Synthesis of nitrogen-substituted methylenecyclopropanes by strain-driven overman rearrangement of cyclopropenylmethyl trichloroacetimidates

James K. Howard  
*University of Tasmania*

Chintan Amin  
*California State University*

Brendan Lainhart  
*California State University*

Jason A. Smith  
*University of Tasmania*

Jack Rimington  
*University of Wollongong*, jr161@uowmail.edu.au

See next page for additional authors

Publication Details

Synthesis of nitrogen-substituted methylenecyclopropanes by strain-driven overman rearrangement of cyclopropenylmethyl trichloroacetimidates

Abstract
Nitrogen-substituted methylenecyclopropanes have been prepared by a strain-driven Overman rearrangement of cyclopropenylmethyl trichloroacetimidates. The reaction proceeds at room temperature and without the need of a transition-metal catalyst. Furthermore, it has been shown that C-3-substituted cyclopropenylmethyl trichloroacetimidates undergo a hydrolytic ring-opening reaction to form allenylcarbinols.

Disciplines
Medicine and Health Sciences | Social and Behavioral Sciences

Publication Details

Authors
James K. Howard, Chintan Amin, Brendan Lainhart, Jason A. Smith, Jack Rimington, and Christopher J. T Hyland

This journal article is available at Research Online: http://ro.uow.edu.au/smhpapers/2314
Synthesis of Nitrogen-Substituted Methylene cyclopropanes by Strain-Driven Overman Rearrangement of Cyclopropenylmethyl Trichloroacetimidates

James K. Howard§, Chintan Amin†, Brendan Lainhart‡, Jason A. Smith§, Jack Rimington‡ and Christopher J. T. Hyland‡* 

‡School of Chemistry, University of Wollongong, New South Wales 2522, Australia. chris_hyland@uow.edu.au

§J. K. Howard, J. A. Smith, School of Physical Sciences (Chemistry), University of Tasmania, Private Bag 75, Hobart TAS 7001 (Australia).

† C. Amin, B. Lainhart, Department of Chemistry and Biochemistry, California State University Fullerton, California, 92831 (United States).

Abstract

Nitrogen-substituted methylenecyclopropanes have been prepared by a strain-driven Overman rearrangement of cyclopropenylmethyl trichloroacetimidates. The reaction proceeds at room temperature and without the need of a transition-metal catalyst. Furthermore, it has been shown that C-3 substituted cyclopropenylmethyl trichloroacetimidates undergo a hydrolytic ring-opening reaction to form allenylcarbinols.
Methylenecyclopropanes are strained, but remarkably stable, unsaturated carbocycles that have attracted significant interest for their strain-driven reactivity.[1-4] Typically, these highly strained systems are susceptible to ring-opening reactions [5-17], cycloaddition reactions [18-23] and ring-expansion reactions [23-28]. They have also proved to be precursors for densely functionalized cyclopropanes via ring-retaining C-C [29-37] and C-heteroatom bond forming reactions to their exocyclic double bond. [38-40]

A range of methods for the synthesis of methylenecyclopropanes exist [4],[41], however, relatively few of these consider the synthesis of heteroatom-substituted structures. Cyclopropenes, bearing an allylic leaving group, can be transformed into methylenecyclopropanes upon nucleophilic attack to the cyclopropene double bond. Such a process is thermodynamically favored due to the relief of strain energy associated with movement of the double bond to the exocyclic position. This approach has been developed for the synthesis of carbon/hydrogen-substituted methylenecyclopropanes [42-47], but is also one of the limited ways to prepare heteroatom-substituted systems. One notable example is the strain-driven [3,3]-sigmatropic rearrangement of cyclopropenylmethyl esters to acetoxy-substituted methylenecyclopropanes by Marek and co-workers (eq 1, Scheme 1) [43]. The groups of Marek [43] and Rubin [47] also reported a [2,3]-sigmatropic rearrangement of cyclopropenes to provide methylenecyclopropylphosphine oxides (eq 2 and 3, Scheme 1). Such heteroatom-substituted systems are of interest as phosphorous, oxygen and nitrogen substituents are ubiquitous in bioactive small molecules. In particular, N-substituted methylenecyclopropanes may act as precursors to
cyclopropylamines and cyclopropylureas, which are found in a range of bioactive molecules. For example,

**Scheme 1.** Previous syntheses of heteroatom-substituted methylenecyclopropanes and proposed Overman rearrangement of cyclopropenylmethyl trichloroacetimidates.

Cyclopropylurea **I** displays anti-HIV activity[48], **II** is a kinase inhibitor[49] and phenylcyclopropylamine **III** is a mono-amine oxidase (MAO) inhibitor (Figure 1).[50] As there are no general methods for the synthesis of nitrogen substituted methylenecyclopropanes there is a need for methodology to allow their preparation.

To address this gap, we hypothesized that an allylic trichloroacetimidate rearrangement (Overman rearrangement) of cyclopropenylmethyl
trichloroacetimidates (eq 4) should afford 2,2,2-trichloro-N-(2-methylene cyclopropyl)acetamides.

The Overman rearrangement is a powerful method for converting allylic alcohols to allylic amines. Typically, allylic trichloroacetimidates undergo either thermal or Pd(II)-catalyzed rearrangement to allylic trichloroacetamides that may be subsequently transformed into allylic amines by hydrolysis. [51-52] The thermal conditions typically require xylenes at reflux, however, we hypothesized that the strain relief associated with a cyclopropenylmethyl trichloroacetimidate undergoing rearrangement to a 2,2,2-trichloro-N-(2-methylene cyclopropyl)acetamide would allow the reaction to occur without a catalyst and without the need for high temperatures. Herein, we report the successful catalyst-free rearrangement of these systems at ambient temperature.

