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BICYCLO[3.3.1]NONANE AND ITS DERIVATIVES—IV[1]

REACTIONS OF SOME CARBONYL DERIVATIVES OF BICYCLO[3.3.1]NONANE WITH DIAZOMETHANE

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Abstract—The reaction of bicyclo[3.3.1]nonane-2,6-dione with diazomethane *in situ* does not lead to the homologous bicyclo[4.3.1]decane-2,7-dione, but mainly to tricyclo[4.4.0.0^{2,9}]decan-9-ol-5-one. The structure of the latter was confirmed by the proton NMR spectra measured with an addition of Eu(DPM)$_3$. A mixture of tricyclo[4.4.0.0^{2,9}]decan-9-ol-5-one and bicyclo[4.3.1]decane-2,7-dione results when solutions of diazomethane are used. The reaction of bicyclo[3.3.1]nonane-2,6-dione monoethyleneacetal with diazomethane *in situ* yields predominantly bicyclo[4.3.1]decane-2,7-dione. Under the same conditions bicyclo[3.3.1]nonan-2-one gives with diazomethane *in situ* only bicyclo[4.3.1]decan-2-one.

INTRODUCTION

As known, the reaction of diazomethane with bicyclic ketones under appropriate conditions can be used to extend the ring and thus to prepare homologous ketones in good yields. In the bicyclo[3.3.1]nonane series this extension was applied only to the preparation of bicyclo[3.3.2]decan-9-one, by using a methanolic solution of diazomethane.[2,3] The reaction of bicyclo[3.3.1]nonane-2,6-dione with diazomethane has not been described.

We found that bicyclo[3.3.1]nonane-2,6-dione reacts with diazomethane *in situ* in methanol with the formation of tricyclo[4.4.0.0^{2,9}]decan-9-ol-5-one (**4**) in 50% yield. The yields are lower when solutions of diazomethane in ether or tetrahydrofuran are used.

