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Synthesis of cyclopropanes via iodine–magnesium exchange between 3-iodomethyl-1-oxacyclopentanes and organomagnesium reagents

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Abstract—Iodine–magnesium exchange occurs upon treatment of 3-iodomethyl-1-oxacyclopentanes with alkyl Grignard reagents or trialkylmagnesate. The resulting organomagnesium compounds undergo intramolecular nucleophilic substitution in ether to afford cyclopropane skeletons in a stereoselective manner.
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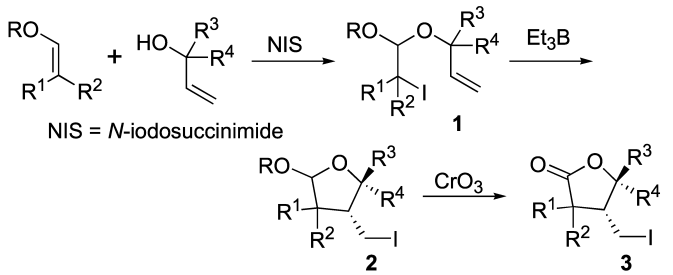
1. Introduction

Cyclopropane rings are highly strained entities and hence attracts much attention. They are not only structurally challenging targets but also found in a wide variety of naturally occurring useful compounds. While many methodologies are available to construct three-membered rings, synthesis of cyclopropanes still gains in importance.[1] Ring closure of alkyl halide having a leaving group at the third position via halogen–lithium exchange is promising.[2] On the other hand, there are a limited number of halogen–metal exchanges with metal reagents other than organolithium to form cyclopropanes.[3]

Iodine–magnesium exchange between Grignard reagents and organic iodides is a convenient method to prepare new organomagnesium compounds.[4] Aryl and vinyl iodides[5] and alkyl iodides bearing another electronegative groups such as CF_3I, $RCHI_2$, and $ROCH_2I$[6] are usually the choice of precursors. In general, the exchange reaction using alkyl iodides is much less widely used because the exchange is complicated by the possible occurrence of Wultz-type



NIS = *N*-iodosuccinimide

	R	R^1	R^2	R^3	R^4
a	C_2H_5	H (or CH_3)	CH_3 (or H)	n-C_5H_{11}	H
b	CH_3	CH_3	CH_3	n-C_5H_{11}	H
c	TBDMS	CH_3	CH_3	H	H
d	TBDMS	CH_3	CH_3	n-C_5H_{11}	H
e	TBDMS	CH_3	CH_3	CH_3	CH_3

TBDMS = t-$C_4H_9(CH_3)_2Si$

Scheme 1.

Keywords: Cyclopropanes; Iodine–magnesium exchange; Ate complex.
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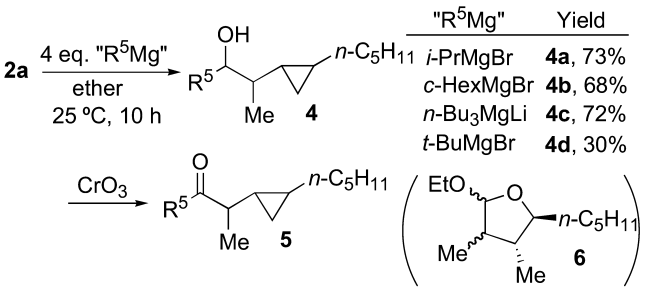
coupling in an ethereal solvent and the fact that complete conversion to product is not achieved.[4c,7] Here we report iodine–magnesium exchange of 3-iodomethyl-1-oxacyclopentane derivatives. Following intramolecular nucleophilic substitution led to the construction of cyclopropane with concomitant opening of the oxacyclopentane ring.

