A Solvent Effect in the Reaction of Sodium Methoxide with Pentafluoronitrobenzene

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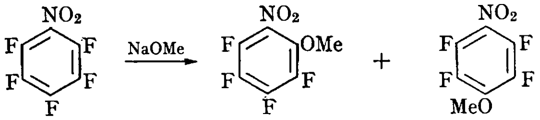
IN recent papers we showed that ammonia (in ether)[1] and methylamine (in 3% ethanol–ether)[2] reacted with pentafluoronitrobenzene to replace mainly (~70%) the fluorine *ortho* to the nitro-group. In contrast, with dimethylamine (in 3% ethanol–ether),[2] with sodium methoxide (in methanol), with pentafluorophenylmagnesium bromide (in tetrahydrofuran),[3] and with pentafluorophenyllithium (in ether),[4] the *para*-fluorine was predominantly (>80%) replaced. In these last reactions, pentafluoronitrobenzene was behaving as do[5] other C_6F_5X compounds in which X is not strongly electron-donating in reacting with nucleophiles mainly (~90%) at the position *para* to X. We attributed[2] the high proportion of *ortho*-replacement in the reactions of ammonia and methylamine with pentafluoronitrobenzene to hydrogen-bonding between the amines and the nitro-group.

We have now found, however, that in ether containing very little methanol, sodium methoxide replaces mainly the *ortho*-fluorine in pentafluoronitrobenzene to a much greater extent than in methanol itself, the ratio of *ortho*- to *para*-replacement decreasing rapidly with increasing methanol content of the solvent.

% (v/v) methanol in ether	3·8	5·0	10	20	50	100
ortho: para ratio	1·0	0·53	0·26	0·08	0·06	0·08



Sodium methoxide (1 equiv.) in methanol–ether (200 ml.) was added dropwise during 2 hr., with stirring, at 15° to a solution of pentafluoronitrobenzene (0·5 g.) in the same methanol–ether mixture (200 ml.) After 2 hr. the reaction mixture was evaporated, the residue diluted with water, and the mixed methoxy-compounds (~100% yield) isolated by methylene chloride extraction; they were analysed both by gas chromatography and proton magnetic resonance spectroscopy.[2]

Until much more data are available, it will not be possible to rationalise this solvent effect with any certainty. Similar, and possibly related,

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[1] G. M. Brooke, J. Burdon, and J. C. Tatlow, *J.*, 1961, 802.
[2] J. G. Allen, J. Burdon, and J. C. Tatlow, *J.*, 1965, 1045.
[3] G. M. Brooke and W. K. R. Musgrave, *J.*, 1965.
[4] D. Callander, P. L. Coe, and J. C. Tatlow, unpublished.
[5] J. C. Tatlow, *Endeavour*, 1963, **22**, 89.

solvent effects have been encountered[6] in the general nucleophilic aromatic substitution field, but none was as obviously pronounced as the one reported here and none has been satisfactorily explained.

While our present findings do not invalidate earlier work on directional effects in the polyfluoro-aromatic field, it is clearly necessary that these replacements be re-investigated in a variety of solvents.

One report of a possible solvent effect in this field has been made already;[7] hydrazine in dioxan reacted with pentafluorophenylhydrazine to give the *meta*- and *para*-disubstituted products in equal amounts, whereas in tetrahydrofuran, the *para*-dihydrazine was the only isolated. The yields were poor, however, and so the result may not represent a true change in position of attack with change of solvent.

(*Received, January 26th*, 1965.)

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[6] W. Greizerstein, and J. A. Brieux, *J. Amer. Chem. Soc.*, 1962, **84**, 1032; G. Illuminati and G. Marino, *Chem. and Ind.*, 1963, 1287; J. H. D. Hertog, and C. Jouwersma, *Rec. Trav. chim.*, 1953, **72**, 44; N. B. Chapman, R. E. Parker, and P. W. Soanes, *J.*, 1954, 2109.

[7] D. G. Holland, G. J. Moore, and C. Tamborski, *J. Org. Chem.*, 1964, **29**, 1562.