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Reactions of 2-Methyleneadamantane and 2-Benzylideneadamantane with Acetyl Nitrate

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Abstract—The reactions of 2-methylene- and 2-benzylideneadamantane with acetyl nitrate have been studied. In the case of 2-methyleneadamantane, the reaction proceeds via addition of nitronium cation at the double bond followed by stabilization of 2-nitromethyl-2-adamantyl carbocation. In the case of 2-benzylidenadamantane, *ortho*-substitution at the benzene ring occurred predominantly.

Keywords: acetyl nitrate, alkylideneadamantane, nitration, electrophilic addition, electrophilic substitution

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Development of novel methods for the synthesis of substituted adamantanes containing functional groups at the bridging carbon atom and the study of their biological activity have been the topics of a number of reports in the field of cage compounds chemistry [1–4]. Reactions of alkylideneadamantanes with nitrosating agents can serve for preparation of such compounds. A few examples of reactions of alkenes with acetyl nitrate to form usually a mixture of nitroacetylated and nitroxynitrated products have been reported in the literature [5–11].

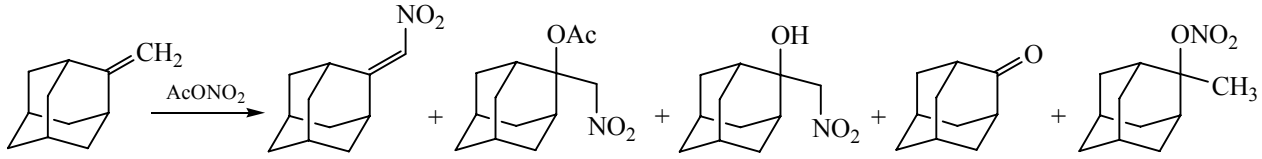
Extending our earlier studies [12–16] on the chemistry of alkylideneadamantanes and their interactions with electrophilic reagents, herein we report on the reactions of 2-methyleneadamantane **1** and 2-benzylideneadamantane **2** with acetyl nitrate (10% molar excess) generated *in situ* from fuming HNO_3 and acetic anhydride in methylene chloride solution at 0°C. In the case of 2-methyleneadamantane, a number of the reaction products **3–7** were isolated by column chromatography.

2-(Nitromethylene)adamantane was **3** was isolated in 26% yield (Scheme 1). Apparently, the reaction of 2-methyleneadamantane **1** with acetyl nitrate proceeded through a four-mem-bered transition state to form carbocation **A**, its stabilization occurring either via proton elimination or by attaching acetate anion to form 2-(nitromethyl)-adamant-2-yl acetate **4** as the major product.

2-(Nitromethyl)adamantan-2-ol **5** can be formed during the decomposition of 2-(nitromethyl)adamant-2-yl acetate **4** on silica in the presence of adsorbed water. The subsequent retro-Henry reaction led to the formation of 2-adamanone **6**. In addition, adamantanone formation could be due to the direct oxidation of 2-methyleneadamantane (Scheme 2).

