Synthesis of Symmetrical Polyenes by Allylzincation

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Received 7 January 2005; revised 8 February 2005

Abstract: Allylzinc bromide reacts with lithium chloroacetylenide to give 4-allyl-4-methylhepta-1,6-diene in good yield. The reaction of allylzinc bromide with acetylene, prop-1-ynylmagnesium bromide and 3-bromoprop-1-yne resulted in the synthesis of 4-methylhepta-1,6-diene, 4,4-dimethylhepta-1,6-diene and 1,1-diallylcyclopropane respectively. These symmetrical polyenes were oxidized by MCPBA to yield the corresponding epoxides (the molar ratio of the reactants determined which epoxide formed).

Key words: allylzinc bromide, alkynes, diastereoselectivity, unconjugated polyenes, epoxidations

It was reported that allylzinc reagents undergo regioselective addition to 1-alkynes to form unconjugated dienes.1–7 These papers underlined the fact that twofold addition is generally more important than single addition to the triple bond when the organozinc reagents react with acetylenic Grignard reagents or lithium acetylenides. Moreover, when there is a nucleofuge group at the α-position of the triple bond, twofold addition allows cyclopropane derivatives to be obtained.2,4,6,8–10 In this report, the synthesis of unconjugated symmetrical polyenes was performed by carrying out the addition of allylzinc bromide with lithium chloroacetylenide, acetylene, prop-1-ynylmagnesium bromide, and 3-bromoprop-1-yne. These polyenes were oxidized by MCPBA to obtain a series of epoxides. These epoxides can be used as starting materials for the synthesis of polyfunctional derivatives since the epoxide ring may be opened by a variety of nucleophilic reagents.11

In a previous paper,4 we reported that cyclohex-2-enylzinc bromide adds to the triple bond of lithium chloroacetylenide to give cyclohex-2-enylacetylene and 1,1-di(cyclohex-2-enyl)ethylene. In this report, we showed that the reaction of lithium chloroacetylenide (2) with an excess of allylzinc bromide (3) yields 4-allyl-4-methylhepta-1,6-diene (7). In the first step, lithium chloroacetylenide (2) was prepared, according to a known procedure,12 by reacting methyllithium with 1,2-dichloroethylene (1). Then, due to the regioselectivity of the addition of allylzinc bromide (3) to 2, the intermediate 4 was formed, which underwent loss of lithium chloride to release the acetylenide 5. Finally, the triple bond of 5 was saturated, using two equivalents of the organozinc reagent 3, to yield the complex 6 whose hydrolysis allowed the hydrocarbon 7 to be isolated in 71% overall yield (Scheme 1).

Scheme 1

The reaction of the triene 7 with MCPBA provides a mixture of monoepoxide 8, diepoxide 9, and triepoxide 10 (the molar ratio between the reactants determines which epoxide forms; Scheme 2).

Scheme 2
Table 1 shows that when the molar ratio of MCPBA/7 <3:1 a mixture of the three epoxides 8, 9, and 10 resulted, which were separated by distillation (Table 1, entries 1 and 2). With a greater than threefold excess of MCPBA the oxidation of 7 provided the triepoxide 10 only, 78% yield (Table 1, entry 3).

\(^1\)H NMR spectra (Table 2) and capillary gas chromatography analysis of compounds 9 and 10 confirmed, as expected, that there was a mixture of two diastereoisomers. For the diepoxide 9, the racemic (RR/SS) and meso (RS) isomers are present in a molar ratio of 1:1. This result was verified by GC analysis (\(t_\text{R} 14.9\) and 15.7 min). For the two diastereoisomers (RR/SS) 10a and (RR/SS) 10b the statistically calculated molar ratio (10a/10b) is 3:1 and 2.7:1 for the observed molar ratio based on GC analysis (\(t_\text{R} 20\) and 20.4 min).

Twofold addition of allylzinc bromide (3) to acetylene (11a) and prop-1-ynylmagnesium bromide (11b) yielded 4-methylhepta-1,6-diene (12a) and 4,4-dimethylhepta-1,6-diene (12b) respectively (Scheme 3).

\[
\text{Scheme 3 Synthesis and epoxidation of 4-methylhepta-1,6-diene (12a) and 4,4-dimethylhepta-1,6-diene (12b)}
\]

Epoxidation of these dienes can give both the monoepoxides 13a,b (MCPBA/12, 1.5:1) and the diepoxides 14a,b (MCPBA/12, 2.5:1; Table 1, entries 4 to 7).

With the molar ratio of MCPBA/12, 1.5:1 the oxidation resulted in the formation of two epoxides 13 and 14. However, the proportion of the diepoxide 14 formed was dependent on the steric hindrance at the carbon-carbon double bonds of 12. The steric hindrance of 12 favors the formation of monoeoxides 13 (Table 1, entries 4 and 6). With an excess of MCPBA we always obtained one compound, the diepoxide 14a (87% yield) from 12a (Table 1, entry 5) or the diepoxide 14b (81% yield) from 12b (Table 1, entry 7).

