SYNTHESIS OF (±)-OXETANOCIN AND RELATED COMPOUNDS

by

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requirements for the degree of Doctor of Philosophy

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© January 1992
To My Parents,

Josef and Anna Hambalek

To My Loving Wife and Colleague,

Kristina
ABSTRACT

Photo-adducts of aldehydes and furan were transformed to substituted monocyclic oxetanes, using a modification of the Fraser-Reid-Mootoo glycosidation procedure, and the chemistry of these oxetanes was studied. The photo-adduct of 2-methylfuran and propionyloxyacetaldehyde was transformed in a one-pot reaction to oxetane 75a, which gave oxetanocin and its epimer as described. The coupling of various oxetanes of the type 75 to nitrogenous bases was also investigated.

During the course of this work, it was found that epoxides of the type 23 could be transformed into bicyclic nucleosides 91 and furanosides 93. Bicyclic nucleosides 99 were also prepared, again using a modified Fraser-Reid-Mootoo coupling procedure.

An investigation into the resolution of photo-adducts of aldehydes and furans was initiated.
RESUME

Des adduits résultant de la cycloaddition photochimiques du furane sur des aldéhydes ont été convertis en oxétanes monocycliques substitués en utilisant une modification du procédé de glycosidation Fraser-Reid—Mootoo. La chimie de ces oxétanes résultant a été également étudiée.

L'adduit dérivé de la photo-condensation du methyl-2 furane et du propionyloxyacetaldehyde a été transformé par trois réactions in situ en l'oxétane 75a dont le couplage avec l'adénine a donné lieu à la formation de l'oxetanocin et de l'épimère correspondant. Une études plus générale sur la couplage des oxétanes du types 75 avec des bases puriques a été également entreprise.

Il a été trouvé dans le cadre de ce travail que des époxides du type 23 pourraient être convertis en nucléosides bicycliques tel que 91 et du furanosides tel que 93. Les nucléosides bicycliques 99 ont également préparés par une modification de la méthode de couplage Fraser-Reid—Mootoo.

Des travaux en vue de parvenir à la séparation des diastéréomères des adduits résultant de la photocondensation des aldéhydes et des furanes ont été entrepris.
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## GLOSSARY OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>Ac</td>
<td>acetyl</td>
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<tr>
<td>Ade</td>
<td>adenine</td>
</tr>
<tr>
<td>AIDS</td>
<td>acquired immunodeficiency syndrome</td>
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<tr>
<td>APT</td>
<td>attached proton test</td>
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<tr>
<td>B</td>
<td>base</td>
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<tr>
<td>Bn</td>
<td>benzyl</td>
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<tr>
<td>Bu</td>
<td>butyl (C₄H₉)</td>
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<td>Bz</td>
<td>benzoyl</td>
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<td>calcd</td>
<td>calculated</td>
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<tr>
<td>Cl</td>
<td>chemical ionization</td>
</tr>
<tr>
<td>coll</td>
<td>sym-collidine</td>
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<tr>
<td>COSY</td>
<td>correlation spectroscopy</td>
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<tr>
<td>Cyt</td>
<td>cytosine</td>
</tr>
<tr>
<td>ddA</td>
<td>2',3'-dideoxyadenosine</td>
</tr>
<tr>
<td>DEAD</td>
<td>diethyl azodicarboxylate</td>
</tr>
<tr>
<td>DIBAL-H</td>
<td>di-iso-butylaluminium hydride</td>
</tr>
<tr>
<td>DMAP</td>
<td>4-dimethylaminopyridine</td>
</tr>
<tr>
<td>DMF</td>
<td>dimethylformamide</td>
</tr>
<tr>
<td>DMS</td>
<td>dimethyl sulfide</td>
</tr>
<tr>
<td>DNA</td>
<td>2'-deoxyribonucleic acid</td>
</tr>
<tr>
<td>E⁺</td>
<td>electrophile</td>
</tr>
<tr>
<td>EC₅₀</td>
<td>effective concentration for 50% inhibition</td>
</tr>
<tr>
<td>ED₅₀</td>
<td>effective dose for 50% inhibition</td>
</tr>
<tr>
<td>El</td>
<td>electron impact</td>
</tr>
<tr>
<td>EBV</td>
<td>Epstein-Barr virus</td>
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<tr>
<td>Et</td>
<td>ethyl (C₂H₅)</td>
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<tr>
<td>ee</td>
<td>enanomeric excess</td>
</tr>
<tr>
<td>equiv.</td>
<td>equivalent(s)</td>
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<tr>
<td>FAB</td>
<td>fast atom bombardment</td>
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<td>g</td>
<td>gram(s)</td>
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<td>GC</td>
<td>gas chromatography</td>
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<tr>
<td>h</td>
<td>hour(s)</td>
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<tr>
<td>HBV</td>
<td>hepatitis B virus</td>
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<td>HCMV</td>
<td>human cytomegalovirus</td>
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<tr>
<td>Abbreviation</td>
<td>Definition</td>
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<td>--------------</td>
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<tr>
<td>HETCOR</td>
<td>heteronuclear correlation</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
</tr>
<tr>
<td>HMDS</td>
<td>1,1,1,3,3,3-hexamethyldisilazane</td>
</tr>
<tr>
<td>HRMS</td>
<td>high-resolution mass spectrometry (spectrum)</td>
</tr>
<tr>
<td>HSV</td>
<td>herpes simplex virus</td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz</td>
</tr>
<tr>
<td>i-</td>
<td>inhibitory concentration which inhibits 50%</td>
</tr>
<tr>
<td>IC50</td>
<td>inhibitory dose which inhibits 50%</td>
</tr>
<tr>
<td>ID50</td>
<td>iodonium di-sym-collidine perchlorate</td>
</tr>
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<td>IDCP</td>
<td>imidazole</td>
</tr>
<tr>
<td>imd</td>
<td>imida70lic</td>
</tr>
<tr>
<td>IR</td>
<td>infra-red</td>
</tr>
<tr>
<td>L</td>
<td>wavelength</td>
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<tr>
<td>LRMS</td>
<td>low-resolution mass spectrometry (spectrum)</td>
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<tr>
<td>M</td>
<td>mega</td>
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<td>M</td>
<td>molar(ity)</td>
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<td>milli</td>
</tr>
<tr>
<td>μ</td>
<td>micro</td>
</tr>
<tr>
<td>MCPBA</td>
<td>meta-chloroperbenzoic acid</td>
</tr>
<tr>
<td>MCMV</td>
<td>murine cytomegalovirus</td>
</tr>
<tr>
<td>Me</td>
<td>methyl (CH₃)</td>
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<tr>
<td>MEM</td>
<td>methoxyethoxymethyl</td>
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<tr>
<td>MIC</td>
<td>minimum inhibitory concentration</td>
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<tr>
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<td>minute(s)</td>
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<td>MMPP</td>
<td>magnesium monoperoxyphthalate</td>
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<td>MOM</td>
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<td>m.p.</td>
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<td>normal(ity)</td>
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<td>N-chlorosuccinimide</td>
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<td>N-iodosuccinimide</td>
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<tr>
<td>Nu</td>
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<tr>
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<tr>
<td>Pr</td>
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<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>PPL</td>
<td>porcine pancreatic lipase</td>
</tr>
<tr>
<td>py</td>
<td>pyridine</td>
</tr>
<tr>
<td>Rf</td>
<td>distance travelled by compound, divided by that travelled by solvent front</td>
</tr>
<tr>
<td>res</td>
<td>resolving power (in HRMS)</td>
</tr>
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<td>RNA</td>
<td>ribonucleic acid</td>
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<td>room temperature</td>
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<tr>
<td>T½</td>
<td>half-life</td>
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<td>t- or tert-</td>
<td>tertiary-</td>
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<td>TBAF</td>
<td>tetrabutylammonium fluoride</td>
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<tr>
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<td>TBDPPhSi</td>
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<td>TEA</td>
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<tr>
<td>Tf</td>
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<td>TMS</td>
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<tr>
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<td>varicella-zoster virus</td>
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1. INTRODUCTION & LITERATURE REVIEW.

1.1 Isolation and Characterization.

In 1986, an article\(^1\) was published describing oxetanocin, a structurally novel nucleoside isolated from the culture filtrate of *Bacillus megaterium* NK 84-0218, which has been shown to possess antibacterial, antiviral and antitumor activity. Oxetanocin was isolated in yields of approximately 17 mg/L of culture filtrate and is only obtained in pure form after lengthy and tedious chromatographic separations.

![Structure of oxetanocin](image)

Oxetanocin is the first natural product which is an oxetanosyl-N-glycoside\(^1\) and the name "oxetanoside" has been proposed by Nitsuma\(^2\), for the glycoside possessing an oxetane ring. The structure of oxetanocin was assigned after extensive analysis of its IR, UV, \(^{13}\)C-NMR, \(^1\)H-NMR and field desorption mass spectra as well as elemental analysis. Its structure was confirmed by X-ray crystallographic studies\(^3\).

Oxetanocin exhibited cytotoxicity against Vero cells (132.6 μg/well, 50% inhibition of cell growth)\(^1\). It also inhibited the growth of HeLa cells in vitro (IC\(_{50}\) 47 μg/mL)\(^1\) and showed activity against both herpes simplex virus-I (IC\(_{50}\) 4.8 μg/mL)\(^4\) and herpes simplex virus II (IC\(_{50}\) 10 μg/mL)\(^1,4,5\). Oxetanocin showed anti hepatitis B virus activity (ID\(_{50}\) 91 μg/mL)\(^6\) and anti human cytomegalovirus activity (IC\(_{50}\) 13 μg/mL)\(^4\). However, oxetanocin did not exhibit any activity against vesicular stomatitis.

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virus (RNA virus) at 100 μg/well. Oxetanocin also showed strong antibacterial activity against Staphylococcus aureus 209P (MIC < 0.1 μg/mL), Bacillus subtilis PCI 219 (MIC < 0.1 μg/mL), Bacillus polymyxa IAM 1210 (MIC < 0.1 μg/mL) and Bacillus megaterium ATCC 14945 (MIC = 1.56 μg/mL).

Adenine and adenosine were strongly antagonistic against oxetanocin in terms of its antibacterial activity. Inosine and guanosine demonstrated only a weak antagonistic effect. However, the most impressive feature of oxetanocin is its activity against the human immunodeficiency virus. Moreover, it is active at very low concentrations (0.5-1.5 μg/mL) and intravenous injections of oxetanocin to mice (200 mg/kg) did not show any signs of toxicity. When allopunol and mycophenolic acid were added to oxetanocin, additive anti-HIV effects were produced.

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1.2 Mode of Action Against Human Immunodeficiency Virus.

The tremendous interest in oxetanocin over the last few years is largely due to its ability to inhibit the HIV virus. The human immunodeficiency virus belongs to a class of viruses that are known as retroviruses. Replication of the HIV virus is a complicated affair involving many steps. This is shown in Figure 1.10

Figure 1. Life Cycle of the Human Immunodeficiency Virus. The first step involves binding of the glycoprotein on the viral envelope to the receptors on the surface of the cell. After the HIV virus has bound to the cell, it fuses with the cell membrane and releases its contents into the cytoplasm. Next, viral RNA and reverse transcriptase escape from their inner protein coat. The reverse transcriptase then binds to the viral RNA and begins synthesizing a complementary viral DNA strand. Reverse transcriptase then proceeds to make a second DNA copy of the first DNA strand. This double stranded DNA is now incorporated into the cellular DNA and is transcribed with the host cell DNA. The transcribed RNA is translated into viral proteins. The viral proteins thus produced undergo modifications to allow them to assemble into virus particles which then escape the cell by budding out of its surface.

10 From AIDS THERAPIES by Yarchoan, R.; Mitsuya, H.; Broder, S., Scientific American, 259, 112 (1988). Copyright © by Scientific American, Inc. All rights reserved.
Interference with any of the six steps shown in Figure 1 would destroy the virus' ability to replicate itself. Oxetanocin possesses anti-HIV activity due to its ability to inhibit the synthesis of viral DNA by the inhibition of HIV reverse transcriptase. The causative agent of this inhibition is oxetanocin triphosphate, formed through cellular phosphorylation mechanisms. A great deal of effort is currently underway to determine the mechanism of inhibition of reverse transcriptase so as to make logical structural changes to known anti-HIV compounds that would enhance their effectiveness.

Oxetanocin Triphosphate

1.3 Syntheses of Oxetanocin.

Shortly after we initiated our project, the first total synthesis of oxetanocin was published in 1987 by Niitsuma\textsuperscript{13}. The synthesis, which used a glucose derivative as its starting point, produced oxetanocin in only 0.008\% overall yield. The key step involved cyclization of an epoxy allylic ether to an oxetane. Unfortunately, this step proceeded in only 5\% yield.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{niitsuma_synthesis.png}
\caption{The Niitsuma synthesis of oxetanocin.}
\end{figure}

Approximately one year later, another equally low yield synthesis was published\textsuperscript{14,15}. This synthesis used cis-2-buten-1,4-diol as its starting point. The starting material was transformed to mesylate I, which was then converted to oxetane II. Coupling of oxetane II with the nitrogenous base yielded protected oxetanocin and epioxetanocin in a 3:1 ratio. Separation of the two isomers was very tedious due to the fact that they had to be converted to their tetrabenzate derivatives before separation was possible.

A few weeks later, Norbeck\textsuperscript{16} reported a 12 step synthesis of oxetanocin starting from adenosine. The synthesis proceeded in 5% overall yield. The key step involved a Wolff rearrangement of diazoketone III. Application of this methodology to the preparation of pyrimidine analogues of oxetanocin has not been reported in the literature.

Figure 4. The Norbeck synthesis of oxetanocin.

The latest synthesis of oxetanocin was published in 1990 by Fleet\(^9\). Diacetone glucose was transformed to lactone IV in 5 steps. Ring contraction of lactone IV gave oxetane ester V. This oxetane ester was then transformed to chlorooxetane VI. The coupling of VI with adenine gave an epimeric mixture (α:β 3:2) of protected oxetanocins which were separated chromatographically. This synthesis also failed to provide oxetanocin in an anomerically pure form without resorting to tedious chromatographic separations.
Figure 5. The Fleet synthesis of oxetanocin.
1.4 Syntheses of Oxetanocin Derivatives.

Although most nucleoside antibiotics contain a β-D-ribofuranose connected to a heterocyclic ring, the fact that oxetanocin exhibits biological activity (antibacterial, antitumor and antiviral) has fueled interest in modifying this novel nucleoside in the hope of increasing its biological activity. The first derivatives, shown in Figure 6, were synthesized from oxetanocin and involved modification of the nitrogenous base, usually by appropriate enzymatic reactions.

![Figure 6. Modified Bases.](image)

None of these derivatives exhibited antibacterial activities except for 2-amino-OXT-A, which demonstrated activity against *Bacillus cereus* IAM 1072 (MIC: 3.13 μg/mL) and *Staphylococcus aureus* 209 p (MIC: 3.13 μg/mL). OXT-G and 2-amino-OXT-A exhibited activity against herpes simplex virus type-II at 9.71 μg/well (50% inhibition of cytopathic effect) and 17.68 μg/well (50% inhibition of cytopathic effect), respectively. The other derivatives were inactive against this virus. In testing for activity against the hepatitis B virus, only OXT-G (ID₅₀ 0.72 μg/mL) and 2-amino-OXT-A (ID₅₀ 0.32 μg/mL) showed activity.

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μg/mL) showed antiviral activity. The antiviral effects of OXT-G and 2-amino-OXT-A were 12 to 27 times as strong as that of ara-A, and they were less cytotoxic. Although the mechanism of inhibition of HBV DNA synthesis is not known, it is thought they affect HBV related reverse transcriptase. OXT-G has also been found to be active against Varicella-zoster virus (ED$_{50}$ 1-2 μg/mL). OXT-G, 2-amino-OXT-A and OXT-H exhibited activity against human cytomegalovirus (IC$_{50}$ 1.0 μg/mL, 2.1 μg/mL and 18 μg/mL, respectively). OXT-X did not show any activity at concentrations up to 50 μg/mL. OXT-G was found to have a very low acute toxicity (600 mg/kg). It has been shown that the triphosphate form of OXT-G (analogous to the triphosphate form of OXT-A shown in section 1.2) inhibits viral replication by impairing viral DNA polymerase. OXT-H, 2-amino-OXT-A and OXT-G also exhibited activity against human immunodeficiency virus (EC$_{50}$ 2.2 μg/mL, 4.7 μg/mL and 7.3 μg/mL, respectively). OXT-X did not show any activity at concentrations up to 100 μg/mL. Allopurinol and mycophenolic acid potentiated the anti-HIV activity of OXT-H. OXT-H also showed the most promise for therapeutic use since its selectivity index was the highest of all of the above mentioned derivatives including OXT-A.

![Modified Bases](image)

**Figure 7. Modified Bases.**

A few months later, 2 more derivatives involving modification of the nitrogenous base were synthesized. No biological data were given for compound VII. Compound VIII exhibited activity against the human cytomegalovirus (IC$_{50}$ 0.67 μg/mL) and the hepatitis B virus. In 1991, showdomycin analogue IX was synthesized by chemists at Nippon Kayaku Co. No information on biological activity was given.

18 Summers, J.; Mason, W. S., Cell, 29, 403 (1982).
Figure 8. Oxetane Modifications.

In 1989, phosphoric acid esters of the type X were prepared. All of these compounds exhibited activity against cytomegalovirus, hepatitis B virus, herpes simplex virus-1, human immunodeficiency virus and Varicella-zoster virus. Oxetanocin derivatives of the type XI were also synthesized, but no biological data is available.

Figure 9. Oxetane Modifications.

There have also been many oxetanocin derivatives synthesized which involved modification of the oxetane ring. In 1990, oxetanocin derivatives XIII, XVI and XVII were synthesized. Compound XIII was found to exhibit anti-HIV activity (IC<sub>50</sub> 5.5 µg/mL) as did compound XVI (IC<sub>50</sub> 0.54 µg/mL). α-Noroxetanocin XVII did not possess any antiviral activity at concentrations up to 100 µg/mL. Saito and coworkers also synthesized oxetanocin derivatives XII, XIII and XVI.
XII was found to possess anti-HIV activity at concentrations of 0.25 μg/mL. Azido derivative XIV and fluoro derivative XV were synthesized by Fleet. Compound XIV was found to be active against the HIV virus (IC50 6 μg/mL) whereas the azido derivative XV showed no significant anti-viral activity at concentrations up to 100 μg/mL. Epioxetanocin XVIII has been synthesized by several groups. Unfortunately, it did not possess any anti-viral activity.

Figure 10. Carbocyclic Analogue.
In addition to all of the derivatives shown above which involved either modified bases and/or modified oxetanes, a series of carbocyclic analogues has also been synthesized over the last few years. The first derivatives made simply replaced the oxetane ring with a cyclobutane ring10,11,12,31,34,35,36. Adenosine and guanosine derivatives of the type XIX exhibited activity against HSV-I, HSV-II, HCMV, HBV, MCMV, VZV and HIV at concentrations between 0.024 µg/mL and 12.0 µg/mL. The guanosine analogue of XIX was also active against EBV (ID₅₀ 0.01 µg/mL). Neither derivative proved to be acutely toxic to mice. No biological data is available for the thymidine and uridine analogues of XIX.

Several isomers of XIX have also been synthesized. Derivatives of the type XX were recently reported by Katagiri and coworkers35. No information is available on their biological activity. Analogues XXI and XXIII were also prepared32,36. The adenosine analogue XXI displayed no detectable activity against HSV-I, HSV-II, HCMV. However, it was active against HIV at concentrations between 10 and 50 µg/mL. The guanosine derivative XXIII exhibited activity against all of the above listed viruses at concentrations of 8.0, 2.0, 2.6 and 10 µg/mL, respectively. Derivatives XXII and XXIV were synthesized by Nishiyama and co-workers32. Both displayed strong activity against HSV-I, HSV-II and HCMV (EC₅₀ 0.12-4.2 µg/mL). Adenosine analogues of the type XXII were found to be inactive against HSV-I and HIV36. The guanosine derivative has not yet been evaluated.

Derivatives XXVI and XXVIII were found to be inactive against HSV-I and HIV36. Earlier this year, Legraverend37 reported the synthesis of XXVII and XXIX. Both of these derivatives were reported to be inactive against the human immunodeficiency virus. The adenosine analogue of the type XXX exhibited no activity against HSV-I and HIV36. No information is available concerning the biological activity of the guanosine analogue.

Cyclopropane analogues of the type XXXI and XXXII were recently synthesized by Katagiri and Kaneko38. Neither type of derivative exhibited any activity against herpes simplex viruses I and II. However, compounds of the type XXXII were active against bovine leukemia virus at 5-50 µg/mL.

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Tricyclic derivatives XXXIII and XXXIV were synthesized in early 1988 by Fleet\textsuperscript{39} as part of his research involving oxetanevin. No information is available on either compound regarding its biological activity.

1.5 Structure-Activity Relationship versus HIV.

Due to the difficulties involved in the synthesis of oxetanocin and oxetanocin derivatives, Marquez\textsuperscript{40} undertook an investigation into the necessity of the oxetane or cyclobutane ring for antiviral activity. Since the tetrahydrofuran ring is known to be an excellent template for reverse transcriptase as demonstrated by the anti-HIV activity of various 2',3'-dideoxynucleosides\textsuperscript{41}, they decided to synthesize hydroxymethyl-substituted 2',3'-dideoxyadenosines XXXV and XXXVI.

![Figure 13](image-url)

In the modelling studies carried out, 2',3'-dideoxyadenosine (ddA) was assumed to have the appropriate geometry and was used as a reference template. Oxetanocin and ddA were shown to have a large common sub-structure with essentially the same geometry and hence can be largely superimposed as shown in Figure 14. Since ddA possesses superior biological activity with respect to oxetanocin, it suggests the the 2' hydroxymethyl side chain in oxetanocin may hinder its ability to fit into the binding sites used by ddA.

When 2'-hydroxymethyl ddA and 3'-hydroxymethyl ddA were modelled, it was found that the 3'-hydroxymethyl isomer closely resembles oxetanocin and does indeed possess anti-HIV activity. On the other hand, the 2'-hydroxymethyl isomer does not closely resemble oxetanocin since its 2'-hydroxymethyl group is in a very different location. Also, the 2'-hydroxymethyl isomer does not exhibit any anti-HIV activity. This seems to suggest that the cleft between the 2' ring systems must be empty for binding to the active site to take place.


Figure 14. Modelling of Oxetanocin and ddA

Figure 15. Modelling of Oxetanocin and Isomeric Hydroxymethyl ddA Analogues\(^4\).

These results seem to indicate that the tetrahydrofuran ring is equivalent to the oxetane ring. It also indicates that the type and position of the side chains may be more important for anti-HIV activity than ring size.
2. RESULTS & DISCUSSION.

2.1 Synthetic Strategy.

The structural features of the novel nucleoside oxetanocin 1β offer a challenging synthetic project. The unprecedented oxetanosyl-N-glycoside presents new challenges in the synthesis of nucleosides and carbohydrates as many of the principles used in furanoside syntheses are not applicable to oxetanoside synthesis. We wanted to design a scheme that was not restricted to the synthesis of oxetanocin only, but one that would enable us to efficiently synthesize derivatives of oxetanocin as it was felt by us at the time of the initiation of the project that derivatives would also be biologically active. This was borne out later in the numerous papers on oxetanocin derivatives.

It was decided from the beginning that our strategy would be based on the coupling of a suitably functionalized oxetanose moiety to the base. This approach would enable us to incorporate pyrimidine as well as purine bases. The difficulty in the coupling reaction was the control of the stereochemistry at the anomeric position. It was hoped that a coupling methodology for oxetanoses could be developed analogous to the ones that have been developed for furanose sugars. Disconnection of the glycosidic bond is shown in Scheme R1.

Scheme R1

\[
\begin{align*}
\text{NH}_2 \\
\text{HO} & \quad \text{O} \\
\text{OH} \\
\end{align*}
\]

\[1\beta, \text{oxetanocin}\]

The sugar moiety can be derived from the well known photocycloaddition of aldehydes and furans\textsuperscript{42,43,44}. These photo-adducts incorporate many of the stereochemical features that characterize
oxetanocin and offer flexibility in altering the 2' and/or 3' substituents with relative ease. It was clear that the choice of protecting and/or participating groups would have to be carefully considered since these would ultimately determine the stereochemistry of the coupling reaction. Control of the stereochemistry about the anomeric position was deemed to be critical since separation of mixtures of anomers is often very tedious and impractical as was shown by Yamamura's\textsuperscript{14,15} and Fleet's\textsuperscript{9} syntheses of oxetanocin. These photo-adducts also offer the benefit of being available from relatively inexpensive starting materials. One drawback of using these photo-adducts as starting materials was that they have never been obtained in enantiomerically pure form and that ultimately a methodology would have to be devised to separate the enantiomers or synthesize them in high enantiomeric excess (ee). The retrosynthesis of the functionalized oxetane is shown in Scheme R2.

Scheme R2

Another possible approach involved coupling of the nitrogenous base directly to a suitably functionalized/modified photo-adduct. The difficulty in this approach was that the oxetane ring has a greater tendency to open up (especially under acidic conditions) than the furan ring. Any conversion of photo-adducts to oxetanocin, or a precursor thereof, must circumvent this ring opening. It was felt that this could be accomplished by modifying the furan part of the photo-adduct in such a way as to destabilize it so that it would open in preference to the oxetane part.
2.2 Initial Attempt.

2.2a Synthesis of (3).

The photo-adduct 2a was prepared from benzaldehyde and furan via a slight modification of the previously described [2+2] Patterno-Buchi photo-cycloaddition\(^{41}\) in large quantities and in consistently good yields, typically 50%. This material served as the model for our initial investigations. Ozonolysis of 2a in methylene chloride at -78°C, followed by dimethyl sulfide reduction provided formate 3 in virtually quantitative yield and with a purity >95%. Attempts to improve the purity by flash chromatography resulted in decomposition of 3\(^ {45} \). Nevertheless, we decided to proceed with this material as obtained and it was hoped that the anomeric formyl group would behave similar to acetate groups in coupling reactions and that the only remaining task would be to transform the aldehyde group into a suitable participating group.

Attempts to reduce the aldehyde function to the alcohol with NaBH\(_4\) in methanol or ethanol at various temperatures resulted in decomposition of the starting material. Reaction with sodium cyanoborohydride in methanol also resulted in decomposition. At this point it was felt that an aprotic solvent was needed since the oxetane ring was probably being destroyed in a base catalyzed hydrolysis of the formate. Therefore, we attempted to carry out the reduction with LiBH\(_4\), DIBAL-H or Zn(BH\(_4\))\(_2\) in tetrahydrofuran or ether. These approaches were also not successful. An even milder approach involved treating a methylene chloride solution of 3 with NaBH\(_4\) on alumina or silica gel. This too did not give the desired alcohol. Since we were not able to reduce the aldehyde, it was decided to form the methyl acetal with cerium trichloride, methanol and trimethyl orthoformate according to the methodology described by Luche\(^ {46} \). However, instead of the desired product, only the tetramethoxy olefin 4 was isolated in 43% yield.

\(^{45}\) Formate 3 had a shelf-life of only 1-2 weeks at -10°C before significant decomposition occurred.
Scheme 1

\[ R \text{CHO} + \text{CHO} \rightarrow \text{OCHO} \]

2a, R=Ph
2b, R=iPr
2c, R=TBDMSiOCH₂
2d, R=BzOCH₂
Figure 16. The 200 MHz $^1$H-NMR spectrum of formate 3 in CDCl$_3$.

Figure 17. The 200 MHz $^1$H-NMR spectrum of tetramethoxy-olefin 4 in CDCl$_3$. 
2.2b Mechanism of Formation of (4).

Compound 4 is presumably formed by a hydrolysis of the formyl group to give the intermediate 3a which tautomerizes readily to the open chain alcohol 3b. Dehydration of 3b, to give the ditaldehyde 3c is not unexpected in view of the instability of β-hydroxy aldehydes. Finally, acetalization of 3c gives the end product.

Scheme 2

2.2c Attempted Coupling of (3) to Nitrogenous Bases.

Since all efforts to transform the aldehyde function of 3 to a suitably protected group failed, we then decided to proceed with the coupling to the nitrogenous base. Our original approach was based on the classical Vorbrüggen methodology\(^\text{47,48,49}\) and was to involve a purine base (adenine) and a pyrimidine base (cytosine) just in case the different classes of bases behaved differently. \(N^6\)-benzoyladenine was synthesized by a described method\(^\text{50}\) and then reacted with chlorotrimethylsilane to yield the bis-silylated base\(^\text{51}\) as a clear yellow glass after bulb to bulb distillation. A stock solution of this material in 1,2-dichloroethane was used for all investigations and was found to be stable for extended

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periods of time if moisture was rigorously excluded. Bis-silylated cytosine was obtained from the unprotected pyrimidine by a known method and gave a white powder.

The coupling of oxetane 3 and bis-(trimethylsilyl)-N6-benzoyladenine catalyzed by trimethylsilyl triflate, trimethylsilyl acetate or tin tetrachloride under various conditions afforded complex mixtures which contained no coupled products or otherwise identifiable compounds. Similar results were obtained when bis-(trimethylsilyl)-cytosine was employed as the nitrogenous base. Therefore, this approach was abandoned and other coupling methods were investigated. Reaction of 3 with bis-(trimethylsilyl)-N6-benzoyladenine in acetonitrile under phase transfer conditions using dibenzo-18-crown-6 and potassium iodide under various conditions gave complex mixtures which contained no coupled products. Attempts to couple oxetane 3 with the sodium salt of adenine in DMF under various conditions also resulted in decomposition of the oxetane. Coupling of 3 with chloromercuri-6-benzamidopurine in 1,2-dichloroethane catalyzed by various Lewis acids under several different conditions also resulted in only decomposition of 3. Our findings regarding the instability of oxetanosyl-formates were corroborated by the Yamamura group at Nippon Kayaku Co. Due to the difficulty in coupling oxetane 3 with nitrogenous bases, it was decided that we had to develop a different sugar component, one that was considerably more stable than 3.

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2.3 Lactone Approach.

Our next attempt involved the synthesis of lactone 5. We felt that the lactone moiety could be activated by a Lewis acid (E⁺), thereby making the anomeric center susceptible to β-attack by the nitrogenous base (B⁻) resulting in opening of the 5-membered ring. The resulting nucleoside (an oxetanocin derivative) could then be transformed into oxetanocin simply by shortening the 2' side chain by one methylene unit.

Scheme 3

2.3a Synthesis of Lactone (5a).

Our initial approach was to try to convert photo-adduct 2a to the desired lactone 5a. Although Schreiber had recently described the oxidation of photo-adducts 2 with m-chloroperbenzoic acid to give compounds of the type 6⁵⁴, we hoped that it would be possible to add a peroxide across the double bond of 2a and then transform the resulting compound 7 to the desired lactone. Unfortunately, all attempts to add t-butylhydroperoxide across the double bond of 2a failed and this approach was abandoned.

Scheme 4

Irradiation of benzaldehyde and 2-O-trimethylsilyl-furan in benzene under various conditions resulted only in recovered starting material and there was no evidence of the desired photo-product 8 or lactone 5a. Attempts to react benzaldehyde and 2-furane in benzene photolytically also failed. However, photolysis of benzaldehyde with 2-acetoxyfuran in benzene gave lactone 5a and acetate 9a in 14% and 5% yield (unoptimized), respectively.

Scheme 5

The lactone is presumably formed from vinyl acetate 9b. Possible pathways for this rearrangement are shown in Scheme 6. No mechanistic studies were carried out to determine by which pathway the reaction proceeds.
Scheme 6

Pathway A

Pathway B

$9b$

$\xrightarrow{\text{\textbf{Ph~O\textsubscript{\textbullet}}} \dots \text{\textbf{Ph~O\textsubscript{\textbullet}}}}$

$9b$

$\xrightarrow{\text{\textbf{Ph~O\textsubscript{\textbullet}}} \dots \text{\textbf{Ph~O\textsubscript{\textbullet}}}}$

$\text{\textbf{Ph~O\textsubscript{\textbullet}}} + \text{\textbf{Ph~O\textsubscript{\textbullet}}}$

$\text{\textbf{OH}} + \text{\textbf{CH\textsubscript{2}}}$

$\text{\textbf{OH}} + \text{\textbf{CH\textsubscript{2}}}$

$\text{\textbf{OH}} + \text{\textbf{CH\textsubscript{2}}}$

$\text{\textbf{OH}} + \text{\textbf{CH\textsubscript{2}}}$
2.3b Attempted Coupling of Lactone (5) to Nitrogenous Bases.

With the lactone 5a in hand, we proceeded with the coupling to the base. Reaction of 5a and bis-(trimethylsilyl)-N’-benzoyladenine in 1,2-dichloroethane catalyzed by various Lewis acids resulted in no reaction taking place if mild conditions were used. On the other hand, if more forcing conditions (e.g. reflux, excess catalyst) were employed, the lactone started to decompose slowly. Attempts to couple lactone 5a with bis-(trimethylsilyl)-N’-benzoyladenine in acetonitrile under phase transfer conditions using dibenzo-18-crown-6 and potassium iodide also did not yield any coupled products. Similar results were obtained when bis-(trimethylsilyl)-cytosine was used as the base. Since we were unable to convert lactone 5a into oxetanocin like material, a new approach had to be devised.
2.4 New Strategy.

After careful consideration, two new strategies were developed. The first one was inspired by the work of Fraser-Reid and Mootoo, who transformed 1-pentenyl glycosides to disaccharides by means of iodonium di-sym-collidine perchlorate (IDCP) and the appropriate sugars\textsuperscript{55,56,57,58}. It was hoped that by functionalizing photo-adducts of the type 2 with appropriate alkenes that it would be possible to selectively open the 5-membered ring of these photo-adducts according to Pathway B to yield monocyclic oxetanes 12 which could then be coupled to nitrogenous bases to yield oxetanocin derivatives. One possible competing reaction would be the opening of the intermediate 11a according to Pathway C to yield a bicyclic compound of the type 13a. We felt that it was not likely that the intermediate would react this way since the approach of the nucleophile is extremely hindered by the substituent on the 4-position (especially pronounced if a bulky group is at C-4) and that the resulting compound would be more strained than compounds of type 12 (predicted by molecular modeling). The other possible side reaction would involve opening of the oxetane ring according to Pathway A to yield a bicyclic compound of type 13. We felt this pathway was only likely in the case where the intermediate iodonium ion 11 was in close proximity to the oxetane oxygen.

The second approach centered around the investigation of the Paterno-Buchi photocycloaddition reaction in order to determine if it is possible to obtain chemoselectivity in the addition of unsymmetrically substituted furans to aldehydes. This would enable us to replace the very unstable anumeric formate group with something more stable, like an acetate (commonly employed in base coupling reactions) or benzoate group.

\textsuperscript{55} Mootoo, D. R.; Date, V.; Fraser-Reid, B., \textit{J. Am. Chem. Soc.}, 110, 2662 (1988).
\textsuperscript{57} Konradsson, P.; Mootoo, D. R.; McDevitt, R. E.; Fraser-Reid, B., \textit{ibid.}, 270 (1990).
Scheme 7

Pathway A

Pathway B

Pathway C
2.5 The Fraser-Reid Approach to Monocyclic Oxetanes.

2.5a Synthesis of (9).

Our first task was to construct a photo-adduct of the type 10. Due to the extreme difficulty that we experienced in our initial attempts to epoxidize the double bond in 2 (discussed in section 2.5d), we decided to carry out our initial studies on model compounds where the hydroxy function would be replaced by a hydrogen or halogen atom in order to see if the method was a viable one and so as not to waste time should this approach fail. We also believed that the halogen could be converted to a hydroxy group if epoxidation proved to be unachievable.

Reaction of 2a with hot methanol gave alcohol 14 in 31% yield. The latter is derived from an acid-catalyzed opening of the oxetane ring. Treatment of photo-adducts 2a and 2b with allyl or methallyl alcohol and catalytic amounts of acetic acid gave the corresponding allyl (15: 30%) and methallyl (16a: 10%, 16b: 11%) acetals. The structural assignment of 14, and therefore of 15, 16a and 16b, was based on a HETCOR carbon-hydrogen correlation, which unambiguously ruled out the bicyclic structure of type 10.

The functionalizing of the bicyclic system 2 proceeded in a more satisfactory manner when a 0.2 M solution of photo-adducts 2a or 2b in the appropriate alcohol was treated with one equivalent of N-bromo or N-iodosuccinimide at room temperature for 1.5 - 2 h, giving bromo or iodo acetals 10 in variable, but frequently high yields. The results are summarized in Table 1.

Compounds of the type 10 were formed by, first, an exo coordination of the halonium ion to the double bond followed by an SN2 type displacement from the endo face. The trans stereochemistry along the C3-C4 bond was confirmed by 1H and COSY NMR, which showed no coupling between H3 and H4 since the two protons had a dihedral angle of approximately 90°. Had they been cis, a coupling would have occurred due to their dihedral angle being approximately 0°. The 13C, APT and HETCOR NMR's also confirmed that we had obtained the desired bicyclic compounds 10. The high purity of selected examples was established by elemental analysis.
The reaction, however, is far from general. All attempts to synthesize chloro derivatives using NCS and various alcohols (allyl, methallyl, dimethallyl, 4-pentenyl, cinnamyl) failed. It was also not possible to synthesize any iodo derivatives using the above mentioned alcohols except for methallyl alcohol. Using NBS, only the reactions with cinnamyl alcohol and 4-penten-1-ol failed. When 4-penten-1-ol was used as the alcohol, reaction with NBS or NIS resulted in intramolecular cyclization giving 2-bromomethyl or 2-iodomethyl tetrahydrofurans. It occurred more rapidly than reaction with the double bond of the photo-adducts. Surprisingly, the iodo derivatives 10d and 10h had life times exceeding 1 year at -10°C, whereas the bromo compounds were considerably less stable with life times of one to fifteen weeks.
2.5b Synthesis of Monocyclic Oxetanes (model studies).

Preliminary work was carried out on acetals 10b - 10f and 10h so that it could be determined which ones would give the best results. Using the protocol established by Fraser-Reid and Mootoo, bromoacetals 10b, 10c, 10e and 10f were treated with iodonium di-sym-collidine perchlorate (IDCP)\textsuperscript{59} and methanol (5 equiv.) in benzene and gave 17b, 17c, 17e and 17f in 27 - 70% yield as a mixture of inseparable and relatively unstable diastereomers. Reaction of iodoacetals 10d and 10h with IDCP and methanol (5 equiv.) in benzene gave 17d and 17h in 67% and 30% yield, respectively. After observation of the compounds for several weeks, it became clear to us that the iodo derivatives were more stable than the corresponding bromo derivatives. We also noticed that the 2-methallyl derivatives were considerably more stable than either the 3,3-dimethallyl or allyl derivatives. These results indicated that future work should be carried out with the iodo methallyl derivatives.

We next explored the reaction of various nucleophiles with 10h. Reaction of the iodo-methallyl acetal 10h with IDCP and a variety of alcohols and carboxylic acids gave, after 4 h, 18a - 18f in variable yields. The results are summarized in Scheme 9 (* yields are based on recovered starting material). As can be seen, acetate 18f could be obtained in respectable yield. All compounds 18 were isolated as mixtures of inseparable diastereomers. All of these compounds decomposed slowly at -10 °C and had to be repurified after 1 - 2 weeks if required for further work. Unfortunately, the range of nucleophiles that can be employed in this reaction is not unrestricted. Attempts to carry out the reaction using bulky nucleophiles such as t-butanol, diacetone glucose, methyl-2,3-isopropylidene-D-ribofuranose, stigmasterol and β-cholestanol failed and only starting material was recovered. This is probably due to their sheer size which prevents them from coordinating with the electropositive centers in the intermediate. We also tried to couple nitrogenous bases [bis-(trimethylsilyl)-N6-benzyladenine and bis-(trimethylsilyl)-cytosine] to 10h. Unfortunately, no reaction occurred and only starting material was recovered even if forcing conditions were used.
Detailed analysis of the $^1$H and $^{13}$C-NMR spectra of these monocyclic oxetanes proves that bicyclic compounds of the types 13 and 13a were not formed. Since two diastereomers are formed in the reaction, one would expect the $^1$H and $^{13}$C-NMR of the bicyclic compound to be quite different for the two diastereomers due to the fact that the system is relatively rigid and thus, the CH$_2$ and CH$_3$ groups would be in significantly different environments. On the other hand, the monocyclic oxetanes would not exhibit any significant differences in chemical shifts between the two diastereomers since the diastereomeric center of the molecule is reasonably removed from the oxetane part of the molecule. Also, since there is free rotation about the carbon-carbon bond which connects the dioxolane moiety to the rest of the molecule, it is not possible for the two diastereomers to be "locked" in a fixed...
configuration (which would exhibit markedly different chemical shifts for the two isomers). This is exactly what we observe in the $^1$H and $^{13}$C-NMR. Also, if one examines the $^1$H and COSY NMR's of 18e and 18f, we can see that of the two "anomeric" protons, the one further downfield (H2) is coupled to the one at $\sim 3.5$ ppm (H3) whereas the other "anomeric" proton (H3') is not coupled to any other protons. This indicates that the monocyclic structure is correct since protons at anomeric positions which have ester substituents are always more deshielded than aceta ls due to the deshielding effects of the carbonyl group.

![Figure 19. The 200 MHz 1H-NMR of oxetane 18e in CDCl$_3$.](image)

2.5c Synthesis of (20).

Having proven that the bicyclic system 2 can be opened in the desired manner using a modification of the Fraser-Reid--Mootoo methodology, we decided to prepare an intermediate which was more closely related to oxetanocin. Since we would have to protect what would eventually become the 4'-hydroxy group, it was decided to use the $\tau$-butyldimethylsilyl protecting group since it is reasonably stable to acid (a requirement for Vorbruggen type couplings), survives ozonolysis and would not interfere with the halonium reagents used in opening of the photo-adduct.
Dimethallyl alcohol was quantitatively converted to the tert-butyldimethylsilyl ether 19 by standard means (TBDMSiCl / imidazole / DMF)\(^{60}\). Ozonolysis in methylene chloride at -78°C, followed by reduction with dimethylsulphide, gave aldehyde 20 in 95% yield. Irradiation of 20 with furan in benzene provided photo-adduct 2e in 34% yield. Treatment of a 0.2 M solution of 2e in methallyl alcohol with 1 equivalent of N-bromo or N-iodosuccinimide gave the corresponding bromo (21a) and iodo (21b) acetals in 34 and 27% yield, respectively. Finally, treatment of 21b with IDCP and acetic acid gave the monocyclic oxetane 22 in 47% yield.

Since oxetanes similar to 22 had been converted to oxetanocin by reaction with bis-(trimethylsilyl)-N\(^5\)-benzoyladenine and tin tetrachloride,\(^{dc}\), we used these reaction conditions and variations thereof to try to convert 22 to an oxetanocin like molecule. However, decomposition occurred before coupling. The instability is probably linked to the presence of the two halogens in 22. Therefore, it was decided that the halogen on C3' would have to be replaced by a hydroxy group and this could be accomplished by either replacing the halogen in compounds 10 or by functionalizing the epoxide of 2 with methallyl alcohol.

Reaction of 10b with excess potassium hydroxide in refluxing tetrahydrofuran / water did not result in replacement of the iodide by a hydroxy group. When silver carbonate in dioxane / water was used, no reaction occurred unless forcing conditions were used. Then, decomposition of the starting material resulted. Since we were unsuccessful in our efforts to replace the iodide with a hydroxy group, it was decided to proceed via the epoxide of 2.

2.5d Epoxidation of Photo-adducts (2), model studies.

Since it was known that MCPBA could not be used for the epoxidation of photo-adducts, other methods had to be explored. Reaction of 2a with peracetic acid\(^{61}\) in methylene chloride / acetic acid resulted in decomposition of the starting material. Similar results were obtained when magnesium monoperoxyphthalate (MMPP)\(^{62}\) was used. At this point we felt that decomposition was occurring because the epoxide was unstable and hence could not be isolated. Therefore, we added methallyl alcohol to the reaction mixtures hoping to open the epoxide, to give the methallyl acetal, before it decomposed. This approach was not successful. When methanol / water solutions of photo-adducts 2a and 2b were treated with sodium percarbonate\(^{63}\), no reaction occurred even when forcing conditions were used. Use of 2-butanone peroxide as the epoxidizing agent also did not yield the desired epoxides and only starting material was recovered. However, when a methylene chloride solution of 2a was submitted to the actions of dimethyl dioxirane in acetone\(^{64,65,66}\), epoxide 23a was obtained in almost quantitative yield as a 9:1 mixture of exo and endo isomers, which were unstable to and therefore unseparable by chromatography. Unfortunately, reaction of 2b with dimethyl dioxirane in acetone / methylene chloride did not give the desired product and no starting material was recovered. Nevertheless, we decided to proceed with our model studies using epoxide 23a.

Since we were interested in establishing the optimum conditions for opening up the epoxide with methallyl alcohol, it was necessary to determine under what conditions the epoxide would survive and react in the desired manner. It was discovered that by dissolving 23a in dry methanol and stirring for 16 hours causes the epoxide to open giving acetal 24a in 61% yield. Although 24a can be isolated and characterized without much difficulty, its lifetime is only 1 - 2 weeks at \(-10^\circ\text{C}\). Acetylation by standard methods (Ac\(_2\)O, py, DMAP) gave acetate 25a in 56% yield. It was necessary to protect the free alcohol so as to increase the stability of the molecule. Reaction of 23a with 5 equivalents of acetic acid in methylene chloride gave, after 18 h, 24b in 56% yield. Acetylation proceeded in 93% yield to give diacetate 25b. This result proved that the epoxide could tolerate controlled acidic conditions. Now that we had an idea of how to functionalize the epoxide, we proceeded to synthesize the methallyl acetal of 23a. Reaction of 23a with 5 equivalents of methallyl alcohol in methylene chloride gave 24c in 63% yield. Protection of the free hydroxy group as an acetate (25c) proceeded in 71% yield.

Being satisfied with the results from our model studies, work proceeded on epoxidizing photo-adduct 2e. Unfortunately, the conditions which were employed for 2a proved to be unsatisfactory for 2e. It was thought that the epoxide of 2e was very unstable and that it could not be isolated. Therefore, we reacted 2e with dimethyl dioxirane in acetone/methylene chloride containing 1 equivalent of methallyl alcohol hoping to open the epoxide in situ before it decomposed. This approach was not successful. It also did not succeed when tried with photo-adduct 2a, but surprisingly, when 2b was employed, epoxide 23b was isolated in 53% yield. No explanation for why methallyl alcohol is necessary to facilitate epoxidation of 2b can be given.

Since we were unable to epoxidize 2e, a new photo-adduct would have to be designed. The tert-butyldimethylsilyl group would now have to be replaced by another protecting group because we felt that the TBMSi group was the source of instability in the epoxide of 2c. After careful consideration, the benzoyl ester was chosen since it is stable to oxidizing agents, acidic conditions used in Vorbruggen coupling reactions, and can be removed under relatively mild conditions.

Dimethallyl alcohol was transformed in quantitative yield to its benzoate ester 26 by standard methods (BzCl, py, DMAP). Ozonolysis, followed by reduction with dimethyl sulfide, gave aldehyde 27, which upon irradiation with furan, provided photo-adduct 2d in 30% yield. Epoxidation with dimethyl
dioxirane in acetone / methylene chloride proceeded smoothly to give epoxide 23d in virtually quantitative yield as a 9:1 mixture of exo and endo isomers which, as expected, were unstable to column chromatography. Treatment of 23d with 10 equivalents of methallyl alcohol in methylene chloride gave hydroxy acetal 28, which was transformed to acetate, methyl oxalate and benzoate 29a-c by standard procedures in 75, 64 and 78% overall yield respectively, from epoxide 23d. Treatment of 29a, b and c with 1,2-DCC and acetic acid (5 equiv.) gave 30a, b and c, whereas the use of benzoic acid as the nucleophile gave 31a, b and c. All of these were obtained in moderate yield. Benzoates 31a, b and c had a shelf life of 3 - 5 weeks at -10°C, whereas the acetates 30a, b and c started decomposing after a few days. The NMR data of 30 and 31 were similar to those of the iodo derivatives 18e, 18f and 22, and confirmed that we had obtained the desired monocyclic oxetanes.

Since we felt that the presence of an iodine in our sugars was a contributing factor to their relative instabilities, we also investigated the reaction of 29a-c with bromonium di-sym-collidine perchlorate and acetic acid, hoping that perhaps the bromides would be more stable than the corresponding iodides. Although tlc indicated that a reaction took place, the products were so unstable that they could not be isolated even in crude form. Hence it was not possible to ascertain whether or not the desired product had formed.
Unfortunately, both 30 and 31 decomposed during attempts to couple with persilylated bases, using Lewis acid catalysis. In order to improve the stability of oxetanes 30 and 31, we attempted to remove the dioxolane moiety reductively by means of zinc in methanol. When the reaction was carried out on oxetanes 30a-c, 31a and 31c, tlc indicated formation of a new product which could have possibly been the desired aldehyde 32. However, the product decomposed almost immediately after it was formed and thus could not be isolated. Only oxetane 31b gave an isolatable, albeit highly unstable ($T_{1/2} \sim 2h$ at

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-10°C), reduction product 32' whose structure was tentatively assigned based only on ^1H-NMR. The spectrum clearly indicated the presence of the monocyclic oxetane ring as well as a methallyl side chain.

Scheme 13

![Scheme 13](image)

The mechanism for the formation of oxetane 32' is shown in Scheme 14. After examination of this scheme, it is quite obvious why the reaction can only proceed through this pathway when a methyl oxalyl protecting group is used. Clearly, this pathway is preferred to the one that would lead to the formation of aldehydes 32.

Tributyltin hydride mediated deiodination of oxetane 31 only gave the desired product 33 (I = H, 50% yield) in the case of 31c. It is stable at -10°C for extended periods of time but could not be converted to oxetanocin like material because of decomposition under mildly Lewis acid conditions. From comparison with anomeric benzoates of type 31c not containing the dioxolane ring (prepared in section 2.6b), we conclude that the dimethyl-dioxolane ring is the source of instability in these types of compounds since the dimethyl-dioxolane moiety is rapidly converted to an aldehyde under acidic
conditions. These aldehydes, as seen from our attempts to convert oxetanes 30 and 31 to aldehydes 32, are extremely unstable and decompose almost immediately after formation.

Scheme 14

2.5e Methallyl Epoxide Approach.

At the same time as we were investigating IDCP initiated monocyclic oxetane formation, we also investigated the epoxidation of allyl type adducts. It was hoped that nitrogenous bases could be added to these epoxides in a manner analogous to the one that we developed for synthesis of monocyclic oxetanes. Again using model compounds, we subjected acetal 10g to the actions of dimethyl dioxirane in acetone / methylene chloride and discovered that bromo epoxide 34a was obtained in 66% yield. Similarly, epoxidation of acetal 21a gave epoxide 34b in 90% yield. However, acetals 10h and 21b did not afford their corresponding epoxides since the starting material was decomposed by the actions of dimethyl dioxirane. We believe that 10h and 21b decomposed (solution turned black) because the iodine was oxidized by dimethyl dioxirane.

