Acid-isomerization of 3,4-Dimethyl-4-homoadamantyl Cation to 3-Ethyl-5-methyl-1-adamantyl Cation. A Unique Method for Construction of an Adamantyl Framework Having Two Alkyl Groups on the Bridgehead Positions

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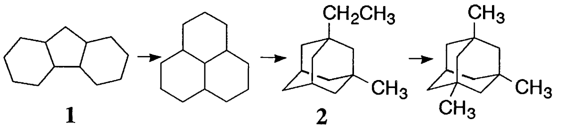
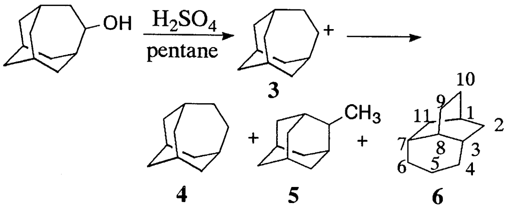
Ionization of 3,4-dimethyl-4-homoadamantanol with FSO_3H/SbF_5 in SO_2ClF irreversibly afforded the 3-ethyl-5-methyl-1-adamantyl cation (**9**) at −30 °C, which was directly observed by ^{13}C NMR. Trapping of **9** with methanol gave the corresponding methyl ether in 71% yield, suggesting that the acid–isomerization of 3,4-dialkyl-4-homoadamantanols may be conveniently used for preparation of 1,3-dialkyladamantane derivatives.

Several methods have been reported on the introduction of alkyl groups to the bridgehead positions of adamantane, but it is not always facile. The direct alkylation of 1-haloadamantanes has been done by using alkyl Grignard reagents and other organometallics.[1,2] Highly reactive 1-adamantyl trifluoromethanesulfonate has also been alkylated with alkyllithiums.[3b] 1-Adamantanol has been reductively alkylated and reduced with trialkylboron/trifluoromethanesulfonic acid.[3a] Further bridgehead halogenation of these 1-alkyladamantanes followed by the second alkylation may afford 1,3-dialkyladamantanes,[1b] but the scope has never been tested. A few 1,3-dialkyl- and 1,3,5-trialkyl-adamantanes have been prepared by the acid-isomerization of condensed alicyclic hydrocarbons: for example, the isomerization of perhydrofluorene (**1**) with $AlCl_3$/*t*-BuCl, aluminum bromide complex, or aluminum halides gave perhydrophenanthrene, 1-ethyl-3-methyladamantane (**2**), and 1,3,5-trimethyladamantane, but isolation of **2** required much effort.[4]

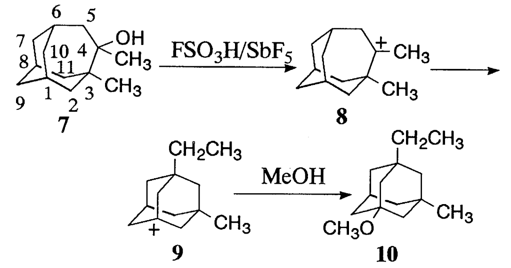


Majerski et al reported that the 4-homoadamantyl cation (**3**) that is generated in the acid-isomerization of 4-homoadamantanol gave homoadamantane (**4**), 2-methyladamantane (**5**), and tricyclo[5.3.1.$0^{3,8}$]undecane (**6**) in a ratio of 1:1:2,[5] but no further study dealing with substituted homoadamantane derivatives has been reported. This observation led us to examine substituted 4-homoadamantyl cations as precursors of alkylated adamantyl cations.



We previously reported a general method for preparing 3-alkyl-4-homoadamantanones that can easily be converted to 3,4-dialkyl-4-homoadamantanols.[6] We now describe that the 3,4-dimethyl-4-homoadamantyl cation (**8**) generated from 3,4-dimethyl-4-homoadamantanol (**7**)[7] in SO_2ClF with 25% Magic Acid (FSO_3H/SbF_5) undergoes clean isomerization that may not be easily predictable, and gives the 3-ethyl-5-methyl-1-adamantyl cation (**9**) in a good yield. The produced cation was directly observed by ^{13}C NMR and trapped by methanol to give 1-ethyl-3-methoxy-5-methyladamantane (**10**).

Scheme 1.



To a suspension of 3,4-dimethyl-4-homoadamantanol (**7**) in SO_2ClF at −120 °C was added 25% Magic Acid (4:1 FSO_3H/SbF_5) with stirring, and the ^{13}C NMR spectrum was measured at −100 °C. The 3,4-dimethyl-4-homoadamantyl cation (**8**) was, however, unstable and rearranged to two carbocations showing the cationic carbon signals at δ 323.0 and 318.0.[8] When the temperature was raised to −30 °C, the cation showing the C^+ signal at δ 318.0 was smoothly and irreversibly converted to the other.