2. Results and discussion

The starting compounds **2a** and **2b** were readily prepared by iodoetherification of vinyl ether with allylic alcohol and *N*-iodosuccinimide and subsequent triethylborane-induced atom transfer radical cyclization (Scheme 1).[8] β-Iodomethyl-γ-lactones **3c**–**3e** were prepared by Jones oxidation of the corresponding cyclic acetals **2c**–**2e**. Radical cyclization of **1a**, **1b** and **1d**, which have R^3=*n*-C_5H_{11} and R^4=H, proceeded with exclusive *trans* selectivity in regard to the pentyl and iodomethyl groups, as is often observed in radical cyclization.[9]

Iodo acetal **2a** (0.50 mmol) was added to an ethereal solution of isopropylmagnesium bromide (2.0 mmol, 4 equiv.) at 0 °C under argon (Scheme 2). The reaction mixture was stirred for 10 h at 25 °C. Usual workup followed by silica gel column purification afforded **4a** in 73% yield. The alcohol **4a** has four stereogenic centers. To simplify the assignment of the stereochemistry, **4a** was subjected to Jones oxidation to provide ketone **5a** in 90% yield. Ketone **5a** consisted of two isomers in a ratio of 71/29. On the other hand, Jones oxidation of **2a** furnished lactone **3a** in a ratio of 70/30. These facts are informative to consider the reaction mechanism (vide infra).

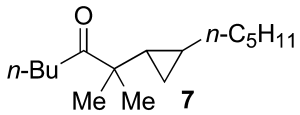
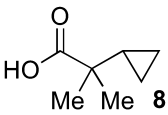
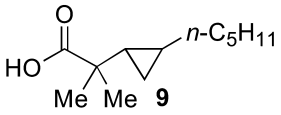
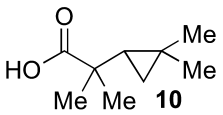


Scheme 2.

Use of three equimolar amounts of isopropyl Grignard reagent resulted in lower yield (58%). An increasing amount of the Grignard reagent (6 equiv.) did not improve the yield of **4a** (75%). It is worth noting that the reaction did not afford **4a** in THF at all, and reduced product **6** was obtained instead as a sole product.[10] *t*-Butyllithium was less effective to give **4d** in 26% yield, in addition to 38% yield of **6**.

Other magnesium reagents effected similar reactions. Reaction with cyclohexyl Grignard reagent furnished the corresponding alcohol **4b** in 68% yield. Use of primary Grignard reagents such as *n*-BuMgBr resulted in the recovery of the starting material. Instead, tributylmagnesate *n*-Bu_3MgLi, prepared from *n*-BuMgBr and 2 equiv. of *n*-BuLi,[11] was suitable to yield the butylated product **4c** (72%).[12] *t*-BuMgBr worked less efficiently, and the corresponding alcohol **4d** was obtained in 30% yield, in addition to remaining starting material (27% yield). Oxidation of **4b**–**4d** proceeded in more than 85% yield.

Table 1. Formation of cyclopropanes from iodomethyl-substituted oxacyclopentanes

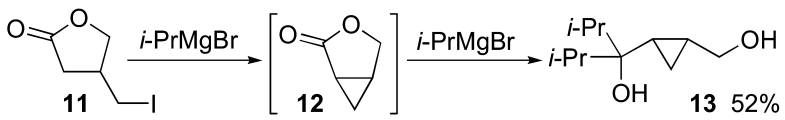
Substrate	Mg reagent	Product	Yield (%)
2b	*n*-Bu_3MgLi		73[a]
3c	*i*-PrMgBr		69
3d	*i*-PrMgBr		79
3e	*i*-PrMgBr		60

[a] Overall yield after Jones oxidation (83% for cyclopropane formation and 88% for oxidation).

