

Rearrangements of Neoclovene Epoxides in Acidic Media*

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Received December 13, 2000

Abstract—Rearrangements of neoclovene epoxides in the presence of a solid superacid ZrO_2/SO_4^{2-} and in formic acid were investigated. In the latter case a ketone was obtained with a previously unknown carbon skeleton. The most probable pathway of its formation was derived from calculations by molecular mechanics and quantum-chemical methods.

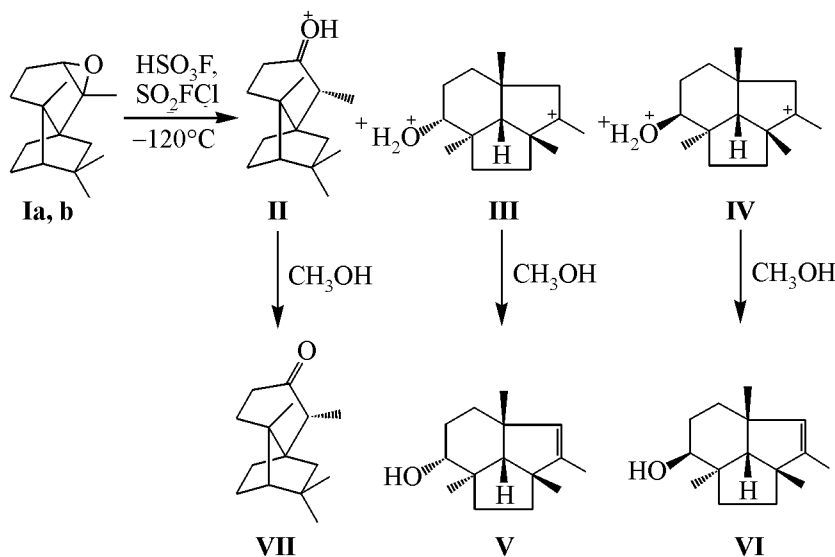
We showed formerly that protonation of a mixture of epimeric neoclovene epoxides (**Ia, b**) by a system HSO_3F-SO_2FCl formed ions **II-IV** that on “quenching” with a mixture ethanol-ethyl ether afforded epimeric alcohols **V** and **VI** in 25 and 14% yield respectively alongside ketone (**VII**) (24%) [1] (Scheme 1).

In extension of investigation on epoxides **Ia, b** rearrangements in various acidic media we studied their behavior in the presence of a solid superacid ZrO_2/SO_4^{2-} at 20°C and at boiling in formic acid. In the former case we obtained a mixture of epimeric ketones **VII** (55%, here and hereinafter the content from GLC data), and (1*S*,2*S*,6*S*,7*S*)-2,6,8,8-

tetramethyltricyclo[5.2.2.0^{1,6}]-undecen-3-one (**VIII**) (24%). After boiling of epoxides **Ia, b** in formic acid was isolated a mixture of ketone (**VII**) (53%) and (1*S*,4*S*,7*S*,9*S*)-5,5,7,9-tetramethyltricyclo[5.4.0.0^{4,9}]-undecen-8-one (**IX**) (33%) (Scheme 2).

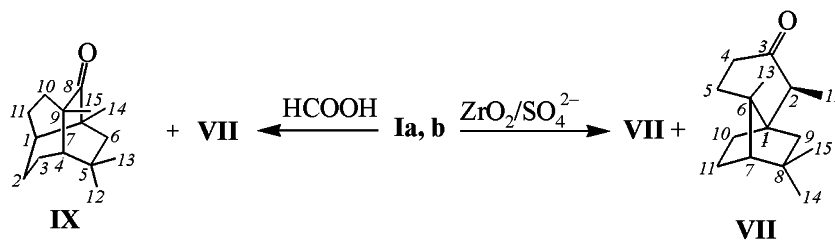
The structure of ketone **VII** was previously derived from ¹H and ¹³C NMR spectra and also from the form of dispersion of optical rotation curve [1]. The structure of epimer **VIII** also was established from ¹H and ¹³C NMR spectra. Ketones **VII** and **VIII** were previously obtained by the other procedures, and their structures were established from the chemical data and dispersion of optical rotation curves [2]. The NMR spectra of ketone **VIII** we recorded for the first

Scheme 1.

