Published in final edited form as:

Synthesis (Stuttg). 2012 ; 44(18): 2843–2850. doi:10.1055/s-0031-1290822.

Functionalized Cyclopropenes and Methylenecyclopropenes from Dianions of 3-Hydroxymethylcyclopropenes

Matthew D. Hassink and Joseph M. Fox*

Brown Laboratories, Department of Chemistry and Biochemistry, University of Delaware, Newark DE 19716, USA

Abstract

1,2-Disubstituted-3-hydroxymethylcyclopropene derivatives have been synthesized by reacting the dianions of 1-alkyl-3-hydroxymethylcyclopropenes with a range of electrophiles. Additionally, a complementary procedure is described for one-pot sequential alkylation/rearrangement to provide a convenient synthesis of a chiral methylenecyclopropane directly from a 1-alkyl-3-hydroxymethylcyclopropene.

Keywords

cyclopropene; chiral; dianion; methylenecyclopropane; rearrangement

As a result of high strain energy and unusual bonding, cyclopropene and its derivatives participate in a diverse range of reactivity.¹ Cyclopropenes with hydroxymethyl substitution at C-3 have been particularly useful building blocks for organic synthesis (Scheme 1). For example, the 3-hydroxymethyl substituent is a powerful directing group for reduction² and carbomagnesation³ reactions of cyclopropenes that give rise to stereochemically rich cyclopropanes, and in carbometallation/elimination cascades that give methylenecyclopropanes and alkylidenecyclopropanes.⁴ Further, derivatives of 3-hydroxymethylcyclopropenes have been utilized in hydroacylation,⁵ ring-opening/ring-closing metathesis,⁶ and in phosphinylation/[2,3]-rearrangement cascades.⁷ The broad utility⁸ of 3-hydroxymethylcyclopropenes prompted us to consider expanding the scope of methods for their preparation.

3-Hydroxymethylcyclopropenes are generally prepared via the reduction of cycloprop-2-ene carboxylic esters, and there are varied methods for preparing enantiomerically enriched cycloprop-2-ene carboxylic esters with a single alkene substituent (“terminal” cyclopropenes).⁹ However, methods of preparing chiral 1,2-disubstituted cyclopropenes (“internal” cyclopropenes) are more limited, despite the utility of such compounds in Pauson-Khand¹⁰ and carbomagnesation protocols.^{3c} Accordingly, a number of groups have sought to prepare chiral internal chiral 1,2-disubstituted cyclopropenes by derivatizing terminal cyclopropenes.

The vinylic hydrogens of cyclopropenes are acidic and can generally be deprotonated and functionalized,¹¹ but the direct route of deprotonating cycloprop-2-ene carboxylic esters is only successful for a limited range of electrophiles that can be added prior to addition of a base. In their studies on functionalization of cycloprop-1-ene carboxylates, Eckert-Maksic

and coworkers found that base addition without the prior addition of an electrophile yielded ring opened products (Eq. 1).¹² Our own studies have confirmed that the anions of cycloprop-1-ene carboxylic esters are very unstable.¹³

(1)

Based on the hypothesis that dianions of cycloprop-1-ene carboxylic acids would be more resilient to undesirable ring opening fragmentation reactions, we developed a more general method for the synthesis of internal cyclopropenes from terminal cyclopropenes via a dianion intermediate.¹³ Additionally, Gevorgyan elegantly developed an Heck-type coupling method to access internal cyclopropenes through the introduction of aryl groups.¹⁴ Lam developed a method to stannylate a terminal cyclopropene followed by a palladium catalyzed cross-coupling with α -aryl iodides and acid chlorides.¹⁵ Rubin has developed a powerful method to functionalize cyclopropene-3-carboxamides via deprotonation.¹⁶ To complement these methods, a direct functionalization of 3-hydroxymethylcyclopropenes is described herein.

It was hypothesized that the dianions of 3-hydroxymethylcyclopropenes would be stable to ring opening fragmentation, due to the lack of a resonance stabilizing carbonyl moiety that could stabilize the anion in the ring-opened form (see Eq. 1).^{12,13} Thus, the stability of the dianion from 1-hexyl-3-hydroxymethylcyclopropene was evaluated (Scheme 2). Thus 1-hexyl-3-hydroxymethylcyclopropene (**1**) was treated with *n*-BuLi at -78°C , followed by warming to r.t. After 2 hours, the reaction was quenched, and ^1H NMR analysis indicated that >95% of the starting material remained. The result compared favorably to earlier observations of the dianion from 2-butyl-1-phenylcycloprop-2-ene carboxylic acid. When this dianion was generated at -78°C , and warmed to 21°C over 15 min., only 32% of starting material was recovered after aqueous quench.^{13b} This observation prompted a fuller investigation of the chemistry of the dianion of 3-hydroxymethylcyclopropenes.

A protocol for the deprotonation and electrophile quench of 3-hydroxymethylcyclopropenes was developed. After screening a number of bases, it was determined that alkyllithium reagents were effective, and MeLi was utilized in further studies. A number of electrophiles were surveyed with 1-hexyl-3-hydroxymethylcyclopropene (**1**) as the starting material. Both octylaldehyde and paraformaldehyde were effective electrophiles, providing adducts **2** and **3** in 73% and 70% yields respectively. Enolizable ketones also functioned as electrophiles: cyclohexanone and 3-heptanone leading to addition products **7** and **9** in 52% and 62% yields, respectively. Alkyl halides also combined with the dianion of **1**; ethyl iodide and methyl iodide provided adducts **5** and **6** in 67% and 70% yield, respectively. Hexyl iodide, a less reactive electrophile, gave adduct **8** in 52% yield. With MOMCl, it was not possible to selectively obtain the product of C-alkylation, but it was possible to isolate dialkylated product **4** in 73% yield when 5 equiv. of MOMCl was added.

Cyclopropenes that are disubstituted at C-3 were also explored. The dianions from 3-hydroxymethyl-3-methyl-1-hexyl cyclopropene (**10**) combined with paraformaldehyde and 3-heptanone to give adducts **11** and **12** in 85% and 70% yield respectively. 1-Hexyl-3-hydroxymethyl-3-phenylcyclopropene (**13**) combined with ethyl iodide, octylaldehyde, and pivaldehyde to give adducts **14–16** in 57–68% yields. Thus, the scope of this reaction includes a number of different electrophiles and tolerates substitution at the 3-position.

