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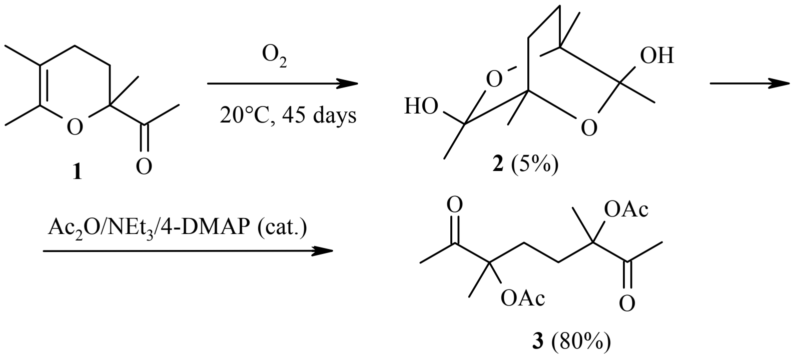
1,3,4,6-TETRAMETHYL-2,5-DIOXABICYCLO-[2.2.2]OCTANE-3,6-DIOL: AN EXAMPLE OF A NEW BICYCLIC HEMIKETAL

M. V. Mavrov and S. G. Zlotin

1,3,4,6-Tetramethyl-2,5-dioxabicyclo[2.2.2]octan-3,6-diol, which is the simplest analog of a natural bicyclic hemiketal, was obtained and characterized.

Keywords: bicyclic hemiketal, dihydropyran, autooxidation.

We have established that 2-acetyl-2,5,6-trimethyl-2,3-dihydropyran (**1**) (the dimer of methyl isopropyl ketone [1]) is transformed by the prolonged action of light in air, albeit with a low yield (4-5%), into the previously unknown bicyclic hemiketal **2**. The structure of 1,3,4,6-tetramethyl-2,5-dioxabicyclo[2.2.2]octane-3,6-diol (**2**) was established on the basis of spectral data and by chemical means, i.e., by transformation into 3,6-diacetoxy-3,6-dimethoxyoctane-2,7-dione (**3**).



The ^1H and ^{13}C NMR spectra of the heterocycle **2** contain five signals of nonequivalent ^1H and ^{13}C nuclei, indicating C_2 symmetry for the molecule. In the ^1H NMR spectrum, recorded under double resonance conditions (NOESY), there are exchange cross peaks from the methylene protons at positions 1,4. The absence of cross lines from interaction of the indicated methylene protons with the protons of the CH_3 groups at positions 3 and 6 probably indicates that they have the *endo* orientation.

In the ^{13}C NMR spectrum of compound **2** there is a signal at δ 98.1 ppm for the hemiacetal $C_{(3)}$ and $C_{(6)}$ atoms. The presence of the hydroxyl groups is confirmed by a strong absorption band in the region of 3400 cm^{-1} in the IR spectrum and by a fragment ion with *m*/*e* 185 [M^+ - OH] in the mass spectrum of compound **2**.

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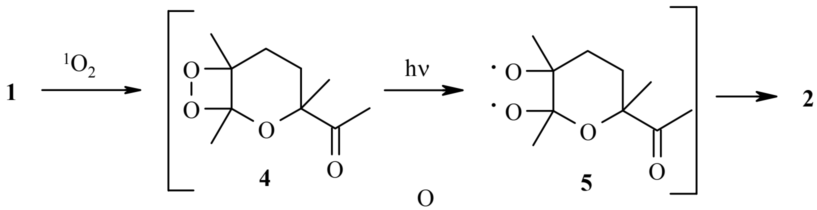
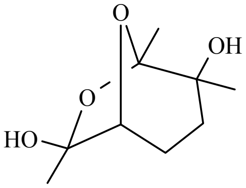
The transformation **1** → **2** probably takes place according to a scheme involving oxidation of the dihydropyran **1** by singlet oxygen from the atmosphere [2, 3], cleavage of the O–O bond in the dioxetane **4**, and reductive heterocyclization of the diradical **5** with the formation of the heterocycle **2**.





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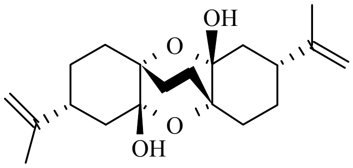
Other directions of ring opening, such as the formation of compound **6**, are possible, but we were unable to identify the position and structural isomers of compound **2** in the ^{1}H and ^{13}C NMR spectra.

The heterocycle **2** is fairly stable in the crystalline state, but in solution it gradually splits at the C–O bonds and is converted into carbonyl-containing compounds. Thus, the ^{13}C NMR spectrum of a solution of **2** in DMSO-d$_6$ after holding at room temperature for 4-6 h contains a strong signal for the carbon atom of a carbonyl group (δ 213.9 ppm) not belonging to compound **2**.