![Figure 1. Representative bioactive N-substituted cyclopropanes.](image)

Initial optimization of both imidate synthesis and subsequent Overman rearrangement utilized p-bromobenzaldehyde-derived cyclopropenylcarbinol 1a, (Table 1). The optimum conditions for trichloroacetimidate synthesis involved treating alcohol 1a with a catalytic amount of DBU in CH₂Cl₂ at -78 °C, followed by addition of trichloroacetonitrile and warming to -15 °C. The imidate 2a could be
identified in the \(^1\)H NMR spectrum by the shift of the singlet corresponding to the proton adjacent to oxygen from 5.63 ppm in \(1a\) downfield to 6.76 ppm for the imidate \(2a\). The use of other bases such as NaH and KH gave only recovered starting material. It was found to be important that the imidation reaction with DBU should be left for no longer than 3 hours and allowed to warm to a maximum of -15 °C. Longer reaction time, or higher temperatures led to decomposition and/or lower yielding partial rearrangement to the amide. The imidate could be obtained after rapid removal of all volatile components under reduced pressure and was used directly without further purification.

Table 1. Optimization of the Overman rearrangement of \(2a\) to yield trichloroacetimidate \(3a\).

<table>
<thead>
<tr>
<th>Entry</th>
<th>additive</th>
<th>conditions</th>
<th>Time</th>
<th>Yield(^{[a]})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>30 °C, CH(_2)Cl(_2)</td>
<td>40 h</td>
<td>21%</td>
</tr>
<tr>
<td>2</td>
<td>1 equiv K(_2)CO(_3)</td>
<td>30 °C, CH(_2)Cl(_2)</td>
<td>40 h</td>
<td>63%</td>
</tr>
<tr>
<td>3</td>
<td>5 mol% PdCl(_2)(MeCN(_2))</td>
<td>30 °C, CH(_2)Cl(_2)</td>
<td>24 h</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>4</td>
<td>1 equiv K(_2)CO(_3)</td>
<td>30 °C, DMF</td>
<td>22 h</td>
<td>53%</td>
</tr>
</tbody>
</table>

\(^{[a]}\) isolated yields.
With conditions for the preparation of the imidate in hand, attention was
turned towards identifying optimum conditions for the Overman rearrangement. We
were delighted to find that imidate 2a underwent efficient [3,3]-sigmatropic
rearrangement under mild conditions (30 °C, CH₂Cl₂, Table 1, entry 1) to yield a
single isomer of 3a. This two-step yield was significantly increased by the addition of
K₂CO₃ as a base. However, changing the solvent to DMF resulted in a faster but
lower yielding reaction (entry 4, full conversion in 22 hours). It also quickly became
apparent that catalysis of the rearrangement by PdCl₂(MeCN)₂ was inefficient in
comparison to the mild thermal conditions (entry 3, Table 1). The Pd-catalyst gave
only trace product accompanied by significant decomposition. Evidence for
methylenecyclopropane formation was indicated by ¹H NMR resonance of the proton
adjacent to the oxygen of the imidate shifting from a singlet at 6.76 ppm to a triplet at
7.13 ppm corresponding to the alkene.

A range of different aryl-substituted cyclopropenylmethyl
trichloroacetimidates was subjected to rearrangement (Table 2). It can be observed
that derivatives with electron-rich (3d-e) and heterocyclic (3b) aryl groups underwent
efficient rearrangement. Halogen-substituted phenyl groups were well tolerated (3a
and 3g), as was ortho-substitution (3g). Highly electron-deficient aryl nitro-
substituted systems however, did not undergo rearrangement at all and just provided
recovered starting material. This lack of reactivity is likely due to the electron-
deficient aryl groups disfavoring the development of positive charge in the transition
state at the oxygen-bearing carbon. This observation, coupled with the higher
reactivity of electron-rich aryl groups, suggest the possibility of a transition state with
ionic character. Curiously, the dodecyl aldehyde-derived cyclopropenylcarbinol 1j
could not be converted to the corresponding imidate despite extended reaction times and excesses of reagents [53].

Table 2. Scope of the Overman rearrangement to yield 2,2,2-trichloro-N-(2-methylenecyclopropyl)acetamides 3.^[a]

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>63%</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>99%</td>
<td></td>
</tr>
<tr>
<td>3c</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td>3d</td>
<td>77%</td>
<td></td>
</tr>
<tr>
<td>3e</td>
<td>98%</td>
<td></td>
</tr>
<tr>
<td>3f</td>
<td>47%</td>
<td></td>
</tr>
<tr>
<td>3g</td>
<td>48%</td>
<td></td>
</tr>
</tbody>
</table>

[a] Isolated yields over two steps, representing a single E-isomer of the product. [b] Imidate was formed but rearrangement did not proceed. [c] Imidate could not be formed.
All of the methylenecyclopropanamides were obtained as a single \( E \)-isomer, suggesting that the reaction likely proceeds through a [3,3] sigmatropic rearrangement mechanism as is normally observed for the Overman rearrangement.[52] The stereochemistry of the rearrangement is assigned based on nOe correlations and is explained by a pseudo chair conformation 4 similar to that proposed by Marek and co-workers.[43]

**Scheme 1. Manipulation of methylenecyclopropane 3a/f under basic conditions to yield ureas 5a/f or oxaacetamide 6.**

Attempts to reduce or hydrolyze the trichloroacetamides to reveal the free amines were not successful. Conditions investigation included: acid hydrolysis (1M HCl, 0\(^\circ\)C), basic hydrolysis (KOH/EtOH) and reductive cleavage (DIBAL-H or NaBH\(_4\)); in each case recovery of starting material along with decomposition was observed. This was attributed to an unstable isocyanate intermediate resulting in the loss of chloroform, as shown by Nishikawa et al.[54] A different course of action was taken, which was to generate the isocyanate intermediate from 3a/3f at -78 \(^\circ\)C with
Cs$_2$CO$_3$ in DMF before capturing it with pyrrolidine to successfully yield the desired ureas 5a/5f respectively. Cyclopropylureas are valuable targets given their occurrence in a range of bioactive molecules, including: kinase inhibitors [49], epoxide hydrolase inhibitors [55] and HIV-1 reverse transcriptase inhibitors [48]. Interestingly when bench grade DMF, which contained traces of water, was used a 2-oxaacetamide 6 can be formed in a moderate yield.[56]

Given the potential of methylenecyclopropanes 3 as precursors to nitrogen-substituted cyclopropanes, a catalytic hydrogenation was also attempted in order to provide the saturated system. Hydrogenation initially yielded a mixture of reduction products identified as various dehalogenated cyclopropanes. Fortuitously, with extended reaction times, hydrogenation yielded the monochloro amide 7 as a 2.5:1 mixture of diastereoisomers in 41% yield. Of note is the remaining chloride in 7, representing a useful handle for further functionalization by substitution or coupling chemistry.