With 34b in hand, we proceeded with the coupling to the nitrogenous base. Reaction of 34b and bis-(trimethylsilyl)-N^6-benzoyladenine in 1,2-dichloroethane catalyzed by various Lewis acids resulted in decomposition of the starting material with no evidence of any coupled products of the type 35a being formed. Similar results were obtained when bis-(trimethylsilyl)-cytosine was used as the base. Believing that perhaps the bromine in epoxide 34b was the cause for its instability, epoxide 34c was prepared by a procedure similar to that used for the preparation of 34b in 87% yield. It was hoped that this epoxide (34c) would be more suitable for coupling reactions due to its increased stability. Unfortunately, we were
unable to achieve any coupling to nitrogenous bases using conditions similar to those used for 34b and this approach was abandoned.

Scheme 15

Since we had experienced difficulty in coupling nitrogenous bases directly to functionalized photo-adducts previously, it was decided to attempt to open the bicyclic compound 34c with a thiol to yield a compound of type 35b. This compound could then be coupled to the base via a mercury catalyst. It was thought that these types of coupling conditions are milder than the Lewis acid catalyzed methods. Reaction of 34c with thiophenol in ether catalyzed by zinc chloride gave alcohol 36 as a mixture of inseparable diastereomers in 64% yield. The product is derived from a zinc chloride catalyzed opening of the oxetane ring and is extremely unstable. Attempts to further characterize 36 by forming an acetate failed. Also, the synthesis of 36 is very difficult and requires very dry conditions (despite the best precautions, only 1 out of 3 attempts gave 36). All other attempts to synthesize compounds of the type 35b failed and this approach was not pursued any further.
Scheme 16

34a, R=TBDMSi, Bz; X=Br, AcO
Nu=Adenine, Cytosine
35b, R=Bz, X=AcO, Nu=SPh

34b, R=TBDMSi, X=Br
34c, R=Bz, X=AcO

35a, R=TBDMSi, Bz; X=Br, AcO
Nu=Adenine, Cytosine
35b, R=Bz, X=AcO, Nu=SPh
2.6 Unsymmetrically Substituted Photo-adducts as Precursors for Oxetanocin.

2.6a Model Studies.

One of the major limitations of the Paterno-Buchi photocycloaddition reaction is the lack of regioselectivity in the addition of aldehydes to unsymmetrically substituted furans. For example, the photochemical reaction between benzaldehyde and 2-methylfuran provides a 1:1.3 mixture of photo-adducts resulting from the exo addition of the aldehyde to the less- and more-substituted double bond of furan, respectively. Separation by chromatographic means is not possible, and therefore it was not possible to convert the appropriate photo-adduct to a suitably protected oxetane due to the fact that the undesired isomer decomposes during the reaction and gives a complex mixture from which it was impossible to isolate the desired sugar.

Since we were interested in synthesizing oxetane sugars directly from photo-adducts by the method developed for the synthesis of 3, an investigation of the reaction of aldehydes with various mono-substituted furans was initiated. It was hoped that a pattern would emerge regarding the effect of electron donating or withdrawing substituents on the furan ring. Another objective of this study was to provide a stock of vinyl substituted photo-adducts which could be used in the synthesis of oxetanocin. We also wanted to see if the use of non alkyl substituents would make separation by chromatographic means feasible. Benzaldehyde was chosen as the carbonyl component due to the fact that it gives relatively stable photo-adducts, its NMR spectrum is simple and does not appear in the same region as the photo-adduct signals and it is readily available in very pure form. The substituted furans chosen were ones that were readily available and contained side chains which could be modified as necessary in our synthesis of oxetanocin.

Irradiation of a benzene solution of benzaldehyde and furfural did not give any photo-products and only starting material was recovered. Similar results were obtained when 2-acetylfuran or 2-methoxyfuran were used as the furan components. However, when furfuryl alcohol 37 was used as the furan component, photo-adducts 37a and 37b were obtained as a 4:7 mixture of regioisomers. Purification by flash chromatography gave the vinyl substituted isomer 37a exclusively, in 20% yield. It was possible to isolate 37a uncontaminated by 37b since the latter is destroyed on the column. This selective destruction is possible since silica gel is slightly acidic and catalyzes the opening of the oxetane ring in the case of the acetal substituted isomer 37b due to the very favourable formation of a tertiary oxo-carbonium ion. The silica gel, however, is not acidic enough to catalyze oxetane ring opening in the vinyl substituted isomer.

68 In retrospect, other aldehydes should have also been investigated (especially benzoyloxyacetaldehyde) since this would have given us a better understanding of the relative stabilities of the photo-adducts under the conditions of flash chromatography.
Encouraged by this result, we then formed 2-(2-hydroxyethyl)-furan 38 in 99% yield by the reaction of furfural with methyl magnesium bromide in ether. Irradiation of benzaldehyde with 38 in benzene gave photo-adducts 38a and 38b as a 3:5 mixture of regioisomers. It was possible to isolate isomer 38a in 26% yield by flash chromatography without contamination of the other isomer 38b. Acetalization of furfural with cerium trichloride, methanol and trimethyl orthoformate gave, in 69% yield, dimethyl acetal 39, which was irradiated with benzaldehyde in benzene to give photo-adducts 39a and 39b in 46% yield as a 2:3 mixture of inseparable regioisomers.

Scheme 17

\[
\begin{align*}
&\text{Ph} = \text{hv, C}_2\text{H}_6 \rightarrow \\
&37, \ R=\text{CH}_2\text{OH} \\
&36, \ R=\text{CH(OH)}\text{CH}_3 \\
&39, \ R=\text{CH(OMe)}_2 \\
&37a, \ R=\text{CH}_2\text{OH} \\
&38a, \ R=\text{CH(OH)}\text{CH}_3 \\
&38b, \ R=\text{CH(OMe)}_2 \\
&39a, \ R=\text{CH(OMe)}_2 \\
&39b, \ R=\text{CH(OMe)}_2
\end{align*}
\]

It is not possible to draw any conclusions from this study since its scope was simply not broad enough. However, we did learn that it was possible to obtain unsymmetrically substituted photo-adducts in a pure form by way of flash chromatography. The isolation of the desired isomer depended solely on the difference of the stabilities of the two regioisomers.

2.6b Synthesis of Benzoate (42) and p-Nitrobenzoate (43).

Since anomeric benzoates 31 were more stable than the corresponding acetates 30, we next proceeded to synthesize 42 (Scheme 18). It was felt that these sugars would be significantly more stable than 31 since they did not contain a dioxolane moiety.

We initially decided to synthesize photo-adduct 41a via [2+2] photocycloaddition of 2-phenylfuran and aldehyde 27. Although we did not expect any regioselectivity in this reaction, it was hoped that the two regio-isomers could be separated by chromatography. Unfortunately, irradiation of 2-phenylfuran, prepared by a described method69, and aldehyde 27 did not give any photo-products and only starting material was recovered. However, when using tributyl-(2 furyl)-stannane, prepared by a known procedure70, as the furan component as described by Schreiber71, photo-adduct 40 was obtained.


46
in 15% yield after flash chromatography without contamination of the other isomer. In order to prevent acid-catalyzed decomposition of the photo-products, the reaction mixtures were buffered with anhydrous potassium carbonate. It was not possible to isolate the other regio-isomer\(^{72}\) due to its instability on silica gel, even when basified with 2% triethylamine. Arylation of 40 using bromobenzene and tetrakis(triphenylphosphine)palladium(0) in refluxing tetrahydrofuran\(^{73}\) proceeded in 80% yield to give 41a. We found that the best results were obtained when the catalyst was added in small portions over the course of the reaction. This is presumably due to the fact that the catalyst becomes poisoned by the tin, which is liberated during the course of the reaction. When the reaction was carried out using iodobenzene instead of bromobenzene, the yield increased to 85%. Ozonolysis of 41a in methylene chloride at -78°C, followed by reduction with dimethyl sulfide and reduction of the aldehyde function with sodium borohydride on alumina gel gave, after acylation, stable tracyloxy oxetane 42a in 33% yield (unoptimized).

With anomeric benzoate 42a in hand, we proceeded with the coupling to the base. Unfortunately, reaction of 42a and bis-trimethylsilyl-N\(^6\)-benzoyladenine in 1,2-dichloroethane catalyzed by various Lewis acids resulted in no reaction taking place even if forcing conditions (reflux, 48 h, excess catalyst) were used. Since benzoate 42a was too unreactive, we decided to substitute the benzoyl group with a p-nitrobenzoyl group in the hope that while at the same time being stable enough to withstand Lewis acid conditions, it would also be a better leaving group, thus allowing coupling with the nitrogenous base to proceed. Hence, 42b was synthesized in 25% yield by a procedure similar to that used for 42a. However, this sugar also proved to be too stable and attempts at coupling to the base proved to be unsuccessful.

---

72 The isomer with the Sn bonded to the acetal carbon was obtained in a 1.20 ratio with respect to the vinyl tributyl tin isomer as determined by integration of 200 MHz proton NMR signals.
2.6c Synthesis of Acetates (47).

We next investigated the photoaddition of 2-trimethylsilylfuran with aldehyde 27. It was thought that the reaction could yield the desired vinyl silane either by chromatographic separation or by achieving high chemoselectivity as we observed earlier when we carried out a photochemical reaction with tributyl-(2-furyl)-stannane. The resultant vinyl silane 43a could then be converted into an oxetane by the method described in Section 2.6b. Unfortunately, irradiation of 2-trimethylsilylfuran with aldehyde 27 gave photo-adducts 43a and 43b in 19% yield (unoptimized) as a 7:4 mixture of 2 inseparable isomers.

Scheme 19
Since we were unable to separate 43a and 43b, we next investigated the photoaddition of 2-methylfuran with benzoyloxyacetaldehyde. It was hoped that we could obtain the desired photo-adduct 44a either by chromatographic separation (as observed on several occasions in our model studies; section 2.6a) or even better, by achieving regioselectivity in the photoreaction. Irradiation of a benzene solution of 2-methylfuran and 27 gave regioisomers 44a and 44b in a ratio of 11:8, which could be isolated by flash chromatography (ethyl acetate / petroleum ether / triethylamine). In the absence of triethylamine, 44b decomposed and the desired photo-adduct 44a was isolated in 30% yield. In a one-pot reaction, 44a was transformed to 47a-c by the following sequence: A methylene chloride solution of 44a was ozonized at -78°C, and the ozonide reduced with dimethyl sulfide to give aldehyde 45. Addition of sodium borohydride on alumina gel, followed by filtration gave alcohol 46. Acylation of the alcohol function (47a: Ac₂O, pyridine, DMAP; 47b: BzCl, NEt₃, DMAP; 47c: MeOCCOCl, NEt₃, DMAP) gave 47a, 47b and 47c in 30% - 55% yield. This result was in sharp contrast to the decomposition that occurred when the corresponding furan derived photo-adduct 2d had been submitted to the same reaction conditions. Clearly, the anomic acetates are much more stable than the corresponding anemic formates. It was possible to isolate and characterize the intermediate aldehyde 45 and alcohol 46, although neither is very stable and thus cannot be stored for extended periods of time without appreciable decomposition occurring.

Figure 20. The 200 MHz ¹H-NMR of photo-adduct 44a in CD₂Cl₂.
Scheme 20

27

BzO  \xrightarrow{hv, C_{6}H_{6}} \quad \text{hv, C}_{6}H_{6} \quad \text{hv, C}_{6}H_{6}

44a

44b

1. O₃, CH₂Cl₂, -78 °C
2. MgSO₄, R.T.

47a, R=CH₃
47b, R=Ph
47c, R=COOCH₃

(TMS)₂Ado Bz
SnCl₄

48a, R=CH₃, 100% α
48b, R=Ph, 100% α
48c, 49; R=COOMe, 91 α β

45

46

48b

BzO

BzO

BzCl, py., DMAP, CH₂Cl₂

NH₃, MeOH

HO

HO

1a

OH

NHBz

NHBz

BzO

BzO

BzO

BzO

BzO

BzO

BzO

BzO

BzO

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BzO

BzO
Figure 21. The 200 MHz $^1$H-NMR of oxctane 47c in CD$_2$Cl$_2$.

As described by Yamamura$^{15}$, reaction of 47b with bis-(trimethylsilyl)-$N^6$-benzoyladenine and tin tetrachloride in 1,2-dichloroethane, gave protected epioxetanocin 48b as the only isolated product in 70% yield$^{74}$. Similar results were obtained when acetate 47a was used as the carbohydrate component. Applying the Vorbruggen coupling to methyl oxalate 47c gave 49 and 48c as a 9:1 mixture of $\alpha$ and $\beta$ anomers in 70% yield.

Since we were interested in studying the biological properties of epioxetanocin, 48b was debenzoylated (MeOH / NH$_3$) to give 1$\alpha$ in 71% yield, after recrystallization from methanol. However, when epioxetanocin was evaluated as an anti-viral agent against HIV in vitro, it showed no anti-viral effects at concentrations up to 100 $\mu$g/mL. These results were corroborated by Fleet$^9$.

$^{74}$ Since we wanted to compare our product to the one obtained by Nishiyama, 48b was benzoylated (BzCl, NEt$_3$, DMAP) to give N,N-dibenzoylepioxetanocin dibenzoate 50 in 89% yield. It was completely identical with the one described by Yamamura in every respect, except for the fact that our product was racemic.
Figure 22. The 200 MHz $^1$H-NMR of epioxetanocin 1a in CD$_3$OD.

2.6d Synthesis of Silyl Oxetanes (54) and (56).

We now turned our attention to obtaining oxetanocin in anomerically pure form. Since the $\alpha$-anomer is formed via a favourable seven-membered intermediate 51b, as shown below, we wanted to design an oxetanose in which it was not possible to form this intermediate (or at least limit its ability to do so), and thus obtain only the $\beta$-anomer. After careful consideration, we decided to protect the hydroxy group in the photo-adduct as a $t$-butylidemethylsilyl ether.

Scheme 21

51a  47c  51b

$\beta$-anomer  $\alpha$-anomer
Unfortunately, irradiation of a benzene solution of 2-methylfuran and t-butyldimethylsilyloxyacetaldehyde did not give the desired photo-adduct. Hence, we had to obtain 53 in an indirect manner. Hydrolysis of photo-adduct 44a with sodium hydroxide in methanol/water resulted in decomposition of the starting material. Similar results were obtained when the hydrolysis was tried using sodium methoxide in methanol. However, when 44a was subjected to the action of lithium aluminum hydride in ether, alcohol 52 was obtained in 60% yield after flash chromatography. Silylation (TBDMSiCl/imidazole/DMF) of 52 gave photo-adduct 53 in 27% yield. In a one-pot reaction, 53 was transformed to diacetate 54 in 19% yield by a procedure similar to that used for syntheses of compounds 47. Reaction of 54 with bis-(trimethylsilyl)-N6-benzoyladenine catalyzed by tetrachloride gave a complex mixture which did not contain the desired product. However, two coupled products were isolated. Their structures could not be determined with any degree of certainty since purification by chromatographic methods was not possible, although we suspect that the oxetane underwent ring expansion before coupling. We felt that replacing the TBDMSi group with the more stable t-butyldiphenylsilyl group would circumvent this problem.

Reaction of 52 with t-butyldiphenylsilyl chloride\(^{75}\) and imidazole in N,N-dimethylformamide gave 55 in 62% yield. Photo-adduct 55 was transformed to oxetanes 56a-c in 18% yield by the same procedure that was used for the synthesis of oxetane 54. All attempts to couple oxetanes 56 with bis-(trimethylsilyl)-N6-benzoyladenine under Lewis acid catalysis gave very complex mixtures. No materials were isolated which contained benzoyladenine connected to an oxetane ring. The coupled products that were isolated in very low yields could not be identified with any degree of certainty due to difficulty of separation and instability of the compounds, but, as in the case with oxetane 54, we suspect that ring expansion was taking place before coupling.

Scheme 22

BzO\(-\)\(\text{LIAIH}_4\) \(\text{B}_2\text{O}\)

HO\(-\)\(\text{imidazole RCl, DMF}\)

RO\(-\)

53, \(R=\text{TBDMSi}\)
55, \(R=\text{TBDPhSi}\)

54

56a, \(R=\text{CH}_3\)
56b, \(R=\text{Ph}\)
56c, \(R=\text{COOCH}_3\)
2.6e Attempted Synthesis of Oxetanes with 4'-Non-Participating Groups.

Due to the difficulties encountered with the silyl protecting groups, we decided to use a benzyl group. It was hoped that this group would be robust enough to withstand Lewis acid catalysis and would not participate in the coupling reaction so as not to favour the α-anomer. Dimethallyl alcohol was quantitatively converted to the benzyl ether 57 by standard means (Bu₄NI / NaH / BnBr / THF). Ozonolysis in methylene chloride saturated with nitrogen at -78°C, followed by reduction with dimethyl sulfide, gave aldehyde 58 in 95% yield. Irradiation of 58 with 2-methylfuran in benzene did not give photo-adducts 59, but surprisingly, photo-adducts 60a and 60b were isolated in 27% yield as a mixture of regioisomers in a ratio of 3:4.

Scheme 23

Photo-adducts 60a and 60b are formed by the photoreaction of benzaldehyde and 2-methylfuran. The benzaldehyde is formed by a Norrish Type II rearrangement as shown below in Scheme 23. Although these types of rearrangements are not uncommon, it was surprising that rearrangement of the aldehyde took place so rapidly so as to exclude formation of the desired photo-adducts 59 entirely.

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77 No photoreaction takes place between 2-methylfuran and acetaldehyde due to the volatility of the aldehyde.
Since we were unable to obtain 59a by photochemical means, we attempted to synthesize it by an indirect route. Benzylation of photo-adduct alcohol 52 by standard methods did not give the desired product and only decomposition of starting material occurred. Unfortunately, when a milder method (BnOH / DEAD / PPh₃ / THF) was employed, the desired product was also not obtained. We attribute failure to the instability of alcohol 52.

Being unable to synthesize 59a, we decided to substitute the benzyl group with the p-anisyl protecting group. Unfortunately, all attempts to form the p-anisyl ether of alcohol 52 failed. Hence, we attempted to form 65 via the photochemical route. Dimethallyl alcohol was protected as its p-anisyl ether 61 by standard methods (p-MeO-C₆H₄-OH / DEAD / PPh₃ / THF) in 97% yield. However, we were unable to generate the aldehyde 62 in pure form by ozonolysis due to oxidation of the phenyl ring, and since purification by distillation or flash chromatography was not possible, a new approach had to be found. Protection of glycerol acetonide as its p-anisyl ether 63 proceeded in 88% yield. Reaction of 63 with acetic acid and water gave diol 64 in 77% yield. Cleavage of the diol with sodium meta-periodate in water / methanol gave the desired aldehyde 62 in quantitative yield. Unfortunately, irradiation of a benzene solution of aldehyde 62 and 2-methylfuran did not give any photoproducts and only starting material was recovered. Hence, this approach was abandoned.

We then attempted to synthesize a photo-adduct with a methoxyethoxymethyl (MEM) protecting group. However, all attempts to protect the alcohol function of 52 as a MEM ether failed. Therefore, the photochemical route to the MEM photo-adduct was investigated. Dimethallyl alcohol was transformed to its MEM ether 66 by standard methods\(^\text{79}\) (NaH / MEM-Cl / THF) in 83% yield. Ozonolysis in methylene chloride (saturated with nitrogen) at -78°C, followed by reduction with dimethyl sulfide, gave aldehyde 67 in only 27% yield. It was very difficult to obtain pure aldehyde due to its inherent instability. Irradiation of 67 with 2-methylfuran in benzene did not give the desired photo-adduct and only decomposed starting materials were recovered. It is not surprising that the reaction failed considering the instability of the aldehyde. We also attempted to synthesize a photo-adduct with a p-nitrobenzoyl protecting group via the photochemical route. Unfortunately, irradiation of a benzene solution of p-nitrobenzoyloxyacetaldehyde 69, obtained from ozonolysis of the p-nitrobenzoate ester of dimethallyl alcohol 68, and 2-methylfuran did not give any photo-products, and only starting material was recovered.

---

Scheme 26

\[
\text{RO} \begin{array}{c}
\text{66, } R=\text{MEM} \\
\text{68, } R=\rho-\text{NO}_2\text{Bz}
\end{array} \\
\text{1 O}_3/\text{CH}_2\text{Cl}_2 \quad \text{2 DMS} \\
\text{RO} \begin{array}{c}
\text{67, } R=\text{MEM} \\
\text{69, } R=\rho-\text{NO}_2\text{Bz}
\end{array}
\]

2.6f Synthesis of Oxetanes (75).

Since we were unable to synthesize a photo-adduct with a robust non-participating group on what would become the 4' position in the oxetane, we then decided to substitute the benzoyl protecting group with a propionyl group since Yarnamun\textsuperscript{15} had reasonable success with this protecting group\textsuperscript{80}. Irradiation of a benzene solution of propionyloxyacetaldehyde 71, obtained by ozonolysis of 1-O-propionyl-3-methyl-2-buten-1-ol 70, with 2-methylfuran gave, after column chromatography, 72a in 23% yield\textsuperscript{81}. Ozonolysis of 72a, followed by dimethyl sulfide gave aldehyde 73 in 92% yield. Reduction with sodium borohydride on alumina gave alcohol 74 in 68% yield. This alcohol could now be protected in many different ways in order to determine which participating group would give the best yield of oxetanocin. We hoped that we could achieve a practical anemic control of the coupling reaction since separation of anomers by chromatographic means requires conversion to their tetrabenzoate derivatives before chromatographic separation is possible (see section 2.6c). This results in a lengthy synthesis with a low overall yield.

\textsuperscript{80} We had considered using an acetate protecting group. However, due to our earlier difficulties with this group (see section 2.7b), we opted for the more stable propionyl protecting group. We also felt that there would be practically no difference in reactivity between these two groups, except for increased stability with the propionyl, since they are very similar in nature.

\textsuperscript{81} The irradiation of aldehyde 71 and 2-methylfuran gave adducts 72a and 72b in a ratio of 16:11 in 33% combined yield. The less stable isomer could be isolated as a mixture of the two isomers simply by basifying the chromatography solvent with 0.5% triethylamine. Lowering the triethylamine content to 0.1% effectively destroys the minor isomer without significant destruction of the more stable (and desired) isomer.
Esterification of hydroxy compound 74 with methyl oxalyl chloride gave 75a in 45% yield. Coupling of 75a with bis-(trimethylsilyl)-M₆-benzoyladenine in 1,2-chloroethane catalyzed by tin tetrachloride proceeded as described by Yamamura and gave protected oxetanocin and epoxetanocin as a 3:1 mixture of inseparable anomers. Use of trimethylsilyl triflate as the Lewis acid catalyst resulted in decomposition of 75a. Although this was an improvement over previous schemes, the β:α ratio was still not large enough (we were aiming for at least 10:1) for a practical synthesis of oxetanocin. Therefore, other participating groups were investigated. It was hoped that these changes would strongly favour participation of the 3′ group over the 4′ group, thus reducing the amount of α-anomer formed.

82 It is not possible to separate the two anomers chromatographically without first forming their tetrabenzoate derivatives.

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We first investigated the use of thiocarbonyl participating groups since the C=S bond length is greater than the C=O bond length, thus aiding formation of the intermediate that leads to β attack. Compounds 75b and c were formed from acylation of the alcohol function of 74 (75b: PhOCSCI, py, DMAP; 75c: (imld)₂CS, pyridine). Compound 75d was obtained from 75e in 35% yield simply by stirring the latter in methanol at R.T. Unfortunately, all of these new oxetanes failed to couple with bis-(trimethylsilyl)-N⁶-benzoyladenine under Lewis acid catalysis. This was probably due to the relative instability of all of these sugars, which lead to decomposition before coupling with the base could occur.

We next investigated the use of the thio-MOM (and derivatives thereof) protecting group. Alcohol 74 was converted to its thio-MOM ether 75e in 20% yield by the method of Pojer. Upon reaction with bis-(trimethylsilyl)-N⁶-benzoyladenine and tin tetrachloride in 1,2-dichloroethane, only the α-anomer 76b was formed in 72% yield. The use of trimethylsilyl triflate also resulted in formation of the α-anomer, but in a much lower yield. Having gone completely in the wrong direction, 75e was converted to sulfoxide 75f and sulfone 75g by oxidation with sodium m-periodate in methanol / water in 76 and 72% yield, respectively. These sugars however, were too stable and did not couple with bis-(trimethylsilyl)-N⁶-benzoyladenine. When forcing conditions were used, slow decomposition of the sugars occurred.

Due to the lack of success with thio participating groups, we decided to synthesize 75h via a Mitsunobu coupling of guaicol and alcohol 74. This proceeded smoothly in 33% yield. Unfortunately, all attempts to obtain any products containing adenine attached to an oxetane ring failed. Since we felt that we needed a participating group that possessed stronger electron donating characteristics than the methyl oxalyl group, it was decided to synthesize an oxamide protected oxetane.

Scheme 28

\[
\begin{align*}
\text{NH} & \xrightarrow{\text{CICOOCOMe}} \text{N-C-C-O Me} & \xrightarrow{\text{K₂CO₃}} \text{N-C-C-OH} \\
& \text{B₂O} & \text{H₂O / MeOH}
\end{align*}
\]

Hence, methyl oxalyl chloride was reacted with pyrrolidine in ether to give 77 in 95% yield. Hydrolysis of 77 with potassium hydroxide in water / methanol resulted in recovery of only pyrrolidine hydrochloride. Evidently, a dihydrolysis had occurred and thus, milder conditions would have to be

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86 When pyrrolidine hydrochloride was accidently reacted with 74 under Mitsunobu conditions, 75j (OR=Cl) was formed in 48% yield.
employed. When the hydrolysis was attempted with potassium carbonate in methanol / water, only acid 78 was isolated, in virtually quantitative yield. A Mitsunobu coupling of 78 and alcohol 74 gave oxetane 75I in 26% yield. Surprisingly, reaction of 75I with bis-(trimethylsilyl)-N\textsuperscript{6}-benzoyladenine and tin tetrachloride in 1,2-dichloroethane gave only the α-anomer which decomposed when subjected to flash chromatography. The structure of 76e was confirmed by deblocking (Na / MeOH) to obtain epioxetanocin 1α.

2.6g Synthesis of Oxetane (84).

Due to our lack of success in converting 75 to oxetanocin, we investigated the possibility of synthesizing oxetanes with a halogen at the 2-position. It was thought that acetates 75 could be converted to chlorides by methods analogous to those developed for furanoses and hexoses. This approach, however, was not pursued since Fleet et al.\textsuperscript{9} published a synthesis of oxetanocin using these types of chloro-oxetanes at the time when we were developing our strategy. We were fortunate that this work was brought to light at this time since Fleet was not able to convert his chloro-oxetanes to oxetanocin exclusively. It was obtained as a 1:1 mixture of α and β, which had to be separated chromatographically.

We were now convinced that no matter what participating group we put on the 3'-position of the oxetanes 75, we would always obtain some α-anomer in the coupling reaction as long as we had a group on the 4'-position that could form a seven-membered ring intermediate. To circumvent the formation of this intermediate, we decided to synthesize photo-adduct 81. The new protecting group on the 4-position can only form a six-membered ring intermediate, thereby hindering α-anomer formation and thus favoring the formation of the intermediate which leads to the β-anomer. Originally, isopropyl glyoxalate 80 was obtained from the ozonolysis of di-isopropyl fumarate 79\textsuperscript{87}. However, we found that it was simpler to prepare aldehyde 80 via a periodic acid cleavage of commercially available di-isopropyl l-tartarate\textsuperscript{88}. Irradiation of a benzene solution of isopropyl glyoxalate 80 and 2-methylfuran gave, after flash chromatography, photo-adduct 81 in 17% yield\textsuperscript{89}. Adduct 81 was then transformed to oxetane 84 by the previously described method in 40% yield. However, all efforts to couple 84 with bis-(trimethylsilyl)-N\textsuperscript{6}-benzoyladenine under Lewis acid catalysis failed. If mild conditions were employed, no reaction would take place. Using more vigorous conditions simply resulted in decomposition of the starting material.

\textsuperscript{87} Di-isopropyl fumarate 79 was obtained from fumaronic acid by esterification with isopropyl alcohol.
\textsuperscript{89} The isomer with the methyl group bonded to the acetal carbon was obtained in less than a 1:20 ratio with respect to the vinyl substituted isomer as determined by integration of 200 MHz proton NMR signals.
2.7 Synthesis of Enantiomerically Enriched Photo-Adducts and Oxetanes.

2.7a The "Chiral Aldehyde" Approach; Synthesis of (85).

In parallel to our synthesis of racemic oxetanocin and derivatives thereof, we also pursued a program of synthesizing chiral intermediates that could be used in our oxetanocin synthesis. Since separation of Mosher acid derivatives is often impractical for larger scale syntheses due to its cost and the necessity of tedious chromatographic separations, we investigated approaches that would eliminate at least one of these obstacles. We also decided that chromatographic separation of the two enantiomers would only be acceptable if it occurred early on in the synthesis. This would enable us to carry out further research with the "wrong" enantiomer so that the undesired enantiomer could be put to some use.

Our first approach involved the [2+2] photoaddition of a chiral aldehyde to a furan. Although Schreiber has recently shown that the furan-carbonyl photocycloaddition proceeds without diastereoface selectivity in relation to the chiral aldehyde, he did demonstrate that photo-products of the reaction of R-glyceraldehyde acetal and 3,4-dimethylfurane can be separated chromatographically. Therefore we decided to synthesize photo-adduct 85 from R-glyceraldehyde acetal and furan, since it was felt that this bicyclic compound would be a good starting point for our synthesis of oxetanocin. The substituent on the C-6 position could be easily transformed into an alcohol by removal of the acetonide followed by sodium periodate/sodium borohydride cleavage to the alcohol, which could then be protected by a suitable group. Irradiation of a benzene solution of furan and R-glyceraldehyde acetal gave photo-adduct 85 in 25% yield as a 1:1 mixture of diastereomers. Unfortunately, separation by flash chromatography proved to be impossible and this approach was abandoned.

Scheme 30

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2.7b Enzymic Resolution of Photo-Adducts (2d) and (87).

Over the past decade, the use of enzymes in synthetic organic chemistry has increased dramatically. Enzyme-catalyzed syntheses are among the best methods for the preparation of enantiomerically pure compounds and in the last few years, methods have even been developed for using enzymes in organic solvents. We felt that our photo-adduct 2d would be a suitable candidate for enzymatic resolution since selective hydrolysis of the ester would enable us to chromatographically separate the alcohol and unreacted ester. It did not matter which enantiomer was hydrolyzed since the alcohol could be reconverted to its ester quite easily. However, we did have some concern using 2d since practically all enzyme hydrolysis are carried out on acetates. Therefore, it was decided to synthesize photo-adduct 87.

Ozonolysis of allyl acetate, followed by reduction with dimethyl sulfide, gave acetoxyacetetaldehyde 86 in 38% yield. Irradiation of 86 with furan provided photo-adduct 87. Unfortunately, the reaction proceeded in very low yield and a great deal of decomposition took place during the reaction which made this an impractical route to 87. Hence, an alternate route to adduct 87 had to be found. Hydrolysis of photo-adduct 2d with sodium hydroxide in methanol / water gave alcohol 88 in 79% yield. Acetylation of the alcohol by standard methods (Ac₂O, py, DMAP) gave 87 in 72% yield.

Scheme 31

With acetate 87 in hand, we were now ready to proceed with our enzymatic resolution. We decided to carry out our hydrolysis with porcine pancreatic lipase (PPL) since its use in these types of reactions is well documented and has been shown to give high ee's. It was hoped that the enzyme would only hydrolyze one enantiomer and thus, the hydrolysis experiment was designed to stop when 50% conversion was obtained. Unfortunately, hydrolysis of 87 with PPL resulted in total decomposition of the starting material. We felt that this decomposition was due to the inherent instability of photo-adduct 87 and not because the enzyme was unsuitable for the reaction. Hence, it was decided to carry out

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the hydrolysis with photo-adduct 2d. Using the same conditions as for acetate 87, we managed to isolate both unreacted photo-adduct -2d (46% yield) and alcohol 88 (42% yield), after flash chromatography. Benzoylation of 88 via standard methods gave +2d in 45% yield. We then measured the rotations of both the benzoyl photo-adducts 2d obtained from the enzyme hydrolysis and found that they were opposite (-2d: [α]_{D}^{20} = -15.5° (c = 3.21, CH₂Cl₂) vs +2d: [α]_{D}^{20} = +18.8° (c = 1.25, CH₂Cl₂)). These numbers proved that we were indeed getting enantiomeric enrichment.

Scheme 32

We did not attempt to establish the enantiomeric purity of resolved 2d by Mosher ester or by the use of ¹H-NMR shift reagents since this project was not the main thrust of our research anymore and we were now concentrating on the use of photo-adducts 44a and 72a in our approach to the synthesis of oxetanocin.

2.7c Enzymic Resolution of Photo-Adducts (44a) and (72a).

As we had recently completed a total synthesis of (±)-oxetanocin²⁹ starting from photo-adduct 72a, we were now interested in synthesizing optically pure oxetanocin. Using the precedent that we established in resolving photo-adduct 2d, we decided to hydrolyze photo-adduct 72a with PPL. Unfortunately, no identifiable products could be isolated from the reaction mixture and the chart measuring the progress of the reaction indicated that there was no selectivity for one enantiomer. Since we had earlier converted photo-adduct 44a to photo-adduct 72a, we decided to hydrolyze 44a and convert the resultant alcohol or unreacted benzoate to enantiomerically pure 72a. Using the same conditions as for photo-adduct 72a, we managed to obtain both unreacted 44a and alcohol 52 (as indicated on tlc). Not surprisingly, we were unable to isolate the alcohol due to its instability. However,
unreacted photo-adduct 44a was isolated by flash chromatography in 36% yield. We then measured the rotation of recovered 44a ([α]^{20}_D = -7.5° (c = 2.22, CH_2Cl_2)) and found that we were obtaining enantiomeric enrichment. Conversion of -44a to oxetane 47b proceeded smoothly as described in section 2.6c. The rotation of 47b was determined to be ([α]^{20}_D = +6.4° (c = 2.51, CH_2Cl_2)). Enantiomerically pure 47b that is the precursor^14 for epioxetanocin has [α]^{20}_D = +41.8°. This meant that our oxetane +47b had an ee of 15.3%.

Scheme 33

![Scheme 33](image)

2.7d Future Considerations.

We established that racemic photo-adduct 2d could be resolved into its two enantiomers quite easily and may only require investigation of other enzymes to determine which ones give the highest ee. On the other hand, resolution of photo-adducts 44a and 72a may require redesigning the hydrolysis experiment so as to eliminate the aqueous conditions which seem to cause decomposition of the photo-adduct alcohol 52. Other enzymes should also be investigated since PPL did not give a very high ee.
2.8 Synthesis of Bicyclic Nucleosides and Derivatives.

During the course of our investigations of suitably functionalized photo-adducts for coupling to nitrogenous bases, epoxides of the type 23 were synthesized, as previously described in section 2.5d. It was hoped that these epoxides would couple to the nitrogenous bases in the manner depicted in Pathway A of Scheme 34 to yield an oxetanocin-like nucleoside. We also realized that there were two other competing routes possible. One would involve a Lewis acid-catalyzed opening of the epoxide followed by attack of the nitrogenous base to yield bicyclic nucleosides (Pathway B), which could then be transformed into furanose nucleosides via the use of well-established methods. The other possibility would simply be the Lewis acid-catalyzed opening of the oxetane ring followed by addition of the base to give furanose nucleosides.

Scheme 34
2.8a Synthesis of Bicyclic Nucleosides (89a) and (89b).

Our initial efforts were carried out with model compounds 23a and 23b. Reaction of these epoxides with persilylated bases and Lewis acids (tin tetrachloride, trimethylsilyl acetate, trimethylsilyl trifluoromethanesulfonate) under various conditions gave very complex mixtures. No materials were isolated which contained nitrogenous bases connected to a sugar component. Similar results were obtained when epoxide 23d was used. However, it was found that by using zinc chloride as the Lewis acid catalyst in a variation of the procedure described by Danishefsky, nucleosides 89a and 89b were obtained in 67 and 66% yield\(^ {95} \), respectively as shown in Scheme 35. It is interesting to note that the free hydroxyl group becomes silylated in situ, presumably by chlorotrimethylsilane generated by reaction of the silylated base with zinc chloride, and survives the work-up even when the reaction mixture is washed with 5% aqueous hydrochloric acid.

\(^ {95} \text{Upon flash chromatography over silica gel with methylene chloride/methanol, epoxide 23d which had not coupled to the base was opened up by the methanol to give 24a'(Ph=}$\text{BzOCH}_2$) in 22% yield.\)
The configuration of nucleoside 89a, and thus of 89b, about H3' and H4' was confirmed by \(^1\)H-NMR spectroscopy (Figure 23), which clearly showed couplings of \(-\) 0\(\text{ Hz}\) for \(J_{\text{H3, H4'}}\). This indicates that the nitrogenous base and protected hydroxyl function are trans to one another with a torsional angle of \(-\) 90°. Had the two substituents been cis, a coupling between H3' and H4' would have been observed.

The bicyclic structure was confirmed by a HETCOR carbon-hydrogen correlation (see Appendix IV) which showed that the \(^{13}\)C signal at 110.45 ppm was coupled to the proton at 6.28 ppm, and the \(^{13}\)C signal at 99.02 ppm was coupled to the proton at 5.94 ppm. This indicates that the nitrogenous base is connected to C3' since O-C-O carbons are always more deshielded than O-C-N carbons.

We also investigated this reaction with purine bases. However, attempts to carry out the coupling reaction with bis-(trimethylsilyl)-N\(^6\)-benzoyladenine and zinc chloride proved to be unsuccessful whether the silylated base was generated \textit{in situ} using HMDS and chlorotrimethylsilane\(^8\) or a stock solution of the silylated base in 1,2-dichloroethane was used. Further investigation of purine couplings to 23d have not been carried out at this time.

Desilylation (Bu\(_4\)NF / THF) of nucleosides 89a and 89b proceeded smoothly giving excellent yields (95 and 93%, respectively) of the desilylated nucleosides 90a and 90b. Fully deprotected 90b was obtained by aminolysis (NH\(_3\) / MeOH), followed by recrystallization from methanol, in 58% yield. Nucleoside 91a was obtained in a similar manner\(^9\) in 65% yield, except that it was purified by flash chromatography prior to recrystallization from methanol. The X-ray crystallographic structure of 91a (Figure 24) confirmed our NMR analyses, clearly showing the nitrogenous base trans to the adjacent hydroxy group. Details of the X-ray crystallographic study of nucleoside 91a are shown in Appendix III.

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\(96\) Nucleosides 91* are enantiomers of nucleosides 91.

Figure 24. The X-ray crystallographic structure of nucleoside 91a.
Scheme 35

23d

$\text{[(CH$_3$_2)$_3$Si)$_2$B. ZnO}_2. \text{ THF.}$

89a, B-Thymine
89b, B-Cytosine

TBAF. THF

90a, B-Thymine
90b, B-Cytosine

NH$_3$. MeOH

91a, B-Thymine
91b, B-Cytosine

92

NH$_3$. MeOH

93

91c

93c
2.8b Synthesis of Furanoside (93).

We also felt that these novel bicyclic nucleosides could be transformed into interesting furanosides simply by opening the oxetane ring, and this is known to proceed stereospecifically in many cases. Reaction of 89a with trifluoroacetic acid in methanol gave the ring opened nucleoside 92 in 89% yield. Debenzylation in methanolic ammonia, followed by flash chromatography and recrystallization from acetone/hexanes gave the deprotected furanoside 93 in 86% yield. All efforts to obtain crystals large enough for X-ray diffraction studies proved to be unsuccessful. Work on the synthesis of other derivatives of 93 may be undertaken in the future pending the outcome of biological evaluation currently underway.

2.8c Attempted Resolution of Enantiomers of Bicyclic Nucleoside (90a).

Since we were interested in eventually developing a method for the synthesis of enantiomerically pure 91, a project involving the chiral derivatization of 90 was initiated. First, 90a was acetylated by standard methods to give 94a in 90% yield. This derivative was made so that we could have a simple model for the purpose of setting GC and HPLC conditions. Since our group is currently involved in developing a practical synthesis of enantiomerically pure α-methylvaleric acid, we decided to make the valerate ester of 90a. Esterification proceeded smoothly giving 94b in 95% yield. Unfortunately, the 2 diastereomers were unseparable by TLC, GC and HPLC. Also, the 1H-NMR exhibited no difference for the two diastereomers. We then decided to synthesize the Mosher ester derivative 98 (94c) of 90a. It was obtained in 82% yield via standard methods. Again, we unable to separate the 2 diastereomers by chromatographic means. However, the 1H-NMR indicated that the diastereomers existed in an approximately 1:1 ratio. Being unable to separate the isomers by derivatization, other methods (mainly enzymatic) of resolution will be investigated in the future if biological evaluation is promising.

\[
\begin{align*}
&\text{BzO} \\
&\text{O} \\
&\text{O} \\
&\text{Thy} \\
&\text{RO} \\
\end{align*}
\]

94a, R=Ac
94b, R=CH₃CH₂CH₂CH(CH₃)CO
94c, R=C₆H₅CO(OCH₃)(CF₃)CO

97 Furanoside 93* is the enantiomer of furanoside 93.

2.9 Direct Coupling of a Nitrogenous Base to a Modified Photo-adduct (via a Modified Fraser-Reid–Mootoo Approach).

2.9a Strategy.

Since all of our efforts to obtain anomerically pure oxetanocin did not succeed, a new strategy based on our modified Fraser-Reid–Mootoo method was designed. We felt that this approach would give us oxetanocin in anomerically pure form since attack from the α face is extremely hindered and attack at the C-3 position of the photo-adduct is extremely unlikely due to steric factors especially when considering that much smaller nucleophiles did not attack via this pathway (see section 2.5b). This approach had been tried earlier and had failed due to the incompatibility of DCP with the nitrogenous bases. To circumvent this problem we decided to synthesize modified photo-adducts of the type 95 which contain halogens. It was thought that we could then couple persilylated bases to adducts of type 95 in the presence of silver salts to afford protected oxetanocin derivatives 96 as shown in Scheme 36. Nucleoside 96 could then be transformed to oxetanocin by deprotection of the aldehyde, followed by cleavage of the hydroxy aldehyde function with sodium peroxide / sodium borohydride to afford the desired alcohol. Fully deprotected oxetanocin could then be obtained by removal of the 4′ protecting group.

Scheme 36
2.9b Synthesis of Bicyclic Nucleosides (99).

Our first task was to construct a modified photo-adduct of the type 95. Unfortunately, all attempts to open epoxide 23d with 2-haloethanol were unsuccessful. However, when 23d was treated with bromo or chloroacetic acid in methylene chloride, acetals 97a and 97b were obtained in 55 and 45% yield, respectively. Acetal 97a was transformed to its tert-butyldimethylsilyl ether 98a in 41% yield by standard means (TBDMSiCl / imidazole / DMF). However, when the same conditions were used to silylate 97b, adduct 98b was obtained in 36% yield. When silylation was carried out using 2,6-lutidine / TBDMSi-OTf in methylene chloride99, 98c was obtained in 58% yield.

Scheme 37

\[ BzO-\overset{CH_2COOH}{\rightarrow} BzO- \]

\[ 23d \]

\[ 97a, \; X=\text{Cl} \]

\[ 97b, \; X=\text{Br} \]

\[ \text{TBDMSiCl, imidazole, DMF} \]

\[ \text{or} \]

\[ \text{TBDMSi-OTf, 2,6-lutidine, CH}_2\text{Cl}_2 \]

\[ BzO-\overset{AcO, \; CH_2Cl_2 ; \text{py, DMAP}}{\rightarrow} BzO- \]

\[ 98a, \; X=\text{Cl} \]

\[ 98b, \; X=\text{imid} \]

\[ 98c, \; X=\text{Br} \]

We were now ready to couple the nitrogenous base to our modified photo-adducts 98. Silver triflate was chosen as the metal salt that would trigger the reaction due to the high affinity of silver ion for halogens and because the triflate anion is an extremely poor nucleophile that would not interfere with the coupling reaction. Unfortunately, reaction of 98a with bis-(trimethylsilyl)-N6-benzoyladenine and silver triflate gave a very complex mixture. No materials were isolated which contained N6-benzoyladenine connected to a sugar moiety. However, when 98c was reacted with bis-(trimethylsilyl)-N6-benzoyladenine and silver triflate under similar conditions, a product 99a containing N6-benzoyladenine connected to a sugar moiety was obtained. Its 1H and 13C-NMR was not consistent with nucleosides of the type 100. Also, the instability of this compound made it difficult to work with since it decomposed shortly after purification. Therefore, we decided to deblock nucleoside 99a not really knowing the exact structure of it. All attempts to remove silyl or benzoyl protecting groups failed.

Being unable to work with nucleoside 99a, it was decided to replace the TBDMSi protecting group with an acetate group since we felt that the TBDMSi group was the cause of the instability. Acetal 97b was acetylated by standard means to afford 101 in 95% yield. Coupling of 101 to bis-(trimethylsilyl)-N6-benzoyladenine in the presence of silver triflate again afforded a nucleoside 99b whose NMR data was not consistent with nucleosides of the type 100. This compound was more stable than the TBDMSi derivative and it was possible to carry out extensive analysis by NMR. Unfortunately, it was not possible to obtain a mass spectrum of either nucleoside 99a or 99b.

Figure 25. The 200MHz 1H-NMR of nucleoside 99b in CD2Cl2.

100 Had we known the structure of nucleoside 99a at this point, we would have obviously not attempted to hydrolyze the benzoyl group since this would open the bicyclic lactone.
Scheme 38

Despite not being able to obtain a mass spectrum of 99b, we were able to assign the structure of 99b, and thus of 99a, with a high degree of confidence based on our extensive NMR experiments. The mechanism for the formation of nucleosides 99 is shown in Scheme 39. The only possible explanation as to why the reaction proceeds via this pathway, considering that we had earlier opened acetalts of type 10, 21 and 29 in the desired manner to yield monocyclic oxetanes (see sections 2.5b - 2.5d), is that the oxetane oxygen is in closer proximity to the acetyl bromide side chain than the furan oxygen.

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101 Nucleoside 99* is the enantiomer of nucleoside 99.
Due to this unexpected result, we reexamined our structural assignment of oxetanes 17, 18, 22, 30 and 31. If we analyze the NMR data of compound 30c (a representative sample), we see that the main distinction between oxetane 30c and furan 102* in the $^1$H-NMR is the chemical shift and coupling pattern of H3. If 102* had been formed, we should see a "ddd" at ~2.5 ppm like was observed in nucleosides 99. Instead, the $^1$H-NMR shows a triplet at 3.51 ppm. The chemical shift is very close to what Yamamura$^{14}$ reports for oxetane 103. Also, if we examine the $^1$H-NMR's of a variety of monocyclic oxetanes, we see that H3 is not affected very much by the substituents on C3' due to the fact that the substituent on C3 is not rigidly attached and can "swing" away to a more stable conformer. If structures of type 102* had been formed, varying the substituents on C4 would affect the chemical shift of H3 since these substituents would be part of the ring and could not orient out of the way.
It may be possible to synthesize deprotected nucleosides of the type 99 simply by starting from an epoxide which has a protecting group that can be removed under neutral conditions and protecting the free alcohol in acetals of type 97 with a group that can also be removed under mild conditions. A problem may arise with the use of purine bases since these are normally benzoylated prior to benzylation and the benzoyl group may be difficult to remove without again destroying the bicyclic lactone as was the case when we attempted to deblock 99a. However, no such problems should arise with the use of pyrimidine bases and this may be an interesting approach to obtain deprotected nucleosides of the type 99.
2.10 Future Outlook.

Due to the unexpected reaction of adducts 98c and 101 with \( \text{bis-(trimethylsilyl)-N}^6 \)-benzoyladenine, a new adduct would have to be designed in which the halide containing side chain could not reach over to the oxetane oxygen. It has not yet been possible to synthesize an endo epoxide of type 23d, which would be required to obtain an \( \text{exo} \) opening of the epoxide, and thus yield an adduct which would have the halide containing side chain closer to the furan oxygen. Therefore, we felt that perhaps an adduct of the type 107 would be suitable and allow the reaction to proceed in the desired manner to give nucleoside 108 since the halide containing side chain is locked in a position that puts it in close proximity to the furan oxygen. Adducts of the type 107 could be synthesized via a \([2+2]\) photocycloaddition of aldehyde \( 105 \) and furan \( 106 \) as shown in Scheme 41 or by building the side chain on to a suitable photo-adduct.

Scheme 41

Although oxetanocin has generated a great deal of interest in oxetane containing nucleosides over the past few years, interest in it and derivatives thereof is slowly waning due to findings that the oxetane ring is not the sole structural feature which is responsible for activity and due to the fact that no one has yet developed a cost efficient synthesis.
3. CONTRIBUTIONS TO KNOWLEDGE

1. A number of trisubstituted monocyclic oxetanes were prepared from photo-adducts of aldehydes and furan using a modification of the Fraser-Reid–Moore glycosidation procedure. The chemistry of these oxetanes was also investigated.

2. Racemic oxetanocin and epioxetanocin were synthesized from photo-adducts of propionyloxyacetalddehyde and 2-methylfuran. The coupling of oxetanes, containing various participating groups, with nitrogenous bases was investigated.

3. Bicyclic nucleosides containing photo-adducts of aldehydes and furan were synthesized. Furanose derivatives of these nucleosides were also prepared.
4. EXPERIMENTAL

4.1 General Methods.

Melting points (m.p.) were determined on a Gallenkamp block and are uncorrected. Gas chromatographic analyses were performed on a Hewlett-Packard 5890 GC equipped with a fused silica capillary column (25m x 0.2 mm), a flame ionization detector and a HP 3392A integrator. UV spectra were obtained on a Hewlett-Packard 8451 diode array spectrophotometer. Infrared spectra were recorded on an Analect AQS-18 spectrometer in the indicated solvent. Optical rotations were measured on a Jasco DIP-140 digital polarimeter in the indicated solvent and concentration in a 1 dm cell. Low-resolution chemical ionization mass spectra were obtained on an HP-5980A quadrupole mass spectrometer in the direct-inlet mode. Low-resolution electron impact mass spectra were obtained on a DuPont 21-492B mass spectrometer in the direct-inlet mode. High-resolution chemical ionization and FAB mass spectra (low-resolution and high-resolution) were obtained on a VG ZAB-2F-HS sector mass spectrometer in the direct-inlet mode. The measurements were carried out at a resolving power (res) of 10000, unless otherwise indicated. Elemental analyses were performed by Guelph Chemical Laboratories Ltd. (Guelph, Ontario, Canada). All compounds were shown to be homogeneous by tlc and high-field NMR, and to have a purity of >95%.

