Synthesis of disubstituted homodiamantanes by acylative ring expansion using benzoyl trifluoromethanesulfonate

Takao Okazaki\textsuperscript{a,}\textsuperscript{*}, Shusaku Mandai\textsuperscript{a}, Toshikazu Kitagawa\textsuperscript{b}, Ken’ichi Takeuchi\textsuperscript{c}

\textsuperscript{a}Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Nishikyo-ku, Kyoto 615-8510, Japan
\textsuperscript{b}Institute for Chemical Research, Kyoto University, Uji, Kyoto 611-0011, Japan
\textsuperscript{c}Takuma National College of Technology, Takuma-cho, Kagawa 769-1192, Japan

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Abstract

Diamantane is a hydrocarbon whose carbon framework is a part of diamond lattices. Acylative ring expansion of 1- and 4-diamantanecarbaldehyde using benzoyl trifluoromethanesulfonate and trifluoromethanesulfonic acid yielded 10-hydroxyhomodiamant-9-yl benzoate and 7-hydroxyhomodiamant-8-yl benzoate, whose skeletal structures are same as pentacyclo[8.3.1.1^{4,13}.0^{2,7}.0^{6,12}]tetradecane.

Keywords: Acylative ring expansion; Cage compound; Super acid

1. Introduction

Diamond lattices are built up by fusing of the carbon framework of adamantane (1: tricyclo[3.3.1.1^{3,7}]decane) [1–9]. Fusing two molecules of adamantane forms diamantane (2: pentacyclo[7.3.1.1^{4,12}.0^{2,7}.0^{6,13}]tetradecane). A hydrocarbon with additional CH\textsubscript{2} into adamantane is called homoadamantane (3: tricyclo[4.3.1.1^{3,8}]undecane). In principle, ring enlargement of diamantane can derive two isomers, homodiamantane (4: pentacyclo[8.3.1.1^{4,13}.0^{2,7}.0^{6,12}]tetradecane) and isohomodiamantane (5: pentacyclo[8.3.1.1^{4,13}.0^{3,8}.0^{6,12}]tetradecane). The preparation and functionalization of elegant structures of these diamondoid hydrocarbons have fascinated chemists [1–6]. Recently the interest in diamondoid structures has been renewed by application in material science [10,11], polymer science [12–15], and medicinal chemistry [16].

Among the diamondoid hydrocarbons, the chemistry of adamantane (1), diamantane (2), and homoadamantane (3) has been extensively developed. However reports of the synthesis of homodiamantane derivatives have been limited [17–19]. Reaction of 1-diamantaneacetaldehyde with benzoyl trifluoromethanesulfonate [20,21], which is known as a strong acylative reagent, was reported to afford 3-hydroxyhomodiamant-4-yl benzoate via carbocation intermediates. This product has been converted into a variety of disubstituted homodiamantane derivatives. In the case that the acylative ring expansion is applied to diamantane derivatives, disubstituted homodiamantane/isohomodiamantane derivatives are expected to be produced. We now report the synthetic results of homodiamantane derivatives with two functional groups by application of acylative ring expansion using benzoyl trifluoromethanesulfonate (Scheme 1).

2. Experimental section

Melting points are uncorrected. NMR spectra were recorded on 400 and 270 MHz instruments. IR spectra were obtained by using an FT-IR spectrometer. Elemental analyses were performed by the Microanalytical Center, Kyoto University, Kyoto. Anhydrous solvents were prepared by standard procedures. A mixture of 1-diamantane-carboxylic acid (6a) and 4-diamantane-carboxylic acid (6b) was prepared according to literature procedures [17].
Other commercially available reagents were of reagent-grade quality and used as received.

