Synthesis of Medium and Large Rings, XLV[◇]

The Reaction of Dimethyl 10-Oxo-3,6-hexanooxepine-4,5-dicarboxylate with Sodium Methoxide/Methanol − A Reinvestigation

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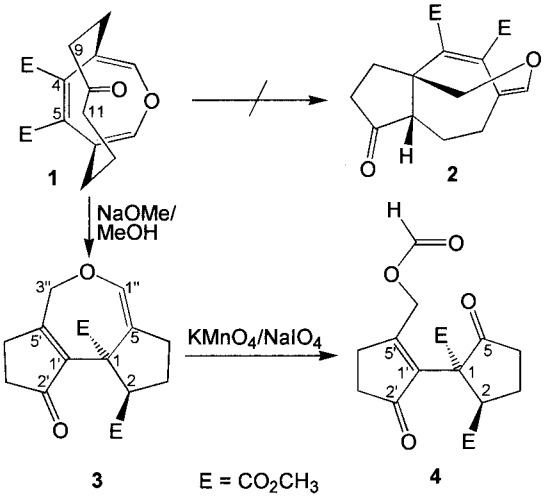
Treatment of the title compound **1** with sodium methoxide in ether in the presence of methanol leads to the bicyclopentyl derivative **3**. The structure of **3** was established by X-ray analysis. The structure **2** proposed earlier has to be corrected in favour of **3**.

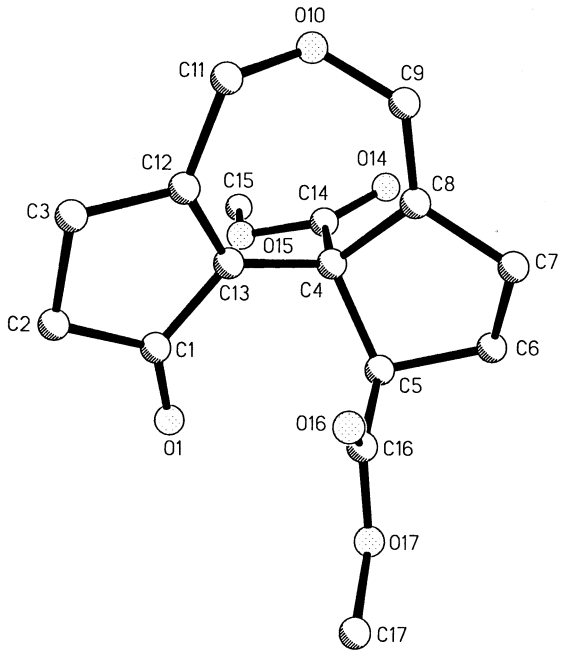
The reaction of the oxepine **1** with a large excess of powdered sodium methoxide in diethyl ether leads to a functionalized hydroazulenone that can be used as starting material for the synthesis of tremulane sesquiterpenoids[1][2][3]. However, when **1** was treated with sodium methoxide in ether in the presence of methanol another isomer of **1** was isolated in 61% yield. For this compound the structure **2** was derived in ref.[1].



1 **2** **3** **4**

With suitable crystals in our hands an X-ray analysis[4] was now possible that revealed the unexpected structure **3** of a bridged bicyclopentyl derivative for this isomer of **1** (See Figure 1). Therefore, the formulae of **2** and its oxidation product in ref.[1] have to be corrected into **3** and **4**. The new assignments of the NMR signals of **3** and **4** are given in the Experimental Section.

Figure 1. A molecule of **3** in the crystal; arbitrary numbering



The formation of **3** from **1** can be explained as follows: The addition of the C(9)=C(10)−O$^-$ enolate to the methoxycarbonyl group on C-4 to give a 1,3-diketone under methanol elimination and protonation is followed by a transannular Michael addition of the C(11)=C(10)−O$^-$ enolate to C-5 and subsequent protonation in α-position to

