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SHORT COMMUNICATIONS

Epoxidation of *N*-(10-Camphorsulfonyl)-*endo*-5-(aminomethyl)-bicyclo[2.2.1]hept-2-ene

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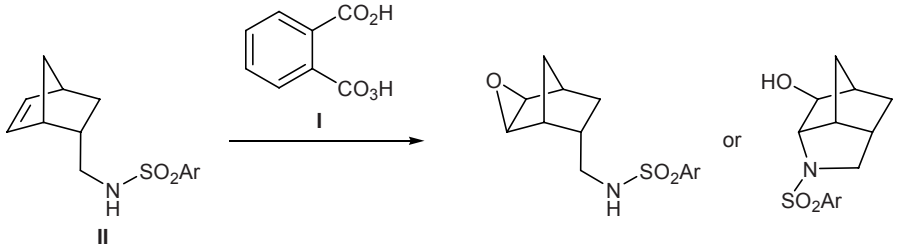
In the past decade a series of studies has been performed on stereochemical aspects of epoxidation of bicyclo[2.2.1]hept-2-en-*exo*-5- and -*endo*-5-ylmethanamine derivatives by the action of peroxyphthalic acid (**I**). Substituted norbornenes with *exo* orientation of substituent in the bicyclic fragment (such as ureas, carboxamides, and sulfonamides) were thus converted into the corresponding epoxy derivatives, while the behavior of their *endo* isomers was ambiguous. Like the corresponding *exo* isomers, carboxamides gave rise to oxirane derivatives [1], and aryl-, arylsulfonyl-, and benzoylureas, as well as phosphonic amides, underwent heterocyclization to produce substituted 4-azatricyclo[4.2.1.$0^{3,7}$]nonanes (azabrendanes) [2]. *endo* Stereoisomers of arenesulfonamides (**II**) reacted along both pathways, depending on the substituent on the nitrogen atom (Scheme 1). Heterocyclization occurred in the epoxidation of all sulfonamides of the *endo* series having one substituent in the benzene ring and some disubstituted analogs [3, 4], but arenesulfonamides having electron-withdrawing substituents or bulky substituents in the *ortho* position of the benzene ring failed to react in such a way [4]. No heterocyclization occurred in the epoxidation of *N*-(bicyclo[2.2.1]hept-2-en-*endo*-5-ylmethyl)cyclohexanesulfonamide [5]. Some epoxides and azabrendanes obtained by the above reactions were found to exhibit biological activity, specifically neurotropic. Azabrendanes, as well as other brendane hetero analogs, showed a strong herbicidal activity and an appreciable growth-stimulating effect [6].

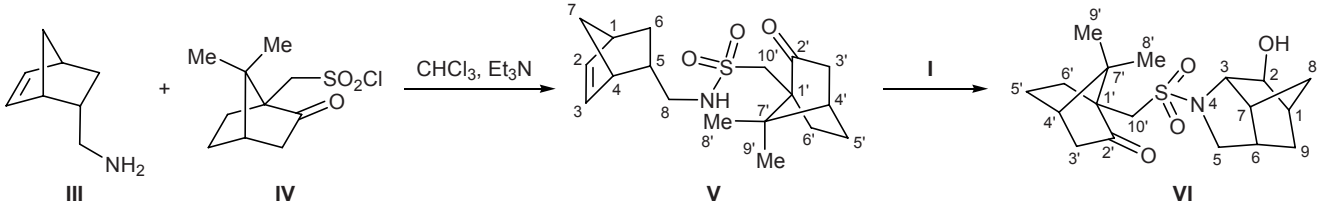
In terms of solving problems relevant to the "structure–properties" relations we examined epoxidation of sulfonamide **V** which was synthesized by reaction of (bicyclo[2.2.1]hept-5-en-*endo*-2-yl)methanamine (**III**) with camphor-10-sulfonyl chloride (**IV**). Molecule **V** contains an additional cage-like fragment at the rear (*endo*) side of the bicyclic skeleton. The oxidation of sulfonamide **V** was carried out using monoperoxyphthalic acid generated *in situ* from phthalic anhydride and 50% aqueous hydrogen peroxide [4, 5]. The only product was tricyclic derivative **VI** whose structure demonstrates that the heterocyclization is not hampered by the presence of a bulky camphor moiety in the vicinity of the reaction center.