2.1. Reduction of a mixture of 1-diamantancarboxylic acid (6a) and 4-diamantancarboxylic acid (6b)

A mixture of 6a [17,18,22,23] and 6b [17,18,23] (1.89 g, 8.13 mmol) in dry THF was dropwise added to a suspension of LiAlH4 (566 mg, 14.9 mmol) in dry THF and the mixture was stirred for 30 min and refluxed for 4.5 h. The solution was cooled to room temperature, and the mixture was stirred for 30 min and refluxed for 4.5 h. The solution was cooled to room temperature, and the reaction was quenched by addition of water. The organic layer was washed with 10% NaOH and water and dried (MgSO4). The resulting mixture was filtered. Removal of the solvents gave colorless crystals. Purification by chromatography on SiO2 using hexane–ether (9:1) and ethanol-water (1:1) gave 6a as colorless crystals (7.19 g, 90%) as colorless oil (204 mg, 2%) using hexane–ether (2:1).

7a: IR (KBr) 3478, 2909, 1714, 1274, 711 cm\(^{-1}\); \(^1\)H NMR (270 MHz, CDCl\(_3\)) \(\delta\) 1.40–1.82 (m, 17H), 1.92 (m, 1H), 2.01 (br, \(J = 13.0\) Hz, 2H), 3.60 (s, 2H), 3.62 (s, 2H), 3.94 (t, \(J = 7.8\) Hz, 1H). Anal. Calcd for C\(_{23}\)H\(_{26}\)O\(_3\); H, 7.74; C, 78.07; Found, H, 7.77; C, 78.07.

7b: mp 192.4–193.5 °C; IR (KBr) 3210, 2876, 1704, 1292, 709 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.26 (brs, 1H), 1.47 (t, \(J = 2.9\) Hz, 6H), 1.68 (brs, 3H), 1.73 (t, \(J = 2.9\) Hz, 6H), 1.77–1.85 (m, 4H), 3.25 (s, 2H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 25.7 (CH), 32.5 (C), 37.2 (3CH), 37.5 (3CH), 37.8 (CH), 39.1 (3CH\(_2\)), 39.8 (3CH\(_2\)), 73.3 (CH\(_2\)). Anal. Calcd for C\(_{16}\)H\(_{12}\)O; H, 10.16; C, 82.52; Found, H, 10.10; C, 82.26.

2.2. 7-Hydroxyhomodiamant-8-yl benzoate (9a) and 10-hydroxyhomodiamant-9-yl benzoate (9b)

9a and 9b were prepared by a general procedure of acylative ring expansion described in the literature [20]. A solution of a mixture of 7a and 7b [24,25] (8:2) (8.02 g, 36.7 mmol) in dry CH\(_2\)Cl\(_2\) (50 mL) was added to a stirred suspension of pyridinium chlorochromate (11.9 g, 55.1 mmol) cooled by water bath under nitrogen atmosphere. The mixture was stirred for 13 h at room temperature and passed through florisil using dry ether. Careful evaporation of the solvent gave a mixture of 1-diamantancarbaldehyde (8a) [18] and 4-diamantancarbaldehyde (8b) [18] as colorless crystals (7.19 g, 90%), which were used for further experiments without purification, since they are oxidized easily to carboxylic acids by air.

8a: \(^1\)H NMR (270 MHz, CDCl\(_3\)) \(\delta\) 1.50–2.00 (m, 17H), 2.04 (brs, 2H), 9.36 (s, 1H).

8b: \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.69 (d, \(J = 3.4\) Hz, 6H), 1.72 (brs, 3H), 1.75 (t, \(J = 3.0\) Hz, 6H), 1.83 (m, 1H), 1.90 (brs, 3H), 9.40 (s, 1H).