1H-NMR spectra were obtained on either a Varian XL-200 or Varian XL-300 spectrometer at 200 MHz and 300 MHz, respectively and the peak assignments were made, in some cases, with the aid of homonuclear decoupling and/or COSY experiments. Chemical shifts are given in the scale of parts per million (ppm). The residual proton signals of chloroform, DMSO, methanol and methylene chloride (assigned values of δ 7.24, 2.49, 3.30 and 5.32 ppm, respectively) were used as reference in these solvents. The multiplicities are recorded using the following abbreviations: s, singlet; d, doublet; dd, doublet of doublets; ddd, doublet of doublet of doublets; dddd, doublet of doublet of doublet of doublet; t, triplet; q, quartet, h7, heptet; m, multiplet, br, broad; ex, exchangeable. 13C-NMR spectra were obtained on a Varian XL-300 spectrometer at 75.4 MHz and the peak assignments were made, in some cases, with the aid of APT and/or HETCOR experiments. The 13C signals of CDCl3, DMSO-d6, CD3OD, CD2Cl2 and C6D6 (assigned values of δ 77.00, 39.50, 49.00, 53.80 and 128.00 ppm, respectively) were used as reference in these solvents. Entries with an asterisk are interchangeable. Selected 2-D experiments are shown in Appendix IV.

Tetrahydrofuran and ether were distilled from sodium benzophenone ketyl. Methylene chloride and 1,2-dichloroethane were distilled from P2O5. Benzene, hexanes, petroleum ether and toluene were dried over sodium wire. Methanol was distilled from magnesium. Pyridine, acetonitrile, di-sym-collidine and triethylamine were distilled from calcium hydride. N,N-Dimethylformamide was dried by shaking with KOH followed by distillation from BaO. Thin-layer chromatography (tlc) was performed on silica.
gel (Kieselgel 60 F\textsubscript{254}) aluminum-backed plates (0.2 mm thickness) and visualized by UV and/or dipping into a solution of 2.5 g ammonium molybdate and 1 g ceric sulfate in 10 mL sulphuric acid / 90 mL water, followed by heating. Kieselgel 60 (Merck 230-400 mesh) silica gel was used for column chromatography\textsuperscript{102}.

Photochemical reactions were carried out in 350 mL or 2 L reaction vessels using a 450 W medium pressure Hg arc lamp equipped with a VYCOR filter. Oxetanes 42, 47, 54, 56, 75 and 84 can be prepared in one-pot from their respective photo-adducts. However, in some cases, an improved yield can be realized if a partial work-up is done at the alcohol stage. The nomenclature of photo-adducts 2a-d, 37a, 38a, 39a, 39b, 40, 41, 43, 44, 52, 53, 55, 72, 81, 85, 87 and 88, and any compounds derived from these adducts, refers to the enantiomer shown.

4.2 Experimental for Section 2.2.

2α-O-Formylxy-3α-C-formyl-4β-phenyl oxetane (3).

Ozone was bubbled through a solution of the photo-adduct 2a (1.025 g, 5.89 mmol) in dry methylene chloride (250 mL) at -78°C until the solution turned blue (1 h). Dimethyl sulfide (2.16 mL, 5 equiv.) was added to the reaction mixture under nitrogen and it was allowed to warm to ambient temperature gradually overnight. The solution was washed with water (2 x 150 mL), brine (150 mL), dried (Na₂SO₄), filtered and the solvent removed in vacuo to yield aldehyde 3 (1.201 g, 99% yield) as a light yellow oil. \(^1\)H-NMR (200 MHz, CDCl₃): δ 3.93 (ddd, 1 H, H₃), 6.22 (d, 1 H, H₄), 6.88 (d, 1H, H₂), 7.26 - 7.39 (m, 5H, phenyl), 8.14 (s, 1 H, OCHO). 9.84 (d, 1H, CHO); J₃-H₃ = 6.2 Hz, J₃-H₃-CHO = 1.0 Hz, J₃-H₂-H₄ = 6.5 Hz, IR (CH₂Cl₂): 1730 cm⁻¹ [CHO], 1743 cm⁻¹ [OCHO].

![Chemical Structure](image)

Tetramethoxy-olefin (4).

To a stirred solution of aldehyde 3 (206 mg, 1.00 mmol) in dry methanol (2.5 mL) under nitrogen at room temperature was added cerium (III) chloride heptahydrate (373 mg, 1.00 mmol) and trimethyl orthoformate (0.80 mL, 7.00 mmol). After stirring for 43 h, another 0.80 mL of trimethyl orthoformate was added. After stirring for another 2 h, the reaction mixture was poured into saturated aqueous sodium bicarbonate (50 mL), extracted with ether (3 x 50 mL), dried (Na₂SO₄), filtered and the solvent removed in vacuo yielding a yellow syrup which was chromatographed over silica gel (hexanes / ether, 2:1 v/v), affording tetramethoxy-olefin 4 as a light yellow oil (108 mg, 43% yield) \(^1\)H-NMR (200 MHz, CDCl₃): δ 3.34, 3.35, 3.41, 3.42 (4s, 12H, MeO), 4.89, 5.03 (2s, 2H, CH(OMe)₂), 7.09 (s, 1H, CH-Ph), 7.32 - 7.39 (m, 5H, phenyl); LRMS (Cl-NH₃): m/e 221 ([MH⁺ - MeOH], 100%).

![Chemical Structure](image)
4.3 Experimentals for Section 2.3.

6β-Phenyl-2,7-dioxabicyclo[3,2,0]-hepta-3-none (5a) and 1-β-acetoxy-6β-phenyl-2,7-dioxabicyclo[3,2,0]-hepta-3-ene (9a).

A mixture of 2-acetoxyfuran (5.90 g, 46.8 mmol) and benzaldehyde (4.90 g, 46.2 mmol) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C and saturated with helium. The solution was then irradiated for 6 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) gave 5a (1.241 g, 14% yield) and 9a (550 mg, 5% yield) as yellow oils. 5a: \( \delta \) 2.80 (A of ABX, 1H, H4a), 2.96 (B of ABX, 1H, H4b), 3.51 (dddd, 1H, H5), 5.42 (d, 1H, H6), 6.37 (d, 1H, H1), 7.35 - 7.44 (m, 5H, phenyl); JH1-H15 = 4.8 Hz, JH4-H14 = 1.3 Hz, JH14-H14b = 10.0 Hz, JH4-H14b = -18.8 Hz, JH5-H6 = 4.4 Hz; \( ^{13}C\)-NMR (75.4 MHz, CDCl3): \( \delta \) 32.64 [C4], 42.77 [C5], 86.79 [C6], 104.75 [C1], 125.24, 128.38, 139.17 [aromatic CH], 128.23 [aromatic C], 175.96 [CO]. IR (CH2Cl2) 1794 cm\(^{-1}\). 9a: \( \delta \) 2.17 (s, 3H, CH3), 3.86 (t, 1H, H5), 5.41 (d, 1H, H6), 5.51 (t, 1H, H4), 6.66 (d, 1H, H3), 7.30 - 7.45 (m, 5H, phenyl); JH3-H14 = 3.4 Hz, JH14-H15 = 3.1 Hz, JH15-H16 = 3.5 Hz; IR (CH2Cl2): 1767 cm\(^{-1}\); LRMS (Cl-NH3): m/e 250 ([M + NH4\(^{+}\), 25.8%], 233 ([M+H\(^{+}\)], 14.2%).

\[ \text{5a} \]
\[ \text{9a} \]
4.4  Experimental for Section 2.5.

General Procedure for the Reaction of N-Halosuccinimide and Alcohols with Photo-adducts.

To a solution of 2 in dry alcohol (0.05 M - 0.20 M) at room temperature under nitrogen was added N-bromo (NBS) or N-iodo (NIS) succinimide (1 equiv.). The reaction mixture was stirred at room temperature until complete consumption of the starting material (1 - 3 h). The remaining alcohol was removed in vacuo and the residue was purified by flash chromatography (petroleum ether / ethyl acetate, 10:1 - 4:1, v/v).

3α-Allyloxy-4β-bromo-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10a).

Photo-adduct 2a (98 mg, 0.56 mmol) and NBS (99 mg, 0.56 mmol) in allyl alcohol (5 mL) gave the title compound (38 mg, 22% yield) as a clear oil. \( {^1}H-NMR \) (200 MHz, CDCl₃): \( \delta \) 3.59 (t, 1H, H5), 4.32 (ddt, br, 2H, H3′, H3″), 4.50 (s, 1H, H4), 5.31 (ddd, br, 2H, H3′′, H3″″), 5.57 (d, 1H, H6), 5.74 (d, 1H, H3), 5.96 (m, 1H, H3″), 6.33 (d, 1H, H1), 7.31 - 7.41 (m, 5H, phenyl), \( J_{\text{H11-H12}} = 4.1 \text{ Hz} \), \( J_{\text{H13-113a}} = -0.3 \text{ Hz} \), \( J_{6-5} = 4.8 \text{ Hz} \).

3α-Methallyloxy-4β-bromo-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10b).

Photo-adduct 2a (435 mg, 2.50 mmol) and NBS (445 mg, 2.50 mmol) in 2-methyl-2-propen-1-ol (25 mL) gave the title compound (108 mg, 17% yield) as a clear oil. \( {^1}H-NMR \) (200 MHz, CDCl₃): \( \delta \) 1.80 (s, 3H, Me), 3.59 (t, 1H, H5), 4.23 (dd, br, 2H, H3′, H3″), 4.51 (s, 1H, H4), 4.96, 5.05 (2s, br, 2H, H3′″, H3″″), 5.57 (d, 1H, H6), 5.72 (d, 1H, H3), 6.33 (d, 1H, H1), 7.30 - 7.41 (m, 5H, phenyl), \( J_{\text{H11-H12}} = 4.1 \text{ Hz} \), \( J_{\text{H13-113a}} = -0.5 \text{ Hz} \), \( J_{\text{H13-113b}} = -12.4 \text{ Hz} \), \( J_{\text{H15-116}} = 4.8 \text{ Hz} \); LRMS (Cl-NH₃): m/e 344, 342 ([M + NH₄⁺], 5.7%, 4.3%), 272, 270 ([MH⁺ - H₂C=C(CH₃)CH₂OH], 15.2%, 11.9%).

3α-Dimethallyloxy-4β-bromo-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10c).

Photo-adduct 2a (87 mg, 0.50 mmol) and NBS (89 mg, 0.50 mmol) in 3-methyl-2-buten-1-ol (5 mL) gave the title compound (129 mg, 76% yield) as a clear oil. \( {^1}H-NMR \) (200 MHz, CDCl₃): \( \delta \) 1.61, 1.78 (2s, br, 6H, Me), 3.57 (t, 1H, H5), 4.31 (ddd, br, 2H, H3′, H3″), 4.48 (s, 1H, H4), 5.40 (m, 1H, H3″), 5.57 (d, 1H, H6), 5.73 (s, 1H, H3), 6.33 (d, 1H, H1), 7.30 - 7.40 (m, 5H, phenyl), \( J_{\text{H11-H12}} = 4.1 \text{ Hz} \), \( J_{\text{H15-116}} = 4.7 \text{ Hz} \); LRMS (Cl-NH₃): m/e 341, 339 ([MH⁺], 5.8%, 6.2%).

![Structural diagram](image-url)
3α-Methallyloxy-4β-iodo-6β-phenyl-2,7-dioxo-bicyclo-[3,2,0]-heptane (10d).

Photo-adduct 2a (87 mg, 0.50 mmol) and NIS (113 mg, 0.50 mmol) in 2-methyl-2-propen-1-ol (5 mL) gave the title compound (186 mg, 100% yield) as a clear oil. \(^1\)H-NMR (200 MHz, CDCl\(_3\)): δ 1.75 (s, 3H, Me), 3.69 (l, 1H, H2'), 4.49 (s, 1H, H4), 4.95, 5.04 (2s, br, 2H, H3''a, H3''b), 5.56 (d, 1H, H6), 5.84 (d, 1H, H3), 6.34 (d, 1H, H1), 7.30 - 7.43 (m, 5H, phenyl), J\(_{\text{H1-1H5}}\) = 4.0 Hz, J\(_{\text{H3-H3'}}\) = -0.6 Hz, J\(_{\text{H3a-H3b}}\) = -12.2 Hz, LRMS (Cl-\(\text{NH}_3\))\(^+$+: m/e 373 ([MH]+, 0.2%), 301 ([MH\(-\text{CH}_2\text{C(CH}_3\text{)}\text{CH}_2\text{OH}]+, 4.2%).

3α-Allyloxy-4β-bromo-6β-\text{-}3-propyl-2,7-dioxo-bicyclo-[3,2,0]-heptane (10e).

Photo-adduct 2b (140 mg, 1.00 mmol) and NBS (178 mg, 1.00 mmol) in allyl alcohol (5 mL) gave the title compound (194 mg, 70% yield) as a colourless oil. \(^1\)H-NMR (200 MHz, CDCl\(_3\)): δ 0.86 (d, 3H, MeCHMe'), 0.89 (d, 3H, MeCHMe'), 0.91 (d, 3H, MeCHMe'), 1.82 (m, 1H, H6'), 3.32 (t, 1H, H5), 4.17 (dd, 1H, H6), 4.23 (m, br, 2H, H3''a, H3''b), 4.25 (s, 1H, H4), 5.25 (dddd, br, 2H, H3''a, H3''b), 5.63 (d, 1H, H3), 5.87 (m, 1H, H3'), 6.02 (d, 1H, H1), J\(_{\text{H1-1H5}}\) = 4.1 Hz, J\(_{\text{H3-H3'}}\) = -0.6 Hz, J\(_{\text{H3a-H3b}}\) = -12.2 Hz, J\(_{\text{H5-1H6}}\) = 4.8 Hz; LRMS (Cl-\(\text{NH}_3\))\(^+$+: m/e 373 ([MH]+, 0.2%), 301 ([MH\(-\text{CH}_2\text{C(CH}_3\text{)}\text{CH}_2\text{OH}]+, 4.2%).

3α-Methallyloxy-4β-bromo-6β-\text{-}3-propyl-2,7-dioxo-bicyclo-[3,2,0]-heptane (10f).

Photo-adduct 2b (140 mg, 1.00 mmol) and NBS (178 mg, 1.00 mmol) in 2-methyl-2-propen-1-ol (5 mL) gave the title compound (27 mg, 9% yield) as a clear oil. \(^1\)H-NMR (200 MHz, CDCl\(_3\)): δ 0.87 (d, 3H, MeCHMe'), 0.91 (d, 3H, MeCHMe'), 1.75 (c, 3H, Me), 1.79 (m, 1H, H6'), 3.34 (t, 1H, H5), 4.15 (dd, br, 2H, H3''a, H3''b), 4.20 (dd, 1H, H6), 4.28 (s, 1H, H4), 4.93, 5.00 (2s, br, 2H, H3''a, H3''b), 5.63 (d, 1H, H3), 6.05 (d, 1H, H1), J\(_{\text{H1-1H5}}\) = 3.8 Hz, J\(_{\text{H3-H3'}}\) = -0.3 Hz, J\(_{\text{H3a-H3b}}\) = -12.4 Hz, J\(_{\text{H5-1H6}}\) = 4.4 Hz, J\(_{\text{H6-1H6}}\) = 8.0 Hz, J\(_{\text{H6'-Me}}\) = 6.9 Hz, J\(_{\text{H6'-Me}}\) = 6.9 Hz).
3α-Dimethallyloxy-4β-bromo-6β-i-propyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10p).

Photo-adduct 2b (140 mg, 1.00 mmol) and NBS (178 mg, 1.00 mmol) in 3-methyl-2-buten-1-ol (5 mL) gave the title compound (228 mg, 75% yield) as a clear oil. \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)) \(\delta\) 0.87 (d, 3H, MeCHMe\(_3\)), 0.91 (d, 3H, MeCHMe\(_3\)), 1.69, 1.75 (2s, br, 6H, Me\(_2\)C), 1.85 (m, 1H, H\(_6\)), 3.32 (t, 1H, H5), 4.19 (ddd, br, 2H, H\(_3\)'a, H\(_3\)'b), 4.24 (s, 1H, H4), 5.35 (m, 1H, H3") 5.63 (s, 1H, H3), 6.04 (d, 1H, H1), J\(_{H1-H5} = 4.2\) Hz, J\(_{H3-H5} = -0.6\) Hz, J\(_{H3\'-b\cdot H3''} = -11.1\) Hz, J\(_{H3\cdot H3''} = 4.8\) Hz, J\(_{H3\cdot H3''} = 7.4\) Hz, J\(_{H5-H6} = 4.5\) Hz, J\(_{H6-H6} = 8.0\) Hz, J\(_{H6-Me} = 6.7\) Hz, J\(_{H6\cdot Me} = 6.7\) Hz.}

3α-Methallyloxy-4β-iodo-6β-i-propyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10h).

Photo-adduct 2b (1.68 g, 12.0 mmol) and NIS (2.71 g, 12.0 mmol) in 2-methyl-2-propen-1-ol (120 mL) gave the title compound (3.84 g, 84% yield) as a clear oil. \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)) \(\delta\) 0.86 (d, 3H, MeCHMe\(_3\)), 0.89 (d, 3H, MeCHMe\(_3\)), 1.74 (s, 3H, Me), 1.81 (m, 1H, H6), 3.44 (t, 1H, H3), 4.13 (dd, br, 2H, H\(_3\)'a, H\(_3\)'b), 4.17 (dd, 1H, H6), 4.26 (s, 1H, H4), 4.92, 4.99 (2s, br, 2H, H3", H3"b), 5.74 (d, 1H, H3), 6.05 (d, 1H, H1), J\(_{H1-H5} = 4.0\) Hz, J\(_{H3-H3} = -0.5\) Hz, J\(_{H3\cdot H3}\) = -12.4 Hz, J\(_{H3\cdot H3\cdot J13'} = -4.8\) Hz, J\(_{H6-H6} = 5.74\) Hz, J\(_{H5-H6} = 4.5\) Hz, J\(_{H6-Me} = 8.0\) Hz, J\(_{H6\cdot Me} = 6.7\) Hz, J\(_{H6\cdot Me} = 6.7\) Hz.}

4,5-Dihydro-4α-(α-hydroxybenzyl)-5β-methoxyfuran (14).

A solution of 2a (489 mg, 2.81 mmol) in anhydrous methanol (50 mL) was refluxed under an atmosphere of nitrogen for 2 h. The solvent was removed under reduced pressure to give a white residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1, v/v) gave the title compound (180 mg, 31% yield) as a clear oil. \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)) \(\delta\) 2.08 (d, ex, 1H, OH), 3.05 (ddd, 1H, H4), 3.42 (s, 3H, MeO), 4.44 (dd, 1H, H4'), 4.59 (t, 1H, H3), 5.42 (d, 1H, H5), 6.39 (dd, 1H, H2), 7.32 - 7.36 (m, 5H, phenyl\), J\(_{H2-H3} = 2.8\) Hz, J\(_{H2-H4} = -2.0\) Hz, J\(_{H3-H4} = 2.8\) Hz, J\(_{H4-H4} = 8.1\) Hz, J\(_{H4-H4} = 2.2\) Hz, J\(_{H4\cdot OH} = 3.0\) Hz; LRMS (EI, 70 eV): m/e 206 ([M\(^+\)]\(^+\), 1.1%).
4,5-Dihydro-4α-(α-hydroxybenzyl)-5β-allyloxyfuran (15).

A solution of 2a (2.00 g, 11.5 mmol) in dry allyl alcohol (200 mL) under nitrogen at room temperature containing acetic acid (13 μL, 0.12 mmol) was refluxed for 2 days. The solution was evaporated to dryness and the residue was dissolved in EtOAc (500 mL), washed with saturated aqueous sodium bicarbonate (400 mL), brine (400 mL), dried (Na2SO4), filtered and the solvent removed under reduced pressure to yield a thick yellow residue. Flash chromatography of the residual syrup (petroleum ether / ethyl acetate, 4:1, v/v) gave the title compound (791 mg, 30% yield) as a light yellow oil and recovered starting material (552 mg). {1H-NMR (200 MHz, CDCl3): δ 2.25 (J, ex, 1H, OH), 3.08 (dddd, 1H, H4), 4.13 (ddd, 2H, H5′, H5′b), 4.43 (dd, 1H, H4′), 4.60 (t, 1H, H3), 5.18 (dddd, br, 2H, H5′a, H5′b), 5.53 (d, 1H, H5), 5.83 (m, 1H, H5′), 6.37 (dd, 1H, H2), 7.27 - 7.39 (m, 5H, phenyl), J H2 ∙ H3 = 2.8 Hz, J H2 ∙ H3 = -1.9 Hz, J H3 ∙ H4 = 2.8 Hz, J H14 ∙ H15 = 2.1 Hz, J H4′ ∙ OH = 2.9 Hz; 13C-NMR (75.4 MHz, CD2Cl2): δ 57.21 [C4], 69.20 [OCH2CH=CH2], 74.63 [C4′], 100.81 [C3], 106.71 [C5], 117.07 [OCH2CH=CH2], 126.68, 128.11, 128.73 [aromatic CH], 134.51 [OCH2CH=CH2], 142.59 [aromatic C], 145.87 [C2]; LRMS (Cl-NH3): m/e 255 ([M + NH4⁺], 1.0%), 233 ([MH⁺], 3.6%).}

4,5-Dihydro-4α-(α-hydroxybenzyl)-5β-methallyloxyfuran (16a).

The title compound was prepared in 10% yield by a procedure similar to that used for the preparation of 15. {1H-NMR (200 MHz, CDCl3): δ 1.59 (s, br, 3H, Me), 1.97 (d, ex, 1H, OH), 3.11 (ddd, 1H, H4), 4.03 (dd, br, 2H, H5′, H5′b), 4.51 (ddd, 1H, H4′), 4.66 (t, 1H, H3), 4.86, 4.88 (2s, br, 2H, H5′a, H5′b), 5.49 (d, 1H, H5), 6.42 (dd, 1H, H2), 7.27 - 7.36 (m, 5H, phenyl), J H2 ∙ H3 = 2.7 Hz, J H2 ∙ H3 = -1.8 Hz, J H13 ∙ H14 = 2.8 Hz, J H14 ∙ H15 = 7.4 Hz, J H14 ∙ H15 = 2.1 Hz, J H4′ ∙ OH = 2.6 Hz, J H5′a ∙ H5′b = -12.6 Hz; LRMS (Cl-NH3): m/e 264 ([M + NH4⁺], 1.9%), 247 ([MH⁺], 5.5%); HRMS (Cl-NH3): m/e calcd. for C15H19O3 [MH⁺], 247.1333; found, 247.1334.

4,5-Dihydro-4α-(4′-hydroxy-4″-methylpropyl)-5β-methallyloxyfuran (16b).

The title compound was prepared in 11% yield by a procedure similar to that used for the preparation of 15. {1H-NMR (200 MHz, CDCl3): δ 0.95 (d, 6H, Me2CH), 1.50 (s, br, ex, 1H, OH), 1.73 (s, br, 3H, Me), 1.76 (m, 1H, Me2CH), 2.91 (ddd, 1H, H4′), 3.19 (ddd, 1H, H4′), 4.08 (dd, br, 2H, H5′a, H5′b), 4.85 (t, 1H, H3), 4.89, 4.98 (2s, br, 2H, H5′a, H5′b), 5.47 (d, 1H, H5), 6.41 (dd, 1H, H2), J H2 ∙ H3 =
2.7 Hz, $J_{H2-H4} = -1.8$ Hz, $J_{H3-H4} = 2.8$ Hz, $J_{H4-H5} = 8.0$ Hz, $J_{H4-CHMe} = 6.5$ Hz, $J_{CHMe-Me} = 6.7$ Hz; LRMS (Cl-NH$_3$): m/e 230 ([M + NH$_4^+$], 12.4%), 213 ([MH$^+$], 39.2%), 141 ([MH$^+$ - H$_2$C=C(CH$_3$)CH$_2$OH], 100%); HRMS (Cl-NH$_3$): m/e calcd. for C$_{13}$H$_{19}$O$_3$ [MH$^+$ - H$_2$C=C(CH$_3$)CH$_2$OH], 213.1490; found, 213.1490).

General Procedure for I$^+$,(sym-collidine)$_2$ClO$_4^-$ Mediated Opening of Acetals 10, 21 and 29.

To a solution of the adduct in dry benzene (0.03 M) under nitrogen at room temperature was added the nucleophile (5 equiv.). After stirring for 10 min., I$^+$,(sym-collidine)$_2$ClO$_4^-$ (1.5 equiv.) was added in small portions over a 20 minute period and the solution allowed to stir until completion of the reaction (1 - 18 h). The excess I$^+$,(sym-collidine)$_2$ClO$_4^-$ was precipitated by the addition of ether (amount equal to total solvent used) and the reaction mixture was filtered through a bed of dry Celite. The filter cake was washed with more diethyl ether and the combined filtrates were washed with saturated aqueous sodium thiosulfate, 5% hydrochloric acid, saturated aqueous sodium bicarbonate, water, dried (Na$_2$SO$_4$), filtered and the solvent removed under reduced pressure to yield a syrup. Flash chl. matography of the residual syrup (petroleum ether / ethyl acetate, 10:1 - 2:1, v/v) gave the unsubstituted monocyclic oxetane.

Oxetane (17b).

Acetal 10b (72 mg, 0.22 mmol) and methanol (45µL, 1.10 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (107 mg, 100% yield) as a colourless oil. 17b-minor: ![1H-NMR](image)

17b-major: ![1H-NMR](image)
Oxetane (17d).

Acetal 10d (74 mg, 0.20 mmol) and methanol (41 μL, 1.10 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6, (71 mg, 67% yield) as a light yellow oil. 17d-minor: $^{1}$H-NMR (200 MHz, CDCl$_3$): δ 1.35 (s, 3H, Me), 3.27 (s, 3H, MeO), 3.36 (s, br, 2H, CHH$_1$, CHH$_{3}$), 3.68 (t, 1H, H3),$^{1}$ 3.82 (dd, 2H, H3''$_a$, H3''$_b$), 4.49 (s, 1H, H3'), 5.48 (d, 1H, H4), 5.84 (s, 1H, H3''), 6.33 (d, 1H, H2), 7.33 - 7.39 (m, 5H, phenyl), $^{13}$C-NMR (75.4 MHz, CDCl$_3$): δ 12.14 [CH$_2$], 20.07 [CH$_3$], 22.75 [C$_3$], 50.22 [C3], 59.86 [MeO], 71.05 [C3''], 74.32 [CCH$_2$], 84.91 [C4], 108.45 [C2], 114.93 [C3''], 125.40, 128.44, 128.74 [aromatic CH], 140.56 [aromatic C]. 17d-major: $^{1}$H-NMR (200 MHz, CDCl$_3$): δ 1.37 (s, 3H, Me), 3.27 (s, 3H, MeO), 3.39 (dd, 2H, CHH$_1$, CHH$_{3}$), 3.68 (t, 1H, H3), 3.79 (dd, 2H, H3''$_a$, H3''$_b$), 4.49 (s, 1H, H3''), 5.46 (d, 1H, H4), 5.84 (s, 1H, H3''), 6.33 (d, 1H, H2), 7.33 - 7.39 (m, 5H, phenyl), $^{13}$C-NMR (75.4 MHz, CDCl$_3$): δ 12.60 [CH$_2$], 20.21 [CH$_3$], 22.71 [C3''], 49.97 [C3], 50.87 [MeO], 70.76 [C3''], 74.30 [CCH$_2$], 84.94 [C4], 108.47 [C2], 114.93 [C3''], 125.40, 128.44, 128.74 [aromatic CH], 140.54 [aromatic C].

Oxetane (17c).

Acetal 10c (68 mg, 0.20 mmol) and methanol (41 μL, 1.00 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 45:55, (70 mg, 70% yield) as a light yellow oil. 17c-minor: $^{1}$H-NMR (200 MHz, CDCl$_3$): δ 1.37 (s, 6H, CH$_3$), 3.23 (s, 3H, MeO), 3.59 (dd, 1H, H3), 3.93 (d, 1H, CHI), 4.23 - 4.51 (m, 2H, H3''$_a$, H3''$_b$), 4.54 (s, 1H, H3''), 5.67 (d, 1H, H4), 5.77 (s, 1H, H3''), 6.32 (d, 1H, H2), 7.34 - 7.41 (m, 5H, phenyl), $^{1}$H-NMR (200 MHz, CDCl$_3$): δ 1.37 (s, 6H, CH$_3$), 3.13 (s, 3H, MeO), 3.59 (dd, 1H, H3), 3.92 (d, 1H, CHI), 4.23 - 4.51 (m, 2H, H3''$_a$, H3''$_b$), 4.52 (s, 1H, H3''), 5.75 (d, 1H, H4), 5.75 (s, 1H, H3''), 6.32 (d, 1H, H2), 7.34 - 7.41 (m, 5H, phenyl), $^{13}$C-NMR (75.4 MHz, CDCl$_3$): δ 12.14 [CH$_2$], 20.07 [CH$_3$], 22.75 [C$_3$], 50.22 [C3], 59.86 [MeO], 71.05 [C3''], 74.32 [CCH$_2$], 84.91 [C4], 108.45 [C2], 114.93 [C3''], 125.40, 128.44, 128.74 [aromatic CH], 140.56 [aromatic C].
Oxetane (17e).

Acetal 10e (56 mg, 0.20 mmol) and methanol (41 µL, 1.10 mmol) gave the title compound (mixture of inseparable diastereomers, 45:55), (24 mg, 24% yield) as a light yellow oil. 17e-minor: [1H-NMR (200 MHz, CDCl₃): δ 0.87 (d, 3H, MeCHMe'), 0.91 (d, 3H, MeCHMe'), 1.64 (m, 1H, H₄'), 3.24 - 3.39 (m, 3H, H₃, CHH', CHH'), 3.43 (s, 3H, MeO), 3.66 (m, 1H, H₃'), 3.84 - 4.18 (m, 3H, H₃', H₂, H₄), 6.03 (d, 1H, H₂), J₁₂.H₃ = 4.1 Hz, J₃'.H₃'' = 2.7 Hz, J₃.H₄ = 6.8 Hz, J₃.H₄ = 6.6 Hz). 17e-major: [1H-NMR (200 MHz, CDCl₃): δ 0.87 (d, 3H, MeCHMe'), 0.91 (d, 3H, MeCHMe'), 1.84 (m, 1H, H₄'), 3.24 - 3.39 (m, 3H, H₃, CHH', CHH'), 3.42 (s, 3H, MeO), 3.66 (m, 1H, H₃'), 3.84 - 4.18 (m, 3H, H₃', H₂, H₄), 6.04 (d, 1H, H₂), J₁₂.H₃ = 4.1 Hz, J₃'.H₃'' = 0 Hz, J₃.CH₇-Me = 6.8 Hz, J₃.CH₇-Me = 6.6 Hz].

Oxetane (17f).

Acetal 10f (27 mg, 0.09 mmol) and methanol (19 µL, 0.46 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (13 mg, 32% yield) as a colourless oil. 17f-minor: [1H-NMR (200 MHz, CDCl₃): δ 0.87 (d, 3H, MeCHMe'), 0.91 (d, 3H, MeCHMe'), 1.30 (s, 3H, Me), 1.85 (m, 1H, H₄'), 3.25 (s, 3H, MeO), 3.32 (s, br, 2H, CHH', CHH'), 3.44 (t, 1H, H₃), 3.75 (dd, 2H, H₃', H₃''), 4.11 (dd, 1H, H₄), 4.28 (s, 1H, H₃'), 5.63 (s, 1H, H₃''), 6.04 (d, 1H, H₂), J₁₂.H₃ = 4.1 Hz, J₃.H₄ = 4.7 Hz, J₃.H₃' = -10.3 Hz, J₃.CH₇-CHH' = -6.8 Hz, J₁₄.H₃ = 6.8 Hz, J₁₄.Mc = 6.6 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 12.21 [CH₂], 16.32, 16.98 [Me₂C₂H], 20.18 [CH₃], 33.63 [C₄'], 49.28 [C₃'], 50.22 [C₃], 52.88 [MeO], 70.58 [C₃''], 74.33 [CH₂], 87.30 [C₄], 107.82 [C₂], 112.93 [C₃']. 17f-major: [1H-NMR (200 MHz, CDCl₃): δ 0.87 (d, 3H, MeCHMe'), 0.91 (d, 3H, MeCHMe'), 1.32 (s, 3H, Me), 1.85 (m, 1H, H₄'), 3.25 (s, 3H, MeO), 3.32 (dd, 2H, CHH', CHH'), 3.44 (t, 1H, H₃), 3.73 (dd, 2H, H₃', H₃''), 4.11 (dd, 1H, H₄), 4.28 (s, 1H, H₃'), 5.63 (s, 1H, H₃''), 6.04 (d, 1H, H₂), J₁₂.H₃ = 4.1 Hz, J₃.H₄ = 4.7 Hz, J₃.H₃' = -9.8 Hz, J₃.CH₇-CHH' = -10.0 Hz, J₁₄.H₃ = 8.0 Hz, J₁₄.Mc = 6.8 Hz, J₁₄.Mc = 6.6 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 12.60 [CH₂], 16.32, 16.98 [Me₂C₂H], 20.30 [CH₃], 33.63 [C₄'], 49.28 [C₃'], 50.22 [C₃], 52.88 [MeO], 70.58 [C₃''], 74.33 [CH₂], 87.30 [C₄], 107.82 [C₂], 112.93 [C₃']].
Oxetane (17h).

Acelal 10h (34 mg, 0.10 mmol) and methanol (20 µL, 0.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6). (15 mg, 30% yield) as a clear oil and recovered starting material (5 mg). 17h-minor: \textit{^1}H-NMR (200 MHz, CDCl$_3$): δ 0.86 (d, 3H, MeCHMe'), 0.89 (d, 3H, MeCHMe'), 1.30 (s, 3H, 1.5°), 1.83 (m, 1H, H4'), 3.25 (s, 3H, MeO), 3.32 (s, br, 2H, CHHl, CHHl), 3.43 (t, 1H, H3), 3.74 (dd, 2H, H3'~a, H3'~b), 4.11 (dd, 1H, H4), 4.27 (s, 1H, H3'), 5.75 (s, 1H, H3~), 6.05 (d, 1H, H2). J$_{112-113}$ = 4.1 Hz, J$_{113-114}$ = 4.6 Hz, J$_{H3''\sim a-H3''\sim b}$ = -10.1 Hz, J$_{CHHl-CHHl} \sim 0$ Hz, J$_{H4-114} = 7.9$ Hz, J$_{114-115} = 7.2$ Hz, J$_{114-115} = 6.7$ Hz. 17h-major: \textit{^1}H-NMR (200 MHz, CDCl$_3$): δ 0.86 (d, 3H, MeCHMe'), 0.89 (d, 3H, MeCHMe'), 1.32 (s, 3H, Me), 1.83 (m, 1H, H4'), 3.25 (s, br, 2H, CHHl, CHHl), 3.69 (dd, 2H, H3'~a, H3'~b), 4.11 (dd, 1H, H4), 4.27 (s, 1H, H3'), 5.75 (s, 1H, H3~), 6.05 (d, 1H, H2). J$_{112-113}$ = 4.1 Hz, J$_{113-114}$ = 4.6 Hz, J$_{H3''\sim a-H3''\sim b}$ = -10.1 Hz, J$_{CHHl-CHHl} = -9.9$ Hz, J$_{114-115} = 7.9$ Hz, J$_{114-115} = 7.2$ Hz, J$_{114-115} = 6.7$ Hz.

Oxetane (18a).

Acelal 10h (34 mg, 0.10 mmol) and ethanol (29 µL, 0.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6). (12 mg, 24% yield) as a clear oil and recovered starting material (26 mg). \textit{LRMS (CI-NH$_3$): m/e 528 ([M + NH$_4^+$], 53.3%), 511 ([M$^+$], 21.8%)}. 18a-minor: \textit{^1}H-NMR (200 MHz, CDCl$_3$): δ 0.86 (d, 3H, MeCHMe'), 0.89 (d, 3H, MeCHMe'), 1.16 (t, 3H, OCH$_2$CH$_3$), 1.30 (s, 3H, Me), 1.81 (m, 1H, H4'), 3.33 (s, br. 2H, CHHl, CHHl), 3.42 (t, 1H, H3), 3.42 (q, 2H, OCH$_2$CH$_3$), 3.73 (dd, 2H, H3'~a, H3'~b), 4.09 (dd, 1H, H4), 4.26 (s, 1H, H3~), 5.75 (s, 1H, H3~), 6.04 (d, 1H, H2). J$_{CH2-CH3} = 6.9$ Hz, J$_{112-113} = 4.2$ Hz, J$_{H3-114} = 4.7$ Hz, J$_{H3''\sim a-H3''\sim b} = -10.0$ Hz, J$_{CHHl-CHHI} \sim 0$ Hz, J$_{114-115} = 7.8$ Hz, J$_{114-115} = 6.8$ Hz, J$_{114-115} = 7.2$ Hz. 18a-major: \textit{^1}H-NMR (200 MHz, CDCl$_3$): δ 0.86 (d, 3H, MeCHMe'), 0.89 (d, 3H, MeCHMe'), 1.17 (t, 3H, OCH$_2$CH$_3$), 1.32 (s, 3H, Me), 1.80 (m, 1H, H4'), 3.35 (dd, 2H, CHHl, CHHl), 3.42 (t, 1H, H3), 3.42 (q, 2H, OCH$_2$CH$_3$), 3.70 (dd, 2H, H3'~a, H3'~b), 4.09 (dd, 1H, H4), 4.26 (s, 1H, H3~), 5.75 (s, 1H, H3~), 6.04 (d, 1H, H2). J$_{CH2-CH3} = 7.0$ Hz, J$_{112-113} = 4.2$ Hz, J$_{113-114} = 4.7$ Hz, J$_{H3''\sim a-H3''\sim b} = -9.8$ Hz, J$_{CHHl-CHHI} = -10.8$ Hz, J$_{114-115} = 7.8$ Hz, J$_{114-115} = 6.8$ Hz, J$_{114-115} = 7.2$ Hz.
Oxetane (18b).

Acetal 10h (68 mg, 0.20 mmol) and i-propanol (77 μL, 1.00 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (29 mg, 27% yield) as a light yellow oil and recovered starting material (37 mg). 18b-minor: \[^{1}H\-NMR\text{ (200 MHz, CDCl}_3\): δ 0.85 (d, 3H, MeCHMe\(^+\)), 0.89 (d, 3H, CHMe\(^+\)), 1.17 (d, 6H, Me\(_2\)CH, anomic), 1.33 (s, 3H, Me), 1.77 (m, 1H, H\(^4\)), 3.34 (s, br, 2H, CHHI, CHHII), 3.42 (t, 1H, H\(^3\)), 3.68 (dd, 2H, H\(^3\), H\(^3\)), 3.77 (m, 1H, H\(^2\)), 4.08 (dd, 1H, H\(^4\)). \(J\text{ H}_2-\text{H}_1 = 4.2\ 	ext{Hz}, J\text{ H}_3' - \text{H}_1 = 10.2\ 	ext{Hz}, J\text{ CHHI-CHHII} = -0.8\ \text{Hz}, J\text{ H}_4'-\text{H}_4 = 4.4\ \text{Hz}, J\text{ CHHII-CHHIII} = -9.7\ \text{Hz}, J\text{ H}_3'-\text{H}_3'' = -10.3\ \text{Hz}\).} 18b-major: \[^{1}H\-NMR\text{ (200 MHz, CDCl}_3\): δ 0.85 (d, 3H, MeCHMe\(^+\)), 0.89 (d, 3H, MeCHMe\(^+\)), 1.12 (d, 6H, Me\(_2\)CH, anomic), 1.34 (s, 3H, Me), 1.76 (m, 1H, H\(^4\)), 3.30 (dd, 2H, H\(^3\), H\(^3\)), 3.77 (m, 1H, H\(^2\)), 4.08 (dd, 1H, H\(^4\)), 4.25 (s, 1H, H\(^3\)), 5.75 (s, 1H, H\(^3\)). \(J\text{ H}_2-\text{H}_1 = 4.1\ \text{Hz}, J\text{ H}_3' - \text{H}_1 = 4.3\ \text{Hz}, J\text{ CHHII-CHHIII} = -9.7\ \text{Hz}, J\text{ H}_3'-\text{H}_3'' = -10.3\ \text{Hz}, J\text{ H}_4'-\text{H}_4 = 6.8\ \text{Hz}, J\text{ H}_4'-\text{Me} = 6.6\ \text{Hz}, J\text{ H}_4'-\text{Me} = 5.7\ \text{Hz}\).}

Oxetane (18c).

Acetal 10h (68 mg, 0.20 mmol) and cyclohexanol (104 μL, 1.00 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (12 mg, 11% yield) as a clear oil and recovered starting material (60 mg). 18c-minor: \[^{1}H\-NMR\text{ (200 MHz, CDCl}_3\): δ 0.88 (d, 6H, MeCHMe\(^+\)), 0.91 (d, 6H, MeCHMe\(^+\)), 1.20 - 1.94 (m, 10H, C\(_6\)H\(_11\)O), 1.26 (s, 3H, Me), 1.81 (m, 1H, H\(^4\)), 2.28 (m, 1H, C\(_6\)H\(_11\)O), 3.21 (dd, 2H, CHHI, CHHII), 3.46 (t, 1H, H\(^3\)), 3.70 (dd, 2H, H\(^3\), H\(^3\)), 4.04 (dd, 1H, H\(^4\)), 4.31 (s, 1H, H\(^3\)), 5.77 (s, 1H, H\(^3\)). \(J\text{ H}_2-\text{H}_1 = 4.1\ \text{Hz}, J\text{ H}_3' - \text{H}_1 = 4.3\ \text{Hz}, J\text{ CHHI-CHHII} = -10.3\ \text{Hz}, J\text{ CHHII-CHHIII} = -9.7\ \text{Hz}, J\text{ H}_3'-\text{H}_3'' = -10.3\ \text{Hz}, J\text{ CHHIII-CHHIV} = -9.7\ \text{Hz}, J\text{ CHHIV-CHHII} = -10.2\ \text{Hz}, J\text{ CHHII-CHHIII} = 5.7\ \text{Hz}\).} 18c-major: \[^{1}H\-NMR\text{ (200 MHz, CDCl}_3\): δ 0.88 (d, 6H, MeCHMe\(^+\)), 0.91 (d, 6H, MeCHMe\(^+\)), 1.20 - 1.94 (m, 10H, C\(_6\)H\(_11\)O), 1.26 (s, 3H, Me), 1.81 (m, 1H, H\(^4\)), 2.28 (m, 1H, C\(_6\)H\(_11\)O), 3.21 (dd, 2H, CHHI, CHHII), 3.46 (t, 1H, H\(^3\)), 3.70 (dd, 2H, H\(^3\), H\(^3\)), 4.04 (dd, 1H, H\(^4\)), 4.31 (s, 1H, H\(^3\)). \(J\text{ H}_2-\text{H}_1 = 4.1\ \text{Hz}, J\text{ H}_3' - \text{H}_1 = 4.3\ \text{Hz}, J\text{ CHHII-CHHIII} = -9.7\ \text{Hz}, J\text{ CHHIII-CHHIV} = -9.7\ \text{Hz}, J\text{ CHHIV-CHHII} = 6.8\ \text{Hz}, J\text{ CHHII-CHHIII} = 6.6\ \text{Hz}, J\text{ CHHIII-CHHIV} = 5.7\ \text{Hz}\).}
Oxetane (18d).

Acetal 10h (68 mg, 0.20 mmol) and benzyl alcohol (105 µL, 1.00 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 3:7), (40 mg, 35% yield) as a light yellow oil and recovered starting material (44 mg). 18d-minor: \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)): \(\delta\) 0.83 (d, 3H, MeCHMe\(_3\)), 0.87 (d, 3H, MeCHMe\(_3\)), 1.40 (s, 3H, Me), 1.77 (m, 1H, H\(_4\)'), 3.43 (t, 1H, H3), 3.44 (s, br, 2H, CHHII, CHHI), 3.84 (dd, 2H, H3\('''\), H3\(''''\)), 4.10 (dd, 1H, H4), 4.25 (s, 1H, H3), 4.49 (s, 2H, OCH\(_2\)Ph), 5.74 (s, 1H, H3\('''\)), 6.05 (d, 1H, H2), 7.26 - 7.36 (m, 5H, phenyl), \(J_{H2·H3} = 4.1\) Hz, \(J_{H3·H4} = 4.4\) Hz, \(J_{H3''·H3'''} = -10.4\) Hz, \(J_{H4·Me} = 9.0\) Hz, \(J_{H4'·Me} = 6.7\) Hz. 18d-major: \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)): \(\delta\) 0.84 (d, 3H, MeCHMe\(_3\)), 0.85 (d, 3H, MeCHMe\(_3\)), 1.43 (s, 3H, Me), 1.77 (m, 1H, H4'), 3.43 (t, 1H, H3), 3.45 (dd, 2H, CHHII, CHHI), 3.81 (dd, 2H, H3\('''\), H3\(''''\)), 4.10 (dd, 1H, H4), 4.25 (s, 1H, H3), 4.50 (s, 2H, OCH\(_2\)Ph), 5.74 (s, 1H, H3), 6.05 (d, 1H, H2), 7.26 - 7.36 (m, 5H, phenyl), \(J_{H2·H3} = 4.1\) Hz, \(J_{H3·H4} = 4.4\) Hz, \(J_{H3''·H3'''} = -9.8\) Hz, \(J_{H4·Me} = 1.7\) Hz, \(J_{H4'·Me} = 5.1\) Hz.

Oxetane (18e).

Acetal 10h (34 mg, 0.10 mmol) and formic acid (19 µL, 0.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (13 mg, 25% yield) as a colourless oil and recovered starting material (12 mg). \(\text{IR (CH}_2\text{Cl}_2\): 1729 cm}^{-1}; \text{LRMS (CI-NH}_3\): m/e 528 ([M + NH\(_4^+\)], 14.2%); HRMS (CI-NH\(_3\)): m/e calcd. for C\(_{13}\)H\(_{24}\)NO\(_2\)S\(_2\), [M + NH\(_4^+\)], 527.9744; found, 527.9744. 18e-minor: \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)): \(\delta\) 0.83 (d, 3H, MeCHMe\(_3\)), 0.86 (d, 3H, MeCHMe\(_3\)), 1.55 (s, 3H, Me), 1.73 (m, 1H, H\(_4\)'), 3.43 (t, 1H, H3), 3.44 (s, br, 2H, CHHII, CHHI), 3.80 (dd, 2H, H3\('''\), H3\(''''\)), 4.07 (dd, 1H, H4), 4.24 (s, 1H, H3), 4.30 (s, 1H, H3), 6.04 (d, 1H, H2), 7.96 (s, 1H, COOH), \(J_{H2·H3} = 4.1\) Hz, \(J_{H3·H4} = 4.4\) Hz, \(J_{H3''·H3'''} = -9.8\) Hz, \(J_{CHHII·CHHI} = -9.7\) Hz, \(J_{H4·H4'} = 5.7\) Hz, \(J_{H4·Me} = 1.7\) Hz, \(J_{H4'·Me} = 5.1\) Hz.

Oxetane (18f).

Acetal 10h (505 mg, 1.50 mmol) and acetic acid (435 µL, 7.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (566 mg, 72% yield) as a clear oil and recovered starting material (88 mg). \(\text{IR (CDCl}_3\): 1734 cm}^{-1}\). 18f-minor: \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)): \(\delta\) 0.83 (d, 3H, MeCHMe\(_3\)), 0.86 (d, 3H, MeCHMe\(_3\)), 1.55 (s, 3H, Me), 1.73 (m, 1H, H\(_4\)'), 1.99 (s, 3H, Ac), 3.40 (t, 1H, H3), 3.66 (s, br, 2H, CHHII, CHHI), 3.90 (dd, 2H, H3\('''\), H3\(''''\)), 4.03 (dd, 1H, H4), 4.20 (s, 1H, H3), 5.71 (s, 1H, H3'), 6.01 (d, 1H, H2), \(J_{H2·H3} = 3.9\) Hz, \(J_{H3·H4} = 4.4\) Hz, \(J_{H3''·H3'''} = -9.5\) Hz, \(J_{CHHII·CHHI} = 0\).
18f-maj or: \{^1\text{H-NMR} (200 \text{ MHz}, \text{CDCl}_3)\}: 5 0.83 (d, 3H, MeCHMe'), 0.86 (d, 3H, MeCHMe'), 1.57 (m, 1H, H4'), 1.73 (m, 1H, H4'), 1.99 (s, 3H, Ac), 3.40 (t, 1H, H3), 3.66 (s, br, 2H, CHH1, CHH1'), 3.90 (dd, 2H, H3”a, H3”b), 4.03 (dd, 1H, H4), 4.20 (d, 1H, H3'), 5.71 (s, 1H, H3"), 6.01 (d, 1H, H2), J_{II4-Me} = 7.9 \text{ Hz}, J_{II4-Me'} = 7.9 \text{ Hz}, J_{II4-Me''} = 7.0 \text{ Hz}, J_{II4-Me''} = 7.0 \text{ Hz}.

\text{t-Butyldimethylsilyloxy-3-methyl-2-butene (19).}

To a solution of 3-methyl-2-buten-1-ol (5.17 g, 60.0 mmol) in dry \text{N,N-dimethylformamide} (100 mL) under nitrogen at room temperature was added imidazole (10.20 g, 0.15 mol) and \text{t-butyldimethylsilyl chloride} (10.85 g, 72.0 mmol) and it was allowed to stir until all of the starting material was consumed (20 h). The reaction mixture was diluted with \text{ethyl acetate} (600 mL), washed with water (3 x 1 L), dried (MgSO4), filtered and the solvent removed \textit{in vacuo} to yield a yellow oil. Distillation of the crude product (196 °C, 760 mm Hg) gave the title compound (11.88 g, 99% yield) as a light yellow oil. \{^1\text{H-NMR} (200 \text{ MHz}, \text{CDCl}_3)\}: 8 0.05 (s, 6H, r-BuSiMe2), 0.92 (s, 9H, r-Bu), 1.61 (d, 3H, CH3), 1.69 (d, 3H, CH3), 4.15 (d, 2H, CH2), 5.26 (m, 1H, CH), J_{CH-Me} = -0.11 \text{ Hz}, J_{CH-Me'} = -1.1 \text{ Hz}, J_{CH-ClI2} = 6.7 \text{ Hz}.

\text{2-t-Butyldimethylsilyloxymethyl-2,7-dioxabicyclo-[3,2,0]-hept-3-ene (20).}

Ozone was bubbled through a solution of 19 (11.88 g, 59.4 mmol) in dry \text{methylene chloride} (1500 mL) at -78°C until the solution turned blue (12 h). \text{Dimethyl sulfide} (21.9 mL, 5 equiv) was added to the reaction mixture under an atmosphere of nitrogen and it was allowed to warm to ambient temperature gradually overnight. The solution was washed with water (2 x 1 L), brine (1 L), dried (Na2SO4), filtered and the solvent removed \textit{in vacuo} to yield the aldehyde 20 (9.84 g, 95% yield) as a light yellow oil. \{^1\text{H-NMR} (200 \text{ MHz}, \text{CDCl}_3)\}: 8 0.10 (s, 6H, t-BuSiMe2), 0.92 (s, 9H, t-BuSiMe2), 4.20 (d, 2H, CH2), 9.69 (s, 1H, CHO), J_{CII2-CHO} = 0.7 \text{ Hz}.