The monoeoxide 13a has two stereogenic carbon atoms which lead to the formation of two diastereoisomers 13a\(_{1}\) (RS/SSR) and 13a\(_{2}\) (RR/SSS) which are not separable by gas chromatography. But, both of these isomers are observed in the \(^1\)H and \(^13\)C NMR spectra through the splitting of several signals (Table 2).

The diepoxides 14a and 14b are also a mixture of two diastereoisomers: an achiral meso-isomer (R/S) and a chiral isomer (RR/SS). For 14a, the diastereoisomers 14a\(_{1}\) and 14a\(_{2}\) are not separable by gas chromatography, however, the diastereoisomers 14b\(_{1}\) and 14b\(_{2}\) are separable by GC (\(t_\text{R} 18.9\) and 19.2 min). \(^1\)H and \(^13\)C NMR spectra (Table 2) allowed us to characterize the two diastereoisomers in the mixture without separating them. In particular, the \(^1\)H NMR spectrum of 14a exhibits a doublet at 1.05 ppm assigned to the methyl group of the meso-isomer (R/S), while the two doublets at 1.04 and 1.07 ppm assigned to the methyl group of the racemic isomer (RR/SS). The \(^1\)H NMR spectrum of 14b shows two signals between 1.38 and 1.65 ppm, assigned to the methylene groups, which allowed us to characterize the two diastereoisomers. It is expected that the steric hindrance of the two epoxide rings in 14b should cause a difference in shielding between the two hydrogen atoms of each methylene group \(\alpha\) to the heterocycle. For the racemic (RR/SS) isomer, the \(^1\)H NMR spectrum exhibits two doublet of doublet at 1.43 and 1.60 ppm which are assigned to each hydrogen atom of the methylene groups. For the meso-isomer (RS) the doublet at 1.50 ppm is assigned to the two methylene groups \(\alpha\) to the heterocycles with each hydrogen atoms undergoing the same shielding due to symmetry.

### Table 1 Epoxidation of Polyenes 7, 12, and 18 with MCPBA

<table>
<thead>
<tr>
<th>Entry</th>
<th>Polyene</th>
<th>Molar Ratio MCPBA/polyene</th>
<th>Epoxide</th>
<th>Yield(^{\text{b}}) (%)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>1.5</td>
<td>8</td>
<td>36</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>2.5</td>
<td>8</td>
<td>10</td>
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<tr>
<td>3</td>
<td>7</td>
<td>3.5</td>
<td>10</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>12a</td>
<td>1.5</td>
<td>13a</td>
<td>21</td>
</tr>
<tr>
<td>5</td>
<td>12a</td>
<td>2.5</td>
<td>14a</td>
<td>63</td>
</tr>
<tr>
<td>6</td>
<td>12b</td>
<td>1.5</td>
<td>13b</td>
<td>34</td>
</tr>
<tr>
<td>7</td>
<td>12b</td>
<td>2.5</td>
<td>14b</td>
<td>49</td>
</tr>
<tr>
<td>8</td>
<td>18</td>
<td>1.5</td>
<td>19</td>
<td>50</td>
</tr>
<tr>
<td>9</td>
<td>18</td>
<td>2.5</td>
<td>20</td>
<td>38</td>
</tr>
</tbody>
</table>

\(^{a}\) All reactions were run at r.t. for 10 h in CH\(_2\)Cl\(_2\).

\(^{b}\) Yields refer to pure isolated products and based on polyene.
Table 2  NMR Data of Polyenes 7, 12, and 18 and their Epoxides 8, 9, 10, 13, 14, 19, and 20

<table>
<thead>
<tr>
<th>Product</th>
<th>$^1$H NMR (CDCl$_3$)</th>
<th>$^{13}$C NMR (CDCl$_3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>$^1$H NMR (CDCl$_3$)</td>
<td>$^{13}$C NMR (CDCl$_3$)</td>
</tr>
<tr>
<td>8</td>
<td>$^1$H NMR (CDCl$_3$)</td>
<td>$^{13}$C NMR (CDCl$_3$)</td>
</tr>
<tr>
<td>9</td>
<td>$^1$H NMR (CDCl$_3$)</td>
<td>$^{13}$C NMR (CDCl$_3$)</td>
</tr>
<tr>
<td>10</td>
<td>$^1$H NMR (CDCl$_3$)</td>
<td>$^{13}$C NMR (CDCl$_3$)</td>
</tr>
<tr>
<td>13a</td>
<td>$^1$H NMR (CDCl$_3$)</td>
<td>$^{13}$C NMR (CDCl$_3$)</td>
</tr>
<tr>
<td>13b</td>
<td>$^1$H NMR (CDCl$_3$)</td>
<td>$^{13}$C NMR (CDCl$_3$)</td>
</tr>
<tr>
<td>14a</td>
<td>$^1$H NMR (CDCl$_3$)</td>
<td>$^{13}$C NMR (CDCl$_3$)</td>
</tr>
<tr>
<td>14b</td>
<td>$^1$H NMR (CDCl$_3$)</td>
<td>$^{13}$C NMR (CDCl$_3$)</td>
</tr>
</tbody>
</table>
It is known\textsuperscript{8–10} that the reaction of the organozinc reagent 15 with 3-bromoprop-1-yne (15) affords 1,1-diallylcyclopropane (18) via the intermediate 17 which then undergoes hydrolysis (Scheme 4).