Scheme 2. Catalytic hydrogenation of methylenecyclopropane 3f to yield saturated amidocyclopropane 7.

We also briefly investigated the Overman rearrangement of cyclopropenylmethyl trichloroacetimidate 9 bearing a gem-dimethyl group at C-3.
While the trichloroacetimidates 9 could be readily prepared, they underwent rapid hydrolytic ring-opening in the presence of silica-gel to form allenylcarbinol 10. This reaction pathway is highly favored due to the stabilization of the allenyl cation by the gem-dimethyl group in conjunction with the relief of ring-strain. Indeed, we have previously demonstrated that related cyclopropenylmethyl acetates undergo ring-opening to allenyl cations 11 in the presence of TiCl4.[57]

**Scheme 3.** Formation of allenylcarbinols 10 by silica gel-induced hydrolytic ring-opening of acetimidate 9 via allenyl cation 11.

**Conclusion**

In summary, we have developed a method for the preparation of functionalized nitrogen-substituted methylene-cyclopropanes via an Overman rearrangement. There are currently no general methods available for these structures, which as we have shown have some potential as precursors to cyclopropylureas. These rearrangements occur under very mild conditions by virtue of strain-relief and also occur with complete stereoselectivity to give the $E$-methylenecyclopropanes. We
have also described initial studies on the manipulation of these systems and divergent reactivity towards the formation of allenyl carbinols when cation-stabilizing groups are present.

**Experimental Section**

**General Methods**

Unless otherwise stated all reactions were carried out under an argon or nitrogen atmosphere in dry glassware. Reactions were monitored by TLC using glass-backed silica gel plates or by GC and GC/MS. Compounds were purified using flash column chromatography or by radial chromatography with a Chromatotron®. Reaction solvents were obtained from a solvent purification system having passed through anhydrous alumina columns. nBuLi was titrated against diphenylacetic acid prior to use. 1,2,2-Tribromo-1-methylpropane [58], 1,1,2-tribromo-2,3,3-trimethylcyclopropane [59], (2-methylcycloprop-1-enyl)(4-bromophenyl)methanol 1a [54], phenyl(2,3,3-trimethylcycloprop-1-en-1-yl)methanol 1c [60], (2-methylcycloprop-1-enyl)(4-methoxyphenyl)methanol 1d [58], 2-methylcycloprop-1-enyl)(4-methylphenyl)methanol 1e [58], phenyl(2,3,3-trimethylcycloprop-1-enyl)methanol 8a [59], and (4-bromophenyl)(2,3,3-trimethylcycloprop-1-enyl)methanol 8b [59] were synthesized and characterized as previously reported. Other reagents were commercially available and used without further purification. The following abbreviations were used to describe ¹H spectra peak splitting patterns; s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dddd = doublet of doublet of doublet of doublets, t = triplet, dt = doublet of triplets, q = quartets, dq = doublet of quartets, bs = broad singlet, m = multiplet and ad
= apparent doublet. IR spectra were recorded as films on NaCl plates (liquids) or in a NaCl solution cells (solids).

**General procedure of the synthesis- of cyclopropenylcarbinols.**

In an oven dried 2-neck flask was added 1,2,2-tribromo-1-methylpropane (1.0 equiv.) and anhydrous Et₂O (20 mL) before cooling to -78 °C and adding n-BuLi (1.45 M, 1.9 equiv.). The resultant solution was warmed to -10°C for 30 min before cooling to -50°C and adding the selected aldehyde. The solution was taken to room temperature after 10 min and left to stir for 2 h before quenching with H₂O (20 mL). The mixture was then extracted with Et₂O (3 x 20 mL), dried on Na₂SO₄ and filtered before the solvent was removed under reduced pressure. The crude oil was the purified by means of flash chromatography on silica gel treated with Et₃N (typically ethyl acetate:hexanes).

**2-Methylcycloprop-1-enyl][1-(p-toluenesulfonyl)pyrrol-2-yl]methanol (Ib).** From N-toluenesulfonylpyrrole-2-carboxaldehyde as a yellow oil using 100% CH₂Cl₂ for purification; 179.5 mg, 29% yield. IR (ATR): 3534, 2948, 2869, 1596, 1362, 1173 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 0.99 (d, J = 8.4 Hz, 1H), 1.05 (d, J = 8.4 Hz, 1H), 2.09 (d, J = 1.5 Hz, 3H), 2.40 (s, 3H), 2.94 (d, J = 6 Hz, 1H), 5.99 (s, 1H), 6.22-6.25 (m, 2H), 7.26-7.30 (m, 3H), 7.73 (d, J = 8.4 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 9.9, 11.5, 21.7, 62.8, 109.1, 110.8, 111.7, 114.3, 123.8, 126.9, 130.0, 134.9, 136.2, 145.2. HRMS (+EI-Orbitrap): m/z for C₁₆H₁₇NO₃SNa calcd 326.0826; found, 326.0821.
1-(2-Methylcycloprop-1-enyl)dodecan-1-ol (Ij) From dodecylaldehyde as a colorless oil using 20% ethyl acetate: hexanes; 345 mg, 57%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.89 (t, $J = 7.0$ Hz, 3H), 0.92 (d, $J_{ab} = 9.0$ Hz, 1H), 0.95 (d, $J_{ab} = 9.0$ Hz, 1H), 1.19 – 1.47 (m, 18H), 1.70 (dd, $J = 7.0$, 15.0 Hz, 2H), 1.87 (br s, 1H), 2.10 (d, $J = 1.5$ Hz, 3H), 4.60 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 8.2, 11.5, 14.1, 22.7, 25.2, 29.3, 29.5, 29.6, 29.6, 31.9, 35.8, 68.0, 108.3, 111.2. IR: 3416 cm$^{-1}$. HRMS (MMI-TOF) (m/z): (M - H)$^+$ calcd for C$_{16}$H$_{29}$O, 237.2213; found, 237.2214.