A solution of 8a and 8b (7.19 g) in dry CCl\(_4\) (12.4 mL) was dropwise added to a solution of PhCOOSO\(_2\)CF\(_3\) [21] (7.30 mL, 14.4 g, 82.6 mmol) in dry CCl\(_4\) (12.4 mL) cooled by ice-water bath under nitrogen atmosphere. After stirring for 15 min, CF\(_3\)SO\(_2\)H (7.31 mL, 14.4 g, 82.6 mmol) was dropwise added. The mixture was stirred for 10 min, and then water (40 mL) was dropwise added. The resulting mixture was diluted with ether. The organic layer was washed with 5% NaHCO\(_3\) and 10% NaCl and dried (MgSO\(_4\)). The solvent was removed by evaporation to give a pale yellow oil, whose purification by SiO\(_2\) column chromatography afforded 9a as colorless crystals (6.06 g, 54%) using hexane–ether (9:1) and 9b as colorless oil (204 mg, 2%) using hexane–ether (7:3).

9a: mp 125.0–126.0 °C [from benzene–hexane (2:8)]; IR (KBr) 3484, 2897, 1704, 1292, 709 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.44–1.61 (m, 4H), 1.67–1.79 (m, 6H), 1.86–2.01 (m, 3H), 2.04 (m, 2H), 2.23 (brs, 1H), 2.29 (brs, 1H), 2.38 (brd, \(J = 11.7\) Hz, 1H), 2.47 (m, 1H), 2.52 (brd, \(J = 12.7\) Hz, 1H), 5.23 (dd, \(J = 10.3, 3.4\) Hz, 1H), 7.44 (dd, \(J = 7.3\) and 7.3 Hz, 2H), 7.56 (t, \(J = 7.3\) Hz, 1H), 8.04 (d, \(J = 7.3\) Hz, 2H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 25.8 (CH), 27.7 (CH), 34.1 (CH\(_2\)), 34.2 (CH\(_2\)), 36.9 (CH), 37.9 (CH\(_2\)), 38.3 (CH\(_2\)), 39.10 (CH), 39.13 (CH), 39.4 (CH), 39.5 (CH\(_2\)), 40.8 (CH\(_2\)), 41.7 (CH), 76.6 (C), 82.6 (CH), 128.3 (2CH), 129.5 (2CH), 130.6 (C), 132.9 (CH), 166.0 (C). Analysis calculated for C\(_{22}\)H\(_{26}\)O\(_3\): H, 7.74; C, 78.07; found, H, 7.77; C, 77.79.

9b: IR (KBr) 3478, 2909, 1714, 1274, 711 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.68–1.89 (m, 13H), 1.95 (brs, 3H), 2.01 (dd, \(J = 13.6, 4.8\) Hz, 1H), 2.37 (brs, 1H), 2.45 (brd, \(J = 13.6\) Hz, 1H), 2.54 (m, 1H), 5.13 (m, 1H), 7.45 (dd, \(J = 7.8\) and 7.8 Hz, 1H), 7.57 (t, \(J = 7.5\) Hz, 1H), 8.06 (d, \(J = 7.5\) Hz, 2H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 26.7 (CH), 36.4 (CH), 37.2 (CH), 37.7 (CH), 37.9 (CH\(_2\)), 38.3 (CH\(_2\)), 38.8 (CH), 39.8 (CH), 40.2 (CH\(_2\)), 40.3 (CH\(_2\)), 40.5 (CH\(_2\)), 43.0 (CH), 43.8 (CH\(_2\)), 72.2 (C), 82.0 (CH), 128.3 (2CH), 129.5 (2CH), 130.4 (C), 132.9 (CH), 166.3 (C).
2.3. Homodiamantane-7,8-diol (10a)

