

REACTIONS OF CAMPHENE OXIDE WITH SULFUR-CONTAINING NUCLEOPHILES

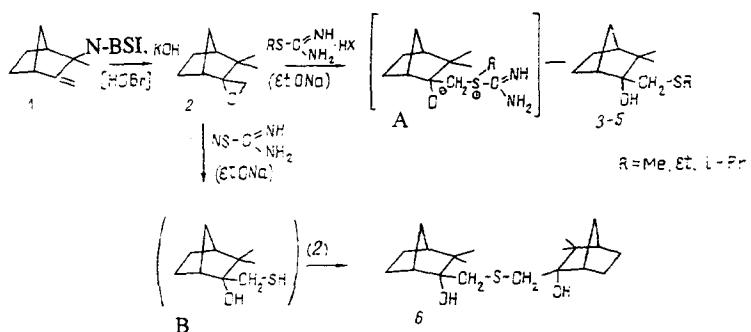
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Sulfur-containing derivatives of the camphene series have been obtained by the nucleophilic addition of isothiouronium salts and thiourea under the conditions of base catalysis.

Reactions of sulfur-containing electrophiles with olefins form one of the commonest methods of introducing a sulfide function into hydrocarbon molecules. In the bicyclic monoterpenoid series the performance of the regio- and, if possible, stereoselective synthesis of terpene sulfides is complicated by the well known tendency of terpenes to undergo isomeric transformations. In view of this, in a number of cases the use of the corresponding terpene oxides as synthons for these purposes is promising.

In contrast to the epoxide of 3-carene or, for example, that of limonene, camphene oxide has scarcely been studied in its reactions with nucleophilic reagents. We obtained camphene oxide (2) by the action of N-bromosuccinimide (N-BSI) on racemic camphene, followed by treatment of the resulting bromohydrin with alkali — by analogy with the method of synthesizing 3-carene oxide [1]. The authors of papers devoted to the synthesis of (2) leave open the question of the steric position of the oxide ring in the molecule [2]. Furthermore, the PMR spectrum of compound (2) does not permit its spatial structure to be deduced but only shows that a camphene oxide, and not other theoretically possible functional derivatives of bicyclo[2.2.1]heptane, has been formed.



The camphene oxide that we obtained most probably had the configuration (2), in accordance with the preferential nature of the electrophilic attack of the vinylidene fragment by the bromine ion from the side of the *endo*-methylene bridge (which is characteristic for bicyclo[2.2.1]heptenes [3]), with subsequent *trans*-addition of a hydroxyl anion.

We then studied the interaction of camphene oxide (2) with S-methyl-, S-ethyl-, and S-isopropylisothiouronium salts and thiourea in the presence of sodium ethanolate. As the result of the reaction, in each case individual products (3-6) were formed (with yields of 48-56%) and were isolated in the pure state by column chromatography on silica gel. The yields of compounds (3-6) were low because of resinification.

The elemental analyses of the products of the reactions of camphene oxide with the isothiouronium salts corresponded to the addition of one thiol fragment to the oxide. According to the PMR spectra of the compounds (3) (R = Me), (4) (R = Et), and (5) (R = i-Pr) (presence of signals of a gem-dimethyl fragment at 0.90-1.05 ppm, of the protons of the $-\text{CH}_2-$ group

TABLE 1. PMR Spectra of Compounds (2-6) (δ , ppm)

Compound	CH ₃ -8,9 (6H)	CH ₂ -10 (2H)	SR	OH
2	0.83 s	2.5 s	—	—
3	0.92 s; 1.05 s	2.63; 2.84 (AB centers) 13 Hz	2.25 s (3H, SCH ₃)	2.63 s
4	0.90 s; 1.00 s	2.58; 2.79 (AB centers) 13 Hz	1.35 t (3H, SCH ₂ CH ₃) 2.50 b (2H, SCH ₂ CH ₃)	2.55 s
5	0.90 s; 1.00 s	2.68; 2.89 (AB centers) 13 Hz	1.25 d, 1.27 d (6H, SCH(CH ₃) ₂) 6.6 Hz 2.86 m (1H, SCH(CH ₃) ₂)	2.70 s
6	1.00 c; 1.10 s	2.63; 2.84 (AB centers) 13.0 Hz (4H-10,10)	—	2.80 s

