CHEMICAL COMMUNICATIONS

The Synthesis and X-Ray Analysis of a Tricyclo [5,3,1,1^{2,6}]dodecane

By G. FERGUSON, W. D. K. MACROSSON, J. MARTIN, and W. PARKER (Chemistry Department, The University, Glasgow, W.2)

An unambiguous synthetic route to simple tricyclo- $[5,3,1,1^{2,6}]$ dodecanes was undertaken to permit an extension of our studies on the reactivity and conformational properties of the bicyclo[3,3,1]nonane system.¹

Without exception, all previously reported syntheses of the tricyclic ring system have been fortuitous and, for the most part, have resulted from the colligation of two heavily substituted aromatic nuclei.² It is noteworthy that the structural evidence for such compounds is based mainly on spectroscopic evidence and mechanistic considerations, and to date no structural confirmation by X-ray crystallographic or exhaustive chemical analysis has been reported. The high degree of substitution in such derivatives and the facility with which they dissociate to their aromatic precursors preclude their use for our purposes. The synthetic route adopted started from

bicyclo[3,3,1]nonan-2-one, readily available from mercuric acetate oxidation of 2-morpholinobicyclo[3,3,1]nonane. Treatment of this ketone with methylmagnesium iodide gave the tertiary carbinol (I) which was dehydrated (0·1 N-HClO₄/ HOAc) and hydroborated to give 2-methylbicyclo-[3,3,1]nonan-3-ol. Jones oxidation to the corresponding ketone (II; R=H) followed by cyanoethylation produced the keto-nitrile (II; R=CH₂. CH₂·CN) in high yield. Basic hydrolysis of (II; R=CH₂·CH₂·CN) gave the keto-acid (II; R= CH₂·CH₂·CO₂H) which was readily transformed to the crystalline enol lactone (III) by standard procedures.

As previously reported from these laboratories,^{3,4} reductive cyclisation of suitably substituted δ -enol lactones affords a highly stereoselective route to 2-hydroxybicyclo[3,3,1]nonan-9-ones in high yield. However, at this stage in our synthesis it was necessary to determine the relative stereochemistry of the methyl and the propionyl side-chain in (II; $R=CH_2\cdot CH_2\cdot CO_2H$). On the occasion of the methyl group being axial, *i.e.*, *exo* to the methylene bridge, cyclisation would lead to a tricyclododecane of configuration shown in (IV), whereas an equatorial (*endo*) configuration of the methyl group would result in a diamantane-like skeleton as depicted in (V).

To this end, the conversion of the keto-acid (II; $R=CH_2 \cdot CH_2 \cdot CO_2H$) into the ketone (II; $R=CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3$) was accomplished by standard techniques. Nuclear magnetic resonance solvent shift studies⁵ on this ketone (II; $R=CH_2 \cdot CH_2 \cdot CH_3 \cdot CH_3 \cdot CH_2 \cdot CH_3 \cdot CH_$

In the event, treatment of the enol-lactone (III) with lithium aluminium hydride gave two major products, one of which was shown to be the ketoalcohol (II; $R=CH_2\cdot CH_2\cdot CH_2\cdot OH$) whereas the other, a highly crystalline solid, proved to be the expected diol (VI; R=H).

Oxidation of (VI; R=H) gave the crystalline diketone (V) which was readily converted into the keto-acid (II; $R=CH_2 \cdot CH_2 \cdot CO_2H$) by treatment

103

with aqueous sodium carbonate. Buchanan *et al.*⁶ have recently described an attempted synthesis of (VIII) from cyclisation of (VII). Unfortunately, the sole isolable product proved to have the grossly rearranged structure (IX). In the above synthesis the β -diketone cleavage to the starting keto-acid (II; R=CH₂·CH₂·CO₂H) confirms that no deep seated rearrangement has taken place in the step (III) to (VI; R=H).

A single-crystal X-ray analysis of (VI; $R=p-I\cdot C_6H_4\cdot CO\cdot$) completely confirms the proposed structure and reveals the precise conformation in the solid state (Figure).