For the reaction of 1-hexyl-2-hydroxymethylcyclopropene (**1**) with MeI, the standard reaction conditions led to the formation of (2-hexyl-3-methylenecyclopropyl)methanol (**17**) in addition to (2-hexyl-3-methylcycloprop-2-en-1-yl)methanol (**6**). Methylenecyclopropanes are strained molecules that possess high reactivity, and much synthetic effort has been devoted to their synthesis. Previously developed synthetic routes to methylenecyclopropanes have included carbene additions to allenes, eliminations including selenoxide eliminations, halogen eliminations, silyl group eliminations, and Wittig based reactions.¹⁷

Of the varied methods for preparing methylenecyclopropanes, syntheses that begin with cyclopropene starting materials are among the most direct and general.^{4,18} Methods had previously been described for the base-promoted isomerization of 1-alkylcyclopropanes to methylenecyclopropanes or alkylidenecyclopropanes,¹⁹ but there was no efficient method for accomplishing alkylation/rearrangement in one pot with terminal cyclopropanes as starting material.^{19o}

It was possible to obtain **17** with a yield of 67% by forming the dianion of **1** in THF with *n*-BuLi (2.2 equiv., -78 °C, then warm to 0 °C), and then adding MeI and heating the reaction to 35 °C for 1 h (Scheme 5). An analogous reaction with *n*-BuLi/*t*-BuOK gave **17** in slightly lower yield (60%). However, the combination of MeLi with TMEDA had a markedly beneficial effect on the yield. With MeLi/TMEDA, starting material **1** was completely consumed within 10 min and **17** was formed in 73% yield.

Complementary reaction conditions that would optimize the formation of (2-hexyl-3-methylcycloprop-2-en-1-yl)methanol (**6**), and minimize rearrangement to methylenecyclopropane **17** were sought. NMO and HMPA were tested as additives under the standard reaction conditions, but they were ineffective in suppressing the rearrangement. Solvent effects are known to be quite pronounced in reactions of organolithium reagents.²⁰ Accordingly, several solvents were screened in order to improve selectivity for cyclopropene formation without rearrangement. Benzene proved to be optimal for the formation of **6** while suppressing rearrangement product to **17**.

In conclusion, a facile synthesis of internal cyclopropanes has been developed in which dianions of 3-hydroxymethylcyclopropanes are combined with electrophiles. Productive electrophiles in this process include primary alkyl iodides, aromatic and aliphatic aldehydes, cyclic and acyclic ketones, and MOMCl. Additionally, a complementary procedure is described for one-pot sequential alkylation/rearrangement to provide a convenient synthesis of a chiral methylenecyclopropane directly from an terminal cyclopropene.

Experimental Section

All reactions were carried out in flame dried round bottom flasks under nitrogen. All commercially available reagents were used as received. THF was distilled from sodium. Chromatography was performed using Silacyle silica gel (40–63D, 60Å). For ¹³C NMR, multiplicities were distinguished using a ATP pulse sequence: typical methylene and quaternary carbons appear 'up'; methine and methyl carbons 'down'. Exceptions are methine carbons of cyclopropanes, which usually have the same phase as 'normal' methylenes and quaternary carbons.

General Procedure A: Preparation of 3-hydroxymethylcyclopropanes

A dry round bottom flask was charged with the cyclopropene carboxylate and THF. The mixture was cooled to -78 °C, and DIBAL (4 equiv.) was added via syringe. The reaction was stirred at -78 °C until the reaction was judged complete by TLC analysis. Sodium sulfate decahydrate (5 equiv.) was added to the reaction at -78 °C and the reaction mixture

was warmed to r.t. and stirred for 3 hr. The mixture was filtered, the filtrate was concentrated in vacuo, and the residue purified by column chromatography.

General Procedure B: Functionalization of Dianions of cyclopropenes

A dry round bottom flask was charged with 3-hydroxymethylcyclopropene (0.5 mmol) and THF (2 mL). The flask was cooled to -78°C then MeLi (1.0 mmol, 0.63 mL) was added via syringe. The flask was warmed to r.t. then electrophile (0.55 mmol) was added via syringe. The mixture was allowed to stir an additional 3 h. at r.t. The reaction was acidified with aqueous HCl (3 M). The aqueous layer was extracted with three portions of diethyl ether. The extracts were dried with MgSO_4 and concentrated in vacuo. The residue was purified by column chromatography to provide the desired compound.

(2-Hexylcycloprop-2-en-1-yl)methanol (1)—General procedure A was followed using ethyl 2-hexylcycloprop-2-ene carboxylate (4.45 g, 22.7 mmol) and DIBAL (20.0 mL, 115 mmol) in THF (20.0 mL). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 2.62 g (17.0 mmol, 75%) of the title compound as a clear oil. Spectral properties agreed with those previously reported.^{3a}

1-(2-Hexyl-3-(hydroxymethyl)cycloprop-1-en-1-yl)hexan-1-ol (2)—General procedure B was followed using (2-hexylcycloprop-2-en-1-yl)methanol (0.075 g, 0.49 mmol), MeLi (0.60 mL, 0.98 mmol), and octyl aldehyde (0.15 mL, 0.98 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.101 g (0.36 mmol, 73%) of a 6:4 (NMR) mixture of diastereomers of the title compound as a colorless oil.

Major Diastereomer:

^1H NMR (400 MHz, CDCl_3) δ 4.65 (t, $J = 6.8$ Hz, 1H), 3.90 (m, 1H), 3.13–3.07 (m, 1H), 2.94 (s, 2H), 2.47–2.35 (m, 2H), 1.80–1.59 (m, 4H), 1.58–1.48 (m, 3H), 1.35–1.23 (m, 14H), 0.91–0.87 (m, 6H);

Minor Diastereomer:

^1H NMR (400 MHz, CDCl_3) δ 4.51 (m, 1H), 3.90 (m, 1H), 3.13–3.07 (m, 1H), 2.94 (s, 2H), 2.47–2.35 (m, 2H), 1.80–1.59 (m, 4H), 1.58–1.48 (m, 3H), 1.35–1.23 (m, 14H), 0.91–0.87 (m, 6H);

^{13}C NMR of both diastereomers (100 MHz, CDCl_3) δ 115.93 (C), 115.90 (C), 115.87 (C), 115.2 (C), 68.9 (CH_2), 68.6 (CH_2), 66.8 (CH), 65.8 (CH), 36.5 (CH_2), 35.5 (CH_2), 31.84 (CH_2), 31.82 (CH_2), 31.6 (CH_2 , 2 non-equiv. carbons), 29.5 (CH_2), 29.4 (CH_2), 29.31 (CH_2), 29.29 (CH_2), 29.07 (CH_2), 29.05 (CH_2), 27.43 (CH_2), 27.39 (CH_2), 25.62 (CH_2), 25.59 (CH_2), 25.47 (CH_2), 25.36 (CH_2), 22.9 (CH), 22.7 (CH_2 , 2 non-equiv. carbons), 22.6 (CH_2 , 2 non-equiv. carbons), 22.0 (CH), 14.12 (CH_3 , 2 non-equiv. carbons), 14.09 (CH_3 , 2 non-equiv. carbons).

