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New entry to the enantioselective formation of substituted cyclohexenes bearing an all-carbon quaternary stereogenic center

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1 | INTRODUCTION

Developing new methods for the efficient synthesis of highly substituted chiral molecules is of great importance in pharmaceuticals and agrochemicals. A cyclohexane having a chiral quaternary carbon center is a common substructure in natural products with significant biological and medicinal activities such as alkaloids and sesquiterpenoids¹⁻⁵ (Figure 1). Various efforts have therefore been devoted to developing new methods to synthesize these frameworks; however, the efficient formation of cyclohexanes bearing an all-carbon quaternary stereogenic center still remains as a challenging task in the field of chiral synthesis.6-8

One representative method to efficiently access these highly functionalized cyclohexanes in chiral forms is the Diels-Alder reaction^{9,10} mediated by asymmetric Lewis acid catalysts or chiral organocatalysts. In the course of

Abstract

Enantioselective formation of cyclohexene derivatives bearing an all-carbon quaternary stereogenic center is described. The racemic cyclohexenes are readily transformed to chiral substituted cyclohexenes in good yield with excellent enantioselectivity and diastereoselectivity by a palladium-mediated deracemization. The resulting products are promising synthetic intermediates of biologically active natural products. This protocol provides us with a new entry to the concise and scalable synthesis of multifunctionalized compounds.

K E Y W O R D S

asymmetric allylic alkylation, cyclohexene, palladium-mediated deracemization, quaternary stereogenic center

our synthetic studies of natural products, we required the practical and scalable method for the preparation of cyclohexene 3 bearing a chiral quaternary carbon center, as a starting material. Our initial attempt was catalytic asymmetric Diels-Alder reaction of 2-substituted butadiene 1 and 2-substituted acrylic aldehyde 2 (Table 1). When the Diels-Alder reaction was performed by MacMillan's imidazolidinone 4,¹¹ cyclohexene 3 with 13% ee was obtained in a poor yield (entry 1). The reaction catalyzed by *tert*-butyl imidazolidinone 5^{12,13} resulted in improvement in the yield of 3, though it was proved to be almost racemic (entry 2). Efforts of Hayashi-Jørgensen's catalyst 6¹⁴⁻¹⁶ (entry 3) and CBS oxazaborolidines,^{17,18} 7 and 8 (entries 4 and 5), were totally fruitless. These results suggest that the bulky C-2 substituent of aldehyde 2 exerted a disadvantageous steric interaction during the [4 + 2] cycloaddition. Finally, we were pleased to find that the reaction using Maruoka's bis (naphthalene)



FIGURE 1 Selected examples of naturally occurring bioactive cyclohexanes bearing an all-carbon quaternary center

diamine catalyst 9^{19} brought about the asymmetric Diels-Alder reaction successfully to afford **3** in a good yield with excellent enantioselectivity (entry 6). However, the catalyst **9** was not easily available, and its starting material, 2,2'-diamino-1,1'-binaphthalene, is expensive. Therefore, we sought other methods feasible for the multigram scale synthesis.

We took an interest in deracemization of cyclic allyl esters, which had been developed by Trost et al.^{20,21} Deracemization of cyclic allyl esters of Trost et al involves differentiating the enantiotopic π -allyl metal intermediate derived from a racemic precursor²² (Scheme 1). In this process, the initial chirality of the substrate is lost, and a symmetric π -allyl palladium complex is generated, which then undergoes а stereoselective neucleophilic acyloxylation to regenerate chiral acyloyl product 11. The cyclic substrates can be adopted to the reaction; however, no example of cyclohexanes bearing a quaternary stereogenic center was reported so far. Herein, we report the deracemization of highly substituted cyclohexenes involving stereoselective quaternalization.