\text{6β-t-Butyldimethylsilyloxymethyl-2,7-dioxabicyclo-[3,2,0]-hept-3-ene (2c).}

A mixture of \text{furan} (15.6 mL, 0.214 mol) and 20 (9.32 g, 53.6 mmol) in dry \text{benzene} (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C and saturated with argon. The solution was
then irradiated for 6 h. Evaporation of the solvent under reduced pressure gave a yellow syrup which was chromatographed over silica gel (petroleum ether / diethyl ether, 4:1 v/v) to give the title compound (4.41 g, 34% yield) as a light yellow oil. {\textsuperscript{1}H-NMR (200 MHz, CDCl\textsubscript{3}): $\delta$ 0.08 (s, 6H, t-BuSiMe\textsubscript{2}), 0.91 (s, 9H, t-BuSiMe\textsubscript{2}), 3.65 (dddd, 1H, J=5), 3.73 (A of ABX, 1H, H6\textsubscript{a}), 3.79 (B of ABX, 1H, H6\textsubscript{b}), 4.56 (dddd, 1H, H6), 5.31 (dd, 1H, H4), 6.26 (dddd, 1H, H1), 6.60 (dd, 1H, H3), $J_{\text{H1-H5}} = -0.8$ Hz, $J_{\text{H1-H5}} = 4.2$ Hz, $J_{\text{H1-H15}} = -0.8$ Hz, $J_{\text{H1-H14}} = 2.9$ Hz, $J_{\text{H13-H13}} = -1.2$ Hz, $J_{\text{H14-H15}} = 2.9$ Hz, $J_{\text{H15-H6}} = 2.9$ Hz, $J_{\text{H6-H6a}} = 2.8$ Hz, $J_{\text{H6-H6b}} = 3.1$ Hz, $J_{\text{H6a-H6b}} = -11.8$ Hz; $^{13}$C-NMR (75.4 MHz, CDCl\textsubscript{3}): $\delta$ 18.26 ([CH\textsubscript{3}], 25.66 [t-BuSiMe\textsubscript{2}], 25.83 ([CH\textsubscript{3}], 45.91 [C5], 64.73 [C6], 91.47 [C6], 104.01 [C4], 107.89 [C1], 147.98 [C3]; LRMS (Cl-NH\textsubscript{3}): m/e 225 ([M+ + H\textsubscript{2}O], 22.0%); HRMS (Cl-NH\textsubscript{3}): m/e calcd. for C\textsubscript{12}H\textsubscript{21}O\textsubscript{2}Si [M+ + H\textsubscript{2}O], 225.1310; found, 225.1310).

TBDMSiO

2c

3β-Methallyloxy-4β-bromo-6β-t-butyldimethylsilyloxyethyl-2,7-dioxo-bicyclo-[3,2,0]-heptane (21a).

Photo-adduct 2c (121 mg, 0.50 mmol) and NBS (89 g, 0.50 mmol) in 2-methyl-2-propen-1-ol (5 mL) gave the title compound (66 mg, 34% yield) as a clear oil. {\textsuperscript{1}H-NMR (200 MHz, CDCl\textsubscript{3}): $\delta$ 0.06, 0.08 (2s, 6H, t-BuSiMe\textsubscript{2}), 0.90 (s, 9H, t-BuSiMe\textsubscript{2}), 1.74 (s, 3H, Me), 3.67 (t, 1H, H5), 3.69 (A of ABX, 1H, H6\textsubscript{a}), 3.74 (B of ABX, 1H, H6\textsubscript{b}), 4.13 (dd, br, 2H, H3\textsubscript{a}, H3\textsubscript{b}), 4.32 (s, 1H, H4), 4.54 (dddd, 1H, H6), 4.90, 4.98 (2s, br, 2H, H3\textsuperscript{1} H3\textsuperscript{2}), 5.63 (d, 1H, H3), 6.02 (d, 1H, H1), $J_{\text{H11-H15}} = 4.0$ Hz, $J_{\text{H13-H13a}} = -0.3$ Hz, $J_{\text{H13a-H13b}} = -12.7$ Hz, $J_{\text{H15-H6a}} = 4.6$ Hz, $J_{\text{H16-H16a}} = 1.9$ Hz, $J_{\text{H16-H16b}} = 3.7$ Hz, $J_{\text{H16a-H16b}} = -11.9$ Hz; $^{13}$C-NMR (75.4 MHz, CDCl\textsubscript{3}): $\delta$ 18.25 [Me\textsubscript{3}], 19.52 [OCH\textsubscript{2}C(CH\textsubscript{3})=CH\textsubscript{2}], 25.70 [Me\textsubscript{3}], 29.45 [Me2C(SiMe\textsubscript{3})], 49.25 [C4], 50.84 [C5], 64.03 [t-BuSiMe\textsubscript{2}OCH\textsubscript{2}], 71.56 [OCH\textsubscript{2}C(CH\textsubscript{3})=CH\textsubscript{2}], 82.11 [C6], 107.95 [C1], 116.0 [OCH\textsubscript{2}C(CH\textsubscript{3})=CH\textsubscript{2}], 112.63 [C3], 141.01 [OCH\textsubscript{2}C(CH\textsubscript{3})=CH\textsubscript{2}]; LRMS (Cl-NH\textsubscript{3}): m/e 323, 321 ([M+ + H\textsubscript{2}C=CH(CH\textsubscript{3})CH\textsubscript{2}OH], 24.5%, 30.9%).

TBDMSiO

21a, X=Br
21b, X=I
3α-Methallyloxy-4β-iodo-6β-t-butyldimethylsilyloxyethyl-2,7-dioxabicyclo[3.2.0]heptane (21b).

Photo-adduct 2c (968 mg, 4.00 mmol) and NIS (900 mg, 4.00 mmol) in 2-methyl-2-propen-1-ol (60 mL) gave the title compound (482 mg, 27% yield) as a clear oil. 1H-NMR (200 MHz, CDCl3) δ 0.06, 0.07 (2s, 6H, t-BuSiMe2), 0.89 (s, 9H, t-BuSiMe2), 1.73 (s, 3H, Me), 3.68 (A of ABX, 1H, H6'), 3.71 (B of ABX, 1H, H6'b), 3.76 (t, 1H, H5), 4.12 (dd, br, 2H, H3'', H3''b), 4.30 (s, 1H, H4), 4.52 (ddd, 1H, H6), 4.89, 4.98 (2s, br, 2H, H3'''a, H3'''b), 5.75 (d, 1H, H3), 6.03 (d, 1H, H1), J111-H5 = 4.1 Hz, J111-H3' = -0.5 Hz, J113''-H3''b = -12.7 Hz, Jm''-H3 = -10.0 Hz, JIII1-H6 = 4.4 Hz, Jh6-H6b = 3.5 Hz, Jh6a-H6b = -11.8 Hz; 13C-NMR (75.4 MHz, CDCl3) δ 18.28 (Me3SiMe2), 19.56 (OCCH2C(CH3)2=CH2), 23.73 [C4], 23.73 [Me3SiMe2], 25.83 [Me3SiMe2], 52.79 [C5], 64.15 [t-BuSiMe2OCH2], 71.60 [OCH2C(CH3)=CH2], 83.94 [C6], 108.30 [C1], 112.65 [OCH2C(CH3)2CH2], 113.98 [C3], 141.21 [OCH2C(CH3)=CH2]; LRMS (Cl-NH3): m/e 644 ([M + NH4]+, 100%), 369 ([MH+ - H2C=C(CH3)2OH], 100%); HRMS (CI-NH3) m/e calcd for C16H29O7Si [MH+], 627.0135, found, 627.0135.

Oxetane (22).

Acetal 21b (220 mg, 0.50 mmol) and acetic acid (150 μL, 1.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (147 mg, 47% yield) as a light yellow oil and recovered starting material (101 mg) IR (CDCl3) 1735 cm−1, LRMS (Cl-NH3): m/e 441 ([MH+], 4%), 369 ([MH+ - H2C=C(CH3)2OH], 100%); HRMS (Cl-NH3) m/e calcd for C16H33O6Si2 [MH+], 627.0135, found, 627.0135. 22-major: 1H-NMR (200 MHz, CDCl3) δ 0.06 (s, 6H, t-BuSiMe2), 0.90 (s, 9H, t-BuSiMe2), 1.57 (s, 3H, Me), 2.01 (s, 3H, Ac), 3.70 (s, br, 2H, CHH1, CHH1i), 3.73 (d, 2H, H4''a, H4''b), 3.73 (t, 1H, H3), 3.94 (dd, 2H, H3''a, H3''b), 4.28 (s, 1H, H3'), 4.41 (dt, 1H, H4), 5.75 (s, 1H, H3''), 6.03 (d, 1H, H2), J112-H11 = 4.1 Hz, J113-H13 = 4.3 Hz, J113-H13' = 10.0 Hz, J113-H13a = 6.0 Hz J111-H11b = 0 Hz. 22-minor: 1H-NMR (200 MHz, CDCl3) δ 0.07 (s, 6H, t-BuSiMe2), 0.90 (s, 9H, t-BuSiMe2), 1.59 (s, 3H, Me), 2.02 (s, 3H, Ac), 3.69 (dd, 2H, CHH1, CHH1i), 3.73 (d, 2H, H4''a, H4''b), 3.73 (t, 1H, H3), 3.93 (dd, 2H, H3''a, H3''b), 4.29 (s, 1H, H3'), 4.41 (dt, 1H, H4), 5.75 (s, 1H, H3''), 6.03 (d, 1H, H2), J112-H11 = 4.1 Hz, J113-H13 = 4.3 Hz, J113-H13' = -9.7 Hz, JCHH1i-CHH1 = -2.5 Hz, J114-H14a14b = 6.0 Hz.
Epoxide (23a) of 6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene.

To a solution of 2a (77 mg, 0.44 mmol) in dry methylene chloride (5 mL) under nitrogen at room temperature was added a 0.1 M solution of dimethylsulfoxide in acetone (4.6 mL, 1.05 equiv.) and it was allowed to stir until the reaction was complete (30 min). The solution was evaporated under reduced pressure to afford the epoxide (mixture of 2 inseparable diastereomers, 9:1, exo:endo), (85 mg, 100% yield) as a light yellow oil. [LRMS (CI-NH₃): m/e 208 ([M + NH₄⁺], 100%), 191 ([MH⁺], 84.8%), HRMS (CI-NH₃): m/e calcd for C₁₅H₁₇O₃ [MH⁺], 238.1010; found, 238.1014].

23a-endo: [¹H-NMR (200 MHz, CDCl₃): δ 3.27 (ddd, 1H, H5), 3.84 (dd, 1H, H4), 5.63 (d, 1H, H3), 5.64 (d, 1H, H6), 6.41 (d, 1H, H1), 7.26 - 7.47 (m, 5H, Ph), J_H1-H5 = 3.8 Hz, J_H3-H4 = 1.8 Hz, J_H4-H5 = 4.2 Hz, J_H5-H6 = 3.8 Hz].

23a-exo: [¹H-NMR (200 MHz, CDCl₃): δ 3.42 (t, 1H, H5), 3.93 (d, 1H, H4), 5.47 (d, 1H, H6), 5.48 (d, 1H, H3), 5.85 (d, 1H, H1), 7.26 - 7.47 (m, 5H, Ph), J_H1-H5 = 3.8 Hz, J_H3-H4 = 1.8 Hz, J_H4-H5 = 4.0 Hz].

Epoxide (23b) of 6β-i-propyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene.

To a stirred solution of 2b (42 mg, 0.30 mmol) in dry methylene chloride (5 mL) under nitrogen at room temperature was added 2-methyl-2-propen-1-ol (25 µL, 0.30 mL) and a 0.1 M solution of dimethylsulfoxide in acetone (3.0 mL, 1.0 equiv.) and it was allowed to stir until the reaction was complete (1 h). The solution was evaporated under reduced pressure to yield the exo-epoxide exclusively (25 mg, 53% yield) as a clear oil. [¹H-NMR (200 MHz, CDCl₃): δ 0.89 (d, 3H, MeCHMe), 0.93 (d, 3H, MeCHMe), 1.93 (m, 1H, H6''), 3.25 (t, 1H, H5), 3.69 (d, 1H, H4), 4.11 (dd, 1H, H6), 5.37 (d, 1H, H3), 5.59 (d, 1H, H1), J_H1-H5 = 3.9 Hz, J_H3-H4 = 1.6 Hz, J_H4-H5 = 4.1 Hz, J_H6-Me = 6.7 Hz, J_H6-Me = 6.7 Hz, LRMS (CI-NH₃): m/e calcd for C₁₅H₁₇O₃ [MH⁺], 257.0859; found, 257.0864].

Epoxide 23a (34 mg, 0.18 mmol) in dry methanol (5 mL) under an atmosphere of nitrogen at room temperature was stirred for 16 h. The solvent was removed in vacuo to give the title compound (25 mg, 63% yield) as a clear oil. [¹H-NMR (200 MHz, CDCl₃): δ 1.97 (d, ex, 1H, OH), 3.17 (dd, 1H, H5), 3.54 (s, 3H, MeO), 4.47 (d, 1H, H4), 5.30 (s, 1H, H3), 5.45 (d, 1H, H6), 6.24 (d, 1H, H1), 7.27 - 7.39 (m, 5H, phenyl), J_H1-H5 = 4.1 Hz, J_H4-OH = 3.4 Hz, J_H5-H6 = 4.8 Hz].

3α-Methoxy-4β-hydroxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (24a).

Epoxide 23a (34 mg, 0.18 mmol) in dry methanol (5 mL) under an atmosphere of nitrogen at room temperature was stirred for 16 h. The solvent was removed in vacuo to give the title compound (25 mg, 63% yield) as a clear oil. [¹H-NMR (200 MHz, CDCl₃): δ 1.97 (d, ex, 1H, OH), 3.17 (dd, 1H, H5), 3.54 (s, 3H, MeO), 4.47 (d, 1H, H4), 5.30 (s, 1H, H3), 5.45 (d, 1H, H6), 6.24 (d, 1H, H1), 7.27 - 7.39 (m, 5H, phenyl), J_H1-H5 = 4.1 Hz, J_H4-OH = 3.4 Hz, J_H5-H6 = 4.8 Hz].
3α-Acetoxy-4β-hydroxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (24b).

To a solution of 23a (41 mg, 0.22 mmol) in dry methylene chloride (5 mL) under an atmosphere of nitrogen at room temperature was added acetic acid (62 µL, 1.10 mmol) and it was allowed to stir for 18 h. The reaction was diluted with methylene chloride (25 mL), washed with saturated aqueous sodium bicarbonate (30 mL), dried (Na₂SO₄), filtered and the solvent removed in vacuo to yield a yellow residue. Purification by flash chromatography (petroleum ether / diethyl ether, 4:1 v/v) afforded 24b (30 mg, 56% yield) as a clear oil. \( \text{[1H-NMR (200 MHz, CDCl₃): } \delta 2.17 \text{ (s, 3H, Ac), 3.30 (dd, 1H, H5), 4.21 (s, br, 1H, OH), 4.58 (s, 1H, H4), 5.42 (d, 1H, H6), 6.28 (d, 1H, H1), 6.49 (s, 1H, H3), 7.32 - 7.41 (m, 5H, phenyl), J_{II1,II5} = 4.1 \text{ Hz, } J_{II5,II6} = 4.8 \text{ Hz}.} \)

3α-Methallyloxy-4β-hydroxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (24c).

To a stirred solution of 23a (40 mg, 0.21 mmol) in dry methylene chloride (5 mL) under an atmosphere of nitrogen at room temperature was added 2-methyl-2-propen-1-ol (90 µL, 1.05 mmol). After 1 h, the reaction mixture was evaporated to dryness and the residue was chromatographed over silica gel (petroleum ether / diethyl ether, 2:1 v/v) to yield the title compound (35 mg, 63% yield) as a clear oil. \( \text{[1H-NMR (200 MHz, CDCl₃): } \delta 1.78 \text{ (s, 3H, Me), 3.18 (dd, 1H, H5), 4.02 (d, ex, 1H, OH), 4.20 (dd, br, 2H, H3'a, H3'b), 4.53 \text{ (d, 1H, H4), 4.93, 5.04 (2s, br, 2H, H3''a, H3''b), 5.42 (d, 1H, H3), 5.51 (d, 1H, H6), 6.34 \text{ (d, 1H, H1), 7.20 - 7.39 (m, 5H, phenyl), } J_{II1,II5} = 4.1 \text{ Hz, } J_{II3,II4} = -0.5 \text{ Hz, } J_{II3,IIa} = -11.9 \text{ Hz, } J_{II4,OH} = 4.5 \text{ Hz, } J_{II5,II6} = 4.8 \text{ Hz}.} \)

3α-Methox-y-4β-acetoxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (25a).

Alcohol 24a (25 mg, 0.11 mmol) was dissolved in dry methylene chloride (5 mL) containing dry pyridine (28 µL, 0.34 mmol) and N,N-dimethylaminopyridine (2 mg, 0.01 mmol) Acetic anhydride (16 µL, 0.17 mmol) was then added dropwise, and the reaction was stirred at room temperature under an atmosphere of nitrogen. After 16 h, the reaction was diluted with methylene chloride (25 mL), washed with 5% hydrochloric acid (30 mL), saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na₂SO₄), filtered and the solvent removed under reduced pressure to yield a light yellow residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) gave the title compound (16 mg, 55% yield) as a clear oil. \( \text{[1H-NMR (200 MHz, CDCl₃): } \delta 2.02 \text{ (s, 3H, Ac), 3.25 (dd, 1H, H5), } \)

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3.57 (s, br, 3H, MeO), 5.33 (s, 1H, H4), 5.35 (d, 1H, H3), 5.54 (d, 1H, H6), 6.23 (d, 1H, H1), 7.28 - 7.42 (m, 5H, phenyl), J_{H1-H5} = 4.1 Hz, J_{H1-OCH_{2}} = -0.8 Hz, J_{H5-H1} = 4.8 Hz; LRMS (CI-NH$_3$): m/e 282 ([M + NH$_4^+$], 0.5%), 265 ([MH$^+$], 5.7%), 233 ([MH$^+$ - MeOH], 73.3%); HRMS (CI-NH$_3$): m/e calcd. for C$_{14}$H$_{17}$O$_5$ [MH$^+$], 265.1075; found, 265.1075.

3α-Acetoxy-4β-acetoxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (25b).

Alcohol 24b was acetylated in 58% yield by a procedure similar to that used for the preparation of 25a. $^1$H-NMR (200 MHz, CDCl$_3$): 2.04 (s, 3H, Ac), 2.19 (s, 3H, Ac, anomeric), 3.32 (t, 1H, H5), 5.45 (s, 1H, H4), 5.53 (d, 1H, H6), 6.26 (d, 1H, H1), 6.56 (s, 1H, H3), 7.34 - 7.42 (m, 5H, phenyl), J_{H1-H5} = 4.1 Hz, J_{H5-H1} = 4.8 Hz; LRMS (CI-NH$_3$): m/e 283 ([MH$^+$], 2.0%), 265 ([MH$^+$ - H$_2$O], 6.3%), 233 ([MH$^+$ - AcOH], 100%); HRMS (CI-NH$_3$): m/e calcd. for C$_{14}$H$_{17}$O$_5$ [MH$^+$], 293.1025; found, 293.1025.

3α-Methallyloxy-4β-acetoxy-6β-phenyl-2,7-dioxa-bicyclo-heptane (25c).

Alcohol 24c was acetylated in 71% yield by a procedure similar to that used for the preparation of 25a. $^1$H-NMR (200 MHz, CDCl$_3$): 1.79 (s, 3H, Me), 2.02 (s, 3H, Ac), 3.26 (dd, 1H, H5), 4.22 (dd, br, 2H, H3$^\alpha$, H3$^\beta$), 4.94, 5.06 (2s, br, 2H, H3$^\gamma$, H3$^\delta$), 5.38 (s, 1H, H4), 5.45 (d, 1H, H3), 5.58 (d, 1H, H6), 6.23 (d, 1H, H1), 7.32 - 7.40 (m, 5H, phenyl), J_{H1-H5} = 4.1 Hz, J_{H3-H5} = -0.5 Hz, J_{H3$^\alpha$-H3$^\beta$} = -12.2 Hz, J_{H5-H1} = 4.8 Hz; LRMS (CI-NH$_3$): m/e 305 ([MH$^+$], 0.5%), 233 ([MH$^+$ - H$_2$C=C(CH$_3$)CH$_2$OH], 44.9%); HRMS (CI-NH$_3$): m/e calcd. for C$_{13}$H$_{13}$O$_4$ [MH$^+$ - H$_2$C=C(CH$_3$)CH$_2$OH], 233.0813; found, 233.0813.

1-O-Benzoyloxy-3-methyl-2-butene (26).

A solution of 3-methyl-2-butene-1-ol (5.17 g, 60.0 mmol) in dry methylene chloride (500 mL) under nitrogen at ambient temperature containing N,N-dimethylaminopyridine (733 mg, 6.00 mmol), pyridine (14.6 mL, 180 mmol) and benzyoyl chloride (10.4 mL, 90 mmol) was stirred for 18 h. The solution was washed with 5% hydrochloric acid (450 mL), saturated aqueous sodium bicarbonate (450 mL), brine (450 mL), dried (Na$_2$SO$_4$), filtered and the solvent removed under reduced pressure to yield a yellow oil. Distillation of the crude product (101-102°C, 1.4 mm Hg) gave the title compound contaminated by an impurity which codistilled. Chromatography over silica gel (petroleum ether / ethyl
acetate, 10:1 v/v) afforded pure 26 in quantitative yield (11.39 g) as a clear oil. \[^1\text{H-NMR (200 MHz, CDCl}_3\text{): }\delta\text{ 1.76 (d, 3H, CH}_3\text{), 1.77 (d, 3H, CH}_3\text{), 4.78 (d, 1H, CHH), 4.82 (d, 1H, CHH), 5.45 (m, 1H, CH), 7.36 - 7.71 (m, 3H, Ph), 8.00 - 8.06 (m, 2H, Ph), J\text{CH-Me} = -1.0 \text{Hz, JCH-Chl} = 7.1 \text{Hz, JCHH-CH} = 7.1 \text{Hz; } ^{13}\text{C-NMR (75.4 MHz, CDCl}_3\text{): }\delta\text{ 25.55 [CH}_3\text{], 25.56 [CHl', 61.47 [CH}_2\text{], 118.58 [CH], 127.95, 130.27, 132.42 [aromatic CH], 129.27 [aromatic C], 138.57 [(CH}_3\text{)C], 166.16 [CO]; IR (CDCl}_3\text{): 1714 cm}^{-1}.\]

2-Benzoyloxyacetaldehyde (27).

2-Benzoyloxyacetaldehyde was obtained from olefin 26 as described for the preparation of aldehyde 20. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) gave the title compound (95% yield) as a viscous light yellow oil. \[^1\text{H-NMR (200 MHz, CDCl}_3\text{): }\delta\text{ 4.88 (d, 2R CH}_2\text{), 7.41 - 7.64 (m, 3H, Ph), 8.03 - 8.12 (m, 2H, Ph), 9.71 (t, 1H, CHO), J\text{CH2-CHO} = 0.6 \text{Hz; } ^{13}\text{C-NMR (75.4 MHz, CDCl}_3\text{): }\delta\text{ 68.94 [CH}_2\text{], 128.47, 129.84, 133.55 [aromatic CH], 128.78 [aromatic C], 165.89 [Ph-CO], 195.83 [CHO]; IR (CDCl}_3\text{): 1728 cm}^{-1}, 1759 cm}^{-1}, 2717 cm}^{-1}, 2825 cm}^{-1}.\]

6β-Benzoyloxymethyl-2,7-dioxabicyclo-[3,2,0]-hept-3-ene (2d).

A mixture of furan (17.5 mL, 240.6 mmol) and 27 (10.11 g, 61.6 mmol) in dry benzene (320 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C and saturated with argon. The solution was then irradiated for 8 h. Evaporation under reduced pressure gave a yellow syrup which was chromatographed over silica gel (petroleum ether / ethyl acetate, 9:1 v/v) to give the title compound (4.31 g, 30% yield) as a light yellow oil, and unreacted aldehyde (5.74 g). \[^1\text{H-NMR (200 MHz, CDCl}_3\text{): }\delta\text{ 3.75 (dd, 1H, H5), 4.55 (d, 2H, H6, H6'), 4.85 (m, 1H, H6), 5.37 (dd, 1H, H4), 6.39 (dd, 1H, H1), 6.64 (dd, 1H, H3), 7.28 - 7.58 (m, 3H, Ph), 8.05 - 8.10 (m, 2H, Ph), J\text{H1-H1} = -0.9 \text{Hz, JH1-H15} = 4.2 \text{Hz, JH1-H6} = -0.8 \text{Hz, JH3-H4} = 2.8 \text{Hz, JH3-H15} = -1.3 \text{Hz, JH5-H15} = 2.9 \text{Hz, JH6-H16} = 3.5 \text{Hz, JH6-H6a} = 3.5 \text{Hz, JH6-H6b} = 3.5 \text{Hz, JH6a-H6b} = 0 \text{Hz; } ^{13}\text{C-NMR (75.4 MHz, CDCl}_3\text{): }\delta\text{ 46.61 [C5], 65.95 [C6'], 88.40 [C6], 103.65 [C4], 107.85 [C1], 128.46, 129.61, 133.27 [aromatic CH], 128.50 [aromatic C], 148.39 [C3], 166.20 [CO]; LRMs (Cl-NH}_3\text{): m/e 250 ([M + NH}_4\text{] \text{+}, 6.5%), 215 ([MH}_2\text{-H}_2\text{O}, 100%); HRMS (Cl-NH}_3\text{): m/e calcd. for C}_13\text{H}_{15}\text{O}_3\text{ [MH}_2\text{-H}_2\text{O}, 205.0709; found, 205.0708]. Anal. calcd. for C}_13\text{H}_{12}\text{O}_4\text{: C, 67.23; H, 5.21. Found: C, 66.87; H, 5.60.\]
Epoxide (23d) of 6β-Benzoyloxyethyl-2,7-dioxa-bicyclo[3,2,0]-hept-3-ene.

Epoxide 23d (mixture of 2 inseparable diastereomers, 9:1 exo / endo) was obtained in quantitative yield from 2d by a procedure similar to that used for 23a. (LRMS (CI-NH₃): m/e 266 ([M + NH₄⁺], 25.8%), 249 ([MH⁺], 100%); HRMS (CI-NH₃): m/e calcd. for C₁₃H₁₃O₈ [MH⁺]: 249.0762; found, 249.0762). 23d-endo: ¹H-NMR (200 MHz, CDCl₃): δ 3.38 (dd, 1H, H5), 3.78 (dd, 1H, H₄), 4.47 (A of ABX, 1H, H₆α), 5.63 (dd, 1H, H₃), 6.22 (d, 1H, H₁), 7.29 - 7.61 (m, 3H, Ph), 8.00 - 8.05 (m, 2H, Ph), J₃-H₅ = 4.2 Hz, J₃-H₆ = 1.5 Hz, J₆α-H₆ = 3.6 Hz, J₆α-H₆b = 4.0 Hz, J₆b-H₃ = 3.0 Hz, J₆b-H₆b = -12.5 Hz; ¹³C-NMR (75.4 MHz, CDCl₃): δ 42.23 [C₅], 55.11 [C₄], 65.25 [C₆α], 76.43 [C₆], 88.33 [C₃], 112.76 [C₁], 128.32, 129.53, 133.14 [aromatic CH], 129.29 [aromatic C], 166.05 [CO]. 23d-exo: ¹H-NMR (200 MHz, CDCl₃): δ 3.58 (t, 1H, H₅), 3.83 (dd, 1H, H₄) 4.46 (A of ABX, 1H, H₆α), 4.56 (B of ABX, 1H, H₆β), 4.77 (dd, 1H, H₆), 5.41 (dd, 1H, H₃), 7.29 - 7.61 (m, 3H, Ph), 8.00 - 8.05 (m, 2H, Ph), J₃-H₅ = 3.6 Hz, J₃-H₆ = 1.4 Hz, J₆α-H₆ = 3.8 Hz, J₆b-H₆b = 3.1 Hz, J₆b-H₆b = -12.6 Hz; ¹³C-NMR (75.4 MHz, CDCl₃): δ 43.57 [C₅], 56.68 [C₄], 65.21 [C₆], 75.62 [C₆], 82.55 [C₃], 107.82 [C₁], 128.48, 129.79, 133.38 [aromatic CH], 129.57 [aromatic C], 166.05 [CO].

3α-Methallyloxy-4β-hydroxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo[3,2,0]-heptane (28).

To a solution of epoxide 23d (313 mg, 1.26 mmol) in dry methylene chloride (50 mL) under nitrogen at room temperature was added 2-methyl-2-propen-1-ol (1.10 mL, 12.60 mmol) and the reaction mixture was allowed to stir for 6 h. Evaporation to dryness gave 28 (359 mg, 89% yield) as a light yellow oil which was used without further purification. ¹H-NMR (200 MHz, CDCl₃): δ 1.72 (s, 3H, Me), 2.88 (s, br, ex, 1H, OH), 3.30 (t, 1H, H₅), 4.11 (dd, br, 2H, H₃α, H₃β), 4.38 (s, br, 1H, H₄), 4.44 (A of ABX, 1H, H₆α), 4.53 (B of ABX, 1H, H₆β), 4.83 (dd, 1H, H₆), 4.89, 4.89 (2s, br, 2H, H₃α, H₃β), 5.36 (d, 1H, H₃), 6.06 (d, 1H, H₁), 7.30 - 7.60 (m, 3H, phenyl), 8.00 - 8.07 (m, 2H, phenyl), J₃-H₅ = 4.0 Hz, J₃-H₆α = -0.2 Hz, J₃-H₆β = -12.5 Hz, J₆α-H₆ = 4.4 Hz, J₆b-H₆b = 4.3 Hz, J₆b-H₆b = 3.2 Hz, J₆b-H₆b = -12.4 Hz; ¹³C-NMR (75.4 MHz, CDCl₃): δ 19.49 [OCH₂C(CH₃)₂=CH₂], 49.95 [C₅], 65.84 [C₆], 71.33 [OCH₂C(CH₃)₂=CH₂], 76.45 [C₄], 76.45 [C₆], 107.84 [C₁], 111.76 [C₃], 112.52 [OCH₂C(CH₃)₂=CH₂], 128.40, 129.59, 133.26 [aromatic CH], 129.46 [aromatic C], 141.20 [OCH₂C(CH₃)₂=CH₂], 166.42 [CO].
3α-Methallyloxy-4β-acetoxy-6β-benzyloxyethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (29a).

Alcohol 28 was acetylated in 84% yield by a procedure similar to that used for the preparation of 25a. \{1H-NMR (200 MHz, CDCl₃): δ 1.72 (s, 3H, Me), 2.04 (s, 3H, Ac), 3.37 (t, 2H, H₅), 4.17 (dd, br, 2H, H₃''₄, H₃''₅), 4.46 (A of ABX, 1H, H₆''₄), 4.56 (B of ABX, 1H, H₆''₅), 4.88 (dd, 1H, H₆), 4.91, 5.03 (2s, br, 2H, H₃''₄, H₃''₅), 5.25 (s, 1H, H₄), 5.41 (d, 1H, H₃), 6.08 (d, 1H, H₁), 7.40 – 7.59 (m, 3H, phenyl), 8.05 – 8.10 (m, 2H, phenyl), J₃H₄·H₅ = 4.1 Hz, J₃H₅·H₃''₄ = -0.8 Hz, J₃H₅·H₃''₅ = -12.5 Hz, J₃H₆·H₆''₄ = 4.6 Hz, J₃H₆·H₆''₅ = 3.4 Hz, J₃H₆·H₆''₅ = -12.4 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 19.59 [OCH₂C(CH₃)=CH₂], 20.74 [C₆CO], 47.51 [C₅], 65.56 [C₆], 71.49 [OCH₂C(CH₃)=CH₂], 76.24 [C₆], 77.90 [C₄], 107.61 [C₁], 109.10 [C₃], 112.94 [OCH₂C(CH₃)=CH₂], 128.39, 129.64, 133.18 [aromatic CH], 129.64 [aromatic Cl, 140.94 [OCH₂C(CH₃)=CH₂], 166.42 [PhCO], 169.71 [CH₃CO]; LRMS (Cl­NH₃): m/e 363 ([MH⁺], 1.4%), 291 ([MH⁺ - H₂C=C(CH₃)CH₂OH], 17.2%)]


To a solution of alcohol 28 (1.290 g, 4.03 mmol) in dry methylene chloride (350 mL) under nitrogen at 0°C was added N,N-dimethylaminopyridine (49 mg, 0.40 mmol), pyridine (97 mL, 1.210 mmol) and methyl oxalyl chloride (55.6 mL, 6.05 mmol). The solution was gradually warmed to ambient temperature (over 1 h) and allowed to stir for 18 h. It was washed with 5% hydrochloric acid (500 mL), saturated aqueous sodium bicarbonate (500 mL), brine (500 mL), dried (Na₂SO₄), filtered and the solvent removed under reduced pressure to yield a yellow syrup. Flash chromatography of the residue (petroleum ether / ethyl acetate, 2:1 v/v) gave the title compound (1.18 g, 72% yield) as a light yellow oil. \{1H-NMR (200 MHz, CDCl₃): δ 1.76 (s, 3H, Me), 3.51 (dd, 1H, H₅), 3.87 (s, 3H, MeO), 4 18 (dd, br, 2H, H₃''₄, H₃''₅), 4.46 (A of ABX, 1H, H₆''₄), 4.58 (B of ABX, 1H, H₆''₅), 4.89 (dd, 1H, H₆), 4.94, 5.02 (2s, br, 2H, H₃''₄, H₃''₅), 5.38 (s, 1H, H₄), 5.50 (d, 1H, H₃), 6.11 (d, 1H, H₁), 7.40 – 7.58 (m, 3H, phenyl), 8.04 – 8.09 (m, 2H, phenyl), J₃H₁·H₁₅ = 4.0 Hz, J₃H₅·H₃''₄ = -1.0 Hz, J₃H₅·H₃''₅ = -12.6 Hz, J₃H₆·H₆''₄ = 4.4 Hz, J₃H₆·H₆''₅ = 3.8 Hz, J₃H₆·H₆''₅ = -12.4 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 19.59 [OCH₂C(CH₃)=CH₂], 47.58 [C₅], 54.10 [MeO], 65.53 [C₆], 72.00 [OCH₂C(CH₃)=CH₂], 76.53 [C₆], 80.59 [C₄], 198.04 [C₁], 109.05 [C₃], 113.04 [OCH₂C(CH₃)=CH₂], 128.84, 129.94, 134.02
3α-Methallyloxy-4β-benzoyloxy-6β-benzyloloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (29c).

Alcohol 28 was benzoylated in 88% yield by a procedure similar to that used for the preparation of 26. {1H-NMR (200 MHz, CDCl₃): δ 1.79 (s, 3H, Me), 3.54 (l, 1H, HS), 4.22 (dd, br, 2H, H₃'., H₃''.), 4.49 (A of ABX, 1H, H₆'), 4.61 (B of ABX, 1H, H₆''), 4.96 (ddd, 1H, H₆), 5.06 (2s, br, 2H, H₃'''., H₃''''), 5.51 (s, 1H, H₄), 5.58 (d, 1H, H₃), 6.16 (d, 1H, H₁), 7.35 - 7.75 (m, 6H, phenyl), 7.96 - 8.12 (m, 4H, phenyl), J_H₂ - H₃ = 4.0 Hz, J_H₃ - H₃ = -0.8 Hz, J_H₃''' - H₃''' = -12.8 Hz, J_H₅ - H₆ = 4.5 Hz, J_H₆ - H₆ = 4.1 Hz, J_H₆'' - H₆'' = 3.3 Hz, J_H₆'' - H₆'' = -12.4 Hz; LRMS (CI-NH₃): m/z 424 ([M + NH₄⁺], 100%).

Oxetane (30a).

Reaction of 29a (298 mg, 0.82 mmol) and acetic acid (269 μL, 4.12 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (113 mg, 25% yield) as a light yellow oil and recovered starting material (70 mg).

30a-minor: {1H-NMR (200 MHz, CDCl₃): δ 1.61 (s, 3H, Mc), 2.01 (s, 3H, Ac) 2.03 (s, 3H, Ac, anomeric), 3.35 (t, 1H, H₃), 3.70 (s, br, 2H, CHH₂, CHH₂), 3.96 (dd, br, 2H, H₃''., H₃''.), 4.47 (A of ABX, 1H, H₄'), 4.55 (B of ABX, 1H, H₄''), 4.77 (ddd, 1H, H₄), 5.27 (s, 1H, H₃'), 5.40 (d, 1H, H₃''), 6.08 (d, 1H, H₁), 7.40 - 7.61 (m, 3H, phenyl), 8.03 - 8.07 (m, 2H, phenyl), J_H₂ - H₃ = 4.0 Hz, J_H₃ - H₃ = -0.9 Hz, J_H₃'' - H₃'' = -9.9 Hz, J_CHH₂ - CHH₂ = 0 Hz, J_H₄ - H₄ = 0.3 Hz, J_H₄'' - H₄'' = -12.4 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 11.10 [CH₂], 20.78 [CH₃], 21.09, 21.98 [CH₃CO], 47.39 [C₃], 65.60 [C₄', 70.92 [C₃''], 76.15 [C₄], 77.81 [C₃'], 79.62 [CCH₂], 107.99 [C₂], 109.62 [C₃''], 128.47, 129.68, 133.28 [aromatic CH], 129.61 [aromatic C], 166.15 [PhCO], 169.72, 170.32 [CH₃CO]).

30a-major: {1H-NMR (200 MHz, CDCl₃): δ 1.61 (s, 3H, Mc), 2.01 (s, 3H, Ac) 2.03 (s, 3H, Ac, anomeric), 3.35 (t, 1H, H₃), 3.70 (s, br, 2H, CHH₂, CHH₂), 3.97 (dd, br, 2H, H₃''., H₃''.), 4.47 (A of ABX, 1H, H₄'), 4.55 (B of ABX, 1H, H₄''), 4.77 (ddd, 1H, H₄), 5.23 (s, 1H, H₃'), 5.41 (d, 1H, H₃''), 6.07 (d, 1H, H₁), 7.40 - 7.61 (m, 3H, phenyl), 8.03 - 8.07 (m, 2H, phenyl), J_H₂ - H₃ = 3.6 Hz, J_H₃ - H₃ = 4.7 Hz, J_H₃'' - H₃'' = -0.8 Hz, J_CHH₂ - CHH₂ = -10.5 Hz, J_H₄'' - H₄'' = -12.4 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 11.10 [CH₂], 20.78 [CH₃], 21.09, 21.98 [CH₃CO], 47.39 [C₃], 65.60 [C₄', 70.92 [C₃''], 76.15 [C₄], 77.81 [C₃'], 79.62 [CCH₂], 107.99 [C₂], 109.62 [C₃''], 128.47, 129.68, 133.28 [aromatic CH], 129.61 [aromatic C], 166.15 [PhCO], 169.61, 170.06 [CH₃CO]).

Oxetane (30b).

Reaction of 29b (32 mg, 0.08 mmol) and acetic acid (25 μL, 0.40 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (7 mg, 15% yield). {IR (CH₂Cl₂): 1717 cm⁻¹, 166.44 (CO); 1H-NMR (CDCl₃): δ 1.19 (s, 3H, Me), 3.54 (l, 1H, HS), 4.22 (dd, br, 2H, H₃'., H₃''.), 4.49 (A of ABX, 1H, H₆'), 4.61 (B of ABX, 1H, H₆''), 4.96 (ddd, 1H, H₆), 5.06 (2s, br, 2H, H₃'''., H₃''''), 5.51 (s, 1H, H₄), 5.58 (d, 1H, H₃), 6.16 (d, 1H, H₁), 7.35 - 7.75 (m, 6H, phenyl), 7.96 - 8.12 (m, 4H, phenyl), J_H₂ - H₃ = 4.0 Hz, J_H₃ - H₃ = -0.8 Hz, J_H₃''' - H₃''' = -12.8 Hz, J_H₅ - H₆ = 4.5 Hz, J_H₆ - H₆ = 4.1 Hz, J_H₆'' - H₆'' = 3.3 Hz, J_H₆'' - H₆'' = -12.4 Hz; LRMS (CI-NH₃): m/z 425 ([M + NH₄⁺], 7.9%), 353 ([M + H₂C=C(CH₃)CH₂OH], 10.2%).
1722 cm\(^{-1}\), 1751 cm\(^{-1}\), 1774 cm\(^{-1}\). 30b-minor: \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)): \(\delta\) 1.62 (s, 3H, Me), 2.02 (s, 3H, Ac), 3.52 (t, 1H, H3), 3.78 (dd, 2H, CH\(_{2}\), CH\(_{2}\)), 3.89 (s, 3H, MeO), 4.00 (dd, br, 2H, H3\(\text{a}\), H3\(\text{b}\)), 4.47 (A of ABX, 1H, H4\(\text{a}\)), 4.59 (B of ABX, 1H, H4\(\text{b}\)), 4.80 (ddd, 1H, H4), 5.39 (s, 1H, H3), 5.54 (d, 1H, H3\(\text{b}\)), 6.10 (d, 1H, H1), 7.42 - 7.62 (m, 3H, phenyl), 8.03 - 8.09 (m, 2H, phenyl), \(J_{112-113} = 3.9\) Hz, \(J_{\text{H3-H4}} = 4.3\) Hz, \(J_{\text{H3-H3-b}} = -0.9\) Hz, \(J_{\text{CH3-CH3}} = -9.7\) Hz, \(J_{114-114\text{a}} = 4.1\) Hz, \(J_{114-114\text{b}} = 3.6\) Hz, \(J_{114\text{a}-114\text{b}} = -12.5\) Hz). 30b-major: \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)): \(\delta\) 1.56 (s, 3H, Me), 2.02 (s, 3H, Ac), 3.52 (t, 1H, H3), 3.79 (dd, 2H, CH\(_{2}\), CH\(_{2}\)), 4.00 (dd, br, 2H, H3\(\text{a}\), H3\(\text{b}\)), 4.59 (B of ABX, 1H, H4\(\text{b}\)), 4.80 (ddd, 1H, H4), 5.38 (s, 1H, H3), 5.54 (d, 1H, H3\(\text{b}\)), 6.12 (d, 1H, H1), 7.42 - 7.62 (m, 3H, phenyl), 8.03 - 8.09 (m, 2H, phenyl), \(J_{112-113} = 3.7\) Hz, \(J_{\text{H3-H4}} = 4.3\) Hz, \(J_{\text{H3-H3-b}} = -0.9\) Hz, \(J_{\text{CH3-CH3}} = -10.3\) Hz, \(J_{114-114\text{a}} = 4.1\) Hz, \(J_{114-114\text{b}} = 3.6\) Hz, \(J_{114\text{a}-114\text{b}} = -12.5\) Hz). Oxetane (39c).

Reaction of 29c (45 mg, 0.11 mmol) and acetic acid (32 \(\mu\)l, 0.53 mmol) gave the title compound (mixture of 2 diastereomers, 4:6), (24 mg, 37% yield) as a light yellow oil and recovered starting material (11 mg). 30c-minor: \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)): \(\delta\) 1.54 (s, 3H, Me), 2.03 (s, 3H, Ac), 3.51 (t, 1H, H3), 3.74 (s, br, 2H, CH\(_{2}\), CH\(_{2}\)), 4.02 (dd, br, 2H, H3\(\text{a}\), H3\(\text{b}\)), 4.49 (A of ABX, 1H, H4\(\text{a}\)), 4.59 (A of ABX, 1H, H4\(\text{b}\)), 4.87 (ddd, 1H, H4), 5.51 (s, 1H, H3\(\text{b}\)), 5.57 (d, 1H, H3\(\text{a}\)), 6.15 (d, 1H, H1), 7.38 - 7.61 (m, 6H, phenyl), 7.96 - 8.10 (m, 4H, phenyl), \(J_{112-113} = 4.1\) Hz, \(J_{113-114} = 4.3\) Hz, \(J_{\text{H3-a-H3-b}} = -1.3\) Hz, \(J_{\text{CH3-CH3}} = 0\) Hz, \(J_{114-114\text{a}} = 4.1\) Hz, \(J_{114-114\text{b}} = 3.4\) Hz, \(J_{114\text{a}-114\text{b}} = -12.5\) Hz). 30c-major: \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)): \(\delta\) 1.64 (s, 3H, Me), 2.03 (s, 3H, Ac), 3.51 (t, 1H, H3), 3.76 (dd, 2H, CH\(_{2}\), CH\(_{2}\)), 4.03 (dd, br, 2H, H3\(\text{a}\), H3\(\text{b}\)), 4.47 (A of ABX, 1H, H4\(\text{a}\)), 4.59 (B of ABX, 1H, H4\(\text{b}\)), 4.87 (ddd, 1H, H4), 5.50 (s, 1H, H3\(\text{b}\)), 5.58 (d, 1H, H3\(\text{a}\)), 6.14 (d, 1H, H1), 7.38 - 7.61 (m, 6H, phenyl), 7.96 - 8.10 (m, 4H, phenyl), \(J_{112-113} = 4.0\) Hz, \(J_{113-114} = 4.3\) Hz, \(J_{\text{H3-a-H3-b}} = -1.0\) Hz, \(J_{\text{CH3-CH3}} = -9.8\) Hz, \(J_{114-114\text{a}} = 4.1\) Hz, \(J_{114-114\text{b}} = 3.4\) Hz, \(J_{114\text{a}-114\text{b}} = -12.5\) Hz).
Oxetane (31a).

Acetal 29a (36 mg, 0.10 mmol) and benzoic acid (61 mg, 0.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 3:7), (40 mg, 66% yield) as a light yellow oil and recovered starting material (7 mg). 31a-minor: {1H-NMR (200 MHz, CDCl₃): δ 1.76 (s, 3H, Me), 2.01 (s, 3H, Ac), 3.37 (t, 1H, H3), 3.84 (dd, 2H, CHHII, CHHII), 4.16 (dd, 2H, H3"a, H3"b), 4.43 (A of ABX, 1H, H4"a), 4.55 (B of ABX, 1H, H4"b), 4.73 (dd, 1H, H4), 5.23 (s, 1H, H3), 5.46 (s, 1H, H3"), 6.08 (d, 1H, H1), 7.37 - 7.57 (m, 6H, phenyl), 7.98 - 8.12 (m, 4H, phenyl), JH2-H3 = 4.1 Hz, JH3-H4 = 4.1 Hz, JH3"a-H3"b = -9.9 Hz, JCHHII-ChHII = -10.9 Hz, JH4-H4"a = 3.7 Hz, JH4-H4"b = 3.9 Hz, JH4"a-H4"b = -12.5 Hz). 31a-major: {1H-NMR (200 MHz, CDCl₃): δ 1.77 (s, 3H, Me), 2.03 (s, 3H, Ac), 3.35 (t, 1H, H3), 3.86 (dd, 2H, CHHII, CHHII), 4.17 (dd, 2H, H3"a, H3"b), 4.43 (A of ABX, 1H, H4"a), 4.55 (B of ABX, 1H, H4"b), 4.73 (dd, 1H, H4), 5.23 (s, 1H, H3), 5.46 (s, 1H, H3"), 6.08 (d, 1H, H1), 7.37 - 7.57 (m, 6H, phenyl), 7.98 - 8.12 (m, 4H, phenyl), JH2-H3 = 4.1 Hz, JH3-H4 = 4.3 Hz, JH3"a-H3"b = -9.8 Hz, JCHHII-ChHII = -10.6 Hz, JH4-H4"a = 3.7 Hz, JH4-H4"b = 3.9 Hz, JH4"a-H4"b = -12.5 Hz).

Oxetane (31b).

Acetal 29b (609 mg, 1.50 mmol) and benzoic acid (920 mg, 7.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 3:7), (578 mg, 59% yield) as a light yellow oil and recovered starting material (56 mg). [IR (CH₂Cl₂): 1717 cm⁻¹, 1722 cm⁻¹, 1751 cm⁻¹, 1774 cm⁻¹]. 31b-minor: {1H-NMR (200 MHz, CDCl₃): δ 1.77 (s, 3H, Me), 3.52 (t, 1H, H3), 3.70 (m, 2H, CHHII, CHHII), 3.88 (s, 3H, MeO), 4.18 (dd, br, 2H, H3"a, H3"b), 4.42 (A of ABX, 1H, H4"a), 4.52 (B of ABX, 1H, H4"b), 4.74 (dd, 1H, H4), 5.39 (s, 1H, H3"), 5.50 (d, 1H, H3"), 6.11 (d, 1H, H1), 7.37 - 7.58 (m, 6H, phenyl), 7.98 - 8.11 (m, 4H, phenyl), JH2-H3 = 4.0 Hz, JH3-H4 = 3.8 Hz, JH3"a-H3"b = -0.9 Hz, JH3"a-H3"b = -10.1 Hz, JH4-H4"a = 0.9 Hz, JH4-H4"b = -12.4 Hz; 13C-NMR (75.4 MHz, CD₂Cl₂): δ 11.68 [CH₂], 21.62 [CH₃], 47.49 [C₃], 54.10 [MeO], 65.48 [C₆], 71.34 [C₃"], 76.53 [C₄], 80.41 [C₃"], 80.53 [CCH₂], 108.18 [C₂], 109.89 [C₃"], 128.79, 128.84, 129.94, 130.36, 133.03, 134.02 [aromatic CH], 129.72, 130.13 [aromatic C], 156.75, 166.38, 166.44, 171.14 [CO]). 31b-major: {1H-NMR (200 MHz, CDCl₃): δ 1.78 (s, 3H, Me), 3.48 (t, 1H, H3), 3.86 (m, 2H, CHHII, CHHII), 3.88 (s, 3H, MeO), 4.19 (dd, br, 2H, H3"a, H3"b), 4.42 (A of ABX, 1H, H4"a), 4.52 (B of ABX, 1H, H4"b), 4.74 (dd, 1H, H4), 5.37 (s, 1H, H3"), 5.57 (d, 1H, H3"), 6.11 (d, 1H, H1), 7.37 - 7.58 (m, 6H, phenyl), 7.98 - 8.11 (m, 4H, phenyl), JH2-H3 = 3.7 Hz, JH3-H4 = 3.9 Hz, JH3"a-H3"b = -0.9 Hz, JH3"a-H3"b = -9.8 Hz, JH4-H4"a = 0.9 Hz, JH4-H4"b = 3.8 Hz, JH4"a-H4"b = -12.4 Hz; 13C-NMR (75.4 MHz, CD₂Cl₂): δ 12.10 [CH₂], 21.78 [CH₃], 47.58 [C₃], 54.10 [MeO], 65.76 [C₆], 71.07 [C₃"], 76.53 [C₄], 80.29 [C₃"], 80.53 [CCH₂], 108.04 [C₂], 109.94 [C₃"], 128.79, 128.84, 129.94, 130.36, 133.63, 134.02 [aromatic CH], 129.72, 130.13 [aromatic C], 156.75, 166.38, 166.44, 171.14 [CO]).
Oxetane (31c).

