145. Formation of 5-Hydroxy-indan-2-one from Attempts to Hydrolyse 9-Ethylenedioxy-bicyclo[3.3.1]nonane-3,7-dione

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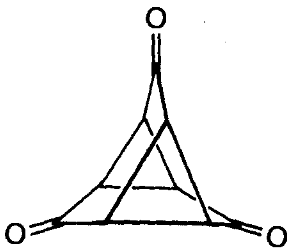
Bildung von 5-Hydroxy-indan-2-on bei Hydrolyseversuchen mit 9-Äthylendioxy-bicyclo[3.3.1]nonan-3,7-dion

Zusammenfassung

Verschiedene Versuche, 9-Äthylendioxy-bicyclo[3.3.1]nonan-3,7-dion (**2**) durch Hydrolyse in das entsprechende Triketon **3** umzuwandeln, führten nur zu 5-Hydroxy-indan-2-on (**4**) und in einem Fall auch noch zu etwas 7,9-Bis(äthylendioxy)-bicyclo-[3.3.1]nonan-3-on (**5**). Unter milderen Hydrolysebedingungen reagierte **2** gar nicht. Die Bildung von **4** aus **2** wird über eine *Wagner-Meerwein*-Umlagerung und nachfolgende Eliminierung von Äthylenglycol formuliert. Das so entstandene Äthylenglycol reagiert mit noch vorhandenem Acetal **2** zum Bis-acetal **5**, was als weitere Bestätigung der Resistenz von **2** gegen Hydrolyse gelten darf.

In connection with our previous work on the synthesis of triasteranetrione (**1**) [1] we attempted to hydrolyse the intermediate 9-ethylenedioxy-bicyclo[3.3.1]nonane-3,7-dione (**2**) in order to obtain the corresponding trione **3**.

Under a variety of conditions, the only products we were able to isolate were 5-hydroxy-indan-2-one (**4**) and 7,9-bis(ethylenedioxy)-bicyclo[3.3.1]nonan-3-one (**5**):



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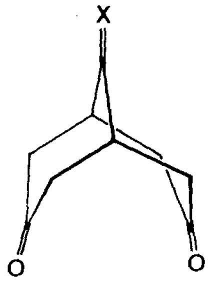

2: X = $-OCH_2CH_2O-$
3: X = O

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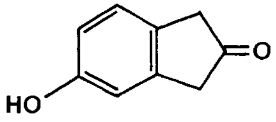
No reaction was observed with 5% aqueous hydrochloric acid, with borontrifluoride etherate followed by aqueous work-up, and under *trans*-acetalisation conditions. With a hydrochloric acetic acid mixture only 5-hydroxy-indan-2-one (**4**) was obtained, while with 10% aqueous hydrochloric acid the ketone **4** was accompanied by a small amount of the bis-acetal **5**.



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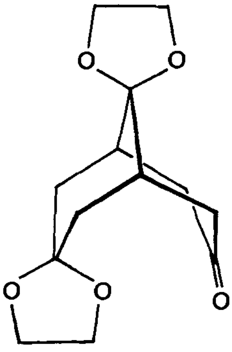


5

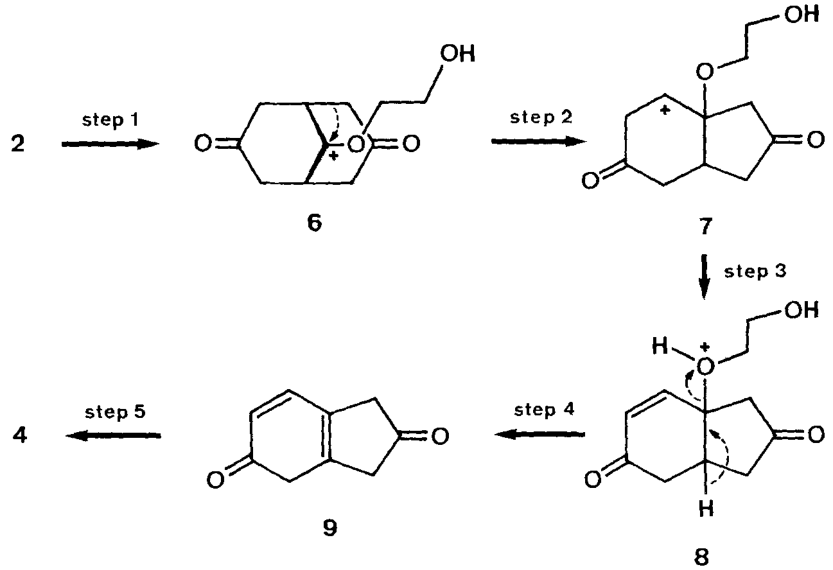
The structure of 5-hydroxy-indan-2-one (**4**) was deduced as follows: The mass spectrum (M^{+}148 *m/e*), in particular the high resolution mass determination, corresponds to a molecular formula of $C_9H_8O_2$ and the base peak is due to the loss of CO. The IR. spectrum shows hydroxyl and carbonyl absorptions at 3300 and 1736 cm^{-1} respectively, the latter suggesting the presence of a five-membered ring, a structural unit not present in the reactant **2**. The ^{1}H-NMR. spectrum contains only one signal in the high field region, namely a singlet at $\delta = 3.00$ for the two accidentally equivalent pairs of hydrogen atoms in the cyclopentenone ring. Of the four low field signals the 1 proton singlet at $\delta = 8.27$ clearly belongs to the phenolic hydroxyl group and the 3 proton signal between $\delta = 6.6$ and 7.3 ppm shows the form which is characteristic for 3,4-dialkyl-phenols (compare [2]).

