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SELECTIVE CARBANION SUBSTITUTION IN A 1,2,3,4-TETRAHYDROFLUOREN-1-ONE

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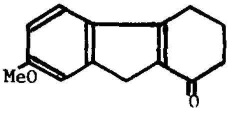
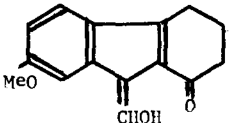
7-Methoxy-1,2,3,4-tetrahydrofluoren-1-one (I) has been found to undergo highly selective substitution at different positions, depending on the reagent and conditions used. This ketone (mp. 111-112°, $\nu_{max}^{CHCl_3}$ 1650 and 1610 cm^{-1}) was obtained by polyphosphoric acid cyclisation of m-methoxybenzyl cyclohexane-2,6-dione (mp. 149.5-150°) in 51% yield, together with 17% of the 5-methoxy isomer (mp. 121-122°).

Formylation of (I) (ethyl formate, sodium methoxide, benzene) gave in 88% yield the 9-formyl ketone (II), mp. 124-124.5°, which according to its NMR spectrum was entirely enolic: $\delta\ ppm_{TMS}^{CDCl_3}$ 7.72 (1H, d, J=13 cps, =C$\underline{H}$OH), 13.62 (1H, d, J=13 cps, =CHO$\underline{H}$), 1.9-3.0 (6H, -CH$_2$-) no indene -CH -. Forced condensation of (I) with dimethyl carbonate and sodium methoxide gave in 41% yield the keto-9-ester (IIIb), mp. 121-122°, $\nu_{max}^{CHCl_3}$ 1735, 1650 and 1605 cm^{-1}; $\delta\ ppm_{TMS}^{CDCl_3}$ 4.60 (1H, broad s, indene -CH-), 1.90-3.0 (6H, -CH$_2$-); together with 11% of its methylation product (1) (IV), mp. 135.5-137°; $\nu_{max}^{CHCl_3}$ 1730, 1655 and 1605 cm^{-1}; $\delta\ ppm_{TMS}^{CDCl_3}$ 1.67



I



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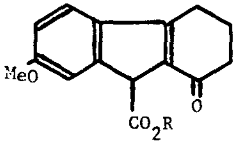

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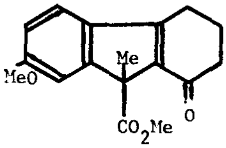
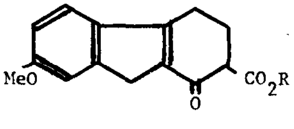
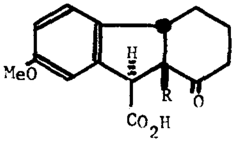


IV

V





VI

a: R=H
b: R=Me

(3H, s, C-Me), 1.9-3.0 (6H, $-CH_2-$), no indene H. Furthermore, conversion of (I) into its enolate with sodium tert.-amyloxide or potassium tert.-butoxide in benzene - dimethoxyethane, followed by treatment with carbon dioxide, led in over 85% yield to the keto-9-acid (IIIa), mp. 128° (decomp.), converted by diazomethane into (IIIb).

On the other hand, carboxylation of (I) either by carbon dioxide treatment of the enolate formed with lithium diisopropylamide, or by treatment with magnesium methyl carbonate (2) gave in variable yields (apart from unchanged material) the keto-2-acid (Va), mp. 110° (decomp.), whose methyl ester (Vb), mp. 127.5-128.5° showed $\nu_{max}^{CHCl_3}$ 1753, 1655 and 1610 cm^{-1}; δ $ppm_{TMS}^{CDCl_3}$ 2.0-3.1 (4H, $-CH_2-$), 3.58 (2H, broad s, indene $-CH_2-$) and 3.90 (1H, overlapping OMe peak, -COCHCO-). Finally, reduction of acid (IIIa) with lithium in liquid ammonia, followed by termination of the reaction with methyl iodide (3), gave the 9a-methylated keto-acid (VIb), mp. 181-183°, $\nu_{max}^{CHCl_3}$ 1700 cm^{-1}; δ ppm $_{TMS}^{CDCl_3}$ 1.42 (3H, s, C-Me), 4.70 (1H, s, indene -CH-), whose suggested stereochemistry is based on analogy with that of the des-methyl acid (VIa). The latter was obtained when the lithium - ammonia reduction was terminated with ammonium chloride; it had mp. 140.5-141° and showed $\nu_{max}^{CHCl_3}$ 1700 cm^{-1}; δppm $_{TMS}^{CDCl_3}$ 4.70 (1H, d, H_9), 3.8-4.15 (1H, m, H_{4a}), 3.50(1H, double d, H_{9a}). On double irradition at H_9 the H_{9a} signal collapsed to a simple doublet; on irradiation at H_{9a} the H_9 signal appeared as a singlet and the H_{4a} signal appeared to simplify to a triplet. These results confirm the above assignments, and the coupling constants thus found: $J_{9,9a}$= 2 cps and $J_{4a,9a}$= 8 cps indicate H_{9a} and H_9 to be trans- and H_{4a} and H_{9a} to be cis-related.

All new compounds mentioned gave satisfactory analyses.

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References.

(1) V.H. Wallingford and D.M. Jones, J. Amer. Chem. Soc., **64**, 578 (1942).

(2) H.L. Finkbeiner and M. Stiles, ibid., **85**, 616 (1963).

(3) G. Stork, P. Rosen, N. Goldman, R.V. Coombs, and J. Tsuji, ibid., **87**, 275 (1965).