Acetal 29c (45 mg, 0.11 mmol) and benzoic acid (65 mg, 0.53 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (32 mg, 45% yield) as a yellow oil and recovered starting material (8 mg). 31c-minor: \(^\text{\textsuperscript{1}H-NMR (200 MHz, CDCl\textsubscript{3}) : \delta 1.81 (s, 3H, Me), 3.50 (t, 1H, H\textsubscript{3}), 3.87 (dd, 2H, H\textsubscript{3\textsuperscript{``}}, H\textsubscript{3\textsuperscript{'''}}), 4.46 (A of ABX, 1H, H\textsubscript{4\textsuperscript{`}}), 4.53 (B of ABX, 1H, H\textsubscript{4\textsuperscript{'''}}), 4.82 (ddd, 1H, H4), 5.50 (s, 1H, H\textsubscript{3\textsuperscript{'''}}), 5.61 (s, 1H, H\textsubscript{3\textsuperscript{''}}), 6.14 (d, 1H, H1), 7.37 - 7.64 (m, 9H, phenyl), 7.93 - 8.13 (m, 6H, phenyl), \(J_{H2\textsubscript{.}H3} = 4.1 \text{ Hz}, J_{H3\textsubscript{.}H4} = 4.4 \text{ Hz}, J_{H3\textsuperscript{``}.H3\textsuperscript{''}} = -9.7 \text{ Hz}, J_{CH\textsubscript{3}.CH\textsubscript{3\textsuperscript{'''}}} = -10.5 \text{ Hz}, J_{H4\textsuperscript{``}.H4\textsuperscript{''}} = 3.7 \text{ Hz}, J_{H4\textsuperscript{``}.H4\textsuperscript{''}} = -12.3 \text{ Hz}; \textsuperscript{13}C-NMR (75.4 MHz, CD\textsubscript{2}Cl\textsubscript{2}) : \delta 11.94 \text{ [C\textsubscript{8}2\textsubscript{1}]}, 21.68 \text{ [CH\textsubscript{3}]}, 47.85 \text{ [C\textsubscript{3}]}, 65.74 \text{ [C6\textsuperscript{'}]}, 71.00 \text{ [C3\textsuperscript{''}]), 76.81 \text{ [C4]}, 78.71 \text{ [C3\textsuperscript{'''}, 80.65 \text{ [CH2\textsubscript{1}]}, 108.30 \text{ [C2]}, 110.73 \text{ [C3\textsuperscript{'''}, 128.70, 128.74, 128.83, 129.96, 130.10, 130.36, 133.58, 133.90, 133.97 \text{ [aromatic CH]}, 128.84, 129.17, 130.39 \text{ [aromatic C]}, 165.67, 166.77, 171.20 \text{ [CO]}).}

31c-major: \(^\text{\textsuperscript{1}H-NMR (200 MHz, CDCl\textsubscript{3}) : \delta 1.80 (s, 3H, Me), 3.50 (t, 1H, H\textsubscript{3}), 3.89 (dd, 2H, H\textsubscript{3\textsuperscript{``}}, H\textsubscript{3\textsuperscript{'''}}), 4.22 (L1d, 2H, H3\textsuperscript{`}), 4.46 (A of ABX, 1H, H\textsubscript{4\textsuperscript{`}}), 4.53 (B of ABX, 1H, H\textsubscript{4\textsuperscript{'''}}), 4.82 (ddd, 1H, H4), 5.49 (s, 1H, H\textsubscript{3\textsuperscript{'''}}), 5.61 (s, 1H, H\textsubscript{3\textsuperscript{''}}), 6.14 (d, 1H, H1), 7.37 - 7.64 (m, 9H, phenyl), 7.93 - 8.13 (m, 6H, phenyl), \(J_{H2\textsubscript{.}H3} = 4.1 \text{ Hz}, J_{H3\textsubscript{.}H4} = 4.4 \text{ Hz}, J_{H3\textsuperscript{``}.H3\textsuperscript{''}} = -9.8 \text{ Hz}, J_{CH\textsubscript{3}.CH\textsubscript{3\textsuperscript{'''}}} = -10.5 \text{ Hz}, J_{H4\textsuperscript{``}.H4\textsuperscript{''}} = 3.7 \text{ Hz}, J_{H4\textsuperscript{``}.H4\textsuperscript{''}} = -12.3 \text{ Hz}; \textsuperscript{13}C-NMR (75.4 MHz, CD\textsubscript{2}Cl\textsubscript{2}) : \delta 11.94 \text{ [C\textsubscript{8}2\textsubscript{1}]}, 21.82 \text{ [CH\textsubscript{2}]}, 47.89 \text{ [C\textsubscript{3}]}, 65.80 \text{ [C6\textsuperscript{'}]}, 71.30 \text{ [C3\textsuperscript{''}]), 76.81 \text{ [C4]}, 78.71 \text{ [C3\textsuperscript{'''}, 80.55 \text{ [CH2\textsubscript{1}]}, 108.34 \text{ [C2]}, 110.73 \text{ [C3\textsuperscript{'''}, 128.70, 128.74, 128.83, 129.96, 130.10, 130.36, 133.58, 133.90, 133.97 \text{ [aromatic CH]}, 128.84, 129.17, 130.39 \text{ [aromatic C]}, 165.56, 166.45, 171.20 \text{ [CO]}].

Oxetane (33).

To a solution of 31e (67 mg, 0.10 mmol) in 7 mL of dry benzene under an atmosphere of nitrogen at room temperature was added pyridine (24 \textmu L, 0.30 mmol) and Bu\textsubscript{3}SnH (54 \textmu L, 0.20 mmol). After refluxing for 15 h, tlc indicated complete disappearance of starting material. The solution was evaporated under reduced pressure and the residue purified by flash chromatography (petroleum ether / ethyl acetate, 2:1 v/v) to afford the deoxygenated compound (27 mg, 50% yield) as a colorless oil. \(^\text{1}H-NMR (200 MHz, CDCl\textsubscript{3}) : \delta 1.65, 1.66 (2s, 6H, Me), 3.56 (t, 1H, H3), 4.03 (dd, br, 2H, H3\textsuperscript{``}, H3\textsuperscript{'''}, 4.36 (A of ABX, 1H, H\textsuperscript{4\textsuperscript{''}}), 4.42 (B of ABX, 1H, H\textsuperscript{4\textsuperscript{'''}}), 4.86 (ddd, 1H, H4), 5.51 (s, 1H, H3\textsuperscript{'''}, 5.64 (d, 1H, H3\textsuperscript{''}).
6.13 (d, 1H, H1), 7.34 - 7.64 (m, 9H, phenyl), 7.93 - 8.12 (m, 6H, phenyl), JH2-H3 = 3.8 Hz, JH3-H4 = 4.6 Hz, JH3-H4-a = -9.8 Hz, JH4-H4-b = 3.6 Hz, JH4-H4 = 3.4 Hz, JH4-H4 = -12.5 Hz; 13C-NMR (75.4 MHz, CDCl3): δ 23.47, 23.53 [CH3], 47.62 [C3], 65.36 [C6], 73.44 [C3'], 76.30 [C4], 78.34 [C3'], 81.27 [C(CH3)2], 107.73 [C2], 110.26 [C3'], 128.21, 128.33, 128.46, 129.48, 129.70, 129.74, 132.59, 133.23, 133.55 [aromatic CH], 129.74, 132.0, 131.57 [aromatic C], 165.35, 165.63, 166.19 [CO]; LRMS (DCI-NH3): m/e 547 ([MH+], 0.9%), 425 ([MH+ - PhCOOH], 26.3%); HRMS (DCI-NH3): m/e calcd. for C24H23O7 [MH+ - PhCOOH], 425.1600; found, 425.1600.

Oxetane (32').

A solution of 31b (33 mg, 0.05 mmol) and activated zinc dust (50 mg, 0.76 mmol) in dry methanol (2 mL) was stirred for 3 h under an atmosphere of nitrogen at room temperature. The zinc was removed by filtration and the filtrate evaporated to dryness in vacuo to give a clear syrup. The residue was dissolved in ether (30 mL), washed with saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na2SO4), filtered and the solvent removed under reduced pressure to give the title compound (mixture of 2 inseparable diastereomers, 3:7), (16 mg, 65% yield) as an extremely unstable clear oil. (IR (CH2Cl2); 1717 cm⁻¹, 1722 cm⁻¹). 32b-minor: {1H-NMR (200 MHz, CDCl3); δ 1.75 (s, 3H, CH), 3.31 (t, 1H, H3), 3.99 (dd, 2H, OCH2C(CH3)=CH2), 4.45 (A of ABX, 1H, H4'), 4.46 (s, 1H, H3'), JH4-H4' = 4.4 Hz, JH3-H3' = 4.4 Hz, JH4-H4' = 3.4 Hz, JH4-H4' = -12.1 Hz). 32-major: {1H-NMR (200 MHz, CDCl3); δ 1.75 (s, 3H, CH), 3.31 (t, 1H, H3), 4.14 (dd, 2H, OCH2C(CH3)=CH2), 4.45 (A of ABX, 1H, H4'), 4.46 (s, 1H, H3'), JH4-H4' = 4.4 Hz, JH3-H3' = 4.4 Hz, JH4-H4' = 3.4 Hz, JH4-H4' = -12.1 Hz).
Epoxide (34a) of 3α-dimethallyloxy-4β-bromo-6β-4-propyl-2,7-dioxa-bicyclo-[3,2,0]-heptane.

Epoxide 34a (mixture of 2 inseparable diastereomers, 2:3) was obtained in 66% yield after flash chromatography (petroleum ether/ethyl acetate, 4:1 v/v) from acetal 10g by a procedure similar to that used for 23a. (LRMS (Cl-NH₃), m/e 340, 338 ([M + NH₄⁺], 4.3%, 4.0%), 323, 321 ([MH⁺], 10%, 1.7%), 221, 219 ([MH⁺ - (H₂C₅C=O(CH₂)₂OH, 28.0%, 29.3%); HRMS (Cl-NH₃). m/e calcd for C₁₃H₂₇NO₇Br, [M⁺ + NH₄⁺], 338.0967; found, 338.0968). 34a-minor: {¹H-NMR (200 MHz, CDCl₃): δ 0.88, 0.91 (d, 3H, CH₃), 1.29, 1.32 (2s, 6H, Me₂C), 1.83 (m, 1H, H6), 3.02 (dd, 1H, H3), 3.33 (dd, 1H, H5), 3.83 (ddd, 2H, H3', H3''), 4.18 (dd, 1H, H6), 4.26 (s, 1H, H4), 5.64 (s, 1H, H3), 6.04 (d, 1H, H1), JH₁-HS = 2.8 Hz, JH₃·H₄ = -11.7 Hz, JH₃·H₆ = 3.2 Hz, JH₆·H₆ = 2.8 Hz, JH₆'-H₆ = 7.0 Hz, JH₅·H₆ = 4.9 Hz, JH₆·H₆ = 6.7 Hz}. 34a-major: {¹H-NMR (200 MHz, CDCl₃): δ 0.88, 0.91 (d, 3H, CH₃), 1.28, 1.32 (2s, 6H, Me₂C), 1.84 (m, 1H, H6), 3.02 (dd, 1H, H3), 3.33 (dd, 1H, H5), 3.82 (ddd, 2H, H3', H3''), 4.18 (dd, 1H, H6), 4.29 (s, 1H, H4), 5.66 (s, 1H, H3), 6.04 (d, 1H, H1), JH₁-HS = 4.1 Hz, JH₃·H₄ = -11.7 Hz, JH₃·H₆ = 5.6 Hz, JH₃·H₆ = 5.8 Hz, JH₅·H₆ = 4.5 Hz, JH₆·H₆ = 4.9 Hz, JH₆·H₆ = 7.0 Hz, JH₆·H₆ = 6.7 Hz}. 34a

Epoxide (34b) of 3α-methylallyloxy-4β-bromo-6β-t-butyldimethylsilyloxyethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane.

Epoxide 34b (mixture of 2 inseparable diastereomers, 2:3) was obtained in 90% yield after flash chromatography (petroleum ether/ether, 4:1 v/v) from acetal 21a by a procedure similar to that used for the preparation of 23a. (LRMS (Cl-NH₃), m/e 323, 321 ([MH⁺ - H₂C₅C=O(CH₂)₂OH, 10.6%, 9.9%]). 34b-minor: {¹H-NMR (200 MHz, CDCl₃): δ 0.07, 0.08 (2s, 6H, t-BuSiMe₂), 0.90 (s, 9H, t-BuSiMe₂), 1.38 (s, 3H, CH₃), 2.72 (dd, 2H, H3', H3''), 3.66 (dd, br, 2H, H3', H3''), 4.18 (dd, 1H, H6), 4.29 (s, 1H, H4), 5.65 (d, 1H, H3), 6.02 (d, 1H, H1), JH₁-HS = 4.0 Hz, JH₃·H₄ = -0.6 Hz, JH₃·H₆ = -11.0 Hz, JH₃·H₆ = -4.8 Hz, JH₅·H₆ = 4.3 Hz, JH₆·H₆ = 3.3 Hz, JH₆·H₆ = 3.2 Hz, JH₆·H₆ = -11.7 Hz}. 34b-major: {¹H-NMR (200 MHz, CDCl₃): δ 0.07, 0.08 (2s, 6H, t-BuSiMe₂), 0.90 (s, 9H, t-BuSiMe₂), 1.35 (s, 3H, CH₃), 2.72 (dd, 2H, H3', H3''), 3.66 (dd, 1H, H5), 3.72 (A of ABX, 1H, H6'), 4.36 (s, 1H, H4), 4.54 (ddd, 1H, H6), 5.65 (d, 1H, H3), 6.02 (d, 1H, H1), JH₁-HS = 4.0 Hz, JH₃·H₄ = -0.6 Hz, JH₃·H₆ = -11.0 Hz, JH₃·H₆ = -4.8 Hz, JH₅·H₆ = 4.3 Hz, JH₆·H₆ = 3.3 Hz, JH₆·H₆ = 3.2 Hz, JH₆·H₆ = -11.7 Hz}.
Epoxide (34c) of 3α-methallyloxy-4β-acetoxy-6β-benzoyloxyethyl-2,7-dioxa-bicyclo[3,2,0]-heptane.

Epoxide 34c (mixture of 2 inseparable diastereomers, 45:55) was obtained in 87% yield after flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) from acetal 29a by a procedure similar to that used for the preparation of 23a. (LRMS (CI-NH): m/e 396 ([M + NH₄⁺], 57.1%), 379 ([MH⁺], 28.8%); Anal. calcd. for C₁₉H₂₂O₈: C, 60.31; H, 5.86; found: C, 59.95; H, 5.47). 34c-minor: [1H-NMR (200 MHz, CDCl₃): δ 1.40 (s, 3H, CH₃), 2.03 (s, 3H, Ac), 2.67 (dd, 2H, H₃''', H₃'''b), 3.36 (dd, 1H, H₅), 3.70 (dd, br, 2H, H₃'', H₃''b), 4.45 (A of ABX, 1H, H₆''), 4.56 (8 of ABX, 1H, H₆''b), 4.82 (ddd, 1H, H₆), 5.27 (s, 1H, H₄), 5.46 (d, 1H, H₃), 6.06 (d, 1H, H₁), 7.39 - 7.61 (m, 3H, phenyl), 8.03 - 8.08 (m, 2H, phenyl). J₃H₃ = 4.1 Hz, J₃H₃b = -11.2 Hz, J₃H₆'' = -4.9 Hz, J₆H₆'' = 4.0 Hz, J₆H₆''b = 4.1 Hz, J₆H₆'b = -12.5 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 18.25 [OCH₂C(CH₃)₂(O)CH₂], 20.73 [CH₃CO], 47.50 [C₅], 51.58 [OCH₂C(CH₃)(O)CH₂], 55.61 [OCH₂C(CH₃)(O)CH₂], 65.49 [C₆], 71.81 [OCH₂C(CH₃)(O)CH₂], 76.23 [C₆], 77.74 [C₄], 107.71 [C₁], 109.83 [C₃], 128.40, 129.62, 133.21 [aromatic CH], 129.57 [aromatic C], 166.10 [PhCO], 169.66 [CH₃CO]].

34c-major: [1H-NMR (200 MHz, CDCl₃): δ 1.37 (s, 3H, CH₃), 2.02 (s, 3H, Ac), 2.73 (dd, 2H, H₃''', H₃'''b), 3.36 (dd, 1H, H₅), 3.79 (dd, br, 2H, H₃'', H₃''b), 4.45 (A of ABX, 1H, H₆''), 4.55 (B of ABX, 1H, H₆''b), 4.82 (ddd, 1H, H₆), 5.23 (s, 1H, H₄), 5.42 (d, 1H, H₃), 6.06 (d, 1H, H₁), 7.39 - 7.61 (m, 3H, phenyl), 8.03 - 8.08 (m, 2H, phenyl). J₃H₃ = 4.1 Hz, J₃H₃b = -11.2 Hz, J₃H₆'' = -4.9 Hz, J₆H₆'' = 4.0 Hz, J₆H₆''b = 4.1 Hz, J₆H₆'b = -12.5 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 18.53 [OCH₂C(CH₃)₂(O)CH₂], 20.73 [CH₃CO], 47.50 [C₅], 51.58 [OCH₂C(CH₃)(O)CH₂], 55.41 [OCH₂C(CH₃)(O)CH₂], 65.49 [C₆], 70.09 [OCH₂C(CH₃)(O)CH₂], 76.23 [C₆], 77.74 [C₄], 107.71 [C₁], 109.83 [C₃], 128.40, 129.62, 133.21 [aromatic CH], 129.57 [aromatic C], 166.10 [PhCO], 169.66 [CH₃CO]].
Thioglycoside (36).

To an ice cooled solution of epoxide 34c (38 mg, 0.10 mmol) and thiophenol (103 μL, 1.00 mmol) in dry ether (5 mL) under nitrogen was added a 1.0 M solution of zinc chloride in ether (100 mL). After stirring for 30 min, the solution was warmed to room temperature, diluted with ether (20 mL), washed with saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na₂SO₄), filtered and the solvent removed in vacuo yielding a yellow residue which was chromatographed over silica gel (petroleum ether / ethyl acetate, 2:1 v/v), affording 36 (mixture of 2 inseparable diastereomers, 45:55) as a light yellow oil (31 mg, 64% yield). **36-minor:** [¹H-NMR (200 MHz, CDCl₃): δ 1.40 (s, 3H, CH₃), 2.02 (s, 3H, Ac), 2.49 (s, br,ex, 1H, OH), 2.73 (dd, 2H, H₂''ₜ, H₂''ₜ'), 3.21 (m, 1H, H₄), 3.70 (dd, 2H, H₂''ₜ, H₂''ₜ'), 4.43 - 4.53 (m, 3H, H₄', H₄''ₜ, H₄''ₜ'), 5.05 (s, 1H, H₃), 5.27 (d, 1H, H₂), 5.72 (d, 1H, H₅), 7.23 - 7.62 (m, 3H, phenyl), 8.05 - 8.12 (m, 2H, phenyl), J₁₄-H₅ = 6.1 Hz, J₁₄-H₂''ₜ = -11.2 Hz, J₁₄-H₂''转型ₜ = -4.4 Hz]. **36-major:** [¹H-NMR (200 MHz, CDCl₃): δ 1.30 (s, 3H, CH₃), 2.02 (s, 3H, Ac), 2.49 (s, br,ex, 1H, OH), 2.75 (dd, 2H, H₂''ₜ, H₂''ₜ'), 3.21 (m, 1H, H₄), 3.71 (dd, 2H, H₂''ₜ, H₂''ₜ'), 4.43 - 4.53 (m, 3H, H₄', H₄''ₜ, H₄''ₜ'), 5.06 (s, 1H, H₃), 5.24 (d, 1H, H₂), 5.72 (d, 1H, H₅), 7.22 - 7.62 (m, 3H, phenyl), 8.05 - 8.12 (m, 2H, phenyl), J₁₄-H₅ = 6.1 Hz, J₁₄-H₂''ₜ = -11.3 Hz, J₁₄-H₂''转型ₜ = -4.4 Hz].
4.5  Experiments for Section 2.6.

3-Hydroxymethyl-6β-phenyl-2,7-dioxa-bicyclo[3,2,0]hept-3-ene (37a).

A mixture of furfuryl alcohol (38.14 g, 388.7 mmol) and benzaldehyde (10.00 g, 94.2 mmol) in benzene (300 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with helium. The solution was then irradiated for 6 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (ether / hexanes, 3:1 v/v) gave exclusively 37a (3.845 g, 20% yield) as a light yellow oil and recovered starting material (15.02 g furfuryl alcohol, 4.05 g benzaldehyde). [1H-NMR (200 MHz, CDCl3): δ 2.06 (t, ex, 1H, OH), 3.68 (ddd, 1H, H5), 4.34 (d, 2H, CH2), 5.39 (d, 1H, H4), 5.57 (d, 1H, H6), 6.55 (d, 1H, H1), 7.31 - 7.42 (m, 5H, Ph); JH1-H5 = 4.4 Hz, JCH2-OH = 6.2 Hz, JH4-H5 = 2.8 Hz, JH5-H6 = 3.2 Hz; LRMS (Cl-NH3), m/e 222 ([M + NH4]+, 28.2%), 205 ([MH]+, 100%), 187 ([MH+ - H2O], 32.9%); HRMS (Cl-NH3): m/e calcd. for C12H11O2, 222; found, 222.0758).

2-(2'-Hydroxyethyl)-furan (38).

To a stirred ice-cooled solution of furfural (2.00 g, 21.8 mmol) in anhydrous ether (100 mL) under an atmosphere of nitrogen was added a 1.0M solution of methylmagnesium bromide in butyl ether (20.8 mL, 20.8 mmol) over a period of 30 min and the mixture allowed to gradually warm to ambient temperature. After 1.5 h, the reaction mixture was poured into ice cold 5% hydrochloric acid (30 mL) and the organic phase was washed with brine (100 mL), dried (Na2SO4), filtered and the solvent removed in vacuo to afford pure racemic 38 (2.31 g, 99% yield) as a colourless oil. [1H-NMR (200 MHz, CDCl3): δ 1.53 (d, 3H, Me), 1.90 (d, ex, 1H, OH), 4.87 (dq, 1H, CH), 6.21, 6.31 (2m, 2H, H3, H4), 7.36 (m, 1H, H5). JCH-OH = 5.0 Hz, JCH-Me = 6.6 Hz].

3-(3'-Hydroxyethyl)-6β-phenyl-2,7-dioxa-bicyclo[3,2,0]hept-3-ene (38a).

A mixture of 38 (528 mg, 4.71 mmol) and benzaldehyde (500 mg, 4.71 mmol) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with helium. The solution was then irradiated for 5 h. The solvent was removed in vacuo to yield a yellow syrup.
Chromatography over silica gel (ether / hexanes, 3:1 v/v) afforded 38a exclusively (mixture of 2 inseparable diastereomers, 1:1), (292 mg, 28% yield) as a light yellow oil and recovered starting material (102 mg 38, 100 mg benzaldehyde). \[^1\text{H-NMR}\ (200\text{ MHz, CDCl}_3): \delta\ 1.47\ (2d, 3H, Me), 2.03\ (d, ex, 1H, OH), 3.65\ (ddd, 1H, H5), 4.50, 4.52\ (2dq, 1H, H3'), 5.31, 5.33\ (2d, 1H, H4), 6.53\ (d, 1H, H1), 7.25 - 7.50\ (m, 5H, Ph); J_{H11-H15} = 4.4\text{ Hz}, J_{H3'-OH} = 5.0\text{ Hz}, J_{H3'-Me} = 6.6\text{ Hz}, J_{H4-H15} = 2.3\text{ Hz}, J_{H5-H6} = 3.0\text{ Hz}.\]

![Diagram of 38a](image)

2-Furaldehyde dimethyl acetal (39).

A solution of furfural (9.61 g, 100.0 mmol) in methanol (210 mL) containing CeCl\(_3\) 7H\(_2\)O (37.25 g, 100.0 mmol) and trimethylorthioformate (87.5 mL, 800 mmol) was allowed to stir for 25 min at room temperature. The reaction mixture was poured into saturated aqueous sodium bicarbonate (1 L) and extracted with ether (4 x 500 mL). The extracts were washed with brine (2 L), dried (Na\(_2\)SO\(_4\)), filtered and the solvent removed in vacuo to afford pure 39 (9.81 g, 69% yield) as a colourless oil. \[^1\text{H-NMR}\ (200\text{ MHz, CDCl}_3): \delta\ 3.34\ (s, 6H, MeO), 5.43\ (s, 1H, CHMe), 6.36, 6.41\ (2m, 2H, H3, H4), 7.39\ (m, 1H, H5)\].

![Diagram of 39](image)

3-Dimethoxymethyl-6\(\beta\)-phenyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (39a) and 1-Dimethoxymethyl-6\(\beta\)-phenyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (39b).

A mixture of 2-furaldehyde dimethyl acetal 39 (2.84 g, 20.0 mmol) and benzaldehyde (2.00 g, 18.8 mmol) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8\(^\circ\)C, and saturated with helium. The solution was then irradiated for 7 h. The solvent was removed in vacuo to yield a yellow residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 6.1 v/v) gave 39a and 39b (mixture of 2 inseparable regioisomers, 3.5), (2.132 g, 46% yield) as a light yellow oil and recovered starting material (1.39 g 2-furaldehyde dimethyl acetal, 869 mg benzaldehyde) 39a: \[^1\text{H-NMR}\ (200\text{ MHz, CDCl}_3): \delta\ 3.45\ (s, 6H, MeO), 3.70\ (ddd, 1H, H5), 5.09\ (t, 1H, H4), 5.58\ (d, 1H, H6), 5.58\ (d, 1H, H3), 6.56\ (dd, 1H, H1), 7.29 - 7.68\ (m, 5H, Ph); J_{H11-H15} = 4.4\text{ Hz}, J_{H3'-H6} = 0.8\text{ Hz}, J_{H3'-H4} = -1.1\text{ Hz}, J_{H4-H5} = 1.1\text{ Hz}, J_{H5-H6} = 2.9\text{ Hz}; \text{LRMS}\ (CI-NH}_3): m/e 231 ([MH\(^+\) - H\(_2\)O], 0.5%).\] 39b: \[^1\text{H-NMR}\ (200\text{ MHz, CDCl}_3): \delta\ 3.40\ (s, 6H, MeO), 3.79\ (ddd, 1H, H5), 4.48\ (s, 1H, H1'), 5.41\ (t, 1H, H4),...
5.58 (d, 1H, H6), 6.73 (dd, 1H, H3), 7.29 - 7.68 (m, 5H, Ph); JH3.H4 = 3.0 Hz, JH3.H5 = -0.9 Hz, JH4.H5 = 2.9 Hz, JH5.H6 = 3.8 Hz; LRMS (Cl-NH3): m/e 231 ([MH+ - H2O], 0.5%).

3-Tri-n-butylstannyl-6-benzoyloxymethyl-2,7-dioxabicyclo[3,2,0]hept-3-ene (40).

A mixture of tributyl-(2-furyl)-stannane (6.43 g, 18.0 mmol), aldehyde 27 (1.64 g, 10.0 mmol) and anhydrous potassium carbonate (3 g) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with helium. The solution was then irradiated for 8 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (petroleum ether/ triethylamine, 1:0.02 v/v) gave 40 (782 mg, 15% yield) as a clear oil and recovered starting material (5.86 g tributyl-(2-furyl)-stannane, 390 mg aldehyde 27). 1H-NMR (200 MHz, CD2Cl2): δ 0.90 (t, 9H, SnCH2CH2CH2CH3), 1.04 (t, 6H, SnCH2CH2CH2CH3), 1.33 (tq, 6H, SnCH2CH2CH2CH3), 1.60 (t, 6H, SnCH2CH2CH2CH3), 3.70 (ddd, 1H, H6'), 4.49 (A of ABX, 1H, H6'), 4.52 (8 of ABX, 1H, H6'), 4.70 (dddd, 1H, H6), 5.47 (d, 1H, H4), 6.36 (dd, 1H, H1), 7.43 - 7.64 (m, 3H, Ph), 8.06 - 8.11 (m, 2H, Ph), JH1.H6 = -0.7 Hz, JH1.H5 = 4.3 Hz, JH4.H5 = 2.8 Hz, JH5.H6 = 2.2 Hz, JH6.H6' = 4.3 Hz, JH6.H6'' = 2.9 Hz, JH6'.'H6'' = -12.1 Hz, JSnCH2CH2 = 7.9 Hz, JCH2CH2 = 7.2 Hz, JCH3.CH2 = 7.1 Hz; 13C-NMR (75.4 MHz, CD2Cl2): δ 10.14 [SnCH1(CH2)2CH3], 13.87 [Sn(CH2)3CH3], 27.59 [Sn(CH2)2CH2CH3], 29.31 [SnCH2CH2CH2CH3], 48.00 [C5], 66.84 [C6], 88.39 [C6], 109.01 [C1], 115.91 [C4], 128.89, 129.98, 133.55 [aromatic CH], 130.42 [aromatic Cl], 166.53 [CO], 167.29 [C3]; LRMS (Cl-NH3): m/e 523 ([MH+]*, 2.8%), 505 ([MH+ - H2O], 100%); HRMS (Cl-NH3): m/e calcd. for C25H37O3120Sn [MH+ - H2O], 505.1765; found, 505.1764.

3-Phenyl-6β-benzoyloxymethyl-2,7-dioxabicyclo[3,2,0]hept-3-ene (41a).

To a stirred solution of 40a (1.042 g, 2.00 mmol) in dry tetrahydrofuran (140 ml) was added iodobenzene (448 µL, 4.00 mmol) and tetrakis(triphenylphosphine)palladium(0) (347 mg, 0.30 mmol; 35 mg added originally, the rest was added in 6 portions during the course of the reaction). The reaction
mixture was refluxed under an atmosphere of nitrogen until tlc indicated complete disappearance of starting material (36 h). The mixture was allowed to cool to room temperature, and pyridine (800 μL) was added followed by 1.2 N pyridinium fluoride solution (1.7 mL). The resulting mixture was stirred for 18 h. Evaporation of the solvent in vacuo gave a black residue which was dissolved in diethyl ether (250 mL). The resulting solution was washed with 5% hydrochloric acid (200 mL), saturated aqueous sodium bicarbonate (200 mL), brine (200 mL), dried (Na₂SO₄), filtered and the solvent removed under reduced pressure to give a brown residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 5:1 v/v) gave the title compound (524 mg, 85% yield) as a light yellow oil. (IH-NMR (200 MHz, CDCl₃): δ 3.94 (ddd, 1H, H₅), 4.58 (d, 2H, H₆', H₆''), 4.90 (ddt, 1H, H₆), 5.11 (d, 1H, H₄), 6.52 (dd, 1H, H₁), 7.26 - 7.67 (m, 8H, Ph), 8.07 - 8.13 (m, 2H, Ph), J₃₅₂₆ = 4.3 Hz, J₅₁₅₆ = -0.7 Hz, J₆₅₁₆₅ = 3.1 Hz, J₆₅₁₆₅₁₆₅ = 3.3 Hz; 13C-NMR (75.4 MHz, CD₂Cl₂): δ 48.55 [C₅], 66.44 [C₆'], 88.57 [C₆], 98.58 [C₄], 108.36 [C₁], 125.75, 128.79, 128.90, 129.46, 129.94, 133.61 [aromatic CH], 130.26, 130.46 [aromatic C], 158.86 [C₃], 166.50 [CO]; LRMS (CI-NH₃): m/e 326 ([MH+ + NH₄⁺], 1.9%), 309 ([MH+], 16.3%), 291 ([MH+ - H₂O], 33.8%); HRMS (CI-NH₃): m/e calcld. for C₁₉H₁₆O₄ [MH+], 309.1128; found, 309.1127).

3-p-Nitrophenyl-6β-benzoyloxymethyl-2,7-dioxo-bicyclo[3,2,2]hept-3-ene (41b).

1-Bromo-4-nitrobenzene and photo-adduct 40a gave 41b in 91% yield by a procedure similar to the one used for the preparation of 41a. (IH-NMR (200 MHz, CDCl₃): δ 4.04 (ddd, 1H, H₅), 4.56 (A of ABX, 1H, H₆'), 4.93 (dddd, 1H, H₆), 6.02 (d, 1H, H₄), 6.55 (dd, 1H, H₁), 7.25 - 7.67 (m, 3H, Ph), 7.83, 8.24 (AB q, 4H, C₆H₄NO₂), 8.09 - 8.14 (m, 2H, Ph), J₃₅₂₆ = -0.9 Hz, J₅₁₅₆ = 4.3 Hz, J₆₅₁₆₅ = 3.3 Hz, J₆₅₁₆₅₁₆₅ = 3.9 Hz, J₁₆₅₁₆₅₁₆₅ = 3.1 Hz, J₁₆₅₁₆₅₁₆₅ = -12.8 Hz; LRMS (CI-NH₃): m/e 371 ([M + NH₄⁺], 0.6%), ([MH⁺], 1.8%), 336 ([MH⁺ - H₂O], 42.1%); HRMS (CI-NH₃): m/e calcld. for C₁₉H₁₄NO₅ [MH⁺], 336.0877; found, 336.0871).

Oxetane (42a).

Ozone was bubbled through a solution of 41a (25 mg, 0.08 mmol) in dry methylene chloride (10 mL) at -78°C until the solution turned blue (5 min). Dimethyl sulfide (60 μL, 0.80 mmol) was added to the reaction mixture under nitrogen and it was allowed to warm to ambient temperature gradually overnight. Next, sodium borohydride on alumina gel (10%), (62 mg, 0.16 mmol) was added and stirring was continued until tlc indicated reduction of the aldehyde was complete (3 h). Pyridine (20 μL, 0.24 mmol), N,N-dimethylaminopyridine (2 mg, 0.01 mmol) and acetic anhydride (12 μL, 0.12 mmol) were added and the reaction was allowed to stir for 16 h. The reaction mixture was diluted with methylene chloride (20 mL), washed with 5% hydrochloric acid (30 mL), saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na₂SO₄), filtered and the solvent removed under reduced pressure to yield a yellow residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 3:1 v/v) gave the
title compound (10 mg, 33% yield) as a light yellow oil. {\textsuperscript{1}H-NMR (200 MHz, CD\textsubscript{2}Cl\textsubscript{2}): \textdelta 1.97 (s, 3H, CH\textsubscript{3}), 3.58 (dddd, 1H, H3'), 4.50 (A of ABX, 1H, H4'), 4.54 (B of ABX, 1H, H3'), 4.62 (B of ABX, 1H, H4'), 5.03 (ddd, 1H, H4), 6.72 (d, 1H, H2), 7.45 - 7.70 (m, 6H, Ph), 8.05 - 8.12 (m, 4H, Ph); J\textsubscript{I-3} = 5.9 Hz, J\textsubscript{H3-3'a} = 4.1 Hz, J\textsubscript{H3-H3'a} = 3.9 Hz, J\textsubscript{H3-H3'b} = -0.2 Hz, J\textsubscript{H3-H4} = 6.3 Hz, J\textsubscript{H4-H4'a} = 4.5 Hz, J\textsubscript{H4-H4'b} = -12.6 Hz. \textsuperscript{13}C-NMR (75.4 MHz, CD\textsubscript{2}Cl\textsubscript{2}): \textdelta 20.48 (CH\textsubscript{3}CO), 40.22 [C3], 60.64 [C3'], 65.42 [C4'], 80.15 [C4], 96.88 [C2], 128.53, 128.59, 129.61, 129.75, 133.29, 133.68 [aromatic CH], 128.72, 129.32 [aromatic Cl], 164.88, 166.05 [CO], 170.62 [CH\textsubscript{3}CO]; \textsuperscript{1}H-NMR (200 MHz, CD\textsubscript{2}Cl\textsubscript{2}): \textdelta 1.98 (s, 3H, CH\textsubscript{3}), 3.60 (dddd, 1H, H3), 4.48 (A of ABX, 1H, H3'), 4.54 (B of ABX, 1H, H3'), 4.56 (B of ABX, 1H, H4'), 5.07 (ddd, 1H, H4), 6.75 (d, 1H, H2), 7.43 - 7.67 (m, 3H, Ph), 7.98 - 8.13 (m, 2H, Ph), 8.27, 8.32 (AB q, 4H, p-NO\textsubscript{2}BzOH); J\textsubscript{AB} = 8.8 Hz, J\textsubscript{H2-H3} = 5.8 Hz, J\textsubscript{H3-3'a} = 4.3 Hz, J\textsubscript{H3-H3'b} = 1.3 Hz, J\textsubscript{H3-H3'b} = -12.9 Hz, J\textsubscript{H3-H4} = 5.9 Hz, J\textsubscript{H4-H4'a} = 4.7 Hz, J\textsubscript{H4-H4'b} = 3.0 Hz, J\textsubscript{H4'-H4'a} = -12.8 Hz; \textsuperscript{13}C-NMR (75.4 MHz, CD\textsubscript{2}Cl\textsubscript{2}): \textdelta 20.80 [CH\textsubscript{3}CO], 40.61 [C3], 60.67 [C3'], 65.57 [C4'], 80.75 [C4], 96.87 [C2], 124.07, 128.91, 131.33, 133.71, 134.77 [aromatic CH], 129.98, 135.07, 151.33 [aromatic C], 166.35, 168.90 [CO], 170.72 [CH\textsubscript{3}CO]; LRMS (CI-NH\textsubscript{3}): m/e 447 ([M + NH\textsubscript{4}\textsuperscript{+}], 100%), 430 ([MH\textsuperscript{+} - NO\textsubscript{2}BzOH], 3.1%); HRMS (CI-NH\textsubscript{3}): m/e calcd. for C\textsubscript{21}H\textsubscript{24}N\textsubscript{2}O\textsubscript{7} [M + NH\textsubscript{4}\textsuperscript{+}], 447.1403; found, 447.1403.

Oxetane (42b).

Oxetane 42b was obtained from 41b in 25% yield by a procedure similar to that used for the preparation of 42a. {\textsuperscript{1}H-NMR (200 MHz, CD\textsubscript{2}Cl\textsubscript{2}): \textdelta 1.98 (s, 3H, CH\textsubscript{3}), 3.60 (dddd, 1H, H3), 4.48 (A of ABX, 1H, H3'), 4.54 (A of ABX, 1H, H4'), 4.56 (B of ABX, 1H, H3'), 4.64 (B of ABX, 1H, H4'), 5.07 (ddd, 1H, H4), 6.75 (d, 1H, H2), 7.43 - 7.67 (m, 3H, Ph), 7.98 - 8.13 (m, 2H, Ph), 8.27, 8.32 (AB q, 4H, p-NO\textsubscript{2}Bz); J\textsubscript{AB} = 8.8 Hz, J\textsubscript{H2-H3} = 5.8 Hz, J\textsubscript{H3-3'a} = 4.3 Hz, J\textsubscript{H3-H3'b} = 1.3 Hz, J\textsubscript{H3-H3'b} = -12.9 Hz, J\textsubscript{H3-H4} = 5.9 Hz, J\textsubscript{H4-H4'a} = 4.7 Hz, J\textsubscript{H4-H4'b} = 3.0 Hz, J\textsubscript{H4'-H4'a} = -12.8 Hz; \textsuperscript{13}C-NMR (75.4 MHz, CD\textsubscript{2}Cl\textsubscript{2}): \textdelta 20.80 [CH\textsubscript{3}CO], 40.61 [C3], 60.67 [C3'], 65.57 [C4'], 80.75 [C4], 96.87 [C2], 124.07, 128.91, 131.33, 133.71, 134.77 [aromatic CH], 129.98, 135.07, 151.33 [aromatic C], 166.35, 168.90 [CO], 170.72 [CH\textsubscript{3}CO]; LRMS (CI-NH\textsubscript{3}): m/e 447 ([M + NH\textsubscript{4}\textsuperscript{+}], 100%), 430 ([MH\textsuperscript{+}], 1.8%), 263 ([MH\textsuperscript{+} - NO\textsubscript{2}BzOH], 3.1%); HRMS (CI-NH\textsubscript{3}): m/e calcd. for C\textsubscript{21}H\textsubscript{23}N\textsubscript{2}O\textsubscript{9} [M + NH\textsubscript{4}\textsuperscript{+}], 447.1403; found, 447.1403.

3-Trimethylsilyl-6β-benzoyloxymethyl-2,7-dioxabicyclo-[3,2,0]hept-3-ene (43a) and 1-Trimethylsilyl-6β-benzoyloxymethyl-2,7-dioxabicyclo-[3,2,0]hept-3-ene (43b).

A mixture of 2-trimethylsilylfuran (2.53 g, 18.0 mmol), aldehyde 27 (1.64 g, 10.0 mmol) and anhydrous potassium carbonate (3 g) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with helium. The solution was then irradiated for 8 h. The solvent was removed in vacuo to afford a yellow syrup. Chromatography over silica gel (petroleum ether / ethyl acetate / triethylamine, 42:7:1 v/v/v) gave photo-adducts 43a and 43b (mixture of 2 inseparable regioisomers, 7:4), (577 mg, 19% yield) as a light yellow oil and recovered starting material (152 mg.
aldehyde 27). 43a: \(^{1}H\)-NMR (200 MHz, CD₂Cl₂): \(\delta \) 0.21 (s, 9H, SiMe₃), 3.74 (ddd, 1H, H₅), 4.48 (A of ABX, 1H, H₆'), 4.54 (ddd, 1H, H₆), 4.74 (ddd, 1H, H₆''), 6.38 (dd, 1H, H₁). 7.41 - 7.66 (m, 3H, Ph), 8.00 - 8.12 (m, 2H, Ph); J₇₃ - H₄ = 4.2 Hz, J₇₃ - H₆ = 0.8 Hz, J₇₃ - H₆' = 2.9 Hz, J₇₅ - H₆ = 3.0 Hz, J₇₅ - H₆' = 5.4 Hz, J₇₅ - H₆'' = 1.5 Hz, J₇₆ - H₆''' = 0.7 Hz, J₇₆ - H₆''' = -13.6 Hz). 43b: \(^{1}H\)-NMR (200 MHz, CD₂Cl₂): \(\delta \) 0.16 (s, 9H, SiMe₃), 3.54 (ddd, 1H, H₅), 4.48 (A of ABX, 1H, H₆'), 4.54 (B of ABX, 1H, H₆''), 4.99 (ddd, 1H, H₆), 5.30 (t, 1H, H₄), 6.69 (dd, 1H, H₃), 7.41 - 7.66 (m, 3H, Ph), 8.00 - 8.12 (m, 2H, Ph); J₉₃ - H₄ = 2.9 Hz, J₉₃ - H₆ = 1.2 Hz, J₉₄ - H₆ = 2.9 Hz, J₉₅ - H₆' = 1.5 Hz, J₉₆ - H₆'' = 0.7 Hz, J₉₆ - H₆''' = -13.6 Hz).

3-Methyl-6β-benzoyloxymethyl-2,7-dioxo-bicyclo-[3.2,0]-hept-3-ene (44a) and 1β-Methyl-6β-benzoyloxymethyl-2,7-dioxo-bicyclo-[3.2,0]-hept-3-ene (44b).

A mixture of 2-methylfuran (17.3 mL, 192 mmol) and aldehyde 27 (15.74 g, 96 mmol) in benzene (1800 mL) was placed in a 2 L photo-reaction vessel, cooled to 8°C, and saturated with argon. The solution was then irradiated for 7 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate / methanol, 10:1:1 v/v/v) gave 44a and 44b (mixture of 2 inseparable regioisomers, 11:8), (11.10 g, 47% yield) as a light yellow oil and recovered starting material (5.62 g aldehyde 27). In the absence of triethylamine, 44b decomposed on the column and photo-adduct 44a was isolated (6.38 g, 27% yield) as a light yellow oil along with recovered starting material (5.62 g aldehyde 27). 44a: \(^{1}H\)-NMR (200 MHz, CD₂Cl₂): \(\delta \) 1.94 (dd, 3H, Me), 3.73 (dddd, 1H, H₅), 4.47 (A of ABX, 1H, H₆'), 4.52 (B of ABX, 1H, H₆''), 4.77 (ddd, 1H, H₆), 5.01 (dd, 1H, H₄), 6.31 (dd, 1H, H₁), 7.44 - 7.66 (m, 3H, Ph), 7.99 - 8.11 (m, 2H, Ph); J₇₃ - H₄ = 4.4 Hz, J₇₃ - H₆ = -0.9 Hz, J₇₃ - Me = -1.4 Hz, J₇₃ - H₆' = 2.8 Hz, J₇₃ - H₆'' = 1.4 Hz, J₇₅ - H₆ = 2.2 Hz, J₇₆ - H₆'' = 4.4 Hz, J₇₆ - H₆''' = 2.9 Hz, J₇₆ - H₆'''' = -12.5 Hz; \(^{13}C\)-NMR (75.4 MHz, CD₂Cl₂): \(\delta \) 13.91 (Me), 48.12 [C₅], 66.48 [C₆], 88.76 [C₆'], 98.91 [C₄], 108.51 [C₁], 129.33, 129.88, 133.52 [aromatic CH], 130.27 [aromatic C], 158.45 [C₃], 166.44 [CO]; LRMS (Cl-NH₃): m/e 264 ([M + NH₄⁺], 1.7%), 247 ([MH⁺], 0.8 %), 225 ([MH⁺ - H₂O], 100%); HRMS (Cl-NH₃): m/e calcld. for C₁₄H₁₃O₃ [MH⁺ - H₂O], 229.0865; found, 229.0864). Anal. calcd. for C₁₄H₁₄O₄: C, 68.28; H, 5.73. Found: C, 68.09; H, 5.67.

44b: \(^{1}H\)-NMR (200 MHz, CD₂Cl₂): \(\delta \) 1.69 (s, 3H, Me), 3.52 (ddd, 1H, H₅), 4.47 (A of ABX, 1H, H₆'). 4.52 (B of ABX, 1H, H₆''), 4.72 (ddd, 1H, H₆), 5.31 (t, 1H, H₄), 6.58 (dd, 1H, H₃), 7.41 - 7.66 (m, 3H, Ph), 7.98 - 8.11 (m, 2H, Ph); J₉₃ - H₄ = 3.0 Hz, J₉₃ - H₆ = -1.0 Hz, J₉₄ - H₆ = 3.0 Hz, J₉₅ - H₆ = 2.9 Hz, J₉₆ - H₆ = 0.7 Hz, J₉₆ - H₆'' = -13.6 Hz).
$\text{H}_2\text{H} = 4.2 \text{ Hz}, J_{\text{H}16\text{-H}16'} = 2.9 \text{ Hz}, J_{\text{H}1\text{-H}1'} = -12.6 \text{ Hz}; ^{13}\text{C-}
\text{NMR (75.4 MHz, CD}_{2}\text{Cl}_2): \delta 23.46 \text{ [Me], 48.53 [C5], 66.31 [C6'], 85.88 [C6], 104.29 [C4], 116.22 [C1], 128.75, 130.01, 133.41 [aromatic CH], 130.23 [aromatic C], 148.43 [C3], 166.44 [CO]; LRMS (Cl-NH}_3): m/e 264 ([M + NH}_4^+], 1.7%), 247 ([MH]' [0.8%], 229 ([MH]' - H}_2\text{O}, 100%); HRMS (Cl-NH}_3): m/e \text{calcd. for C}_{14}\text{H}_{13}\text{O}_3 [MH}^+ - \text{H}_2\text{O}, 229.0865; \text{found, 229.0864}].

\begin{align*}
\text{BzO} & \quad \text{BzO} \\
\text{O} & \quad \text{O} \\
44a & \quad 44b
\end{align*}

2α-Acetoxy-3α-C-formyl-4β-benzoyloxymethyl oxetane (45).

Ozone was bubbled through a solution of the photo-adduct 44a (73 mg, 0.30 mmol) in dry methylene chloride (45 mL) at -78°C until the solution turned blue (15 min). Dimethyl sulfide (218 mL, 10 equiv.) was added to the reaction mixture under nitrogen and it was allowed to warm to ambient temperature gradually overnight. The reaction mixture was diluted with methylene chloride (25 mL), washed with water (2 x 25 mL), brine (25 mL), dried (Na$_2$SO$_4$), filtered and the solvent removed in vacuo to yield aldehyde 45 (78 mg, 94% yield) as a light yellow oil. $^1\text{H-NMR (200 MHz, CD}_{2}\text{Cl}_2): \delta 2.06 (s, 3H, Ac), 4.02 (dt, 1H, H3), 4.29 (A of ABX, 1H, H4'), 4.39 (B of ABX, 1H, H4'), 5.41 (ddd, 1H, H4), 6.58 (d, 1H, H2), 7.25 - 7.67 (m, 3H, Ph), 7.91 - 8.11 (m, 2H, Ph), 9.76 (d, 1H, CHO), J_{\text{H2-H3}} = 6.4 \text{ Hz}, J_{\text{H3-C1O}} = 1.0 \text{ Hz}, J_{\text{H13-H14}} = 6.1 \text{ Hz}, J_{\text{H14-H14'a}} = 3.8 \text{ Hz}, J_{\text{H14-H14'b}} = 3.1 \text{ Hz}, J_{\text{H14'a-H14'b}} = -12.9 \text{ Hz}; ^{13}\text{C-}
\text{NMR (75.4 MHz, CDCl}_3): \delta 20.75 \text{ [CH}_3\text{CO], 50.61 [C3], 64.72 [C4'], 75.95 [C4], 95.66 [C2], 128.48, 129.61, 133.40 [aromatic CH], 129.24 [aromatic C], 166.01 [PhCO], 169.29 [CH}_3\text{CO], 194.98 [CHO]; LRMS (Cl-NH}_3): m/e 296 ([M + NH}_4^+], 100%), 279 ([MH}' [3.9%), 219 ([MH}' - AcOH), 3.3%; HRMS (Cl-NH}_3): m/e \text{calcd. for C}_{14}\text{H}_{18}\text{NO}_6 [MH}^+ - \text{H}_2\text{O}, 296.1135; \text{found, 296.1134}].

\begin{align*}
\text{BzO} & \quad \text{BzO} \\
\text{OAc} & \quad \text{OAc} \\
45 & \quad 45
\end{align*}

2α-Acetoxy-3α-hydroxymethyl-4β-benzoyloxymethyl oxetane (46).