The formation of **4** can be rationalized by the mechanism depicted in the *scheme*: The acetal ring cleavage (step 1) is accompanied by a 1,2-*Wagner-Meerwein* shift (step 2), deprotonation (step 3), elimination of ethylene glycol (step 4) and finally enolization with aromatization (step 5).

The structure of the bis-acetal **5** was evident from the strong molecular peak at *m/e* 254 in the mass spectrum, which corresponds to the weight of the reactant **2** plus ethylene glycol minus water, and from the strong band at 1710 cm^{-1} and the several even stronger ones in the 1200–1000 cm^{-1} region of the IR. spectrum, absorptions which are also found in the reactant **2** but in a reversed intensity relation. The ^{1}H-NMR. spectrum of **5** contains two separate 4 proton signals at $\delta = 4.02$ and 3.88 ppm for the two non-equivalent ethylenedioxy-groups aside from a 10 proton multiplet at $\delta = 3.3$–1.2 ppm.

Our results suggest that there may be sufficient steric hindrance to the attack of water at C(9) of **6** and/or sufficient strain release in the conversion of the bicyclo[3.3.1]-to the bicyclo[4.3.0]-system (step 2) to permit the rearrangement **2** → **4** to compete favourably with the simple hydrolysis **2** → **3**. The resistance which the acetal **2** shows

Scheme



towards hydrolysis is also demonstrated by the fact that any unrearranged **2** prefers to be acetalized to **5** by the ethylene glycol, which must be formed in step 4 and thus can reach a reasonable concentration only after the concentration of **2** has already been appreciably reduced.

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Experimental Part

General. Symbols, abbreviations and other notations used here have been described in [3] apart from the following modifications or additions. Working up: The term 'dried' refers to the use of anhydrous magnesium or sodium sulfate. The IR. spectra were measured on a *Perkin-Elmer* 21,257 or 421 spectrometer. The mass spectra were measured on a *CEC* 21-110B or an *Atlas* CH-5 instrument operated at 70 eV. The accurate mass measurements were obtained with an *AEI* MS 9 (double focusing) instrument. ^{1}H-NMR.-Integration units are designated H instead of pr.

5-Hydroxy-indan-2-one (**4**). A solution of 0.5 g (2.38 mmol) of 9-ethylenedioxy-bicyclo[3.3.1]-nonane-3,7-dione (**2**) in 22 ml acetic acid and 8 ml conc. hydrochloric acid was heated under reflux for 6 h. The solvent was removed under reduced pressure and the residue was shaken with 50 ml saturated NaCl-solution and 50 ml chloroform. Further extraction of the aqueous phase with chloroform followed by drying of the organic phase and evaporation of the solvent yielded 80 mg of an orange solid. Purification by preparative TLC. on silica gel using 30% ethyl acetate/hexane gave 50 mg (14%) of **4** as a yellow solid, m.p. 179–182°; sublimation at 95–100°/0.04 Torr raised the m.p. to 188–191°. – IR. (KBr): 3300*s* br. (OH); 2895*w*; 1736*s* (C=O); 1625*m*; 1586*s*; 1505*m*; 1475*s*; 1390*s*; 1346*s*; 1291*m*; 1232*m*; 1189*m*; 1156*m*; 1140*m*; 1085*m*; 969*m*; 946*m*; 870*w*; 862*w*; 820*m*; 790*w*; 751*w*; 680*w*. – ^{1}H-NMR. (60 MHz, d_6-acetone): $\delta = 8.27$/*s*, 1H (OH); 7.14/br.*d* ($J = 8$), 1H (H–C(6) or H–C(7)); 6.83/br.*s*, 1H (H–C(4)); 6.77/*d*×*d* ($J = 3$ and 8) part of the signal is covered by the singlet at 6.83, 1H (H–C(7) or H–C(6)); 3.00/*s*, 4H (2×H–C(1), 2×H–C(3)). – MS.: 148/50 (M^+); 121/12; 120/100 ($M^+ - CO$); 119/15; 91/44. High resolution MS.: 148.0521, calc. for $C_9H_8O_2$ 148.0524.