The product structure was confirmed by IR and ^{1}H and ^{13}C NMR spectroscopy, including homo- (COSY)

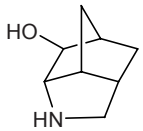
Scheme 1.



Scheme 2.



and ^{1}H–^{13}C heteronuclear correlation techniques (HMQC, HMBC). The ^{1}H NMR spectrum of oxidation product **VI** lacked signals from protons typical of epoxy norbornanes (δ 3.10–3.20 ppm), but a singlet at δ 3.71 ppm and a doublet at δ 3.61 ppm ($^{3}J_{3,7}$ = 5.1 Hz) were present; the latter signals were assigned to 2-H and 3-H in the azabrendane fragment [3–5]. The ^{13}C NMR spectrum of **VI** contained signals from C^{2} (δ_C 81.5 ppm) and C^{3} (δ_C 69.5 ppm), as well as other signals typical of parent structure **VII** [1].



VII

The fact that the carbonyl group in the camphor fragment remained intact (δ_C 215.4, 216.0 ppm) indicated its inertness in the oxidation according to Baeyer–Villiger. Some signals were doubled due to the presence of diastereoisomeric heterocyclization products.

***N*-(Bicyclo[2.2.1]hept-5-en-*exo*-2-ylmethyl)-(7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-methanesulfonamide (V).** A solution of 0.80 g (3.2 mol) of sulfonyl chloride **IV** was added dropwise under stirring to a mixture of 0.40 g (3.2 mmol) of amine **III**, 0.32 g (3.2 mmol) of triethylamine in 8 ml of chloroform, and the mixture was stirred until the reaction was complete according to the TLC data. The solvent was removed, and the residue was washed with 10 ml of 5% hydrochloric acid and recrystallized from propan-2-ol. Yield 75%, mp 94–95°C, R_f 0.91. IR spectrum, ν, cm^{-1}: 3300, 3072, 1741, 1335, 1154, 730. ^{1}H NMR spectrum, δ, ppm: 0.49 d (1H, *exo*-6-H), 0.79 s and 1.01 s (3H each, CH_3), 1.22 d (1H, *anti*-7-H), 1.33 d.d (1H, *syn*-7-H), 1.39 d.d (1H, *endo*-5′-H), 1.51 m (1H, *endo*-6′-H), 1.79 d.d.d (1H, *exo*-6-H), 1.91 m (1H, *endo*-3′-H), 1.94 m (1H, *exo*-5′-H), 2.04 t (1H, 4′-H), 2.18 m (1H, 5-H), 2.33 d.d (1H, *exo*-3′-H), 2.36 m (1H, *exo*-6′-H), 2.61 m (1H, 8-H_A), 2.72 m (1H, 8-H_B), 2.76 m (1H, 1-H), 2.84 br.s (1H, 10′-H_A), 2.86 s (1H, 4-H), 3.26 m (1H, 10′-H_B), 5.97 d.d (1H, 3-H), 6.16 d.d (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 20.0 and 20.2 ($C^{8'}$, $C^{9'}$), 25.2 ($C^{6'}$), 27.0 ($C^{5'}$), 30.5 (C^{6}), 39.6 (C^{5}), 42.7 ($C^{3'}$, $C^{4'}$), 42.8 (C^{1}), 44.3 (C^{4}), 47.4 (C^{8}), 48.1 ($C^{10'}$), 48.2 ($C^{7'}$), 49.6 (C^{7}), 58.5 ($C^{1'}$), 133.0 (C^{3}), 137.8 (C^{2}), 215.4 ($C^{2'}$).