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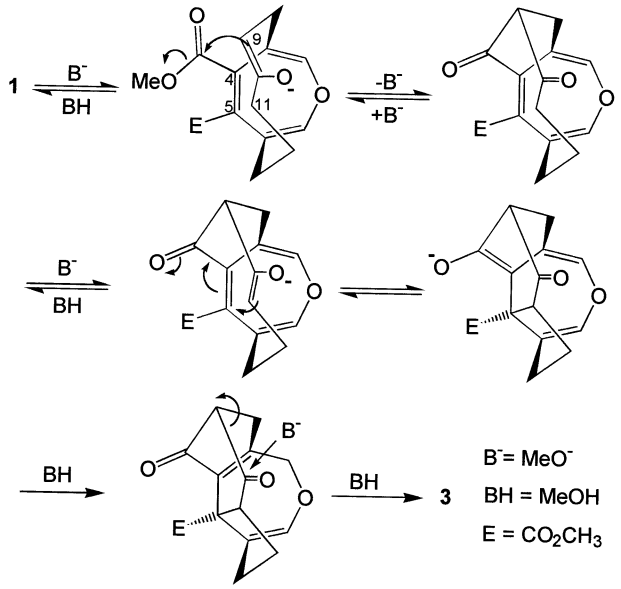
  1434−193X/98/0303−0507 $ 17.50+.50/0

the oxepine oxygen atom. Final cleavage of the bond between the two oxo groups by methoxide and protonation gives **3**[5].



Experimental Section

IR: Perkin-Elmer 1600 FTIR. − ^{1}H NMR: TMS int.; Bruker DRX 500. − ^{13}C NMR: TMS int.; Bruker AM 300, DRX 500.

1. *(1R*,2S*)-(±)-Dimethyl 5,5′-(2′′-Oxaprop-3′′-yl-1′′-ylidene)-2′-oxobicyclopent-1′-ene-1,2-dicarboxylate* (**3**)[1]: IR (KBr): $\tilde{\nu}$ = 1730 cm^{-1} (s, ester C=O), 1690 cm^{-1} (ketone C=O). − ^{1}H NMR (C_6D_6, 500 MHz): δ = 1.55 (ddddd, ^2J = 18.0 Hz, $^3J_{4',\,3'}$ = 5.2 Hz, $^3J_{4',\,3'}$ = 5.2 Hz, $^4J_{4',\,3''}$ = 0.9 Hz, $^4J_{4',\,3''}$ = 0.9 Hz, 1 H, 4′-H), 1.64 (ddddd, ^2J = 18.0 Hz, $^3J_{4',\,3'}$ = 5.1 Hz, $^3J_{4',\,3'}$ = 4.9 Hz, $^4J_{4',\,3''}$ = 2.2 Hz, $^4J_{4',\,3''}$ = 0.9 Hz, 1 H, 4′-H), 1.87 (dddd, ^2J = 13.2 Hz, ^3J = 8.2 Hz, ^3J = 3.0 Hz, ^3J = 1.4 Hz, 1 H, 3-H), 2.01 (ddd, ^2J = 13.9 Hz, $^3J_{3',\,4'}$ = 5.2 Hz, $^3J_{3',\,4'}$ = 4.9 Hz, 1 H, 3′-H), 2.04 (ddd, ^2J = 13.9 Hz, $^3J_{3',\,4'}$ = 5.2 Hz, $^3J_{3',\,4'}$ = 5.1 Hz, 1 H, 3′-H), 2.35 (m, 1 H, 4-H), 2.43 (m, 1 H, 4-H), 2.48 (dddd, ^2J = 13.2 Hz, ^3J = 9.6 Hz, ^3J = 9.6 Hz, ^3J = 7.9 Hz, 1 H, 3-H), 3.27 (s, 3 H, $COOCH_3$ at C-2), 3.30 (s, 3 H, $COOCH_3$ at C-1), 4.09 (ddd, ^2J = 17.1 Hz, $^4J_{11,\,3}$ = 0.9 Hz, $^4J_{11,\,3}$ = 0.9 Hz, 1 H, 3′′-H), 4.17 (dddd, ^2J = 17.1 Hz, $^4J_{3'',\,4'}$ = 2.2 Hz, $^4J_{3'',\,4'}$ = 0.9 Hz, $^4J_{3'',\,1''}$ = 0.8 Hz, 1 H, 3′′-H), 4.41 (m, 1 H, 2-H), 6.49 (ddd, $^4J_{1'',\,4}$ = 1.9 Hz, $^4J_{1'',\,4}$ = 1.9 Hz, $^4J_{1'',\,3''}$ = 0.8 Hz, 1 H, 1′′-H). − ^{13}C NMR (C_6D_6, 125 MHz): δ = 26.43 (t, C-4), 27.03 (t, C-4′), 27.87 (t, C-3), 33.14 (t, C-3′), 50.51 (q, $COOCH_3$ at C-2), 51.20 (d, C-2), 52.00 (q, $COOCH_3$ at C-1), 56.87 (s, C-1), 69.41 (t, C-3′′), 130.57 (s, C-5), 137.49 (s, C-1′), 141.94 (d, C-1′′), 169.13 (s, C-5′), 171.29 (s, $COOCH_3$ at C-1), 173.78 (s, $COOCH_3$ at C-2), 205.41 (s, C-2′).

