Tetrahedron Letters No. 43, pp 4175 - 4178.
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0040-4039/78/1022-4175$02.00/0

THE BASE-INDUCED REARRANGEMENT OF ENDO-7,7-DIMETHYLBICYCLO[3.3.1]NONAN-3-OL-9-ONE

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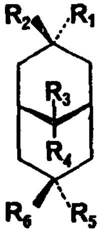
We have recently described[1] rapid reversible 3,7-hydride transfer in the alkoxide of exo-bicyclo[3.3.1] nonan-7-ol-3-one (1). We now report the base-induced rearrangement of the title compound (3) to anti-7,7-dimethylbicyclo[3.3.1]nonan-9-ol-3-one (4), a process involving 3,9-hydride transfer within the same molecular framework.



1 $R_1 = R_2 = O$, $R_3 = H$, $R_4 = H$, $R_5 = H$, $R_6 = OH$
2 $R_1 = H$, $R_2 = OH$, $R_3 = R_4 = O$, $R_5 = CH_3$, $R_6 = CH_3$
3 $R_1 = OH$, $R_2 = H$, $R_3 = R_4 = O$, $R_5 = CH_3$, $R_6 = CH_3$
4 $R_1 = R_2 = O$, $R_3 = H$, $R_4 = OH$, $R_5 = CH_3$, $R_6 = CH_3$
5 $R_1 = R_2 = O$, $R_3 = OH$, $R_4 = H$, $R_5 = CH_3$, $R_6 = CH_3$
6 $R_1 = R_2 = O$, $R_3 = R_4 = O$, $R_5 = CH_3$, $R_6 = CH_3$

The epimeric ketols, 2 and 3, were prepared by sequential lithium : liquid ammonia reduction and deketalization of the 9-ethylene ketal[2] of the dione 6, and both were treated with base. The endo-epimer (3) was converted smoothly ($t_{\frac{1}{2}}$ = 15 min. in 0.4M refluxing ethanolic potassium ethoxide) into an isomeric ketol whose structure (4) follows from its spectral properties and the chemical evidence presented below. Examination of the reaction mixture by G.L.C.[3] after 12 h. showed that the product was, in fact, a 1.04 : 98.96 mixture of 3 and 4. The same mixture was formed when pure 4 was resubjected to the reaction conditions. The exo-epimer (2) was unchanged under the same conditions.

That no skeletal reorganization had occurred in the course of the reaction was demonstrated by chromic acid oxidation of ketols 2, 3, and 4, to the same dione, 6. The position of the alcohol function in 4 is shown by the alcohol methine hydrogen signal (t, J = 2.8 Hz, at δ 4.12) in its NMR spectrum.[4] The orientation of this

9-hydroxyl (syn or anti to the 3-carbonyl) is not evident from the spectral data, but, reduction of the lithium enolate[5] of dione, 6, with lithium aluminium hydride at -78°C gave only two reduction products. One of these was shown, by spectral and chromatographic comparison, to be identical to the rearrangement product. The other was a fourth isomeric ketol (5), which also showed a triplet alcohol methine signal (J = 3 Hz) but at 0.3 ppm higher field than the corresponding signal in the NMR spectrum of 4, consistent with deshielding of this hydrogen by the 3-carbonyl group in ketol 4, but not in 5.

For conditions comparable with those used in the rearrangement of ketol 1, ketol 3 was dissolved in t-butanol at 35°C and one molar equivalent of potassium t-butoxide added, the reaction being monitored by G.L.C. The rearrangement of 3 then had a half-life of six minutes, corresponding to a rate of 2.10^{-3} sec.$^{-1}$, almost 10^2 slower than the rearrangement of 1.[6]

The rearrangement was also effected with NaOD in D_2O. Under these conditions, the alcohol methine hydrogen was not exchanged, although deuterium was incorporated into the product by exchange of hydrogens adjacent to the 3-carbonyl.

The most economical accommodation of the experimental data is that the rearrangement of 3 to 4 is a further example[7] of reversible intramolecular transfer of hydride from alcohol methine to carbonyl carbon (see Figure).