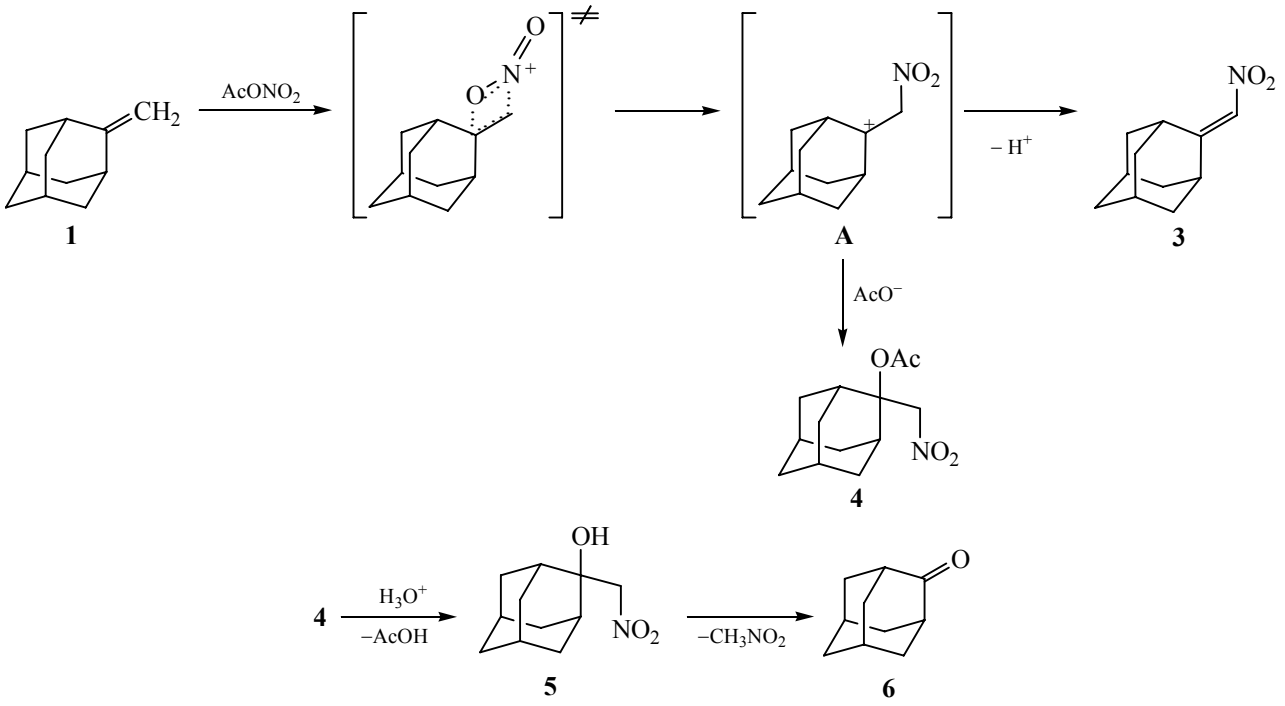
Finally, the formation of 2-methyl-2-adamantyl nitrate **7** could be explained by the electrophilic addition of nitric acid at the double bond. It should be noted that the addition of nitric acid to alkenes to form

Scheme 1.

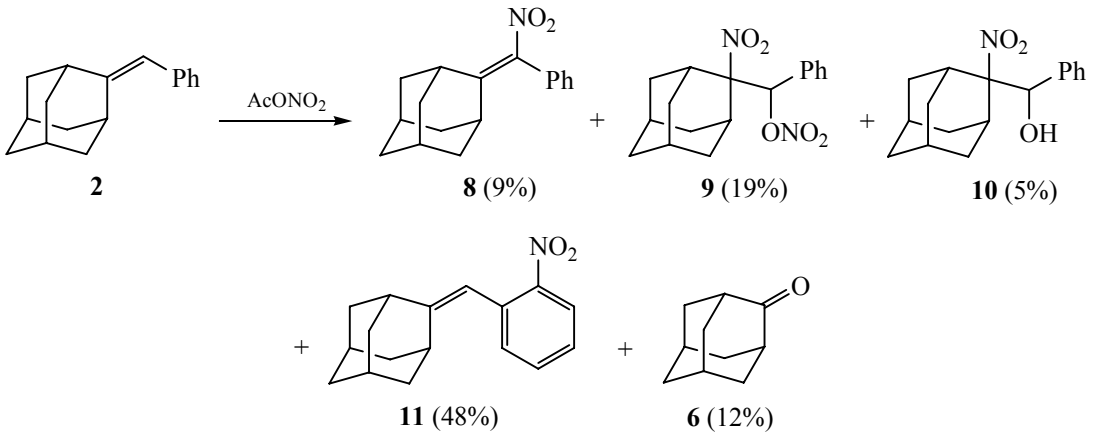


1 **3** (26%) **4** (44%) **5** (7%) **6** (4%) **7** (4%)

Scheme 2.



