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# Titanium carbenoid-mediated cyclopropanation of allylic alcohols: selectivity and mechanism†

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A new method for the chemo- and stereoselective conversion of allylic alcohols into the corresponding cyclopropane derivatives has been developed. The cyclopropanation reaction was carried out with an unprecedented titanium carbenoid generated *in situ* from Nugent's reagent, manganese and methylene diiodide. The reaction involving the participation of an allylic hydroxyl group, proceeded with conservation of the alkene geometry and in a high diastereomeric excess. The scope, limitations and mechanism of this metal-catalysed reaction are discussed.



## Introduction

A cyclopropane ring is a key component of a large number of compounds that possess valuable biological activities.[1] The range of these biological activities together with the utility of the cyclopropane ring in generating other structural units, has led to considerable interest in the development of novel and alternative methods of cyclopropanation.[2,3] Many approaches to the synthesis of the cyclopropane ring have been reviewed.[4] One of the most powerful methods is a carbenoid-based methylene addition to an allylic alcohol, especially when it leads to the stereoselective synthesis of cyclopropyl alcohols. A number of modifications of the original zinc–copper couple based Simmons–Smith methodology have recently been reported.[4b,5]

The ease with which titanium undergoes the one-electron changes linking titanium(III) and (IV) has led to the $Cp_2TiCl_2$/$Cp_2TiCl$ couple being used in both single-electron oxidative addition and single-electron reductive elimination reactions. This facile one-electron change can form the basis of reactions that are sub-stoichiometric or even catalytic in titanocene in the presence of electron sources such as manganese or zinc dust.[6] This has widened the scope of titanium(III)-mediated reactions resulting in a number of useful synthetic procedures, which have recently been reviewed.[7]

Esters, ketones, amides and other carbonyl compounds can be methylated using three different titanium-based reagents: the Tebbe reagent, titanocyclobutanes and dimethyltitanocene.[8] In addition, some cyclopropanation methods using Ti(IV) carbenoid complexes have been reported.[9] In this context the intra- and intermolecular reaction of *gem*-dihalides and thioacetals with olefins to give cyclopropanes,[10] and the carbonyl cyclopropanation, specially the Kulinkovich reaction yielding cyclopropanols from esters and amides are of interest.[11] Recently an ambiphilic titanium carbenoid equivalent was used in amide cyclopropanation.[12] Although there are a large number of reactions of this type including metallocarbene-mediated tandem carbonyl olefination and olefin cyclopropanation, as far as we know there are no precedents for the formation of a titanium-carbenoid and its application to the construction of a cyclopropane ring by a direct carbenoid mediated methylene addition reaction to a C–C double bond. A theoretical study by Zhang[13] in 2007 predicted that a titanium-carbenoid species could be one of the most highly reactive cyclopropanating reagents.

In the light of these experimental and theoretical studies and the known reactivity of $Cp_2TiCl$ (Nugent's reagent)[14] with allylic halides[15] and its ability to coordinate with heteroatoms,[6f] we decided to investigate the use of a titanium-carbenoid in the development of new strategies for the direct cyclopropanation of alkenes. In this paper we describe the use of a low-valent titanium(III) species derived from Nugent's reagent to generate *in situ* a titanium-carbenoid from a haloalkane in order to cyclopropanate an allylic alcohol and thus to provide support for Zhang's theoretical predictions.

## Results and discussion

We used the methodology of Gansaeuer[16] and other authors[17] to reduce the Ti(IV) complex to generate catalytic quantities of

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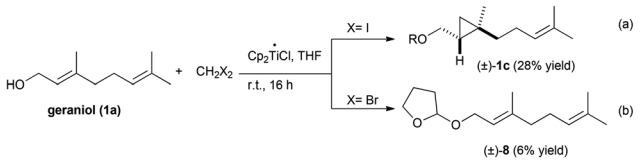
†Electronic supplementary information (ESI) available: Copies of $^1H$ and $^{13}C$ NMR spectra for all new compounds appearing in the schemes and $^1H$ NMR spectrum for known compounds prepared by the general procedure of cyclopropanation. See DOI: 10.1039/c5ob00544b




**Scheme 1** Preliminary experiment.

titanocene(III) chloride. Thus $Cp_2Ti^{IV}Cl_2$ (0.2 equiv.) was treated with excess Mn powder (8.0 equiv.) under argon in carefully deoxygenated THF (13 mL). After 15 minutes, the reaction mixture turned to the characteristic green colour of Ti(III) solutions. A solution of the allylic alcohol geraniol (**1a**) (1 equiv.) together with $CH_2I_2$ (4 equiv.) was then added and the mixture was stirred for 16 hours. The reaction was quenched with water and the crude product was purified (Scheme 1).