(2-Methylcycloprop-1-enyl)(3-methoxyphenyl)methanol (If). From 3-methoxybenzaldehyde as pale yellow oil using 20% ethyl acetate: hexanes; 45.5 mg, 20% yield. IR (ATR): 3403, 2943, 2869, 1260 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.02 (d, $J = 8.4$ Hz, 1H), 1.06 (d, $J = 8.4$ Hz, 1H), 2.09 (d, $J = 1.2$ Hz, 3H), 3.80 (s, 3H), 5.64 (bs, 1H), 6.82-6.86 (m, 1H), 6.96-6.99 (m, 2H), 7.27 (t, $J = 8.1$ Hz, 1H). $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 20.0, 20.9, 55.3, 112.6, 113.5, 119.9, 121.1, 128.3, 129.7, 138.1, 159.8, 162.3. HRMS (+EI-Orbitrap): m/z for C$_{12}$H$_{15}$O$_2$ calcd 191.1072; found, 191.1067.

(2-Methylcycloprop-1-enyl)(2-chlorophenyl)methanol (Ig). From 2-chlorobenzaldehyde as a clear oil using 20% ethyl acetate: hexanes; 184.8 mg >99% yield. IR (ATR): 3357, 2964, 2871, 1441 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.03 (s, 2H), 2.06 (s, 3H), 2.59 (bs, 1H), 6.03 (bs, 1H), 7.22-7.28 (m, 2H), 7.30-7.37 (m, 1H), 7.50-7.53 (m, 1H). $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 9.1, 11.4, 67.2, 109.7, 110.6, 127.1, 127.9, 128.9, 129.6, 132.3, 138.7. HRMS (+EI-Orbitrap): m/z for C$_{11}$H$_{12}$ClO calcd 195.0571; found, 195.0569.
2-Methylcycloprop-1-enyl)(4-nitrophenyl)methanol (Ih). From 4-nitrobenzaldehyde as a yellow semi-solid using 50% Et₂O:pentane; 335.1 mg, 94% yield. IR (ATR): 3594, 3054, 2986, 1268 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 1.05 (d, Jₐb = 8.3 Hz, 1H), 1.08 (d, Jₐb = 8.3 Hz, 1H), 2.11 (d, J = 1.4 Hz, 3H), 5.80 (s, 1H), 7.61 (d, J = 8.9 Hz, 2H), 8.24 (d, J = 8.9 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 9.1, 11.4, 69.2, 110.0, 111.6, 123.8, 127.0, 148.4. HRMS (MMI-TOF): m/z for (2M + NH₄)⁺ calcd for C₂₂H₂₆N₃O₆, 428.1822; found: 428.1828.

(2-Methylcycloprop-1-enyl)(3-nitrophenyl)methanol (II). From 3-nitrobenzaldehyde as an off-white semi-solid without need for purification by column; 309.2 mg, 88% yield. IR (ATR): 3583, 2857, 1529, 1350 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.04 (d, J = 8.3 Hz, 1H), 1.08 (d, J = 8.3 Hz, 1H), 2.11 (d, J = 1.4 Hz, 3H), 5.79 (s, 1H), 7.55 (t, J = 7.9 Hz, 1H), 7.81 – 7.72 (m, 1H), 8.14 - 8.18 (m, 1H), 8.29 – 8.31 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 9.1, 11.4, 69.1, 109.9, 111.5, 121.4, 122.8, 129.5, 132.5, 143.4, 189.9. HRMS (+EI-Orbitrap): m/z for C₁₁H₁₁NO₃Na calcd 228.0636; found, 228.0631.

(2-Fluorophenyl)(2,3,3-trimethylcycloprop-1-en-1-yl)methanol (8c). From 2-fluorobenzaldehyde as a clear oil using 20% ethyl acetate: hexanes for purification; 610.5 mg, 20% yield. IR (ATR): 3447, 2957, 1610, 1487, 1454, 1032, 1032, 754 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.03 (s, 3H), 2.10 (3, 3H), 1.63 (bs, 1H), 1.97 (s, 3H), 5.93 (s, 1H), 7.03 (app t, J = 8.7 Hz, 1H), 7.12 (t, J = 7.2 Hz, 1H), 7.26-7.28 (m, 1H), 7.47 (t, J = 7.2 Hz). ¹³C NMR (75 MHz, CDCl₃): δ 8.6, 22.2, 25.3, 25.6, 65.1 (d, J = 4.6 Hz), 115.3 (d, J = 21.8 Hz), 124.6 (d, J = 13.8 Hz), 124.9 (d, J =
3.5 Hz), 128.5 (d, J = 4.6 Hz), 129.9 (d, J = 8.1 Hz), 159.9 (d, J = 245.1 Hz). HRMS (ASAP-TOF): m/z For C_{13}H_{15}FO +H – H_2O calcd 189.1080; found, 189.1071.