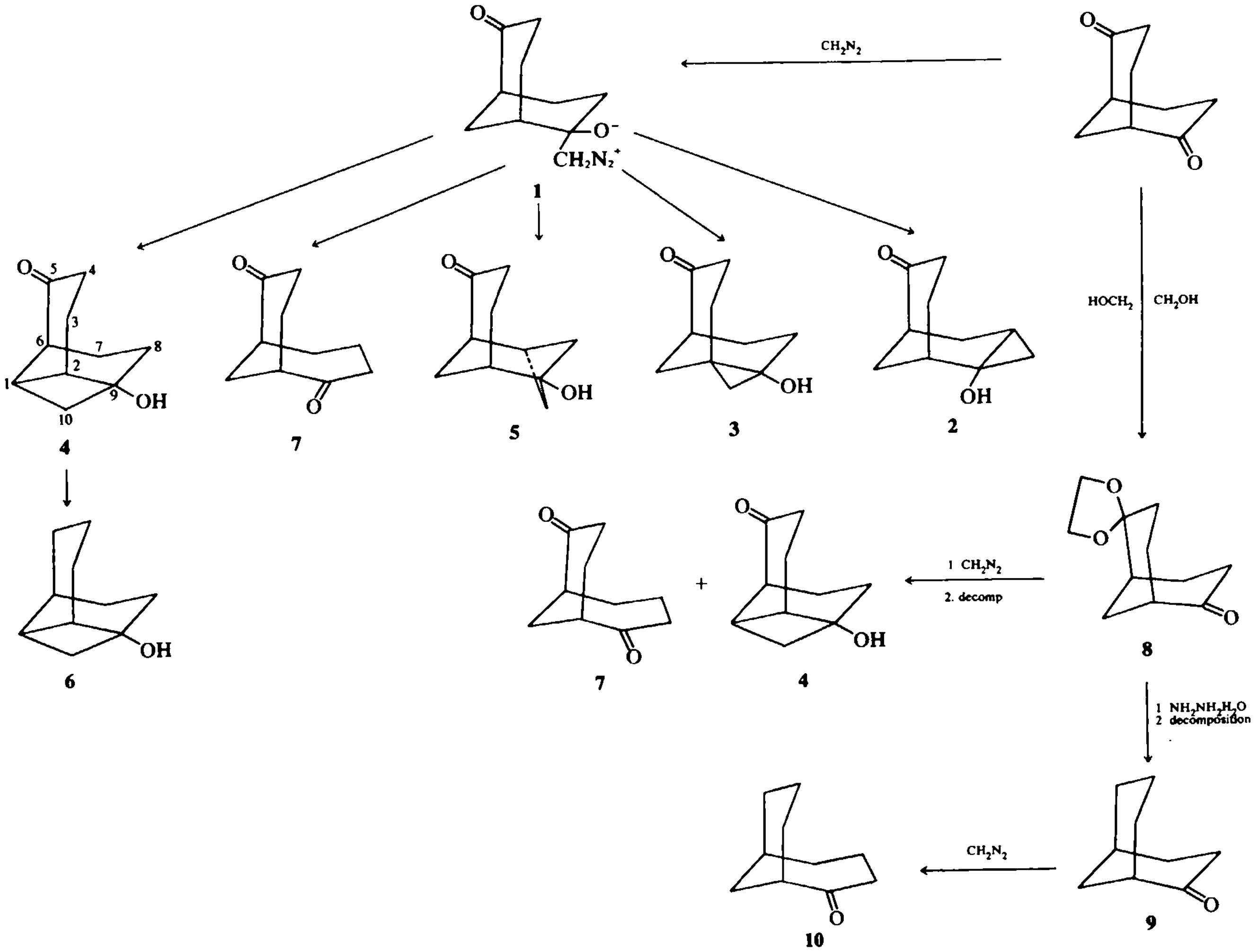
RESULTS AND DISCUSSION

The formation of tricyclo[4.4.0.0^{2,9}]decan-9-ol-5-one (**4**) from bicyclo[3.3.1]nonane-2,6-dione can be explained (Scheme 1) on the basis of a nucleophilic attack of the carbonyl carbon by diazomethane from the *exo*-side of the bicyclo skeleton and the formation of the intermediate product (**1**). This intermediate product can, with the liberation of nitrogen, form the compound **4** or tricyclo[3.3.1.1^{2,4}]decan-2-ol-6-one (**5**), both compounds containing a 4-membered ring. Less easy is the formation of tricyclo[4.3.1.0^{2,4}]decan-2-ol-7-one (**2**) or tricyclo[4.3.1.0^{1,3}]decan-3-ol-7-one (**3**), containing a 3-membered ring. In addition, bicyclo[4.3.1]decane-2,7-dione (**7**) can be formed through the classical rearrangement.

The analysis of IR and PMR spectra and a comparison with the published data[4,5] eliminate the structures involving the 3-membered ring. This was also supported by the ^{13}C NMR measurements of the tricyclic hydroxyketone (**4**) and comparison with the data,[6] and the types of carbon atoms found as given in Table 1.

After the structure had been established, the starting hydroxyketone **4** was reduced with hydrazinehydrate to yield the hydroxy compound **6** (Scheme 1), whose NMR spectra were measured with the addition of the shift reagent Eu(DPM)$_3$[7]. We calculated the slopes Δ_i of the plots $\delta_{i,obs}$ *vs* R_p, where $\delta_{i,obs}$ is the chemical shift for the i-th proton of the compound in the presence of the shift reagent and R_p the molar ratio of the reagent to the compound studied. These slopes Δ_i (the bound chemical shifts) were used for the solution of the equation of the pseudocontact shift,[8] $\Delta_i = K(3\cos\Theta_i - 1)/r_i^3$, where Θ_i is the angle between two vectors, one of which connects the lanthanide with oxygen and the other the lanthanide with the i-th proton, r_i is the magnitude of the latter vector, and K is a constant. We applied the method of nonlinear regression[9] for solving this problem and assumed the lanthanide to lie on the prolonged connecting line carbon–oxygen. For the calculations we took into account six of the most probable structures, *viz* **6a**, **6b**, **5a**, **5b**, **11a** and **11b**, containing a 4-membered ring (Table 2) (the structures **11a** and **11b** were included for a check, although they are not formed from the intermediate **1**). For the most probable was taken that structure, whose set of calculated values of bound chemical shifts, $\Delta_{i,cal}$, showed the least deviations from the experimental values $\Delta_{i,obs}$. The assembly of data were evaluated by using the parameter[10] $P = [\sum_i (\Delta_{i,cal} - \Delta_{i,obs})^2 / (\sum_i \Delta_{i,obs})^2]^{1/2}$, whose values along with the distances c of europium from oxygen in the complex adducts for the six structures mentioned are given in Table 2. The least value of the parameter P was obtained for the structure **6a**, with the observed and calculated values of Δ_i as given in Table 3.