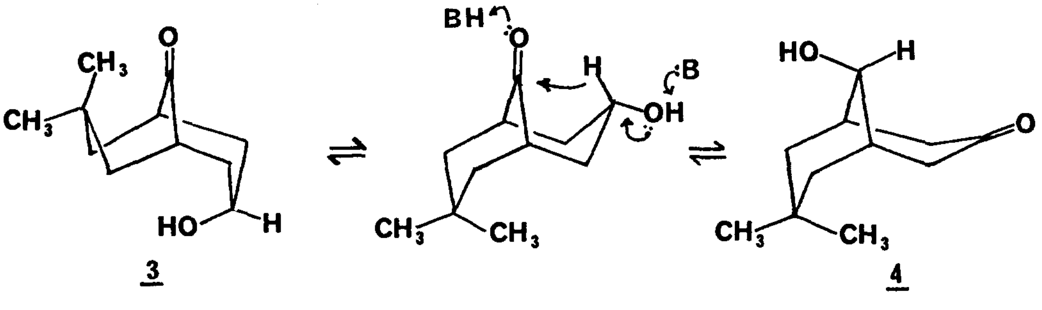


Figure *

The reacting centres at C_3 and C_9 are only placed in proximity when the cyclohexanol ring has adopted a boat conformation. However, the shape of the alcohol methine hydrogen signal (m, W = 14 Hz) in the NMR spectrum of 3 shows that this ring preferentially adopts a chair conformation (in $CDCl_3$ solution at least).[8] The necessity for a conformational pre-equilibrium in the rearrangement of 3, but not in 1, could account for the slowness of the 3,9-hydride transfer compared to the 3,7-shift.

Finally, the equilibrium constant in the rearrangement indicated that ketol 4 is 2.7 kcal.mol.$^{-1}$ more stable than its isomer, 3. This difference can, no doubt, be rationalized in terms of relief of steric interactions and, indeed, equilibrium constants for simple rearrangements of this type should provide useful benchmarks for the oxygen force fields now being developed.

Physiochemical Data.

All IR data (cm^{-1}) taken in CCl_4, and all NMR data (δ) taken in $CDCl_3$

2. Oil.

MS: m/e Found 182.1307, Calc. 182.1307; IR: 3607, 3405 (OH), 1724 (C = O); PMR: 0.90 (s, 3H), 0.98 (s, 3H), 1.4 to 3.0 (unresolved, 12H), 3.2 (s, 1H, exchanges with D_2O), 4.59 (m, 7 lines, width 32 Hz, 1H).

3. White crystalline solid.

M.p. 116.5 - 117.5°; MS: m/e Found 182.1309, Calc. 182.1307; IR: 3609 and 3440 (OH), 1710 (C = O); PMR: 0.89 (s, 3H), 0.98 (s, 3H), 1.4 to 3.0 (unresolved, 12H), 3.27 (s, 1H, exchanges with D_2O), 4.17 (m, 7 lines, width 14 Hz).

4. White crystalline solid.

M.p. 114 - 115°; MS: m/e Found 182.1311, Calc. 182.1307; IR: 3610 and 3450 (OH), 1715 (C = O); PMR: 0.89 (s, 3H), 0.97 (s, 3H), 1.3 (d, J = 13.5 Hz, 2H), 1.7 to 2.8 (unresolved, 8H), 2.52 (s, 1H, exchanges with D_2O), 4.12 (t, J = 2.8 Hz, 1H).

5. Oil.

MS: m/e Found 182.1310, Calc. 182.1307; IR: 3610 and 3420 (OH), 1710 (C = O); PMR: 0.89 (s, 3H), 0.93 (s, 3H), 1.66 (m, 4H), 2.18 (d, J = 19 Hz, 2H), superimposed on 2.28 (m, 2H), 2.71 (d of d, J = 19 and 8 Hz, 2H), 3.77 (t, J = 3 Hz, 1H).

6. White crystalline solid.

M.p. 35 - 36°; MS: Found 180.1158; Calc. 180.1150; IR: 1730 (C = O); PMR: 0.94 (s, 3H), 1.0 (s, 3H), 1.82 (d of d, J = 15 Hz, and J = 3 Hz, 2H), 2.1 (m, unresolved, 2H), 2.65 (m, unresolved, 6H).

[*] Illustrated thus for brevity. We have no information on the molecularity of the reaction.

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(Received in UK 24 August 1978; accepted for publication 4 September 1978)