IR (film, CHCl_3 , cm^{-1}) 3428, 3156, 2930, 2858, 1866, 1794, 1467, 1381, 1097, 1011, 909, 734, 651.

HRMS-Cl (NH_3) m/z : [M-OH] calcd for $\text{C}_{18}\text{H}_{33}\text{O}$, 265.2526; found 265.2522

(3-Hexylcycloprop-2-ene-1,2-diyl)dimethanol (3)—General procedure B was followed using (2-hexylcycloprop-2-en-1-yl)methanol (0.075 g, 0.49 mmol), MeLi (0.60 mL, 0.98 mmol), and paraformaldehyde (0.074 g, 2.45 mmol). Silica gel chromatography

using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.063 g (0.34 mmol, 70%) of the title compound as a colorless oil.

^1H NMR (400 MHz, CDCl_3) δ 4.64 (d, $J_{AB} = 14.2$ Hz, 1H), 4.46 (d, $J_{AB} = 14.2$ Hz, 1H), 3.90 (dd, $J = 3.6, 10.3$ Hz, 1H), 3.19 (dd, $J = 6.3, 10.3$ Hz, 1H), 2.43 (t, $J = 7.4$ Hz, 2H), 2.28 (s, 2H), 1.81 (dd, $J = 3.7, 6.3$ Hz, 1H), 1.59–1.51 (m, 2H), 1.39–1.27 (m, 6H), 0.91 (t, $J = 6.7$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 116.8 (C), 112.9 (C), 68.6 (CH_2), 56.4 (CH_2), 31.7 (CH_2), 29.1 (CH_2), 27.5 (CH_2), 25.7 (CH_2), 23.1 (CH), 22.7 (CH_2), 14.2 (CH_3).

IR (film, CHCl_3 , cm^{-1}) 3387, 2932, 2859, 1869, 1711, 1465, 1364, 1224, 1016, 935, 881, 773, 689.

HRMS-Cl (NH_3) m/z : $[\text{M}+\text{Na}]$ calcd for $\text{C}_{11}\text{H}_{20}\text{O}_2\text{Na}$, 207.1361; found 207.1358.

1-Hexyl-3-((methoxymethoxy)methyl)-2-(methoxymethyl)cycloprop-1-ene (4)—

General procedure B was followed using (2-hexylcycloprop-2-en-1-yl)methanol (0.050 g, 0.33 mmol), MeLi (0.62 mL, 0.99 mmol), and chloromethyl methyl ether (0.125 mL, 1.65 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.058 g (0.24 mmol, 73%) of the title compound as a colorless oil.

^1H NMR (400 MHz, CDCl_3) δ 4.65 (d, $J_{AB} = 6.8$ Hz, 1H), 4.65 (d, $J_{AB} = 6.8$ Hz, 1H), 4.41 (s, 2H), 3.51–3.42 (m, 2H), 3.40 (s, 3H), 3.37 (s, 3H), 2.48 (t, $J = 7.3$ Hz, 2H), 1.77 (t, $J = 5.0$ Hz, 1H), 1.62–1.54 (m, 2H), 1.40–1.27 (m, 6H), 0.91 (t, $J = 6.9$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 118.6 (C), 111.0 (C), 96.1 (CH_2), 75.0 (CH_2), 67.4 (CH_2), 58.4 (CH_3), 55.1 (CH_3), 31.7 (CH_2), 29.2 (CH_2), 27.5 (CH_2), 25.9 (CH_2), 22.7 (CH_2), 20.7 (CH), 14.2 (CH_3).

IR (film, CHCl_3 , cm^{-1}) 3156, 2931, 2863, 1868, 1461, 1379, 1150, 1100, 1038, 919, 752, 715, 652.

HRMS-Cl (NH_3) m/z : $[\text{M}+\text{Na}]$ calcd for $\text{C}_{14}\text{H}_{26}\text{O}_3\text{Na}$, 265.1780; found 265.1767

(2-Ethyl-3-hexylcycloprop-2-en-1-yl)methanol (5)—General procedure B was followed using (2-hexylcycloprop-2-en-1-yl)methanol (0.075 g, 0.49 mmol), MeLi (0.81 mL, 1.1 mmol), and ethyl iodide (0.058 mL, 0.72 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.057 g (0.33 mmol, 67%) of the title compound as a colorless oil.

^1H NMR (400 MHz, CDCl_3) δ 3.54–3.48 (m, 2H), 2.44–2.37 (m, 4H), 1.59 (t, $J = 4.5$ Hz, 1H), 1.57–1.49 (m, 2H), 1.37–1.25 (m, 7H), 1.14 (t, $J = 7.5$ Hz, 3H), 0.89 (t, $J = 7.0$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 115.4 (C), 113.9 (C), 69.3 (CH_2), 31.7 (CH_2), 29.2 (CH_2), 27.9 (CH_2), 25.7 (CH_2), 22.8 (CH), 22.7 (CH_2), 19.3 (CH_2), 14.2 (CH_3), 12.5 (CH_3).

IR (film, CHCl_3 , cm^{-1}) 3438, 2959, 2931, 2859, 1872, 1720, 1656, 1461, 1380, 1111, 1009, 914, 743, 719, 651.

HRMS-Cl (NH_3) m/z : $[\text{M}+\text{H}]$ calcd for $\text{C}_{12}\text{H}_{23}\text{O}$, 183.1749; found 183.1746

(2-Hexyl-3-methylcycloprop-2-en-1-yl)methanol (6)—A dry round bottom flask was charged with (2-hexylcycloprop-2-en-1-yl)methanol (0.050 g, 0.33 mmol) and benzene (2

mL). The flask was cooled to 0 °C then MeLi (0.41 mL, 0.65 mmol) was added via syringe. The flask was warmed to r.t. then methyl iodide (0.020 mL, 0.32 mmol) was added via syringe. The mixture was allowed to stir an additional 3 h. at r.t. The reaction was acidified with aqueous HCl (3 M). The aqueous layer was extracted with three portions of diethyl ether. The extracts were dried with MgSO₄ and concentrated in vacuo. Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.039 g (0.23 mmol, 70%) of the title compound.

¹H NMR (400 MHz, CDCl₃) δ 3.58–3.47 (m, 2H), 2.38 (t, *J* = 7.3 Hz, 2H), 2.05 (s, 3H), 1.59–1.49 (m, 3H), 1.37–1.26 (m, 6H), 1.03 (t, *J* = 4.9 Hz, 1H), 0.89 (t, *J* = 6.6 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 114.7 (C), 109.9 (C), 69.0 (CH₂), 31.7 (CH₂), 29.2 (CH₂), 27.7 (CH₂), 25.7 (CH₂), 22.9 (CH), 22.7 (CH₂), 14.2 (CH₃), 11.0 (CH₃).

