A new method for the direct reduction of products of ozonolysis of 1-alkylcycloalkenes to ketols

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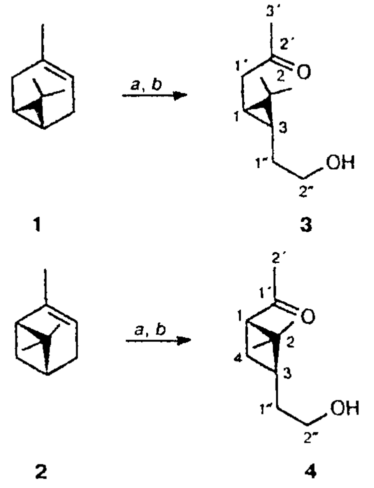
A method for the direct reduction of peroxide products of ozonolysis of 1-alkylcycloalkenes (with Δ^3-carene and α-pinene as examples) to the corresponding ketols with $NaBH(OAc)_3$ was proposed.

Key words: 1-alkylcycloalkene, ozonolysis, Δ^3-carene, α-pinene, reduction, sodium triacetoxyborohydride, ketols.

The known ozonolysis-based methods for the conversion of 1-alkylcycloalkenes to ketols include the initial transformation of peroxide products into keto-aldehydes with subsequent reduction of the formyl group to the hydroxy group by hydride reagents such as $Li(OBu^t)_3AlH$ [1] or $NaBH(OAc)_3$,[2] or by direct reduction of ozonides either under the action of borane complexes with pyridine, Et_3N, or THF or electrochemically on a lead cathode.[4] The second approach seems to be more promising, though it is characterized by comparatively low yields (<65%) of the target ketols.

In a development of this approach, we demonstrated with Δ^3-carene (**1**) (*ee* 87%) and α-pinene (**2**) (*ee* 66%) as examples that $NaBH(OAc)_3$ is a highly efficient reductive agent for the corresponding peroxide products of ozonolysis. The target ketols **3** and **4** were obtained in high yields (>85%), the content of admixtures of the corresponding diols being not higher than 3% (GLC data).



Reagents: *a*. $O_3/AcOH/CH_2Cl_2$; *b*. $NaBH(OAc)_3$.

Experimental

IR spectra were recorded on a UR-20 instrument (thin film). ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300 and 75.47 MHz, respectively) in $CDCl_3$ with Me_4Si as the internal standard. Products were chromatographed on a Chrom-5 instrument (column length 1.2 m, silicone SE-30 (5%) on Chromaton N-AW-DMCS (0.16—0.20 mm) as the stationary phase, operating temperature 50—300 °C, helium as carrier gas). Optical rotation was measured on a Perkin—Elmer 241-MC polarimeter.

Synthesis of ketols (general procedure). An oxygen—ozone mixture (ozonizer capacity was 40 mmol of O_3 per hour) was bubbled with stirring through a solution of an olefin (2.0 g, 14.4 mmol) and glacial AcOH (1.72 g, 28.7 mmol) in 40 mL of CH_2Cl_2 at −4 to −2 °C until 0.72 g (15 mmol) of ozone was absorbed. The reaction mixture was blown with argon, diluted with 20 mL of CH_2Cl_2, and added with stirring at 10 °C to a suspension of $NaBH(OAc)_3$ preliminarily prepared by addition of a solution of glacial AcOH (11.9 g, 198.0 mmol) in 20 mL of CH_2Cl_2 to a suspension of $NaBH_4$ (2.5 g, 66.0 mmol) in 100 mL of CH_2Cl_2 with subsequent stirring for 2 h. Then the reaction mixture was heated to ~20 °C, stirred for 3 h, and cooled to 10 °C, and a 4.3% aqueous solution of NaOH was added. The organic layer was separated, washed with a saturated solution of NH_4Cl and water, dried with Na_2SO_4, and concentrated to give the corresponding ketol.