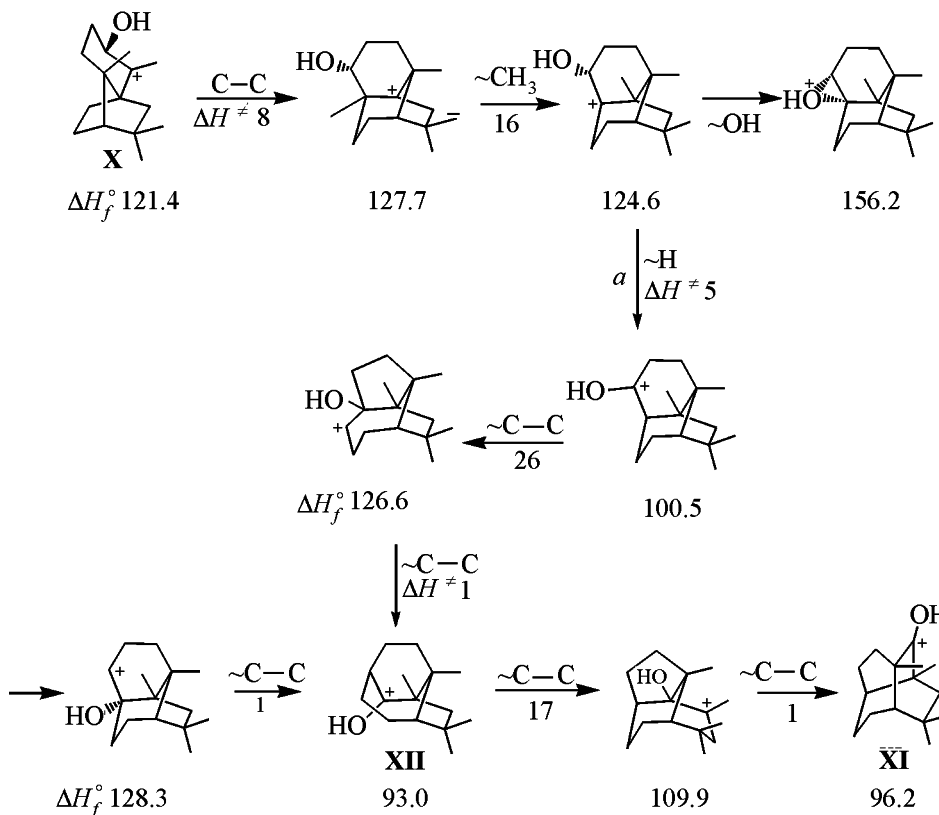


* The authors are grateful to the Russian Foundation for Basic Research for financial support in acquiring a license for using the Cambridge Structural Database (grant no. 99-07-90133).

Scheme 2.



Scheme 3.