IR (film, CHCl₃, cm^{−1}) 3458, 2959, 2930, 2859, 1873, 1775, 1462, 1440, 1382, 1349, 1176, 1066, 996, 923, 905, 746, 733.

HRMS-EI *m/z*: [M⁺] calcd for C₁₁H₂₀O, 168.1514; found 168.1488

1-(2-Hexyl-3-(hydroxymethyl)cycloprop-1-en-1-yl)cyclohexanol (7)—General procedure B was followed using (2-hexylcycloprop-2-en-1-yl)methanol (0.050 g, 0.33 mmol), MeLi (0.62 mL, 0.99 mmol), and cyclohexanone (0.14 mL, 1.3 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.043 g (0.17 mmol, 52%) of the title compound as a colorless oil.

¹H NMR (400 MHz, CDCl₃) δ 3.89 (dd, *J* = 3.6, 10.5 Hz, 1H), 3.15 (dd, *J* = 6.4, 10.5 Hz, 1H), 2.73 (brs, 1H), 2.43 (m, 2H), 1.95–1.88 (m, 1H), 1.83–1.43 (m, 10H), 1.37–1.22 (m, 8H), 0.89 (t, *J* = 6.8 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 117.8 (C), 115.4 (C), 70.1 (C), 69.0 (CH₂), 38.1 (CH₂), 37.0 (CH₂), 31.7 (CH₂), 29.2 (CH₂), 27.5 (CH₂), 25.7 (CH₂), 25.6 (CH₂), 23.4 (CH₂), 23.1 (CH₂), 22.7 (CH₂), 21.6 (CH), 14.2 (CH₃).

IR (film, CHCl₃, cm^{−1}) 3413, 2934, 2859, 1865, 1450, 1380, 1343, 1259, 1144, 1060, 1009, 960, 924, 892, 758, 709, 649.

HRMS-CI (NH₃) *m/z*: [M-OH] calcd for C₁₆H₂₇O, 235.2056; found 235.2052

(2,3-Dihexyl-1-methylcycloprop-2-en-1-yl)methanol (8)—General procedure B was followed using (2-hexylcycloprop-2-en-1-yl)methanol (0.050 g, 0.33 mmol), MeLi (0.43 mL, 0.69 mmol), and hexyliodide (0.063 mL, 0.43 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.041 g (0.17 mmol, 52%) of the title compound as a colorless oil.

¹H NMR (400 MHz, CDCl₃) δ 3.51 (d, *J* = 4.6 Hz, 2H), 2.38 (t, *J* = 7.2 Hz, 4H), 1.58–1.48 (m, 6H), 1.36–1.24 (m, 12H), 0.88 (t, *J* = 6.7 Hz, 6H).

¹³C NMR (100 MHz, CDCl₃) δ 114.2 (C), 69.3 (CH₂), 31.7 (CH₂), 29.2 (CH₂), 27.8 (CH₂), 25.8 (CH₂), 22.7 (CH), 22.7 (CH₂), 14.2 (CH₃).

IR (film, CHCl₃, cm^{−1}) 3463, 2930, 2858, 1857, 1757, 1464, 1381, 1110, 1045, 994, 930.

HRMS-CI (NH₃) *m/z*: [M+H] calcd for C₁₆H₃₁O, 239.2374; found 239.2374

3-(2-Hexyl-3-(hydroxymethyl)cycloprop-1-en-1-yl)heptan-3-ol (9)—General procedure B was followed using (2-hexylcycloprop-2-en-1-yl)methanol (0.075 g, 0.49 mmol), MeLi (0.60 mL, 0.98 mmol), and 3-heptanone (0.12 mL, 0.74 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.082 g (0.30 mmol, 62%) of the title compound, a clear oil that is an inseparable mixture of diastereomers.

^1H NMR of both diastereomers (400 MHz, CDCl_3) δ 3.90 (m, 1H), 3.19–3.12 (m, 1H), 2.90–2.60 (br s, 1H), 2.42 (t, $J = 7.4$ Hz, 2H), 1.80–1.64 (m, 5H), 1.57–1.49 (m, 2H), 1.40–1.29 (m, 11H), 1.00–0.86 (m, 9H);

^{13}C NMR of both diastereomers (100 MHz, CDCl_3) δ 118.0 (C, 2 non-equiv. carbons), 115.4 (C), 115.2 (C), 73.45 (C), 73.37 (C), 69.1 (CH_2 , 2 non-equiv. carbons), 39.3 (CH_2), 38.9 (CH_2), 32.5 (CH_2), 32.4 (CH_2), 31.6 (CH_2 , 2 non-equiv. carbons), 29.1 (CH_2 , 2 non-equiv. carbons), 27.44 (CH_2), 27.43 (CH_2), 26.3 (CH_2), 26.1 (CH_2), 25.5 (CH_2 , 2 non-equiv. carbons), 23.2 (CH_2), 23.1 (CH_2), 22.80 (CH), 22.76 (CH), 22.6 (CH_2 , 2 non-equiv. carbons), 14.16 (CH_3), 14.11 (CH_3), 14.09 (CH_3 , 2 non-equiv. carbons), 8.5 (CH_3), 8.3 (CH_3).

IR (film, CHCl_3 , cm^{-1}) 3425, 3019, 2960, 2932, 2861, 1864, 1711, 1464, 1379, 1216, 1144, 1048, 1010, 909, 761, 669.

HRMS-Cl (NH_3) m/z : [M-OH] calcd for $\text{C}_{17}\text{H}_{31}\text{O}$, 251.2369; found 251.2366

(2-Hexyl-1-methylcycloprop-2-en-1-yl)methanol (10)—General procedure A was followed using ethyl 2-hexyl-1-methylcycloprop-2-ene carboxylate⁴ (1.92 g, 9.14 mmol) and DIBAL (6.78 mL, 36.6 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 1.02 g (6.07 mmol, 66%) of the title compound as a colorless oil.

^1H NMR (400 MHz, CDCl_3) δ 6.71 (s, 1H), 3.56–3.48 (m, 2H), 2.44 (m, 2H), 1.58–1.50 (m, 2H), 1.40–1.25 (m, 6H) 1.12 (s, 3H), 0.90 (bs, 1H), 0.89 (t, $J = 6.9$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 132.1 (C), 107.1 (CH), 68.9 (CH_2), 31.6 (CH_2), 29.0 (CH_2), 27.4 (CH_2), 25.7 (CH_2), 24.4 (C), 22.6 (CH_2), 22.0 (CH_3) 14.1 (CH_3).

IR (film, CHCl_3 , cm^{-1}) 3554, 2959, 2932, 2860, 1753, 1459, 1425, 1379, 1305, 1204, 1048, 997, 923, 891, 752, 725, 709, 650.

