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SHORT COMMUNICATIONS

Amidation of Adamantane and Diamantane with Acetonitrile and Bromotrichloromethane in the Presence of $Mo(CO)_6$ in Aqueous Medium

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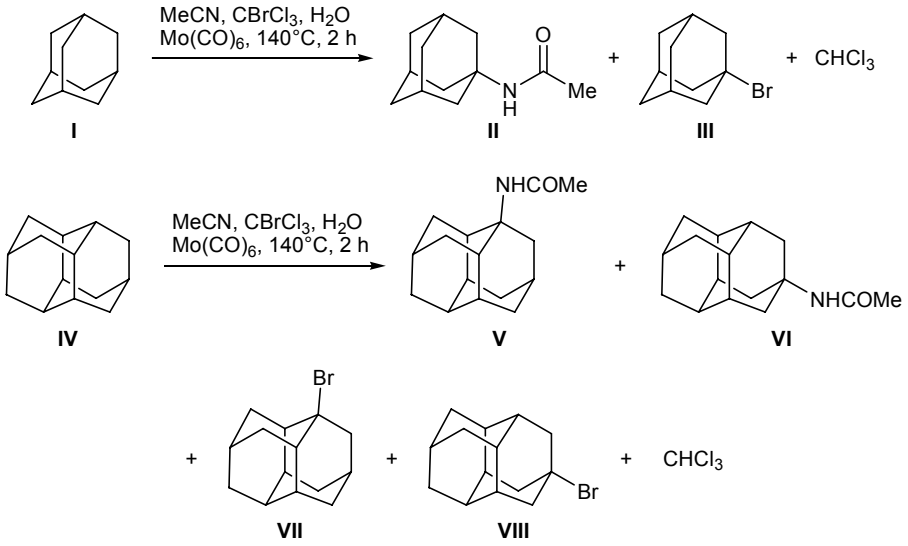
N-(1-Adamantyl)acetamide and its derivatives are starting compounds in the synthesis of biologically active aminoadamantanes possessing antimicrobial and antiviral activity and used in the treatment and prophylactics of influenza, herpes, and pneumonia. Removal of acetyl protection from *N*-(1-adamantyl)acetamide yields 1-aminoadamantane which is the active component of the known drug midantane for the treatment of Parkinson's disease [1–5].

Known methods for the preparation of *N*-acetyl derivatives of 1-aminoadamantane are based on reactions of 1-X-substituted adamantanes (X = Br, I, OMe, Cl, F, OH, CF_3COO, O_2NO) with acetonitrile in the presence of excess catalyst such as NO_2BF_4 [6], $NOPF_6$ [7], $(CF_3SO_2)_2O$ [8], CF_3COOH, $BF_3 \cdot Et_2O$ [9], and H_2SO_4 [10]. Baklan et al. [11] synthesized *N*-(1-adamantyl)acetamide (**II**) by reaction of adamantane (**I**) with acetonitrile in bromine as solvent and catalyst and subsequent hydrolysis. Liberated hydrogen bromide was not trapped during the process, for the target amide did not react with HBr under these conditions [11]. The presence of an oxidant, sodium peroxosulfate $Na_2S_2O_5$ was necessary to obtain compound **II** in high yield.

We performed direct one-pot amidation of adamantane (**I**) with acetonitrile in the presence of molybdenum hexacarbonyl $Mo(CO)_6$ and bromotrichloromethane $BrCCl_3$ in aqueous medium. The reaction



occurred at 140–150°C in 2–5 h and afforded 90–95% of compound **II**, the conversion of initial adamantane (**I**) being complete. 1-Bromoadamantane (**III**) was formed as by-product (yield 5–10%). Under analogous conditions, diamantane (**IV**) was completely converted into a mixture of *N*-(1- and 4-diamantyl)acetamides **V** and **VI** and 1- and 4-bromodiamantanes **VII** and **VIII** at a ratio of 2:1:0.5:0.4. The reactant and catalyst ratio $Mo(CO)_6$–**I** (or **IV**)–$BrCCl_3$–MeCN–H_2O was 3:100:100:150:200.

Apart from compounds **II**, **III**, and **V**–**VIII**, the reaction mixtures contained chloroform (according to the GLC amd GC–MS data); the amount of the latter was equal to the amount of compound **II**, indicating direct participation of $BrCCl_3$ in the amidation of **I** and **IV** with acetonitrile. No reaction occurred in the absence of $BrCCl_3$. When $BrCCl_3$ was replaced by CBr_4, the yield of amide **II** was 34%; a probable reason for the lower yield of **II** is that the initial reactants and the product are solids. In methylene chloride the yield of **II** increased to 72%. The yield of amide **II** was 22% in the presence of $MoO(acac)_2$ as catalyst. The structure of 1-bromoadamantane (**III**), and 1- and 4-bromodiamantanes **VII** and **VIII** was proved by comparison with authentic samples [1, 12].