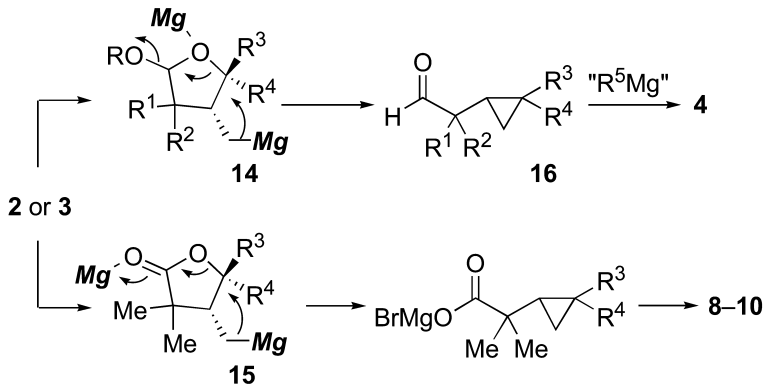
Other substrates were subjected to the transformation (Table 1). Treatment of **2b** with tributylmagnesate afforded **7** in good yield after Jones oxidation. Exclusive formation of the *trans* isomer was deduced by analysis of the coupling constants of the protons on cyclopropane ring,[13] which indicates the stereospecificity of the reaction. Lactones **3c**–**3e** also participated in the reaction to provide 2-cyclopropylisobutyric acids. However, treatment of lactone **11** with isopropyl Grignard reagent did not afford the expected product, instead giving diol **13** (Scheme 3). Formation of the enolate of **11** followed by intramolecular nucleophilic substitution gave bicyclic **12**. Addition of the Grignard reagent to **12** afforded **13**.

We assume the reaction mechanism as shown in Scheme 4. Iodine–magnesium exchange occurs upon treatment of 3-iodomethyl-1-oxacyclopentane **2** or **3** with a Grignard reagent. The resulting organomagnesium species **14** or **15** undergoes intramolecular nucleophilic substitution in ether to afford the cyclopropane skeleton. However, in THF as aforementioned, no cyclopropanes were obtained. This fact implies that the coordination of **14** or **15** to Lewis acidic magnesium species in the substitution step would play a critical role.

To confirm the stereochemistry of the cyclopropanation



Scheme 3.

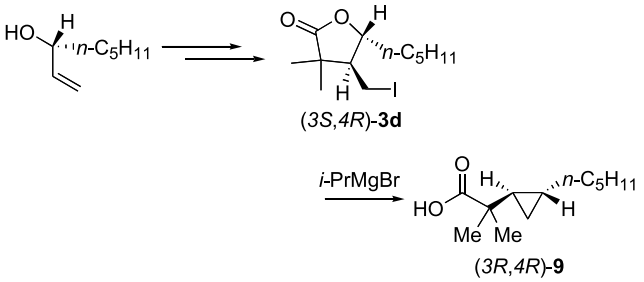


Scheme 4.

step, we prepared optically pure lactone (*3S,4R*)-**3d** from (*R*)-1-octen-3-ol (Scheme 5). Upon treatment of (*3S,4R*)-**3d** with isopropyl Grignard reagent, carboxylic acid **9** was obtained as a single enantiomer (Fig. 1). We assume that its absolute stereochemistry would be (*3R,4R*) and that the cyclopropanation would proceed with inversion of configuration.

3. Conclusion

Iodine–magnesium exchange between 3-iodomethyl-1-oxacyclopentanes and organomagnesium reagents in ether led to the formation of cyclopropane skeleton. The present reaction probably constructs 1,1,2,2-tetrasubstituted cyclopropane, starting from a proper 3-iodomethyl-1-oxacyclopentane derivative. Synthesis of 1,1,2,2,3-penta- or 1,1,2,2,3,3-hexasubstituted cyclopropane through the present method seems difficult because the synthesis requires halogen–magnesium exchange of secondary or tertiary alkyl halide at the initial stage. Although lacking functional group compatiblitity because of the use of organomagnesium reagents, this method can construct highly complex stereodefined cyclopropanes from simple starting materials, vinyl ether, allylic alcohol, and Grignard reagent, in a few steps.