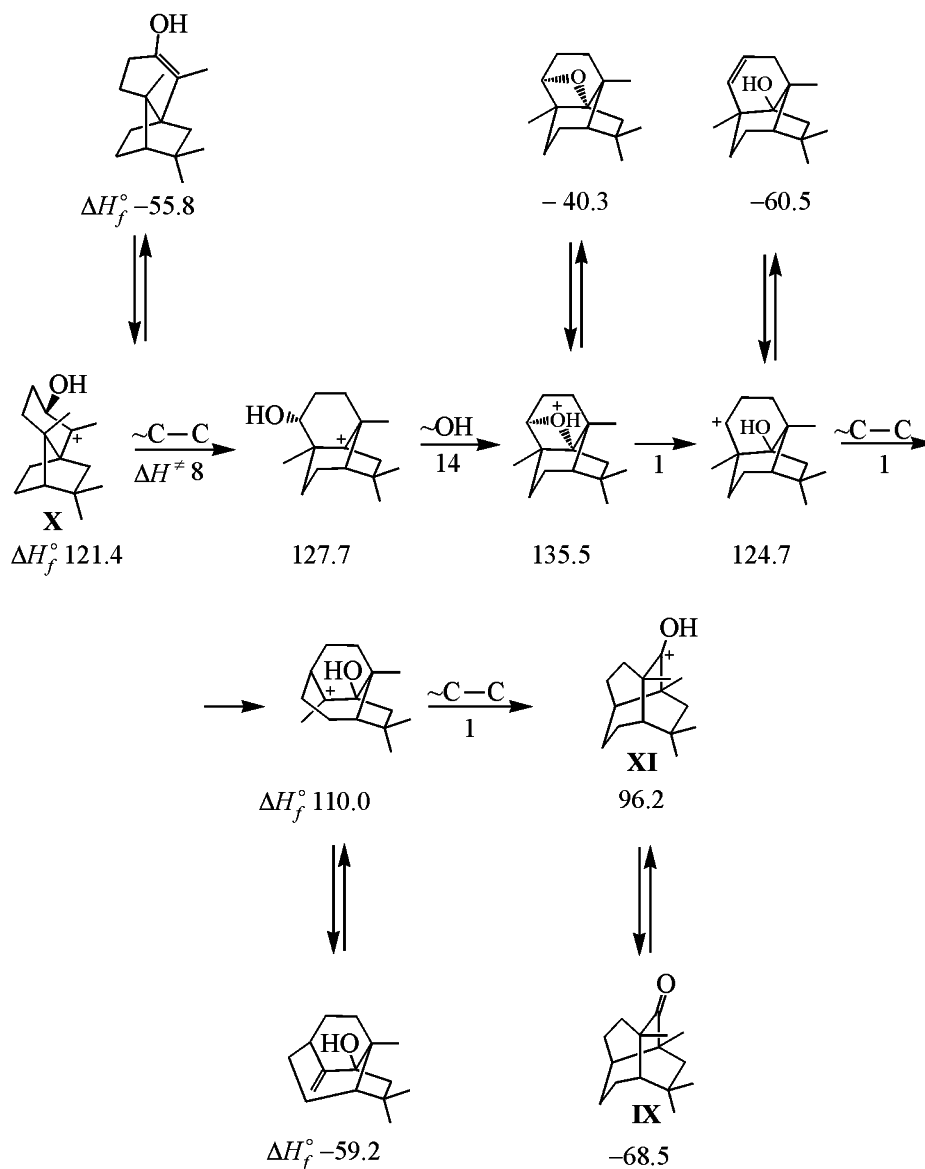


-time. The structure of ketone **IX** was derived from two-dimensional correlation spectrum ^{13}C - ^{13}C (2D-INADEQUATE).

We did not find any compounds with the structure of ketone **IX** in the Cambridge Structural Database [3]. We performed a search for probable pathways of intramolecular rearrangement of the original cation **X** into the final cation **XI** with the use of ICAR software [4]. Since ketone **VII** on boiling in formic acid do not yield compound **IX**, and thus cation **II** is stable under these conditions, we do not consider as the initial ion the ion epimeric to cation **X**. As previously [5] we regarded as permissible only 1,2-shifts of C-C and C-H bonds; thus we obtained the shortest 7-stage route of rearrangements (Scheme 3, path *a*).

The drawback of this route is a large "ascent" (the difference ΔH_f° between the least and the most stable ions along the total route calculated in kcal mol⁻¹ here and further in all the Schemes) equal to 26.1 kcal mol⁻¹. Addition to the permissible shifts of 1,2 C-O bond shift provides the shortest 7-stage route (Scheme 3, path *b*). However this rearrangements path has the same disadvantage: the "ascent" equals to 34.8 kcal mol⁻¹. Besides in the path appears ion **XII** that is more stable than the final experimental ion **XI**. Therefore we added to the permissible shifts 1, *n*-shifts of the C-O bond. As a result we found the shortest 5-stage route containing a 1,3-shift of OH group (Scheme 4). This rearrangement version is significantly more feasible since here the "ascent" amounts to 14.1 kcal mol⁻¹.