The reactions were carried out in a 20-ml glass ampule or in a 17-ml stainless-steel high-pressure reactor; the results of parallel runs were almost similar. A reactor (ampule) was charged with 0.1 mmol of $Mo(CO)_6$, 10 mmol of adamantane (**I**) or diamantane (**IV**), 10 mmol of $BrCCl_3$, 15 mmol of acetonitrile, and 20 mmol of water. The reactor was hermetically closed (the ampule was sealed) and heated for 2–5 h at 140–150°C. After cooling to room temperature, the reactor (ampule) was opened, the organic phase was separated, the aqueous phase was extracted with methylene chloride (3×5 ml), the extracts were combined with the organic phase, the solvent was distilled off, and the residue was crystallized from ethanol. The yields are given for the isolated compounds. Compounds **II**, **V**, and **VI** were purified by column chromatography on aluminum oxide of activity grade II using methylene chloride–hexane (1:3, by volume) as eluent.

***N*-(1-Adamantyl)acetamide (II).** Yield 90%, mp 147–147.5°C (from ethanol); published data [9]: mp 147–148°C (from petroleum ether). IR spectrum, ν, cm^{-1}: 3220 (NH), 1645 (C=O), 1545 (δNH). ^{13}C NMR spectrum, δ_C, ppm: 25.40 (CH_3), 30.85 (C^3, C^5, C^7), 36.42 (C^4, C^6, C^{10}), 41.5 (C^2, C^8, C^9), 51.61 (C^1), 160.86 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 193 (43) $[M]^+$, 192 (9), 150 (7), 137 (8), 136 (100), 135 (24), 134 (25), 100 (8), 94 (45), 93 (18), 92 (16), 91 (17), 79 (15), 77 (14), 58 (8), 55 (7), 43 (31), 42 (12), 41 (21), 39 (14).

***N*-(1-Diamantyl)acetamide (V).** Yield 52%, mp 168–168.5°C (from ethanol); published data [12]: mp 167–168°C (from acetone). IR spectrum, ν, cm^{-1}: 3283 (NH), 1645 (C=O), 1572, 1549 (δNH). ^{13}C NMR spectrum, δ_C, ppm: 23.46 (CH_3), 25.54 (C^4), 28.57 (C^9), 33.27 (C^3, C^{14}), 36.93 (C^6), 37.50 (C^5), 37.79 (C^8, C^{10}), 39.13 (C^7, C^{11}), 40.37 (C^2, C^{12}), 41.66 (C^{13}), 56.63 (C^1), 171.44 (C=O).

***N*-(4-Diamantyl)acetamide (VI).** Yield 26%, sublimes at 98°C (10 mm). IR spectrum, ν, cm^{-1}: 3280 (NH), 1645 (C=O), 1549 (δNH). ^{13}C NMR spectrum, δ_C, ppm: 23.46 (CH_3), 25.36 (C^9), 35.94 (C^1, C^7, C^{11}), 37.15 (C^8, C^{10}, C^{13}), 40.24 (C^2, C^6, C^{12}), 42.26 (C^3, C^5, C^{14}), 54.19 (C^4), 170.98 (C=O). Found, %: C 77.89; H 9.18; N 5.59. $C_{16}H_{23}NO$. Calculated, %: C 78.32; H 9.45; N 5.71.

The IR spectra were measured in the range from 3600 to 550 cm^{-1} on a Bruker Vertex 70V spectrometer from samples pelleted with KBr or dispersed in mineral oil. The ^{13}C NMR spectra were recorded on a Bruker Avance-400 spectrometer at 100.62 MHz using $CDCl_3$ as solvent. The mass spectra were obtained on a Shimadzu QP-2010 Plus GC–MS system (Supelco PTE-5 capillary column, 30 m×0.35 mm). The elemental composition was determined on a Carlo Erba 1106 analyzer.

The progress of reactions and the purity of products were monitored by GLC on a Khrom-5 chromatograph equipped with a flame ionization detector (1.2- and 3-m columns, 3.3 mm i.d., stationary phase 5% of SE-30 on Chromaton-N-HMDS, 0.125–0.160 mm; oven temperature programming from 50 to 280°C at a rate of 8 deg/min; carrier gas helium, flow rate 50 ml/min).

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