at 2.58-2.89 ppm (AB centers), of the hydroxyl protons at 2.55-2.80 ppm, and of the hydrogen atoms of the thioalkyl function) the nucleophilic thioalkylation of camphene oxide had taken place regiospecifically with retention of the camphene skeleton of the molecule. The IR spectra of compounds (3-5) contained the bands of O—H stretching vibrations (ν 3500 cm⁻¹) and of deformation and stretching vibrations of a C—O bond (ν 1115 cm⁻¹) that are characteristic for compounds with tertiary hydroxyls. The spectral results unambiguously showed the formation of the 10-alkylthiocamphan-3-ols (3-5), probably proceeding through the intermediate A. The spatial position of the hydroxyl in compounds (3-5) is given in accordance with the presumed structure of the oxide (2).

On the basis of the results of elementary analysis (S = 9.72%) and of IR (absence of bands corresponding to vibrations of a S—H bond) and PMR spectroscopies (Table 1), the product of the reaction of camphene oxide (2) with thiourea was assigned the structure of 10,10-thiodi(camphan-3-ol) (6). Compound (6) was most probably formed through intermediate B, which, under the reaction conditions (EtONa), readily attacked an oxide molecule, leading to the formation of an adduct with two terpene fragments. The structure of the sulfide (6) and the scheme of its formation are in harmony with results that we obtained previously on the reactions of 3-carene oxides with thiourea [4].

Thus, the nucleophilic thiylation reactions of camphene oxide, being characterized by a high degree of regioselectivity (on the isolation of compound (3-6) by column chromatography no other regioisomers were detected) form a convenient method for the synthesis of sulfur-containing derivatives of the camphene series.

EXPERIMENTAL

PMR spectra were measured in CCl₄ on Bruker WM-250 (250 MHz) and Varian HA-100 (100 MHz) spectrometers, with TMS as internal standard, IR spectra (CCl₄) on a Specord 75 IR spectrometer, and refractive indices on a IRF-454 BM refractometer. Elementary analyses corresponded to the calculated figures.

Syntheses of Compounds (3-6). A solution of sodium ethanolate (0.5 g (0.02 mole) of Na in 30 ml of C₂H₅OH (abs.)) was prepared in a three-necked flask fitted with a stirrer, a calcium chloride tube, and a reflux condenser, after which 0.01 mole of camphene oxide and 0.015 mole of an isothiouronium salt were added. The reaction mixture was stirred at 90°C for 5 h, and it was then poured into 100 ml of water and extracted with ether. The extract was dried with MgSO₄, the ether was distilled off, and compounds (3-6) were isolated by column chromatography on silica gel (hexane—ether). Yields: 3 (C₁₁H₂₀OS) — 58%, 4 (C₁₂H₂₂OS) — 50%, 5 (C₁₃H₂₄OS) — 52%, 6 (C₂₀H₃₄O₂S) — 48%.

n_d^{20} : 3 — 1.5160, 4 — 1.5155, 5 — 1.5020. mp 6 — 89-91°C. R_f (hexane—ether, 10:1): 3' — 0.25, 4 — 0.30, 6 — 0.1.

REFERENCES

1. B. A. Arbuzov, Z. G. Isaeva, and I. B. Nemirovskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1401 (1969).
2. B. A. Arbuzov, *Investigations in the Field of Isomeric Transformations of Bicyclic Terpene Hydrocarbons and their Oxides* [in Russian], Kazan' (1936).
3. Kurita Yasuyuki and Takayama Chiyozo, *Tetrahedron*, **46**, 3789 (1990).
4. N. P. Artemova, G. Sh. Bikbulatova, V. V. Plemenkov, and Yu. Ya. Efremov, *Zh. Obshch. Khim.*, **61**, 1484 (1991).