(1*R*,3*S*)-3-(2-Hydroxyethyl)-1-(2-oxopropyl)-2,2-dimethylcyclopropane (3). Yield 2.11 (85%), colorless liquid (purity 97%, GLC data), $[\alpha]_D^{20}$ −16.7° (*c* 0.67, MeOH).[5] The parameters of the ^1H NMR and IR spectra of compound 3 are virtually identical with those described earlier.[1,6] ^{13}C NMR, δ:

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14.7 (q, *cis*-$\underline{C}H_3C(2)$); 16.4 (s, C(2)); 21.1 (d, C(1), J = 159.3 Hz); 22.6 (d, C(3), J = 162.5 Hz); 27.6 (t, C(1″)); 28.5 (q, *trans*-$\underline{C}H_3C(2)$); 29.1 (q, C(3′)); 39.1 (t, C(1′)); 62.9 (t, C(2″)); 210.1 (s, C(2′)).

(1*R*,3*S*)-3-(2-Hydroxyethyl)-1-(1-oxoethyl)-2,2-dimethylcyclobutane (4). Yield 2.17 g (87%), colorless liquid (purity 99%, GLC data), $[\alpha]_D^{20}$ +41.2° (*c* 0.4, MeOH).[5] The parameters of the ^{1}H NMR and IR spectra of compound **4** are virtually identical with those described earlier.[1,6] ^{13}C NMR, δ: 16.0 (s, *cis*-$\underline{C}H_3C(2)$); 22.9 (t, C(4), J = 137.3 Hz); 29.7 (q, C(2′)); 30.1 (q, *trans*-$\underline{C}H_3C(2)$); 32.8 (t, C(1″), J = 125.31 Hz); 38.5 (d, C(3), J = 133.0 Hz); 43.0 (s, C(2)); 54.1 (d, C(1), J = 132.9 Hz); 60.4 (t, C(2″), J = 143.7 Hz); 208.1 (s, C(1′)).

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Acylation of sterically hindered 2-propargyl-1,3-diketones

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Sterically hindered 2-propargyl-1,3-diketones were acylated at the terminal acetylenic group by acyl chlorides in the presence of CuCl. Some peculiarities of the reaction were revealed.

Key words: 2-propargyl-1,3-diketones, steric hindrances, acylation, Cu and Pd catalysis, isomerization, acetylenic and allenic triketones.

We have described previously[1] the preparation of a new type of sterically hindered compounds containing two reaction centers: 1,3-dicarbonyl fragment and propargyl group. Acylation at the terminal acetylenic group is one of the possible ways of their further functionalization. Products of this reaction (triketones) can find use in the synthesis of polyfunctional heterocyclic compounds.[2,3]

In the present work, we studied for the first time acylation of sterically hindered propargyl-substituted 1,3-diketones in the presence of CuCl.[4]

2-Propargyl-1,3-diketones **1a—c**, in which the structure of the substituent bound to one of the carbonyl groups remained unchanged and that of the substituent bound to the second group was sterically hindered, were used as the starting substrates:

The reactions of diketones **1a—c** with chlorides of branched aliphatic carboxylic acids **2a,b** in the presence of catalytic quantities of CuCl afford acetylenic triketones **3a—e** in 67—88% yields. The structures of the compounds obtained were confirmed by the data of elemental analysis and IR and ^{1}H NMR spectra. The IR spectra of triketones **3a—e** contain absorption bands corresponding to stretching vibrations of the CO groups (1670, 1700, and 1740 cm^{-1}) and the triple bond (2210 cm^{-1}). The ^{1}H NMR spectra exhibit signals of diastereotopic protons of the CH_2—C≡C group as two doublets of doublets (ABX system) in the 2.45—3.10 ppm region and a triplet of the methine proton of the β-dicarbonyl fragment at 4.58—5.15 ppm.

A by-product was formed (according to the TLC data) during isolation of triketone **3b**. It has been shown by special experiments that compound **3b** is transformed into this by-product during chromatography on Al_2O_3 (66% yield). Its IR spectrum contains an absorption band at 1550 cm^{-1} characteristic of the C=C bond of the furan cycle,[5] and the ^{1}H NMR spectrum exhibits a singlet at 6.85 ppm corresponding to the proton of this heterocycle.

Based on the elemental analysis and spectral data, we ascribed the structure of 2-isopropyl-3-(2-methyl-2-methoxy-1-oxopropyl)-5-(3-methyl-2-oxobutyl)furan (**4**)

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