2 | MATERIALS AND METHODS

2.1 | General methods

Where appropriate, reactions were carried out in flamedried glassware under an argon atmosphere. Extracts were dried with MgSO₄ and concentrated by rotary evaporation below 30°C at 25 Torr unless otherwise noted. Commercially sourced reagents and solvents were used as supplied with the following exceptions. Tetrahydrofuran (THF) was purified by filtration through a column of activated alumina under an argon atmosphere. Dichloromethane (CH₂Cl₂), toluene, triethylamine, and pyridine were distilled from CaH₂. Methanol (MeOH) was distilled over Na. Column chromatography was carried out by using silica gel (particle size 100-210 µm [regular]). Optical rotations were recorded with a digital polarimeter at ambient temperature. Infrared spectra (Fourier transform infrared [FTIR]) were measured with an FTIR spectrometer. ¹H-NMR (500 or 400 MHz) and ¹³C-NMR (125 or 100 MHz) spectra were measured by using CDCl₃ as solvent, and chemical shifts are reported as δ values in ppm based on internal CHCl₃ (¹H: δ = 7.26 ppm; ¹³C: δ = 77.0 ppm). Mass spectra (MS) and high-resolution MS (HRMS) were recorded in electron ionization (EI) (dual focusing sector field) or electrospray ionization (ESI) (time of flight [TOF]) mode.

2.1.1 | General procedure for 11

To a solution of sodium hydride (60%, dispersion in paraffin liquid; 24.7 mg, 0.616 mmol) and tetrahexylammonium bromide (268 mg, 0.616 mmol) in degassed CH₂Cl₂ (6 mL) was added propionic acid (0.055 mL, 0.724 mmol) at rt. In another vessel, to a solution of (S,S)-DACH-phenyl Trost ligand (63.8 mg, 0.0925 mmol) in degassed CH₂Cl₂ (2 mL) was added allylpalladium (II) chloride dimer (11.2 mg, 0.0308 mmol) at rt, and the mixture was stirred at the same temperature for 10 minutes. The latter mixture was added to the former one, and stirring was continued for 20 minutes. To the resulting mixture was added racemic cyclohexene derivative 10 (0.308 mmol) at rt; the reaction mixture was stirred at the same temperature until disappearance of the starting material was observed by thin-layer chromatography (TLC). The mixture was concentrated in vacuo, and the residue was purified by silica gel chromatography to afford compound 11.

2.2 | Methyl (1*R*,5*R*)-1-((benzyloxy) methyl)-5-(propionyl-oxy)cyclohex-3-ene-1carboxylate (14)

According to general procedure, **14** (77.1 mg, 0.232 mmol, 82%) was obtained from **13** as a colorless oil. Compound **14** (39.9 mg, 0.120 mmol, 38%) was also transformed from **21**. $[\alpha]_D^{27}$ + 87.4 (*c* 1.00, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) δ 7.36-7.26 (m, 5H), 5.97-5.93 (m, 1H), 5.68 (d, *J* = 10.0 Hz, 1H), 5.29 (brs, 1H), 4.50 (s, 2H), 3.68 (s, 3H), 3.61 (d, *J* = 8.4 Hz, 1H), 3.44 (d, *J* = 8.4 Hz, 1H), 2.72 (d, *J* = 18.8 Hz, 1H), 2.27 (q, *J* = 8.0 Hz, 2H), 2.13-2.03 (m, 3H), 1.12 (t, *J* = 8.0 Hz, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 175.0, 173.9, 138.0, 130.3, 128.3, 127.6, 127.4, 124.2, 74.8, 73.2, 66.3, 51.8, 45.2, 32.2, 29.8, 27.6, 8.9; FTIR (neat) 2942, 2869, 1727, 1444, 1360, 1183, 1085,





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TABLE 1 (Continued)



^aNo reaction.

^bDetermined by chiral high-performance liquid chromatography (HPLC).





1006 cm⁻¹; MS (ESI) m/z 165 (100), 166, 181, 281, 355 [(M + Na)⁺]; HRMS (ESI) calcd for C₁₉H₂₄NaO₅ [(M + Na)⁺] 355.1521, found 355.1550.

2.2.1 | Methyl (1*R*,5*R*)-1-benzyl-5-(propionyloxy)cyclohex-3-ene-1-carboxylate (16)

According to general procedure, **16** (79.5 mg, 0.263 mmol, 80%) was obtained as a colorless oil. $[\alpha]_D^{25}$ + 44.7 (*c* 0.95, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 7.28-7.20 (m, 3H), 7.07 (d, *J* = 8.0 Hz, 2H), 5.96 (dt, *J* = 10.0, 3.0 Hz, 1H),