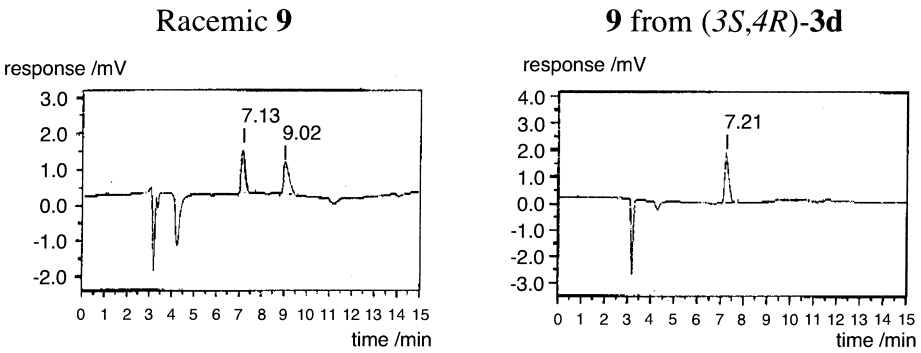


Scheme 5.

4. Experimental

4.1. General

^{1}H NMR (300 MHz) and ^{13}C NMR (75.3 MHz) spectra were taken on a Varian GEMINI 300 spectrometer in $CDCl_3$ as a solvent, and chemical shifts were given in δ value with tetramethylsilane as an internal standard IR spectra were



Retention time /min	7.13	9.02
Area	12756	14276

Figure 1. Chromatograms of racemic **9** and optically pure **9** derived from (*3S,4R*)-**3d**.

determined on a JASCO IR-810 spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University. The optical purity of **9** was established by chiral HPLC analysis (CHIRALCEL® AS-H column 4.6 mm×250 mm Daisel Chemical Industries, Hexane/2-propanol/trifluoroacetic acid=100/1/0.1 eluent, 1.0 mL/min, 25 °C, and RI detector).

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Ether was purified over slices of sodium. THF was distilled from sodium benzophenone ketyl. Dichloromethane was stored over molecular sieves 3A. (*R*)-1-Octen-3-ol was purchased from Tokyo Kasei Kogyo Co.

4.2. Preparation of iodo compounds 2 and 11

Iodo acetal **1** was prepared by treatment of an equimolar mixture of the corresponding vinyl ether and allylic alcohol with an equal amount of *N*-iodosuccinimide in dichloromethane at 0 °C for 2 h. Preparation of **1a**–**d** was efficient (more than 90% yield). However, preparation of **1e** resulted in a lower yield (15%, not optimized).

Preparation of **2a** is representative. Iodo acetal **1a** (10.2 g, 30.0 mmol) was dissolved in hexane (25 mL). The solution was flushed with argon in a toy balloon. A solution of triethylborane in hexane (1.0 M, 6.0 mL, 6.0 mmol) was added to iodo acetal. After being stirred for 2 h at ambient temperature, the reaction mixture was evaporated. Silica gel column purification (hexane/ethyl acetate=20/1) provided **2a** (9.31 g, 27.4 mmol) in 91% yield. The diastereomer ratio of **2a** was determined by ^{1}H NMR spectra to be 55/18/15/12.

Iodo compound **11** was prepared according to the literature.[8]

4.3. Synthesis of cyclopropanes 4 from cyclic acetals 2

Iodo acetal **2a** (0.170 g, 0.500 mmol) in ether (2 mL) was added to an ethereal solution of isopropylmagnesium bromide (1.0 M ether solution, 4 equiv., 2.0 mL, 2.0 mmol) at 0 °C under argon. The reaction mixture was stirred at ambient temperature for 10 h. The mixture was poured into a saturated NH_4Cl solution. The product was then extracted with ethyl acetate (20 mL×3). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/ethyl acetate=20/1) to furnish alcohol **4a** (0.077 g, 0.36 mmol) in 73% yield.

4.4. Reaction of β-iodomethyl-γ-lactones 3

Under argon, iodo lactone **3c** (0.170 g, 0.500 mmol) in ether (2 mL) was added to isopropylmagnesium bromide (1.0 M ether solution, 2 equiv., 1.0 mL, 1.0 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 10 h. The mixture was poured into 1 M HCl solution. The product was extracted with ether (10 mL×3). Sodium hydroxide (2 M, 5 mL) was added to the combined organic layer to transfer the carboxylate into the aqueous layer. After removal of the organic layer, 1 M HCl was then added to the aqueous solution until the solution became acidic. Extraction with ethyl acetate (20 mL×3) and concentration afforded colorless oil. Purification on silica gel with hexane/ethyl acetate=3/1 as an eluent yielded carboxylic acid **8** (0.044 g, 0.34 mmol) in 69% yield.

