Synthesis of Disubstituted Homodiamantanes by Acylative Ring Expansion Using Benzoyl Trifluoromethanesulfonate

Takao Okazaki, Shusaku Mandai, Toshikazu Kitagawa, and Ken'ichi Takeuchi

Abstract

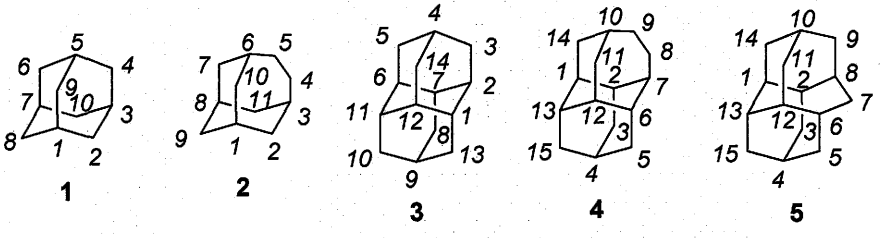
Diamantane is a hydrocarbon whose carbon framework is a part of diamond lattices. Acylative ring expansion of 1- and 4-diamanatanecarbaldehydes using benzoyl trifluoromethanesulfonate and trifluoromethanesulfonic acid yielded 10-hydroxyhomodiamant-9-yl benzoate and 7-hydroxy-homodiamant-8-yl benzoate,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

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 (**3**: pentacyclo[7.3.1.1^{4,12}.0^{2,7}.0^{6,11}]tetradecane). A hydrocarbon with additional CH_2 into adamantane is called homoadamantane (**2**: 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^{2,8}.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**), homoadamantane (**2**), and diamantane (**3**) has been extensively developed. However reports of the synthesis of homodiamantane derivatives have been limited.[17-19] Reaction of 1-adamantanecarbaldehyde with benzoyl trifluoromethanesulfonate,[20,21] which is known as a strong acylative reagent, was reported to afford 3-hydroxyhomoadamant-4-yl benzoate via carbocation intermediates. This product has been converted into a variety of disubstituted homoadamantane 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. Structures of diamondoid hydrocarbons.

Results and discussion

Synthetic scheme is summarized in Figure 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 $LiAlH_4$ 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.

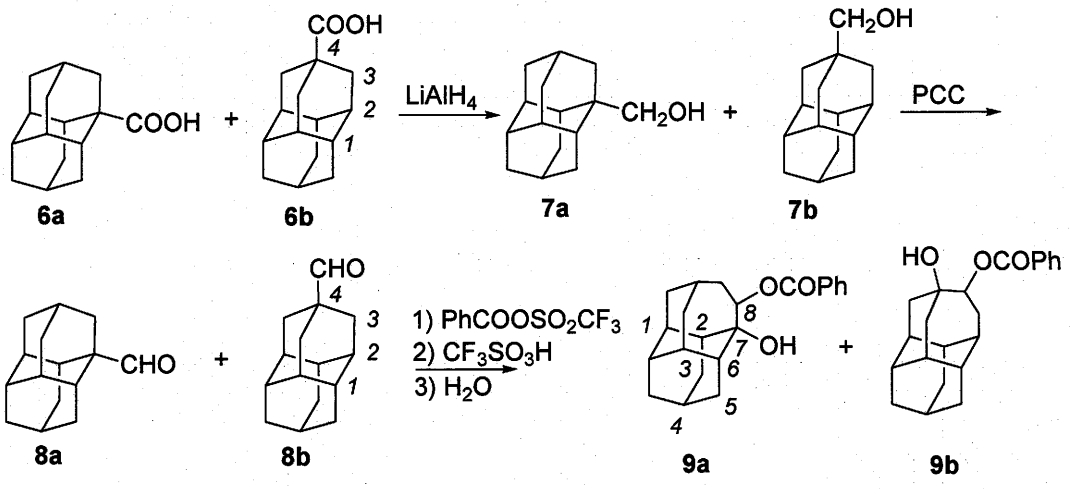


Figure 1. Synthetic scheme for the preparation of homodiamantane derivatives using acylative ring expansion.