5.71 (d, J = 10.0 Hz, 1H), 5.41 (brs, 1H), 3.65 (s, 3H), 3.07 (d, J = 13.5 Hz, 1H), 2.76 (d, J = 13.5 Hz, 1H), 2.50 (brd, J = 18.0 Hz, 1H), 2.31-2.25 (m, 3H), 2.05-2.00 (m, 2H), 1.13 (t, J = 7.5 Hz, 3H); ¹³C-NMR (125 MHz, CDCl₃) δ 175.5, 173.9, 136.5, 130.6, 129.8, 128.2, 126.8, 124.0, 66.6, 51.6, 45.3, 44.6, 35.9, 31.6, 27.7, 9.0; FTIR (neat) 3033, 2944, 1737, 1449, 1358, 1205, 1075, 957, 803 cm⁻¹; MS (EI) m/z 91 (100), 137, 155, 246, 302 (M⁺); HRMS (EI) calcd for C₁₈H₂₂O₄ (M⁺) 302.1518, found 302.1521.

2.2.2 | Methyl (1*R*,5*R*)-1-(oct-7-enyl)-5-(propionyloxy)cyclo-hex-3-ene-1carboxylate (18)

According to general procedure, **18** (99.0 mg, 0.307 mmol, 99%) was obtained as a colorless oil. $[\alpha]_D^{25}$ + 83.5 (*c* 0.86, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) δ 5.97-5.92 (m, 1H), 5.80 (ddt, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.69 (brd, *J* = 10.4 Hz, 1H), 5.29 (brs, 1H), 4.98 (d, *J* = 17.2 Hz, 1H), 4.92 (d, *J* = 10.4 Hz, 1H), 3.67 (s, 3H), 2.64 (brd, *J* = 18.0 Hz, 1H), 2.28 (q, *J* = 7.6 Hz, 2H), 2.11 (dd, *J* = 14.0, 5.6 Hz, 1H), 2.05-1.99 (m, 3H), 1.90 (d, *J* = 18.0 Hz, 1H), 1.71 (td, *J* = 12.4, 4.0 Hz, 1H), 1.43 (td, *J* = 12.4, 4.0 Hz, 1H), 1.37-1.20 (m, 8H), 1.12 (t, *J* = 7.6 Hz, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 176.5, 174.1, 139.1, 130.5, 124.4, 114.2, 66.8, 51.6, 43.8, 38.4, 35.5, 33.6, 32.4, 29.6, 28.8, 28.7, 27.6, 24.1, 8.9; FTIR (neat) 2930, 2856, 1734, 1454, 1356, 1189, 1003,

905, 714 cm⁻¹; MS (EI) m/z 91, 137 (100), 207, 322 (M⁺); HRMS (EI) calcd for $C_{19}H_{30}O_4$ (M⁺) 322.2144, found 322.2148.

2.2.3 | Methyl (1*R*,5*R*)-1-methyl-5-(propionyloxy)cyclohex-3-ene-1-carboxylate (20)

According to general procedure, **20** (66.8 mg, 0.295 mmol, 97%) was obtained as a yellow oil. $[\alpha]_D^{27}$ + 48.1 (*c* 1.00, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) δ 5.91 (dt, *J* = 10.0, 4.0 Hz, 1H), 5.67 (d, *J* = 10.0 Hz, 1H), 5.34 (brs, 1H), 3.68 (s, 3H), 2.61 (d, *J* = 18.0 Hz, 1H), 2.28 (q, *J* = 7.6 Hz, 2H), 2.09 (dd, *J* = 14.0, 6.0 Hz, 1H), 1.98 (dd, *J* = 14.0, 5.6 Hz, 1H), 1.93 (d, *J* = 18.0 Hz, 1H), 1.26 (s, 3H), 1.12 (t, *J* = 7.6 Hz, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 177.1, 174.0, 129.9, 124.5, 67.1, 51.8, 40.3, 36.4, 33.7, 27.6, 24.1, 8.9; FTIR (neat) 2946, 1736, 1459, 1195, 1125, 1079, 1013 cm⁻¹; MS (EI) *m/z* 93 (100), 111, 152, 170, 226 (M⁺); HRMS (EI) calcd for C₁₂H₁₈O₄ (M⁺) 226.1205, found 226.1202.