To a stirred solution of aldehyde 45 (78 mg, 0.28 mmol) in methylene chloride (45 mL) at 0°C under an atmosphere of nitrogen was added sodium borohydride on alumina gel (10%), (225 mg, 0.61 mmol) and the mixture was warmed to ambient temperature gradually over 1 h. After 5 h, reduction of the aldehyde was complete. The reaction mixture was filtered through a bed of dry Celite and the filtrate was washed with 5% hydrochloric acid (40 mL), saturated aqueous sodium bicarbonate (40 mL), dried (Na$_2$SO$_4$), filtered and the solvent removed in vacuo to yield the title compound (55 mg, 70% yield) as a
light yellow oil. For purposes of characterization, a small sample of alcohol 46 was chromatographed over silica gel (petroleum ether/ethyl acetate, 1:1 v/v). $^{1}H$-NMR (200 MHz, CD$_2$Cl$_2$): $\delta$ 0.88 (s, br, ex, 1H, OH), 2.13 (s, 3H, Ac), 3.32 (ddddd, 1H, H3), 3.88 (A of ABX, 1H, H3$^\beta$), 3.94 (B of ABX, 1H, H3$^\alpha$), 4.46 (A of ABX, 1H, H4$^\beta$), 4.57 (B of ABX, 1H, H4$^\alpha$), 4.96 (ddddd, 1H, H4), 6.48 (d, 1H, H2), 7.42 - 7.65 (m, 3H, Ph), 7.98 - 8.11 (m, 2H, Ph), J$_{112-113}$ = 5.9 Hz, J$_{113-113'}$ = 5.6 Hz, J$_{113-113''}$ = 7.2 Hz, J$_{113''-113}$ = -11.7 Hz, J$_{113-114}$ = 6.1 Hz, J$_{114-114''}$ = 4.6 Hz, J$_{114-114'}$ = 3.0 Hz, J$_{114'-114}$ = -12.6 Hz; $^{13}$C-NMR (75.4 MHz, CD$_2$Cl$_2$): $\delta$ 21.28 [CII 3 CO], 43.11 [C3], 59.33 [C3$'$], 66.03 [C4$'$], 79.50 [C4], 97.75 [C2], 128.69, 129.93, 133.60 [aromatic CH], 130.13 [aromatic C], 166.49 [PhCO], 169.98 [CH$_3$CO], LRMS (Cl-NH$_3$): m/e 298 ([M + NH$_4^+$], 100%), 211 ([M$^+$ - AcOH], 60.6%), HRMS (Cl-NH$_3$): m/e calcd for C$_{14}$H$_{20}$N$_2$O$_6$ [M + NH$_4^+$], 298.1289; found, 298.1290.

Oxetane (47a).

Oxetane 47a was obtained from photo-adduct 44a in 54% yield by a procedure similar to that used for the preparation of 42a. $^{1}H$-NMR (200 MHz, CD$_2$Cl$_2$): $\delta$ 1.99 (s, 3H, Ac), 2.11(s, 3H, anomic Ac), 3.45 (dddt, 1H, H3), 4.38 (d, 2H, H3$'$, H3$''$), 4.45 (A of ABX, 1H, H4$'$), 4.57 (B of ABX, 1H, H4$''$), 4.93 (dddd, 1H, H4), 6.47 (d, 1H, H2), 7.44 - 7.66 (m, 3H, Ph), 7.98 - 8.12 (m, 2H, Ph), J$_{112-113}$ = 5.9 Hz, J$_{113-113'}$ = 7.1 Hz, J$_{113-114}$ = 6.1 Hz, J$_{114-114'\alpha}$ = 4.5 Hz, J$_{114'\alpha-114}$ = 3.3 Hz, J$_{114'\alpha-114\beta}$ = -12.6 Hz; $^{13}$C-NMR (75.4 MHz, CD$_2$Cl$_2$): $\delta$ 20.86, 21.17 [CH$_3$], 40.28 [C3], 60.91 [C3$'$], 65.77 [C4$'$], 80.45 [C4], 96.48 [C2], 128.87, 129.94, 133.63 [aromatic CH], 130.10 [aromatic C], 166.37 [PhCO], 169.80, 170.94 [CH$_3$CO]; LRMS (Cl-NH$_3$): m/e 340 ([M + NH$_4^+$], 100%), 323 ([M$^+$], 0.5%), 261 ([M$^+$ - AcOH], 34.4%), HRMS (Cl-NH$_3$): m/e calcd for C$_{16}$H$_{22}$N$_2$O$_6$ [M + NH$_4^+$], 340.1397; found, 340.1396.

Oxetane (47b).

To a solution of alcohol 46 (28 mg, 0.10 mmol) in dry methylene chloride (15 mL) under nitrogen at 0°C was added N,N-dimethylaminopyridine (1 mg, 0.01 mmol), pyridine (24 $\mu$L, 0.30 mmol) and benzoyl chloride (17 $\mu$L, 0.15 mmol). The solution was gradually warmed to room temperature (1 h) and allowed to stir for 16 h. It was then diluted with methylene chloride (15 mL), washed with 5% hydrochloric acid (30 mL), saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na$_2$SO$_4$), filtered and the solvent removed in vacuo to yield a yellow syrup. Purification by flash chromatography (petroleum ether/ethyl acetate, 2:1 v/v) afforded the title compound (18 mg, 47% yield from photo-adduct 44a) as a colourless oil. $^{1}H$-NMR (200 MHz, CD$_2$Cl$_2$): $\delta$ 2.10 (s, 3H, Ac), 3.61 (ddddd, 1H, H3), 4.52 (A of ABX, 1H, H4$'$), 4.64 (B of ABX, 1H, H4$''$), 4.65 (A of ABX, 1H, H3$'$), 4.70
(B of ABX, 1H, H3'\_b), 5.05 (ddd, 1H, H4), 6.58 (d, 1H, H2), 7.34 - 7.76 (m, 6H, Ph), 7.90 - 8.11 (m, 4H, Ph), J_{H12.H3} = 6.0 Hz, J_{H3.H3'\_a} = 6.9 Hz, J_{H3.H3'\_b} = 7.7 Hz, J_{H3.H4} = -11.5 Hz, J_{H3.H4'} = 6.2 Hz, J_{H4.H4'\_a} = 4.4 Hz, J_{H4.H4'\_b} = 3.2 Hz, J_{H4'\_a.H4'\_b} = -12.6 Hz; \textsuperscript{13}C-NMR (75.4 MHz, CD\textsubscript{2}Cl\textsubscript{2}): \delta 21.18 [CH\textsubscript{3}], 40.49 [C3], 61.44 [C3'], 65.85 [C4'], 80.31 [C4], 96.58 [C2], 128.84, 128.90, 129.91, 130.42, 133.59, 134.14 [aromatic CH], 129.27, 129.86 [aromatic Cl], 166.47, 169.84, 170.98 [CO]; LRMS (Cl-NH\textsubscript{3}): m/e 402 ([M + NH\textsubscript{4}\textsuperscript{+}], 100%), 385 ([MH\textsuperscript{+} - AcOH], 34.4%); HRMS (Cl-NH\textsubscript{3}): m/e calcld. for C\textsubscript{21}H\textsubscript{21}NO\textsubscript{3} [M + NH\textsubscript{4}\textsuperscript{+}], 385.1286; found, 385.1287).

**Oxetane (47c).**

To a solution of alcohol 46 (56 mg, 0.20 mmol) in dry methylene chloride (30 mL) under nitrogen at 0°C was added N,N-dimethylaminopyridine (2 mg, 0.02 mmol), triethylamine (140 \\mu L, 1.00 mmol) and methyl oxalyl chloride (37 \\mu L, 0.40 mmol). The solution was gradually warmed to room temperature (1 h) and allowed to stir for 16 h. It was then diluted with methylene chloride (20 mL), washed with 5% hydrochloric acid (40 mL), saturated aqueous sodium bicarbonate (40 mL), brine (40 mL), dried (Na\textsubscript{2}SO\textsubscript{4}), filtered and the solvent removed in vacuo to yield a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate, 2:1 v/v) afforded the title compound (39 mg, 53% yield from photo-adduct 44a) as a colourless oil. \textsuperscript{1}H-NMR (200 MHz, CD\textsubscript{2}Cl\textsubscript{2}): \delta 2.12 (s, 3H, Ac), 3.58 (ddd, 1H, H3), 3.85 (s, 3H, MeO), 4.46 (A of ABX, 1H, H4'\_a), 4.59 (B of ABX, 1H, H4'\_b), 4.59 (A of ABX, 1H, H3'\_b), 4.63 (B of ABX, 1H, H3'\_b), 4.96 (ddd, 1H, H4), 6.50 (d, 1H, H2), 7.44 - 7.66 (m, 3H, Ph), 8.02 - 8.10 (m, 2H, Ph), J_{H2.H3} = 6.0 Hz, J_{H3.H3'\_a} = 7.1 Hz, J_{H3.H3'\_b} = 7.2 Hz, J_{H3'H3'\_b} = -11.5 Hz, J_{H11.H4} = 5.8 Hz, J_{H11.H4'\_a} = 4.2 Hz, J_{H11.H4'\_b} = 3.3 Hz, J_{H4'\_a.H4'\_b} = -12.7 Hz; \textsuperscript{13}C-NMR (75.4 MHz, CD\textsubscript{2}Cl\textsubscript{2}): \delta 21.14 [CH\textsubscript{3}CO], 39.95 [C3], 63.16 [C3'], 65.57 [C4'], 79.92 [C4], 96.07 [C2], 128.90, 129.98, 133.68 [aromatic CH], 129.88 [aromatic C], 157.69, 158.05 [OCOCOOMe], 166.38 [PhCO], 169.70 [CH\textsubscript{3}CO]; LRMS (Cl-NH\textsubscript{3}): m/e 384 ([M + NH\textsubscript{4}\textsuperscript{+}], 100%), 307 ([MH\textsuperscript{+} - AcOH], 41.6%); HRMS (Cl-NH\textsubscript{3}): m/e calcld. for C\textsubscript{17}H\textsubscript{22}NO\textsubscript{3} [M + NH\textsubscript{4}\textsuperscript{+}], 384.1293; found, 384.1294.

![Diagram](image-url)
Nucleoside (48a).

To a solution of oxetane 47a (13 mg, 0.04 mmol) in dry 1,2-dichloroethane (0.5 mL) under an atmosphere of nitrogen at room temperature was added a stock solution of bis-(trimethylsilyl)-N6-adenine in 1,2-dichloroethane (0.339 M solution, 250 µL, 0.085 mmol) and tin tetrachloride (7.1 µL, 0.06 mmol). After stirring for 1 h, the reaction mixture was diluted with methylene chloride (25 mL), washed with saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na2SO4), filtered and the solvent removed in vacuo yielding a white residue. Purification by flash chromatography (methylene chloride/methanol, 100:3 v/v) afforded nucleoside 48a (14 mg, 70% yield) as a white foam. 

\[ ^1H-NMR (200 MHz, CDCl_3): \delta 2.05 (s, 3H, Ac), 3.47 (dddd, 1H, H2',a, H2'b, H3',a, H3'b), 4.42 (m, 4H, H2'-b, H2"t, H3"t, H3'b), 5.47 (ddd, 1H, H3'), 6.26 (d, 1H, H1'), 7.32 - 7.56 (m, 6H, Ph), 7.79 - 7.84 (m, 1H, Ph), 7.92 - 8.00 (m, 3H, Ph), 8.26 (s, 1H, H2), 9.39 (s, br, ex, 1H, NH), J_H1'-H2' = 3.3 Hz, J_H2'-H3' = 2.2 Hz; \] 

\[ ^13C-NMR (75.4 MHz, CD2Cl2): \delta 20.95 ([CH]CO), 51.39 (C2'-t), 62.28 ([C2"t], 74.13 (C3'p), 76.23 ([Cl'], 123.98 [C5], 128.12, 128.98, 129.23, 129.85, 133.08, 133.96 [aromatic CH], 130.03 [aromatic C-COOCH2], 135.76 [aromatic C-CON2], 141.36 [C8], 149.87 [C4], 151.96 [C6], 152.86 [C2], 164.76, 166.16 [PhCO], 170.90 ([CH2]CO); UV (methanol), \lambda_{max} 234 nm and 282 nm). \]

Nucleoside (48b).

Nucleoside 48b was obtained from oxetane 48b by a procedure similar to that used for the preparation of nucleoside 48a. 

\[ ^1H-NMR (200 MHz, CDCl_3): \delta 3.64 (dddd, 1H, H2'), 4.48 (A of ABX, 1H, H3'), 4.53 (B of ABX, 1H, H3'q), 4.66 (A of ABX, 1H, H3'p), 4.76 (B of ABX, 1H, H2'b), 5.60 (ddd, 1H, H3'), 6.44 (d, 1H, H1'), 7.37 - 7.72 (m, 9H, Ph), 7.84 - 7.88 (m, 1H, Ph), 7.98 - 8.14 (m, 5H, Ph), 8.31 (s, 1H, H8), 8.64 (s, 1H, H2), 9.07 (s, br, ex, 1H, NH), J_H1'-H2' = 3.2 Hz, J_H2'-H3' = 7.0 Hz, J_H1'-H2'b = 5.6 Hz, J_H2'-H3'b = -1.6 Hz, J_H2'-H3' = 1.6 Hz, J_H1'-H3' = 2.5 Hz, J_H1'-H3'b = 5.0 Hz, J_H1'-H3'b = -10.8 Hz; \]

\[ ^13C-NMR (75.4 MHz, CD2Cl2): \delta 51.52 [C2'], 62.95 [C2"q], 74.16 [C3'p], 76.23 [C3'], 89.80 [C1'], 124.02 [C5], 128.21, 128.83, 128.94, 129.09, 129.83, 129.93, 132.96, 133.71, 133.93 [aromatic CH], 129.42, 129.76 [aromatic C-COOCH2], 134.30 [aromatic C-CON2], 141.36 [C8], 149.97 [C4], 151.86 [C6], 152.86 [C2], 165.19, 166.11, 166.39 [CO]; LRMS (FAB-glycerol): m/e 564 ([MH]+, 12.1%); HRMS (FAB-glycerol): m/e calc'd. for C31H26N6O6 [MH]+, 564.1884; found, 564.1883). \]
N,N-Benzoylepoxetanocin-dibenzoate (50).

A solution of nucleoside 48b (36 mg, 0.064 mmol) in dry methylene chloride (1 mL) under nitrogen at ambient temperature containing N,N-dimethylaminopyridine (8 mg, 0.064 mmol), pyridine (52 μL, 0.64 mmol) and benzoyl chloride (37 μL, 0.32 mmol) was stirred for 18 h. The solution was diluted with methylene chloride (25 mL), washed with 5% hydrochloric acid (25 mL), saturated aqueous sodium bicarbonate (25 mL), brine (25 mL), dried (Na₂SO₄), filtered and the solvent removed under reduced pressure to yield a yellow oil. Chromatography over silica gel (methylene chloride / methanol, 50:1 v/v) afforded pure 50 (38 mg, 89% yield) as a white foam. (1H-NMR (200 MHz, CDCl₃): δ 3.64 (dddd, 1H, H₂'), 4.48 (A of ABX, 1H, H₃'''), 5.44 (B of ABX, 1H, H₃'''), 4.66 (A of ABX, 1H, H₂'''), 4.76 (B of ABX, 1H, H₃'''), 6.62 (ddd, 1H, H₃'''), 6.44 (m, 12H, Ph), 7.25 - 7.65 (m, 12H, Ph), 7.78 - 7.91 (m, 3H, Ph), 7.95 - 8.07 (m, 3H, Ph), 8.36 (s, 1H, H₈), 8.49 (s, 1H, H₁), J H₂'·H₂''' = 3.0 Hz, J H₁·H₂' = 7.2 Hz, J H₂'. H₂''' = 5.6 Hz, J H₁·H₂'' = -11.5 Hz, J H₂'·H₂'' = 2.7 Hz, J H₃'·H₃''' = 2.8 Hz, J H₃'·H₃''' = 5.7 Hz, J H₃'·H₃''' = -10.9 Hz; ¹³C-NMR (75.4 MHz, DMSO-d₆): δ 49.22 [C₂', 62.74 [C₂''], 72.76 [C₃''], 75.79 [C₃'], 87.17 [C₁', 125.56 [C₅], 128.85, 128.90, 129.07, 129.10, 129.65, 129.81, 129.88, 129.97, 133.29, 133.39, 133.72, 133.77 [aromatic CH], 132.96, 129.76 [aromatic C-COOCH₂], 134.00, 134.32 [aromatic CON], 145.77 [C₈], 151.27 [C₄'], 152.15 [C₆], 152.74 [C₂], 165.90, 166.23 [PhCOO], 172.47, 177.77 [OCNCO]; LRMS (FAB-glycerol): m/e 564 ([MH+], 12.1%); HRMS (FAB-glycerol): m/e calcd. for C₃₁H₂₆N₃O₆ [MH+], 564.1884; found, 564.1883.

Epioxetanocin (1a).

To a solution of nucleoside 48a (28 mg, 0.056 mmol) in anhydrous methanol (1 mL) under an atmosphere of nitrogen at room temperature was added sodium (8 mg, 0.348 mmol) and the mixture allowed to stir for 16 h. Amberlite weakly acidic resin was added until the pH was adjusted to 7 and the reaction mixture was filtered. The solvent was then removed in vacuo and the residue was crystallized from methanol to afford pure epioxetanocin (10 mg, 71% yield) as white needles (m.p. 117-118°C). Nucleosides 48b and 79b were deblocked in a similar manner. (1H-NMR (200 MHz, CD₃OD): δ 2.84 (ddd, 1H, H₂'), 3.73 (A of ABX, 1H, H₂''), 3.77 (B of ABX, 1H, H₂''), 4.08 (A of ABX, 1H, H₃''), 4.12 (B of ABX, 1H, H₃'''), 4.35 (ddd, 1H, H₃'''), 6.10 (d, 1H, H₁'), 8.20 (s, 1H, H₈), 8.37 (s, 1H, H₂), J H₁·H₂ = 3.4 Hz, J H₂·H₃' = 6.9 Hz, J H₂·H₃'' = 6.2 Hz, J H₂·H₃'' = -11.1 Hz, J H₂·H₃'' = 2.3 Hz, J H₂·H₃'' = 3.0 Hz, J H₂·H₃'' = 4.6 Hz, J H₂·H₃'' = -9.6 Hz; ¹³C-NMR (75.4 MHz, CD₃OD): δ 57.44 [C₂'], 61.90 [C₂''], 74.25 [C₃''], 77.13 [C₃'], 88.58 [C₁'], 129.33 [C₅], 130.64 [C₄], 133.61 [C₆], 141.95 [C₈], 153.60 [C₆]
3-Methyl-6β-hydroxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (52).

To a stirred solution of photo-adduct 44a (1.024 g, 4.16 mmol) in dry diethyl ether (80 mL) under nitrogen at 0°C was added lithium aluminum hydride (240 mg, 6.24 mmol) and it was allowed to warm to ambient temperature. After 30 min, water (240 µL), 15% aqueous sodium hydroxide solution (240 µL) and water (720 µL) were added to destroy excess hydride. The reaction mixture was filtered through a bed of dry Celite and the filter cake washed with ether (80 mL). Evaporation of the filtrate in vacuo gave a colourless syrup which was chromatographed over silica gel (petroleum ether / ethyl acetate, 1:1 v/v) to afford the title compound (349 mg, 59% yield) as a clear oil. {1H-NMR (200 MHz, CDCl₃): δ 1.94 (dd, 3H, Me), 2.27 (s, br, ex, tH, OH), 3.64 (dddd, 1H, H₅), 3.69 (A of ABX, 1H, H₆₄), 3.77 (B of ABX, 1H, H₆₅), 4.60 (ddddd, 1H, H₆), 4.93 (dd, 1H, H₄), 6.25 (dd, 1H, H₁); J₃₁₁-₅₅ = 4.4 Hz, J₃₁₁-H₆ = -0.8 Hz, J₅₅-Me = -1.3 Hz, J₅₅-H₁₁ = 2.8 Hz, J₅₅-Me = 1.4 Hz, J₅₅-H₁₆ = 2.5 Hz, J₁₆-₁₆'₅ = 3.7 Hz, J₁₆-H₆₅ = 2.9 Hz, J₁₆-H₆₅ = -12.7 Hz; 13C-NMR (75.4 MHz, CD₂Cl₂): δ 13.87 [C₅], 47.31 [C₅], 64.75 [C₆], 92.35 [C₆], 99.16 [C₇], 108.56 [C₈], 115.08 [C₉]; LRMS (CI-NH₃): m/z 160 ([M+NH₄⁺], 3.5%), 143 ([MH⁺], 100%), 125 ([MH⁺ - H₂O], 47.4%); HRMS (CI-NH₃): m/e calcld. for C₇H₁₀O₃ [MH⁺], 143.0708; found, 143.0708.

3-Methyl-6β-t-butyldimethylsilyloxy methyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (53).

Photo-adduct alcohol 52 was silylated by a procedure similar to that used for the preparation of 19. Purification by flash chromatography (petroleum ether / ether, 10:1 v/v) gave the title compound in 27% yield as a clear oil. {1H-NMR (200 MHz, CDCl₃): δ 0.07, 0.09 (2s, 6H, t-BuSiMe₂), 0.91 (s, 9H, t-BuSiMe₂), 1.92 (t, 3H, Me), 3.61 (dddd, 1H, H₅), 3.72 (A of ABX, 1H, H₆₅), 3.78 (B of ABX, 1H, H₆₅), 4.50 (dddd, 1H, H₆), 4.91 (dd, 1H, H₄), 6.21 (dd, 1H, H₁), J₃₁₁-H₅ = 4.4 Hz, J₃₁₁-H₆ = -0.9 Hz, J₃₁₁-Me = -1.4 Hz, J₅₅-H₁₅ = 2.7 Hz, J₅₅-Me = 1.4 Hz, J₅₅-H₁₆ = 3.1 Hz, J₁₆-₁₆'₅ = 3.0 Hz, J₁₆-H₆₅ = 3.3 Hz, J₁₆-H₆₅ = -11.7 Hz; LRMS (Cl-NH₃): m/e 274 ([M + NH₄⁺], 0.5%), 257 ([MH⁺], 7.7%), 239 ([MH⁺ - H₂O], 100%); HRMS (Cl-NH₃): m/e calcld. for C₁₃H₂₃O₂Si [MH⁺ - H₂O], 239.1468, found, 239.1467.
3-Methyl-6β-t-butyldiphenylsilyloxymethyl-2,7-dioxo-bicyclo-[3,2,0]-hept-3-ene (55).

To a solution of photo-adduct alcohol 52 (78 mg, 0.55 mmol) in dry N,N-dimethylformamide (2 mL) under nitrogen at room temperature was added imidazole (79 mg, 1.10 mmol) and t-butyldiphenylsilyl chloride (150 μL, 0.58 mmol) and it was allowed to stir until all of the starting material was consumed (18 h). The solvent was removed in vacuo and the residue was chromatographed over silica gel (petroleum ether / ethyl acetate, 20:1 v/v) to afford the title compound (129 mg, 62% yield) as a clear oil.

{\(^{1}\)H-NMR (200 MHz, CD\(_2\)Cl\(_2\)): δ 1.11 (s, 9H, t-BuSiPh\(_2\)), 1.95 (t, 3H, Me), 3.75 (dddd, 1H, H5), 3.82 (A of ABX, 1H, H6'), 3.86 (B of ABX, 1H, H6'), 4.54 (dddd, 1H, H6), 4.98 (dd, 1H, H4), 6.32 (dd, 1H, H1), 7.37 - 7.52 (m, 6H, Ph), 7.66 - 7.79 (m, 4H, Ph); \(J_{H1-H5} = 4.4\) Hz, \(J_{H1-H6} = -0.9\) Hz, \(J_{H4-H5} = 2.7\) Hz, \(J_{H5-Me} = 1.4\) Hz, \(J_{H5-H6} = 1.4\) Hz, \(J_{H6-H6'a} = 3.0\) Hz, \(J_{H6-H6'b} = 3.0\) Hz, \(J_{H6'a-H6'b} = -11.7\) Hz; \(^{13}\)C-NMR (75.4 MHz, CD\(_2\)Cl\(_2\)): δ 14.04 [Me], 19.55 [CH\(_3\)SiMe\(_2\)], 27.02 [(CH\(_3\))\(_3\)SiMe\(_2\)], 47.64 [C5], 66.13 [C6'], 91.72 [C6], 99.25 [C4], 108.66 [C1], 128.13, 128.28, 130.13, 130.17, 135.91, 136.02 [aromatic CH], 133.69, 133.80 [aromatic C-Si], 158.10 [C3]; LRMS (CI-NH\(_3\)): \(m/e\) 398 (M + NH\(_4^+\), 2.7%), 381 (MH\(^+\), 100%), 363 (MH\(^+\) - H\(_2\)O), 6.7%); HRMS (CI-NH\(_3\)): \(m/e\) calcd. for C\(_{23}\)H\(_{29}\)O\(_3\)S\(_1\) (MH\(^+\), 381.1886; found, 381.1885).

Oxetane (54).

Oxetane 54 was obtained from adduct 53 in 19% yield by a procedure similar to that used for the preparation of oxetane 42a. \(^{1}\)H-NMR (200 MHz, CD\(_2\)Cl\(_2\)): δ 0.09, 0.10 (2s, 6H, t-BuSiMe\(_2\)), 0.93 (s, 9H, t-BuSiMe\(_2\)), 2.01 (s, 3H, Ac), 2.09 (s, 3H, anomeric Ac), 3.38 (dddd, 1H, H3), 3.71 (A of ABX, 1H, H4'), 3.81 (B of ABX, 1H, H4'), 4.31 (A of ABX, 1H, H3'), 4.36 (B of ABX, 1H, H3'), 4.58 (dddd, 1H, H4), 6.37 (d, 1H, H2), \(J_{H2-H3} = 5.9\) Hz, \(J_{H3-H3'a} = 7.3\) Hz, \(J_{H3-H3'b} = 7.7\) Hz, \(J_{H3'-H4} = 5.6\) Hz, \(J_{H3'-H3'b} = -11.4\) Hz, \(J_{H4-H4'a} = 3.5\) Hz, \(J_{H4'-H4'b} = 2.9\) Hz, \(J_{H4'a-H4'b} = -12.1\) Hz; LRMS (CI-NH\(_3\)): \(m/e\) 350 (M + NH\(_4^+\), 10.2%), 333 (MH\(^+\), 1.5%); 273 (MH\(^+\) - AcOH), 100%); HRMS (CI-NH\(_3\)): \(m/e\) calcd. for C\(_{13}\)H\(_{25}\)O\(_4\)Si [MH\(^+\) - AcOH], 273.1522; found, 273.1522.

![Diagram](54)
Aldehyde (56).

Adduct 55 was transformed to aldehyde 56 in 93% yield by a procedure similar to that used for the preparation of aldehyde 45. {\(^1\)H-NMR (200 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 1.10 (s, 9H, t-Bu), 2.10 (s, 3H, Ac) 4.14 (dt, 1H, H3), 4.52 (A of ABX, 1H, H4\(_a\)), 4.63 (B of ABX, 1H, H4\(_b\)), 5.16 (ddd, 1H, H4), 6.63 (d, 1H, H2), 7.36 - 7.51 (m, 6H, Ph), 7.64 - 7.85 (m, 4H, Ph), 9.82 (d, 1H, CHO), \(J_{H2-H3} = 6.2\) Hz, \(J_{H3-C11O} = 1.4\) Hz, \(J_{H3-H4} = 6.1\) Hz, \(J_{H4-H4'a} = 7.0\) Hz, \(J_{H4-H4'b} = 7.7\) Hz, \(J_{H4'a-H4'b} = -11.5\) Hz].

Oxetane (56a).

Oxetane 56a was obtained from adduct 55 in 18% yield by a procedure similar to that used for the preparation of oxetane 42a. {\(^1\)H-NMR (200 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 1.09 (s, 9H, t-BuSiPh\(_2\)), 1.99 (s, 3H, Ac), 2.10 (s, 3H, anomic Ac), 3.51 (dddd, 1H, H3), 3.76 (A of ABX, 1H, H4\(_a\)), 3.87 (B of ABX, 1H, H4\(_b\)), 4.31 (A of ABX, 1H, H3\(_a\)), 4.36 (B of ABX, 1H, H3\(_b\)), 4.64 (ddd, 1H, H4), 6.46 (d, 1H, H2), 7.31 - 7.49 (m, 6H, Ph), 7.62 - 7.74 (m, 4H, Ph), \(J_{H2-H3} = 5.8\) Hz, \(J_{H3-H3'a} = 7.3\) Hz, \(J_{H3-H3'b} = 7.6\) Hz, \(J_{H3'a} = -11.4\) Hz, \(J_{H3-H4} = 6.2\) Hz, \(J_{H4-H4'a} = 3.5\) Hz, \(J_{H4-H4'b} = 2.9\) Hz, \(J_{H4'a-H4'b} = -12.0\) Hz; LRMS (Cl-NH\(_3\)): m/e 474 ([M + NH\(_4^+\), 100%]; HRMS (Cl-NH\(_3\)): m/e calcd. for C\(_{25}\)H\(_{36}\)NO\(_6\)Si [M + NH\(_4^+\)], 474.2310; found, 474.2311).

Oxetane (56b).

Oxetane 56b was obtained from adduct 55 in 18% yield by a procedure similar to that used for the transformation of photo-adduct 44a to oxetane 47b. {\(^1\)H-NMR (200 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 1.08 (s, 9H, t-BuSiPh\(_2\)), 2.08 (s, 3H, Ac), 3.67 (dddt, 1H, H3), 3.80 (A of ABX, 1H, H4\(_a\)), 3.91 (B of ABX, 1H, H4\(_b\)), 4.60 (d, 2H, H3\(_a\), H3\(_b\)), 4.76 (dddd, 1H, H4), 6.54 (d, 1H, H2), 7.33 - 7.60 (m, 9H, Ph), 7.66 - 7.74 (m, 4H, Ph), 7.95 - 8.06 (m, 2H, Ph), \(J_{H12-H13} = 5.9\) Hz, \(J_{H13-H13'a} = 7.2\) Hz, \(J_{H13-H13'b} - 0\) Hz, \(J_{H13-H4} = 6.0\) Hz, \(J_{H4-H4'a} = 3.4\) Hz, \(J_{H4-H4'b} = 2.8\) Hz, \(J_{H4'a-H4'b} = -12.1\) Hz; LRMS (Cl-NH\(_3\)): m/e 536 ([M + NH\(_4^+\), 74.9%]), 459 ([MH\(_\text{+AcOH}\), 100%]; HRMS (Cl-NH\(_3\)): m/e calcd. for C\(_{30}\)H\(_{38}\)NO\(_6\)Si [M + NH\(_4^+\)], 536.2469; found, 536.2468).
Oxetane (56c).

Oxetane 56c was obtained from adduct 55 in 18% yield by a procedure similar to that used for the transformation of photo-adduct 44a to oxetane 47c. [H-NMR (200 MHz, CD2Cl2): δ 1.08 (s, 9H, t-BuSiPh2), 2.11 (s, 3H, Ac), 2.86 (s, 3H, MeO), 6.49 (d, 1H, H2), 7.35 - 7.73 (m, 10H, Ph), JH2-H3 = 5.8 Hz; 13C-NMR (75.4 MHz, CD2Cl2): δ 19.50 [SiC(CH3)3], 21.19 [CH2CO], 26.95 [SiC(CH3)3], 38.91 [C3], 52.95 [CH2Si], 63.42 [C4], 65.03 [C4'], 82.26 [C4], 96.19 [C2], 128.05, 128.14, 130.19, 130.34, 135.93, 136.03 [aromatic CH], 133.48, 133.53 [aromatic C-Si], 157.12, 158.16 [OCOCOMe], 169.76 [CH3CO]; LRMS (CI-NH3): m/e 518 ([M + NH4]+, 40.5%); HRMS (CI-NH3): m/e calculated for C26H36NO8Si [M + NH4]+, 518.2212; found, 518.2210].

1-O-Benzyl-3-methyl-2-butene (57).

Sodium hydride (60% oil dispersion, 3.60 g, 90.0 mmol) was added to an ice-cooled solution of 3-methyl-2-buten-1-ol (5.17 g, 60.0 mmol) and tert-n-butylammonium iodide (2.22 g, 6.0 mmol) in dry tetrahydrofuran (500 mL) under an atmosphere of nitrogen. After complete evolution of hydrogen (1 h), benzyl bromide (12.30 g, 72.0 mmol) was added dropwise and stirring was continued for 20 h. Florsil (10 g) was added and the reaction mixture was stirred for another 30 min. Removal of the solvent in vacuo gave a residue which was washed with pentane (5 x 200 mL). Evaporation of the washings gave a yellow oil which was chromatographed over silica gel (petroleum ether/ethyl acetate, 70:1 v/v) to afford the title compound (10.46 g, 99% yield) as a colourless oil. [H-NMR (200 MHz, CDCl3): δ 1.64 (s, br, 3H, CH), 1.75 (s, br, 3H, CH3'), 3.99 (d, 2H, CH2), 4.49 (s, 2H, CH2Ph), 5.40 (t, br, 1H, CH), 7.26 - 7.37 (m, 5H, Ph), JCH2-CH = 0.7 Hz; 13C-NMR (75.4 MHz, CDCl3): δ 25.67 [CHJ, 66.44 [CH2Ph], 71.90 [CH2Ph], 121.02 [CH], 127.36, 127.66, 128.19 [aromatic CH], 136.97 [aromatic C], 138.47 [Me2C]].

BnO

57, X=O(CH3)2 58, X=O

2-Benzylacetaldelyde (58).

Ozone and nitrogen were bubbled through a solution of 57 (17.60 g, 100.0 mmol) in dry methylene chloride (1600 mL) at -78°C until the solution turned blue (4.5 h). Dimethyl sulfide (73.4 mL, 1.0 mol) was added to the reaction mixture under an atmosphere of nitrogen and it was allowed to warm to ambient temperature gradually overnight. The solution was washed with water (2 x 1 L), brine (1 L), dried (Na2SO4), filtered and the solvent removed in vacuo to yield aldehyde 58 (14.25 g, 95% yield) as a light yellow oil. [H-NMR (200 MHz, CDCl3): δ 4.00 (d, 2H, CH2CHO), 4.51 (s, 2H, CH2Ph), 7.25 - 7.29 (m, 5H, Ph), 9.58 (t, 1H, CHO), JCH2-CHO = 0.8 Hz; 13C-NMR (75.4 MHz, CDCl3): δ 73.40
[CH₂CHO], 75.08 [CH₂Ph], 127.84, 127.99, 128.40 [aromatic CH], 136.70 [aromatic C], 200.20 [CHO]).

1-O-p-Anisyloxy-3-methyl-2-butene (61).
To a stirred solution of 3-methyl-2-buten-1-ol (8.61 g, 100.0 mmol) and p-methoxyphenol (37.24 g, 300.0 mmol) in dry tetrahydrofuran (300 mL) under nitrogen at ambient temperature was added triphenylphosphine (34.10 g, 130.0 mmol) and diethyl azodicarboxylate (22.64 g, 130.0 mmol). The mixture was then refluxed for 2 h. Evaporation of the solvent in vacuo gave a white solid which was chromatographed over silica gel (petroleum ether/ethyl acetate, 100:1) to afford 61 (18.70 g, 97% yield) as a clear oil. [¹H-NMR (200 MHz, CDCl₃): δ 1.71 (d, 3H, CH₃), 1.77 (d, 3H, CH₃'), 3.75 (s, 3H, MeO), 4.43 (d, 2H, CH₂), 5.47 (m, tH, CH), 6.81, 6.83 (AB quartet, 4H, Ph), JCH-Me = -0.3 Hz, JCH-Me' = -1.2 Hz, JCH₂CH = 6.8 Hz, JAB = 9.6 Hz].

2-p-Anisyloxyacetalddehyde (62).
To a stirred solution of diol 64 (4.16 g, 20.0 mmol) in methanol (100 mL) and water (100 mL) at ambient temperature was added sodium m-pentanode (4.28 g, 20.0 mmol). After 30 min, the sodium iodate precipitate was filtered off and the methanol was evaporated in vacuo. The remaining solution was then extracted with methylene chloride (3 × 250 mL), washed with brine (250 mL), dried (Na₂SO₄), filtered and the solvent again removed in vacuo to afford aldehyde 62 (3.22 g, 97% yield) as a clear oil. [¹H-NMR (200 MHz, CDCl₃): δ 3.75 (s, 3H, MeO), 4.51 (d, 2H, CH₂), 6.81, 6.84 (AB quartet, 4H, Ph), 9.83 (t, 1H, CHO), JCH₂-CHO = 1.1 Hz, JAB = 1.9 Hz; LRMS (Cl-NH₃): m/e 184 ([M + NH₄⁺], 100%)].

Glycerol-1-O-p-anisyl-2,3-O-acetonide (63).
Compound 63 was obtained in 88% yield from solketal by a procedure similar to that used for the preparation of 61. [¹H-NMR (200 MHz, CDCl₃): δ 1.38, 1.44 (2s, 6H, CMc₂), 3.74 (s, 3H, MeO), 3.87 (A of ABX, 1H, H₁a) *, 3.87 (A of ABX, 1H, H₃a) *, 4.00 (B of ABX, 1H, H₁b) *, 4.14 (B of ABX, 1H, H₃b) *, 4.44 (ddddd, 1H, H2), 6.82, 6.83 (AB q, 4H, Ph), JH₂-H₂ = 5.9 Hz, JH₁a-H₁b = 5.4 Hz, JH₁b-H₁a = -9.2 Hz, JAB = 1.2 Hz, JH₂-H₃a = 5.9 Hz, JH₁b-H₃b = 6.4 Hz, JH₁a-H₃b = -8.6 Hz].
1-O-p-anslyloxyglycerol (64).

A solution of 63 (26.61 g, 107.3 mmol) in acetic acid (240 mL) and water (60 mL) was stirred at ambient temperature for 17 h. Evaporation of the solvent in vacuo gave a white solid which was dissolved in methylene chloride (1 L), washed with saturated aqueous sodium bicarbonate (3 x 800 mL), brine (800 mL), dried (Na$_2$SO$_4$), filtered and the solvent removed under reduced pressure to give a white residue. Purification by flash chromatography (ethyl acetate / petroleum ether, 2:1 v/v) afforded the title compound (18.75 g, 84% yield) as a white solid (m.p. 74.5-75.5°C). {^1H-NMR (200 MHz, CDCl$_3$): $\delta$ 2.41 (t, ex, 1H, OH on C3), 2.91 (d, ex, 1H, OH on C2), 3.74 (s, 3H, MeO), 3.74 (dddd, 2H, H$_3$H$_3$), 4.05 (m, 1H, H2), 3.95 (m, 2H, H$_1$H$_1$), 6.81, 6.82 (AB q, 4H, Ph), $J_{OH-H2} = 4.5$ Hz, $J_{OH-H3aH3b} = 6.0$ Hz, $J_{AB} = 0.6$ Hz}.  

\begin{center}
\entrymodifiers={++<0.5em>}
\begin{tikzpicture}
\node[shape=circle,draw,inner sep=1pt] (a) at (0,0) {p-MeO-C$_6$H$_4$O};
\end{tikzpicture}
\end{center}

1-O-Methoxyethoxymethyloxy-3-methyl-2-butene (66).

Sodium hydride (60% oil dispersion, 7.20 g, 180.0 mmol) was added to an ice-cooled solution of 3-methyl-2-buten-1-ol (12.92 g, 150.0 mmol) in dry tetrahydrofuran (500 mL) under an atmosphere of nitrogen. After complete evolution of hydrogen (1 h), 2-methoxyethoxymethyl chloride (22.42 g, 180.0 mmol) was added dropwise and allowed to stir for 16 h at room temperature. The reaction mixture was then cooled to 0°C and excess hydride was destroyed by careful addition of 0.1% hydrochloric acid. Removal of the solvent in vacuo gave a residue which was dissolved in methylene chloride (1 L), washed with saturated aqueous sodium bicarbonate (800 mL), brine (800 mL), dried (Na$_2$SO$_4$), filtered and the solvent removed under reduced pressure to yield a yellow oil. Distillation of the crude product (69-71°C, 0.5 mm Hg) gave the title compound (21.59 g, 83% yield) as a light yellow oil. {^1H-NMR (200 MHz, CDCl$_3$): $\delta$ 1.65 (s, br, 3H, CH$_3$), 1.72 (d, 3H, CH$_3$), 3.37 (s, 3H, MeO), 3.54 (m, 2H, OCH$_2$), 3.68 (m, 2H, OCH$_2$), 4.04 (d, 2H, OCH$_2$CH), 4.69 (s, 2H, OCH$_2$O), 5.30 (m, 1H, CH), $J_{Me-CH} = 0$ Hz, $J_{Me'-CH} = -1.0$ Hz, $J_{CH2-CH} = 7.1$ Hz}.  

\begin{center}
\entrymodifiers={++<0.5em>}
\begin{tikzpicture}
\node[shape=circle,draw,inner sep=1pt] (a) at (0,0) {X};
\end{tikzpicture}
\end{center}

\begin{itemize}
\item 66, R=C(CH$_3$)$_2$
\item 67, R=O
\end{itemize}

2-Methoxyethoxymethyloxycetaldehyde (67).

Aldehyde 67 was obtained in 27% yield from olefin 66 by a procedure similar to that described for the preparation of aldehyde 58. {^1H-NMR (200 MHz, CDCl$_3$): $\delta$ 3.37 (s, 3H, MeO), 3.54 (m, 2H,
OCH₂), 3.72 (m, 2H, OCH₂), 4.19 (d, 2H, CH₂CHO), 4.82 (s, 2H, OCH₂O), 9.70 (t, 1H, CHO), JCH₂-CHO = 0.9 Hz; IR (CHCl₃): 1738 cm⁻¹.

1-O-p-Nitrobenzoyloxy-3-methyl-2-butene (68).

A solution of 3-methyl-2-buten-1-ol (8.61 g, 100.0 mmol) in dry methylene chloride (125 mL) under nitrogen at ambient temperature containing N,N-dimethylaminopyridine (1.22 g, 10.0 mmol), pyridine (24.3 mL, 300 mmol) and p-nitrobenzoyl chloride (22.27 g, 120.0 mmol) was stirred for 18 h. The solution was diluted with methylene chloride (1 L), washed with 5% hydrochloric acid (450 mL), saturated aqueous sodium bicarbonate (450 mL), brine (450 mL), dried (Na₂SO₄), filtered and the solvent removed under reduced pressure to yield a yellow solid which was chromatographed over silica gel (hexanes / ethyl acetate, 97:3 v/v) to afford 68 as a light yellow solid (21.60 g, 92% yield, m.p. 61.5-63.5°C). [¹H-NMR (200 MHz, CDCl₃): δ 1.76 (d, 3H, CH₃), 1.78 (d, 3H, CH₃'), 4.84 (d, 1H, CH₂), 5.45 (m, 1H, CH), 8.19, 8.25 (AB q, 4H, Ph), JCH₂-Me = -1.2 Hz, JCH-Me = -1.0 Hz, JCH₂-CH = 7.3 Hz, JAB = 9.2 Hz].

2-p-Nitrobenzoyloxyacetaldehyde (69).

2-p-Nitrobenzoyloxyacetaldehyde was obtained from 68 as described for the preparation of aldehyde 20. Purification by flash chromatography (petroleum ether / ethyl acetate, 2:1 v/v) gave the title compound (95% yield) as a viscous light yellow oil. [¹H-NMR (200 MHz, CDCl₃): δ 4.98 (s, 2H, CH₂), 8.26, 8.31 (AB q, 4H, Ph), 9.71 (s, 1H, CHO), JAB = 9.2 Hz]
Propionyloxyacetaldheyde (71).

Propionyloxyacetaldheyde was obtained from 70 as described for the preparation of aldehyde 20. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) gave the title compound (85% yield) as a clear oil. \[^{1}\text{H-NMR} (200 \text{ MHz, CDCl}_3)\]: \(\delta \) 1.18 (t, 3H, CH\(_3\)), 2.46 (q, 2H, CH\(_2\)CH\(_3\)), 4.65 (s, 2H, CH\(_1\)CHO), 9.59 (s, 1H, CHO), \(J_{\text{CH3-CH2}} = 7.6 \text{ Hz}; \[^{13}\text{C-NMR} (75.4 \text{ MHz, CDCl}_3)\]: \(\delta \) 8.55 [CH\(_3\)CH\(_2\)], 26.60 [CH\(_3\)CH\(_2\)], 68.25 [OCH\(_1\)CH\(_3\)], 173.43 [EtCO], 195.71 [CHO]).

\[
\begin{align*}
\text{EtCOO} & \xrightarrow{X} \text{X} \\
70, \ x=-(CH_3)_2 \\
71, \ x=O
\end{align*}
\]

3-Methyl-6\(^\beta\)-propionyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (72a) and 1\(^\beta\)-Methyl-6\(^\beta\)-propionyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (72b).

A mixture of 2-methylfuran (17.3 mL, 192 mmol) and aldehyde 71 (11.14 g, 96 mmol) in benzene (1800 mL) was placed in a 2 L photo-reaction vessel, cooled to 8°C, and saturated with argon. The solution was then irradiated for 8 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate / triethylamine, 10:1:0.01 v/v/v) gave 72a and 72b (mixture of 2 inseparable regioisomers, 16:11), (6.36 g, 33% yield) as a light yellow oil and recovered starting material (4.64 g aldehyde 71). In the absence of triethylamine, 72b decomposed on the column and photo-adduct 72a was isolated (4.37 g, 23% yield) as a light yellow oil along with recovered starting material (4.64 g aldehyde 71). 72a: \[^{1}\text{H-NMR} (200 \text{ MHz, CDCl}_3)\]: \(\delta \) 1.15 (t, 3H, CH\(_3\)), 1.92 (dd, 3H, CH\(_3\)), 2.40 (q, 2H, CH\(_3\)CH\(_1\)), 3.59 (dddd, 1H, HS), 4.22 (A of ABX, 1H, H6'), 4.26 (B of ABX, 1H, H6''), 4.63 (dddd, 1H, H6), 6.22 (dd, 1H, H4), J\(_{\text{H3-H5}}\) = 4.4 Hz, J\(_{\text{H5-H6}}\) = -0.8 Hz, J\(_{\text{H6-A}}\) = 1.4 Hz, J\(_{\text{H6-B}}\) = 2.7 Hz, J\(_{\text{H6-C}}\) = 1.4 Hz, J\(_{\text{H6-D}}\) = 2.8 Hz, J\(_{\text{H6-E}}\) = 4.3 Hz, J\(_{\text{H6-F}}\) = 3.2 Hz, J\(_{\text{CH3-CH2}}\) = 7.5 Hz; \[^{13}\text{C-NMR} (75.4 \text{ MHz, CDCl}_3)\]: \(\delta \) 9.18 [CH\(_3\)CH\(_2\)], 23.12 [Me], 47.89 [C], 65.80 [C6], 88.57 [C6], 98.81 [C4], 108.34 [C1], 158.23 [C3], 174.04 [CO]; LRMS (CI-NH\(_3\)): m/e 199 ([MH\(^+\)], 0.5%), 181 ([MH\(^+\)-H\(_2\)O], 100%); HRMS (CI-NH\(_3\)): m/e calcld. for C\(_{10}\)H\(_{13}\)O\(_3\) [MH\(^+\)-H\(_2\)O], 181.0865; found, 181.0864. 72b: \[^{1}\text{H-NMR} (200 \text{ MHz, CDCl}_3)\]: \(\delta \) 1.15 (t, 3H, CH\(_3\)CH\(_2\)), 1.71 (s, 3H, CH\(_3\)), 2.39 (q, 2H, CH\(_3\)CH\(_2\)), 3.37 (ddd, 1H, H5), 4.26 (d, 2H, H6', H6''), 4.59 (dt, 1H, H6), 5.23 (t, 1H, H4), 6.54 (dd, 1H, H3), J\(_{\text{H3-H4}}\) = 3.0 Hz, J\(_{\text{H3-H5}}\) = -1.0 Hz, J\(_{\text{H4-H5}}\) = 2.9 Hz, J\(_{\text{H5-H6}}\) = 4.3 Hz, J\(_{\text{H6-H6'-H6''}}\) = 4.1 Hz, J\(_{\text{H6-H6'-H6''}}\) = 0 Hz, J\(_{\text{CH3-CH2}}\) = 7.6 Hz; \[^{13}\text{C-NMR} (75.4 \text{ MHz, CDCl}_3)\]: \(\delta \) 9.18 [CH\(_3\)CH\(_2\)], 23.12 [Me], 27.61 [CH\(_3\)CH\(_2\)], 48.39 [C5], 56.67 [C6], 85.73 [C6], 104.25 [C4], 116.08 [C1], 148.37 [C3], 174.20 [CO]; LRMS (CI-NH\(_3\)): m/e 199
2α-Acetoxy-3α-O-formyl-4β-propionyloxymethyl oxetane (73).

Photo-adduct 72a was transformed to aldehyde 73 in 92% yield by a procedure similar to that used for the preparation of aldehyde 45. \(^{1}H\text{-NMR} (200 \text{ MHz, CDCl}_3): \delta 1.12 (t, 3H, CH\text{CH}_2), 2.08 (s, 3H, Ac), 2.37 (q, 2H, CH\text{CH}_3), 3.93 (dt, 1H, H3), 4.15 (A of ABX, 1H, H4a), 4.37 (B of ABX, 1H, H4b), 5.30 (ddd, 1H, H4), 6.55 (d, 1H, H2), 9.73 (d, 1H, CHO). J\text{H2-H3} = 6.4 \text{ Hz}, J\text{H3-H4} = 1.0 \text{ Hz}, J\text{H4-H4a} = 6.1 \text{ Hz}, J\text{H4-H4b} = 3.8 \text{ Hz}, J\text{H4a-H4b} = -12.9 \text{ Hz}, J\text{Cl3-Cl2} = 7.5 \text{ Hz}; ^{13}C\text{-NMR} (75.4 \text{ MHz, CDCl}_3). \delta 8.94 [\text{CH}_3\text{CH}_2], 20.75 [\text{CH}_3\text{CO}], 27.28 [\text{CH}_3\text{CH}_2], 50.50 [\text{C3}], 64.19 [\text{C4}], 75.76 [\text{C4}], 95.59 [\text{C2}], 169.30 [\text{CH}_3\text{CO}], 173.94 [\text{EtCO}], 195.09 [\text{CHO}]; LRMS (CI-NH\text{3}): m/e 248 ([M + NH\text{4}^+] , 100%), 171 ([MH\text{+} - \text{AcOH}], 59.2%); HRMS (CI-NH\text{3}): m/e calcd. for C\text{10}H\text{11}N\text{O}_6 [M + NH\text{4}^+], 248.1133; found, 248.1134.

2α-Acetoxy-3α-hydroxymethyl-4β-propionyloxymethyl oxetane (74).