Hydrolysis with aqueous hydrochloric acid solutions. A series of hydrolyses were carried out with various concentrations of the acid. A typical run was as follows: A solution of 0.2 g (0.95 mmol) of 9-ethylenedioxy-bicyclo[3.3.1]nonane-3,7-dione (**2**) [1] in 20 ml of a 10% aqueous hydrochloric acid solution was heated under reflux for 16 h. The solution on cooling was saturated with NaCl and extracted with chloroform. The combined extracts were dried and evaporated to leave 0.2 g of a solid residue. An alternative procedure for the extraction of the product was to evaporate the aqueous solution to dryness and then to extract the product with hot chloroform. The residue was then chromatographed on silica gel using ethyl acetate/pentane 1:1 to give 18 mg (13%) of the *indanone* **4** (identified by its ^{1}H-NMR. spectrum) and 60 mg (30%) of reactant **2**. A third fraction (80 mg) also contained traces of **2** as shown by its ^{1}H-NMR. spectrum. The 80 mg fraction was rechromatographed, using the same solvent system as used above, and sublimed at 90°/0.5 Torr to give 40 mg of a solid. Recrystallization from ethyl acetate/pentane removed most of **2** to leave 32 mg (13%) of 7,9-bis-(ethylenedioxy)-bicyclo[3.3.1]nonan-3-one (**5**) as a white powder, m.p. 85–95°. The ^{1}H-NMR. spectrum indicated the sample to be >90% pure. It had: – IR. (Nujol): 1710*s* (C=O); 1441*m*; 1421*m*; 1410*m*; 1398*s*; 1355*m*; 1348*m*; 1310*m*; 1300*m*; 1240*m*; 1208*m*; 1170*s*; 1125*s*; 1090*s*; 1040*s*; 1025*s*; 980*s*; 961*s*; 940*s*; 915*m*; 872*w*; 788*w*; 775*w*; 745*m*; 675*m*. – ^{1}H-NMR. (60 MHz, $CDCl_3$): $\delta = 4.02$/*s*, 4H ($-OCH_2CH_2O-$); 3.88/apparent *qa*, sometimes seen as *t* ($J = 3$), 4H ($-OCH_2CH_2O-$); 3.3–1.2/complex *m*, 10H (H–C(1), H–C(5), 2 × H–C(2), 2 × H–C(4), 2 × H–C(6), 2 × H–C(8)). – MS.: 254/40 (M^+); 182/10; 154/24 ($M^+ - C_5H_8O_2$); 141/14; 140/15; 139/10; 138/11; 129/11; 126/25 ($M^+ - C_5H_8O_2 - CO$); 125/10; 123/10; 114/20; 113/91; 112/25; 111/10; 100/18; 99/100; 97/20; 96/11; 95/20. – High resolution MS.: 254,1154, calc. for $C_{13}H_{18}O_5$ 254,1154.

Other reactions carried out were as follows: 5% aqueous HCl-solution gave only reactant **2**. 7% aqueous HCl-solution gave 75% of **2** and 5% of the *indanone* **4**. 18% aqueous HCl-solution gave no isolable reactant or product. In some reactions the 10% hydrochloric acid hydrolysis gave as little as 4% of the *indanone* **4**.

Attempts at trans-*acetalisation of 9-ethylenedioxy-bicyclo*[*3.3.1*]*nonane-3,7-dione* (**2**) *with acetone.* A solution of 0.25 g (1.19 mmol) of acetal **2** in 25 ml acetone (or 5 ml acetone and 20 ml benzene) and a catalytic amount of *p*-toluene-sulfonic acid (~20 mg) was heated under reflux for 18 h. After evaporation of the solvent and recrystallization of the residue from ethyl acetate over 90% of **2** was recovered, as identified by its ^{1}H-NMR. spectrum.

Attempted hydrolysis using borontrifluoride etherate. To a solution of 0.25 g (1.2 mmol) acetal **2** in 25 ml methylene chloride was added 0.5 ml of a 48% solution of borontrifluoride etherate. The solution was heated under reflux (or left to stand at RT.) for 24 h and water was then added. The extracts were washed with aqueous sodium carbonate solution, water, dried and evaporated to leave 0.22 g of an off-white solid whose TLC. properties and ^{1}H-NMR. spectrum show it to contain ~90% of reactant **2**.

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[3] *C. B. Chapleo & A. S. Dreiding*, Helv. *57*, 873 (1974).