Scheme 3.



tertiary alkyl nitrates has been earlier described in [17].

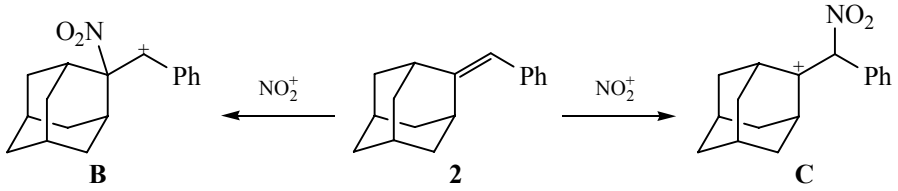
The reaction of 2-benzylideneadamantane **2** with acetyl nitrate also afforded a mixture of compounds **6**, **8**–**11** isolated by column chromatography (Scheme 3).

Note that in the case of 2-benzylideneadamantane **2**, both the bridging and benzylidene carbon atoms could be involved in the electrophilic attack to generate two different carbocations **B** and **C** (Scheme 4).

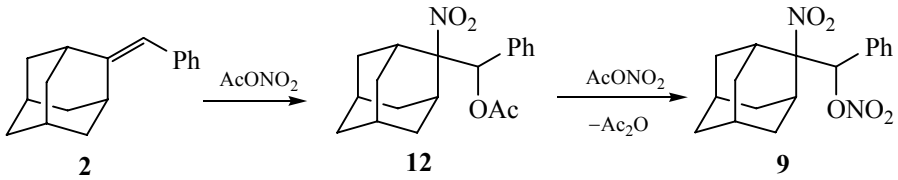
Formation of 2-[nitro(phenyl)methyl]adamantane **8** could be explained by the stabilization of carbocation **B** via proton elimination. IR spectrum of nitroalkene **8** contained strong absorption bands corresponding to vibrations of C–H bonds of adamantane fragment (2851, 2920 cm^{-1}), exocyclic double bond C=C (1655 cm^{-1}), and nitro group (1516, 1366 cm^{-1}). Mass spectrum of compound **8** contained a weak molecular ion peak and a peak of $[M - NO_2]^+$ ion with m/z = 223 (I_{rel} = 100%). The ^1H NMR spectrum revealed certain deshielding of the protons in the positions 1 and 3 of the adamantane core (δ = 2.97 and 2.48 ppm).

Nitronitrate **9** couls be regarded as a product of interaction of nitroacetate **12**, initially formed

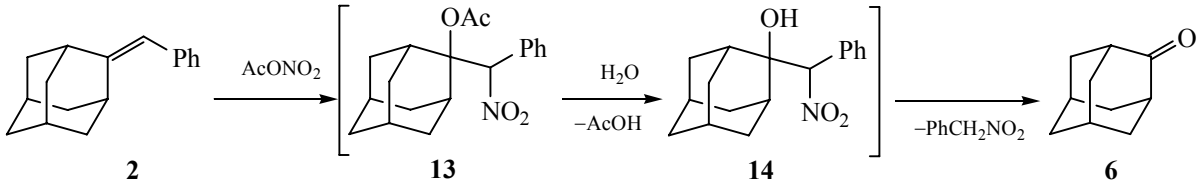
Scheme 4.



Scheme 5.



Scheme 6.



from unstable carbocation **B**, with acetyl nitrate (Scheme 5).