9a (1.26 g, 3.73 mmol) was added to a stirred solution of KOH (1.04 g, 18.5 mmol) in 90% MeOH (70 mL). The solution was refluxed for 4 h. The mixture was poured into water and extracted with CHCl₃. The organic layer was washed with 10% NaCl and dried (MgSO₄). The solvent was evaporated, and recrystallization of the residue from toluene–hexane gave 10a as colorless crystals (714 mg, 82%); mp 210.0–210.8 °C; IR (KBr) 3362, 2902, 1038, 991 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.48–1.64 (m, 7H), 1.74 (brs, 3H), 1.83–1.92 (m, 2H), 1.93–2.04 (m, 4H), 2.28 (brs, J = 12.7 Hz, 1H), 2.37 (m, 2H), 2.61 (s, 1H), 2.72 (d, J = 3.9 Hz, 1H), 3.71 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 25.9 (CH), 27.7 (CH), 34.3 (CH₂), 36.7 (CH), 37.2 (CH), 37.4 (CH), 38.6 (CH), 39.56 (CH₂), 39.60 (CH), 42.3 (CH₂), 42.7 (CH), 77.5 (C), 78.6 (CH). Analysis calculated for C₁₅H₂₂O₂: H, 9.46; C, 76.88; found: H, 9.46; C, 76.69.

2.4. Homodiamantane-9,10-diol (10b)

9b (4.87 g, 14.4 mmol) was added to a stirred solution of KOH (2.42 g, 4.31 mmol) in 90% MeOH (100 mL). The mixture was refluxed for 4 h. The mixture was poured into water and extracted with CHCl₃. The organic layer was washed with 10% NaCl and dried (MgSO₄). The solvent was evaporated, and recrystallization of the residue from benzene gave 10b as pale yellow crystals (2.79 g, 83%); colorless crystals; mp 178.2–188.4 °C [from benzene–hexane (1:2)]; IR (KBr) 3342, 2869, 1445, 1041, 1023 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.19–1.29 (m, 1H), 1.57 (m, 1H), 1.63–1.94 (m, 15H), 1.97 (s, 1H), 2.29 (d, J = 13.7 Hz, 1H), 2.35–2.44 (m, 2H), 3.69 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 26.5 (CH), 26.7 (CH), 34.3 (CH₂), 36.7 (CH), 37.2 (CH), 37.4 (CH), 38.6 (CH), 39.2 (CH₂), 40.4 (CH₂), 40.9 (CH₂), 42.2 (CH), 42.5 (CH and CH₂), 76.6 (CH). Analysis calculated for C₁₅H₂₀O: H, 9.16; C, 76.88; found: H, 9.56; C, 70.03.

2.5. Pinacol rearrangement of homodiamantane-9,10-diol (10b)

A solution of 10b (432 mg, 1.84 mmol) and p-toluenesulfonyl chloride (349 mg, 1.83 mmol) in pyridine (3.7 mL) was stirred at room temperature for 16 d. The mixture was poured into water and extracted with ether. The combined organic layer was washed with water and 5% NaHCO₃ and dried over MgSO₄. Removal of the solvent gave colorless crystals, whose purification by chromatography on SiO₂ gave homodiamantane-9-one (11b) [18,19] as colorless crystals (166 mg, 42%) using hexane–ether (8:2) and 10b as colorless crystals (220 mg) using ether.

11b: mp 180.8–181.5 °C (from hexane); IR (KBr) 2878, 1701, 1021 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.64 (brs, 1H), 1.72–1.94 (m, 16H), 2.59 (d, J = 4.4 Hz, 2H), 2.64 (t, J = 6.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 26.5 (CH), 32.6 (2CH₂), 35.7 (CH), 36.8 (2CH), 38.8 (CH₂), 39.0 (CH), 39.4 (2CH), 40.4 (2CH₂), 47.4 (CH), 47.6 (CH₂), 217.4 (C). Analysis calculated for C₁₅H₂₀O: H, 9.32; C, 83.29; found: H, 9.57; C, 83.24.