After chromatography and final purification by HPLC compound (±)-**1c** was obtained in 28% yield. This corresponds to a chemo- and diastereoselective cyclopropanation of the proximal alkene of geraniol. When other alkyl halides, *e.g.* $CH_2Br_2$, were used the cyclopropanation reaction was unsuccessful and only a THF ether, (±)-**8**, was detected as a minor (6%) by-product.

Although Nugent's reagent can be used in other solvents such as DME, the allylic cyclopropanation reaction only occurred in THF, highlighting the important role of the solvent in this reaction. Our further studies will examine the role played by the THF and whether the mild tetrahydrofuranylation of geranyl alcohols promoted by Ti(III) species in the presence of alkyl dibromides, can be extended to other allylic alcohols.

During our optimization studies with geraniol and different amounts of titanocene and Mn (Table 1), we observed that an increase in the initial Ti(IV) and Mn equivalents resulted in a better yield (65%) of the cyclopropanation reaction. However yields were not improved by using stoichiometric amounts of Ti(IV) (entry 4, Table 1). Then we examined the reaction variables using the Simplex algorithm[18] which has recently been applied to organic synthesis.[19]

The cyclopropanation reaction was dramatically improved when the reaction was carried out at 40 °C and using 0.5 equiv. of $Cp_2TiCl_2$, 12.8 equiv. of Mn and 5 equiv. of $CH_2I_2$ (entry 3, Table 1).

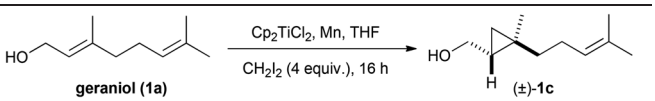
Titanium plays a clear role in the reaction, as was evidenced by the quantitative recovery of geraniol in the absence of $Cp_2TiCl_2$ (entry 6, Table 1). With this observation in hand, we sought to gain insight into the scope and mechanism of this titanium-catalysed cyclopropanation protocol. Initially we set out to determine the role of titanium and manganese and the nature of the potential carbenoid reagent formed in the cyclopropanation event.

The initial generation of Ti(III) species from Ti(IV) and Mn(0) was required, as no reaction was observed without this initial reduction reaction. The cyclopropanation reaction did not occur in the absence of Ti(IV) or manganese dust, indicating that both titanium and manganese participated in the reaction.

Recently, in a series of interesting papers, the Ashfeld research group has described the generation of highly reactive organometallic reagents under mild conditions through the titanocene-catalysed reductive transmetalation of alkyl halides.[20] In contrast to metal activation employed in the conventional method for the generation of organometallic reagents,[21] this strategy utilized titanocene as a catalytic substrate activator to facilitate the overall metal insertion into C–X bonds.[22] In order to clarify the role of the Mn in our cyclopropanation reaction and to study the formation and the possible participation of a titanocene-catalysed manganese carbenoid species, several experiments were carried out, (entries 7–9, Table 1). No reaction was observed when the reaction was carried out in the absence of titanocene using manganese activated with HCl.[23] Interestingly, when cyclopropanation was carried out under the same conditions but using lithium-activated Rieke manganese,[24] 42% of cyclopropanated geraniol ((±)-**1c**) was obtained. However, approximately the same yield of (±)-**1c** was obtained when the reaction was carried out in the absence of both Ti(IV) and Mn(0), indicating that this particular cyclopropanation reaction arose from a lithium carbenoid[2d–f,25] formed in the manganese activation reaction (entry 9, Table 1).

On the basis of our findings, we can rule out the titanocene activation of diiodomethane and the formation of a manganese carbenoid under our reaction conditions. Following the precedents of samarium,[26] indium[27] and lanthanum[28] metal-assisted cyclopropanation reaction reported, we envisioned the formation of a Ti(IV) carbenoid, $Cp_2Ti(OR)CH_2I$, (**D**, Scheme 2), similar to that of the Simmons–Smith-type titanium carbenoid intermediate, proposed by Lin *et al.* in the amide cyclopropanation.[12]

