Formation and Possible Intermediacy of a Spiro-lactone in the Nitrative Cyclisation of Methyl β-Arylisovalerate to a Nitrohydrocoumarin

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Summary Nitration of methyl β-arylisovalerate produces a nitro spiro-lactone in addition to a nitrohydrocoumarin, suggesting possible intervention of an addition-elimination sequence in the formation of the latter compound.

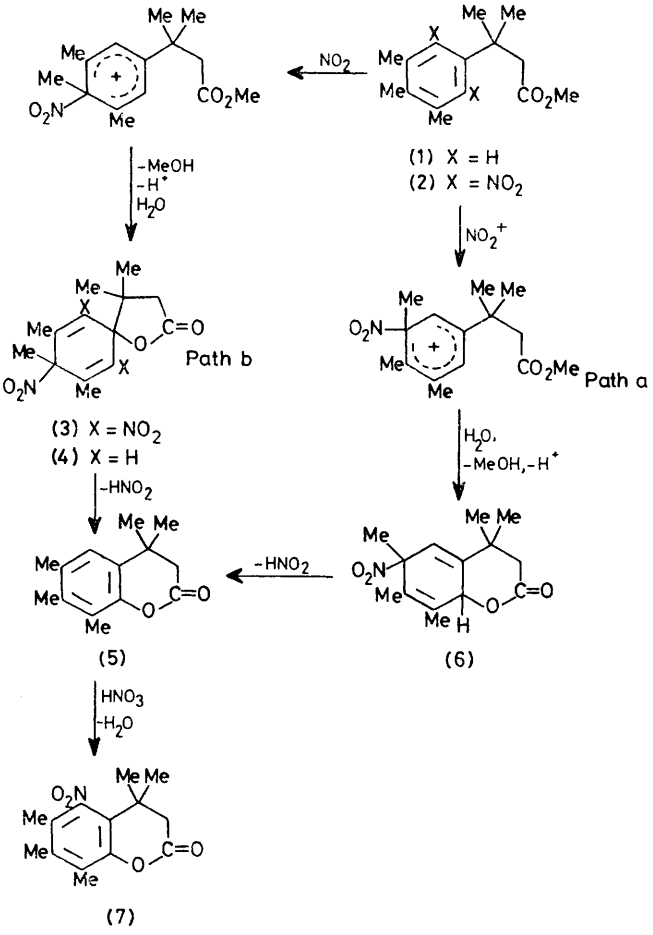
NITRATION of the isovalerate (**1**) produces the nitrodihydrocoumarin (**7**) in good yield.[1] However, the scope and mechanism of this interesting reaction remain unclarified. We now report the isolation of a spiro-lactone (**3**) from the

nitration of (**1**), which suggests the possibility of an addition–elimination sequence playing a role in the conversion of (**1**) into (**7**).

Nitration was effected by adding a solution of KNO_3 in H_2SO_4 to a solution of (**1**) in $CHCl_3$ at 0 °C and allowing the temperature to rise gradually to room temperature. Dilution with water, followed by fractional crystrllization of the precipitate from ethanol gave (**3**) as pale yellow needles (*ca.* 20%), m.p. 143—144 °C (decomp.) in addition to (**7**) and the 2,6-dinitro derivative (**2**). Compound (**3**) was more easily obtained in 50—60% yield by treating (**2**) with excess of HNO_3 (d = 1·5).

Compound (**3**) has the empirical formula $C_{14}H_{17}N_3O_8$; m/e 281 ($M^+ - NO_2 - CO$), 264 ($M^+ - HNO_2 - CO_2$), 226 ($M^+ - C_4H_8 - CO - NO - Me$), and 204 ($M^+ - 2NO_2 - CO_2 - Me$). The i.r. spectrum (KBr) demonstrated the presence of a γ-lactone ring (1810, 1190, and 1025 cm^{-1}), carbon–carbon double bonds (1615 cm^{-1}), and nitro groups (1565, 1540, and 1340 cm^{-1}), while its ^1H n.m.r. spectrum [100 MHz; $(CD_3)_2SO$] showed signals at δ 1·38, 1·98, 2·06, and 2·84, relative intensity 6 : 6 : 3 : 2. The ^{13}C n.m.r. spectrum (90 MHz; $CDCl_3$) provided evidence for the presence of the 1-oxaspiro [4·5]deca-6,9-dien-2-one unit (δ 41·6, 46·9, 83·2, 93·6, 136·0, 148·3, and 171·6) and five methyl groups (δ 14·4, 21·0, and 28·3). Its u.v. spectrum (MeOH) did not exhibit an absorption maximum above 220 nm. Compound (**3**) is only sparingly soluble in normal solvents and in trifluoroacetic acid it decomposed to a complex mixture which contained β-(2,6-dinitro-3,4,5-trimethylphenyl)isovaleric acid in addition to several unidentified substances, which lends support to the proposed structure.

Nitrative cyclisation of (**1**) to (**7**) may well be explained by an addition–elimination mechanism (Scheme, path a), which involves an *ipso* attack of a nitronium ion at the C-5 ring carbon in (**1**), followed by intramolecular trapping of an ester oxygen atom by C-2 to form the hydrocoumarin structure (**6**), although this route does not follow the normal pattern of reactivity of the 1,2,3,5-tetra-alkylbenzene nucleus. However, the ready formation of the spirolactone (**3**) from (**2**) also suggests an alternative possibility; the rearrangement–elimination sequence proposed by Fischer and his co-workers,[2] in which a concerted acid-catalysed loss of the nitro group from a *gem*-adduct (**4**) and a 1,2-migration of the acyloxy group produces the hydrocoumarin (**5**), which upon further nitration yields (**7**) (Scheme, path b). The conversion of (**2**) into (**3**) represents the first case of coupled *ipso* attack on the benzene ring by an external electrophile and internal nucleophile in aromatic nitration.[3]



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[2] A. Fischer and J. N. Ramsay, *Canad. J. Chem.*, 1974, **52**, 3960; A. Fischer and D. R. A. Leonard, *ibid.*, 1976, **54**, 1795.
[3] For a review of non-conventional processes which occur as the consequences of *ipso* attack, see S. R. Hartshorn, *Chem. Soc. Rev.*, 1974, **3**, 167; R. B. Moodie and K. Schofield, *Accounts Chem. Res.*, 1976, **9**, 287; H. Suzuki, *Synthesis*, 1977, 217.