1-(*exo*-2-Hydroxy-4-azatricyclo[4.2.1.0^{3,7}]nonan-4-ylmethylsulfonyl)-7,7-dimethylbicyclo[2.2.1]-heptan-2-one (VI). A 50% aqueous solution of hydrogen peroxide, 0.44 g (6.7 mmol), was added dropwise under stirring to a suspension of 0.75 g (2.2 mmol) of sulfonamide **V**, 0.06 g (1.1 mmol) of urea, and 0.66 g (4.4 mmol) of phthalic anhydride in 10 ml of ethyl acetate. The mixture was stirred until the reaction was complete according to the TLC data. Phthalic acid was neutralized with a saturated solution of sodium carbonate, the organic phase was separated, and the aqueous phase was extracted with three portions of chloroform. The extracts were combined, dried over calcined magnesium sulfate, and evaporated. Yield 67%, oily substance, R_f 0.74. IR spectrum, ν, cm^{-1}: 3500, 1755, 1341, 1164, 855. ^{1}H NMR spectrum, δ, ppm: 0.89 s (3H, $C^{8'}H_3$), 1.00 m (1H, *endo*-9-H), 1.13 s (3H, $C^{9'}H_3$), 1.44 m (2H, *anti*-8-H, *endo*-5′-H), 1.64 m (1H, *endo*-6′-H), 1.92 m (2H, *syn*-8-H, *exo*-9-H), 1.96 d (1H, *endo*-3′-H), 2.05 m (1H, *exo*-5′-H), 2.11 m (1H, 4′-H), 2.19 br.s (1H, 1-H), 2.36 br.s (2H, 6-H, *exo*-3′-H), 2.51 m (1H, *exo*-6′-H), 2.68 m (1H, 7-H), 2.84 d.d (1H, 10′-H_A), 3.28 m (1H, 5-H_A), 3.40 m (1H, 5-H_B), 3.48 m (1H, 10′-H_B), 3.61 d (1H, 3-H), 3.71 br.s (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 20.0 and 20.2 ($C^{8'}$, $C^{9'}$), 25.4 ($C^{6'}$), 27.2 ($C^{5'}$), 33.0 (C^{9}), 34.1 (C^{8}), 37.2 (C^{6}), 41.6 (C^{1}), 42.9 ($C^{8'}$), 43.0 ($C^{4'}$), 45.2 (C^{7}), 46.1 ($C^{3'}$), 48.2 ($C^{7'}$), 54.6 (C^{5}), 58.5 ($C^{1'}$), 69.5 (C^{3}), 81.5 (C^{2}), 216.0 (C=O).

The IR spectra were recorded in KBr on a UR-20 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured on a Varian VXR spectrometer at 400 and 100 MHz, respectively, from solutions in chloroform-*d* using tetramethylsilane as internal reference. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using diethyl ether as eluent; development with iodine vapor.

REFERENCES

1. Kasyan, L.I., Tarabara, I.N., Savel'eva, O.A., and Kasyan, A.O., *Heteroatom Chem*., 2001, vol. 12, p. 119.
2. Kas'yan, L.I., Kas'yan, A.O., Okovityi, S.I., and Tarabara, I.N., *Alitsiklicheskie epoksidnye soedineniya. Reaktsionnaya sposobnost'* (Alicyclic Epoxy Compounds. Reactivity). Dnepropetrovsk: Dnepropetr. Univ., 2003.
3. Kasyan, L.I., Sereda, S.V., Potekhin, K.A., and Kasyan, A.O., *Heteroatom Chem*., 1997, vol. 8, p. 177.
4. Kas'yan, A.O., Karpenko, D.V., and Kas'yan, L.I., *Russ. J. Org. Chem*., 2005, vol. 41, p. 1764.
5. Kasyan, L.I., Tarabara, I.N., Kasyan, A.O., Okovityy, S.I., Tokar, A.V., Shishkina, S.V., and Shishkin, O.V., *Tetrahedron*, 2007, vol. 63, p. 1790.
6. US Patent no. 4828603, 1989; *Ref. Zh., Khim*., 1992, no. 1O428P.