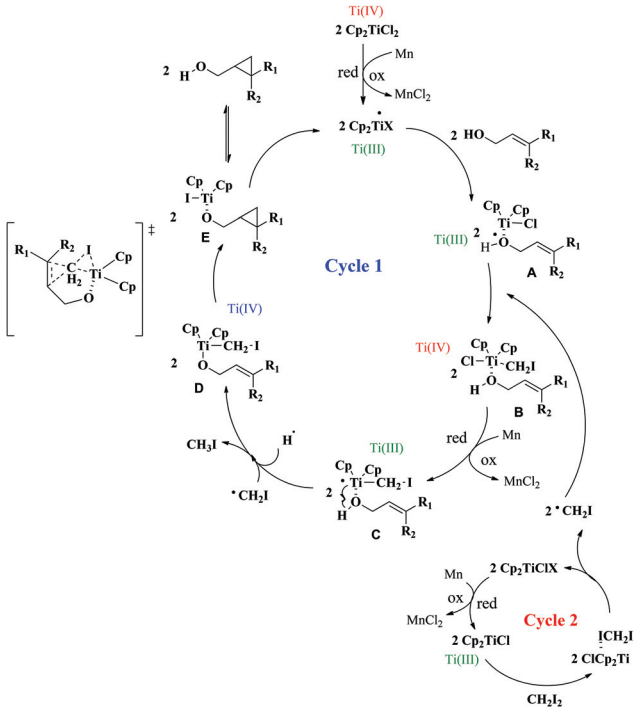
**Table 1** Optimization of cyclopropanation reaction conditions with geraniol




| Entry | Ti(IV) (equiv.) | Mn (equiv.) | *T* | Products[a] (yield %) |
|---|---|---|---|---|
| 1 | 0.27 | 8.0 | r.t. | (±)-**1c** (28%) |
| 2 | 0.50 | 12.8 | r.t. | (±)-**1c** (65%) |
| 3 | 0.50 | 12.8 | 40 °C | (±)-**1c** (81%) |
| 4 | 1.00 | 12.8 | r.t. | (±)-**1c** (8%) |
| 5 | 1.00 | 0 | 40 °C | n.r. |
| 6 | 0 | 12.8 | r.t. | n.r. |
| 7 | 0 | 12.8[b] | r.t. | n.r. |
| 8 | 0 | 12.8[c] | r.t. | (±)-**1c** (42%) |
| 9 | 0 | 0[d] | r.t. | (±)-**1c** (40%) |

[a] Yields were evaluated by GC. [b] Mn was activated by HCl. [c] Rieke-manganese obtained by reduction of $MnCl_2$ by Li and naphthalene. [d] 25.6 equiv. of Li were used together with 5 equiv. of $CH_2I_2$.




Scheme 2 Proposed mechanism for allylic alcohol cyclopropanation.

In order to generalise the cyclopropanation reaction we carried out the reaction with different substrates, yielding good yields of compounds **1c–7c** (entries 1–7, Table 2) using the Simplex algorithm.[18]

The structures of the cyclopropyl derivatives, **1c–7c**, were established by analysis of their NMR and mass spectroscopic data and by comparison with those reported in the literature.[29] The stereochemistry of the cyclopropyl derivatives was assigned by extensive NOE experiments. The fragmentation patterns and the molecular ions in the low and high resolution mass spectra were consistent with the proposed structures.

The presence of a free hydroxyl group is an essential prerequisite for cyclopropanation. The reaction did not take place when the hydroxyl group was protected (substrates **1b–5b**, and **7b**, Table 2) or if the hydroxyl group was not in the allylic position (entries 9 and 10, Table 2). Furthermore a methyl group geminal to the allylic hydroxyl group appears to prevent the reaction, possibly due to steric hindrance (entry 8, Table 2).

A distinctive feature of the reaction is the chemo- and diastereoselectivity in affording the product that is *syn* to the hydroxyl group on the proximal alkene (entries 5 and 6, Table 2). The reaction proceeds with the conservation of the alkene geometry (entries 1, 2 and 7, Table 2). Treatment of *cis*-carveol (**5a**) under the optimized conditions, gave the enantiomerically pure cyclopropyl product (**5c**).[30] However the more sterically congested **6a** gave both diastereoisomers with a 90% de of cyclopropyl derivatives.

We considered that the excess Mn present in the reaction mixture would lead to the regeneration of Ti(III) and thus the process would be susceptible to catalysis by titanium (Scheme 2). We also noted that the $CH_2I_2$, in addition to being the reagent for the formation of the titanium-carbenoid, appeared to play a role in generating the Ti(III) species, possibly by providing an iodine source to replace the chlorine.

The detailed study of the reaction conditions together with the high chemo- and diastereoselectivity which we have observed, has led us to propose the following reaction mechanism (Scheme 2).