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 benzoyl 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%). Presumably, the carboxylic acids were formed by air oxidation during aqueous work-up 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 Figure 2.[20] The reaction with benzoyl 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**.

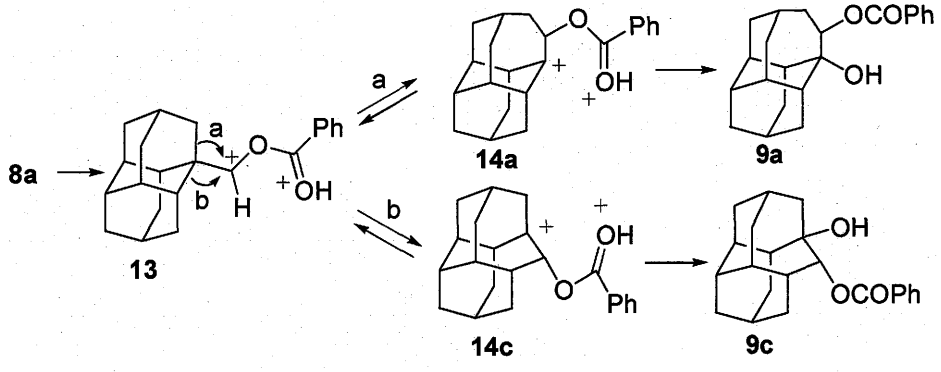


Figure 2. Possible reaction mechanism of the acylative ring expansion of 1-diamantanecarbaldehyde **8a**.

Base-catalyzed hydrolysis converted **9a** and **9b** into **10a** and **10b**, quantitatively (Figure 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 days afforded a mixture of the starting material (**10b**) and ketone **11b**, which could be separated by chromatography on SiO_2 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.

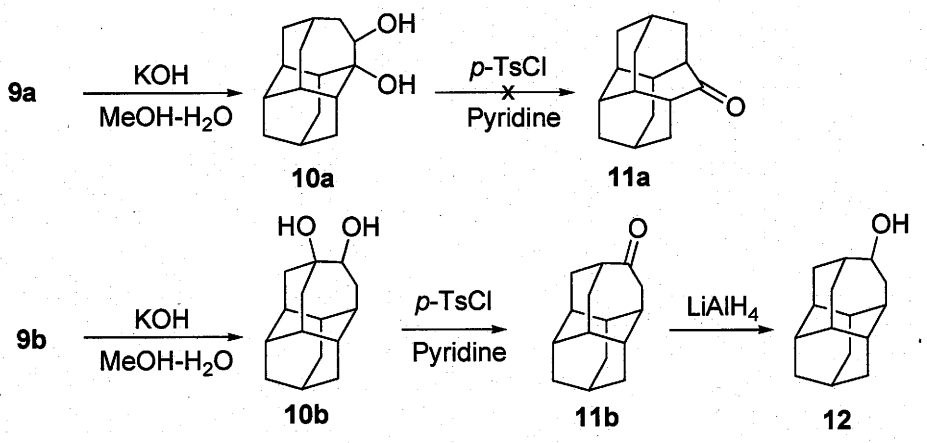


Figure 3. Synthetic scheme for reactions of homodiamantane derivatives

Conclusion

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**.

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-diamantanecarboxylic acid (**6a**) and 4-diamantanecarboxylic acid (**6b**) was prepared according to literature procedures.[17] Other commercially available reagents were of reagent-grade quality and used as received.

Reduction of a mixture of 1-diamantanecarboxylic acid (6a) and 4-diamantane carboxylic 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 $LiAlH_4$ (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 reaction was quenched by addition of water. The organic layer was washed with 10% NaOH and water and dried ($MgSO_4$). The resulting mixture was filtered. Removal of the solvents gave colorless crystals. Purification by chromatography on SiO_2 using hexane-ether (1:1) afforded a mixture of **7a** and **7b** (2:1) as colorless crystals (1.14g, 64%). Recrystallization from benzene gave a small amount of **7b** as colorless crystals (75 mg).

7a:[24,25] ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.40-1.82 (m, 17H), 1.92 (m, 1H), 2.01 (brd, J = 13.0 Hz, 2H), 3.60 (s, 2H).