2.2.4 | Methyl (1*S*,5*R*)-1-((benzyloxy) methyl)-5-(propionyl-oxy)cyclohex-3-ene-1carboxylate (23)

According to general procedure, **23** (98.4 mg, 0.296 mmol, 100%) was obtained as a yellow oil. $[\alpha]_D^{28} + 12.0$ (*c* 1.00, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) δ 7.35-7.26 (m, 5H), 5.86 (brd, *J* = 10.0 Hz, 1H), 5.65 (brd, *J* = 10.0 Hz, 1H), 5.40 (brs, 1H), 4.49 (s, 2H), 3.70 (s, 3H), 3.55 (s, 2H), 2.58 (d, *J* = 18.4 Hz, 1H), 2.36 (dd, *J* = 13.6, 6.0 Hz, 1H), 2.29 (q, *J* = 7.6 Hz, 2H), 2.19 (d, *J* = 18.4 Hz, 1H), 1.80 (dd, *J* = 13.6, 7.2 Hz, 1H), 1.11 (t, *J* = 7.6 Hz, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 175.0, 173.9, 138.1, 129.0, 128.3, 127.6, 127.3, 125.5, 75.1, 73.1, 67.1, 52.1, 46.7, 32.6, 29.7, 27.7, 8.9; FTIR (neat) 3036, 2944, 2869, 1729, 1447, 1359, 1181, 1088, 1009, 736, 695 cm⁻¹; MS (ESI) *m*/*z* 165 (100), 166, 208, 355 [(M + Na)⁺]; HRMS (ESI) calcd for C₁₉H₂₄NaO₅ [(M + Na)⁺] 355.1521, found 355.1475.

2.2.5 | Methyl (1*R*,5*R*)-1-((benzyloxy) methyl)-5-(phenoxy-carbonyl)cyclohex-3ene-1-carboxylate (24)

According to general procedure, **24** (99.5 mg, 0.262 mmol, 87%) was obtained as a colorless oil. $[\alpha]_D^{28}$ + 161.8 (*c* 1.26, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 8.01 (d, *J* = 8.5 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.35-7.32 (m, 2H), 7.30-7.26 (m, 3H), 6.05-6.01

(m, 1H), 5.84-5.80 (m, 1H), 5.53-5.50 (m, 1H), 4.51 (s, 2H), 3.64 (d, J = 9.0 Hz, 1H), 3.53 (s, 3H), 3.47 (d, J = 9.0 Hz, 1H), 2.81 (brd, J = 19.0 Hz, 1H), 2.30 (dd, J = 14.5, 5.0 Hz, 1H), 2.19 (dd, J = 14.5, 5.0 Hz, 1H), 2.13 (brd, J = 19.0 Hz, 1H); ¹³C-NMR (125 MHz, CDCl₃) δ 174.9, 166.0, 137.9, 132.9, 130.8, 130.3, 129.6, 128.3, 128.2, 127.6, 127.4, 124.0, 75.2, 73.2, 67.1, 51.9, 45.3, 32.3, 30.0; FTIR (neat) 3033, 2950, 1717, 1602, 1452, 1274, 1207, 1111, 1025 cm⁻¹; MS (ESI) m/z 270, 281, 403 [(M + Na)⁺]; HRMS (ESI) calcd for C₂₃H₂₄NaO₅ [(M + Na)⁺] 403.1521, found 403.1472.

2.2.6 | Methyl (1*R*,5*R*)-1-((benzyloxy) methyl)-5-((pyridin-2-yloxy)carbonyl) cyclohex-3-ene-1-carboxylate (25)

