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LETTERS TO THE EDITOR

Reactions of 2-(*N*,*N*-Dialkyl)amino-2-adamantylcarbonitriles with Grignard Reagents

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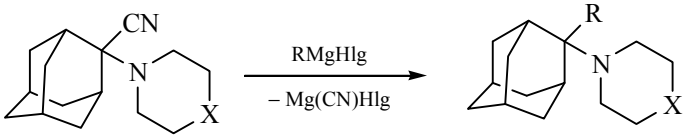
2-Substituted adamantane derivatives have valuable medical and biological properties [1]. It seems interesting to synthesize new compounds containing adamantyl moiety like 2-amino derivatives of adamantane aiming further to test their antiviral activity.

In order to obtain adamantane derivatives containing both alkylamino and keto groups at the position 2, we made an attempt to synthesize new 2-(*N*,*N*-dialkyl)amino-2-acyladamantanes by reacting 2-(*N*,*N*-dialkyl)aminoadamantane-2-carbonitriles [2] with the Grignard reagents.

2-*N*-Piperidino-2-cyanoadamantane **Ia** and 2-*N*-morpholino-2-cyanoadamantane **Ib** were used as starting materials, and methylmagnesium iodide, ethylmagnesium bromide, and allylmagnesium chloride as the Grignard reagents. Reactions were carried out in tetrahydrofuran at a molar ratio of the reactants of 1:(1.5–2) at a temperature of 30–45°C for 3–5 h.



Ia, Ib **IIa–IId**

X = CH_2 (**Ia**), O (**Ib**); X = CH_2, R = CH_3 (**IIa**); X = CH_2, R = C_2H_5 (**IIb**); X = CH_2, R = $CH_2CH{=}CH_2$ (**IIc**); X = O, R = CH_3 (**IId**).

However, 2-alkyl-2-(*N*,*N*-dialkyl)aminoadamantanes **IIa**–**IId** were isolated instead of the expected 2-(*N*,*N*-dialkyl)amino-2-acyladamantanes. The composition and structure of the compounds obtained were confirmed by GC-MS and NMR spectroscopy methods.

General procedure of the synthesis of 2-alkyl-2-(*N*,*N*-dialkyl)aminoadamantanes (IIa–IId). To the Grignard reagent prepared from 0.025 mol of magnesium and 0.018 mol of an alkyl halide in 15–20 mL of tetrahydrofuran was added a solution of 0.009 mol of aminonitrile **I** in 10 mL of tetrahydrofuran. The mixture was heated at 40°C with stirring for 4 h, then cooled and mixed with 0.5 g of water. After separating the solid phase, the filtrate was evaporated. The target product was distilled in a vacuum.

2-Methyl-2-(*N*-piperidino)adamantane (IIa). Yield 75%, bp 171–172°C (20 mm Hg), n_D^{20} 1.5312. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.19–1.84 m (14H, adamantane; 6H, piperidine, 0.86 s (3H, CH_3), 2.20 d [2H, N(CH_2), *J* 14.5], 2.78 d [2H, N(CH_2), *J* 13.7]. Mass spectrum (EI, 70 eV), *m*/*e* (I_{rel}, %): 232.0 (2) [*M* – 1], 218.2 (100) [*M* – CH_3], 84.1 (3).

2-Ethyl-2-(*N*-piperidino)adamantane (IIb). Yield 68%, bp 181–182°C (20 mm Hg), mp 72–74°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.77 t [3H, CH_3, *J* 12.0], 1.11–2.17 m (14H, adamantane; 2H, CH_2; 8H, piperidine), 2.94 d [2H, N(CH_2), *J* 17.6]. Mass spectrum (EI, 70 eV), *m*/*e* (I_{rel}, %): 248.1 (2) $[M]^+$, 246.2 (4), 219.2 (14), 218.4 (100) [*M* – C_2H_5], 84.2 (2).

2-Allyl-2-(*N*-piperidino)adamantane (IIc). Yield 65%, bp 203–205°C (20 mm Hg). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.08–2.25 m (14H, adamantane; 6H, piperidine, 2.37 t [4H, $N(CH_2)_2$, *J* 17.8], 2.91 d (2H, CH_2, *J* 13.4), 4.80–4.96 m (2H, $=CH_2$), 4.80–4.96 m (1H, CH=). Mass spectrum (EI, 70 eV), *m*/*e* (I_{rel}, %): 258.2 (5) [*M* – 1], 219.2 (17), 218.3 (100) [*M* – $CH_2CH=CH_2$].

2-Methyl-2-(*N*-morpholino)adamantane (IId). Yield 84%, bp 191–192°C (20 mm Hg), mp 40–42°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.92 s (3H, CH_3), 1.22–2.21 m (14H, adamantane), 2.46 t [4H, $N(CH_2)_2$, *J* 15.4], 3.39 t [2H, $(CH_2)O$, *J* 14.5], 3.66 t [2H, $(CH_2)O$, *J* 15.4]. Mass spectrum (EI, 70 eV), *m*/*e* (I_{rel}, %): 237.0 (2) [*M* – 1], 236 (8), 220.5 (100) [*M* – CH_3].

The NMR spectra were recorded on a Varian Mercury 300BB spectrometer (300 MHz) using carbon tetrachloride as a solvent, internal reference hexamethyldisiloxane. Mass spectra were recorded on a Varian Saturn 2100 T/GC 3900GC-mass spectrometer (70 eV).

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