Russian Journal of Organic Chemistry, Vol. 39, No. 2, 2003, pp. 275–276. Translated from Zhurnal Organicheskoi Khimii, Vol. 39, No. 2, 2003, pp. 297–298.

SHORT COMMUNICATIONS

Epoxidation of Stereoisomeric Benzoylureas of Norbornene Series

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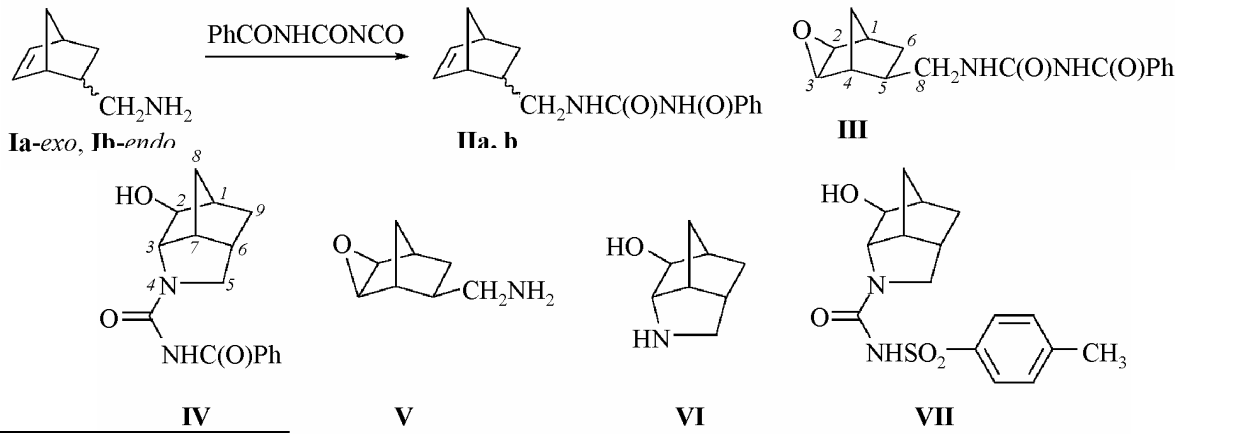
Received December 4, 2002

This work continues the studies on the synthesis of new derivatives of *exo*- and *endo*-5-aminomethylbicyclo[2.2.1]hept-2-enes (**Ia, b**), in particular, of ureas from norbornene series. It was shown previously that the direction of transformations of this group compounds under treatment with peracids depended on the orientation of substituents attached to the cage fragment: The reactions either afforded epoxides or heterocyclization products, substituted azatricyclo [4.2.1.$0^{3,7}$]-nonanes (azabrendanes) [1, 2].

The subject of this report is the synthesis and epoxidation of stereoisomeric benzoylureas **IIa, b**. Among the acylated ureas of various origin were found vitamins and drugs (barbital, biotin, caffeine, riboflavin etc.) [3]. Ureides including bicyclic carbon skeletons are poorly undersood although among them were found compounds possessing anticonvulsant and analgesic properties stronger that the respective qualities of related amides [4].

Steroisomeric amines (**Ia** *exo*, **Ib** *endo*) were prepared by a known procedure of reducing individual *exo*- and *endo*-5-cyanobicyclo[2.2.1]hept-2-enes with lithium aluminum hydride [5]. Benzoylureas **IIa, b** were synthesized by reaction of the amines with benzoyl isocyanate. Epoxidation of compounds **IIa, b** was carried out with monoperphthalic acid *in statu nascendi* obtained from phthalic anhydride and water solution of hydrogen peroxide.

It was established that oxidation of *exo*-isomer **IIa** gave rise to epoxide **III**, and from *endo*-isomer **IIb** arose substituted azabrendane **IV**. Epoxide **III** and azabrendane **IV** were also obtained by treating with benzoyl isocyanate epoxyamine **V** [6] and tricyclic amine **VI** described in [7].



The structure and homogeneity of compounds **II–IV** were confirmed by IR and ^{1}H NMR spectra. In the IR spectrum of compound III was observed a strong band in the region 858 cm^{-1} [ν(CO) in the epoxynorbornane fragment]. In the ^{1}H NMR spectrum the proton signals of this fragment appeared at 2.92 and 2.91ppm for H^2 and H^3 respectively. In the ^{1}H NMR spectrum of azabrendane **IV** were present characteristic signals: a doublet and a singlet belonging respectively to protons H^3 and H^2 at 3.11 and 3.39 ppm. In contrast to

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compound **VII**, epoxidation product of (*N*-tosyl)-carbamoyl-*endo*-5-aminomethylbicyclo[2.2.1]hept-2-ene [2], in whose ^{1}H NMR spectrum appeared two sets of signals with close values of chemical shift corresponding to two kinds of molecules, in the spectrum of compound **IV** was observed a single set of signals consistent with the assigned structure.

Amines **Ia, b** were prepared as described in [5], amines **V** and **VI** as described in [6, 7]. The characteristics of amines were consistent with the published data.

Benzoylureas (IIa, b, III, IV). To a solution of 0.22 g (0.0015 mol) of benzoyl isocyanate in 5 ml of benzene was added 0.0015 mol of an appropriate amine in 5 ml of benzene. The reaction completion was monitored by TLC. The separated precipitate was filtered off, washed with benzene, dried, and purified by crystallization from aqueous ethanol.

