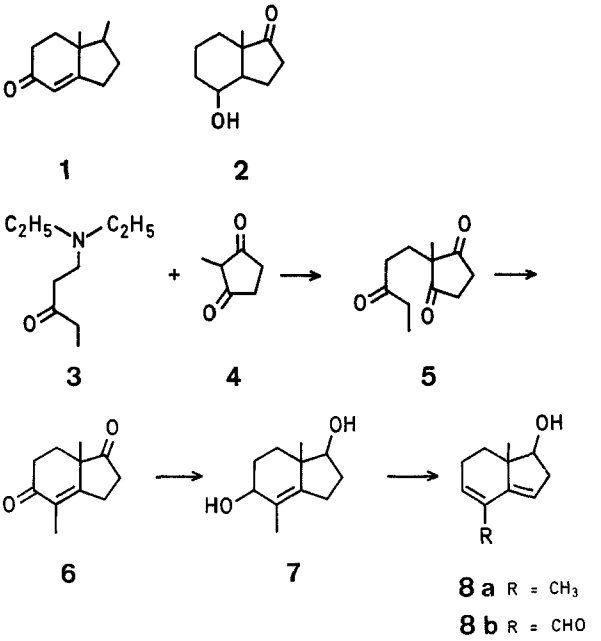
Synthesis of 2-Formyl-6-methyl-7β-hydroxybicyclo-[4.3.0]nona-2,9-diene

D. K. BANERJEE*, A. S. VITTAL RAO, S. D. VENKATARAMU, V. SURENDRANATH, V. B. ANGADI

Department of Organic Chemistry, Indian Institute of Science, Bangalore - 560012, India

Bicyclo[4.3.0]nonanes (**1** and **2**) have been successfully employed in the synthesis of steroids[1,2] and *seco*-steroids[3,4]. It appeared to us that 2-formyl-6-methyl-7β-hydroxybicyclo[4.3.0]-nona-2,9-diene (**8b**) might also serve as an intermediate in the total synthesis of *d,l*-steroids and be particularly useful in the stereospecific formation of asymmetric centres. The synthesis of **8b** is described in the present communication.



The preparation of 2,6-dimethyl-3,7-dioxobicyclo[4.3.0]-nonene (**6**), the starting material, by the condensation of 2-methyl-1,3-dioxocyclopentane (**4**) with ethyl vinyl ketone has been reported[5] in 32% yield. It has now been possible to improve the yield (51%) by refluxing the Mannich base **3** and the dione **4** in xylene containing pyridine, followed by cyclization of the crude trione **5** with *p*-toluenesulfonic acid. Sodium borohydride reduction of **6** in ethanol gave the diol **7** in 95% yield as a crystalline solid. Treatment of **7** with dilute methanolic sulfuric acid furnished a crystalline product which on purification by chromatography and distillation gave the pure dienol **8a** in 43% yield, spectral data agreeing with the assigned structure. Oxidation[6,7,8] of **8a** with selenium dioxide[9] in dimethyl sulfoxide afforded the crystalline hydroxydienaldehyde **8b** in 55% yield; spectral data confirmed the structure. The β-configuration (steroid nomenclature) has been assigned to the hydroxy group on the basis of well known analogy.

1-Diethylamino-3-oxopentane (3):
This was prepared according to the procedure of Robinson[10] in an improved yield by replacing the solvent ether with benzene. Thus from β-chloroethyl methyl ketone (280 g), diethylamine (336 g), and benzene (1050 ml), there was obtained 1-diethylamino-3-oxopentane (**3**); yields: 245 g (67%) as a colorless liquid; b.p. 73°/10 torr (Lit.[10]: 84°/13 torr).

I.R. (film): $\nu_{max} = 1715\ cm^{-1}$.

^{1}H-N.M.R. (CCl_4): $\delta = 1.00$ (9H, t, CH_3), 2.34–2.82 ppm (10H, m, CH_2).

2,6-Dimethyl-3,7-dioxobicyclo[4.3.0]nonene (6):
A mixture of 2-methyl-1,3-dioxocyclopentane (**4**; 36.6 g), 1-diethylamino-3-oxopentane (**3**; 49.4 g), dry pyridine (70 ml), dry xylene (300 ml), and hydroquinone (200 mg) was refluxed for 24 h, the cooled solution was then diluted with water and extracted with chloroform (5 × 200 ml). The extract was washed with cold dilute hydrochloric acid (5 × 100 ml) and then thoroughly with water. Following the complete removal of the chloroform and drying, the xylene solution was refluxed for 48 h after the addition of *p*-toluenesulfonic acid (1 g). The cooled reaction mixture was washed with aqueous sodium hydrogen carbonate and water. The xylene was removed and the residue on distillation gave pure **6**; yield: (30 g), b.p. 120°/0.8 torr (Lit.[5]: 104°/0.4 torr); dioxime, m.p. 234–235°, from ethanol (Lit.[5]: m.p. 236°).