X-ray Structure Analysis of **3**[4]: The data of a crystal (acetone/*n*-pentane) with the approximate dimensions 0.45 × 0.50 × 0.90 mm were obtained with a Siemens P4 diffractometer (Mo-K_α radiation, graphite monochromator). Cell dimensions were refined from 60 reflections; a = 1268.6(1), b = 965.8(1), c = 1238.1(1) pm, β = 98.238(1)°, V = 1501.2(2)·10^6 pm^3, monoclinic, space group $P2_1/c$, Z = 4, $\rho_{calcd.}$ = 1.355 g/cm^3, 3448 unique intensities, of which 2917 [$F_o > 3\sigma(F)$] were observed in the θ range 1.75−27.5°, measured with ω-scan technique. The structure was solved by using direct-phase determination and refined on F by using SHELXTL-Plus. Positional parameters, anisotropic displacement parameters for all atoms except for hydrogen atoms, groupwise isotropic displacement parameters for all hydrogen atoms, treated as rigid groups. R = 0.064, R_w = 0.069, $w = 1/\sigma^2(F)$.

2. *(1R*,2R*)-(±)-Dimethyl 5′-Formyloxymethyl-2′,5-dioxobicyclopent-1′-ene-1,2-dicarboxylate* (**4**)[1]: ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.31 (m, 1 H, 3-H), 2.34 (m, 1 H, 3-H), 2.39 (m, 1 H, 3′-H), 2.41 (m, 1 H, 3′-H), 2.46 (ddd, ^2J = 18.8 Hz, $^3J_{4,\,3}$ = 8.8 Hz, $^3J_{4,\,3}$ = 8.8 Hz, 1 H, 4-H), 2.68 (ddddd, ^2J = 19.1 Hz, $^3J_{4',\,3'}$ = 5.0 Hz, $^3J_{4',\,3'}$ = 3.8 Hz, ^4J = 1.1 Hz, ^4J = 1.1 Hz, 1 H, 4′-H), 2.73 (ddddd, ^2J = 19.1 Hz, $^3J_{4',\,3'}$ = 5.3 Hz, $^3J_{4',\,3'}$ = 4.0 Hz, ^4J = 1.1 Hz, ^4J = 1.1 Hz, 1 H, 4′-H), 2.86 (ddd, ^2J = 18.8 Hz, $^3J_{4,\,3}$ = 8.4 Hz, $^3J_{4,\,3}$ = 6.8 Hz, 1 H, 4-H), 3.58 (s, 3 H, $COOCH_3$), 3.77 (s, 3 H, $COOCH_3$), 4.17 (dd, $^3J_{2,\,3}$ = 7.0 Hz, $^3J_{2,\,3}$ = 6.9 Hz, 1 H, 2-H), 4.94 (ddd, ^4J = 1.1 Hz, ^4J = 1.1 Hz, ^4J = 1.0 Hz, 2 H, CH_2O), 8.12 (dd, ^4J = 1.0 Hz, ^4J = 1.0 Hz, 1 H, formyl H). − ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 23.45 (t, C-3), 28.81 (t, C-4′), 32.76 (t, C-3′), 37.35 (t, C-4), 49.88 (d, C-2), 52.06 (q, $COOCH_3$), 53.80 (q, $COOCH_3$), 61.86 (t, CH_2O), 62.85 (s, C-1), 137.89 (s, C-1′), 160.06 (d, CHO), 167.90 (s, C-5′), 169.68 (s, $COOCH_3$ at C-1), 172.89 (s, $COOCH_3$ at C-2), 207.12 (s, C-2′), 209.92 (s, C-5).

[1] W. Tochtermann, T. Habeck, C. Wolff, E.-M. Peters, K. Peters, H. G. von Schnering, *Chem. Ber.* **1993**, *126*, 2691−2696.
[2] T. Habeck, C. Wolff, W. Tochtermann, *Tetrahedron Lett.* **1995**, *36*, 2041−2044.
[3] K. Peters, E.-M. Peters, T. Panitzsch, W. Tochtermann, *Z. Kristallogr.*, *NCS*, in press.
[4] The atomic coordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW. Any request should be accompanied by the deposition number CCDC-100628 and the full literature citation for this communication.
[5] For further details see: T. Panitzsch, Dissertation, University of Kiel, **1997**.

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