IR spectrum of compound **9** contained the absorption bands assigned to stretching of NO_2 (ν_{as} 1531, ν_s 1358 cm^{-1}) and ONO_2 groups (1647, 1277, 837 cm^{-1}). The signal of deshielded benzylic proton was observed at 6.61 ppm in the ^1H NMR spectrum. In addition, the deshielding of the C^1H and C^3H protons of the adamantane core was observed, that could be explained by the influence of the electron-withdrawing moieties. Generally, ^{13}C NMR spectra 2,2-disubstituted adamantane core contain 7 signals. Since in most cases conformational interconversion barrier of the enantiomers is low, the dynamic symmetry plane appears whereby three pairs of carbon atoms at the positions 1 and 3, 4 and 9, 8 and 10 of adamantane moiety become equivalent. However, the enhanced steric hindrance hampers the rotation, and these pairs of carbon atoms become magnetically nonequivalent. As a result, the carbon atoms of adamantane moiety will resonate as 10 signals instead of 7 in the ^{13}C NMR spectrum; that observed in the case of nitronitrate **9**. The value for the chemical shift of the carbon atom associated with nitro group was of 97.8 ppm.

When eluting the reaction mixture on silica gel, nitronitrate **9** transformed into (2-nitro-2-adamantyl)-(phenyl)methanol **10**. Its ^1H NMR spectrum contained the signal of strongly deshielded benzylic proton at 6.39 ppm and a broad singlet signal of hydroxyl group at 2.83 ppm. As in the case of nitronitrate **9**, the ^{13}C NMR spectrum of compound **10** contained 10 signals of the adamantane moiety. The carbon atom adjacent to the hydroxyl group resonated at 91.0 ppm. The signal at 95.9 ppm was assigned to the carbon atom at position 2 of the adamantane moiety.

Formation of adamantanone **6** in the reaction of alkene **2** with acetyl nitrate could be explained by hydrolysis of unstable nitroacetate **13** (the latter formed through the intermediate carbocation **B**) when treating the reaction mixture to form unstable 2-(nitrobenzyl)adamantan-2-ol **14**, followed by the retro-Henry reaction (Scheme 6).

In the case of 2-benzylidenadamantane **2**, the benzene ring might also be a site of the electrophilic attack, and electrophilic aromatic substitution was the major direction. The preferential formation of 2-(2-nitrobenzylidene)adamantane **11** and the presence of a minor amount (about 1%, according to GC–MS) of the *para*-nitrated product could be explained by the fact that electrophilic nitration at the *ortho*-position of the benzene ring could occur probably via pre-coordination of nitrating reagent with the double C=C

bond. IR spectrum of nitro compound **11** contained the absorption bands assigned to stretching of C–H bonds of the adamantane fragment (2847, 2920 cm^{-1}), double C_{Ad}=C bond (1651 cm^{-1}), aromatic ring (1605 cm^{-1}), and nitro group (1520, 1358 cm^{-1}). The ^1H NMR spectral data clearly indicated the formation of the *ortho*-substituted product; the ^1H NMR spectrum contained a signal of strongly deshielded proton at the double bond, at 6.40 ppm.

Noteworthily, reactions of methyleneadamantane **1** and benzylideneadamantane **2** with acetyl nitrate did not affect the tertiary C–H bonds of adamantane moiety.

In summary, the reaction of 2-methyleneadamantane with acetyl nitrate afforded a wide range of the products due to generation of 2-nitromethyl-2-adamantyl carbocation. In the case of 2-benzylideneadamantane **2**, nitration of the benzene ring competed with nitronium cation attack at the bridging carbon atom of the adamantane scaffold.

EXPERIMENTAL

Mass spectra were recorded using a Thermo Finnigan Trace DSQ instrument by direct injection of the material into the ion source at the ionizing electrons energy of 70 eV. ^1H and ^{13}C NMR spectra (400 and 100 MHz, respectively) of the solutions in $CDCl_3$ or CD_3CN were obtained using a JEOL JNM-ECX400 spectrometer with internal TMS reference. IR spectra were registered using a Shimadzu FTIR-8400S spectrometer (KBr pellets). Elemental analysis was performed using a EuroVector EA-3000 automated CHNS analyzer. Melting points were determined by capillary method using a PTP-M instrument.

