Acetylation of 2,3-Dimethylbenzofuran. The First Example of a 'Non-conventional' Friedel–Crafts Reaction

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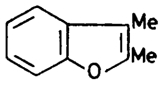
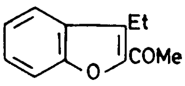
Summary In the acetylation of 2,3-dimethylbenzofuran (I) by Ac_2O and $SnCl_4$ in 1,2-dichloroethane, besides the main product of the reaction, 6-acetyl-2,3-dimethylbenzofuran (IV), 2-acetyl-3-ethylbenzofuran (II) is also obtained in 9% yield, probably *via* attack of the electrophile at the 2-position of (I) and subsequent rearrangement of the 2-methyl group.

SIDE-CHAIN electrophilic substitution of alkylaromatic compounds is one of the most important examples of that class of reactions, called 'non-conventional electrophilic aromatic substitutions,' where the decomposition of the first formed σ-complex does not lead to the displacement of a group by another.[1,2] Since the discovery of the electrophilic side-chain halogenation of polymethylbenzenes[3] the scope of this reaction has been considerably widened to include bromination,[4] iodination,[5] thiocyanation,[6] hydrogen exchange,[7] sulphonation,[8] and nitration.[2] In this note we report on what seems to be the first case of a 'non-conventional' Friedel–Crafts reaction observed in the acetylation of 2,3-dimethylbenzofuran (I).

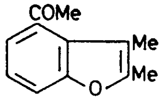
A solution of (I) in 1,2-dichloroethane was added dropwise to a stirred mixture (1 : 10) of $SnCl_4$ and Ac_2O so that the final concentration of reactants was 0·05 M. The mixture was allowed to react at room temperature for 48 h and, after usual work up, was analysed by g.l.c.–mass spectrometry on a 5% SE-30 column. The mass spectrum of each of the three products (II)—(IV) exhibited the parent ion peak at *m/e* 188 and the base peak at $(M-15)$ thus confirming the structures where an acetyl group had replaced a hydrogen atom of (I). The overall yield of acetylated products was *ca.* 30% (some starting material was still present), and the ratio of (II) : (III) : (IV) (in the order of their retention times) was 9 : 2 : 89. For preparative purposes the yield could be increased to up to 60% by using an equimolar amount of catalyst and heating at reflux for 12 h, but under these conditions the distribution of products changes in favour of (III) and (IV).



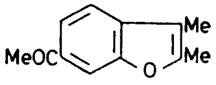
(I)



(II)



(III)

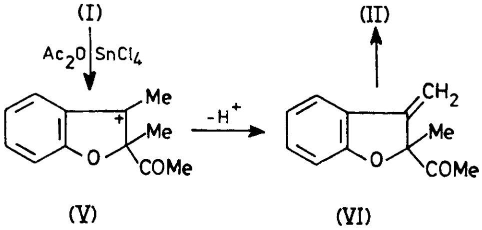


(IV)

The crude mixture was then separated by chromatography on silica gel, eluting with light petroleum–diethyl ether, and the samples obtained were purified further by preparative g.l.c. The good agreement of their i.r.[9] and n.m.r.[10] spectra with those reported in the literature proved that the main product (IV) was, as expected,[11,12] 6-acetyl-2,3-dimethylbenzofuran whereas (III) was the 4-acetyl derivative.

On the basis of compelling spectral evidence [ν(CO) 1675 cm^{-1}, typical of an aromatic ketone; δ (CCl_4) 1·30 (3H, t, *J* 7 Hz, CH_2*Me*), 2·51 (3H, s, COMe), 3·07 (2H, q, *J* 7 Hz, C*H*$_2$Me), 7·0—7·7 (4H, m, ArH)], compound (II) (m.p. 37 °C) was formulated as 2-acetyl-3-ethylbenzofuran. This structure was subsequently confirmed by comparison with an authentic specimen prepared by acetylation[13] of 3-ethylbenzofuran obtained from benzofuran-3(2*H*)-one[14] and EtMgBr.[15]

It seems reasonable to suggest that (II) derives from (I) by the mechanism already proposed for the side-chain electrophilic substitutions of alkylaromatic compounds (see Scheme). The electrophile attacks the most reactive position of the benzofuran ring (C-2)[16] forming the σ-complex (V) which, in turn, can lose a proton from the 3-methyl group giving the intermediate (VI). The subsequent rearrangement of (VI) gives (II) and it is interesting to note that here the migrating group is the 2-methyl group, and not the attacking electrophile, as is the case in other 'non-conventional' processes leading to side-chain substitution.



SCHEME

The low relative amount of (II) obtained can probably be ascribed to the reversibility of the steps leading to the σ-complexes.[17] The subsequent loss of the proton from the 3-methyl group of (V) is probably slower than the loss of the proton from the σ-complex *en route* to the 6-acetyl derivative.

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[1] E. Baciocchi and G. Illuminati, *Progr. Phys. Org. Chem.*, 1967, **5**, 1.

[2] S. R. Hartshorn, *Chem. Soc. Rev.*, 1974, **3**, 167.

[3] E. Baciocchi and G. Illuminati, *Tetrahedron Letters*, 1962, 637; E. Baciocchi, A. Ciana, G. Illuminati, and C. Pasini, *J. Amer. Chem. Soc.*, 1965, **87**, 3953.

[4] E. Baciocchi, M. Casula, G. Illuminati, and L. Mandolini, *Tetrahedron Letters*, 1969, 1275; E. Baciocchi, S. Clementi, and G. V. Sebastiani, *J.C.S. Perkin II*, 1974, 1882; 1976, 266.

[5] L. J. Andrews and R. M. Keefer, *J. Amer. Chem. Soc.*, 1964, **86**, 4158.

[6] E. Baciocchi, P. Faggioni, and G. Illuminati, *Gazzetta*, 1973, **103**, 1311.

[7] C. Eaborn and G. J. Wright, *J. Chem. Soc.* (*B*), 1971, 263.

[8] H. Cerfontain, A. Koeberg-Telder, C. Ris, and C. Schenk, *J.C.S. Perkin II*, 1975, 966.

[9] Y. Kawase and M. Takashina, *Bull. Chem. Soc. Japan*, 1967, **40**, 1224.

[10] Y. Kawase, S. Takata, and T. Miwa, *Bull. Chem. Soc. Japan*, 1970, **43**, 1796.

[11] E. Bisagni and R. Royer, *Bull. Soc. chim. France*, 1962, 925.

[12] Y. Kawase and S. Hori, *Bull. Chem. Soc. Japan*, 1970, **43**, 3496.

[13] E. Bisagni, N. P. Buu Hoi, and R. Royer, *J. Chem. Soc.*, 1955, 3688.

[14] A. K. Bose and P. Yates, *J. Amer. Chem. Soc.*, 1952, **74**, 4703.

[15] R. Stoermer and E. Barthelmes, *Ber.*, 1915, **48**, 62.

[16] S. Clementi, P. Linda, and G. Marino, *J. Chem. Soc.* (*B*), 1971, 79.

[17] R. W. Alder, R. Baker, and J. M. Brown, 'Mechanism in Organic Chemistry', Wiley-Interscience, London, 1971, p. 287.