According to general procedure, 25 (67.0 mg, 0.176 mmol, 59%) was obtained as a yellow oil. $[\alpha]_{D}^{28} + 105.2$ (*c* 1.32, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 8.76 (brd, J = 5.0Hz, 1H), 8.07 (d, J = 7.5 Hz, 1H), 7.82 (t, J = 7.5 Hz, 1H), 7.45 (dd, J = 7.5, 4.5 Hz, 1H), 7.36-7.26 (m, 5H), 6.01 (dt, J = 10.0, 4.0 Hz, 1H), 5.86-5.82 (m, 1H), 5.62-5.59 (m, 1H), 4.52 (s, 2H), 3.64 (d, J = 8.5 Hz, 1H), 3.58 (s, 3H), 3.51 (d, J = 8.5 Hz, 1H), 2.75 (brd, J = 18.5 Hz, 1H), 2.31 (dd, *J* = 14.0, 5.5 Hz, 1H), 2.28 (dd, *J* = 14.0, 5.5 Hz, 1H), 2.15 (brd, J = 18.5 Hz, 1H); ¹³C-NMR (125 MHz, CDCl₃) δ 174.9, 164.4, 149.9, 148.1, 137.9, 136.8, 130.8, 128.3, 127.5, 127.4, 126.7, 125.1, 123.9, 74.5, 73.2, 68.2, 52.0, 45.5, 32.0, 29.9; FTIR (neat) 3033, 2949, 1739, 1582, 1438, 1336, 1305, 1244, 1133 cm⁻¹; MS (ESI) m/z 281, 404 $[(M + Na)^+]$; HRMS (ESI) calcd for C₂₂H₂₃NaO₅ $[(M + Na)^+]$ Na)⁺] 404.1474, found 404.1431.

2.2.7 | Methyl (1*R*,5*R*)-5-(acryloyloxy)-1-((benzyloxy)methyl)-cyclohex-3-ene-1carboxylate (26)

According to general procedure, **26** (48.2 mg, 0.146 mmol, 49%) was obtained as a colorless oil. $[\alpha]_D^{28}$ + 116.6 (*c* 0.97, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 7.36-7.26 (m, 5H), 6.39 (dd, *J* = 17.0, 1.5 Hz, 1H), 6.06 (dd, *J* = 17.0, 10.0 Hz, 1H), 6.00-5.97 (m, 1H), 5.81 (dd, *J* = 10.0, 1.5 Hz, 1H), 5.73-5.70 (m, 1H), 5.37-5.34 (m, 1H), 4.50 (s, 2H), 3.65 (s, 3H), 3.61 (d, *J* = 8.5 Hz, 1H), 3.45 (d, *J* = 8.5 Hz, 1H), 2.75 (brd, *J* = 18.5 Hz, 1H), 2.18-2.07 (m, 3H); ¹³C-NMR (125 MHz, CDCl₃) δ 174.8, 165.6, 137.9, 130.8, 130.7, 128.5, 128.3, 127.6, 127.4, 123.9, 74.9, 73.2, 66.7, 52.0, 45.3, 32.2, 30.0; FTIR (neat) 3033, 2949, 1713, 1633, 1452, 1402, 1265, 1181, 1091 cm⁻¹; MS (ESI) *m/z* 270, 281, 286, 353 [(M + Na)⁺]; HRMS (ESI) calcd for C₁₉H₂₂NaO₅ [(M + Na)⁺] 353.1365, found 353.1330.

TABLE 2 Palladium-mediated deracemization of cyclohexenes bearing quaternary stereogenic center

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TABLE 2 (Continued)



^aOne enantiomer of racemic compounds is shown.

^bConversion yield based on the recovered starting material.

^cDetermined by ¹H-NMR spectra.

^dDetermined by chiral high-performance liquid chromatography (HPLC).

2.2.8 | Methyl (1*R*,5*R*)-1-((benzyloxy) methyl)-5-(but-2-ynoyloxy)cyclohex-3-ene-1-carboxylate (27)

According to general procedure, **27** (33.4 mg, 0.0975 mmol, 33%) was obtained as a yellow oil. $[\alpha]_D^{27}$ + 157.2 (*c* 1.10, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 7.35-7.26 (m, 5H), 5.99 (dt, *J* = 10.0, 3.0 Hz, 1H), 5.69 (brd, *J* = 10.0 Hz, 1H), 5.34-5.31 (m, 1H), 4.50 (s, 2H), 3.71 (s, 3H), 3.59 (d, *J* = 8.5 Hz, 1H), 3.44 (d, *J* = 8.5 Hz, 1H), 2.75 (brd, *J* = 18.5 Hz, 1H), 2.17-2.06 (m, 3H), 1.96 (s, 3H); ¹³C-NMR (125 MHz, CDCl₃) δ 174.6, 153.2, 137.9, 131.4, 128.3, 127.6, 127.4, 123.2, 85.4, 74.7, 73.2, 72.5, 68.2, 52.1, 45.2, 32.1, 30.0, 3.7; FTIR (neat) 3033, 2950, 2861, 2239, 1699, 1450, 1362, 1330, 1240, 1059 cm⁻¹; MS (ESI) *m*/*z* 281 (100), 365 [(M + Na)⁺]; HRMS (ESI) calcd for C₂₀H₂₂NaO₅ [(M + Na)⁺] 365.1365, found 365.1335.