Aldehyde 73 was reduced to alcohol 74 in 68% yield by a procedure similar to that used for the preparation of alcohol 46. \(^{1}H\text{-NMR} (200 \text{ MHz, CD}_2\text{Cl}_2): \delta 0.88 (s, br, ex, 1H, OH), 1.14 (t, 3H, CH\text{CH}_2), 2.13 (s, 3H, Ac), 2.40 (q, 2H, CH\text{CH}_3), 3.19 (ddd, 1H, H3), 3.83 (A of ABX, 1H, H3a), 3.90 (B of ABX, 1H, H3b), 4.20 (A of ABX, 1H, H4a), 4.33 (B of ABX, 1H, H4b), 4.82 (ddd, 1H, H4), 6.41 (d, 1H, H2), J\text{H2-H3} = 6.0 \text{ Hz}, J\text{H3-H3a} = 5.7 \text{ Hz}, J\text{H3-H3b} = 5.6 \text{ Hz}, J\text{H3a-H3b} = -11.8 \text{ Hz}, J\text{H4-H4a} = 6.2 \text{ Hz}, J\text{H4-H4b} = 4.8 \text{ Hz}, J\text{H4a-H4b} = 3.0 \text{ Hz}, J\text{H4a-H4b} = -12.6 \text{ Hz}, J\text{Cl3-Cl2} = 7.5 \text{ Hz}; ^{13}C\text{-NMR} (75.4 \text{ MHz, CD}_2\text{Cl}_2): \delta 8.94 [\text{CH}_3\text{CH}_2], 20.98 [\text{CH}_3\text{CO}], 27.31 [\text{CH}_3\text{CH}_2], 40.78 [\text{C3}], 58.79 [\text{C3}], 65.10 [\text{C4}], 79.34 [\text{C4}], 97.23 [\text{C2}], 169.62 [\text{CH}_3\text{CO}], 174.14 [\text{EtCO}]; LRMS (CI-NH\text{3}): m/e 250 ([M + NH\text{4}^+] , 100%), 233 ([MH\text{+}], 1.5%), 173 ([MH\text{+} - \text{AcOH}], 49.5%); HRMS (CI-NH\text{3}): m/e calcd. for C\text{10}H\text{12}N\text{O}_6 [M + NH\text{4}^+], 250.1291; found, 250.1290.
Oxetane (75a).

Oxetane 75a was obtained from photo-adduct 72a in 41% yield by a procedure similar to that used for the transformation of photo-adduct 44a to oxetane 47c. \(^{1}H\)-NMR (200 MHz, CDCl\(_3\)): \(\delta\) 1.15 (t, 3H, CH\(_{3}\)CH\(_2\)), 2.11 (s, 3H, Ac), 2.39 (q, 2H, CH\(_{3}\)CH\(_2\)), 3.44 (dddd, 1H, H\(_3\)), 3.89 (s, 3H, MeO), 4.19 (A of ABX, 1H, H\(_4'\)), 4.34 (B of ABX, 1H, H\(_4''\)), 4.55 (A of ABX, 1H, H\(_3'\)), 4.60 (B of ABX, 1H, H\(_3''\)), 4.82 (ddd, 1H, H\(_4\)), 6.46 (d, 1H, H2), J\(_{1\text{H}2-H\text{H}3} = 5.9\) Hz, J\(_{\text{H}3-\text{H}3'} = 7.3\) Hz, J\(_{\text{H}3'-\text{H}3''} = -11.6\) Hz, J\(_{\text{H}4-H\text{H}4\text{a}} = 6.2\) Hz, J\(_{\text{H}4\text{a}-\text{H}4\text{b}} = 4.3\) Hz, J\(_{\text{H}4\text{b}-\text{H}4\text{a}} = 3.3\) Hz, J\(_{\text{H}3-\text{H}3'} = -11.6\) Hz, J\(_{\text{H}3'-\text{H}3''} = 7.5\) Hz; \(^{13}\)C-NMR (75.4 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 9.05 [CH\(_{3}\)CH\(_2\)], 20.92 [CH\(_3\)CO], 27.48 [CH\(_3\)CH\(_2\)], 39.67 [C\(_3\)], 53.75 [MeO], 63.00 [C\(_3'\)], 64.86 [C\(_4'\)], 79.62 [C4], 95.96 [C2], 157.56, 158.00 [OCOCOOMe], 169.58 [CH\(_3\)CO], 174.09 [EtCO]; LRMS (Cl-NH\(_3\)): m/e 336 ([M + NH\(_4^+\)], 56.8%), 259 ([MH\(^+\) - AcOH], 25.8%); HRMS (Cl-NH\(_3\)): m/e calcd. for C\(_{13}\)H\(_{22}\)NO\(_6\) [M + NH\(_4^+\)], 336.1296; found, 336.1294.

Oxetane (75b).

To a solution of alcohol 74 (70 mg, 0.30 mmol) in dry methylene chloride (5 mL) under an atmosphere of nitrogen at 0°C was added N,N-dimethylaminopyridine (7 mg, 0.06 mmol), pyridine (170 \(\mu\)L, 2.10 mmol) and phenyl chlorothioformate (124 \(\mu\)L, 0.60 mmol). The solution was gradually warmed to room temperature (over 1 h) and allowed to stir for 16 h. The reaction mixture was then diluted with methylene chloride (20 mL), washed with 5% hydrochloric acid (25 mL), saturated aqueous sodium bicarbonate (25 mL), brine (25 mL), dried (Na\(_2\)SO\(_4\)), filtered and the solvent removed in vacuo to yield a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) afforded the title compound (24 mg, 35% yield) as a light yellow oil. \(^{1}H\)-NMR (200 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 1.16 (t, 3H, CH\(_{3}\)CH\(_2\)), 2.14 (s, 3H, Ac), 2.43 (q, 2H, CH\(_3\)CH\(_2\)), 3.59 (ddd, 1H, H3), 4.22 (A of ABX, 1H, H4').
4.37 (B of ABX, 1H, H4''), 4.80 (A of ABX, 1H, H3''), 4.85 (ddd, 1H, H4), 4.88 (B of ABX, 1H, H3'b'), 6.47 (d, 1H, H2), 7.08 - 7.14 (m, 2H, Ph), 7.27 - 7.49 (m, 3H, Ph), J_{1H-1H} = 5.9 Hz, J_{1H-1H} = 7.1 Hz, J_{1H-1H} = 7.5 Hz, J_{1H-1H} = -11.3 Hz, J_{1H-1H} = 6.7 Hz, J_{1H-1H} = 4.5 Hz, J_{1H-1H} = 3.2 Hz, J_{1H-1H} = -12.6 Hz, J_{1H-1H} = 7.5 Hz; LRMS (CI-NH3): m/e 386 ([M + NH4^+] , 13.3%), 369 ([MH^+] , 4.9%), 259 ([MH^+ - AcOH], 100%); HRMS (CI-NH3): m/e calcd. for C_{17}H_{21}O_7S [MH^+], 369.1007; found, 369.1008.

Oxetane (7Sc).

A solution of alcohol 74 (70 mg, 0.30 mmol) and N,N'-thiocarbonyldiimidazole (80 mg, 0.45 mmol) in dry methylene chloride (5 mL) was refluxed under an atmosphere of nitrogen for 2 h. Evaporation of the solvent in vacuo gave a yellow residue which was chromatographed over silica gel (petroleum ether / ethyl acetate, 1:1 v/v) to afford the title compound (69 mg, 67% yield) as a light yellow oil. \( ^1{H}-\text{NMR} (200 MHz, CD_2Cl_2) \): \( \delta \) 1.14 (t, 3H, CH_3CH_2), 2.09 (s, 3H, Ac), 2.40 (q, 2H, CH_3CH_2), 3.60 (dddd, 1H, H3), 4.25 (A of ABX, 1H, H4''), 4.36 (B of ABX, 1H, H4'b), 4.87 (ddd, 1H, H4), 4.92 (A of ABX, 1H, H3''), 4.98 (B of ABX, 1H, H3'b'), 6.49 (d, 1H, H2), 7.02, 7.63 (2d, 2H, N-CH=CH-N), 8.31 (s, 1H, N-CH=N), J_{1H-1H} = 5.9 Hz, J_{1H-1H} = 6.6 Hz, J_{1H-1H} = 7.5 Hz, J_{1H-1H} = -11.5 Hz, J_{N-CH=CH-N} = 1.3 Hz, J_{1H-1H} = 5.7 Hz, J_{1H-1H} = 4.3 Hz, J_{1H-1H} = 3.3 Hz, J_{1H-1H} = -12.7 Hz, J_{1H-1H} = 7.6 Hz; LRMS (CI-NH3): m/e 343 ([MH^+] , 38.8%), 292 ([MH^+ - AcOH], 100%); HRMS (CI-NH3): m/e calcd. for C_{14}H_{19}N_2O_6S [MH^+], 343.0965; found, 343.0963.

Oxetane (7Sd).

Oxetane 7Sd (38 mg, 0.11 mol) was dissolved in anhydrous methanol (10 mL) and allowed to stir for 24 h under an atmosphere of nitrogen at room temperature. Evaporation of the solvent in vacuo gave a yellow residue which was chromatographed over silica gel (petroleum ether / ethyl acetate, 2:1 v/v) to afford the title compound (23 mg, 68% yield) as a clear oil. \( ^1{H}-\text{NMR} (200 MHz, CD_2Cl_2) \): \( \delta \) 1.14 (t, 3H, CH_3CH_2), 2.11 (s, 3H, Ac), 2.40 (q, 2H, CH_3CH_2), 3.50 (dddd, 1H, H3), 4.04 (s, 3H, MeO), 4.19 (A of ABX, 1H, H4'''), 4.34 (B of ABX, 1H, H4'b), 4.70 (A of ABX, 1H, H3'''), 4.78 (B of ABX, 1H, H3'b'), 4.81 (ddd, 1H, H4), 6.43 (d, 1H, H2), J_{1H-1H} = 5.9 Hz, J_{1H-1H} = 7.2 Hz, J_{1H-1H} = 7.4 Hz, J_{1H-1H} = -11.3 Hz, J_{1H-1H} = 6.1 Hz, J_{1H-1H} = 4.5 Hz, J_{1H-1H} = 3.3 Hz, J_{1H-1H} = -12.6 Hz, J_{1H-1H} = 7.5 Hz; LRMS (CI-NH3): m/e 324 ([M + NH4^+] , 42.3%), 307 ([MH^+] , 10.3%), 247 ([MH^+ - AcOH], 100%); HRMS (CI-NH3): m/e calcd. for C_{12}H_{19}O_7S [MH^+], 307.0852; found, 307.0851.

Oxetane (7Se).

To a stirred solution of alcohol 74 (696 mg, 3.00 mmol) in dimethyl sulfoxide (9.8 mL) under an atmosphere of nitrogen at room temperature was added acetic acid (2.0 mL) and acetic anhydride (6.4
mL}. After stirring for 24 h, the reaction mixture was poured into 10% aqueous sodium carbonate (500 mL) and extracted with methylene chloride (3 x 350 mL). The combined extracts were washed with water (1 L), brine (1 L), dried (Na₂SO₄), filtered and the solvent evaporated in vacuo to afford a yellow residue.

Purification by flash chromatography (petroleum ether / ethyl acetate, 3:1 v/v) gave the title compound (280 mg, 32% yield) as a clear oil.

**Oxetane (75f).**

To a solution of oxetane 7Se (64 mg, 0.22 mmol) in methanol (0.5 mL) was added a solution of sodium periodate (51 mg, 0.23 mmol) in water (0.5 mL), and it was stirred for 18 h at room temperature. After filtration of the inorganic precipitates, the filtrate was diluted with methylene chloride (50 mL) and dried (Na₂SO₄). Evaporation of the solvent under reduced pressure yielded a light yellow oil which was chromatographed over silica gel (ethyl acetate / hexanes / methanol, 5:3:1 v/v/v) to afford 7Se (mixture of 2 inseparable diastereomers, 1:1), (52 mg, 77% yield) as a clear oil. **{1H-NMR (200 MHz, CDCl₃): δ 1.12 (t, 3H, CH₃CH₂), 2.09 (s, 3H, Ac), 2.36 (q, 2H, CH₂CH₂), 2.52 (s, 3H, CH₃SO), 3.31 (m, 1H, H3), 3.97 - 4.50 (m, 6H, H₃ₐ, H₃ₐ, H₃₉, H₄ₐ, H₄ₐ, H₄₉), 4.73 (m, 1H, H4), 6.39, 6.40 (2d, 1H, H2), J_H2-H3 = 5.9 Hz, J_H3-H₃ₐ = 6.2 Hz, J_H₃ₐ-H₄ₐ = 6.0 Hz, J_H₄ₐ-H₄₉ = 7.6 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 8.97 [CH₃CH₂], 20.96 [CH₃SO], 23.73 [CH₃CH₂], 34.67, 34.77 [CH₃SO], 40.37 [C₃], 64.87, 64.92 [C₃’], 70.14, 70.17 [C₄’], 79.56, 79.60 [C₄’], 87.68, 87.82 [OCH₃SO], 95.97, 96.03 [t, J = 169.35, 169.38 [CH₃CO], 174.03 [CH₃CO]; LRMS (Cl-NH₃): m/e 310 ([M + NH₄⁺], 100%), 293 ([MH⁺], 9.3%), 233 ([MH⁺ - AcOH], 26.0%); HRMS (Cl-NH₃): m/e calcd. for C₁₂H₂₁O₇S [MH⁺], 309.1057; found, 309.1058).**

**Oxetane (75g).**

To a solution of oxetane 7Se (58 mg, 0.20 mmol) in methanol (0.5 mL) was added a solution of sodium periodate (94 mg, 0.44 mmol) in water (0.5 mL), and it was stirred for 18 h at room temperature. After filtration of the inorganic precipitates, the filtrate was diluted with methylene chloride (50 mL) and dried (Na₂SO₄). Evaporation of the solvent under reduced pressure yielded a light yellow oil which was chromatographed over silica gel (hexanes / ethyl acetate, 1:1 v/v) to afford 7Sg (60 mg, 93% yield) as a
clear oil. \(^{1}\text{H-NMR} (200 \text{ MHz, CDCl}_3): \delta \text{ 1.15 (t, 3H, CH}_3\text{CH}_2, 2.09 \text{ (s, 3H, Ac), 2.39 (q, 2H, CH}_3\text{CH}_2), 2.88 \text{ (s, 3H, CH}_2\text{SO}_2), 3.32 \text{ (ddddd, 1H, H3), 4.13 \text{ (A of ABX, 1H, H4'}^\text{a}, 4.20 \text{ (A of ABX, 1H, H3'}^\text{a}, 4.23 \text{ (B of ABX, 1H, H3'}^\text{b}, 4.34 \text{ (B of ABX, 1H, H4'}^\text{b}, 4.45 \text{ (s, 2H, OCH}_2\text{S}), 4.76 \text{ (dddd, 1H, H4), 6.44 \text{ (d, 1H, H2), J}_{H2-H3} = 5.9 \text{ Hz, J}_{H3-H3'}^\text{a} = 4.6 \text{ Hz, J}_{H3-H3'}^\text{b} = -8.5 \text{ Hz, J}_{H3-H3'}^\text{b} = 6.0 \text{ Hz, J}_{H4-H4'}^\text{a} = 7.2 \text{ Hz, J}_{H4-H4'}^\text{b} = -12.6 \text{ Hz, J}_{CH_2-CH_2} = 7.5 \text{ Hz; LRMS (Cl-NH}_3): m/e 342 (M + NH}_4^+, \text{ 100%), 325 ([MH}^+], 0.6%); HRMS (Cl-NH}_3): m/e \text{ calcd. for C}_{12}\text{H}_{24}\text{NO}_8\text{S [M + NH}_4^+, 342.1222; found, 342.1222).}}

**Oxetane (75b).**

To a stirred solution of alcohol 74 (116 mg, 0.50 mmol) and guaiacol (186 mg, 1.50 mmol) in dry tetrahydrofuran (2.5 mL) under nitrogen at ambient temperature was added triphenylphosphine (170 mg, 0.65 mmol) and diethyl azodicarboxylate (108 mg, 0.65 mmol). The mixture was then refluxed for 3 h. Evaporation of the solvent in vacuo gave a white solid which was chromatographed over silica gel (petroleum ether / ethyl acetate, 100:1) to afford 75b (90 mg, 53% yield) as a clear oil. \(^{1}\text{H-NMR} (200 \text{ MHz, CDCl}_3): \delta \text{ 1.14 (t, 3H, CH}_3\text{CH}_2), 1.92 \text{ (m, 4H, CH}_2\text{CH}_2\text{N), 2.12 \text{ (s, 3H, Ac), 2.39 (q, 2H, CH}_3\text{CH}_2), 3.56 \text{ (dddd, 1H, H3), 3.81 (s, 3H, MeO), 4.21 \text{ (A of ABX, 1H, H4'}^\text{a}, 4.27 \text{ (A of ABX, 1H, H3'}^\text{a}, 4.33 \text{ (B of ABX, 1H, H3'}^\text{b}, 4.38 \text{ (B of ABX, 1H, H4'}^\text{b}, 4.86 \text{ (dddd, 1H, H4), 6.51 (d, 1H, H2), 6.85 - 7.01 (m, 4H, Ph), J}_{H2-H3} = 5.9 \text{ Hz, J}_{H3-H3'}^\text{a} = 8.5 \text{ Hz, J}_{H3-H3'}^\text{b} = 2.0 \text{ Hz, J}_{H3-H3'}^\text{b} = -9.9 \text{ Hz, J}_{H3-H4} = 6.2 \text{ Hz, J}_{H4-H4'}^\text{a} = 4.8 \text{ Hz, J}_{H4-H4'}^\text{b} = 2.7 \text{ Hz, J}_{H4-H4'}^\text{b} = -12.6 \text{ Hz, J}_{CH_2-CH_2} = 7.6 \text{ Hz; LRMS (Cl-NH}_3): m/e 356 ([M + NH}_4^+, 100%), 339 ([MH}^+], 0.5%); 279 ([MH}^+ - AcOH], 3.8%); HRMS (Cl-NH}_3): m/e \text{ calcd. for C}_{17}\text{H}_{23}\text{O}_7\text{S [MW], 339.1444; found, 339.1443).}}

**Oxetane (75i).**

To a stirred solution of alcohol 74 (70 mg, 0.30 mmol) and acid 78 (43 mg, 0.30 mmol) in dry methylene chloride (2 mL) under an atmosphere of nitrogen at ambient temperature was added N,N-dimethylaminopyridine (37 mg, 0.30 mmol) and N,N'-dicyclohexylcarbodiimide (74 mg, 0.36 mmol). After 18 h, the solvent was removed in vacuo to yield a yellow residue which was chromatographed over silica gel (petroleum ether / ethyl acetate, 1:1) affording 75i (28 mg, 26% yield) as a white solid. \(^{1}\text{H-NMR} (200 \text{ MHz, CDCl}_3): \delta \text{ 1.14 (t, 3H, CH}_3\text{CH}_2), 1.92 \text{ (m, 4H, CH}_2\text{CH}_2\text{N), 2.12 (s, 3H, Ac), 2.38 (q, 2H, CH}_3\text{CH}_2), 3.44 (ddddd, 1H, H3), 3.49 (t, 2H, CH}_2\text{CH}_2\text{N), 3.58 (t, 2H, CH}_2\text{CH}_2\text{N), 4.18 \text{ (A of ABX, 1H, H4'}^\text{a}, 4.34 \text{ (B of ABX, 1H, H4'}^\text{b}, 4.50 \text{ (A of ABX, 1H, H3'}^\text{a}, 4.58 \text{ (B of ABX, 1H, H3'}^\text{b}, 4.82 \text{ (dddd, 1H, H4), 6.45 (d, 1H, H2), J}_{H2-H3} = 5.9 \text{ Hz, J}_{H3-H3'}^\text{a} = 7.6 \text{ Hz, J}_{H3-H3'}^\text{b} = 7.3 \text{ Hz, J}_{H3-H4} = -11.6 \text{ Hz, J}_{NCH_2CH_2} = 6.5 \text{ Hz, J}_{NCH_2CH_2} = 6.8 \text{ Hz, J}_{CH_2CH_2} = 5.4 \text{ Hz, J}_{H3-H4} = 6.0 \text{ Hz, J}_{H4-H4'}^\text{a} = 4.5 \text{ Hz, J}_{H4-H4'}^\text{b} = 3.2 \text{ Hz, J}_{H4'-H4'}^\text{b} = -12.7 \text{ Hz, J}_{CH_2CH_2} = 7.6 \text{ Hz; }^{13}\text{C-NMR (75i MHz, CDCl}_3): \delta 9.12 \text{ [CH}_3\text{CH}_2), 21.08 \text{ [CH}_3\text{CO), 24.18, 26.22 \text{ [CH}_2\text{CH}_2\text{N), 27.56 \text{ [CH}_3\text{CH}_2), 39.72 \text{ [C3), 46.26, 4757 [CH}_2\text{CH}_2\text{N),}}

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Oxetane (75j).

To a stirred solution of alcohol 74 (70 mg, 0.30 mmol) and pyrrolidine hydrochloride (43 mg, 0.40 mmol) in dry tetrahydrofuran (10 mL) under an atmosphere of nitrogen at ambient temperature was added triphenylphosphine (79 mg, 0.30 mmol) and diethyl azodicarboxylate (47 mg, 0.30 mmol). After 3 days, the solvent was removed in vacuo to give a white solid which was chromatographed over silica gel (petroleum ether / ethyl acetate, 4:1) affording 75j (36 mg, 48% yield) as a clear oil. \( ^1H\)-NMR (200 MHz, CD\(_2\)Cl\(_2\)): \( \delta \) 1.15 (t, 3H, CH\(_3\)CH\(_2\)), 2.13 (s, 3H, Ac), 2.39 (q, 2H, CH\(_3\)CH\(_2\)), 3.38 (ddd, 1H, H\(_3\)), 3.75 (s, 1H, H\(_3\)'s), 3.79 (d, 1H, H\(_3\)'b), 4.19 (A of ABX, 1H, H\(_4\)'s), 4.37 (B of ABX, 1H, H\(_4\)'b), 4.76 (ddd, 1H, H\(_4\)), 6.43 (d, 1H, H\(_2\)), \( J_{H_2-H_3} = 5.8 \text{ Hz} \), \( J_{H_3-H_3'b} = 2.4 \text{ Hz} \), \( J_{H_3-H_4} = 5.9 \text{ Hz} \), \( J_{H_4-H_4'a} = 4.5 \text{ Hz} \), \( J_{H_4-H_4'b} = 3.0 \text{ Hz} \), \( J_{H_4'a-H_4'b} = -12.7 \text{ Hz} \), \( J_{\text{CH}_3-\text{CH}_2} = 7.5 \text{ Hz} \); \( ^13\text{C}-\text{NMR} \) (75.4 MHz, CD\(_2\)Cl\(_2\)): \( \delta \) 9.20 (CH\(_3\)CH\(_2\)), 21.14 (CH\(_3\)CO), 27.70 (CH\(_3\)CH\(_2\)), 40.75 (C\(_3\)), 43.05 (C\(_3\)), 65.10 (C\(_2\)), 81.39 (C\(_2\)), 169.69 (CH\(_3\)CO), 174.23 (EtCO); LRMS (Cl-NH\(_3\)): m/e 375 ([M + NH\(_4^+\]), 25.4%), 358 ([MH\(^+\)], 100%), 298 ([MH\(^+\) - AcOH], 90.7%); HRMS (Cl-NH\(_3\)): m/e calcd. for C\(_{16}\)H\(_{24}\)NO\(_5\) [MH\(^+\)], 358.1502; found, 358.1501.

Nucleoside (76b).

Nucleoside 76b was obtained in 65% yield from oxetane 75e by a procedure similar to that used for the preparation of nucleoside 48a. \( ^1H\)-NMR (200 MHz, CD\(_2\)Cl\(_2\)): \( \delta \) 1.15 (t, 3H, CH\(_3\)CH\(_2\)), 2.19 (s, 3H, CH\(_3\)S), 2.33 (q, 2H, CH\(_3\)CH\(_2\)), 3.13 (ddt, 1H, H\(_2\)'), 3.86 (d, 2H, H\(_2\)'a, H\(_2\)'b), 4.26 (A of ABX, 1H, H\(_3\)'a), 4.34 (B of ABX, 1H, H\(_3\)'b), 4.63 (ddd, 1H, H\(_3\)'), 4.72 (s, 2H, OCH\(_2\)S), 6.33 (d, 1H, H\(_8\)'), 7.50 - 7.67 (m, 3H, Ph), 7.99 - 8.03 (m, 2H, Ph), 8.31 (s, 1H, H\(_8\)), 8.73 (s, 1H, H\(_2\)), 8.67 (s, br, ex, 1H, NH), \( J_{\text{H_1'-H_2} = 3.6 \text{ Hz} \), \( J_{\text{H2'-H2'aH2''b} = 5.6 \text{ Hz} \), \( J_{\text{H2'-H3} = 1.9 \text{ Hz} \), \( J_{\text{H3'-H3'a} = 2.1 \text{ Hz} \), \( J_{\text{H3'-H3'b} = 4.9 \text{ Hz} \), \( J_{\text{H3'a-H3'b} = -10.6 \text{ Hz} \), \( J_{\text{CH}_3-\text{CH}_2 = 7.6 \text{ Hz} \).}

Methyl Oxalyl Pyrrolidinamide (77).

Pyrrolidine (3.56 g, 50.2 mmol) was dissolved in dry ether (250 mL). Methyl oxalyl chloride (2.30 mL, 25.1 mmol) was then added dropwise, and the reaction was stirred at room temperature under
an atmosphere of nitrogen. After 2 h, the reaction was washed with 5% hydrochloric acid (200 mL), saturated aqueous sodium bicarbonate (200 mL), brine (200 mL), dried (Na₂SO₄), filtered and the solvent removed under reduced pressure to yield a light yellow residue. Purification by flash chromatography (ethyl acetate) gave the title compound (3.75 g, 95% yield) as a white solid. \( ^{1}H\)-NMR (200 MHz, CDCl₃): \( \delta \) 1.90 (m, 4H, CH₂CH₂N), 3.51 (t, 2H, CH₂N), 3.61 (t, 2H, CH₂N), 3.83 (s, 3H, MeO); J CH₂. CH₂N = 6.5 Hz, J CH₂-CH₂N = 6.7 Hz; \( ^{13}C\)-NMR (75.4 MHz, CDCl₃): \( \delta \) 23.56, 25.69 [CH₂CH₂N], 44.58, 47.19 [CH₂N], 52.32 [MeO], 157.96, 162.27 [CO]; LRMS (EI): m/e 157 ([M⁺], 48.9%), 98 ([M⁺ - COOMe], 100%); IR (CH₂Cl₂): 1651 cm⁻¹ [NCO], 1741 cm⁻¹ [COOMe]).

Pyrrolidine Oxamic acid (78).

To a stirred solution of 77 (419 mg, 2.67 mmol) in methanol (100 mL) and water (50 mL) at room temperature was added potassium carbonate (738 mg, 5.34 mmol). After 1 h, the solution was adjusted to pH 2.5 with 5% hydrochloric acid and evaporated to dryness. The residue was dissolved in methylene chloride (100 mL), washed with water (100 mL), brine (100 mL), dried (Na₂SO₄), filtered and the solvent removed in vacuo to yield essentially pure 78 (362 mg, 95% yield) as a white solid. \( ^{1}H\)-NMR (200 MHz, CDCl₃): \( \delta \) 1.94 (m, 4H, CH₂CH₂N), 3.56 (t, 2H, CH₂N), 3.94 (t, 2H, CH₂N), 6.70 (s, br, ex, 1H, OH), J CH₂-CH₂N = 6.6 Hz, J CH₂CH₂N = 6.6 Hz; \( ^{13}C\)-NMR (75.4 MHz, CDCl₃): \( \delta \) 23.94, 26.81 [CH₂CH₂N], 48.52, 49.47 [CH₃], 157.32, 159.89 [CO]; LRMS (Cl-NH₃): m/e 161 ([M + NH₄⁺], 38.5%), 144 ([MH⁺], 52.4%); IR (CH₂Cl₂): 1654 cm⁻¹ [NCO], 1783 cm⁻¹ [COOMe]).

Diisopropyl Fumarate (79)

Fumaric acid (29.02 g, 250.0 mmol) was dissolved in dry isopropyl alcohol (600 mL). Chlorotrimethylsilane (140 mL, 1.1 mol) was then added dropwise, and the reaction was stirred at room temperature under an atmosphere of nitrogen for 3 days. Evaporation to dryness gave a thick residue which was chromatographed over silica gel (petroleum ether / ethyl acetate, 10:1 v/v) to afford the title compound (48.03 g, 96% yield) as a clear oil. \( ^{1}H\)-NMR (200 MHz, CDCl₃): \( \delta \) 1.26 (d, 6H, Me₂CH), 5.08 (h, 1H, Me₂CH), 6.78 (s, 1H, =HCO), J CH=Me = 6.3 Hz).
i-Propyl Glyoxylate (80).

To a stirred solution of diisopropyl L-tartrate (23.43 g, 100.0 mmol) in dry ether (500 mL) cooled to 5°C was added periodic acid (22.79 g, 100.0 mmol) in portions over 1 h under an atmosphere of nitrogen. The milky reaction mixture was stirred for 1 h until the solution became clear and a white solid separated. The solid was filtered off and the filtrate was dried with sodium sulfate. Evaporation of the solvent in vacuo afforded the title compound (11.02 g, 95% yield) as a clear oil. The 1H-NMR spectrum indicated that the aldehyde exists largely in a polymeric form and only a small amount of free aldehyde was present.

\[ \text{i-PrOOC} \]

3-Methyl-6β-i-propylformyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (81).

A mixture of 2-methylfuran (7.4 mL, 82 mmol) and i-propyl glyoxylate (2.38 g, 20.5 mmol) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with argon. The solution was then irradiated for 25 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (hexanes / ethyl acetate, 10:1 v/v) gave 81 (700 mg, 17% yield) as a light yellow oil. \{1H-NMR (200 MHz, CDCl₃): δ 1.28 (d, 6H, Me₂CH), 1.94 (dd, 3H, Me), 3.69 (dddd, 1H, H5), 4.80 (d, 1H, H6), 5.01 (dd, 1H, H4), 5.11 (h7, 1H, Me₂CH), 6.41 (d, 1H, H1); J_H1-H5 = 4.3 Hz, J_H4-Me = -1.3 Hz, J_H4-H5 = 2.6 Hz, J_H5-Me = 1.4 Hz, J_H5-H6 = 3.1 Hz, J_Ch-Me₂ = 6.3 Hz; \} 13C-NMR (50.3 MHz, CDCl₃): δ 13.56 [Me], 21.46, 21.64 [Me₂CH], 50.35 [C5], 69.10 [Me₂CH], 86.59 [C6], 98.30 [C4], 159.24 [C3], 170.73 [CO]; LRMS (CI-NH₃): m/e 216 ([M + NH₄⁺], 16.7%), 199 ([MH⁺], 35.3%), 181 ([MH⁺ - H₂O], 80.4%); HRMS (CI-NH₃): m/e calcd. for C₁₀H₁₄O₄ [MH⁺], 199.0971; found, 199.0970. Anal. calcd. for C₁₀H₁₄O₄: C, 60.59; H, 7.12. Found: C, 60.84; H, 6.86.

\[ \text{i-PrOOC} \]

2α-Acetoxy-3α-formyl-4β-i-propylformyl oxetane (82).

Photo-adduct 81 was transformed to aldehyde 82 in 90% yield by a procedure similar to that used for the preparation of aldehyde 45. \{1H-NMR (200 MHz, CD₂Cl₂): δ 1.26 (d, 3H, CH₃CH), 1.28 (d, 3H, CH₃CH), 2.09 (s, 3H, Ac), 4.07 (ddd, 1H, H3), 5.09 (m, 1H, Me₂CH), 5.38 (d, 1H, H4), 6.66 (d, 1H, H2), 9.75 (d, 1H, CHO), J_H2-H3 = 6.4 Hz, J_H3-CHO = 1.2 Hz, J_H3-H4 = 6.2 Hz, J_Ch-Me = 6.2 Hz, J_Ch-Me₂ = 6.0 Hz; LRMS (CI-NH₃): m/e 248 ([M + NH₄⁺], 100%), 231 ([MH⁺], 0.2%), 171 ([MH⁺ - AcOH], 0.6%); HRMS (CI-NH₃): m/e calcd. for C₁₀H₁₅O₆ [MH⁺], 231.0868; found, 231.0868.\}
2α-Acetoxy-3α-hydroxymethyl-4β-i-propoxyformyl oxetane (83).

Aldehyde 82 was reduced to alcohol 83 in 62% yield by a procedure similar to that used for the preparation of alcohol 46. \( ^1H-NMR (200 \text{ MHz, } CD_2Cl_2) \): \( \delta \) 0.89 (s, br, ex, 1H, OH), 1.25 (d, 3H, CH₃CH), 1.28 (d, 3H, CH₃CH'), 2.13 (s, 3H, Ac), 3.27 (m, 1H, H3), 3.89 (m, 2H, H3', H3''), 4.90 (d, 1H, H4), 5.08 (m, 1H, Me₂CH), 6.52 (d, 1H, H2), \( J_{H2-H3} = 5.2 \text{ Hz}, J_{H3-H4} = 6.3 \text{ Hz} \), \( J_{CH-Me} = 6.3 \text{ Hz} \), \( J_{CH-Me} = 6.2 \text{ Hz} \); LRMS (Cl-NH₃): m/e 250 ([M + NH₄⁺], 70.8%), 233 ([MH⁺], 8.8%), 173 ([MH⁺ - AcOH], 3.4%); HRMS (Cl-NH₃): m/e calcd. for C₁₀H₁₇O₆ [MH⁺], 233.1026; found, 231.1025.

Oxetane (84).

Oxetane 84 was obtained from photo-adduct 81 in 39% yield by a procedure similar to that used for the transformation of photo-adduct 44a to oxetane 47c. \( ^1H-NMR (200 \text{ MHz, } CDCl₃) \): \( \delta \) 1.25 (d, 3H, CH₃CH), 1.26 (d, 3H, CH₃CH'), 2.12 (s, 3H, Ac), 3.60 (ddt, 1H, H3), 3.89 (s, 3H, MeO), 4.63 (d, 2H, H3', H3''), 4.93 (d, 1H, H4), 5.11 (m, 1H, Me₂CH), 6.58 (d, 1H, H2), \( J_{H2-H3} = 5.9 \text{ Hz} \), \( J_{H3-H4} = 6.9 \text{ Hz} \), \( J_{CH-Me} = 6.2 \text{ Hz} \); \( ^13C-NMR (75.4 \text{ MHz, } CD₂Cl₂) \): \( \delta \) 21.06 [CH₃CO], 21.73 [(CH₃)₂CH], 42.20 [C3], 53.94 [CH₃O], 62.72 [C3'], 69.95 [(CH₃)₂CH'], 77.37 [C4], 96.50 [C2], 157.54, 157.99 [OCOCOOMe], 169.40, 169.63 [CO]; LRMS (Cl-NH₃): m/e 336 ([M + NH₄⁺], 100%), 319 ([MH⁺], 13%); HRMS (Cl-NH₃): m/e calcd. for C₁₃H₁₉O₉ [MH⁺], 319.1030; found, 319.1029.
Photo-adduct (85).

A mixture of furan (3.0 mL, 41.2 mmol) and R-glyceraldehyde acetonide (1.090 g, 8.38 mmol) in dry benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C and saturated with helium. The solution was then irradiated for 8 h. Evaporation under reduced pressure gave a yellow syrup which was chromatographed over silica gel (petroleum ether / ethyl acetate, 9:1 v/v) to afford the title compound (mixture of 2 inseparable diastereomers, 1:1), (415 mg, 25% yield) as a light yellow oil. ($^1$H-NMR (200 MHz, CDCl$_3$): $\delta$ 1.36, 1.40, 1.44, 1.47 (4s, 6H, CMe$_2$), 3.62 - 4.46 (m, 4H, H$_6$, H$_6'$, H$_6''$, H$_6'''$), 3.68 (m, 1H, H5), 5.32, 5.33 (2t, 1H, H4), 6.28 (m, 1H, H1), 6.61 (m, 1H, H3), J$_{H3-H4}$ = 2.9 Hz, J$_{H4-H5}$ = 2.9 Hz; $^{13}$C-NMR (75.4 MHz, CDCl$_3$): $\delta$ 25.11, 26.02, 26.21, 26.62 [CMe$_2$], 46.68 [C5], 64.49, 65.84 [C6], 76.95, 77.35 [C6'], 88.56, 90.49 [C6], 103.71, 103.87 [C4], 108.36, 108.65 [C1], 109.76, 109.84 [CMe$_2$], 148.54 [C3]).

$\beta$-Acetoxyacetaldehyde (86).

2-Acetoxyacetaldehyde was obtained from allyl acetate in 38% yield by a procedure similar to that used for the preparation of aldehyde 20. ($^1$H-NMR (200 MHz, CDCl$_3$): $\delta$ 2.05 (s, 3H, Ac), 4.55 (d, 2H, CH$_2$), 9.47 (t, 1H, CHO), J$_{CH2-CHO}$ = 0.3 Hz; IR (CDCl$_3$): 1746 cm$^{-1}$, 1762 cm$^{-1}$, 2713 cm$^{-1}$, 2817 cm$^{-1}$).

6$\beta$-Hydroxymethyl-2,7-dioxo-bicyclo-[3,2,0]-hept-3-ene (88).

To a stirred solution of photo-adduct 2d (928 mg, 4.00 mmol) in methanol (100 mL) at room temperature was added aqueous sodium hydroxide (15% w/v, 10.7 mL, 40.1 mmol). After 30 min, the solution was neutralised with 0.1% hydrochloric acid, concentrated in vacuo, extracted with ether (5 x 100 mL). The ether extracts were dried (Na$_2$SO$_4$), filtered and the solvent removed under reduced pressure to yield a yellow oil. Purification by flash chromatography (petroleum ether / ethyl acetate, 1:1 v/v) afforded the title compound (403 mg, 79% yield) as a clear oil. ($^1$H-NMR (200 MHz, CDCl$_3$): $\delta$ 2.24 (s, br, ex, 1H, OH), 3.68 (ddd, 1H, H5), 3.73 (A of ABX, 1H, H6'), 3.82 (B of ABX, 1H, H6''), 4.64 (ddd, 1H, H6), 5.37 (t, 1H, H4), 6.30 (d, 1H, H1), 6.62 (dd, 1H, H3), J$_{H1-H5}$ = 4.3 Hz, J$_{H3-H4}$ = 2.9
Hz, $J_{113-115} = -1.1$ Hz, $J_{114-115} = 2.9$ Hz, $J_{115-116} = 3.0$ Hz, $J_{116-116a} = 3.4$ Hz, $J_{116-116b} = 2.8$ Hz, $J_{116a-116b} = 12.8$ Hz; LRMS (CI-NH$_3$): m/e 146 ([M + NH$_4^+$], 31.4%), 129 ([MH$^+$], 100%), 111 ([MH$^+$ - H$_2$O], 70.9%); HRMS (CI-NH$_3$): m/e calcd. for C$_6$H$_9$O$_3$ [MH$^+$], 129.0552; found, 129.0551.

6β-Acetoxymethyl-2,7-dioxa-bicyclo[3,2,0]hept-3-ene (87).

Alcohol 88 was acetylated in 72% yield by a procedure similar to that used for the preparation of 25a. [$^1$H-NMR (200 MHz, CDCl$_3$): δ 2.07 (s, 3H, Ac), 3.58 (dddd, 1H, H$_5$), 4.19 (A of ABX, 3H, H$_6$), 4.24 (8 of ABX, 1H, H$_6^a$), 4.63 (dddd, 1H, H$_6$), 5.33 (t, 1H, H$_4$), 6.24 (t, 3H, H$_1$), 6.59 (1H, H$_3$), $J_{H1-H5} = 4.3$ Hz, $J_{H1-116} = -0.8$ Hz, $J_{H13-H4} = 2.9$ Hz, $J_{H13-115} = -1.2$ Hz, $J_{H14-115} = 2.9$ Hz, $J_{115-116} = 3.2$ Hz, $J_{H16-116a} = 4.7$ Hz, $J_{116-116b} = 3.5$ Hz, $J_{116a-116b} = -12.3$ Hz; LRMS (CI-NH$_3$): m/e 188 ([M + NH$_4^+$], 24.0%), 171 ([MH$^+$], 1.1%), 153 ([MH$^+$ - H$_2$O], 100%); HRMS (CI-NH$_3$): m/e calcd. for C$_8$H$_{11}$O$_4$ [MH$^+$], 171.0656; found, 171.0657.

Enzyme-Catalyzed Hydrolysis of (2d).

Porcine pancreatic lipase (215 mg) was added to a stirred suspension of 2d (232 mg, 1.00 mmol) in phosphate buffer (10.0 mL, 10 mM, pH 7.00). Aliquots of a 0.1 N NaOH solution were added as required to maintain the pH of the mixture between 6.95 and 7.05. After 4.5 h, a total of of 500 mL of base solution had been added (50% conversion). The reaction mixture was extracted with ether (6 x 50 mL), and the combined extracts were washed with saturated aqueous sodium bicarbonate (200 mL) and brine (200 mL). The organic layer was dried (Na$_2$SO$_4$), filtered and the solvent removed in vacuo to give a yellow syrup which was chromatographed over silica gel (petroleum ether / ethyl acetate, 4:1 v/v, then 1:1 v/v) to afford the starting ester (46% yield) and alcohol (42% yield). Benzoylation of alcohol 88 via standard methods yielded benzoate +2d in 45% yield. -2d: [α]$^{20}_D$ = -15.5° (c = 3.21, CH$_2$Cl$_2$). +2d: [α]$^{20}_D$ = +18.8° (c = 1.25, CH$_2$Cl$_2$), respectively.

Enzyme-Catalyzed Hydrolysis of (44a).

Porcine pancreatic lipase (100 mg) was added to a stirred suspension of 44a (123 mg, 0.50 mmol) in phosphate buffer (10.0 mL, 10 mM, pH 7.00). Aliquots of a 0.1 N NaOH solution were added as required to maintain the pH of the mixture between 6.95 and 7.05. After 4.5 h, a total of of 2.50 mL of base solution had been added (50% conversion). The reaction mixture was extracted with ether (5 x 30 mL), and the combined extracts were washed with saturated aqueous sodium bicarbonate (100 mL).
brine (100 mL). The organic layer was dried (Na₂SO₄), filtered and the solvent removed in vacuo to give a yellow syrup which was a mixture of unreacted ester -44a and very small amounts of alcohol 52 (as indicated by ¹H-NMR). Purification by flash chromatography (petroleum ether / ethyl acetate, 6:1 v/v) afforded only the starting ester (36% yield). The enantiomerically enriched photo-adduct -44a was transformed to oxetane +47b by the method described earlier. +47b: [α]²⁰_D = -7.5° (c = 2.22, CHCl₃).
4.7 Experiments for Section 2.8.

3′α-Thymeryl-4′β-O-trimethylsilyl-6′β-benzoyloxymethyl-2′,7′-dioxo-bicyclo-[3,2,0]-heptane (89a)

To a stirred solution of epoxide 23d (263 mg, 1.06 mmol) in dry tetrahydrofuran (5 mL) at room temperature under an atmosphere of nitrogen was added bis-(trimethylsilyl)-thymine (860 mg, 3.18 mmol) and zinc chloride (1.0M solution in ether, 1.06 mL, 1.06 mmol). After 18 h, the reaction mixture was poured into cold saturated aqueous sodium bicarbonate (50 mL), extracted with methylene chloride (5 x 50 mL) and washed with brine (5 x 50 mL). The combined organic phases were then dried (Na₂SO₄), filtered and the solvent removed under reduced pressure to yield a clear syrup which was chromatographed over silica gel (methylene chloride / methanol, 100:1 v/v) affording nucleoside 89a (312 mg, 66% yield) as a white foam. (1H-NMR (200 MHz, CD₂Cl₂): δ 0.18 (s, 9H, Me₃Si), 1.92 (d, 3H, CH₃) at CS₂, 3.34 (t, 1H, H₅′), 4.35 (ddd, 1H, H₆′), 4.41 (A of ABX, 1H, H₆″), 4.52 (B of ABX, 1H, H₆″), 4.74 (s, 1H, H₄′), 5.94 (s, 1H, H₃′), 6.28 (d, 1H, H₁′), 7.43 - 7.65 (m, 3H, Ph), 7.95 (d, 1H, H₆), 8.02 - 8.08 (m, 2H, Ph), 9.69 (s, br, ex, 1H, NH), J₆″·₅″ = 4.1 Hz, J₅″·₄″ = 4.4 Hz, J₆″·₆″ = 3.4 Hz, J₅″·₆″ = -11.8 Hz, J₆·₆″ = -11.8 Hz, J₅·₅″ = -11.8 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ -0.12 ([CH₃]₃Si), 12.52 ([CH₃]₂Si), 50.97 [C5'], 65.15 [C6'], 76.76 [C6'], 78.11 [C4'], 99.02 [C3'], 109.47 [C5], 110.45 [C1'], 128.39, 129.52 and 133.32 [aromatic CH], 129.17 [aromatic C], 135.68 [C6], 151.00 [C2], 164.55 [C4], 165.96 [CO]; LRMS (CI·NH₃): m/e 464 ([M + NH₄⁺], 28.6%), 447 ([M⁺], 100%), 357 ([MH⁺ - Me₃SiOH], 78.9%); HRMS (Cl·NH₃): m/e calcd. for C₁₂H₂₇N₂O₇Si [MH⁺], 447.1589; found, 447.1587.

Epoxide 23d and bis-(trimethylsilyl)-cytosine afforded nucleoside 89b in 58% yield by a procedure similar to the one used for the preparation of nucleoside 89a. (1H-NMR (200 MHz, CDCl₃): δ 0.16 (s, 9H, Me₃Si), 3.25 (t, 1H, H₅′), 4.23 (ddd, 1H, H₆′), 4.38 (A of ABX, 1H, H₆″), 4.51 (B of ABX, 1H, H₆″), 4.74 (s, 1H, H₄′), 5.78 (d, 1H, H₅), 5.95 (s, 1H, H₃), 6.24 (d, 1H, H₁), 7.35 (s, br, ex, 2H, NH₂), 7.39 - 7.61 (m, 3H, Ph), 8.00 - 8.06 (m, 2H, Ph), 8.11 (d, 1H, H₆), J₆·₅″ = 4.3 Hz, J₅·₅″ = 4.0 Hz, J₆·₆″ = 3.8 Hz, J₅·₅″·₆″ = 3.9 Hz, J₆·₆″·₆‴ = -12.4 Hz, J₅·₆‴·₆″ = 7.6 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 0.07 ([CH₃]₃Si), 51.08 [C5'], 65.24 [C6'], 76.74 [C6'], 77.76 [C4'], 93.85 [C5], 99.85 [C3'], 142
3α-Methoxy-4β-hydroxy-6β-benzoyloxyethyl-2,7-dioxo-bicyclo[3,2,0]-heptane (24a').

Acetal 24a' was formed when epoxide 23d was subjected to flash chromatography using methylene chloride / methanol as eluent. ¹H-NMR (200 MHz, CDCl₃): δ 1.95 (d, ex, 1H, OH), 3.29 (t, 1H, H5), 3.48 (s, 3H, MeO), 4.37 (d, 1H, H4), 4.42 (A of ABX, 1H, H6α), 4.52 (B of ABX, 1H, H6β), 4.73 (ddd, 1H, H6), 5.25 (s, 1H, H3), 6.06 (d, 1H, H1), 7.44 - 7.65 (m, 3H, phenyl), 8.04 - 8.09 (m, 2H, phenyl), J₃H-H₅ = 4.1 Hz, J₁₄-OH = 5.0 Hz, J₁₅-H₆α = 4.3 Hz, J₁₆-H₆a = 3.1 Hz, J₁₆-H₆b = -12.4 Hz; LRMS (CI-NH₃): m/z 281 ([MW + NH₃]⁺, 10.9%), 249 ([MH - MeOH]⁺, 98.1%).

3α-Thyminyl-4β-hydroxy-6β-benzoyloxymethyl-2',7'-dioxa-bicyclo[3,2,0]-heptane (90a).

To a stirred solution of nucleoside 89a (322 mg, 0.722 mmol) in dry tetrahydrofuran (20 mL) at room temperature under an atmosphere of nitrogen was added tetra-n-butylammonium fluoride (1.0 M solution in tetrahydrofuran, 1.08 mL, 1.08 mmol). After 1 h, the solvent was removed in vacuo to yield a white solid which was chromatographed over silica gel (methylene chloride / methanol, 20:1 v/v) affording nucleoside 90a as a white solid (246 mg, 91% yield). ¹H-NMR (200 MHz, CDCl₃): δ 1.91 (d, 3H, CH₃ at C5), 3.29 (t, 1H, H5'), 3.48 (s, br, ex, 1H, OH), 4.33 (ddd, 1H, H6'), 4.46 (A of ABX, 1H, H6α), 4.57 (B of ABX, 1H, H6β), 5.92 (s, 1H, H3'), 6.27 (d, 1H, H1'), 7.41 - 7.63 (m, 3H, Ph), 7.92 (d, 1H, H6), 8.02 - 8.14 (m, 2H, Ph), 10.20 (s, br, ex, 1H, NH), J₁₅-H₁₅ = 4.1 Hz, J₁₅-H₆ = 4.2 Hz, J₁₆-H₆a = 4.1 Hz, J₁₆-H₆b = 3.8 Hz, J₁₆-H₆a-H₆b = -12.3 Hz, J₁₆-Me = -1.1 Hz; ¹³C-NMR (75.4 MHz, CDCl₃): δ 12.64 [CH₃ at C5], 49.61 [C5'], 65.08 [C6'], 77.53 [C6'], 78.89 [C4'], 100.02 [C3'], 110.50 [C5], 110.97 [C1'], 128.56, 129.72, 133.48 [aromatic CH], 129.35 [aromatic C], 135.71 [C6], 151.48 [C2], 164.55 [C4], 166.12 [PhCO]; LRMS (CI-NH₃): m/e 392 ([MH + NH₄⁺], 8.4%), 375 ([MH⁺, 100%), 357 ([MH⁺ - H₂O], 49.1%); HRMS (CI-NH₃): m/e calcd. for C₁₅H₁₉N₂O₇ [MH⁺], 375.1192; found, 375.1192.

3'α-Cytosinyl-4β-hydroxy-6β-benzoyloxymethyl-2',7'-dioxa-bicyclo[3,2,0]-heptane (90b).

Nucleoside 90b was obtained in 96% yield as a white foam by a procedure identical to the one described for the preparation of nucleoside 90a. ¹H-NMR (200 MHz, CD-OD): δ 3.41 (t, 1H, H5'), 4.34 (A of ABX, 1H, H6"a), 4.39 (ddd, 1H, H6'), 4.44 (B of ABX, 1H, H6"b), 4.65 (s, 1H, H4'), 5.88 (d, 1H, H5), 6.00 (s, 1H, H3'), 6.26 (d, 1H, H1), 7.47 - 7.68 (m, 3H, Ph), 8.04 - 8.10 (m, 2H, Ph), 8.24 (d, 1H,
H6), J_H1'-H5 = 4.4 Hz, J_H6'-H6' = 4.1 Hz, J_H6'-H6'b = 2.8 Hz, J_H6'b-H6'b = -12.5 Hz, J_H5.
H6 = 7.5 Hz; LRMS (Cl - NH3): m/e 377 ([M + NH4]+, 1.3%), 360 ([MH+], 100%), 249 ([MH+ -
cytosine], 20.2%); HRMS (Cl - NH3): m/e calcd. for C17H18N3O6 [MH+], 360.1196; found, 360.1195.

\[
\begin{align*}
\text{BzO} & \quad \text{O} \\
\text{HO} & \quad \text{\textbullet} \\
\text{\textbullet} & \quad \text{B}
\end{align*}
\]

90a, B = Thymine
90b, B = Cytosine

3'α-Thyminyl-4'β-hydroxy-6'β-hydroxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (91a).