Scheme 4.



Note that experimentally obtained ketone **IX** is the most stable among the neutral compounds appearing in Scheme 4.

The calculation of gas-phase formation heats of carbocations were carried out by semiempirical AM1 procedure [6], those of the neutral compounds were performed by MMX routine. The height of barriers to rearrangements save that of 1,3-shift of OH group were estimated taking into account the orbital factor along procedure [7]. The barrier of the 1,3-shift of OH group was evaluated by AM1 procedure.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were registered on spectrometer Bruker AM-400 at operating frequencies 400.13 MHz (^1H) and 100.61 MHz (^{13}C) from solutions in $\text{CCl}_4\text{-CDCl}_3$ (~1:1 by volume). The signal of chloroform was used as internal reference (δ 7.24, δ_{C} 76.90 ppm).

The structure of ketone **IX** was derived from two-dimensional correlation spectra $^{13}\text{C}\text{-}^{13}\text{C}$ (2D-INADEQUATE, the recording conditions were

optimized for $^1J_{C-C}$ 35 Hz) and $^{13}C-^1H$ (COSY, the value $^1J_{C-H}$ used was 134 Hz). β -Configuration was assigned to the methyl group attached to C^2 carbon in ketone **VIII** proceeding from the data of [1, 2].

The checking of purity of the initial reagents and the analysis of reaction products was carried out by GLC on chromatograph Biokhrom -1 equipped with flame-ionization detector, oven temperature 110–180°C, carrier gas helium, and the following columns: (a) glass capillary column 53000×0.26 mm, stationary phase XE-60; b) quartz capillary column 13000×0.3 mm, stationary phase CE-54. Elemental composition of compounds obtained was derived from high resolution mass spectra measured with Finnigan MAT 8200 instrument. GC-MS analysis of reaction products was carried out on Hewlett Packard 618100A device. The specific rotations were measured with spectrometer Polamat A from solutions in $CHCl_3$. IR spectrum was registered on Bruker Vector 22 instrument. The procedure for preparation of sulfated zirconium oxide was described in [8]. The catalyst was calcined just before the experiment for 2 h at 500°C. The solvent CH_2Cl_2 was passed through a column with calcined alumina. The compounds obtained were separated by column chromatography on SiO_2 (Czechia).

The initial neoclovene was prepared by procedure [9], $[\alpha]_{580}^{27} -62.4^\circ$ (c 9.3, $CHCl_3$), epoxides **Ia**, **b** were obtained by procedure [1].

Isomerization of epoxides Ia, b on ZrO_2/SO_4^{2-} . To a dispersion of 0.4 g of ZrO_2/SO_4^{2-} in 10 ml of CH_2Cl_2 was added 0.2 g of epoxides **Ia**, **b** in 2 ml of CH_2Cl_2 , and the mixture was stirred for 0.5 h at 20°C. After workup of the reaction mixture it was passed through a column packed with alumina of **IV** grade activity, eluent ethyl ether. As a result we obtained 0.194 g of a mixture of ketones **VII** (55%) and **VIII** (24%) according to GLC data. This mixture was twice subjected to column chromatography on SiO_2 (40–100 μ , Czechia), gradient elution with a mixture hexane–ethyl ether (from 0 to 20%). We separated 0.03 g of ketone **VII**, $[\alpha]_{580}^{27} -84.7^\circ$ (c 2.9, $CHCl_3$), 1H and ^{13}C spectra correspond to the published data [1]; and 0.042 g of ketone **VIII**, $[\alpha]_{580}^{25} -45.8^\circ$ (c 2.4, $CHCl_3$). Found: M 220.18238. $C_{15}H_{24}O$. Calculated: M 220.18270. 1H NMR spectrum (δ , ppm, J , Hz): 0.84 d (H^{9n} , $J_{9n,9k}$ 12), 1.02 s and 1.23 s ($C^{14}H_3$, $C^{15}H_3$), 1.07 d ($C^{12}H_3$, $J_{12,2}$ 7.5), 1.23 m and 1.39 m ($2H^{10}$), 1.40 d ($C^{13}H_3$, $J_{13,5a}$ 1), 1.42 d (H^7 , $J_{7,11k}$ 4), 1.50 d.m (H^{5e} , $J_{5e,5a}$