4.5. Characterization data

Spectral data for **8** was found in the literature.[14]

4.5.1. 2-Ethoxy-4-iodomethyl-3-methyl-5-pentyltetrahydrofuran (2a, diastereomer ratio is 55/18/15/12). IR (neat) 2930, 2860, 1458, 1377, 1188, 1084, 1051, 962 cm^{-1}; ^{1}H NMR ($CDCl_3$) For the most abundant isomer: δ 0.89 (t, *J*=6.6 Hz, 3H), 0.95 (d, *J*=7.2 Hz, 3H), 1.18 (t, *J*=7.2 Hz, 3H), 1.23–1.60 (m, 8H), 2.31–2.40 (m, 1H), 2.57–2.68 (m, 1H), 2.99 (t, *J*=10.5 Hz, 1H), 3.16–3.21 (m, 1H), 3.25–3.45 (m, 1H), 3.62–3.77 (m, 2H), 4.71 (s, 1H); ^{13}C NMR ($CDCl_3$) For the most abundant isomer: δ 2.58, 10.82, 14.12, 15.28, 22.68, 26.07, 31.87, 36.81, 43.60, 48.87, 62.21, 82.34, 108.33. Found: C, 46.13; H, 7.40%. Calcd for $C_{13}H_{25}IO_2$: C, 45.89; H, 7.41%.

4.5.2. 4-Iodomethyl-2-methoxy-3,3-dimethyl-5-pentyltetrahydrofuran (2b, single isomer). IR (neat) 1468, 1369, 1188, 1099, 1020, 978 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.90 (t, *J*=6.6 Hz, 3H), 0.91 (s, 3H), 1.09 (s, 3H), 1.26–1.40 (m, 5H), 1.50–1.60 (m, 2H), 1.78–1.90 (m, 1H), 2.22 (ddd, *J*=6.0, 8.4, 8.4 Hz, 1H), 3.05 (dd, *J*=8.4, 10.2 Hz, 1H), 3.20 (dd, *J*=6.0, 10.2 Hz, 1H), 3.30 (s, 3H), 3.70 (dt, *J*=2.7, 8.4 Hz, 1H), 4.31 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 1.48, 14.04, 20.18, 21.43, 22.61, 26.09, 31.75, 37.82, 47.28, 52.84, 54.28, 85.50, 111.59. Found: C, 45.88; H, 7.12%. Calcd for $C_{13}H_{25}IO$: C, 45.89; H, 7.41%.

4.5.3. 4-Iodomethyl-3,3-dimethyldihydrofuran-2(3*H*)-one (3c). IR (neat) 1757, 1342, 1196, 1115, 1097, 1013 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.10 (s, 3H), 1.30 (s, 3H), 2.66 (dddd, *J*=4.8, 7.2, 9.3, 11.1 Hz, 1H), 3.04 (dd, *J*=9.9, 11.1 Hz, 1H), 3.24 (dd, *J*=4.8, 9.9 Hz, 1H), 3.87 (dd, *J*=9.6, 9.6 Hz, 1H), 4.49 (dd, *J*=7.2, 9.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ −0.21, 18.03, 23.90, 43.16, 48.67, 71.01, 181.37. Found: C, 33.09; H, 4.39%. Calcd for $C_7H_{11}IO_2$: C, 33.09; H, 4.36%.

