ISSN 1070-3632, Russian Journal of General Chemistry, 2013, Vol. 83, No. 12, pp. 2350–2351. © Pleiades Publishing, Ltd., 2013.
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LETTERS TO THE EDITOR

Synthesis of Adamantyl-Containing Spirooxazines and Spirooxazolidines

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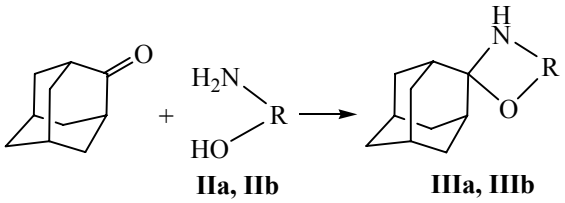
Received July 22, 2013

DOI: 10.1134/S1070363213120268

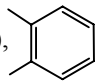
Nitrogen-containing heterocyclic compounds including saturated cycles with one or two nitrogen atoms, morpholine group, wherein adamantyl moiety is bound to the nitrogen atom, occupy a special place among the biologically active adamantane derivatives. 1(2)-Aminoadamantane derivatives, in which molecules the nitrogen atom is a part of the heterocyclic moiety, are of interest as anti-viral and anti-parkinsonian medicals [1, 2].

It is known that reaction of adamantan-2-one with *o*-aminothiophenol and 2-amino-1-thioethane in the presence of a catalyst is accompanied by cyclization to form spiroheterocyclic structures [3]. However, there are no data on the synthesis of similar oxazolidines [4].

We synthesized adamantly-containing spirooxazolidines by reacting adamantan-2-one **I** with aminoethanol **IIa** and *o*-aminophenol **IIb**. It is found that condensation of ketone **I** with amines **IIa**, **IIb** proceeds readily in the absence of a catalyst by refluxing the reactants in toluene with azeotropic removal of water. Reaction of adamantan-2-one **I** with amine **IIa** proceeds also in toluene in the presence of toluenesulfonic acid.

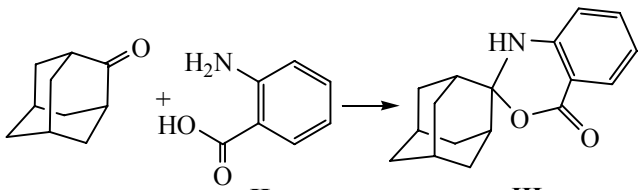


IIa, IIb **IIIa, IIIb**

R = CH_2CH_2 (**IIa, IIIa**),  (**IIb, IIIb**).

Since the synthesis of heterocyclic oxazolidine **IIIb** occurs in the absence of a catalyst, the formation of ketimine intermediate and intramolecular alkylation of the C=N bond may be due to the high acidity of phenolic hydroxy group of **IIb**.

Reaction of ketone **I** and anthranilic acid **IIc** in toluene in the absence of a catalyst can also proceed as condensation and intramolecular cyclization of ketimine to form adamantly-containing 1,3-oxazin-5-one **IIIc**.



IIc **IIIc**

Purification of the product **IIIa** was performed by distillation in vacuum; compounds **IIIb** and **IIIc** were purified by recrystallization from propan-2-ol. Structure and composition of the obtained heterocycles was confirmed by ^{1}H NMR and IR spectroscopy, gas chromatography-mass spectrometry and elemental analysis data. The IR spectra of compounds **IIIa**, **IIIb** contain absorption bands of the NH-group in the region of 3200–3400 cm^{-1}. The presence of characteristic proton signals of the NH-group at 3.5 (**IIIb**) or 7.3 ppm (**IIIc**) confirms intramolecular cyclization of the intermediate ketimines. Downfield shifting of the signal in the spectrum of **IIIc** is due to the influence of the carbonyl group *ortho*-positioned relative to the nitrogen atom. For all cases, in the ^{1}H NMR spectra there are no signals of the OH protons of the carboxyl groups of the intermediate imines.

Thus, we developed a convenient preparative method of obtaining a series of adamantyl-containing spiroheterocycles.

Spiro-1,3-oxazolidine-2,2'-tricyclo[3.3.1.1^{3,7}]-decane (IIIa). A solution of 3 g (0.02 mol) of adamantanone **I** and 1.5 g (0.025 mol) of amine **IIa** in 20 mL of toluene was refluxed for 3 h with azeotropic distillation of water. Then the excess of amine and toluene were distilled off. The residue was distilled under vacuum. Yield 3.5 g (91%), bp 155–157°C (20 mm Hg). ^{1}H NMR spectrum, δ, ppm: 1.39–2.03 m (14H, 1H, 2,2-Ad, NH), 2.99 t (2H, CH_2N, *J* 11.4 Hz), 3.57 t (2H, CH_2O, *J* 11.4 Hz). Mass spectrum (EI, 70 eV), *m*/*e* (I_{rel}, %): 194.0 [M^+] (100), 193.1 (49), 163.0 (49), 150.2 (31), 112.0 (14), 98.0 (19). Found, %: C 74.62; H 9.85; N 7.26. $C_{12}H_{19}NO$. Calculated, %: C 74.57; H 9.91; N 7.25.

3*H*-Spiro-1,3-benzoxazole-2,2'-tricyclo[3.3.1.1^{3,7}]-decane (IIIb) was prepared analogously from 3 g (0.02 mol) of adamantanone **I** and 2.7 g (0.025 mol) of amine **IIb**. Yield 4.1 g (85%), mp 156–157°C. ^{1}H NMR spectrum, δ, ppm: 1.59–1.88 m (10H, Ad), 1.99 s (2H, Ad), 2.20 d (2H, Ad, *J* 12.4 Hz), 3.68 s (1H, NH), 6.49–6.58 m (5H, 1,2-C_6H_4). Mass spectrum (EI, 70 eV), *m*/*e* (I_{rel}, %): 242.3 [M^+] (100), 241.5 (16). Found, %: C 75.67; H 7.96; N 5.79. $C_{16}H_{19}NO$. Calculated, %: C 75.63; H 7.94; N 5.80.

Spiro-3,1-benzoxazine-2,2'-tricyclo[3.3.1.1^{3,7}]-decan-4(1*H*)-one (IIIc) was prepared analogously from 3 g (0.02 mol) of adamantanone **I** and 2.75 g (0.02 mol) of amine **IIb**. Yield 4.85 g (90%). Compound **IIIc** is poorly soluble in propan-2-ol and insoluble in toluene, mp 246°C (subl.). IR spectrum, ν, cm^{-1}: 3364 (N–H), 1714 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.60–2.14 m (14 H, 2,2-Ad), 6.70 t (1H, 1,2-C_6H_4, *J* 5.5 Hz), 6.93 d (1H, 1,2-C_6H_4, *J* 5.0 Hz), 7.26 s (1H, NH), 7.34 t (1H, 1,2-C_6H_4, *J* 6.2 Hz), 7.59 d (1H, 1,2-C_6H_4, *J* 5.6 Hz). Mass spectrum (EI, 70 eV), *m*/*e* (I_{rel}, %): 269.1 [M^+] (69), 224.5 (100), 119.1 (68). Found, %: C 77.85; H 7.08; N 5.18. $C_{17}H_{19}NO_2$. Calculated, %: C 75.81; H 7.11; N 5.20.

^{1}H NMR spectra were recorded in CCl_4 on a Varian Mercury-300 (300 MHz) spectrometer relative to internal HMDS or TMS. Mass spectra were registered on a gas chromatography-mass spectrometer Varian Saturn 2100 T/GC 3900 (70 eV).

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