HRMS-EI m/z : [M+] calcd for $\text{C}_{11}\text{H}_{20}\text{O}$, 168.1514; found 168.1501

(3-Hexyl-1-methylcycloprop-2-ene-1,2-diyl)dimethanol (11)—General procedure B was followed using (2-hexyl-1-methylcycloprop-2-en-1-yl)methanol (0.050 g, 0.30 mmol), MeLi (0.47 mL, 0.75 mmol), and paraformaldehyde (0.074 g, 2.45 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.050 g (0.27 mmol, 85%) of the title compound as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 4.61 (d, $J_{AB} = 14.1$ Hz, 1H), 4.47 (d, $J_{AB} = 14.1$ Hz, 1H), 3.77 (d, $J_{AB} = 10.3$ Hz, 1H), 3.35 (d, $J_{AB} = 10.3$ Hz, 1H), 2.42 (t, $J = 7.4$ Hz, 2H), 1.90 (br s, 2H), 1.58–1.50 (m, 2H), 1.41–1.27 (m, 6H), 1.18 (s, 3H), 0.91 (t, $J = 6.6$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 122.7 (C), 118.2 (C), 70.3 (CH_2), 56.2 (CH_2), 31.8 (CH_2), 29.4 (CH_2), 28.0 (CH_2), 27.4 (C), 25.1 (CH_2), 22.8 (CH_2), 20.9 (CH_3), 14.3 (CH_3).

IR (film, CHCl_3 , cm^{-1}) 3412, 2954, 2931, 2860, 1857, 1726, 1454, 1005, 907, 738, 725.

HRMS-Cl (NH_3) m/z : [M-OH] calcd for $\text{C}_{12}\text{H}_{21}\text{O}$, 181.1587; found 181.1592.

3-(2-Hexyl-3-(hydroxymethyl)-3-methylcycloprop-1-en-1-yl)heptan-3-ol (12)—

General procedure B was followed using (2-hexyl-1-methylcycloprop-2-en-1-yl)methanol (0.050 g, 0.30 mmol), MeLi (0.56 mL, 0.90 mmol), and 3-heptanone (0.10 mL, 0.69 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.058 g (0.21 mmol, 70%) of the title compound, a colorless oil that is an inseparable mixture of diastereomers. Also isolated was starting material (2-hexyl-1-methylcycloprop-2-en-1-yl)methanol (0.006 g, 0.036 mmol, 12%).

^1H NMR (400 MHz, CDCl_3) δ 3.77 (d, $J_{AB} = 10.2$ Hz, 1H), 3.34 (d, $J_{AB} = 10.2$ Hz, 1H), 2.53 (brs, 1H), 2.39 (t, $J = 7.6$ Hz, 2H), 1.81–1.59 (m, 5H), 1.52–1.45 (m, 2H), 1.38–1.25 (m, 10H), 1.18 (s, 3H), 0.96–0.87 (m, 9H).

^{13}C NMR (100 MHz, CDCl_3) δ 122.73 (C), 122.70 (C), 121.0 (C), 120.9 (C), 74.6 (C), 74.5 (C), 70.5 (CH_2 , 2 non-equiv. carbons), 39.4 (CH_2), 38.9 (CH_2), 32.7 (CH_2), 32.3 (CH_2), 31.6 (CH_2 , 2 non-equiv. carbons), 29.3 (CH_2 , 2 non-equiv. carbons), 27.8 (CH_2 , 2 non-equiv. carbons), 27.14 (C), 27.06 (C), 26.4 (CH_2), 26.1 (CH_2), 24.9 (CH_2 , 2 non-equiv. carbons), 23.2 (CH_2), 23.1 (CH_2), 22.6 (CH_2 , 2 non-equiv. carbons), 21.5 (CH_3 , 2 non-equiv. carbons), 14.2 (CH_3), 14.11 (CH_3 , 2 non-equiv. carbons), 14.09 (CH_3), 8.6 (CH_3), 8.2 (CH_3).

IR (film, CHCl_3 , cm^{-1}) 3455, 3156, 2960, 2933, 2860, 1852, 1794, 1642, 1465, 1381, 1096, 994, 903, 732, 651.

HRMS-Cl (NH_3) m/z : [M+Na] calcd for $\text{C}_{18}\text{H}_{34}\text{O}_2\text{Na}$, 305.2457; found 305.2452.

(2-Hexyl-1-phenylcycloprop-2-en-1-yl)methanol (13)—General procedure A was followed using methyl 2-hexyl-1-phenylcycloprop-2-enecarboxylate (1.58 g, 6.48 mmol) and DIBAL (1.80 mL, 9.71 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 1.13 g (4.91 mmol, 76%) of the title compound as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.35–7.30 (m, 2H), 7.27–7.23 (m, 2H), 7.22–7.17 (m, 1H), 6.81 (s, 1H), 4.18 (dd, $J = 5.4, 11.1$ Hz, 1H), 4.03 (dd, $J = 6.1, 10.9$ Hz, 1H), 2.60–2.46 (m, 2H), 1.66–1.54 (m, 2H), 1.42–1.26 (m, 7H), 0.91 (t, $J = 6.9$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 145.8 (C), 128.2 (CH), 126.2 (CH), 126.1 (CH), 125.4 (CH), 101.4 (C), 67.6 (CH_2), 31.6 (CH_2), 31.5 (C), 29.0 (CH_2), 27.3 (CH_2), 24.9 (CH_2), 22.6 (CH_2), 14.1 (CH_3).

IR (film, CHCl_3 , cm^{-1}) 3456, 3061, 3026, 9658, 2931, 2859, 1771, 1667, 1600, 1494, 1465, 1380, 1194, 1063, 1000, 925, 774.

HRMS-Cl (NH_3) m/z : [M-OH] calcd for $\text{C}_{16}\text{H}_{21}$, 213.1643; found 213.1653

(2-Ethyl-3-hexyl-1-phenylcycloprop-2-en-1-yl)methanol (14)—General procedure B was followed using (2-hexyl-1-phenylcycloprop-2-en-1-yl)methanol (0.050 g, 0.23 mmol), MeLi (0.26 mL, 0.542 mmol) and ethyl iodide (0.023 mL, 0.28 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.034 g (0.13 mmol, 57%) of the title compound as a colorless oil.

