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LETTERS TO THE EDITOR

A New Route to *N*-(1-Adamantyl)nicotinamide

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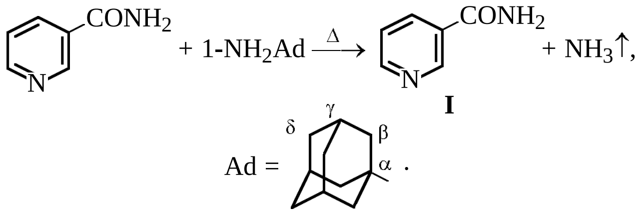
N-(1-Adamantyl)nicotinamide **I** was prepared previously by the reaction of nicotinoyl chloride with 1-aminoadamantane on heating in anhydrous pyridine [1] or by the Ritter reaction [2] from 1-hydroxyadamantane and nicotinonitrile in trifluoroacetic acid acting as catalyst and solvent.

We found that compound **I** can be prepared in 91% yield by heating nicotinamide with 1-aminoadamantane without solvent:



It is known that amides can act as acylating agents toward amines [3]. Heating of amides with primary amines is accompanied by exchange of amino group (often without additional catalyst), but these reactions go to completion only if the released amine is volatile. It was also reported that 1-bromoadamantane reacts amides R'CONHR in the presence of Ag_2SO_4 at 100°C. With *N*-methylacetamide, the yield of the reaction product, 1-*N*-methylacetamidoadamantane, is 43% [4].

We found that nicotinamide can be adamantylated with 1-bromoadamantane without adding a silver salt.

Also, we prepared compound **I** by adamantylation of nicotinamide with 1-hydroxyadamantane in the presence of traces of water. Protic solvents (water in our case) exert an electrophilic accelerating effect on S_N1 reactions. It is known that the rate of solvolysis of 1-BrAd in aqueous ethanol increases by a factor of 4900 with an increase in the water content from 10 to 60 vol % [5]. Apparently, under severe conditions 1-hydroxyadamantane also generates an Ad-carbenium ion with the assistance of water.

***N*-(1-Adamantyl)nicotinamide I.** *a*. A mixture of 0.151 g of 1-aminoadamantane and 0.610 g of nicotinamide was heated on a sand bath to 210–215°C; until the ammonia evolution started, the released gases were passed through a bubbler. The mixture was kept at 210–215°C for 30–40 min. After cooling, it was treated with water, and the precipitate was dried. Adamantylated nicotinamide was obtained in a yield of 0.233 g (91%); mp 164–166°C (published data: mp 164–167°C [1]). IR spectrum, ν, cm^{-1}: 3345 (NH), 2909–2853 (CH$_2$ of adamantane), 1662 (C=O). ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 1.68 (6H^δ), 2.08 (3H^γ + 6H^β) (adamantane protons); 7.87 (NH), 7.44 (H^5), 8.15 (H^4), 8.67 (H^6), 8.97 (H^2) (pyridine protons). ^{13}C NMR spectrum (CDCl$_3$), $δ_C$, ppm: 29.97 (C^γ), 37.15 (C^δ), 41.91 (C^β), 52.85 (C^α), 124.27 (C^5), 132.43 (C^3), 136.16 (C^4), 149.54 (C^6), 152.45 (C^2), 165.63 (CO).

b. A mixture of 1 mmol of 1-XAd [X = Br, OH] and 5 mmol of nicotinamide was heated similarly to procedure *a*. Compound **I** was isolated; yield 66 (from 1-BrAd, sample **Ia**) or 53% (from 1-HOAd, sample **Ib**). The structure of **Ia** and **Ib** was proved by NMR and IR spectroscopy and by comparison of their physicochemical characteristics with the published data [1, 2] and with the characteristics of the product prepared by procedure *a*.

The IR spectra were recorded on a Vector-22 IR Fourier spectrometer in KBr pellets. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-Avance DPX-200W spectrometer (Krasnoyarsk Regional Center of Collective Use, Siberian Division, Russian Academy of Sciences).

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