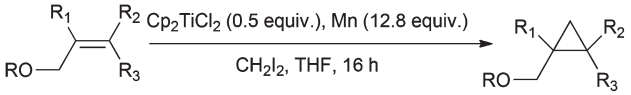
In prior work, the identity of the Ti(III) species generated in THF by the Mn based reduction of $Cp_2TiX_2$ (X = Cl, Br, I) has been clarified.[6e,f] The principal species that are formed are a mixture of $Cp_2TiX$ and $(Cp_2TiX)_2$ in which it is assumed that any free coordination site will be occupied by a THF molecule.

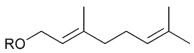
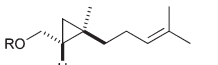
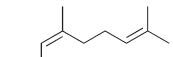
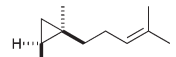
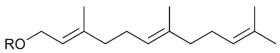
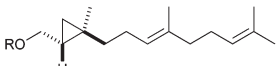
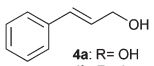
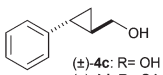
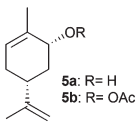
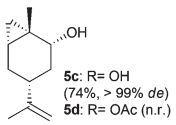
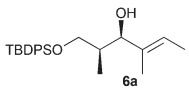
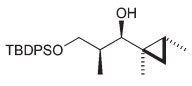
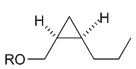
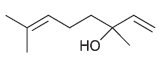
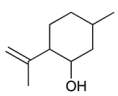
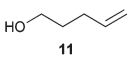
It is worth noting that the progressive colour change observed in the reaction solution, which turns from red to dark blue, passing through green, has led us confirm the involvement of Ti(IV)/Ti(III) species in the cyclopropanation reaction.[31]

A plausible reaction mechanism might involve coupled cycles in which the Ti(III) species is regenerated at various stages by the excess Mn. In one cycle (labelled cycle 2 in Scheme 2) the methylene iodide radical is generated from methylene diiodide by the Ti(III) species and introduced into the main cycle (cycle 1). In this cycle 1 the $Cp_2TiCl_2$ in THF (red solution) is first reduced by Mn to $Cp_2TiCl$ which then complexes with the allylic alcohol (green colour). Reaction with the methylene iodide radical gives a Ti(IV) species (red solution) which is reduced by the Mn again to give a $Ti^{III}$-carbenoid species (green colour). Although, it has been proposed that alcohols bind poorly to titanocene(IV) and Ti(III) reagents,[32] 45 min after $CH_2I_2$ addition, the solution turns deep blue indicating that a potential geranyloxytitanium(IV) bond was formed.[31,32] Following the theoretical proposal, the cyclopropane derivative is formed by a concerted [1 + 2] addition *via* a 'butterfly-type' transition state. This is accompanied by a migration of the halide from the carbon to the metal. Finally displacement of the $Cp_2TiI$ affords the cyclopropyl alcohol. The selectivity for allylic alcohols must depend on their stereo-electronic ability to displace THF from a coordination site on the Ti(III) species.

A final piece of evidence, which supported the proposed mechanism and revealed the existence of a geranyloxytitanium bond, was obtained by a mass spectrometry (MS) study of the cyclopropanation reaction mixture. Detection by MS of $\alpha$-terpinene and $\alpha$-phellandrene implied the existence and cyclisation of the geranyl radical to give an $\alpha$-terpinyl radical, a precursor of the indicated monoterpenes.[33] Thus, the geranyl radical, originating from homolysis of the corresponding C–O bond in compound **D** (Scheme 2), could cyclise to the terpinyl radical yielding the indicated monoterpenes by a proton loss. Furthermore, determination of methyl iodide would indicate a direct hydrogen atom transfer (HAT) from the geraniol–Ti complex to the iodomethylene radical, according to the reported data, *i.e.* step compound **C** to **D**.[32] Finally, when the reaction was quenched by the addition of ethyl acetate, transesterification was observed affording the acetate derivatives of geraniol and