^1H NMR (400 MHz, CDCl_3) δ 7.41–7.29 (m, 2H), 7.23–7.13 (m, 3H), 4.12 (d, $J_{AB} = 10.8$ Hz, 1H), 4.10 (d, $J_{AB} = 10.8$ Hz, 1H), 2.61–2.40 (m, 4H), 1.63–1.53 (m, 2H), 1.41–1.27 (m, 7H), 1.19 (t, $J = 7.5$ Hz, 3H), 0.90 (t, $J = 6.9$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 146.1 (C), 128.2 (CH), 126.1 (CH), 124.9 (CH), 115.2 (C), 114.1 (C), 67.8 (CH_2), 33.2 (C), 31.6 (CH_2), 29.2 (CH_2), 28.0 (CH_2), 24.2 (CH_2), 22.6 (CH_2), 17.8 (CH_2), 14.1 (CH_3), 12.7 (CH_3).

IR (film, CHCl_3 , cm^{-1}) 3457, 3061, 3026, 2958, 2931, 2859, 1882, 1771, 1667, 1600, 1494, 1465, 1380, 1194, 1115, 1063, 1000, 926, 774, 701, 645.

HRMS-Cl (NH_3) m/z : [M-OH] calcd for $\text{C}_{18}\text{H}_{25}$, 241.1951; found 241.1952

1-(2-Hexyl-3-(hydroxymethyl)-3-phenylcycloprop-1-en-1-yl)octan-1-ol (15)—

General procedure B was followed using (2-hexyl-1-phenylcycloprop-2-en-1-yl)methanol (0.050 g, 0.23 mmol), MeLi (0.32 mL, 0.51 mmol) and octyl aldehyde (0.044 mL, 0.28 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.048 g (0.13 mmol, 58%) of the title compound, a colorless oil that is a 6:4 (NMR) mixture of diastereomers.

Major Diastereomer:

^1H NMR (400 MHz, CDCl_3) δ 7.32–7.23 (m, 4H), 7.18 – 7.14 (m, 1H), 4.61 (t, J = 6.3 Hz, 1H), 4.54 (d, J = 10.9 Hz, 1H), 3.61 (d, J = 10.9 Hz, 1H), 2.65–2.44 (m, 2H), 2.41 (s, 2H), 1.89–1.80 (m, 1H), 1.66–1.46 (m, 4H), 1.43–1.25 (m, 15H), 0.94–0.87 (m, 6H);

Minor Diastereomer:

^1H NMR (400 MHz, CDCl_3) δ 7.32–7.23 (m, 4H), 7.18 – 7.14 (m, 1H), 4.78 (t, J = 6.7 Hz, 1H), 4.46 (d, J = 10.9 Hz, 1H), 3.66 (d, J = 10.9 Hz, 1H), 2.65–2.44 (m, 2H), 2.41 (s, 2H), 1.89–1.80 (m, 1H), 1.66–1.46 (m, 4H), 1.43–1.25 (m, 15H), 0.94–0.87 (m, 6H);

^{13}C NMR of both diastereomers (100 MHz, CDCl_3) δ 146.1 (C), 145.7 (C), 128.2 (CH), 128.1 (CH), 126.1 (CH, 2 non-equiv. carbons), 125.1 (CH), 125.0 (CH), 116.2 (C), 115.9 (C), 115.8 (C), 115.4 (C), 68.65 (CH_2), 68.57 (CH_2), 66.6 (CH), 65.5 (CH), 36.6 (CH_2), 36.5 (CH_2), 34.4 (C), 34.2 (C), 31.8 (CH_2), 31.7 (CH_2), 31.6 (CH_2), 31.5 (CH_2), 29.5 (CH_2 , 2 non-equiv. carbons), 29.3 (CH_2 , 2 non-equiv. carbons), 29.1 (CH_2 , 2 non-equiv. carbons), 27.7 (CH_2), 27.6 (CH_2), 25.5 (CH_2 , 2 non-equiv. carbons), 24.32 (CH_2), 24.29 (CH_2), 22.7 (CH_2), 22.61 (CH_2), 22.57 (CH_2), 22.55 (CH_2), 14.10 (CH_3), 14.07 (CH_3), 14.06 (CH_3), 14.04 (CH_3).

IR (film, CHCl_3 , cm^{-1}) 3390, 3060, 3025, 2957, 2930, 2858, 1871, 1600, 1494, 1465, 1379, 1115, 1060, 1002, 913, 904, 735, 700.

HRMS-ESI m/z : [M+Na] calcd for $\text{C}_{24}\text{H}_{38}\text{O}_2\text{Na}$, 381.2770; found 381.2757.

1-(2-Hexyl-3-(hydroxymethyl)-3-phenylcycloprop-1-en-1-yl)-2,2-dimethylpropan-1-ol (16)—

General procedure B was followed using (2-hexyl-1-phenylcycloprop-2-en-1-yl)methanol (0.050 g, 0.23 mmol), MeLi (0.43 mL, 0.69 mmol) and pivaldehyde (0.10 mL, 0.69 mmol). Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.024 g (0.075 mmol, 34%) of the faster eluting diastereomer and 0.024 g (0.075 mmol, 34%) of the slower diastereomer. Both diastereomers are colorless oils.

Faster Eluting Diastereomer:

^1H NMR (400 MHz, CDCl_3) δ 7.32–7.21 (m, 4H), 7.16–7.11 (m, 1H), 4.62 (d, J = 10.1 Hz, 1H), 4.26 (s, 1H), 3.50 (d, J = 10.9 Hz, 1H), 2.55–2.45 (m, 2H), 2.19 (brs, 2H), 1.48–1.39 (m,

2H), 1.31-1.19 (m, 6H), 1.06 (s, 9H), 0.84 (t, $J = 6.7$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 145.7 (C), 128.2 (CH), 126.1 (CH), 125.0 (CH), 115.6 (C), 113.3 (C), 73.9 (CH), 69.0 (CH₂), 35.4 (C), 32.7 (C), 31.5 (CH₂), 29.2 (CH₂), 27.2 (CH₂), 25.6 (CH₃), 24.7 (CH₂), 22.5 (CH₂), 14.0 (CH₃).

IR (film, CHCl_3 , cm^{-1}) 3423, 2956, 2933, 2871, 1869, 1600, 1494, 1466, 1364, 1111, 1046, 1008, 925, 801, 700, 646.

HRMS-Cl (NH_3) m/z : [M-OH] calcd for $\text{C}_{21}\text{H}_{31}\text{O}$, 299.2369; found 299.2367

Slower Eluting Diastereomer:

^1H NMR (400 MHz, CDCl_3) δ 7.31-7.27 (m, 4H), 7.19-7.13 (m, 1H), 4.47 (d, $J = 10.9$ Hz, 1H), 4.45 (s, 1H), 3.65 (d, $J = 10.9$ Hz, 1H), 2.72-2.62 (m, 1H), 2.58-2.48 (m, 1H), 2.01 (br s 2H), 1.68-1.59 (m, 2H), 1.45-1.37 (m, 2H), 1.35-1.27 (m, 4H), 0.91 (t, $J = 6.9$ Hz, 3H), 0.82 (s, 9H).