3 | RESULTS AND DISCUSSION

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We examined the asymmetric allylic acyloxylation of racemic quaternalized (benzyloxymetyl)cyclohexene **13**, readily prepared from commercially available methyl 3-cyclohexene-1-carboxylate in six steps (Data S1), with propionic acid using 10 mol% of allyl palladium (II) chloride dimer and 30 mol% of (*S*,*S*)-DACH-phenyl ligand **12**, which was derived from (1*S*,2*S*)-1,2-cyclohexanediamine and 2-diphenylphosphino-benzoic acid according to Trost's report¹⁹ (Table 2). In this particular case, propionyloxy product **14** was generated in a good yield and 97% ee along with excellent diastereomeric ratio (entry 1). Encouraged by this result, various substrates were next examined. The reactions of benzyl-substituted substrate **15** and 7-octenyl-substituted substrate **18** in

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80% yield (94% conversion) with 95% ee, in 99% yield with 93% ee, respectively (entries 2 and 3). On the other hand, the reaction of methyl-substituted substrate 19 exhibited the moderate enantioselectivity, although the yield and diastereoselectivity were both rather high (entry 4). Notably, the reaction of the substrates bearing a bulky group provided the products in high enantioselectivity. Compared with methyl carbonate 13, acetate 21 was found to be a poor substrate with regard to reaction rate, although the reaction proceeded with high enantioselectivity and diastereoselectivity (entry 5). Interestingly. the reaction of benzyloxymethylsubstituted substrate 22, a diastereomer of 13, afforded compound 23 in excellent yield and high diastereoselectivity; however, the enantioselectivity was merely 36% ee. In case of compound 22, the carbonate and ester are in anticonfiguration. To our knowledge, deracemization of such cyclic allyl esters of anticonfiguration has not been reported previously. The stereochemical outcome of the reaction of 22 indicates that the acyloxylation took place with high diastereoselectivity via the π -allyl palladium complex where the palladium moiety was syn to the ester. Although the precise reason for the resulting poor enantioselectivity is not clear, the ester possibly interacts with the palladium metal leading to the conformational change of the π -allyl palladium complex, which may be responsible for the low enantioselectivity observed.

To probe the generality of the asymmetric allylic acyloxylation, we next turned our attention to the reaction using various acids (Table 3). When benzoic acid was subjected to the reaction of **13** in place of propionic acid, compound **24** was generated in good yield with 80% ee (entry 1). The use of 2-pyridinecarboxylic acid led to the small decline of the yield and enantioselectivity of **25**. On the other hand, the reaction of acrylic acid resulted in excellent enantioselectivity and acceptable conversion yield of **26**. In addition, tetrolic acid was also feasible to afford **27** in moderate yield with high enantioselectivity.

The mechanism of the reaction was assumed to be the same as that proposed by Trost et al from their seminal studies. The diastereomeric ratios were determined by comparison of the nuclear magnetic resonance (NMR) spectral data of the corresponding secondary alcohols. The configurations of all products were determined by modified Mosher's method after hydrolysis and conversion of the secondary alcohols to the corresponding MTPA esters. The enantiomeric ratios were determined by chiral high-performance liquid chromatography (HPLC) analysis of the benzoylated products after hydrolysis and benzoylation.

TABLE 3 Palladium-mediated deracemization of 13 with some acids



^aConversion yield based on the recovered starting material. ^bDetermined by ¹H-NMR spectra.

^cDetermined by chiral high-performance liquid chromatography (HPLC).

4 | CONCLUSION

In summary, we have successfully synthesized the substituted cyclohexenes bearing an all-carbon quaternary stereogenic center with good to excellent enantioselectivity and diastereoselectivity by deracemization of racemic cyclic allyl esters, which are readily prepared from commercially available methyl 3cyclohexene-1-carboxylate in five steps. The present method is scalable and highly practical in terms of yield, enantioselectivity, and diastereoselectivity. Further synthetic application for biologically active compounds is undertaken in our laboratory.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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