4.5.4. 4-Iodomethyl-3,3-dimethyl-5-pentyldihydrofuran-2(3*H*)-one (3d). IR (neat) 2932, 2860, 1771, 1466, 1389, 1223, 1148, 1117, 1007, 934 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.90 (t, *J*=6.9 Hz, 3H), 1.16 (s, 3H), 1.26–1.50 (m, 5H), 1.37 (s, 3H), 1.50–1.70 (m, 2H), 1.87–2.00 (m, 1H), 2.28 (ddd, *J*=7.2, 7.2, 9.3 Hz, 1H), 3.12 (d, *J*=7.2 Hz, 1H), 3.13 (d, *J*=7.2 Hz, 1H), 4.00 (dt, *J*=3.0, 9.3 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ −2.16, 14.08, 18.56, 22.55, 25.15, 25.42, 31.54, 34.52, 43.93, 52.94, 82.43, 180.68. Found: C, 44.57; H, 6.65%. Calcd for $C_{12}H_{21}IO_2$: C, 44.46; H, 6.53%.

4.5.5. 4-Iodomethyl-3,3,5,5-tetramethyldihydrofuran-2(3*H*)-one (3e). IR (neat) 2341, 1757, 1462, 1377, 1286, 1099, 1065, 941 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.22 (s, 3H), 1.37 (s, 3H), 1.38 (s, 3H), 1.58 (s, 3H), 2.48 (dd, *J*=7.5,

8.1 Hz, 1H), 3.13 (dd, *J*=8.1, 10.5 Hz, 1H), 3.21 (dd, *J*=7.5, 10.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ −2.78, 20.32, 22.77, 27.23, 30.28, 44.11, 56.37, 84.19, 180.17. Found: C, 38.26; H, 5.37%. Calcd for $C_9H_{15}IO_2$: C, 38.32; H, 5.36%.

4.5.6. 2-Methyl-4-(2-pentylcyclopropyl)-3-pentanone (5a, diastereomer ratio is 71/29). IR (neat) 2964, 2926, 2874, 2855, 1713, 1468, 1381, 1350, 1092, 1016 cm^{-1}; ^{1}H NMR ($CDCl_3$) For major isomer: δ 0.19–0.32 (m, 1H), 0.34–0.40 (m, 1H), 0.43–0.67 (m, 2H), 0.88 (t, *J*=6.6 Hz, 3H), 1.06 (d, *J*=6.9 Hz, 6H), 1.13 (d, *J*=6.9 Hz, 3H), 1.05–1.14 (m, 2H), 1.20–1.40 (m, 6H), 1.92 (dq, *J*=9.3, 6.9 Hz, 1H), 2.77 (qq, *J*=6.9, 6.9 Hz, 1H), for minor isomer, δ 0.19–0.32 (m, 1H), 0.34–0.40 (m, 1H), 0.43–0.67 (m, 2H), 0.86 (t, *J*=7.2 Hz, 3H), 1.07 (d, *J*=6.9 Hz, 6H), 1.09 (d, *J*=6.9 Hz, 3H), 1.05–1.14 (m, 2H), 1.20–1.40 (m, 6H), 1.95 (dq, *J*=9.3, 6.9 Hz, 1H), 2.77 (qq, *J*=6.9, 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) For major isomer: δ 12.14, 14.18, 16.68, 18.19, 18.21, 18.71, 22.11, 22.74, 29.29, 31.77, 34.08, 39.36, 49.25, 217.62. Found: C, 79.88; H, 12.76%. Calcd for $C_{14}H_{26}O$: C, 79.94; H, 12.46%.