^{13}C NMR (100 MHz, CDCl_3) δ 146.6 (C), 128.1 (CH), 126.4 (CH), 125.1 (CH), 117.5 (C), 116.3 (C), 75.4 (CH), 69.3 (CH₂), 35.2 (C), 34.7 (C), 31.6 (CH₂), 29.2 (CH₂), 27.6 (CH₂), 25.7 (CH₃), 24.5 (CH₂), 22.6 (CH₂), 14.1 (CH₃).

IR (film, CHCl_3 , cm^{-1}) 3411, 2960, 2932, 2872, 1863, 1600, 1493, 1465, 1384, 1365, 1151, 1111, 1044, 1009, 793, 701, 675, 594.

HRMS-Cl (NH_3) m/z : [M+Na] calcd for $\text{C}_{21}\text{H}_{32}\text{O}_2\text{Na}$, 339.2300; found 339.2296

One-Pot Methylenecyclopropane synthesis via Alkylation/Rearrangement: (2-Hexyl-3-methylenecyclo-propyl)methanol (17)—A dry round bottom flask was charged with (2-hexylcycloprop-2-en-1-yl)methanol (0.511 g, 3.32 mmol) and THF (2 mL). The flask was cooled to -78°C then MeLi (5.20 mL, 8.29 mmol) was added via syringe. The flask was warmed to r.t. then tetramethylethylenediamine (0.996 mL, 6.64 mmol) and methyl iodide (0.207 mL, 3.32 mmol) were added. The mixture was allowed to additional 10 min. at 35°C . The reaction was acidified with aqueous HCl (3 M). The aqueous layer was extracted with three portions of diethyl ether. The extracts were dried with MgSO_4 and concentrated in vacuo. Silica gel chromatography using a gradient of ethyl acetate (0–10%) in hexane as the eluent gave 0.410 g (2.44 mmol, 73%) of the title compound as a colorless oil.

^1H NMR (400 MHz, CDCl_3) δ 5.41 (m, 2H), 3.64-3.48 (m, 2H), 1.46-1.24 (m, 13H), 0.88 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 139.1 (C), 103.6 (CH₂), 65.3 (CH₂), 32.3 (CH₂), 31.9 (CH₂), 29.5 (CH₂), 29.1 (CH₂), 25.1 (CH), 22.8 (CH₂), 21.8 (CH), 14.2 (CH₃).

IR (film, CHCl_3 , cm^{-1}) 3465, 3070, 2959, 2928, 2857, 1753, 1462, 1385, 1197, 1139, 1019, 824, 590.

HRMS-EI m/z : [M+] calcd for $\text{C}_{11}\text{H}_{20}\text{O}$, 168.1514; found 168.1510

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Reviews: Miege F, Meyer C, Cossy J. Beilstein J Org Chem. 2011; 7:717. [PubMed: 21804867]
Marek I, Simaan S, Masarwa A. Angew Chem, Int Ed. 2007; 46:7364. Rubin M, Rubina M,

- Gevorgyan V. Chem Rev. 2007; 107:3117. [PubMed: 17622181] Rubin M, Rubina M, Gevorgyan V. Synthesis. 2006; 8:1221. Fox JM, Yan N. Curr Org Chem. 2005; 9:719. Nakamura M, Isobe H, Nakamura E. Chem Rev. 2003; 103:1295. [PubMed: 12683784] Halton B, Banwell MG, Patai S, Rappoport Z. In The Chemistry of the Cyclopropyl Group. WileyChichester 1987:1224. Baird MS. Top Curr Chem. 1988; 144:139. Baird MS, Schmidt T, de Meijere. In Carbocyclic Three-Membered Ring Compounds. Georg Thieme Verlag Stuttgart 1996:114.
2. (a) Vincens M, Dumont C, Vidal M, Domnin IN. Tetrahedron. 1983; 39:4281. (b) D'yakonov IA, Kostikov RR. J Gen Chem USSR (Engl Transl). 1964; 34:1722. (c) Vincens M, Fadel R, Vidal M. Bull de Soc Chim Fr. 1987; 3:462.
3. Liao L, Fox JM. J Am Chem Soc. 2002; 124:14322. [PubMed: 12452703] Liu X, Fox JM. J Am Chem Soc. 2006; 128:5600. [PubMed: 16637603] Yan N, Liu X, Fox JM. J Org Chem. 2008; 73:563. [PubMed: 18085796] Richey HG Jr, Bension RM. J Org Chem. 1980; 45:5036. For carbomagnesation reactions that are directed by allylic hydroxyl substituents: Simaan S, Marek I. Org Lett. 2007; 9:2569. [PubMed: 17536813]
4. Yang Z, Xie X, Fox JM. Angew Chem Int Ed. 2006; 45:3960. Xie X, Yang Z, Fox JM. J Org Chem. 2010; 75:3847. [PubMed: 20462206] For related work with allylic hydroxyl substituents: Masarwa A, Stanger A, Marek I. Angew Chem Int Ed. 2007; 46:8039. Simaan S, Masarwa A, Bertus P, Marek I. Angew Chem Int Ed. 2006; 45:3963.
5. Phan DHT, Kou KGM, Dong VM. J Am Chem Soc. 2010; 132:16354–16355. [PubMed: 21028819] (b) Bugaut X, Liu F, Glorius F. J Am Chem Soc. 2011; 133:8130. [PubMed: 21520959]
6. Miege F, Meyer C, Cossy J. Org Lett. 2010; 12:248. [PubMed: 19994906]
7. Rubina M, Woodward EW, Rubin M. Org Lett. 2007; 9:5501. [PubMed: 18020352]
8. Additional reactions of 3-hydroxymethylcyclopropenes, include: Allylindanation reactions: Araki S, Kenji O, Shiraki F, Hirashita T. Tetrahedron Lett. 2002; 43:8033. Carbozincation reactions: Kramer K, Leong P, Lautens M. Org Lett. 2011; 13:819. [PubMed: 21250749]
9. (a) Doyle MP, Protopova M, Müller P, Ene D, Shapiro EA. J Am Chem Soc. 1994; 116:8492. (b) Davies HML, Lee GH. Org Lett. 2004; 6:1233. [PubMed: 15070305] (c) Briones J, Hansen J, Hardcastle K, Autschbach J, Davies HML. J Am Chem Soc. 2010; 132:17211. (d) Lou Y, Horikawa M, Kloster R, Hawryluk N, Corey EJ. J Am Chem Soc. 2004; 126:8916. [PubMed: 15264821] (e) Goto T, Takeda K, Shimada N, Nambu H, Anada M, Shiro M, Ando K, Hashimoto S. Angew Chem, Int Ed. 2011; 50:6803. (f) Boruta DT, Dmitrenko O, Yap GPA, Fox JM. Chemical Science. 2012 in press. 10.1039/c2sc01134d
10. (a) Pallerla MK, Fox JM. Org Lett. 2007; 9:5625. [PubMed: 18031057] (b) Pallerla MK, Fox JM. Org Lett. 2005; 7:3593. [PubMed: 16048350] (c) Pallerla MK, Yap GPA, Fox JM. J Org Chem. 2008; 73:6137. [PubMed: 18637694] (d) Kireev SL, Smit VA, Ugrak BI, Nefedov OM. Bull Acad Sci USSR (Engl Transl). 1991; 40:2240.
11. (a) Nakamura M, Isobe H, Nakamura E. Chem Rev. 2003; 103:1295. [PubMed: 12683784] (b) Closs GL, Closs LE. J Am Chem Soc. 1963; 85:99. (c) Avezov IB, Bolesov IG, Levina RY. J Org Chem (USSR), Engl Trans. 1974; 10:2129. (d) Isaka M, Matsuzawa S, Yamago S, Ejiri S, Miyachi Y, Nakamura E. J Org Chem. 1989; 54:4727. (e) Kirms MA, Primke H, Stohlmeier M, de Meijere A. Recl Trav Chim Pays-Bas. 1986; 105:462. (f) Schipperijn AJ, Smael P. Recl Trav Chim Pays-Bas. 1973; 92:1159.
12. (a) Zrinski I, Novak-Coumbassa N, Eckert-Maksic M. Organometallics. 2004; 23:2806. (b) Zrinski I, Eckert-Maksi M. Synth Commun. 2003; 33:4071.
13. (a) Liao L, Yan N, Fox JM. Org Lett. 2004; 6:4937. [PubMed: 15606104] (b) Fisher LA, Fox JM. J Org Chem. 2008; 73:8474. [PubMed: 18850746]
14. Chuprakov S, Rubin M, Gevorgyan V. J Am Chem Soc. 2005; 127:3714. [PubMed: 15771503]
15. Fordyce EAF, Luebbbers T, Lam HW. Org Lett. 2008; 10:3993. [PubMed: 18722460]
16. Kim R, Sherrill WM, Rubin M. Tetrahedron. 2010; 66:4947.
17. Audran G, Pellissier H. Adv Synth Catal. 2010; 352:575.
18. Formal SN2': Nueske H, Braese S, Meijere A. Synlett. 2000; 10:1467. Babin D, Pilorge F, Delbarre LM, Demoute JP. Tetrahedron. 1995; 51:9603. Simaan S, Masarwa A, Bertus P, Marek I. Angew Chem, Int Ed. 2006; 118:4067. Weatherhead-Kloster RA, Corey EJ. Org Lett. 2006; 8:171. [PubMed: 16381595] Reduction with Allylic Transposition: Simaan S, Marek I. Chem Commun.