**General procedure for the synthesis of nitrogen-substituted alkylidenecyclopropanes.**

To a stirred solution of cyclopropenylcarbinol (1 equiv.) in CH_{2}Cl_{2} (~0.1 M), was added DBU (0.15 equiv.) followed by trichloroacetonitrile (1.5 equiv.) at -78 °C. The resulting solution was allowed to warm to -10 °C over a period of 2 h before the reaction mixture was evaporated to dryness under reduced pressure. The resulting oil was in most cases identified as the intermediate imidate by NMR of the crude reaction mixture and was used directly in the rearrangement step. Where the \(^1\)H NMR of the crude imidate was clean a listing of the signals is provided below. A solution of crude imidate (1 equiv.) and K_{2}CO_{3} (1.5 equiv.) in CH_{2}Cl_{2} (1 mL) was allowed to stir at 30 °C for 40 h. After this time the solution was filtered before removal of solvent by evaporation under reduced pressure. The crude semisolid was purified by means of flash chromatography on a neutral alumina column (ethyl acetate/hexanes) to yield the exocyclic cyclopropenyl trichloroacetamide.

1-[(E)-2-(4-Bromophenyl)methylidene-1-methylcyclopropylamino]-2,2,2-trichloro-1-ethanone (3a). From 1a as an off-white semi-solid after purification with 20% ethyl acetate: hexanes; 51 mg, 63% yield over two steps. **Imidate:** \(^1\)H NMR (300 MHz, CDCl_{3}): \(\delta\) 1.06 (d, J = 8.3 Hz, 1H), 1.14 (d, J = 8.3 Hz, 1H), 2.09 (d, J = 1.5 Hz, 3H), 6.76 (s, 1H), 7.34 (d, J = 8.3 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H), 8.43 (s, 1H). **3a:** IR (ATR): 3289, 2922, 2850, 1694, 1506 cm^{-1}. \(^1\)H NMR (300 MHz, CDCl_{3}): \(\delta\) 1.60 (s, 3H), 1.76 (dd, J = 10.9, 2.6 Hz, 1H), 1.83 (dd, J = 10.9, 2.6 Hz, 1H), 7.07 (s, 1H), 7.13 (t, J = 2.6 Hz, 1H), 7.39 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 8.6 Hz, 2H). \(^{13}\)C NMR
(75 MHz, CDCl$_3$): $\delta$ 19.9, 20.9, 29.9, 120.3, 121.8, 128.7, 128.8, 131.8, 135.6, 162.3. HRMS (+EI-Orbitrap): $m/z$ for C$_{13}$H$_{11}$BrCl$_3$NONa calcd 403.8987; found, 403.8982.

1-[(E)-2-[[1-(p-Tolylsulfonyl)-1H-pyrrol-2-yl]methylidene]-1-methylcyclopropylamino]-2,2,2-trichloro-1-ethanone (3b). From 1b as a yellow oil after purification with 100% CH$_2$Cl$_2$; 275 mg, >99% yield over two steps. IR (ATR): 3364, 2969, 2027, 1713, 1494, 1367, 1174 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.55 (s, 3H), 1.55-1.59 (m, 1H), 1.62 (dd, $J = 11.1$, 2.7 Hz, 1H), 2.36 (s, 3H), 6.27 (t, $J = 3.9$ Hz, 1H), 6.52-6.52 (m, 1H), 6.99 (s, 1H), 7.26 (d, $J = 8.1$ Hz, 2H), 7.34 (dd, $J = 4.8$, 1.5 Hz, 1H), 7.64 (t, $J = 2.7$ Hz, 1H), 7.72 (d, $J = 8.1$ Hz, 2H). $^{13}$C NMR (75 MHz, CHCl$_3$): $\delta$ 19.6, 21.0, 21.7, 31.4, 110.5, 112.5, 112.7, 123.1, 127.1, 128.5, 130.1, 131.9, 135.9, 145.1, 161.98. HRMS (+EI-Orbitrap): $m/z$ for C$_{18}$H$_{17}$Cl$_3$N$_2$O$_3$S $+H$ calcd 447.0103; found, 447.0098.

1-[(E)-2-Phenylmethylidene-1-methylcyclopropylamino]-2,2,2-trichloro-1-ethanone (3c). From 1c as an off-white semisolid after purification with 20% ethyl acetate: hexanes; 80.1 mg, 83% yield over two steps. **Imidate:** $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.07 (d, $J = 8.4$ Hz, 1H), 1.15 (d, $J = 8.4$ Hz, 1H), 2.09 (d, $J = 1.4$ Hz, 3H), 6.82 (s, 1H), 7.32-7.40 (m, 3H), 7.45-7.48 (m, 2H), 8.42 (s, 1H). **1c:** IR (ATR): 3415, 3054, 2986, 1719, 1492, 1421, 1265, 895 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.61 (s, 3H), 1.80 (dd, $J = 10.8$, 2.6 Hz, 1H), 1.86 (dd, $J = 10.8$, 2.6 Hz, 1H), 7.06 (bs, 1H), 7.19 (t, $J = 2.6$ Hz, 1H), 7.27-7.38 (m, 3H), 7.45-7.56 (m, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 20.0, 21.0, 29.9, 121.2, 127.2, 127.9, 128.0, 128.7, 136.6, 162.3. HRMS (MMI-TOF) $m/z$: (M + H)$^+$ calcd for C$_{13}$H$_{13}$NOCl$_3$: 304.0064; found: 304.0057.
1-[\{(\text{E})-2-(4-Methoxyphenyl)methylidene-1-methylcyclopropylamino\}]-2,2,2-trichloro-1-ethanone (3d). From 1d as an off-white semi-solid after purification with 30% ethyl acetate: hexanes; 145.6 mg, 77% yield over two steps. *Imidate:* $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.09 (dd, $J = 23.7$, 8.4 Hz, 2H), 2.09 (d, $J = 1.5$ Hz, 3H), 3.79 (s, 3H), 6.75 (s, 1H), 6.85-6.92 (m, 2H), 7.38 (d, $J = 8.7$, 2H), 8.38 (s, 1H). 3d: IR (ATR): 3423, 3054, 2986, 1717, 1512, 1421, 1265, 705 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.60 (s, 3H), 1.75 (dd, $J = 8.6$, 2.4 Hz, 1H), 1.81 (dd, $J = 10.7$, 2.8 Hz, 1H), 3.81 (s, 3H), 6.89 (d, $J = 8.8$ Hz, 2H), 7.12 (t, $J = 2.6$ Hz, 1H), 7.48 (d, $J = 8.7$ Hz, 2H). $^{13}$C NMR (75 MHz, CHCl$_3$): $\delta$ 19.8, 21.0, 29.9, 55.3, 114.1, 120.5, 125.5, 128.4, 129.4, 159.4, 162.3. HRMS (MMI-TOF) $m/z$: (M + H$^+$) calcd for C$_{14}$H$_{15}$NO$_2$Cl$_3$: 334.0170; found: 334.0157.

