

Ozonolysis of Alkenes and Study of Reactions of Polyfunctional Compounds: LXIII.* A New Procedure for Direct Reduction of 1-Methylcycloalkene Ozonolysis Products to Hydroxyketones**

G. Yu. Ishmuratov, R. Ya. Kharisov, M. P. Yakovleva, O. V. Botsman,
R. R. Muslukhov, and G. A. Tolstikov

Institute of Organic Chemistry, Ufa Research Center, Russian Academy of Sciences,
pr. Oktyabrya 71, Ufa, 450054 Bashkortostan, Russia

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Abstract—A procedure was proposed for direct reduction of peroxide products resulting from ozonolysis of 1-methylcycloalkenes to the corresponding hydroxyketones by the action of sodium triacetoxohydridoborate.

One of the most important problems in the synthesis of low-molecular bioregulators is development of convenient preparative routes to aliphatic α,ω -functionalized compounds capable of being selectively modified through the terminal groups. A promising method of synthesis of such compounds is based on ozonolysis of cycloalkenes.

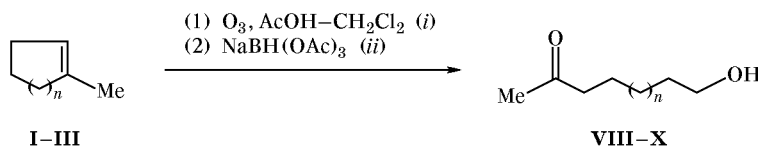
The known procedures for transformation of 1-methylcycloalkenes into hydroxyketones through ozonolysis include initial conversion of primary peroxide products into ketoaldehydes and subsequent transformation of the formyl group into hydroxy by the action of hydride reagents, e.g., $\text{Li}(t\text{-BuO})_3\text{AlH}$ [3] or $\text{NaBH}(\text{OAc})_3$ [4]; also, direct reduction of the ozonides by BH_3 complexes with pyridine, triethylamine, and THF [5] and electrochemical reduction [6] were reported. The second approach seems to be more attractive, though the yields of the target hydroxyketones do not exceed 65%.

In an attempt to develop this approach we have demonstrated the high efficiency of using sodium triacetoxohydridoborate as reducing agent for products of ozonolysis of 1-methylcycloalkenes **I–VII**. The target hydroxyketones **VIII–XIV** (Schemes 1, 2) were obtained in high yields (> 85%), and impurities of the corresponding diols did not exceed 3% (according to GLC). Compound **VII** possessing two equivalent double bonds was subjected to partial ozonolysis under the conditions described in [7].

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer from thin films. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 instrument operating at 300.13 MHz for ^1H and 75.47 MHz for ^{13}C ; chloroform-*d* was used as solvent; the chemical shifts were measured relative to tetramethylsilane. Gas-liquid

Scheme 1.

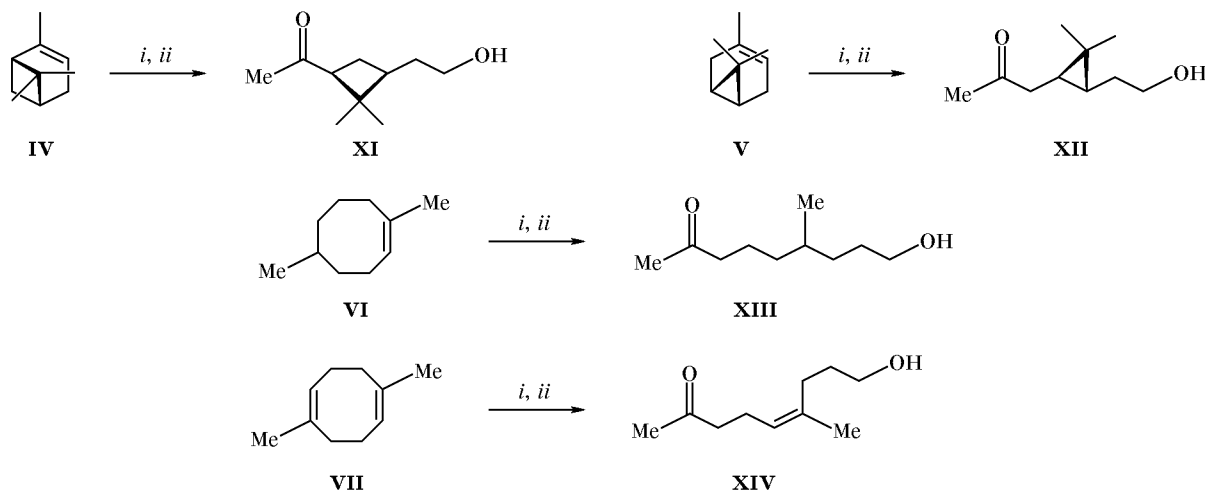


I, VIII, $n = 1$; **II, IX**, $n = 2$; **III, X**, $n = 6$.