7b: mp 192.4-193.5 °C; IR (KBr) 3210, 2876, 1054, 1046, 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 25.7 (CH), 32.5 (C), 37.2 (3CH), 37.5 (3CH), 37.8

($3CH_2$), 39.8 ($3CH_2$), 73.3 (CH_2). Anal. Calcd for $C_{15}H_{22}O$; H, 10.16; C, 82.52; Found, H, 10.10; C, 82.26.

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_2Cl_2 (50 mL) was added to a stirred suspension of pyridinium chlorochromate (11.9g, 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-diamantanecarbaldehyde (**8a**)[18] and 4-diamantanecarbaldehyde (**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, $CDCl_3$) δ 1.50-2.00 (m, 17H), 2.04 (brs, 2H), 9.36 (s, 1H).

8b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 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 $PhCOOSO_2CF_3$[21] (7.30 mL, 11.0 g, 43.4 mmol) in dry CCl_4 (12.4 mL) cooled by ice-water bath under nitrogen atmosphere. After stirring for 15 min, CF_3SO_3H (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 (6.06g, 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}; ^1H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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). Anal. Calcd 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}; ^1H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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).

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 hrs. The mixture was poured into water and extracted with $CHCl_3$. The organic layer was washed with 10% NaCl and dried ($MgSO_4$). 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, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9

(CH), 27.7 (CH), 34.3 (CH_2), 34.4 (CH_2), 36.9 (CH_2), 37.1 (CH), 37.5 (CH), 38.9 (CH), 39.56 (CH_2), 39.60 (CH), 42.3 (CH_2), 42.7 (CH), 77.5 (C), 78.6 (CH). Anal. Calcd for $C_{15}H_{22}O_2$: H, 9.46; C, 76.88; Found: H, 9.56; C, 70.03.

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 solution was refluxed for 11 h. The mixture was concentrated. The residue was diluted with wate and extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$). The solvent was evaporated, and recrystallization of the residue from benzene gave **10b** as pale yellow crystals (2.79 g, 83%): colorless crystals; mp 187.2-188.4 °C [from benzene-hexane (1:2)]; IR (KBr) 3342, 2869, 1445, 1041, 1023 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.49 (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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7 (CH), 36.7 (CH), 37.5 (CH), 37.6 (CH), 37.9 (CH), 38.3 (CH_2), 39.0 (CH_2), 39.3 (CH_2), 40.2 (CH_2), 40.3 (CH_2), 40.8 (CH) 42.7 (CH), 45.1 (CH_2), 73.0 (C), 78.2 (CH). Anal. Calcd for $C_{15}H_{22}O_2$: H, 9.46; C, 76.88; Found: H, 9.46; C, 76.69.

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 days. The mixture was poured into water and extracted with ether. The combined organic layer was washed with water and 5% $NaHCO_3$ and dried over $MgSO_4$. Removal of the solvent gave colorless crystals, whose purification by chromatography on SiO_2 gave homodiamantan-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, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5 (CH), 32.6 ($2CH_2$), 35.7 (CH), 36.8 (2CH), 38.8 (CH_2), 39.0 (CH), 39.4 (2CH), 40.4 ($2CH_2$), 47.4 (CH), 47.6 (CH_2), 217.4 (C). Anal. Calcd for $C_{15}H_{20}O$: H, 9.32; C, 83.29; Found: H, 9.57; C, 83.24.

Homodiamantan-9-ol (12)

Reduction of homodiamantan-9-one (**11b**) (166 mg, 0.77 mmol) with $LiAlH_4$ (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, 1437, 1023 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.39 (s, 1H), 1.46-1.57 (m, 3H), 1.65-2.01 (m, 16H), 2.44 (m, 1H), 3.96 (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 27.0 (CH), 30.2 (CH_2), 36.65 (CH_2), 36.74 (CH), 37.2 (CH), 37.4 (CH), 38.6 (CH), 38.8 (CH), 39.2 (CH_2), 40.4 (CH_2), 40.9 (CH_2), 42.2 (CH), 42.5 (CH and CH_2), 76.6 (CH). Anal. Calcd for $C_{15}H_{22}O$; H, 10.16; C, 82.52; Found: H, 10.43, C, 87.86.

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