1-[\{(\text{E})-2-(4-Methylphenyl)methylidene-1-methylcyclopropylamino\}]-2,2,2-trichloro-1-ethanone (3e). From 1e as an off white semisolid after purification with 30% ethylacetate: hexanes; 281 mg, 98% yield over two steps. *Imidate:* $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.06 (d, $J = 8.4$ Hz, 1H), 1.14 (d, $J = 8.4$ Hz, 1H), 2.10 (d, $J = 1.5$ Hz, 3H), 2.36 (s, 3H), 6.78 (s, 1H), 7.19 (d, $J = 7.9$ Hz, 2H), 7.35 (d, $J = 7.9$ Hz, 2H), 8.39 (s, 1H). 3e: IR (cm$^{-1}$): 3417, 3050, 3030, 2971, 2929, 2864, 1715, 1513, 1489, 1236, 821, 711. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.60 (s, 3H), 1.77 (dd, $J = 10.6$, 2.6 Hz, 1H), 1.83 (dd, $J = 10.7$, 2.6 Hz, 1H), 2.35 (s, 3H), 7.01 (bs, 1H), 7.11-7.19 (m, 3H), 7.44 (d, $J = 8.1$ Hz, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 20.1, 23.1, 21.5, 30.0, 121.1, 126.9, 127.2, 129.5, 134.0, 138.0, 162.4. HRMS (MMI-TOF) $m/z$: (M + H$^+$) calcd for C$_{14}$H$_{15}$NOCl$_3$: 318.0221; found: 318.0214.
1-[(E)-2-(3-Methoxyphenyl)methylidene-1-methylcyclopropylamino]-2,2,2-trichloro-1-ethanone (3f). From 1f an off white semisolid after purification with 30% ethyl acetate: hexanes; 38 mg, 47% yield over two steps. 3f: IR (cm⁻¹): 3443, 2957, 1600, 1511, 1249, 1170, 1030. §H NMR (300 MHz, CDCl₃): δ 1.60 (s, 3H), 1.79 (dd, J = 10.9, 2.6 Hz, 1H), 1.86 (dd, J = 10.9, 2.6 Hz, 1H), 3.82 (s, 3H), 6.81-6.86 (m, 1H), 7.06 (s, 1H), 7.09 (t, J = 2.4 Hz, 1H), 7.12 (ap, 1H), 7.15-7.16 (m, 1H), 7.27 (t, J = 7.8 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 20.0, 20.9, 29.9, 55.3, 92.6, 112.6, 113.5, 119.9, 121.1, 128.3, 129.7, 138.1, 159.8, 162.3. MS: m/z 356 (M+Na, 100), 213 (17). HRMS (+El-Orbitrap): m/z for C₁₄H₁₂Cl₃NO₂Na calcd 355.9987; found, 355.9982.

1-[(E)-2-(2-Chlorophenyl)methylidene-1-methylcyclopropylamino]-2,2,2-trichloro-1-ethanone (3g). From 1g as an off-white semisolid after purification with 20% ethyl acetate: hexanes; 88.8 mg, 48% yield over two steps. Imidate: §H NMR (300 MHz, CDCl₃): δ 1.08 (d, J = 8.4 Hz, 1H), 1.26 (d, J = 8.4 Hz, 1H), 2.08 (d, J = 1.5 Hz, 3H), 7.15 (s, 1H), 7.25-7.32 (m, 2H), 7.38-7.41 (m, 1H), 7.53-7.56 (m, 2H), 8.46 (s, 1H). 3g: IR (ATR): 3317, 2968, 1695, 1495 cm⁻¹. §H NMR (300 MHz, CDCl₃): δ 1.62 (s, 3H), 1.81 (dd, J = 11.1, 2.6 Hz, 1H), 1.88 (dd, J = 11.1, 2.6 Hz, 1H), 7.10 (bs, 1H), 7.18-7.25 (m, 2H), 7.38 (dd, J = 7.7, 1.6 Hz, 1H), 7.58 (t, J = 2.6 Hz, 1H), 7.79 (dd, J = 7.6, 1.8 Hz, 1H). ¹³C NMR (75 MHz, CHCl₃): δ 20.1, 20.9, 30.0, 117.1, 126.8, 127.2, 129.0, 129.9, 130.7, 133.6, 134.2, 162.2. HRMS (+El-Orbitrap): m/z for C₁₃H₁₁Cl₄NONa calcd 359.9492; found, 359.9487.

1-[(E)-2-[(4-Bromophenyl)methylidene]-1-methylcycloproplamino]-1-pyrrolidinyl]formaldehyde (5a). To a solution of 3a (62 mg, 0.16 mmol) in anhydrous DMF (2 mL) under nitrogen was added Cs₂CO₃ (140 mg, 0.43 mmol) at -78 °C. The mixture was allowed to stir for 1 h before the slow addition of pyrrolidine (140 μL,
120 mg, 1.69 mmol), which was subsequently allowed to warm to room temperature over 18 h. After this time the mixture was diluted with 50% ethyl acetate in hexanes and washed with water. The crude mixture was dried on Na$_2$SO$_4$, filtered and had the solvent removed under reduced pressure. The crude oil was purified by means of flash chromatography with 100% ethyl acetate to afford 5a as a yellow oil in a 39% yield (21.0 mg, 0.06 mmol). IR (ATR): 3252, 2970, 1689, 1489, 1383, 1161 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.56 (s, 3H), 1.74-1.77 (m, 4H), 2.02 (s, 3H), 2.41-2.47 (m, 2H), 2.68-2.72 (m, 2H), 6.65 (bs, 1H), 7.33 (d, $J = 8.4$ Hz, 2H), 7.53 (d, $J = 8.4$ Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 11.8, 23.9, 24.5, 46.2, 77.9, 122.1, 129.7, 130.3, 131.0, 131.5, 158.5, 171.7. HRMS (+EI-Orbitrap): $m/z$ For C$_{16}$H$_{19}$BrN$_2$O +H calcd 335.0759; found, 335.0754.