An ice-cold solution of nucleoside 90a (381 mg, 1.02 mmol) in anhydrous methanol (20 mL)
was saturated with ammonia gas and allowed to warm to room temperature. After 20 h, the reaction
was heated to boiling for 0.5 h, allowed to cool and the solvent removed under reduced pressure to yield
a white solid which was washed repeatedly with ether. Recrystallization from methanol yielded bone
white crystals of nucleoside 91a (226 mg, 82% yield, m.p. 194-196°C). \(^{1}H\)-NMR (200 MHz,
CD\(_3\)OD): \(\delta\) 1.86 (d, 3H, CH\(_3\) at C5), 3.28 (t, 1H, H5'), 3.63 (A of ABX, 1H, H6''), 3.69 (8 of ABX, 1H,
H6''), 4.14 (ddd, 1H, H6'), 4.59 (s, 1H, H4'), 5.97 (s, 1H, H3'), 6.17 (d, 1H, H1'), 8.05 (d, 1H,
H6), J_H1'-H5 = 4.2 Hz, J_H5'-H6 = 4.4 Hz, J_H6'-H6'' = 3.8 Hz, J_H6''-H6'' = 3.2 Hz, J_H6'ax-H6'b = -12.6 Hz, J_H16-Me = -1.2 Hz; \(^{13}C\)-NMR (75.4 MHz, CD\(_3\)OD): \(\delta\) 13.57 [CH\(_3\) at C5], 51.42 [C5'], 65.22 [C6'], 80.06 [C6'], 82.63 [C4'],
101.48 [C3'], 110.92 [C5], 112.86 [C1'], 138.38 [C6'], 153.42 [C2], 167.46 [C4]; LRMS (Cl-NH3): m/e
271 ([MH+], 100%), 253 ([MH+ - H\(_2\)O], 7.7%); HRMS (Cl-NH\(_3\)): m/e calcd. for C\(_{11}\)H\(_{15}\)N\(_2\)O\(_6\) [MH+],
271.0931; found, 271.0930). Anal. calcd. for C\(_{11}\)H\(_{14}\)N\(_2\)O\(_6\): C, 48.89; H, 5.22; N, 10.37, found: C, 48.52;
H, 5.49; N, 10.46.

\[
\begin{align*}
\text{HO} & \quad \text{O} \\
\text{HO} & \quad \text{\textbullet} \\
\text{\textbullet} & \quad \text{B}
\end{align*}
\]

91a, B = Thymine
91b, B = Cytosine

3'α-Cytosinyl-4'β-hydroxy-6'β-hydroxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (91b).

Nucleoside 91b was obtained in 77% yield as a white powder by a procedure identical to the one
described for the preparation of nucleoside 91a. \(^{1}H\)-NMR (200 MHz, CD\(_3\)OD): \(\delta\) 3.24 (t, 1H,
H5'), 3.67 (A of ABX, 1H, H6''), 3.69 (B of ABX, 1H, H6''), 4.52 (s, 1H, H4'), 5.83 (d, 1H,
H5), 5.94 (s, 1H, H3'), 6.13 (d, 1H, H1'), 8.21 (d, 1H, H6), J_H1'-H5 = 4.1 Hz, J_H5'-H6 = 4.6 Hz, J_H6'-H6'' =
4.1 Hz, J_H6''-H6'' = 3.2 Hz, J_H6'-H6'' = -12.6 Hz, J_H15-H6 = 7.5 Hz; \(^{13}C\)-NMR (75.4 MHz, CD\(_3\)OD): \(\delta\)
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Nucleoside (92).

To a stirred solution of nucleoside 92a (322 mg, 0.72 mmol) in anhydrous methanol (22 mL) under an atmosphere of nitrogen at room temperature was added trifluoroacetic acid (63 mL, 0.72 mmol). After 30 min, the solution was evaporated to dryness. The residue was redissolved in methylene chloride (100 mL), washed with saturated aqueous sodium bicarbonate (100 mL), brine (100 mL), dried (Na$_2$SO$_4$), filtered and the solvent removed in vacuo to yield the title compound in quantitative (493 mg) yield as a white foam. \(^1H\text{-NMR} (200 MHz, CD$_2$Cl$_2$): \(\delta\) 1.82 (d, 3H, CH$_3$ at C5), 2.45 (ddd, 1H, H3'), 3.42 (s, 3H, MeO), 4.31 - 4.45 (m, 5H, H2', H3", H3"', H3"", OH), 5.33 (d, ex, 1H, OH), 5.34 (d, 1H, H4'), 5.94 (d, 1H, H1''), 7.34 - 7.62 (m, 3H, Ph), 7.49 (d, 1H, H6), 8.03 - 8.08 (m, 2H, Ph), 10.39 (s, br, ex, 1H, NH), \(J_{III'\cdot II''} = 5.2\) Hz, \(J_{III''\cdot III'''} = 4.5\) Hz, \(J_{OH\cdot H1''} or H3' = 0.8\) Hz, \(J_{H16\cdot Me} = -0.8\) Hz; \(^13C\text{-NMR} (75.4 MHz, CDCl$_3$): \(\delta\) 12.36 [CH$_3$ at C5], 54.26 [C3'], 56.26 [C1301], 67.71 [C3"'], 67.86 [C3"''], 77.28 [C2'], 90.90 [C1'], 105.40 [C4'], 109.96 [C5], 128.41, 129.76, 133.26 [aromatic CH], 129.66 [aromatic C], 136.64 [C6], 151.87 [C2], 164.32 [C4], 166.84 [PhCO]; LRMS (CI-NH$_3$): m/e 424 ([M + NH$_4^+$], 2.6%), 407 ([MH$^+$], 22.2%), 375 ([MH$^+$ - MeOH], 100%), 281 ([MH$^+$ - thymine], 12.3%); HRMS (CI-NH$_3$): m/e calcd. for C$_{19}$H$_{23}$N$_2$O$_8$ [MH$^+$], 407.1454; found, 407.1453.

Nucleoside (93).

Nucleoside 93 was obtained in 86% yield as a white powder by a procedure identical to the one described for the preparation of nucleoside 91a. \(^1H\text{-NMR} (200 MHz, CD$_3$OD): \(\delta\) 1.85 (d, 3H, CH$_3$ at C5), 2.19 (ddd, 1H, H3'), 3.39 (s, 3H, MeO), 3.51 (A of ABX, 1H, H3"'), 3.56 (B of ABX, 1H, H3"'), 3.85 (ddd, 1H, H3"), 4.16 (t, 1H, H2'), 5.10 (d, 1H, H4'), 6.01 (d, 1H, H1'), 7.52 (d, 1H, H6), \(J_{III'\cdot II''} = 7.2\) Hz, \(J_{II2\cdot III} = 8.2\) Hz, \(J_{II2\cdot III'} = 4.4\) Hz, \(J_{H3'\cdot H3''} = 7.4\) Hz, \(J_{III\cdot H1}\cdot H3^\prime\cdot II'' = -4.4\) Hz, \(J_{H3''\cdot H3'''} = -10.9\) Hz, \(J_{H16\cdot Me} = -1.3\) Hz; \(^13C\text{-NMR} (75.4 MHz, CD$_3$OD): \(\delta\) 12.36 [CH$_3$ at C5], 55.29 [C3'], 56.14 [CH$_3$O], 65.93 [C3"''], 71.24 [C3"'], 75.91 [C2'], 88.63 [C1'], 105.18 [C4'], 112.18 [C5], 137.82 [C6], 152.77 [C2], 166.11 [C4]; LRMS (CI-NH$_3$): m/e 303 ([MH$^+$], 39.1%), 271 ([MH$^+$ - MeOH], 100%), 246 ([MH$^+$ - H$_2$O], 100%), 221 ([MH$^+$ - H$_2$O - MeOH], 100%), 199 ([MH$^+$ - 2H$_2$O], 100%), 175 ([MH$^+$ - 3H$_2$O], 100%).
100%); HRMS (Cl-NH₃): m/e calcld. for C₁₂H₁₉N₂O₇ [MH⁺], 303.1191; found, 303.1192. Anal. calcld. for C₁₂H₁₈N₂O₂H₂O: C, 45.00; H, 6.29; N, 8.75; found: C, 44.83; H, 6.19; N, 8.67.

3'α-Thyminyl-4'β-acetoxy-6'β-benzoyloxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (94a).

Nucleoside 90a was acetylated in 90% yield by a procedure similar to that used for the preparation of 25a. (¹H-NMR (200 MHz, CDCl₃): δ 1.92 (d, 3H, CH₃), 2.10 (s, 3H, Ac), 3.40 (t, 1H, HS'), 4.47 (A of ABX, 1H, H₆'α), 4.55 (ddd, 1H, H₆'), 4.64 (B of ABX, 1H, H₆''), 5.55 (s, 1H, H₄'), 6.22 (s, 1H, H₃'), 6.23 (d, 1H, H₁'), 7.41 - 7.62 (m, 3H, Ph), 7.83 (d, 1H, H₆), 8.02 - 8.07 (m, 2H, Ph), 9.18 (s, br, ex, 1H, NH), J₉₆.₇₆ = 4.1 Hz, J₉₆.₇₆ = 3.5 Hz, J₉₆.₇₆ = 3.1 Hz, J₉₆.₇₆ = 3.0 Hz, J₉₆.₇₆ = 11.9 Hz, J₉₆-Me = 1.1 Hz; ¹³C-NMR (75.4 MHz, CDCl₃): δ 12.80 [CH], 20.88 [CI], 49.00 [C₅'], 64.78 [C₆'], 77.39 [C₆'], 79.71 [C₄'], 95.73 [C₃'], 109.69 [C₁'], 110.55 [C₅], 128.48, 129.60, 133.38 [aromatic CH], 129.23 [aromatic C], 134.95 [C₆], 150.39 [C₂], 163.68 [C₄], 165.83 [PhCO], 169.32 [CH₃CO]).

3'α-Thyminyl-4'β-(α-methylvaleryloxy)-6'β-benzoyloxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (94b).

To a stirred solution of nucleoside 90a (37 mg, 0.10 mmol) and 2-methylvaleric acid (125 µL, 1.00 mmol) in dry acetonitrile (5 mL) at room temperature under an atmosphere of nitrogen was added N,N-dimethylaminopyridine (24 mg, 0.20 mmol) and 1,3-dicyclohexylcarbodiimide (206 mg, 1.00 mmol). After 18 h, acetic acid (13 µL) and methanol (66 µL) were added and stirring was continued for 30 min. The reaction mixture was poured into saturated aqueous sodium bicarbonate (50 mL) and extracted with methylene chloride (3 x 50 mL). The organic layer was dried (Na₂SO₄), filtered, and the solvent removed in vacuo to afford a white solid. Purification by flash chromatography (methylene chloride / methanol, 30:1 v/v) gave the title compound (mixture of 2 inseparable diastereomers, 1:1), (45 mg, 95% yield) as a white solid. (¹H-NMR (200 MHz, CDCl₃): δ 0.87, 0.88 (2t, 3H, CH₃CH₂), 1.13, 1.15 (2d, 3H, CH₃CH), 1.18 - 1.81 (m, 4H, CH₂CH₂), 1.92 (s, br, 3H, CH₃ at C5), 2.47 (m, 1H, CHCO), 3.33, 3.34 (2t, 1H, H₅'), 4.47 (A of ABX, 1H, H₆''), 4.55 (m, 1H, H₆), 4.64 (B of ABX, 1H, H₆''), 5.52, 5.54 (2s, 1H, H₄'), 6.22 (s, 1H, H₃'), 6.23 (d, 1H, H₁'), 7.41 - 7.86 (m, 3H, Ph), 7.83 (s, br, 1H, H₆), 8.02
- 8.08 (m, 2H, Ph), 8.81, 8.86 (2s, br, ex, 1H, NH), J_{H1'-H5} = 4.1 Hz, J_{CH-Me} = 6.9 Hz, 7.0 Hz, J_{CH3-CH2} = 7.0 Hz, 7.1 Hz, J_{H5-H6} = 4.2 Hz, 4.4 Hz, J_{H6-H6'} = 2.9 Hz, J_{H6'-H6''} = 3.0 Hz, J_{H6''-H6'''} = -11.9 Hz).

3'α-Thyminyl-4'β-(α-methoxy-α-(trifluoromethyl)-phenylacetoxy)-6'β-benzoyloxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (94c).

Nucleoside 90a (37 mg, 0.10 mmol) and 2-methoxy-2-(trifluoromethyl)-phenylacetic acid (234 mg, 1.00 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 1:1), (48 mg, 82% yield) as a white solid by a procedure analogous to the one used for the preparation of 94b. \{^1\text{H-NMR (200 MHz, CDCl}_3\}: δ 1.86 (s, br, 3H, CH at C5), 3.31 (t, 1H, H5'), 3.76 (s, 3H, MeO), 4.21 - 4.86 (m, 3H, H6', H6''a, H6''b), 4.70, 4.74 (2s, 1H, H4'), 5.91, 6.02 (2s, 1H, H3'), 6.26 (d, 1H, H1'), 7.29 - 7.68 (m, 8H, Ph), 7.93 (s, br, 1H, H6), 8.02 - 8.06 (m, 2H, 'γ'), 9.25 (s, br, ex, 1H, NH), J_{H1'-H5} = 3.9 Hz, J_{H5'-H6'} = 4.1 Hz\}. 

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4.8 Experiments for Section 2.9.

3α-Chloroacetoxy-4β-hydroxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (97a).

To a solution of epoxide 23d (50 mg, 0.20 mmol) in dry methylene chloride (5 mL) under nitrogen at room temperature was added chloroacetic acid (19 mg, 0.20 mmol) and the reaction mixture was allowed to stir for 16 h. The solution was diluted with methylene chloride (25 mL), washed with saturated aqueous sodium bicarbonate (25 mL), brine (25 mL), dried (Na₂SO₄), filtered and the solvent removed in vacuo to yield a yellow syrup. Chromatography over silica gel (petroleum ether:ethyl acetate, 1:1 v/v) afforded 97a (31 mg, 45% yield) as a clear oil. {IH-NMR (200 MHz, CDCl₃): δ 2.67 (s, br, ex, IH, OH), 3.40 (dt, 1H, H₅), 4.13 (s, 2H, CH₂Cl), 4.49 (A of ABX, 1H, H₆'), 4.53 (s, 1H, H₄), 4.58 (B of ABX, 1H, H₆''), 4.75 (ddd, 1H, H₆), 6.15 (d, 1H, H1), 6.50 (d, 1H, H3), 7.40 - 7.63 (m, 3H, Ph), 8.03 - 8.08 (m, 2H, Ph); J₃₁-3₅ = 4.0 Hz, J₃₅-3₇ = -1.0 Hz, J₃₅-3₆ = 4.3 Hz, J₃₆-3₈ = 4.2 Hz, J₃₈-3₉ = 3.2 Hz, J₃₉-3₁ = -12.5 Hz).

3α-Bromoacetoxy-4β-hydroxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (97b).

Epoxide 23d (42 mg, 0.17 mmol) and bromoacetic acid (24 mg, 0.17 mmol) gave the title compound (36 mg, 55% yield) as a light yellow oil by a procedure similar to the one used for the preparation of 97a. {IH-NMR (300 MHz, CDCl₃): δ 3.19 (d, ex, 1H, OH), 3.39 (t, 1H, H₅), 3.89 (s, 1H, CHHBr), 3.90 (s, 1H, CHHBr), 4.47 (A of ABX, 1H, H₆'), 4.57 (B of ABX, 1H, H₆''), 4.58 (d, 1H, H₄); J₃₅-3₆ = 4.0 Hz, J₃₆-3₈ = 4.3 Hz, J₃₈-3₉ = 3.2 Hz, J₃₉-3₁ = -12.5 Hz; 13C-NMR (75.4 MHz, CDCl₃): δ 25.79 [CH₂Br], 49.37 [C5], 65.54 [C6], 76.31 [C4], 76.72 [C6], 106.77 [C3], 109.04 [C1], 128.52, 129.65, 133.45 [aromatic CH], 129.32 [aromatic C], 166.22, 166.38 [CO]; LRMS (Cl-NH₃): m/e 406, 404 ([M + NH₄⁺ 34.6%, 34.9%], 389, 387 ([MH⁺ 4.6%, 3.3%], 249 ([MH⁺ - BrCH₂COOH], 37.9%); HRMS (Cl-NH₃): m/e calcd. for C₁₅H₁₉NO₇Br [M + NH₄⁺], 404.0346; found, 404.0344).

3α-Chloroacetoxy-4β-t-butyldimethylsilyloxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (98a).

Alcohol 97a was silylated by a procedure similar to that used for the preparation of 19. Purification by flash chromatography (hexanes/ethyl acetate, 9:1 v/v) gave the title compound in 41%
yield as a clear oil. $^1$H-NMR (200 MHz, CDCl$_3$): $\delta$ 0.07, 0.09 (2s, 6H, t-BuSiMe$_2$), 0.84 (s, 9H, t-BuSiMe$_2$), 3.23 (dt, 1H, H5), 4.13 (s, 2H, CH$_2$Cl), 4.41 (s, 1H, H4), 4.49 (A of ABX, 1H, H6'), 3.46 (B of ABX, 1H, H6'), 4.72 (ddd, 1H, H6), 6.14 (dd, 1H, H1), 6.40 (d, 1H, H3), 7.41 - 7.62 (m, 3H, Ph), 8.03 - 8.09 (m, 2H, Ph); $J_{F1-H5} = 4.1$ Hz, $J_{H1-H5} = -0.9$ Hz, $J_{H5-H6} = 4.4$ Hz, $J_{H6-H6'} = 3.8$ Hz, $J_{H6'-H6'b} = -12.2$ Hz).

3α-$N^1$-Imidazoylacetoxyl-4β-t-butyldimethylsilyloxy-6β-benzoyloxyethyl-2,7-dioxabicyclo-[3,2,0]-heptane (98b).

To a solution of alcohol 97b (39 mg, 0.10 mmol) in dry $N,N$-dimethylformamide (0.5 mL) under nitrogen at room temperature was added imidazole (21 mg, 0.30 mol) and t-butyldimethylsilyl chloride (23 mg, 0.15 mmol) and it was allowed to stir until all of the starting material was consumed (72 h). The reaction mixture was diluted with ethyl acetate (30 mL), washed with water (3 x 25 mL), brine (25 mL), dried (Na$_2$SO$_4$), filtered and the solvent removed $\textit{in vacuo}$ to yield a yellow syrup. Purification by flash chromatography (petroleum ether/ethyl acetate, 1:1 v/v) afforded the title compound (17 mg, 36% yield) as a light yellow oil. $^1$H-NMR (200 MHz, CDCl$_3$): $\delta$ 0.04, 0.06 (2s, 6H, t-BuSiMe$_2$), 0.83 (s, 9H, t-BuSiMe$_2$), 3.18 (s, 1H, H5), 4.30 (s, 1H, H4), 4.34 (ddd, 1H, H6), 4.44 (A of ABX, 1H, H6'), 4.52 (B of ABX, 1H, H6'), 4.79 (s, 2H, CH$_2$), 6.12 (d, 1H, H1), 6.39 (s, 1H, H3), 6.98 - 7.07 (2d, 2H, N-CH=CH-N), 7.41 - 7.63 (m, 3H, Ph), 7.45 (s, 1H, N-CH=N), 8.04 - 8.09 (m, 2H, Ph); $J_{H1-H5} = 4.0$ Hz, $J_{H5-H6} = 4.3$ Hz, $J_{H6-H6'} = 4.1$ Hz, $J_{H6'-H6'b} = -12.2$ Hz, $J_{NCH-NCH} = 0.7$ Hz; $^{13}$C-NMR (75.4 MHz, CDCl$_3$): $\delta$ 17.95 [(CH$_3$)$_3$SiMe$_2$], 25.55 [t-BuSiMe$_2$], 25.55 [(CH$_3$)$_3$SiMe$_2$], 48.27 [CH$_2$], 50.51 [C5], 65.71 [C6'], 76.25 [C6], 77.31 [C4], 106.66 [C3], 109.11 [C1], 120.23 [N-CH=CH-N], 128.54, 129.69, 133.43 [aromatic CH], 129.47 [aromatic C], 133.62 [N-CH=N], 166.02, 166.22 [CO]; LRMS (CI-NH$_3$): m/e 489 [(MH$^+$), 100%], 363 [(MH$^+$ - (imid-CH$_2$COOH)), 20.8%].
material was consumed (2 h). The reaction mixture was diluted with methylene chloride (30 mL), washed with cold 5% aqueous sodium carbonate (25 mL), brine (25 mL), dried (Na₂SO₄), filtered and the solvent removed in vacuo to yield a clear residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 3:1 v/v) afforded the title compound (29 mg, 58% yield) as a colourless oil. ¹H-NMR (200 MHz, CD₂Cl₂): δ 0.11, 0.12 (2s, 6H, t-BuSiMe₃), 0.88 (s, 9H, t-BuSiMe₃), 3.29 (dd, 1H, H₇), 3.95 (s, 2H, CH₂Br), 4.46 (t, 1H, H₄), 4.48 (A of ABX, 1H, H₆'), 4.57 (B of ABX, 1H, H₆'), 4.77 (ddd, 1H, H₆), 6.14 (d, 1H, H₁), 6.53 (s, 1H, H₃), 7.44 - 7.66 (m, 3H, Ph), 8.05 - 8.10 (m, 2H, Ph); J₉₁,H₅ = 4.1 Hz, J₉₅-H₆₄ = 4.5 Hz, J₉₆₄-H₆₅ = 3.9 Hz, J₉₆₅-H₆₆ = -12.3 Hz; ¹³C-NMR (75.4 MHz, CD₂Cl₂): δ 20.84 [CH₃Si], 26.27 [CH₂Br], 47.69 [C₅], 65.61 [C₆], 76.82 [C₆], 77.57 [C₄], 104.20 [C₃], 109.07 [C₁], 128.86, 129.90, 133.65 [aromatic CH], 134.01 [aromatic C], 166.22, 166.38 [CO]; LRMS (Cl-NH₃): m/e 520, 518 ([MH+], 15.1%, 20.8%), 503, 501 ([MH⁺], 1.3%, 1.0%), HRMS (Cl-NH₃): m/e calcd. for C₂₁H₃₀O₇Si₇⁹Br [MH⁺], 501.0941; found, 501.0944.

3α-Bromoacetoxy-4β-acetoxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo[3.2.0]-heptane (101).

Alcohol 97b was acetylated in 95% yield by a procedure similar to that used for 25a. ¹H-NMR (200 MHz, CDCl₃): δ 2.07 (s, 3H, CH₃), 3.45 (t, 1H, H₅), 3.91 (s, 2H, CH₂Br), 4.51 (A of ABX, 1H, H₆'), 4.60 (B of ABX, 1H, H₆'), 4.86 (dd, 1H, H₆), 5.36 (s, 1H, H₄), 6.14 (d, 1H, H₁), 6.53 (s, 1H, H₃), 7.41 - 7.62 (m, 3H, Ph), 8.04 - 8.09 (m, 2H, Ph); J₉₁-H₅ = 4.1 Hz, J₉₅-H₆₄ = 4.3 Hz, J₉₆₄-H₆₅ = 4.0 Hz, J₉₆₅-H₆₆ = 3.3 Hz, J₉₆₆-H₆₇ = -12.5 Hz; ¹³C-NMR (75.4 MHz, CD₂Cl₂): δ 20.84 [CH₃], 26.27 [CH₂Br], 47.69 [C₅], 65.61 [C₆], 76.82 [C₆], 77.57 [C₄], 104.20 [C₃], 109.07 [C₁], 128.86, 129.90, 133.65 [aromatic CH], 134.01 [aromatic C], 166.22, 166.38 [CO]; LRMS (Cl-NH₃): m/e 520, 518 ([MH+], 15.1%, 20.8%), 503, 501 ([MH⁺], 1.3%, 1.0%), HRMS (Cl-NH₃): m/e calcd. for C₁₇H₁₈O₈Si₇⁹Br [MH⁺], 429.0185; found, 429.0185.

Bicyclic Furanoside (99a).

To a solution of 98c (50 mg, 0.10 mmol) in dry acetonitrile (500 µL) under an atmosphere of nitrogen at room temperature was added a stock solution of bis-(trimethylsilyl)-N⁶ adenine in 1,2-dichloroethane (0.339 M solution, 324 µL, 0.11 mmol) and silver triflate (26 mg, 0.10 mmol). After stirring for 1 h, the reaction mixture was diluted with methylene chloride (25 mL), washed with saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na₂SO₄), filtered and the solvent removed in vacuo to yield a clear residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 3:1 v/v) afforded the title compound (29 mg, 58% yield) as a colourless oil. ¹H-NMR (200 MHz, CD₂Cl₂): δ 0.11, 0.12 (2s, 6H, t-BuSiMe₃), 0.88 (s, 9H, t-BuSiMe₃), 3.29 (dd, 1H, H₇), 3.95 (s, 2H, CH₂Br), 4.46 (t, 1H, H₄), 4.48 (A of ABX, 1H, H₆'), 4.57 (B of ABX, 1H, H₆'), 4.77 (dd, 1H, H₆), 6.14 (d, 1H, H₁), 6.53 (s, 1H, H₃), 7.44 - 7.66 (m, 3H, Ph), 8.05 - 8.10 (m, 2H, Ph); J₉₁,H₅ = 4.1 Hz, J₉₅-H₆₄ = 4.5 Hz, J₉₆₄-H₆₅ = 3.9 Hz, J₉₆₅-H₆₆ = -12.3 Hz; ¹³C-NMR (75.4 MHz, CD₂Cl₂): δ 20.84 [CH₃Si], 26.27 [CH₂Br], 47.69 [C₅], 65.61 [C₆], 76.82 [C₆], 77.57 [C₄], 104.20 [C₃], 109.07 [C₁], 128.86, 129.90, 133.65 [aromatic CH], 134.01 [aromatic C], 166.22, 166.38 [CO]; LRMS (Cl-NH₃): m/e 520, 518 ([MH+], 15.1%, 20.8%), 503, 501 ([MH⁺], 1.3%, 1.0%), HRMS (Cl-NH₃): m/e calcd. for C₁₇H₁₈O₈Si₇⁹Br [MH⁺], 429.0185; found, 429.0185.
**Bicyclic Furanoside (99b).**

Acetal 101 (43 mg, 0.10 mmol) and a stock solution of bis-(trimethylsilyl)-N-adenine in 1,2-dichloroethane (0.339 M solution, 324 µL, 0.11 mmol) gave the title compound (41 mg, 70% yield) as an unstable white foam by a procedure analogous to the one used for the preparation of nucleoside 99a. 

$^1$H-NMR (200 MHz, CD$_2$Cl$_2$): $\delta$ 2.01 (s, 3H, Ac), 2.39 (ddd, 1H, H2'), 3.81 (s, 2H, OCH$_2$CO), 4.17 (A of ABX, 1H, H2", $\alpha$), 4.33 (B of ABX, 1H, H2", $\beta$), 4.37 (ddd, 1H, H2"), 5.16 (d, 1H, H3'), 5.60 (s, 1H, H4'), 5.86 (d, 1H, H1'), 7.44 - 7.88 (m, 6H, Ph), 7.94 - 8.04 (m, 4H, Ph), 8.58 (s, 1H, H8), 8.76 (s, 1H, H2), 11.43 (s, br, ex, 1H, NH), $J_{HH':HH'} = 4.6$ Hz, $J_{HH':H2'} = 3.3$ Hz; $^{13}$C-NMR (75.4 MHz, CDCl$_3$): $\delta$ 20.78 [CH$_3$CO], 25.30 [OCH$_2$CO], 55.80 [C2], 66.76 [C2"], 68.03 [C2"], 78.59 [C3], 90.68 [C1'], 100.93 [C4'], 113.10 [C5], 128.52, 128.61, 129.33, 129.59, 132.68, 133.47 [aromatic CH], 129.00 [aromatic C-COOCH$_2$], 134.29 [aromatic C-CON], 145.92 [C8], 146.42 [C4], 154.27 [C2], 156.59 [C6], 165.13, 166.13, 166.80 [CO], 169.99 [CH$_3$CO]).
5. APPENDICES.

APPENDIX I. Antifeedant Testing of Photo-Adducts.

Protecting our food supply from predatory insect attack in an ecologically responsible manner has led to increased interest in behavior altering chemicals from natural sources. The Indian neem tree, Azadirachta Indica A. Juss (Meliaceae)\textsuperscript{103} has provided a large quantity of materials, of which one component, azadirachtin has received a great deal of attention\textsuperscript{104}. Azadirachtin possesses extremely potent biological activity as a growth regulatory and antifeedant agent\textsuperscript{105}.

\begin{center}
\includegraphics[width=0.5\textwidth]{Azadirachtin.png}
\end{center}

Azadirachtin

This has led to a great deal of research into the understanding of the structure activity relationships and to synthesize simpler compounds which exhibit similar biological activity\textsuperscript{104}. Recently, it was reported that antifeedancy can be demonstrated using relatively simple hydroxytricyclic hydrofuran derivatives of the type \textsuperscript{106}. In studies carried out by Ley, it was shown that salannin and derivatives thereof are poor antifeedants, thus indicating that the left hand side of azadirachtin is not responsible for its biological activity\textsuperscript{104}.

Due to the similarities between 109 and photo-adducts of aldehydes and furans, Dr. T. H. Chan thought that our photo-adducts might possess biological activity as antifeedants against spruce budworm. The bioassay\textsuperscript{107} conducted involved feeding laboratory-colony spruce budworm larvae an artificial diet\textsuperscript{108} containing 0.2\% (wet weight) of test compounds. The assay showed the development of larvae reared from second instar on test diets was only significantly retarded by compounds 40 and 41a. The results are shown in Table 2.

Table 2

<table>
<thead>
<tr>
<th>Compound #</th>
<th>Compound</th>
<th>Mean Instar\textsubscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Control</td>
<td>5.30</td>
</tr>
<tr>
<td>2c</td>
<td>R = TBDMSiOCH\textsubscript{2}, R' = H</td>
<td>5.22</td>
</tr>
<tr>
<td>2d</td>
<td>R = BzOCH\textsubscript{2}, R' = H</td>
<td>5.18</td>
</tr>
<tr>
<td>40</td>
<td>R = BzOCH\textsubscript{2}, R' = SnBu\textsubscript{3}</td>
<td>2.00</td>
</tr>
<tr>
<td>41a</td>
<td>R = BzOCH\textsubscript{2}, R' = Ph</td>
<td>2.94</td>
</tr>
<tr>
<td>44a</td>
<td>R = BzOCH\textsubscript{2}, R' = CH\textsubscript{3}</td>
<td>5.18</td>
</tr>
<tr>
<td>72a</td>
<td>R = EtCOCH\textsubscript{2}, R' = CH\textsubscript{3}</td>
<td>5.22</td>
</tr>
<tr>
<td>81</td>
<td>R = tPrOOC, R' = CH\textsubscript{3}</td>
<td>NA</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Maximum = 6.00 (all larvae 6\textsuperscript{th} instars)

Since reduction in development rate could be caused by factors other than feeding, compounds 40 and 41a are currently being evaluated by an assay that will provide a true reflection of the amount of food ingested by sixth instar larvac. Also, both of these compounds are being evaluated at lower concentrations so as to determine the limits of their effectiveness.

\textsuperscript{107} Bioassays were carried out by A. W. Thomas at Canadian Forestry Service Maritimes, Fredericton, N.B., Canada E3B 5P7.

APPENDIX II. Analysis of ABX systems in $^1$H-NMR spectra.

The chemical shifts and coupling constants of second order AB portions of ABX systems were calculated by the method shown below$^{109}$.

The ABX spectrum is divided into two AB systems.

$\begin{align*}
\text{AB } \#1 \\
\text{AB } \#2
\end{align*}$

$J_{A,B} = (8 - 6) = (7 - 5) = (4 - 2) = (3 - 1)$

$\begin{align*}
\vartheta_1 &= (1 + 3 + 5 + 7) / 4 \\
(\Delta \vartheta_1) / 2 &= [(1 - 7)(3 - 5)]^{1/2} / 2 \\
\Delta 1^+ &= \vartheta_1 + (\Delta \vartheta_1) / 2 \\
\Delta 1^- &= \vartheta_1 - (\Delta \vartheta_1) / 2 \\
\vartheta_A &= (\Delta 1^+ + \Delta 2^+) / 2 \\
J_{AX} &= \Delta 1^+ - \Delta 2^+ \\
\text{or} \\
\vartheta_A &= (\Delta 1^+ + \Delta 2^-) / 2 \\
J_{AX} &= \Delta 1^+ - \Delta 2^-
\end{align*}$

$\begin{align*}
\vartheta_2 &= (2 + 4 + 6 + 8) / 4 \\
(\Delta \vartheta_2) / 2 &= [(2 - 8)(4 - 6)]^{1/2} / 2 \\
\Delta 2^+ &= \vartheta_2 + (\Delta \vartheta_2) / 2 \\
\Delta 2^- &= \vartheta_2 - (\Delta \vartheta_2) / 2 \\
\vartheta_B &= (\Delta 1^+ + \Delta 2^+) / 2 \\
J_{BX} &= \Delta 1^+ - \Delta 2^+ \\
\text{or} \\
\vartheta_B &= (\Delta 1^- + \Delta 2^-) / 2 \\
J_{BX} &= \Delta 1^- - \Delta 2^-
\end{align*}$

Two possible sets of values are generated, but one gives unrealistic coupling constants.

---

APPENDIX III. X-Ray Structure Determination of Nucleoside (91a).

An X-Ray study was carried out on nucleoside 91a. The diffraction measurement was made on a Rigaku diffractometer and the data obtained is shown in the tables below.

Table XR-1
Crystal data and course of structure determination

<table>
<thead>
<tr>
<th>Compound name</th>
<th>Nucleoside 91a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Formula</td>
<td>C_{11}H_{14}N_{2}O_{6}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>270.24</td>
</tr>
<tr>
<td>Crystal Habit</td>
<td>rectangular prism</td>
</tr>
<tr>
<td>X-ray specimen size (mm)</td>
<td>0.10 x 0.20 x 0.25</td>
</tr>
<tr>
<td>Radiation</td>
<td>Graphite monochromated CuKα</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P-1</td>
</tr>
<tr>
<td>Lattice Constants</td>
<td></td>
</tr>
<tr>
<td>a (Å)</td>
<td>10.0636(17)</td>
</tr>
<tr>
<td>b (Å)</td>
<td>10.4054(20)</td>
</tr>
<tr>
<td>c (Å)</td>
<td>11.9771(15)</td>
</tr>
<tr>
<td>α (°)</td>
<td>96.552(15)</td>
</tr>
<tr>
<td>β (°)</td>
<td>108.031(11)</td>
</tr>
<tr>
<td>γ (°)</td>
<td>90.498(14)</td>
</tr>
<tr>
<td>V (Å³)</td>
<td>1182.5(3)</td>
</tr>
<tr>
<td>No. of formula in a cell</td>
<td>4</td>
</tr>
<tr>
<td>F (000)</td>
<td>567.90</td>
</tr>
<tr>
<td>Calculated density (g cm⁻³)</td>
<td>1.518</td>
</tr>
<tr>
<td>μ for CuKα (mm⁻¹)</td>
<td>1.02</td>
</tr>
<tr>
<td>λ (Å)</td>
<td>1.54056</td>
</tr>
<tr>
<td>2θ max (°)</td>
<td>110.0</td>
</tr>
<tr>
<td>h, k, l ranges</td>
<td>-10 10, 0 11, -12 12</td>
</tr>
<tr>
<td>No. of reflections measured</td>
<td>3182</td>
</tr>
<tr>
<td>No. of unique reflections</td>
<td>2975</td>
</tr>
</tbody>
</table>
Table of crystallographic data:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of reflections with $I_{\text{ref}} &gt; 2.5\sigma(I_{\text{ref}})$</td>
<td>1975</td>
</tr>
<tr>
<td>For significant reflections</td>
<td>$RF = 0.084, \ R_w = 0.054, \ G_0^f = 3.31$</td>
</tr>
<tr>
<td>For all reflections</td>
<td>$RF = 0.143, \ R_w = 0.056$</td>
</tr>
<tr>
<td>Maximum shift / $\sigma$ ratio</td>
<td>0.061</td>
</tr>
<tr>
<td>Deepest hole in D-map ($e / \text{Å}^3$)</td>
<td>-0.580</td>
</tr>
<tr>
<td>Highest peak in D-map ($e / \text{Å}^3$)</td>
<td>0.380</td>
</tr>
<tr>
<td>Secondary extinction coefficient</td>
<td>0.019(5)</td>
</tr>
<tr>
<td>Merging R</td>
<td>1.2%</td>
</tr>
<tr>
<td>Drop of standard intensities (avg.)</td>
<td>0.2%</td>
</tr>
<tr>
<td>Method of structure determination</td>
<td>Solved by direct methods using SHELXS$^{110}$</td>
</tr>
<tr>
<td>Method of structure refinement</td>
<td>Refined using NRCVAX system programs$^{111}$</td>
</tr>
</tbody>
</table>

Cell dimensions were obtained from 21 reflections with 20 angle in the range 15.00° - 25.00°.
The intensity data were collected using the 0/20 scan mode.

$$RF = \Sigma (F_o - F_c) / \Sigma (F_o)$$
$$R_w = (\Sigma w (F_o - F_c)^2 / \Sigma (wF_o^2))^{1/2}$$
$$G_0^f = (\Sigma w (F_o - F_c)^2 / \Sigma (# \text{of reflections} - # \text{of parameters}))^{1/2}$$

![Figure XR-1. X-ray crystallographic structure of nucleoside 91a.](image)

---


Figure XR-2. Unit cell of nucleoside 91a.
Table XR-2
Atomic Parameters X, Y, Z and $B_{eq}$. E. S. Ds. refer to the last digit printed.

<table>
<thead>
<tr>
<th>Atom</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>$B_{eq}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-2</td>
<td>0.2995(5)</td>
<td>0.8956(5)</td>
<td>0.7867(4)</td>
<td>3.5 (3)</td>
</tr>
<tr>
<td>O-4</td>
<td>0.6723(6)</td>
<td>1.1332(5)</td>
<td>0.7676(5)</td>
<td>4.1 (3)</td>
</tr>
<tr>
<td>O-2'</td>
<td>0.2566(5)</td>
<td>1.1484(5)</td>
<td>1.0577(4)</td>
<td>2.9 (3)</td>
</tr>
<tr>
<td>O-4'</td>
<td>0.0176(5)</td>
<td>0.9666(5)</td>
<td>0.8876(4)</td>
<td>3.8 (3)</td>
</tr>
<tr>
<td>O-7'</td>
<td>0.2146(5)</td>
<td>1.3524(5)</td>
<td>0.9833(5)</td>
<td>3.8 (3)</td>
</tr>
<tr>
<td>O-6''</td>
<td>-0.0601(6)</td>
<td>1.4532(6)</td>
<td>0.8801(5)</td>
<td>5.9 (4)</td>
</tr>
<tr>
<td>N-1</td>
<td>0.3627(6)</td>
<td>1.0859(5)</td>
<td>0.9081(5)</td>
<td>2.4 (3)</td>
</tr>
<tr>
<td>N-3</td>
<td>0.4848(6)</td>
<td>1.0174(5)</td>
<td>0.7788(5)</td>
<td>2.8 (3)</td>
</tr>
<tr>
<td>C-2</td>
<td>0.3760(8)</td>
<td>0.9925(7)</td>
<td>0.8205(6)</td>
<td>2.8 (4)</td>
</tr>
<tr>
<td>C-4</td>
<td>0.5806(8)</td>
<td>1.1208(7)</td>
<td>0.8137(6)</td>
<td>2.9 (4)</td>
</tr>
<tr>
<td>C-5</td>
<td>0.5682(8)</td>
<td>1.2118(7)</td>
<td>0.9122(6)</td>
<td>3.1 (4)</td>
</tr>
<tr>
<td>C-5-Mc</td>
<td>0.6757(9)</td>
<td>1.3203(7)</td>
<td>0.9681(7)</td>
<td>4.1 (5)</td>
</tr>
<tr>
<td>C-6</td>
<td>0.4587(8)</td>
<td>1.1905(7)</td>
<td>0.9524(6)</td>
<td>2.8 (4)</td>
</tr>
<tr>
<td>C-6''</td>
<td>0.0296(10)</td>
<td>1.4222(9)</td>
<td>0.8144(8)</td>
<td>5.6 (6)</td>
</tr>
<tr>
<td>O-2A</td>
<td>-0.5015(5)</td>
<td>0.8567(5)</td>
<td>0.5729(4)</td>
<td>3.4 (3)</td>
</tr>
<tr>
<td>O-4A</td>
<td>-0.7071(6)</td>
<td>0.4809(5)</td>
<td>0.3563(5)</td>
<td>5.7 (4)</td>
</tr>
<tr>
<td>O-2A'</td>
<td>-0.2178(5)</td>
<td>0.8636(5)</td>
<td>0.3961(4)</td>
<td>2.8 (3)</td>
</tr>
<tr>
<td>O-4A'</td>
<td>-0.1710(6)</td>
<td>1.0119(6)</td>
<td>0.6482(5)</td>
<td>5.9 (3)</td>
</tr>
<tr>
<td>O-7A'</td>
<td>-0.0747(5)</td>
<td>0.6836(4)</td>
<td>0.4420(4)</td>
<td>2.80 (25)</td>
</tr>
<tr>
<td>O-6A''</td>
<td>0.2075(5)</td>
<td>0.7237(5)</td>
<td>0.5876(4)</td>
<td>3.2 (3)</td>
</tr>
<tr>
<td>N-1A</td>
<td>-0.3970(6)</td>
<td>0.7544(5)</td>
<td>0.4457(5)</td>
<td>2.1 (3)</td>
</tr>
<tr>
<td>N-3A</td>
<td>-0.6019(6)</td>
<td>0.6682(6)</td>
<td>0.4621(5)</td>
<td>3.0 (3)</td>
</tr>
<tr>
<td>C-2A</td>
<td>-0.5007(7)</td>
<td>0.7655(7)</td>
<td>0.4993(6)</td>
<td>2.7 (4)</td>
</tr>
<tr>
<td>C-4A</td>
<td>-0.6101(8)</td>
<td>0.5598(7)</td>
<td>0.3808(7)</td>
<td>3.3 (4)</td>
</tr>
<tr>
<td>C-5A</td>
<td>-0.4987(8)</td>
<td>0.5532(7)</td>
<td>0.3287(6)</td>
<td>2.8 (4)</td>
</tr>
<tr>
<td>C-5-Mc-A</td>
<td>-0.4954(9)</td>
<td>0.4410(8)</td>
<td>0.2392(7)</td>
<td>4.3 (5)</td>
</tr>
<tr>
<td>C-6A</td>
<td>-0.4004(8)</td>
<td>0.6484(7)</td>
<td>0.3624(6)</td>
<td>2.7 (4)</td>
</tr>
<tr>
<td>C-3A'</td>
<td>-0.2973(7)</td>
<td>0.8697(7)</td>
<td>0.4757(6)</td>
<td>2.5 (4)</td>
</tr>
<tr>
<td>C-4A'</td>
<td>-0.1918(8)</td>
<td>0.8784(7)</td>
<td>0.6012(6)</td>
<td>3.0 (4)</td>
</tr>
<tr>
<td>C-5A'</td>
<td>-0.0559(7)</td>
<td>0.8321(7)</td>
<td>0.5838(6)</td>
<td>2.6 (4)</td>
</tr>
<tr>
<td>C-1A'</td>
<td>-0.0820(8)</td>
<td>0.8220(6)</td>
<td>0.4505(6)</td>
<td>2.5 (4)</td>
</tr>
<tr>
<td>C-6A'</td>
<td>-0.0342(8)</td>
<td>0.6867(7)</td>
<td>0.5702(6)</td>
<td>2.7 (4)</td>
</tr>
<tr>
<td>C-6A''</td>
<td>0.1124(8)</td>
<td>0.6484(7)</td>
<td>0.6217(6)</td>
<td>2.9 (4)</td>
</tr>
</tbody>
</table>

$B_{eq}$ is the mean of the principal axes of the thermal ellipsoid.
**Table XR-3**

Calculated Hydrogen Atom Parameters.

<table>
<thead>
<tr>
<th>Atom</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>$B_{iso}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-O-4'</td>
<td>-0.086</td>
<td>0.971</td>
<td>0.826</td>
<td>4.5</td>
</tr>
<tr>
<td>H-O-6'</td>
<td>-0.124</td>
<td>1.530</td>
<td>0.842</td>
<td>6.8</td>
</tr>
<tr>
<td>H-N3</td>
<td>0.496</td>
<td>0.946</td>
<td>0.710</td>
<td>3.6</td>
</tr>
<tr>
<td>H5-Me_a</td>
<td>0.777</td>
<td>1.280</td>
<td>1.001</td>
<td>5.0</td>
</tr>
<tr>
<td>H5-Me_b</td>
<td>0.679</td>
<td>1.379</td>
<td>0.900</td>
<td>5.0</td>
</tr>
<tr>
<td>H5-Me_c</td>
<td>0.651</td>
<td>1.378</td>
<td>1.039</td>
<td>5.0</td>
</tr>
<tr>
<td>H6</td>
<td>0.501</td>
<td>1.186</td>
<td>1.047</td>
<td>3.4</td>
</tr>
<tr>
<td>H3'</td>
<td>0.259</td>
<td>0.960</td>
<td>0.983</td>
<td>3.7</td>
</tr>
<tr>
<td>H4'</td>
<td>0.109</td>
<td>1.058</td>
<td>0.781</td>
<td>3.7</td>
</tr>
<tr>
<td>H5'</td>
<td>-0.052</td>
<td>1.206</td>
<td>0.894</td>
<td>3.6</td>
</tr>
<tr>
<td>H1'</td>
<td>0.108</td>
<td>1.278</td>
<td>1.090</td>
<td>3.9</td>
</tr>
<tr>
<td>H6'</td>
<td>0.178</td>
<td>1.278</td>
<td>0.803</td>
<td>4.6</td>
</tr>
<tr>
<td>H6''</td>
<td>-0.030</td>
<td>1.392</td>
<td>0.723</td>
<td>6.8</td>
</tr>
<tr>
<td>H6''_b</td>
<td>0.094</td>
<td>1.506</td>
<td>0.815</td>
<td>6.8</td>
</tr>
<tr>
<td>H-O-4'A</td>
<td>0.097</td>
<td>1.019</td>
<td>0.736</td>
<td>5.7</td>
</tr>
<tr>
<td>H-O-6'A</td>
<td>0.263</td>
<td>0.803</td>
<td>0.652</td>
<td>4.0</td>
</tr>
<tr>
<td>H-N3A</td>
<td>-0.675</td>
<td>0.679</td>
<td>0.512</td>
<td>3.8</td>
</tr>
<tr>
<td>H5-Me_aA</td>
<td>-0.491</td>
<td>0.351</td>
<td>0.277</td>
<td>4.9</td>
</tr>
<tr>
<td>H5-Me_bA</td>
<td>-0.589</td>
<td>0.436</td>
<td>0.164</td>
<td>4.9</td>
</tr>
<tr>
<td>H5-Me_cA</td>
<td>-0.407</td>
<td>0.449</td>
<td>0.207</td>
<td>4.9</td>
</tr>
<tr>
<td>H6A</td>
<td>-0.301</td>
<td>0.604</td>
<td>0.395</td>
<td>3.4</td>
</tr>
<tr>
<td>H3'A</td>
<td>-0.355</td>
<td>0.957</td>
<td>0.471</td>
<td>3.4</td>
</tr>
<tr>
<td>H4'A</td>
<td>-0.227</td>
<td>0.818</td>
<td>0.655</td>
<td>3.7</td>
</tr>
<tr>
<td>H5'A</td>
<td>0.036</td>
<td>0.891</td>
<td>0.637</td>
<td>3.4</td>
</tr>
<tr>
<td>H1'A</td>
<td>0.000</td>
<td>0.870</td>
<td>0.427</td>
<td>3.3</td>
</tr>
<tr>
<td>H6'A</td>
<td>-0.108</td>
<td>0.634</td>
<td>0.599</td>
<td>3.6</td>
</tr>
<tr>
<td>H6''_A</td>
<td>0.119</td>
<td>0.547</td>
<td>0.592</td>
<td>3.7</td>
</tr>
<tr>
<td>H6''_bA</td>
<td>0.138</td>
<td>0.660</td>
<td>0.717</td>
<td>3.7</td>
</tr>
</tbody>
</table>

Hydrogen atom positions calculated assuming C/N-H distance of 1.08 Å.
$B_{iso}$ is derived from $U_{iso}$ of the bonded atom plus 0.01.
Table XR-4
Bond Distances in Angstroms

<table>
<thead>
<tr>
<th>Bond</th>
<th>Bond Distance</th>
<th>Bond</th>
<th>Bond Distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>O(2) - C(2)</td>
<td>1.215(9)</td>
<td>O(2A) - C(2A)</td>
<td>1.220(8)</td>
</tr>
<tr>
<td>O(4) - C(4)</td>
<td>1.226(9)</td>
<td>O(4A) - C(4A)</td>
<td>1.210(9)</td>
</tr>
<tr>
<td>O(2') - C(3')</td>
<td>1.415(8)</td>
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### Table XR-6

#### Torsion Angles in Degrees

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APPENDIX IV. 2-D NMR Spectra.

1. The 200 MHz COSY spectrum of acetal 10h.

![2-D NMR Spectra Diagram]
2. The 300 MHz HETCOR spectrum of acetal 10h.
3. The 300 MHz COSY spectrum of oxetane 18e.
4. The 300 MHz HETCOR spectrum of acetal 29a.
5. The 300 MHz HETCOR spectrum of oxetane 33.
6. The 300 MHz HETCOR spectrum of tribenzoate 48b.
7. The 300 MHz HETCOR spectrum of photo-adduct 72a.
8. The 300 MHz HETCOR spectrum of octane 75a.
9. The 300 MHz HETCOR spectrum of bicyclic nucleoside 89a.

\[ \text{Diagram of HETCOR spectrum} \]
10. The 300 MHz HETCOR spectrum of nucleoside 93*. 

![HETCOR spectrum of nucleoside 93* with chemical structures and spectral data.](image-url)
11. The 300 MHz HETCOR spectrum of bicyclic nucleoside 99b.

![HETCOR spectrum of bicyclic nucleoside 99b]