Chemical evidence for the lability of the heterocyclic system of the hemiketal **2** is provided by its transformation into the diketodiacetate **3** with a yield of 80% by the action of a mixture of acetic anhydride and triethylamine in methylene chloride at 20°C.

It should be noted that the structure of bridged cyclic bissemiacetals is encountered in living nature. Thus, the diacetal **7**, isolated from *Cymbopogon martini* Graminae (a bushy plant of the grass family) and containing the structural fragment of 2,5-dioxabicyclo[2.2.2]octane-3,6-diol, was described recently [4].



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The oxidation of carbonyl-containing isoprenoids by atmospheric oxygen in the light can probably take place in the cells of living organisms (probably under the influence of biocatalysts) and can be regarded as a possible method of converting the energy of sunlight into chemical energy.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 instrument (500 and 126 MHz respectively). The ^{1}H and ^{13}C chemical shifts were determined with reference to Me$_4$Si. The mass spectra were recorded on an MAT-112 instrument at 70 eV. The IR spectra were recorded on a Specord M-80 spectrophotometer. The initial dihydropyran **1** was prepared by the previously described method [1]; the ^{1}H and ^{13}C NMR spectra were not given in [1].

6-Acetyl-2,3,6-trimethyl-5,6-dihydropyran (1). ^{1}H NMR spectrum (deuterochloroform), δ, ppm (*J*, Hz): 1.08* and 1.23 (3H, two s, CH_3); 1.32-1.56 (2H, m, CH_2); 1.49* and 1.52 (3H, two s, CH_3); 1.68-1.80 (1H, m, CH_2); 1.77 (3H, s, CH_3); 2.04-2.18 (1H, m, CH_2); 2.12 (3H, s, CH_3). ^{13}C NMR spectrum (deuterochloroform), δ, ppm (*J*, Hz): 212.3, 142.9, 101.9, 81.4, 28.9, 28.1,* 24.2, 23.8, 20.3,* 17.6, 16.4, 13.6.*

1,3,4,6-Tetramethyl-2,5-dioxobicyclo[2.2.2]octane-3,6-diol (2). A freshly prepared solution of the dihydropyran **1** (16.4 g, 0.1 mol) was kept in the light at ~20°C for 45 days. The precipitate was filtered off and recrystallized from ethyl acetate. Yield 0.75 g (~4.5%); mp 139-140°C, R_f 0.46 (chloroform–methanol). IR spectrum (potassium bromide), ν, cm^{-1}: 3384 bs (OH), 2992, 2984, 2976, 2936, 1456, 1376, 1184, 1152, 1128, 1116, 1056, 968, 856. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 0.98 (6H, s, CH_3); 1.62 (2H, br. q, $J \approx 6.8$, CH_2); 1.88 (2H, br. q, $J \approx 6.8$, CH_2); 5.73 (2H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 98.1, 72.3, 27.0, 23.5, 21.2. Mass spectrum, *m/z* (I_{rel}, %): $[M]^+$ (absent), 185 $[M^+ - OH]$ (40), 167 (16), 142 (63), 141 (65), 125 (30), 124 (37), 123 (40), 109 (57), 100 (21), 99 (57), 97 (23), 95 (27), 88 (43), 86 (38), 85 (100), 72 (72), 71 (40), 59 (19), 57 (58). Found %: C 59.21; H 9.04. $C_{10}H_{18}O_4$. Calculated %: C 59.38; H 8.97.

3,6-Diacetoxy-3,6-dimethoxyoctane-2,7-dione (3). A solution of compound **2** (0.41 g, 2.01 mmol), acetic anhydride (5 ml), triethylamine (5 ml), and a catalytic amount of 4-dimethylaminopyridine in methylene chloride (15 ml) was kept at 20°C for 24 h. Methanol (6 ml) was then added slowly, the solution was cooled, and after the usual treatment the crystalline diacetate **3** was isolated. Yield 0.46 g (~80%); mp 118°C (ethyl acetate), R_f 0.61 (chloroform–methanol, 10:1). IR spectrum (potassium bromide), ν, cm^{-1}: 1724, 1372, 1360, 1256, 1232, 1132, 1096, 1024, 952. ^{1}H NMR spectrum (deuterochloroform), δ, ppm: 1.37 (6H, s, CH3); 1.62-1.97 (4H, m, CH_2); 2.02 (6H, s, CH_3); 2.05 (6H, s, CH_3). ^{13}C NMR spectrum (deuterochloroform), δ, ppm: 206.4, 170.1, 85.1, 28.6, 23.9, 20.9, 20.4. Mass spectrum, *m/z* (I_{rel}): $[M]^+$ (absent), 243 (21), 201 (24), 141 (100), 125 (21), 124 (26), 123 (31), 115 (20), 107 (20), 99 (37), 97 (27), 95 (29), 85 (29), 85 (27), 55 (18). Found %: C 58.49; H 7.61. $C_{14}H_{22}O_6$. Calculated %: C 58.73; H 7.25.

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* The signals of the minor conformer (~15%).