2.6. Homodiamantan-9-ol (12)

Reduction of homodiamantan-9-one (11b) (166 mg, 0.77 mmol) with LiAlH₄ (18 mg, 0.47 mmol) in dry ether yielded colorless crystals. Purification by recrystallization from hexane gave 12 as colorless crystals in 66% yield; mp 131.2–131.8 °C; IR (KBr) 3274, 2903, 1023 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.39 (s, 3H), 1.46–1.57 (m, 3H), 1.65–2.01 (m, 16H), 2.44 (m, 1H), 3.96 (m, 1H); ¹³C NMR (67.8 MHz, CDCl₃) δ 27.0 (CH), 30.2 (CH₂), 36.65 (CH₂), 36.74 (CH), 37.2 (CH), 37.4 (CH), 38.6 (CH), 38.8 (CH), 39.2 (CH₂), 40.4 (CH₂), 40.9 (CH₂), 42.2 (CH), 42.5 (CH and CH₂), 76.6 (CH). Analysis calculated for C₁₅H₂₂O: H, 10.16; C, 82.52; found: H, 10.43; C, 87.86.

3. Results and discussion

Synthetic scheme is summarized in Fig. 1. A mixture of 1- and 4-diamantanecarboxylic acids (6a and 6b) was prepared according to the literature procedure [17]. Reduction of the carboxylic acid by LiAlH₄ afforded a mixture of 1-diamantanemethanol (7a) [17,18] and 4-diamantanemethanol (7b), of which careful recrystallization from benzene gave pure 7b, although recrystallization of a mixture containing relatively abundant 7a gave colorless crystals containing both the alcohols.

Oxidation of a mixture of alcohols 7a and 7b (8:2) with pyridinium chlorochromate produced corresponding carbaldehydes 8a [18] and 8b [18], whose ring expansion using benzyol trifluoromethanesulfonate with trifluoromethanesulfonic acid gave hydroxyhomodiamantyl benzoates 9a and 9b. Chromatographic separation of the product mixture afforded a mixture of unchanged carbaldehydes 8a and 8b and carboxylic acids 6a and 6b in 25% yield in addition to both benzoates 9a (54%) and 9b (2%), respectively. Presumably, the carboxylic acids were formed by air oxidation during aqueous workup and/or chromatographic purification. Significantly larger amount of starting material was recovered than in acylative ring expansion of 1-adamantanecarbaldehyde, which suggests that diamantane is more robust than adamantane to ring expansion.

1-Diamantanecarbaldehyde (8a) has possibility of the formation of two isomers (9a and 9c) by acylative ring expansion shown in Fig. 2 [20]. The reaction with benzyol trifluoromethanesulfonate and trifluoromethanesulfonic acid would produce diamantylmethyl cation 13, and rearrangement by path a would yield carbocation 14a, which is expected to afford 9a by addition of water. The other possible product, 9c, has the same carbon skeleton as 5 and can be formed through path b. Compounds with the structure of isohomodiamantane 5 have never been
synthesized. This hydrocarbon 5 and its derivatives remain challenging compounds in synthetic chemistry. In the present work, the former isomer (9a) was obtained selectively in experiments. This selectivity suggests that carbocationic intermediate 14a is much more stable than intermediate 14c.

Base-catalyzed hydrolysis converted 9a and 9b into 10a and 10b, quantitatively (Fig. 3). 10a and 10b were isolated as pure forms in 82% and 83% yields by recrystallization. Pinacol rearrangement of 10b in pyridine containing p-toluenesulfonyl chloride at room temperature for 16 d afforded a mixture of the starting material (10b) and ketone 11b, which could be separated by chromatography on SiO2 to afford pure 11b as colorless crystals in 42% yield. Reduction of 11b gave the corresponding alcohol (12) in a good yield.
The other diol (10a) was reacted under similar conditions, but polymeric products were yielded, no evidence of the formation of 11a being obtained by NMR analysis.

4. Summary

In summary, acylative ring expansion of 1- and 4-homodiamantanecarbaldehydes (8a and 8b) using benzoyl trifluoromethanesulfonate with trifluoromethanesulfonic acid resulted in the formation of the disubstituted homodiamantanes (9a and 9b). The pinacol rearrangement of 10b produced ketone 11b. Ketone 11a and benzoate 9c with isohomodiamantane structure 5 were not formed either by the acylative ring expansion of 8a or by the pinacol rearrangement of 10a.

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