Reaction of 2-methyleneadamantane 1 with acetyl nitrate. Acetyl nitrate was obtained by adding 2.6 mL of fuming (~96%) nitric acid to a mixture of 22.5 mL of Ac_2O and 20 mL of dichloromethane with stirring at 0–5°C. The nitrating mixture was added dropwise to a solution of 6 g (0.04 mol) of 2-methyleneadamantane **1** in 60 mL of dichloromethane upon vigorous stirring at 0–5°C. The mixture was incubated during 12 h at 3–4°C and then poured into 150 g of ice. The organic layer was separated, and the aqueous layer was extracted with dichloromethane. The extract was washed with $NaHCO_3$, dried with Na_2SO_4, and evaporated in vacuum. The residue was purified by silica gel column chromatography eluting with a hexane–dichloromethane mixture (100 : 1). The following compounds were isolated: 2-(nitromethylene)adamantane **3** (2.03 g, 26%), 2-(nitromethyl)adamant-2-yl acetate **4** (4.51 g, 44%), 2-(nitromethyl)adamantan-2-ol **5** (0.60 g, 7%), 2-adamantanone **6** (0.24 g, 4%), 2-methyl-2-adamantyl nitrate **7** (0.34 g, 4%). Physico-chemical and spectral parameters of compounds **3**–**7** coincided with those reported in [11, 18].

Reaction of benzylideneadamantane 2 with 2-acetyl nitrate was performed similarly, using a solution of 4.48 g (0.02 mol) of 2-benzylideneadamantane **2** in 30 mL of methylene chloride and a solution of acetyl nitrate prepared from 12 mL of Ac_2O, 1.3 mL of fuming HNO_3 and 10 mL of methylene chloride. After silica gel column chromatography (eluent – hexane–dichloromethane, 100 : 1), compound **8**–**11** and 2-adamantanone **6** (0.36 g, 12%) were isolated.

2-[Nitro(phenyl)methylene]adamantane (8). Yield 0.48 g (9%), mp 108–110°C (hexane) (mp 108.5–109.5°C [19]). IR spectrum (KBr), ν, cm^{-1}: 2920, 2851 (CH_{Ad}), 1655 (C_{Ad}=C), 1516 (NO_2), 1447, 1366 (NO_2), 1261, 1099, 953, 756, 733, 702. ^1H NMR spectrum (CD_3CN), δ, ppm: 1.81–2.03 m (12H, H_{Ad}), 2.48 br. s and 2.97 br. s (2H, $H^{1,3}_{Ad}$), 7.34–7.37 m (2H, Ph), 7.41–7.44 m (3H, Ph). ^{13}C NMR spectrum (CD_3CN), δ_C, ppm: 27.5 (2CH), 34.1 (2CH), 35.9 (CH_2), 38.5 ($2CH_2$), 38.6 ($2CH_2$), 129.0 ($2CH_{Ph}$), 129.4 ($2CH_{Ph}$), 129.5 (CH^4_{Ph}), 132.0 (C^1_{Ph}), 142.4 (C–NO_2), 149.5 (C^2_{Ad}). Mass spectrum, *m*/*z* (I_{rel}, %): 269 (7) $[M]^+$, 239 (7) $[M - NO]^+$ 223 (100) $[M - NO_2]^+$, 211 (14) $[M - CNO_2]^+$, 181 (6), 178 (5), 167 (13), 165 (12), 143 (9), 141 (10), 129 (13), 128 (17), 115 (22), 105 (36), 91 (28), 79 (11), 77 (14) $[Ph]^+$. Found, %: C 75.90; H 7.01; N 5.11. $C_{17}H_{19}NO_2$. Calculated, %: C 75.81; H 7.11; N 5.20.