A view (along a) of the tricyclo $[5,3,1,1^{2,6}]$ dodecyl moiety showing the deviations from the ideal cyclohexane chair conformation. The point of attachment of the p-iodobenzoate group is indicated by the broken bond at C-5.

The three six-membered rings of (VI; R = p- $I \cdot C_6 H_4 \cdot CO \cdot$) adopt chair conformations but mutual repulsion between methylene groups at C-4 and C-11 causes the ring containing C-4 to be deformed so that C-4 in only 0.32 Å from the plane of C-2-3-5-6 (in an undistorted cyclohexane chair the displacement would be 0.73 Å). Overcrowding of the hydroxyl group and C-9 is relieved by similar bond-angle distortions and the ring containing C-9 is deformed in an almost identical manner (C-9 is 0.31 Å from the plane C-1-7-8-10). As a measure of the congestion around the hydroxyl group C-12 is 2.23 Å from the C-1-7-8-10 plane while the hydroxyl oxygen displacement is 2.84 Å; in the absence of distortion these distances would have had the same value (2.18 Å).

CHEMICAL COMMUNICATIONS

The solid-state infrared spectra, ν_{max} (KCl disc) 3471 cm.⁻¹ is indicative of O-H $\cdot \cdot \cdot$ O hydrogen bonding. This is also confirmed by the X-ray analysis; the hydroxyl group is close (2.90 Å) to the carbonyl oxygen of a neighbouring molecule related by a two-fold screw axis.

The mono-p-iodobenzoate crystallised from ethanol in the monoclinic system, space group $P2_1/c$ with four molecules in a unit cell of dimensions a = 10.36, b = 11.62, c = 15.47 Å, $\beta =$ 104.2°. From equi-inclination Weissenberg photographs taken with $Cu-K_{\alpha}$ radiation, 2943 independent structure amplitudes were estimated. The co-ordinates of the heavy atom were found from a three-dimensional Patterson synthesis. The structure was completely revealed in the first electrondensity distribution derived from iodine phases and observed amplitudes. The atomic parameters for all the non-hydrogen atoms have been improved by Fourier and least-squares methods.* R is now 0.15and further refinement is being continued.



(Received, December 12th, 1966; Com. 980.)

* Using programs devised by the Glasgow group: Fourier program, Dr. J. G. Sime; least-squares program, Professor D. W. J. Cruickshank and J. G. F. Smith.

¹ (a) W. A. C. Brown, G. Eglinton, J. Martin, W. Parker, and G. A. Sim, Proc. Chem. Soc., 1964, 57; (b) G. Eglinton, J. Martin, and W. Parker, J. Chem. Soc., 1965, 1243; (c) W. A. C. Brown, J. Martin, and G. A. Sim, J. Chem. Soc., 1965, 1844; (d) W. D. K. Macrosson, J. Martin, and W. Parker, Tetrahedron Letters, 1965, 2589.
² (a) A. G. Perkin and A. B. Steven, J. Chem. Soc., 1906, 802; (b) T. Severin, Chem. Ber., 1959, 92, 1517; (c) A. J. Birch, D. N. Butler, and J. B. Siddall, J. Chem. Soc., 1964, 2932; (d) H. J. Teuber and G. Steinmetz, Chem. Ber., 1965, 98, 666; (e) H. Davies, H. Endtman, and M. Nilsson, Tetrahedron Letters, 1966, 2491.
³ J. Martin, W. Parker, and R. A. Raphael, J. Chem. Soc., 1964, 289.

⁴ J. Martin, W. Parker, B. Shroot, and T. Stewart, J. Chem. Soc., in the press.

⁵ J. Connolly and R. McCrindle, Chem. and Ind., 1965, 379, 2066.

⁶G. L. Buchanan, G. Ferguson, A. M. Lawson, and D. R. Pollard, Tetrahedron Letters, 1966, 5303.