**Table 2** Titanium carbenoid-mediated cyclopropanation[a]




| Entry | Substrate | $CH_2I_2$ (equiv.)/$T$ | Products[b] (yield %) |
|---|---|---|---|
| 1 |  **1a**: R = H **1b**: R = OBn | 5/40 °C |  (±)-**1c**: R = H (81%) (±)-**1d**: R = OBn (n.r.) |
| 2 |  **2a**: R = H **2b**: R = OBn | 5/40 °C |  (±)-**2c**: R = H (76%) (±)-**2d**: R = OBn (n.r.) |
| 3 |  **3a**: R = H **3b**: R = OAc | 5/40 °C |  (±)-**3c**: R = H (73%) (±)-**3d**: R = OAc (n.r.) |
| 4 |  **4a**: R= OH **4b**: R= Ac | 6/40 °C |  (±)-**4c**: R= OH (68%) (±)-**4d**: R= OAc (n.r.) |
| 5 |  **5a**: R= H **5b**: R= OAc | 4.5/35 °C |  **5c**: R= OH (74%, > 99% *de*) **5d**: R= OAc (n.r.) |
| 6 |  **6a** | 5/r.t. |  *syn* : *anti* **6c** 19 (56%) : 1 (3%) 90 % *de* |
| 7 |  **7a**: R= H **7b**: R= Ac | 5/r.t. |  **7c**: R= H (40%) **7d**: R= Ac (n.r.) |
| 8 |  **9** | 5/40 °C | — |
| 9 |  **10** | 5/r.t. | — |
| 10 |  **11** | 5/r.t. | — |

[a] Ti(III) species was generated *in situ* using THF as a solvent, under argon. [b] Yields were evaluated by GC.

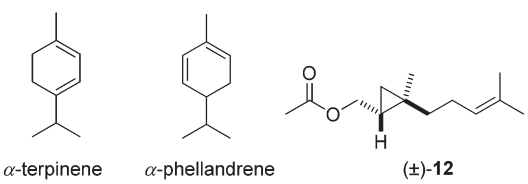



**Fig. 1** Structures of α-terpinene, α-phellandrene and (±)-**12**.

its cyclopropyl derivative (±)-**12**, indicating that an activated species of geraniol (**D**) and cyclopropylgeraniol (**E**) was present in the reaction (Fig. 1).

## Conclusions

We have described the *in situ* preparation of an unprecedented titanium-carbenoid which we have used in the cyclopropana-

tion of allylic alcohols. The major advantage of the reaction is that it proceeds with a high chemo- and diastereoselectivity and in good yield under mild conditions. Further studies are in progress to extend this reaction to *gem*-dimethyl cyclopropyl derivatives.

# Experimental

### General procedures

Unless otherwise noted, materials and reagents were obtained from commercial suppliers and were used without further purification. Tetrahydrofuran was freshly distilled from Na and strictly deoxygenated for 30 minutes under argon prior to use. Dichloromethane was freshly distilled from $CaH_2$. Air- and moisture-sensitive reactions were performed under an argon atmosphere. Purification by semipreparative and analytical HPLC was performed with a Hitachi/Merck L-6270 apparatus equipped with a differential refractometer detector (RI-7490). A LiChrospher® Si 60 (5 μm) LiChroCart® (250 mm × 4 mm) column and a LiChrospher® Si 60 (10 μm) LiChroCart® (250 mm × 10 mm) were used in isolation experiments. Silica gel (Merck) was used for column chromatography. TLC was performed on Merck Kieselgel 60 F254, 0.25 mm thick melting points were measured with a Reichert-Jung Kofler block and are uncorrected. Optical rotations were determined with a digital polarimeter. Infrared spectra were recorded on a FT-IR spectrophotometer and reported as wave numbers ($cm^{-1}$). $^1H$ and $^{13}C$ NMR measurements were recorded on an Agilent 500 MHz spectrometer with $SiMe_4$ as the internal reference. Chemical shifts were referenced to $CDCl_3$ ($\delta_H$ 7.25, $\delta_C$ 77.0). NMR assignments were made using a combination of 1D and 2D techniques. Multiplicities are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quarter; quint = quintuplet; sext = sextuplet; m = multiplet, br = broad. High-Resolution Mass Spectroscopy (HRMS) was recorded with a double-focusing magnetic sector mass spectrometer in positive ion mode or with a QTOF mass spectrometer in positive ion electrospray mode at 20 V cone voltage or in positive ion APCI mode.

### Synthesis of the substrates

**Preparation of 5a.** This compound was obtained by means of the procedure described in the literature and its spectroscopic data were identical to those described in the literature.[34]

**Preparation of 6a.** This compound was obtained by means of the procedure described in the literature and its spectroscopic data were identical to those described in the literature.[35]

**General procedure for the preparation of acetyl derivatives 5b and 7b.** Pyridine (2 drops) was added to a solution of the corresponding alcohol (1 mmol) in acetic anhydride (0.5 mL) at room temperature for 18 h. Then, cyclohexane was added (2 mL) and the solvent was evaporated under reduced pressure. This procedure was repeated three times to give quantitatively the corresponding acetates **5b**[36] and **7b**[37] whose spectroscopic data were identical to those described in the literature.