4.5.7. 1-Cyclohexyl-2-(2-pentylcyclopropyl)-1-propanone (5b, diastereomer ratio is 72/28). IR (neat) 2928, 2855, 1709, 1450, 1373, 993 cm^{-1}; ^{1}H NMR ($CDCl_3$) For major isomer: δ 0.24–0.31 (m, 1H), 0.36–0.39 (m, 1H), 0.45–0.60 (m, 2H), 0.88 (t, *J*=6.6 Hz, 3H), 1.12 (d, *J*=6.9 Hz, 3H), 1.06–1.15 (m, 1H), 1.17–1.45 (m, 12H), 1.60–1.70 (m, 1H), 1.70–1.84 (m, 4H), 1.90 (dq, *J*=9.6, 6.9 Hz, 1H), 2.49 (m, 1H), for minor isomer, δ 0.24–0.31 (m, 1H), 0.36–0.39 (m, 1H), 0.45–0.60 (m, 2H), 0.88 (t, *J*=6.6 Hz, 3H), 1.07 (d, *J*=6.6 Hz, 3H), 1.06–1.15 (m, 1H), 1.17–1.45 (m, 12H), 1.60–1.70 (m, 1H), 1.70–1.84 (m, 4H), 1.90 (dq, *J*=9.6, 6.9 Hz, 1H), 2.49 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 12.08, 14.18, 16.64, 18.17, 22.00, 22.74, 25.73, 25.94, 28.32, 28.87, 29.30, 31.77, 33.98, 34.08, 49.34, 49.64, 216.92. Found: C, 81.25; H, 11.95%. Calcd for $C_{17}H_{30}O$: C, 81.54; H, 12.08%.

4.5.8. 2-(2-Pentylcyclopropyl)-3-heptanone (5c, diastereomer ratio is 71/29). IR (neat) 2959, 2928, 2856, 1713, 1458, 1373, 1259, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$): For major isomer δ 0.23–0.35 (m, 1H), 0.38–0.43 (m, 1H), 0.46–0.55 (m, 2H), 0.88 (t, *J*=8.1 Hz, 3H), 0.90 (t, *J*=7.5 Hz, 3H), 1.13 (d, *J*=6.9 Hz, 3H), 1.22–1.40 (m, 10H), 1.49–1.59 (m, 2H), 1.69–1.80 (m, 1H), 2.38–2.57 (m, 2H), for minor isomer, δ 0.23–0.35 (m, 1H), 0.38–0.43 (m, 1H), 0.46–0.55 (m, 2H), 0.88 (t, *J*=8.1 Hz, 3H), 0.90 (t, *J*=7.5 Hz, 3H), 1.09 (d, *J*=6.9 Hz, 3H), 1.22–1.40 (m, 10H), 1.49–1.59 (m, 2H), 1.69–1.80 (m, 1H), 2.38–2.57 (m, 2H); ^{13}C NMR ($CDCl_3$) For major isomer δ 12.23, 14.01, 14.18, 16.23, 18.38, 22.20, 22.49, 22.74, 25.80, 29.29, 31.76, 34.08, 40.87, 51.13, 214.01. HRMS (*m*/*z*) Found: 224.2149. Calcd for $C_{15}H_{28}O$: 224.2140.

4.5.9. 2,2-Dimethyl-4-(2-pentylcyclopropyl)-3-pentanone (5d, diastereomer ratio is 72/28). IR (neat) 2964, 2926, 2855, 1705, 1477, 1466, 1367, 1049, 991 cm^{-1}; ^{1}H NMR ($CDCl_3$) For major isomer: δ 0.16–0.29 (m, 2H), 0.41–0.55 (m, 1H), 0.65–0.78 (m, 1H), 0.87 (t, *J*=6.9 Hz, 3H), 1.10 (s, 9H), 1.12 (d, *J*=6.6 Hz, 3H), 1.18–1.40 (m, 8H), 2.24 (dq, *J*=9.3, 6.9 Hz, 1H), for minor isomer, δ 0.16–0.29 (m, 2H), 0.41–0.55 (m, 1H), 0.65–0.78 (m, 1H), 0.87 (t, *J*=6.9 Hz, 3H), 1.08 (d, *J*=6.9 Hz, 3H), 1.11 (s, 9H), 1.18–1.40 (m, 8H), 2.24 (dq, *J*=9.3, 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) For major isomer δ 12.20, 14.20, 18.06, 19.02, 22.76, 22.93, 26.02, 29.33, 31.80, 34.15, 44.00, 44.10, 206.09. Found: C, 80.08; H, 12.58%. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58%.