* For communication LXII, see [1].

** For preliminary communication, see [2].

Scheme 2.



chromatography was performed on a Chrom-5 instrument [1.2-m column packed with 5% of SE-30 on Chromaton N-AW-DMCS (0.16–0.20 mm); oven temperature 50–300°C; carrier gas helium]. The specific rotations were determined on a Perkin-Elmer 241MC polarimeter.

General procedure for synthesis of hydroxyketones VIII–XIII. An ozone–oxygen mixture was bubbled through a solution of 14.4 mmol of olefin I–VI and 28.7 mmol of glacial acetic acid in 40 ml of methylene chloride, stirred at –4 to –2°C until 15 mmol of ozone was absorbed (ozonizer efficiency 40 mmol/h). The mixture was purged with argon, diluted with 20 ml of methylene chloride, and added with stirring (10°C) to a suspension of NaBH(OAc)₃, [which was preliminarily prepared by adding a solution of 11.9 g (198 mmol) of glacial acetic acid in 20 ml of methylene chloride to a suspension of 2.5 g (66 mmol) of sodium tetrahydridoborate in 100 ml of methylene chloride and subsequent stirring for 2 h]. The mixture was allowed to warm up to room temperature, stirred for 3 h, and cooled to 10°C, and a solution of 4.5 g of sodium hydroxide in 100 ml of water was added. The organic phase was separated, washed in succession with a saturated solution of ammonium chloride and water, dried over sodium sulfate, and evaporated.

7-Hydroxyheptan-2-one (VIII). Yield 86%, purity 99% (GLC) [8]. IR spectrum, ν , cm⁻¹: 3200–3600 (O–H), 1710 (C=O), 1055 (C–O). ¹H NMR spectrum (CDCl₃), δ , ppm: 2.13 s (3H, CH₃CO), 3.60 t (2H, *J* = 6.5 Hz).

8-Hydroxyoctan-2-one (IX). Yield 85%, purity 98% (GLC) [9]. IR spectrum, ν , cm⁻¹: 3200–3600 (O–H), 1711 (C=O), 1055 (C–O). ¹H NMR spec-

trum (CDCl₃), δ , ppm): 2.12 s (3H, CH₃CO), 3.59 t (2H, *J* = 6.5 Hz).

12-Hydroxydodecan-2-one (X). Yield 89%, purity 99% (GLC) [9]. IR spectrum, ν , cm⁻¹: 3200–3600 (O–H), 1711 (C=O), 1055 (C–O). ¹H NMR spectrum (CDCl₃), δ , ppm: 2.13 s (3H, CH₃CO), 3.61 t (2H, *J* = 6.5 Hz).

(1R,3S)-1-[3-(2-Hydroxyethyl)-2,2-dimethylcyclobutyl]ethanone (XI). Yield 87%, purity 99% (GLC), [α]_D²⁰ = +41.2° (*c* = 0.4; CH₃OH) [10]. The IR and ¹H NMR spectra of XI were almost identical to those reported in [3, 11]. ¹³C NMR spectrum (CDCl₃), δ _C, ppm: 16.04 (*cis*-3-CH₃), 22.91 (C⁴, *J* = 137.3 Hz), 29.72 (C^{2'}, 30.14 (*trans*-3-CH₃), 32.81 (C^{1''}, *J* = 125.31 Hz), 38.46 (C³, *J* = 133.0 Hz), 43.02 (C²), 54.12 (C¹, *J* = 132.9 Hz), 60.40 (C^{2''}, *J* = 143.7 Hz), 208.09 (C^{1'}).