The ^{13}C NMR spectrum (Figure 1) suggests that the cation observed at −30 °C was the 3-ethyl-5-methyl-1-adamantyl cation (**9**). The absorptions at δ 323.0, 97.1, and 91.8 may be assigned to the cationic carbon and two quaternary bridgehead carbons, respectively. For a comparison, the 3,5-dimethyl-1-adamantyl cation has been reported to show the respective absorptions at δ 296.2 (C^+) and 94.0 (C(3), C(5)).[9]

The trapping experiment unambiguously supported the structure of the observed cation **9**. To the cation solution was added cold methanol at −30 °C. Aqueous work-up followed by separation by liquid chromatography on SiO_2 gave a colorless oil

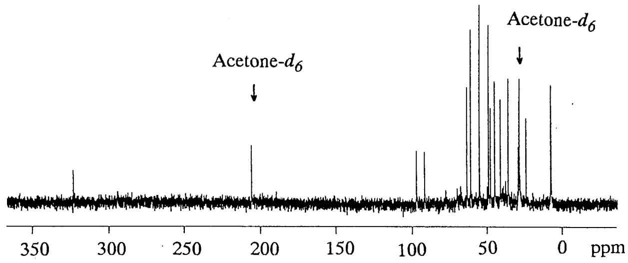
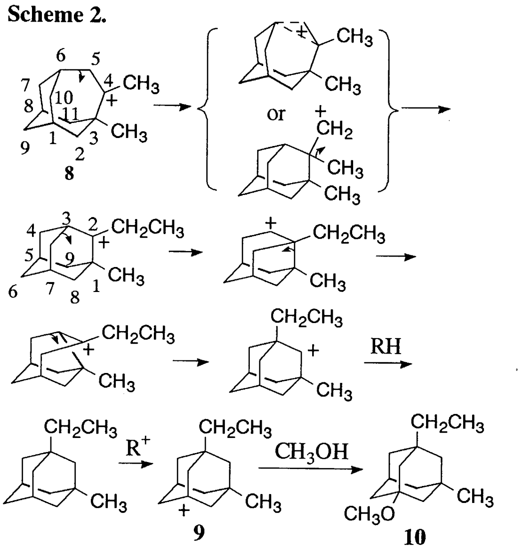


Figure 1. The 67.8 MHz ^{13}C NMR of 3-ethyl-5-methyl-1-adamantyl cation (**9**) generated by FSO_3H/SbF_5 in SO_2ClF at −30 °C (chemical shifts given from an internal capillary of acetone-*d6*).

in 71% yield,[10,11] whose IR and NMR spectra were identical to those of 1-ethyl-3-methoxy-5-methyladamantane (**10**) that was prepared by the methanolysis of 1-bromo-3-ethyl-5-methyladamantane.[4a]

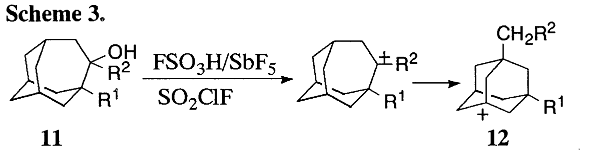
Scheme 2 shows one of plausible isomerization pathways of cation **8** to cation **9**. After ionization of **7**, cation **8** may irreversibly rearrange to the 2-ethyl-1-methyl-2-adamantyl cation by ring contraction.[5] This cation, which might be the other one observed at –100 °C, would subsequently rearrange to the 1-ethyl-3-methyl-2-adamantyl cation *via* the two protoadamantyl cations,[12] and finally give **9** by the intermolecular hydride shift.[12]

Scheme 2.



The present isomerization has potentiality to convert relatively easily prepared 3,4-dialkyl-4-homoadamantanols (**11**)[6] to various adamantyl cations containing R^1 and R^2CH_2 substituents on the different two bridgehead positions (**12**), which may be derived to various dialkyladamantane derivatives (Scheme 3). The study along this line is underway and the results will be reported elsewhere.

Scheme 3.



References and Notes

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7 3,4-Dimethyl-4-homoadamantanol (**7**): mp 162.5–163.0 °C; IR (KBr) 3484, 2902, 1456, 1369, 1096, 902 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.93 (3H, s), 1.24 (3H, s), 1.29 (2H, m), 1.42–1.55 (4H, m), 1.62–1.86 (4H, m), 1.91 (2H, m), 2.00 (3H, brs), 2.28 (1H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 28.3 (CH), 28.4 (CH), 29.5 (CH_3), 29.8 (CH_3), 30.5 (CH), 36.5 (CH_2), 37.1 (CH_2), 38.0 (CH_2), 40.1 (CH_2), 40.5 (CH_2), 40.6 (C), 53.3 (CH_2), 78.3 (C). Analytical data were unsatisfactory presumably because of the hygroscopic nature. Found: C, 79.94; H, 11.62%. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41%. However, the *p*-nitrobenzoate gave satisfactory analytical data (see below). 3,4-Dimethyl-4-homoadamantyl *p*-nitrobenzoate: mp 226.0–227.5 °C (in sealed tube). Found: C, 69.95; H, 7.49%. Calcd for $C_{20}H_{25}NO_4$: C, 69.95; H, 7.34%.

8 A methanol trapping experiment at –100 °C gave a complex mixture, no trace amount of 4-methoxy-3,4-dimethyl-homoadamantane having been detected.

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10 1-Ethyl-3-methoxy-5-methyladamantane (**10**): IR (liquid film) 2923, 1088 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (3H, t, J = 7.5 Hz), 0.88 (3H, s), 1.10 (2H, brs), 1.20 (2H, q, J = 7.5 Hz), 1.25–1.44 (8H, m), 1.60 (2H, brs), 2.22 (1H, m), 3.23 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.2 (CH_3), 30.3 (CH_3), 30.6 (CH), 33.2 (C), 35.6 (CH_2), 36.1 (C), 39.7 (CH_2), 40.2 (CH_2), 43.2 (CH_2), 44.5 (CH_2), 47.4 (CH_2), 48.0 (CH_3), 48.2 (CH_2), 73.7 (C). Found: C, 80.50; H, 11.69%. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61%.

11 No other methyl ether was obtained.

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