The oxidation of 18 with MCPBA provided a mixture of epoxides 19 and 20 depending on the molar ratio MCPBA/18 (Scheme 5).

Table 1 shows that with a 1.5:1 molar ratio of MCPBA/18 (entry 8) the epoxidation yielded a mixture of two compounds in which the monoepoxide 19 is the main product, however an excess of MCPBA in the reaction resulted in diepoxide 20 as the sole product in 80\% yield (entry 9).

Both \textsuperscript{1}H NMR spectra and capillary gas chromatography analysis of compound 20 confirmed, as expected, that there was a mixture of two diastereoisomers. In terms of the effect of steric hindrance, compound 20 can be compared to 14b. The \textsuperscript{1}H NMR spectrum of the racemic isomer (RR/SS) of 20 exhibits two doublet of doublets at 1.46 and 1.65 ppm, which are assigned to each hydrogen atom of the methylene groups linked to the epoxide rings. For the meso-isomer (RS) of 20 the doublet at 1.57 ppm is assigned to the two methylene groups a to the heterocycles, with both hydrogen atoms showing the same shielding due to symmetry.

In conclusion, this work described a new synthesis of unconjugated symmetrical dienes and trienes via organozinc reagents. Epoxidation of these polyenes allowed new oxirane derivatives to be obtained. These polypeoxides are often a mixture of two diastereoisomers, which are characterized by capillary gas chromatography, mass spectrometry, and \textsuperscript{1}H and \textsuperscript{13}C NMR spectroscopy. Our aim is to separate these diastereoisomers by preparative chromatography to obtain pure oxirane derivatives, which can be used as starting materials for synthesis.
fied by GC (HP 5890A, II) coupled with a mass spectrometer. A 25 m x 0.25 mm fused silica capillary column (HP5-MS) was directly inserted into the ion source of the HP quadruple mass spectrometer through a heated (250 °C) interface box. Helium was used as carrier gas; flow rate: 0.7 mL/min. The temperature was programmed to rise at a rate of 10 °C/min. The temperature of the ion source was 200 °C. C, H analyses were within ±0.4% of theoretical values. Microanalyses were carried out at the service central d’analyse CNRS, Ver- naison, France.

**Allylzinc Bromide (3)**

In a dried, nitrogen-filled round-bottomed flask fitted with stirrer and addition funnel, a solution of allyl bromide (24.19 g, 200 mmol) in anhyd THF (100 mL) was added dropwise to zinc (13.07 g, 200 mmol) at 20 °C. The resulting solution was stirred at r.t. for 1 h.

**Lithium Chloroacetylene (2)**

In a dried, nitrogen-filled round-bottomed flask fitted with stirrer and addition funnel, 1.6 M MeLi (62.5 mL, 100 mmol) was diluted in anhyd Et2O (60 mL). A solution of 1,2-dichloroethylene (1, 4.85 g, 50 mmol) in anhyd Et2O (60 mL) was added dropwise at 0 °C. The reaction mixture was then stirred at r.t. for 30 min.

**4-Allyl-4-methylhepta-1,6-diene (7)**

Lithium chloroacetylene (2, 50 mmol) was added dropwise to allylzinc bromide (3, 200 mmol) at r.t.; the temperature increased to 40 °C during the addition. The reaction mixture was stirred at 40 °C for 2 h, then quenched with a mixture of crushed ice (100 g) and concd HCl (25 mL). The phases were separated and the aqueous layer extracted with Et2O (4 x 20 mL). The combined organic phases were washed with brine (4 x 10 mL), neutralized with 5%aq K2CO3 (3 x 10 mL), washed again with brine (4 x 20 mL), and dried (MgSO4). The solvent was evaporated under normal pressure and the crude product distilled.