(1R,3S)-1-[3-(2-Hydroxyethyl)-2,2-dimethylcyclopropyl]-2-propanone (XII). Yield 85%, purity 97% (GLC), [α]_D²⁰ = –16.7° (*c* = 0.67; CH₃OH) [10]. The IR and ¹H NMR spectra of XII were almost identical to those reported in [3, 11]. ¹³C NMR spectrum (CDCl₃), δ _C, ppm: 14.74 (*cis*-2-CH₃), 16.41 (C²), 21.07 (C¹, *J* = 159.3 Hz), 22.62 (C³, *J* = 162.5 Hz), 27.57 (C^{1''}), 28.52 (*trans*-2-CH₃), 29.10 (C^{3'}), 39.11 (C^{1'}), 62.94 (C^{2''}), 210.11 (C^{2'}).

9-Hydroxy-6-methylnonan-2-one (XIII). Yield 89% (GLC) [12]. IR spectrum, ν , cm⁻¹: 3200–3600 (O–H), 1710 (C=O), 1055 (C–O). ¹H NMR spectrum (CDCl₃), δ , ppm: 0.89 d (3H, CH₃, *J* = 5.8 Hz), 1.05–1.66 m (9H, CH₂, CH), 2.12 s (3H, CH₃CO), 2.41 t (2H, CH₂CO, *J* = 7.0 Hz), 2.82 br.s (1H, OH), 3.62 t (2H, CH₂O, *J* = 6.5 Hz).

(Z)-9-Hydroxy-6-methyl-5-nonen-2-one (XIV). An ozone–oxygen mixture was bubbled at 5°C through a solution of 16 mmol of diene **VII** in 48 ml of cyclohexane containing 32 mmol of glacial acetic acid until 14.4 mmol of ozone was absorbed (ozonizer efficiency 40 mmol/h). The mixture was purged with argon, the solvent was separated from the ozonide by decanting, 45 ml of methylene chloride was added, and the mixture was treated following the general procedure described above. Yield of **XIV** 85%, purity 97% (GLC data). The IR and ¹H NMR spectra of **XIV** were almost identical to those reported in [4].

REFERENCES

1. Kukovinets, O.S., Kasradze, V.G., Chernukha, E.V., Odinokov, V.N., Galin, F.Z., Fedorov, P.I., and Tolstikov, G.A., *Russ. J. Org. Chem.*, 2000, vol. 36, no. 2, pp. 211–213.
2. Ishmuratov, G.Yu., Kharisov, R.Ya., Yakovleva, M.P., Botsman, O.V., Muslukhov, R.R., and Tolstikov, G.A., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 1999, no. 1, pp. 198–199.
3. Satoh, T., Okuda, T., Kaneko, Y., and Yamakawa, K., *Chem. Pharm. Bull.*, 1984, vol. 32, no. 4, pp. 1401–1410.
4. Odinokov, V.N., Akhmetova, V.R., Ishmuratov, G.Yu., Botsman, L.P., and Tolstikov, G.A., *Zh. Org. Khim.*, 1986, vol. 32, no. 5, pp. 953–957.
5. Flippia Lee, A., Gallagher, D.W., and Jalali-Araghi, K., *J. Org. Chem.*, 1989, vol. 54, no. 6, pp. 1430–1432.
6. Gora, J., Smigielski, K., and Kula, J., *Synthesis*, 1982, no. 4, pp. 310–312.
7. Odinokov, V.N., Akhunova, V.R., Bakeeva, R.S., Galeeva, R.I., Semenovskii, A.V., Moiseenkov, A.M., and Tolstikov, G.A., *Zh. Org. Khim.*, 1977, vol. 13, no. 3, pp. 532–538.
8. Stetter, H. and Hesse, R., *Monatsh. Chem.*, 1967, vol. 98, no. 3, pp. 755–762.
9. Cottier, L. and Descotes, G., *Bull. Soc. Chim. Fr.*, 1971, no. 12, pp. 4557–4562.
10. Kula, J., *Justus Liebigs Ann. Chem.*, 1983, no. 5, pp. 890–893.
11. Shaffer, G.W., Doerr, A.B., and Purzycki, K.L., *J. Org. Chem.*, 1972, vol. 37, no. 1, pp. 25–29.
12. Obol'nikova, E., Davydova, L.P., Kaboshina, L.N., Valashek, I.E., Yanotovskii, M.Ts., and Samokhvalov, G.I., *Zh. Obshch. Khim.*, 1964, vol. 34, no. 12, pp. 3975–3979.