13), 1.61 m ($2H^{11}$), 1.96 d.d (H^{9k} , J 12, $J_{9k,10k}$ 3.5), 2.08 m (H^{5a}), 2.14 d.d.d.d (H^{4e} , $J_{4e,4a}$ 13.5, $J_{4e,5a}$ 5, $J_{4e,5e}$ 1.5, $J_{4e,2}$ 1.5), 2.31 br.q (H^{2e} , J 7.5), 2.68 d.d.d (H^{4a} , J 13.5, $J_{4a,5a}$ 13, $J_{4a,5e}$ 5). ^{13}C NMR spectrum (δ_C , ppm): 52.76 s (C^1), 49.82 d (C^2), 216.91 s (C^3), 33.64 t (C^4), 30.11 t (C^5), 48.25 s (C^6), 56.16 d (C^7), 37.50 s (C^8), 46.41 t (C^9), 35.79 t (C^{10}), 22.52 t (C^{11}), 13.91 q (C^{12}), 21.82 q (C^{13}), 31.69 q and 31.66 q (C^{14} , C^{15}).

Isomerization of epoxides Ia, b in formic acid.

A solution of 0.5 g of epoxides **Ia**, **b** in 20 ml of $HCOOH$ was boiled for 2 h. After workup the residue (0.41 g) was passed through a column packed with alumina of **IV** grade activity, eluent ethyl ether. We obtained 0.37 g of a mixture of ketones **VII** and **IX** containing by GLC data 53 and 37% respectively. The mixture was subjected to column chromatography on SiO_2 (100–160 μ , Czechia), eluents hexane and 2% solution of ethyl ether in hexane. We isolated 0.09 g of ketone **IX**, $[\alpha]_{580}^{23} +210.5^\circ$ (c 2.26, $CHCl_3$), and 0.136 g of ketone **VII** (characterized by 1H NMR spectrum). Mass spectrum of ketone (**IX**), m/z (I , %): 220 (100) M^+ , 137 (33), 136 (50), 125 (54), 123 (34), 108 (63), 96 (32), 91 (30), 41 (38). Found: M 220.18245. $C_{15}H_{24}O$. Calculated: M 220.18270. IR spectrum (CCl_4 , c 2%, d 0.1, cm^{-1}): 1718 ($C=O$). 1H NMR spectrum of ketone **IX** (δ , ppm, J , Hz): 0.77 s and 0.85 s ($C^{12}H_3$, $C^{13}H_3$), 0.83 s ($C^{14}H_3$), 0.94 s ($C^{15}H_3$), 1.15 d (H^6 , $J_{6,6'}$ 14), 1.23 d.d.d (H^{10} , $J_{10,10'}$ 13.5, $J_{10,11'}$ 10, $J_{10,11}$ 1.5), 1.32 d.d (H^4 , $J_{4,3}$ 4, $J_{4,3'}$ 4), 1.36 br.d.d (H^{11} , $J_{11,11'}$ 14, $J_{10,11'}$ 10), 1.45 m ($H^{11'}$), 1.47 m (H^2), 1.63 m (H^1), 1.73 m (H^3), 1.93 d ($H^{6'}$, J 14), 1.96–2.08 m ($H^{3'}$, $H^{2'}$), 2.18 d.d.d ($H^{10'}$, J 13.5, $J_{10',11}$ 10, $J_{10',11'}$ 10). ^{13}C NMR spectrum (δ_C , ppm): 45.95 d (C^1), 28.34 t (C^2), 24.82 t (C^3), 55.38 d (C^4), 34.22 s (C^5), 49.76 t (C^6), 45.83 c (C^7), 225.63 s (C^8), 48.25 s (C^9), 38.51 t (C^{10}), 24.85 t (C^{11}), 32.53 q and 29.61 q (C^{12} , C^{13}), 22.57 q (C^{14}), 25.57 q (C^{15}).

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