Thus NMR spectroscopy with the application of the shift reagent gives preference to the structure **6a**; hence it can be stated with a high probability that the reaction of


CH2N2
O
O
O⁻
CH2N2⁺
1
HOCH2
CH2OH
O
5
4
3
6
7
8
2
1
9
OH
10
4
7
5
OH
3
OH
2
OH
6
OH
O
O
8
1 CH2N2
2. decomp
+
7
4
OH
1 NH2NH2H2O
2 decomposition
CH2N2
10
9

SCHEME 1.

Table 1. ^{13}C NMR spectrum of tricyclo[4.4.0.0^{2,9}]decan-9-ol-5-one (4)

Number of carbons	Type of carbons	Shift with respect to CS_2 (ppm)
1	$>C{=}O$	−31·4
1	$>C{-}OH$	+113·0
3	$>C{-}H$	+134·5, +152·0, +152·2
5	$>C(H)_2$	+161·1, +161·6, +166·1, +167·0, 168·5

Table 2. Calculated values of the parameter P and the distance c between europium and oxygen for tricyclic hydroxyketones with a 4-membered ring

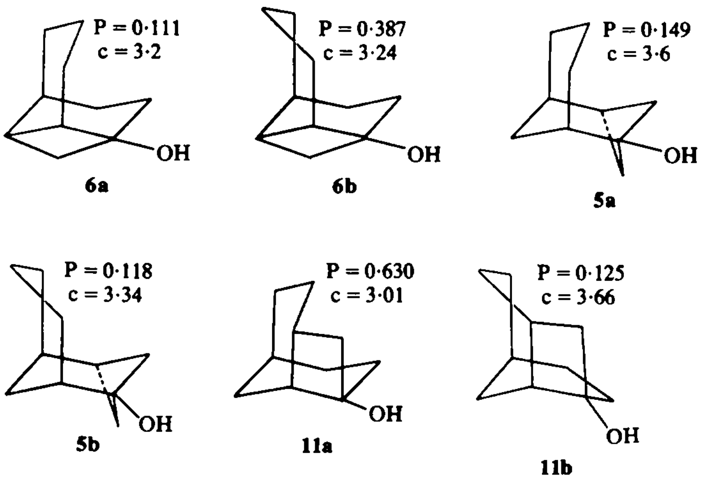


Table 3. Observed and calculated values of bound chemical shifts, $\Delta_{i,obs}$, $\Delta_{i,cal}$, of tricyclo[4.4.0.0^{2,9}]decan-9-ol (6)

Proton	$\Delta_{i,obs}$	$\Delta_{i,cal}$	Proton	$\Delta_{i,obs}$	$\Delta_{i,cal}$
8e	12·17	13·08	7a	5·04	6·08
2	11·80	11·57	3a	4·57	4·79
10a	12·17	12·02	1	4·57	5·67
8a	11·80	10·28	7e	3·89	3·71
10e	10·03	9·78	4e	4·31	4·64
3e	10·03	8·37	6	4·31	4·09
4a	5·04	6·77	5a	3·89	3·47
			5e	3·31	3·18

bicyclo[3.3.1]nonane-2,6-dione with diazomethane *in situ* leads to tricyclo[4.4.0.0^{2,9}]decan-9-ol-5-one. The structure **5b** must be, however, also taken into consideration, as its parameter P approaches very closely that of the structure **6a**.

For a comparison with the reactions *in situ*, several reactions of bicyclo[3.3.1]nonane-2,6-dione were performed with solutions of diazomethane in ether and in tetrahydrofuran, respectively. In this arrangement bicyclo[3.3.1]nonane-2,6-dione was less active and the content of the compound **4** in the reaction mixture amounted only to 16·9%.

In order to clarify the role of the keto groups of the initial compound in the formation of the compound **4**, we prepared monoethyleneacetal of bicyclo[3.3.1]nonane-2,6-dione (**8**) and investigated its reaction with diazomethane *in situ*. We isolated only 6·8% of **4** from the mixture after the decomposition of the acetals with dilute sulfuric acid. This indicates that both of the keto groups participate in the formation of the tricyclic hydroxyketone **4**.

From the monoethyleneacetal **8**, ethyleneacetal of bicyclo[3.3.1]nonan-2-one was prepared by reduction with hydrazinehydrate, and bicyclo[3.3.1]nonan-2-on was obtained by the treatment with dilute sulfuric acid. This ketone reacted with diazomethane *in situ* with the formation of bicyclo[4.3.1]decan-2-on **10**) only (Scheme 1). The position of the keto group was confirmed by PMR measurements with the addition of Eu(DMP)$_3$: the highest spectral shift was found for the group of three protons, which lie in the close vicinity of the keto group.