**General procedure for the preparation of benzyl ethers 1b and 2b.** Sodium hydride (60% in oil, 184.8 mg, 4.62 mmol) was washed twice with hexane, suspended in dry dimethylformamide (7.9 mL). A solution of the corresponding alcohol (2.57 mmol) dissolved in dry dimethylformamide (0.5 mL) was added and the mixture was stirred for 10 min. Then, a solution of benzyl chloride (0.45 mL, 3.85 mmol) was added and the mixture was allowed to warm for 8 h. The mixture was poured into water, the layers were separated and the aqueous layer was extracted three times with diethyl ether (3 × 50 mL). Combined extracts were washed with brine, dried over sodium sulfate and concentrated. The resulting crude product was purified by column chromatography on silica gel using mixtures of hexanes and ethyl acetate as the eluent, followed by analytical HPLC purification, yielding the corresponding benzyl derivatives **1b** (73%) and **2b** (65%). Spectroscopic data of compounds **1b** and **2b** were identical to those described in the literature.[38]

**General procedure for cyclopropanation mediated by $Cp_2Ti^{III}Cl$.** A mixture of $Cp_2TiCl_2$ (81.5 mg, 0.32 mmol) and Mn dust (434 mg; 8.19 mmol) in strictly deoxygenated THF (12.7 mL) under an Ar atmosphere was stirred at room temperature until the red solution turned green. Then, a solution of the corresponding alcohol (0.64 mmol) and $CH_2I_2$ (0.25 mL, 3.20 mmol) in strictly deoxygenated THF (2.5 mL) was added, and the mixture was stirred for 16 hours. The reaction was quenched with distilled water (20 mL), extracted with ethyl acetate (3 × 50 mL), dried with anhydrous $Na_2SO_4$, and evaporated under reduced pressure. The resulting crude product was purified by column chromatography on silica gel using mixtures of hexanes and ethyl acetate as the eluent, followed by analytical HPLC purification, yielding the corresponding cyclopropyl derivatives, in the yields shown in the manuscript.

**(±)-(1*R**,2*R**)-2-Hydroxymethyl-1-methyl-1-(4-methylpent-3-enyl)cyclopropane ((±)-1c).** Spectroscopic data of compound (±)-**1c** were identical to those described in the literature.[29a,c]

**(±)-(1*S**,2*R**)-2-Hydroxymethyl-1-methyl-1-(4-methylpent-3-enyl)cyclopropane ((±)-2c).** Spectroscopic data of compound (±)-**2c** were identical to those described in the literature.[29a]

**(±)-(1*R**,2*R**,3′*E*)-2-Hydroxymethyl-1-methyl-1-(4,8-dimethylnona-3,8-dienyl)cyclopropane ((±)-3c).** Spectroscopic data of compound (±)-**3c** were identical to those described in the literature.[29c]

**(±)-(1*R**,2*R**)-1-Phenyl-2-hydroxymethylcyclopropane ((±)-4c).** Spectroscopic data of compound (±)-**4c** were identical to those described in the literature.[29b]

**(1*S*,2*R*,4*R*,6*R*)-1-Methyl-4-(prop-1-en-2-yl)bicyclo[4.1.0]heptan-2-ol (5c).** White solid; mp 48–50 °C; $t_R$ = 19.4 min, petroleum ether : ethyl acetate (85 : 15), flow = 3.0 mL $min^{-1}$; $[\alpha]_D^{20}$ −54.2° (*c* 0.14 in $CHCl_3$; >99% de); IR (film) $\nu_{max}$ 3350, 3059, 2994, 2964, 2932, 2864, 1438, 1042, 888 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 4.64 (1H, s br.), 4.61 (1H, s br.), 3.92 (1H, dd, *J* 10.8, 5.0, Hz), 2.08–2.00 (1H, m), 1.86 (1H, m), 1.79 (1H, ddt, *J* 12.6, 5.0, 2.0 Hz), 1.64 (3H, s), 1.24–1.13 (1H, m), 1.18 (3H, s), 0.95 (1H, dddd, *J* 14.0, 8.8, 5.2, 2.0 Hz), 0.83 (1H, dd, *J* 12.6,

10.8 Hz), 0.42 (1H, dd, *J* 8.8, 5.2 Hz), 0.33 (1H, t, *J* 5.2 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 148.9, 108.8, 74.0, 41.9, 35.2, 30.0, 24.1, 22.6, 21.7, 20.6, 16.5; HRMS ($APCI^+$): calcd for $C_{11}H_{19}O$ $[M + H]^+$ 167.1436, found 167.1424.