- 2009; 3:292. Simaan S, Masarwa A, Zohar E, Stanger A, Marek I, Bertus P. Chem Eur J. 2009; 15:8449. [PubMed: 19609999] Allylic Chlorination: Arnaud R, Choubani S, Subra R, Vidal M, Vincens M. Can J Chem. 1985; 63:2512. Vincens M, Choubani S, Vidal M. Tetrahedron Lett. 1981; 22:4695. Sigmatropic Rearrangement: Rubina M, Woodward EW, Rubin M. Org Lett. 2007; 9:5501. [PubMed: 18020352] Masarwa A, Stanger A, Marek I. Angew Chem, Int Ed. 2007; 119:8185. Simaan S, Masarwa A, Zohar E, Stanger A, Marek I, Bertus P. Chem Eur J. 2009; 15:8449. [PubMed: 19609999]
19. (a) Yamago S, Nakamura M, Wang X, Yanagawa M, Tokumitsu S, Nakamura E. J Org Chem. 1998; 63:1694. (b) Yamago S, Nakamura E. J Am Chem Soc. 1989; 111:7285. (c) Vincens M, Dumont C, Vidal M. Tetrahedron. 1981; 37:2683. (d) Audo D, Vincens M, Dumont C, Vidal M. Can J Chem. 1981; 59:2199. (e) Vidal M, Vincens M, Arnaud P. Bull Soc Chim Fr. 1972; 2:665. (f) Padwa A, Wannamaker W. Tetrahedron. 1991; 32:6139. (g) Okazaki R, O-oka M, Akiyama T, Inamoto N, Niwa J, Kato S. J Am Chem Soc. 1987; 109:5413. (h) Stierman TJ, Johnson RP. J Am Chem Soc. 1983; 105:2492. (i) Formanovskii AA, Leonova LI, Yakushkina NI, Bakhbukh M, Grishin YuK, Bolesov IG. Zhurnal Organicheskoi Khimii. 1977; 13:1883. (j) Nakamura M, Toganoh M, Wang X, Yamago S, Nakamura E. Chem Lett. 2000; 6:664. (k) Vincens M, Vidal M. Bull Soc Chim Fr. 1985; 5:900. (l) Richey H, Wilkins C, Bension R. J Org Chem. 1980; 45:5042. (m) Warkentin J, Woollard J. Can J Chem. 1997; 75:289. (n) Vincens M, Dumont C, Vidal M. Bull Soc Chim Fr. 1974; 12:2811. (o) Schipperijn AJ, Smael P. Recueil des Travaux Chimiques des Pays-Bas. 1973; 92:1159.
20. Jackman LM, Smith BD. J Am Chem Soc. 1988; 110:3829.

Scheme 1.

Selected, known reactions of 3-hydroxymethyl cyclopropene derivatives

Scheme 2.
Comparison of Dianion Stability

Scheme 3. Synthesis of 1,2-disubstituted cyclopropenes from 1-hexyl-3-hydroxymethylcyclopropene

^a6:4 mixture of diastereomers; ^bReaction run in benzene

Scheme 4. Synthesis of internal cyclopropenes from 3-hydroxymethylcyclopropenes with quaternary carbons

^a6:4 mixture of diastereomers; ^bYield based on recovered starting material

Base (2.2 eq.)	Additive	Reaction time (min)	Yield of 17 (%)
nBuLi	None	60	67
nBuLi/tBuOK	None	60	60
MeLi	TMEDA	10	73

Scheme 5.

Formation of (2-Hexyl-3-methylenecyclopropyl)methanol (**17**) via sequential alkylation/base promoted rearrangement

Solvent	Conversion ^a	6:17^a
DME	<5%	NA
Pyridine	<5%	NA
Hexane	90%	95:5
Dioxane	93%	95:5
Toluene	>95%	95:5
Benzene	>95%	>95:5

Scheme 6. Solvent screen for selective formation of (2-hexyl-3-methylcycloprop-2-en-1-yl)methanol (**6**)

^aBased on NMR integrations against an internal standard