EXPERIMENTAL

The gas-chromatographic analyses were carried out on an instrument CHROM II with a 50 m stainless capillary, inner dia 0·25 mm, with the stationary phase SE-30. The IR spectra were measured on a spectrophotometer Perkin-Elmer 325 in cells 0·1 and 0·4 mm thick, in CCl_4 (**6**, **10**) and $CHCl_3$ (**4**, **7**) solutions. The mass spectra were obtained from a single-focusing apparatus Gas Chromatograph-Mass Spectrometer LKB 9000. The NMR spectra were measured on a spectrometer Varian XL-100 under the following conditions: PMR spectra—100·1 MHz, $CDCl_3$ solutions, 37°, TMS; ^{13}C NMR spectra—25·2 MHz, $CDCl_3$ solns, 37°, CS_2, with noise decoupling or off-resonance decoupling. The distances of the individual protons from the paramagnetic centre, whose values are required for the evaluation of the spectra with the addition of the shift reagent, were measured on Dreiding models (Laboratoriums Technik, Büchi, Switzerland).

Tricyclo[4.4.0.0^{2,9}]*decan-9-ol-5-one* (**4**). The initial bicyclo[3.3.1]nonane-2,6-dione was prepared according to the original paper[11] with minor modifications.[12] Bicyclo[3.3.1]nonane-2,6-dione (19·4 g, 0·128 mole), MeOH p.a. (195 ml) and KOH (12·1 g, 0·216 mole) in 12 ml water were mixed in a 0·5 l. flask, cooled to −5°, and 43·7 g (0·204 mole) of N - nitroso - N - methyl - *p* - toluenesulfonamide, i.e. a 1·6 fold excess with respect to one keto group of the initial dione, were added during 50 min with constant stirring and cooling. After the nitroso compound had beed added, the temp was allowed to rise to the ambient temp. The solid was filtered off on a frit and washed with MeOH, and the filtrate was concentrated, diluted with an equal volume of water, and extracted with 3 × 100 ml $CHCl_3$. The combined $CHCl_3$ extracts were washed with water and dried over Na_2SO_4. The $CHCl_3$ was distilled off and the crystalline residue (14·1 g) was recrystallized from benzene; 10·6 g (50% of the theory) of the compound **4** were obtained, m.p. (corr.) 193·7–195·9°. Determination of active hydrogen: calculated 0·61%, found 0·64%. (Found: C, 72·20; H, 8·45. Calc C, 72·26; H, 8·49%). IR spectrum: bands 1030, 1060, 1143, 1324, 1450, 1460, 1710, 2865, 2945, 3600 cm^{-1}; Mass spectrum: M$^+$ 166 (55%), 55 (100%), 32 (71%), 83 (41%), 112 (38%), 41 (23%); NMR spectrum: multiplet 1·2–2·4 ppm.

Tricyclo[4.4.0.0^{2,9}]*decan-9-ol* (**6**). Compound **4** (0·5 g; 3·0 mole), 0·6 ml of 80% hydrazinehydrate (9·0 mole), 0·3 g fine ground KOH (5·5 mmole), and 2 ml of ethyleneglycol were heated in a 25 ml flask with a reflux condenser on a metal bath at 120–130° for 2 h. The mixture of hydrazinehydrate and water was then distilled off and the temp was kept at 195° for 4 h. After cooling, the mixture was diluted with an equal amount of water and extracted with 3 × 10 ml of ether. The extract was washed with dil HCl and water and dried over Na_2SO_4. Ether was distilled off and the residue dissolved in a small amount of n-hexane and transferred to a column with activated silica gel (8 h at 130°), with the substance-to-adsorbent ratio 1:30. The column was washed with 1290 ml of hexane, 260 ml of a mixture n-hexane–benzene (1:1), and 1330 ml of benzene. From the benzene eluates were obtained 0·15 g of a substance, which sublimed at 100°/atm. 0·12 g (yield 26%) of the compound **6** were obtained, m.p. (corr.) 132·8–134·7°. (Found: C, 79·00; H, 10·77, $C_{10}H_{16}O$ requires: C, 78·89; H, 10·59%); IR spectrum: 940, 1070, 1160, 1465, 2930, 3610 cm^{-1}; Mass spectrum: M$^+$ 152 (65%), 109 (100%), 96 (60%), 55 (55%), 70 (50%), 41 (39%), 95 (40%), 94 (38%), 83 (34%); NMR spectrum: multiplet 1·0–2·2 ppm.