1-[(E)-2-[(3-Methoxyphenyl)methylidene]-1-methylcyclopropylamino](1-pyrrolidinyl)formaldehyde (5f). To a solution of 3f (88.1 mg, 0.26 mmol) in anhydrous DMF (2 mL) under nitrogen was added Cs$_2$CO$_3$ (214.5 mg, 0.75 mmol) at -78°C. The mixture was allowed to stir for 1 h before the slow addition of pyrrolidine (130 $\mu$L, 112 mg, 1.57 mmol), which was subsequently allowed to warm to room temperature over 18 h. After this time the mixture was diluted with 50% ethyl acetate in hexanes and washed with water. The crude mixture was dried on Na$_2$SO$_4$, filtered and had the solvent removed under reduced pressure. The crude oil was purified by means of flash chromatography with 30% ethyl acetate: hexanes to afford 5f as a yellow oil in a 24% yield (18.3 mg, 0.06 mmol). IR (ATR): 3222, 2964, 2834, 1689, 1600, 1578 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.57 (s, 3H), 1.75-1.78 (m, 4H), 2.03 (s, 3H), 2.42-2.47 (m, 2H), 2.69-2.74 (m, 2H), 3.82 (s, 3H), 6.54 (bs, 1H), 6.86-6.89 (m, 1H), 7.01-7.03 (m, 2H), 7.32 (t, $J = 8.4$ Hz, 1H). $^{13}$CNMR (100 MHz, CDCl$_3$): $\delta$ 11.8, 23.9, 24.5, 46.7, 55.3, 77.7, 113.7, 114.9, 121.8, 129.3, 130.7, 132.7, 158.2,
159.5, 172.1. HRMS (+EI-Orbitrap): m/z For C_{17}H_{22}N_{2}O_{2} +H calcd 287.1759; found, 287.1754.

1-\{(E)-2-[(m-Methoxyphenyl)methylidene]-1-methylcyclopropylamino\}-2-(1-pyrrolidinyl)-1,2-ethanedione (6). To a solution of 3f (19.8 mg, 0.06 mmol) in DMF (1 mL, bench grade) under nitrogen was added pyrrolidine (50 μL, 43 mg, 0.6 mmol) followed by Cs_{2}CO_{3} (45.0 mg, 0.14 mmol) at -78 °C. The mixture was subsequently allowed to warm to room temperature over 18 h. After this time the mixture was diluted with 50% ethyl acetate in hexanes (5 mL) and washed with water (5 x 5 mL). The crude mixture was dried on Na_{2}SO_{4}, filtered and had the solvent removed under reduced pressure. The crude oil was purified by means of flash chromatography with 30% ethyl acetate: hexanes to afford 6f as a yellow oil in 58% yield (10.8 mg, 0.03 mmol). IR (ATR): 3297, 2969, 1687, 1623, 1428 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 1.56 (s, 3H), 1.76 (dq, J = 10.8, 2.8 Hz, 2H), 1.83 (p, J = 6.6 Hz, 2H), 1.95 (p, J = 6.6 Hz, 2H), 3.52 (t, J = 6.8 Hz, 2H), 4.00 (dt, J = 6.8, 3.6 Hz, 2H), 6.79-6.82 (m, 1H), 7.07-7.12 (m, 3H), 7.25 (t, J = 8.0 Hz, 1H), 7.9 (bs, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 19.9, 21.5, 23.5, 26.9, 28.5, 48.0, 48.8, 55.3, 112.4, 113.3, 119.9, 120.4, 129.6, 129.7, 138.6, 159.3, 159.9, 161.4. HRMS (+EI-Orbitrap): m/z For C_{18}H_{22}O_{3}N_{2} +Na calcd 337.1528; found, 337.1523.

2-Chloro-1-\{(2-[(m-Methoxyphenyl)methyl]-1-methylcyclopropylamino\}-1-ethanone (7). Under an atmosphere of H₂, 3f (88.9 mg, 0.26 mmol) was stirred in ethanol (10 mL) for 2 days with Pd/C (8.0 mg) at room temperature. After this time the mixture was passed through a short plug of Celite® before the solvent was removed under reduced pressure to reveal a brown oil which was subsequently purified be means of
flash chromatography with 30% ethyl acetate: hexanes to reveal 7 as a slightly yellow oil in a 41% yield (30.3 mg, 0.11 mmol). IR (ATR): 3292, 3096, 2959, 1663, 1489, 1251 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 0.57 (t, J = 6.0 Hz minor isomer), 0.68 (t, J = 6.0 Hz major isomer), 1.01 (dd, J = 9.0, 6.0 Hz, 1H, major isomer), 1.05 (dd, J = 10.0, 6.0 Hz, 1H, minor isomer), 1.20-1.28 (m, 1H, major isomer), 1.28-1.34 (m, 1H, major isomer), 1.44 (s, 3H, major isomer), 1.49 (s, 3H, minor isomer), 2.51 (dd, J = 15.0, 8.0 Hz, 1H, minor isomer), 2.62 (dd, J = 15.0, 8.0 Hz, 1H, major isomer), 2.83 (dd, J = 15.0, 7.0 Hz, 1H, major isomer), 2.93 (dd, J = 15.0, 6.0 Hz, 1H, minor isomer), 3.83 (s, 3H, major isomer), 3.83 (s, 3H, minor isomer), 3.99 (s, 2H, minor isomer), 4.03 (s, 2H, major isomer), 6.78-6.90 (m, 3H, minor and major isomer), 7.25 (t, J = 8.0 Hz, 1H, major isomer), 7.25 (t, J = 8.0 Hz, 1H, major isomer). ¹³C NMR (100 MHz, CDCl₃): δ 18.3, 20.4, 20.6, 23.6, 25.4, 26.2, 33.3, 33.5, 35.0, 35.3, 42.8, 42.9, 55.3, 55.3, 111.4, 111.5, 114.1, 114.3, 120.6, 120.8, 129.5, 129.7, 142.7, 142.9, 159.8, 159.9, 166.0, 166.8. HRMS (+EI-Orbitrap): m/z For C₁₄H₁₈ClNO₂ +Na calcd 290.0923; found, 290.0918.