***exo*-5-(Benzoylureidomethyl)bicyclo[2.2.1]-hept-2-ene (IIa)**, yield 85%, mp 135–136°C. R_f (ether) 0.81. IR spectrum, cm^{-1}: 3340, 3164, 3058, 1718, 1668, 1537, 1280, 730. ^{1}H NMR spectrum, δ, ppm: 6.11 d.d (H^2), 6.05 d.d (H^3), 3.38 d.d (H^{8A}), 3.24 d.d (H^{8B}), 2.85 m (H^1), 2.70 m (H^4), 1.66 m (H^5), 1.43 d (H^{7a}), 1.35 d (H^{7s}), 1.30 d.d.d (H^{6x}), 1.24 d.t (H^{6n}), 10.51 s, 8.86 t (NH), 8.01 d, 7.54 d.d, 7.44 d (H arom). Found, %: N 10.31. $C_{16}H_{18}N_2O_2$. Calculated, %: N 10.37.

***endo*-5-(Benzoylureidomethyl)bicyclo[2.2.1]-hept-2-ene (IIb)**, yield 82%, mp 121–123°C. R_f (ether) 0.85. IR spectrum, cm^{-1}: 3375, 3051, 1700, 1665, 1570, 1522, 1264, 1240, 735. ^{1}H NMR spectrum, δ, ppm: 6.18 d.d (H^2), 6.03 d.d (H^3), 3.08 d.d (H^{8A}), 2.90 m (H^1), 2.88 d.d (H^{8B}), 2.84 m (H^4), 2.34 m (H^5), 1.90 d.d.d (H^{6x}), 1.44 d (H^{7s}), 1.29 d (H^{7a}), 0.62 d.t (H^{6n}), 10.48 s, 8.76 t (NH), 8.01 d, 7.54 d.d, 7.44 d (H arom). Found, %: N 10.41. $C_{16}H_{18}N_2O_2$. Calculated, %: N 10.37. *exo*-5-(Benzoylureidomethyl)-*exo*-2,3-epoxybicyclo[2.2.1]heptane (**III**), yield 87%, mp 126 C. R_f (ether) 0.78. IR spectrum, cm^{-1}: 3320, 3250, 3042, 1686, 1664, 1550, 1272, 1232, 858. ^{1}H NMR spectrum, δ, ppm: 3.19 d.d (H^{8A}), 3.17 d.d (H^{8B}), 2.92 d (H^2), 2.91 d (H^3), 2.43 m (H^1), 2.37 m (H^4), 1.81 m (H^5), 1.52 d.d.d (H^{6x}), 1.19 d (H^{7s}), 1.17 d.t (H^{6n}), 0.92 d (H^{7a}), 10.53 s, 8.82 t (NH), 8.01 d, 7.54 d.d, 7.44 d (H arom). Found, %: N 9.71. $C_{16}H_{18}N_2O_3$. Calcd., %: N 9.79.

4-(Benzoylcarbamoyl)-*exo*-2-hydroxy-4-azatricyclo[4.2.1.0^{3,7}]nonane (IV), yield 84%, mp 122°C (decomp.). R_f (ether) 0.77. IR spectrum, cm^{-1}: 3323, 3067, 1682, 1674, 1548, 1276, 1244, 1176, 1080. ^{1}H NMR spectrum, δ, ppm: 3.39 d.d (H^{5A}), 3.36 s (H^2), 3.18 d (H^{5B}),3.11 d (H^3), 2.45 m (H^7), 2.26 m (H^6), 2.12 m (H^1), 1.84 d (H^{8s}),1.80 m (H^{9x}), 1.45 d (H^{8a}), 0.81 d (H^{9n}), 10.53 s, 8.82 t (NH), 8.01 d, 7.54 d.d, 7.44 d (H arom). Found, %: N 9.81. $C_{16}H_{18}N_2O_3$. Calculated, %: N 9.79.

Epoxidation of benzoylureas (IIa, b). To a suspension of 0.40 g (0.0015 mol) of benzoylurea, 0.04 g (0.00075 mol) of carbamide, and 0.31 g (0.29 ml. 0.003 mol) of 35% water solution of hydrogen peroxide in 10 ml of ethyl acetate was added at stirring (20–25°C) 0.44 g (0.003 mol) of phthalic anhydride, and the stirring was continued till the end of reaction (TLC monitoring). The reaction mixture was treated with a saturated solution of sodium hydrogen carbonate till alkaline reaction, the organic layer was separaated, dried with calcined magnesium sulfate, the solvent was removed, the reaction product was crystallized from aqueous 2-propanol.

***exo*-5-(Benzoylureidomethyl)-*exo*-2,3-epoxy-bicyclo[2.2.1]heptane (III)**, yield 96%, the characteristics are in agreement with described above.

4-(Benzoylcarbamoyl)-*exo*-2-hydroxy-4-aza-tricyclo[4.2.1.0^{3,7}]nonane (IV), yield 76%, the characteristics are in agreement with described above.

IR spectra were recorded on a spectrometer Specord 75IR from samples pelletized with KBr. ^{1}H NMR spectra were registered on spectrometer Bruker DRX at operating frequency 500 MHz from solutions in deuterochloroform, internal reference TMS. The reaction progress was monitored and the purity of compounds synthesized was checked by TLC on Selicagel 60 F 254, eluent ether, development in iodine vapor. Elemental analysis was performed on Karlo Erba analyzer.

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