(2-Nitro-2-adamantyl)(phenyl)methyl nitrate (9). Yield 1.26 g (19%), mp 149–151°C. IR spectrum, ν, cm^{-1}: 2916–2854 (CH_{Ad}), 1647 (ONO_2), 1531 (NO_2), 1516, 1358 (NO_2), 1277 (ONO_2), 837 (ONO_2). ^1H NMR spectrum (CD_3CN), δ, ppm: 1.77–2.06 m (12H, H_{Ad}), 2.48 s (1H, H_{Ad}), 3.03 s (1H, H_{Ad}), 6.61 s (1H, CH), 7.22–7.44 m (5H, Ph). ^{13}C NMR spectrum (CD_3CN), δ_C, ppm: 25.9 and 26.2 ($2CH^{5,7}$), 31.6 and 31.8 ($2CH^{1,3}$), 33.3 (CH_2), 33.6 (CH_2), 33.7 (CH_2), 38.5 (CH_2), 38.6 (CH_2), 81.1 (C–O), 97.8 (C^2), 126.1 ($C^{2,6}_{Ph}$), 129.0 ($C^{3,5}_{Ph}$), 129.9 (C^4_{Ph}), 149.5 (C^1_{Ph}). Mass spectrum, *m*/*z* (I_{rel}, %): 239 (5) $[C_{17}H_{19}O]^+$, 223 (12) $[C_{17}H_{19}]^+$, 211 (60) $[C_{16}H_{19}]^+$, 150 (23), 105 (100), 91 (85). Found, %: C 61.39; H 5.97; N 8.33. $C_{17}H_{20}N_2O_5$. Calculated, %: C 61.44; H 6.07; N 8.43.

(2-Nitro-2-adamantyl)(phenyl)methanol (10). Yield 0.29 g (5%), mp 102–104°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.69–2.20 m (13H, Ad), 2.38 d (1H, Ad, *J* 13.3 Hz), 2.83 br. s (1H, OH), 6.39 s (1H, C<u>H</u>OH), 7.36–7.48 m (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 25.7 and 26.0 ($2CH^{5,7}$), 32.8 and 33.1 ($2CH^{1,3}$), 34.1 (CH_2), 34.2 (CH_2), 34.3 (CH_2), 34.5 (CH_2), 37.7 (CH_2), 91.0 (CHOH), 95.9 (C^2), 128.5 (C^1_{Ph}), 128.7 ($2CH_{Ph}$), 129.2 ($2CH_{Ph}$), 130.8 (CH^4_{Ph}). Found, %: C 70.96; H 7.30; N 4.79. $C_{17}H_{21}NO_3$. Calculated, %: C 71.06; H 7.37; N 4.87.

2-(2-Nitrobenzylidene)adamantane (11). Yield 2.58 g (48%), mp 69–70°C. IR spectrum, ν, cm^{-1}: 3067 (CH_{Ph}), 2910, 2847 (CH_{Ad}), 1651 (C_{Ad}=C), 1605 (C=C_{Ar}), 1566, 1520 (NO_2), 1443, 1358 (NO_2), 1323, 1296, 1277, 1099, 1076, 953, 891, 845, 783, 756, 725. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.73–2.05 m (12H, H_{Ad}), 2.58 s (1H, H_{Ad}), 2.68 s (1H, H_{Ad}), 6.40 s (1H, C=CH), 7.27–7.37 m (2H, $H^{4,6}$), 7.52 t (1H, H^5, *J* = 7.6 Hz), 7.93 d (1H, H^3, *J* = 7.6 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 269 (3) $[M]^+$, 252 (16) $[M - OH]^+$, 240 (23), 224 (7), 165 (11), 150 (9), 120 (45), 119 (100), 115 (17), 92 (67), 91 (47), 79 (40), 77 (25) $[Ph]^+$. Found, %: C 75.76; H 7.67; N 5.16. $C_{17}H_{19}NO_2$. Calculated, %: C 75.81; H 7.11; N 5.20.

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