**(1*R*,2*R*,1′*R*,2′*S*)-1-(1-Hydroxy-2-methyl-3-(*tert*-butyldiphenylsilyloxy)propyl)-1,2-dimethylcyclopropane (*β*-6c)‡.** Colourless oil; $t_R$ = 44 min, petroleum ether : ethyl acetate (95 : 5), flow = 3.0 mL min$^{-1}$; $[\alpha]_D^{20}$ −4.6° (*c* 0.1 in $CHCl_3$; 90% de); IR (film) $\nu_{max}$ 3446, 2930, 2858, 1472, 1428, 1112, 1021, 702 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.67–7.64 (4H, m), 7.44–7.35 (6H, m), 3.66 (1H, dd, *J* 10.0, 4.5 Hz), 3.50 (1H, dd, *J* 10.0, 6.0 Hz), 2.69 (1H, d, *J* 8.5 Hz), 1.91–1.84 (1H, m), 1.69 (1H, s), 1.12 (3H, d, *J* 7.0 Hz), 1.06 (9H, s), 0.86 (3H, s), 0.78 (1H, d, *J* 6.0 Hz), 0.61 (1H, m), 0.50 (1H, dd, *J* 8.5, 4.5 Hz), −0.16 (1H, t, *J* 4.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 135.74 (2C), 135.66 (2C), 133.7, 133.6, 129.63, 129.59, 127.63, 127.61, 81.5, 66.4, 39.1, 26.9 (3C), 23.1, 19.3, 18.3, 15.4, 13.9, 12.8, 12.2; HRMS ($ESI^+$): calcd for $C_{25}H_{36}O_2SiNa$ $[M + Na]^+$ 419.2382, found 419.2387.

**(1*S**,2*R**)-1-Hydroxymethyl-2-propylcyclopropane ((±)-7c).** Colourless oil; $t_R$ = 31 min, petroleum ether : ethyl acetate (88 : 12), flow = 0.8 mL min$^{-1}$; IR (film) $\nu_{max}$ 3330, 2960, 2925, 2873, 1458, 1065 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.65 (1H, ddd, *J* 11.5, 7.0, 5.0 Hz), 3.57 (1H, m), 1.47–1.38 (2H, m), 1.21–1.18 (1H, m), 1.09 (1H, ddq, *J* 8.2, 7.0, 5.0 Hz), 0.92 (3H, t, *J* 7.5 Hz), 0.70 (1H, dt, *J* 8.2, 5.0 Hz), −0.04 (1H, q, *J* 5.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 63.4, 30.7, 23.2, 18.1, 15.9, 14.0, 9.4; HRMS ($ESI^+$): calcd for $C_7H_{14}ONa$ $[M + Na]^+$ 137.0937, found 137.0941.

**Attempts of cyclopropanation mediated by activated Mn with HCl.** Mn previously activated with HCl[23] (434 mg, 8.19 mmol) in strictly deoxygenated THF (12.7 mL) under an Ar atmosphere was stirred at room temperature. Then, a solution of geraniol (100 mg, 0.64 mmol) and $CH_2I_2$ (0.25 mL; 3.20 mmol) in strictly deoxygenated THF (2.5 mL) was added, and the mixture was stirred for 16 hours. The reaction was quenched with distilled water (10 mL), extracted with ethyl acetate (3 × 50 mL), dried with anhydrous $Na_2SO_4$, and evaporated under reduced pressure. The analysis of the reaction by GC showed only the starting material.

**Attempts of cyclopropanation mediated by Rieke-Mn.** To the mixture of lithium (120.7 mg, 17.4 mmol), naphthalene (223.0 mg, 1.74 mmol) and $MnCl_2$ (1094.8 mg, 8.7 mmol) was added *via* a syringe freshly distilled and degassed THF (12.7 mL) at room temperature and then the resulting mixture was allowed to stir at room temperature for 3 h.[24] A black slurry solution was obtained and then, a solution of geraniol (100 mg, 0.64 mmol) and $CH_2I_2$ (0.25 mL, 3.20 mmol) in strictly deoxygenated THF (2.5 mL) was added, and the mixture was stirred for 16 hours. The reaction was quenched with distilled water (10 mL), extracted with ethyl acetate (3 × 50 mL), dried with anhydrous $Na_2SO_4$, and evaporated under reduced pressure. The analysis of the reaction by GC showed that (±)-**1c** was obtained in 42% yield.