Bicyclo[4.3.1]*decane-2,7-dione*. Compound **8** required for the synthesis was prepared as a colourless oil, yield 73·4%, b.p. 146–153°/9 Torr, n_D^{20} = 1·5078[12] (Ref 13 reports a 70% yield, b.p. 120–123°/1 Torr, n_D^{20} = 1·5079). 4·7 g (24·0 mmole) of monoethyleneacetal **8**, 2·08 g (37·2 mmole) of KOH in 2·1 ml of water, and 35 ml of MeOH p.a. were mixed in a 250 ml flask, cooled down to −10°, and 7·65 g (35·3 mmole) of N - nitroso - N - methyl - *p* - toluenesulfonamide were added during 45 min under constant cooling and stirring. Further procedure was the same as in the case of **4**. 5 g of monoethyleneacetals obtained in the reaction with diazomethane were stirred with 50 ml of 10% H_2SO_4 for 5 h at 55–60°. The mixture was then extracted with 3 × 30 ml of $CHCl_3$, the combined extracts were washed with $NaHCO_3$ aq and water and dried over Na_2SO_4, and $CHCl_3$ was distilled off. The composition of the residue was as follows: 22·1% of unreacted bicyclo[3.3.1]nonane-2,6-dione, 6·8% of **4**, 60·8% of **7**, and 10·3% of an unidentified substance. The mixture was transferred in a benzene soln on a column of 20 g of activated silica gel and the column was washed with benzene. From 840 ml of benzene, eluate 1·05 g of substance containing a small amount of bicyclo[3.3.1]nonane-2,6-dione were obtained. The diketone **7** was then purified by using the gas chromatography apparatus CHROM III (column 2 m, dia 6 mm, 4% SE-30 on Porovina (unglazed tile); temp of the column 180°, that of the detector 200°, pressure of the carrying gas (hydrogen) 1·05 kp/cm^2). The preparation gave 0·15 g of the substance, which was then sublimed at 100°/10 Torr; m.p. of **7** (corr.) 117·3–118·6°, (Found: C, 72·10; H, 8·44, theory for $C_{10}H_{14}O_2$: C, 72·26; H, 8·49%); IR spectrum: 960, 1313, 1450, 1695, 2940 cm^{-1}; Mass spectrum: M$^+$ 166 (42%), 55 (100%), 84 (68%), 41 (41%), 83 (39%). NMR spectrum: multiplet 1·2–3·0 ppm.

Bicyclo[4.3.1]*decan-2-one* (**10**). Monoethyleneacetal **8** was first reduced with hydrazinehydrate,[12] and 64·5% of ethyleneacetal of bicyclo[3.3.1]nonan-2-one, b.p. 109–114°/11 Torr, n_D^{20} = 1·4954, were obtained (Ref 13 reports 85% of the theory, b.p. 121–123°/13 Torr, n_D^{20} = 1·4958). This substance was decomposed by stirring with 10% H_2SO_4 at 55–60° for 4 h. We obtained 92·5% of **9**, m.p. 130·6–133·0°; Ref 13 reports 98% yield, m.p. 134–135°. From this ketone **9**, ketone **10** was prepared by the following procedure. 0·5 g (3·62 mmole) of **9**, 0·34 g (6·0 mmole) of KOH aq (50% soln), and 5 ml of MeOH were cooled in a 25 ml flask with a side tube to −10°, and 0·62 g (6·0 mmole) of N - nitroso - N - methylurea were added during 20 min under constant stirring. The mixture was stirred for additional 2 h under cooling and then allowed to stand overnight. The ppt was filtered off on a frit and washed with MeOH. The solvent was distilled off and 0·3 g (54·5% of the theory) of **10** were obtained and sublimed at 70°/12 Torr, m.p. (corr) 82·0–84·2°. (Found: C, 78·77; H, 10·57; $C_{10}H_{16}O$ requires: C, 78·89; H, 10·59%); IR spectrum: 930, 965, 1325, 1465, 1705, 2850, 2920 cm^{-1}; Mass spectrum: M$^+$ 152 (28%), 81 (100%), 41 (93%), 67 (80%), 55 (72%), 39 (70%); NMR spectrum: multiplet 1·2–2·9 ppm.

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