General procedure for the synthesis of allenylcarbinols 10

To a stirred solution of the appropriate cyclopropenylcarbinol 8 (1 equiv.) in CH₂Cl₂ (~0.1 M), was added DBU (0.15 equiv.) followed by trichloroacetonitrile (1.5 equiv.) at -78 °C. The resulting solution was allowed to warm to -10 °C over a period of 2 h before the reaction mixture was evaporated to dryness under reduced pressure. The resulting oil was in most cases identified as the intermediate imidate by crude ¹H NMR and was also used directly in the allene-formation step. The crude imidate (1 equiv.) was dissolved in reagent-grade CH₂Cl₂ (~0.01 M), cooled to -10 °C and silica gel (500 mg per 0.1 mmol of imidate) added. The reaction was stirred vigorously and
allowed to warm to room temperature. After consumption of the starting material (typically about 3 h), the reaction was filtered, evaporated to dryness and purified by flash column chromatography (15% Ethyl acetate:hexanes) to yield the pure allenyl carbinol.

2,3-Dimethyl-5-phenylpenta-3,4-dien-2-ol (10a). From 8a as a pale yellow oil after filtration and evaporation to dryness and purification with 15% ethyl acetate:hexanes; 14.1 mg, 48% yield. IR (ATR): 3593, 3054, 2986, 1421, 1265, 733, 705 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.45 (s, 6H), 1.90 (d, \(J = 2.9\) Hz, 3H), 6.21 (q, \(J = 2.9\) Hz, 1H), 7.18-7.33 (m, 5H). \(^1\)C (100 MHz, CDCl\(_3\)) \(\delta\) 14.5, 29.0, 29.3, 71.7, 96.5, 111.9, 126.6, 126.9, 128.7, 135.2, 200.6. HRMS (MMI-TOF): \(m/z\) For C\(_{13}\)H\(_{16}\)O -H calcd 187.1201; found, 187.187.1258.

5-(2-Bromophenyl)-2,3-dimethylpenta-3,4-dien-2-ol (10b). From 8b as a pale orange viscous oil after purification with 15% ethyl acetate: hexanes; 22 mg, 61% yield over two steps. Imidate: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 1.22 (s, 3H), 1.29 (s, 3H), 2.16 (s, 3H), 7.27 (3, 1H), 7.38 (t, \(J = 7.5\) Hz, 1H), 7.54 (t, \(J = 7.5\) Hz, 1H), 7.78 (d, \(J = 8.0, 1.5\) Hz, 1H), 7.81 (d, \(J = 8.0, 1.5\) Hz, 1H), 8.67 (s, 1H). IR (ATR): 3313, 2977, 1953, 1492, 1235 cm\(^{-1}\). 10b: \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 1.41 (s, 6H), 1.88 (d, \(J = 2.0\) Hz, 3H), 6.62 (d, \(J = 2.0\) Hz), 7.01 (t, \(J = 8.0\) Hz, 1H), 7.21 (t, \(J = 7.5\) Hz, 1H), 7.37 (d, \(J = 8.0, 1.5\) Hz, 1H), 7.50 (d, \(J = 8.0, 1.5\) Hz, 1H). \(^1\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 14.6, 29.2, 29.3, 71.8, 95.5, 112.2, 122.6, 127.6, 128.3, 128.3, 133.3, 134.7, 201.9. HRMS (ASAP-TOF): \(m/z\) For C\(_{13}\)H\(_{15}\)BrO +H calcd 267.0385; found, 267.0378.
5-(2-Fluorophenyl)-2,3-dimethylpenta-3,4-dien-2-ol (10c). From 8c as a clear oil after purification with 20% ethyl acetate: hexanes; 38.6 mg, 30% yield. IR (ATR): 3313, 2977, 1953, 1492, 1235 cm\(^{-1}\). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 1.43 (s, 6H), 1.89 (d, \(J = 2.5\) Hz), 6.40 (s, 1H), 7.01 (t, \(J = 10\) Hz, 1H), 7.07 (t, \(J = 7.0\) Hz, 1H), 7.13-7.18 (m, 1H), 7.31 (dt, \(J = 7.5, 1.5\) Hz). \(^1^3\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 14.4, 28.9, 29.0, 71.5, 88.8, 111.5, 115.6 (d, \(J = 20.9\) Hz), 122.7 (d, \(J = 11.5\) Hz), 124.1, 128.0, 128.1, 159.8 (d, \(J = 246.0\) Hz), 201.5. HRMS (ASAP-TOF): \(m/z\) For C\(_{13}\)H\(_{15}\)FO +H – H\(_2\)O calcd 189.1080; found, 189.1051.

**Associated Content**

**Supporting Information**

NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

Wollongong and University of Tasmania is gratefully acknowledged. The acquisition of an NMR spectrometer at California State University, Fullerton was funded by NSF CHE-0521665. This work was partially supported by the NSF REU program summer research scholarship to BL.

**References**


[53] While the reason for this lack of reactivity is unclear it is potentially due to the long alkyl chain adopting a conformation that reduces the nucleophilicity of the alcohol.