**Attempts of cyclopropanation by lithium and $CH_2I_2$.** To the mixture of lithium (120.7 mg, 17.4 mmol) and $CH_2I_2$ (0.25 mL, 3.20 mmol) in freshly distilled and degassed THF (12.7 mL) at room temperature was added a solution of geraniol (100 mg, 0.64 mmol) in strictly deoxygenated THF (2.5 mL), and the mixture was stirred for 16 hours. The reaction was quenched with distilled water (10 mL), extracted with ethyl acetate (3 × 50 mL), dried with anhydrous $Na_2SO_4$, and evaporated under reduced pressure. The analysis of the reaction by GC showed that (±)-**1c** was obtained in 40% yield.

**Preparation of compound (±)-8.** Compound (±)-**8** was prepared by following the general procedure of cyclopropanation using 0.2 equiv. of $Cp_2Ti^{IV}Cl_2$, 8.0 equiv. of Mn powder and 4.0 equiv. of $CH_2Br_2$ at room temperature to yield (±)-**1c** (28%) together with (±)-**8** (6%).

**(±)-(*E*)-2-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)tetrahydrofuran ((±)-8).** Yellow oil; IR (film) $\nu_{max}$ 2968, 2916, 1442, 1377, 1084, 1036, 919 cm$^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$) $\delta$ 5.31 (1H, m), 5.13 (1H, dd, *J* 4.4, 2.2 Hz), 5.07 (1H, m), 4.15 (1H, dd, *J* 11.8, 6.6 Hz), 3.96 (1H, dd, *J* 11.8, 7.2 Hz), 3.85 (2H, m), 2.10–1.65 (8H, m), 1.66 (6H, s), 1.58 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 140.2, 131.5, 124.0, 120.5, 102.9, 66.8, 63.5, 39.6, 32.3, 26.4, 25.6, 23.5, 17.6, 16.4; HRMS ($APCI^+$): calcd for $C_{14}H_{25}O_2$ $[M + H]^+$, 225.1855, found 225.1856.

**Transesterification of geraniol (1a).** A mixture of $Cp_2TiCl_2$ (81.5 mg, 0.32 mmol) and Mn dust (434 mg, 8.19 mmol) in strictly deoxygenated THF (12.7 mL) under an Ar atmosphere was stirred at room temperature until the red solution turned green. Then, a solution of geraniol (100 mg, 0.64 mmol) and $CH_2I_2$ (0.25 mL, 3.20 mmol) in strictly deoxygenated THF (2.5 mL) was added, and the mixture was stirred for 2.5 hours. The reaction was quenched with ethyl acetate (10 mL) and stirred for further 1.5 h. The crude product was pushed through a pad of silica with ethyl acetate (100 mL) and the solvent was removed under reduced pressure. The resulting crude product was purified by column chromatography on silica gel using mixtures of hexanes and ethyl acetate as the eluent, followed by analytical HPLC purification, yielding quantitatively a 1 : 2 mixture of the corresponding geranyl acetate (41.8 mg)[39] and (±)-**12** (88.7 mg).

**(±)-((1*R**,2*R**)-2-Methyl-2-(4-methylpent-3-enyl)cyclopropyl)-methyl acetate ((±)-12).** Colourless oil; $t_R$ = 18 min, petroleum ether : ethyl acetate (95 : 5), flow = 0.8 mL min$^{-1}$; IR (film) $\nu_{max}$ 2950, 2925, 1742, 1650, 1450, 1380, 1233, 1090, 830 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.08 (1H, m), 4.19 (1H, dd, *J* 11.5, 6.5 Hz), 3.90 (1H, dd, *J* 11.5, 8.5 Hz), 2.08–2.00 (5H, m), 1.66 (3H, s), 1.59 (3H, s), 1.32 (1H, ddd, *J* 13.6, 9.8, 6.2 Hz), 1.12 (1H, ddd, *J* 13.6, 10.0, 6.3 Hz), 1.06 (3H, s), 0.88 (1H, m), 0.54 (1H, dd, *J* 8.7, 4.8 Hz), 0.17 (1H, t, *J* 4.8 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 171.3, 131.2, 124.4, 65.9, 41.0, 26.3, 25.7, 25.3, 21.9, 20.2, 18.1, 17.7, 17.3; HRMS ($ESI^+$): calcd for $C_{13}H_{22}O_2Na$ $[M + Na]^+$ 233.1512, found 233.1517.

‡The minor cyclopropyl compound (1*S*,2*S*,1′*R*,2′*S*)-1-(1-hydroxy-2-methyl-3-(*tert*-butyldiphenylsilyloxy)propyl)-1,2-dimethylcyclopropane could not be purified.

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