4.5.10. 2-Methyl-2-(2-pentylcyclopropyl)-3-heptanone (7). IR (neat) 2959, 2928, 2856, 1709, 1468, 1364, 1042 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.17 (ddd, *J*=5.1, 5.1, 8.7 Hz, 1H), 0.44 (ddd, *J*=5.1, 5.1, 8.7 Hz, 1H), 0.58 (ddd, *J*=5.1, 5.1, 8.7 Hz, 1H), 0.63–0.71 (m, 1H), 0.88 (t, *J*=6.9 Hz, 3H), 0.90 (s, 3H), 0.91 (t, *J*=7.5 Hz, 3H), 0.97 (s, 3H), 1.15–1.40 (m, 10H), 1.49–1.59 (m, 2H), 2.54 (t, *J*=7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 8.21, 13.96, 14.05, 14.81, 21.69, 22.47, 22.55, 22.64, 26.00, 26.45, 29.20, 31.72, 34.28, 36.95, 46.18, 215.57. Found: C, 80.32; H, 12.82%. Calcd for $C_{16}H_{30}O$: C, 80.61; H, 12.68%.

4.5.11. 2-Methyl-2-(2-pentylcyclopropyl)propionic acid (9). IR (neat) 2924, 2856, 2569, 1703, 1474, 1412, 1296, 1155, 943 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.17 (ddd, *J*=5.1, 5.1, 8.7 Hz, 1H), 0.47 (ddd, *J*=5.1, 5.1, 8.7 Hz, 1H), 0.62–0.74 (m, 1H), 0.77 (ddd, *J*=5.1, 5.1, 8.7 Hz, 1H), 0.87 (t, *J*=6.6 Hz, 3H), 1.05 (s, 3H), 1.07 (s, 3H), 1.20–1.40 (m, 8H), 11.20 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 8.23, 14.18, 14.83, 22.77, 22.91, 23.30, 27.23, 29.25, 31.76, 34.29, 41.21, 184.53. Found: C, 72.89; H, 11.03%. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18%.

4.5.12. 2-(2,2-Dimethylcyclopropyl)-2-methylpropionic acid (10). IR (neat) 2874, 2571, 1703, 1458, 1412, 1379, 1294, 1175, 1028, 941, 827 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.42 (d, *J*=8.4 Hz, 2H), 0.78 (t, *J*=8.4 Hz, 1H), 1.04 (s, 3H), 1.11 (s, 3H), 1.17 (s, 3H), 1.30 (s, 3H), 11.74 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 16.51, 16.80, 19.86, 24.79, 27.52, 29.21, 33.43, 41.33, 184.77. Found: C, 68.99; H, 10.11%. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32%.

4.5.13. 3-(2-Hydroxymethylcyclopropyl)-2,4-dimethyl-3-pentanol (13). IR (neat) 3285, 2966, 2878, 1470, 1385, 1367, 1238, 1005, 899 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.64–0.72 (m, 2H), 0.72–0.84 (m, 1H), 0.94–1.02 (m, 1H), 0.99 (d, *J*=6.9 Hz, 6H), 1.00 (d, *J*=6.9 Hz, 6H), 1.92 (qq, *J*=6.9, 6.9 Hz, 1H), 1.98 (qq, *J*=6.9, 6.9 Hz, 1H), 2.33 (bs, 2H), 3.86 (dd, *J*=5.1, 11.4 Hz, 1H), 3.95 (dd, *J*=5.1, 11.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 4.42, 17.39, 17.70, 17.87, 17.98, 18.32, 20.20, 36.12, 36.79, 61.34, 76.73. Found: C, 71.16; H, 11.96%. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90%.

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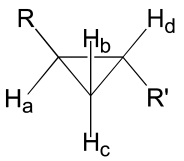
13. The stereochemistry of the cyclopropane was deduced by characteristic coupling constants of *trans*-1,2-disubstituted cyclopropane $J_{ab}=J_{bc}=J_{cd}$=ca. 5 Hz, $J_{ac}=J_{bd}$=ca. 8 Hz. For example, Taylor, R. E.; Risatti, C. A.; Engelhardt, F. C.; Schmitt, M. J. *Org. Lett.* **2003**, *5*, 1377–1379



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