**Epoxides 8, 9, 10, 13, 14, 19, 20: General Procedure**

In a dried, nitrogen-filled round-bottomed flask fitted with stirrer and addition funnel, MCPBA (17.26 g for 75 mmol, 28.76 g for 125 mmol, 40.27 g for 175 mmol) was dissolved in CH2Cl2 (2.5 mL/mmol). A polyene (7 or 12 or 18, 50 mmol) was added dropwise at 0 °C. The reaction mixture was stirred at r.t. for 10 h, then filtered. The filtrate was then neutralized with 10%aq NaOH (2 x 20 mL), washed with brine (in 20 mL fraction until pH 7), and dried (MgSO4). The solvent was evaporated under normal pressure and the crude product distilled.

**4-(2,3-Epoxypropyl)-4-methylhepta-1,6-diene (8)**

Obtained from triene 7 (Table 1).

**4,4-Dimethylhepta-1,6-diene (12b)**

In a dried, nitrogen-filled round-bottomed flask fitted with stirrer and addition funnel, propynylmagnesium bromide (11b, 0.5 M, 150 mL, 75 mmol) was added dropwise to organometallic reagent 3 (200 mmol). The solution was stirred at 60 °C for 2 h, then quenched with a mixture of crushed ice (100 g) and concd HCl (20 mL). After the usual work-up described above, the crude product was distilled.

**Diastereoisomer 9a**

Yield: 5.77 g (62%); bp 118–120 °C; tR 5.2 min.

IR (film): 3060, 2990, 1635 (C=O) cm⁻¹.

MS (EI, 70 eV): m/z (%) = 109 (M – CH2, 2), 83 (M – CH2CH=CH2, 43), 82 (15), 55 (100), 42 (1.5), 41 (CH2CH=CH=CH2, 30), 39 (13).


1,1-Diallylcyclopropane (18); Typical Procedure

In a dried, nitrogen-filled round-bottomed flask fitted with stirrer and addition funnel, 3-bromoprop-1-yn-1-ene (15, 7.5 mL, 50 mmol) was added dropwise to organometallic reagent 3 (200 mmol). The solution was stirred at 60 °C for 1 h, then quenched with a mixture of crushed ice (100 g) and concd HCl (20 mL). After the usual treatments described above, the crude product was distilled.

Yield: 3.6 g (59%); bp 60–62 °C/71 torr; tR 2.1 min.

IR (film): 3060, 2990, 1635 (C=O) cm⁻¹.

MS (EI, 70 eV): m/z (%) = 122 (M, 1), 94 (7), 93 (13), 83 (30), 81 (M – CH2CH=CH2, 55), 80 (34), 79 (100), 42 (2), 41 (CH2CH=CH2, 45), 39 (50).

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**Diastereoisomer 9β**  
$t_R$ 15.7 min.

MS (EI, 70 eV): $m/z$ (%) = 125 (M – CH₃, 0.2), 81 (50), 79 (69), 67 (59), 57 (CH₃CHOCH₂, 13), 55 (80), 43 (CH₂CHO, 43), 42 (7), 41 (CH₂CH=CH₂, 100), 39 (45).

MS (Cl): $m/z$ = 183 (M + 1).

**1,1,1-Tris(2,3-epoxypropyl)ethane (10)**  
Obtained from triene 18 (Table 1).

Yield: 7.73 g (78%); $t_R$ 20.4 min.

IR (film): 3035 (OCH), 2985 (OCH), 1260 (epoxide), 845 (epoxide) cm⁻¹.


**Diastereoisomer RRS/SSR-10α**  
$t_R$ 20 min.

MS (EI, 70 eV): $m/z$ (%) = 141 (M – CH₃CHOCH₂, 1), 81 (51), 57 (CH₂CHOCH₂, 15), 55 (59), 43 (CH₂CHO, 59), 42 (10), 41 (CH₂CH=CH₂, 100), 39 (41).

MS (Cl): $m/z$ = 199 (M + 1).

**Diastereoisomer RRR/SSS-10β**  
$t_R$ 20.4 min.

MS (EI, 70 eV): $m/z$ (%) = 141 (M – CH₃CHOCH₂, 1), 81 (50), 57 (CH₂CHOCH₂, 15), 55 (61), 43 (CH₂CHO, 59), 42 (10), 41 (CH₂CH=CH₂, 100), 39 (41).

MS (Cl): $m/z$ = 199 (M + 1).

**6,7-Epoxy-4-methylhept-1-ene (13a)**  
Obtained from diene 18 (Table 1).

Yield: 3.45 g (50%); bp 82–84 °C/33 torr; $t_R$ 9.4 min.

IR (film): 3065 (OCH), 3035 (OCH), 1637 (C=C), 830 (epoxide) cm⁻¹.


**1-Allyl-1-(2,3-epoxypropyl)cyclopropane (19)**  
Obtained from the cyclopropane 18 (Table 1).

Yield: 3.45 g (50%); bp 82–84 °C/33 torr; $t_R$ 9.4 min.

IR (film): 3065 (OCH), 3040 (OCH), 1637 (C=C), 830 (epoxide) cm⁻¹.

References