2,6-Dimethyl-3,7-dihydroxybicyclo[4.3.0]nonene (7):
To the cooled and stirred solution of the dione (**6**; 5 g) in ethanol (25 ml) was added sodium borohydride (1.25 g) in small portions and the stirring was continued for 20 h. The cooled reaction mixture was acidified with glacial acetic acid (2 ml) and most of the ethanol was removed under diminished pressure. The residue was diluted with water and extracted with chloroform and the extract was washed with aqueous sodium hydrogen carbonate and brine. The solid obtained after removal of the solvent was crystallized from acetone/petroleum ether (40–60°) to furnish the pure diol **7**; yield: 4.9 g (95%); m.p. 140–144°.

$C_{11}H_{18}O_2$	calc.	C 72.49	H 9.96
(182.25)	found	72.79	10.09

I.R (KBr): $\nu_{max} = 3450$–$3200\ cm^{-1}$

^{1}H-N.M.R. (DMSO-d_6): $\delta = 0.83$ (3H, s, 6-CH_3), 1.49 (3H, s, 2-CH_3), 1.1–2.17 (8H, m, 4-, 5-, 8- and 9-CH_2), 3.35 (1H, t, 7-CHOH), 3.78 (1H, t, 3-CHOH), 4.46 and 4.61 ppm (2H, d, $J = 3$ Hz and 2Hz, 7- and 3-CHOH, disappear on treatment with D_2O).

2,6-Dimethyl-7-hydroxybicyclo[4.3.0]nona-2.9-diene (8a):
A solution of the diol (**7**; 2 g) in 50% aqueous methanol (15 ml) containing 4 drops of sulfuric acid (d = 1.84) was refluxed for 30 min and the methanol was distilled off. The cooled residue was poured into crushed ice and the separated solid was extracted with ether/benzene. The extract was washed with aqueous sodium bicarbonate and water. Removal of the solvent furnished a solid (1.7 g, 94%), m.p. 76°, which showed two spots in the T.L.C. using ethyl acetate/hexane (1:4).

A sample (0.5 g) of the crude product was passed through a column of neutral alumina (20 g) and eluted with hexane/benzene (3:2). The first two fractions (0.18 g), a gummy product, showed two spots in the T.L.C. and the later fractions (0.23 g), showing only one spot, were further purified practically without loss by short-path distillation; b.p. 70–75°/1 torr; m.p. 84–85°. The pure product deteriorates on standing and should be immediately used up for the next step.

$C_{11}H_{16}O$	calc.	C 80.44	H 9.83
(164.24)	found	80.11	9.93

U.V. (ethanol): $\lambda_{max} = 236$ ($\varepsilon = 22010$), 240 (21720), 252 nm (14480).
I.R. (nujol): $\nu_{max} = 3450$–3200, $830\ cm^{-1}$.
^{1}H-N.M.R. (CCl_4): $\delta = 0.88$ (3H, s, 6-CH_3), 1.10–1.45 (2H, m, 5-CH_2), 1.75 (3H, s, 2-CH_3), 2.22 (1H, s, CHOH, disappears on treatment with D_2O), 2.12–2.63 (4H, m, 4- and 8-CH_2), 3.90 (1H, t, CHOH), 5.28 and 5.48 ppm (2H, t, C=CH).

2-Formyl-6-methyl-7-hydroxybicyclo[4.3.0]nona-2.9-diene (8b):
A stirred mixture of the freshly prepared pure dienol (**8a**; 1.27 g), selenium dioxide[9] (1.22 g), and dimethyl sulfoxide (24 ml) was heated at 120–125° under nitrogen for 1 h. The cooled black solution was poured into water and extracted with ethyl acetate (4 × 50 ml). The extract was washed with aqueous sodium hydrogen carbonate and water, and dried (Na_2SO_4). The solvent was removed and the residue (1.2 g) was subjected to short-path distilla-

tion. After removal of an initial fraction at b.p. 100°/1 torr the main fraction (0.7 g) distilled at b.p. 135–145°/1 torr and solidified. A further quantity of 50 mg of the crystalline solid could be obtained from the initial fraction, bringing the total yield to 55%. After crystallization from ether/benzene the pure **8b** melted at 85°

$C_{11}H_{14}O_2$	calc.	C 74.15	H 7.86
(178.22)	found	74.59	7.81

U.V. (ethanol): $\lambda_{max}=216$ nm ($\varepsilon=17560$)

I.R (CCl_4): $\nu_{max}=3625$, 2730, 1695, 1660, 1635, 845 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): $\delta=0.86$ (3H, s, 6-C$\underline{H}_3$), 1.10–2.08 (2H, m, 5-C$\underline{H}_2$), 1.98 (1H, s, CHO$\underline{H}$, disappears on treatment with D_2O), 2.36–2.60 (4H, m, 4- and 8-C$\underline{H}_2$), 3.94 (1H, t, C$\underline{H}$OH), 6.34 and 6.62 (2H, t, C=C$\underline{H}$), 9.41 ppm (1H, s, C$\underline{H}$O).

The 2,4-dinitrophenylhydrazone was prepared in ethanol containing a trace of hydrochloric acid and crystallized from ethanol; m.p. 230–231°.

$C_{17}H_{18}N_4O_5$	calc.	C 56.98	H 5.06	N 15.64
(358.35)	found	57.22	5.26	16.01

U.V. ($CHCl_3$): $\lambda_{max}=385$ nm ($\varepsilon=14378$)[11].

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