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# UNUSUAL DEALKYLATIONS AND REARRANGEMENTS IN AROMATIC NUCLEOPHILIC SUBSTITUTION

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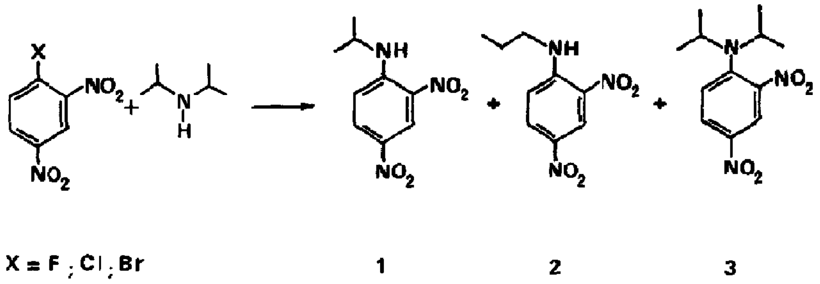
SUMMARY: The reaction of 2,4-dinitrohalobenzenes with di-isopropylamine produces mainly N-(2,4-dinitrophenyl)-isopropylamine and N-(2,4-dinitrophenyl)-n-propylamine instead of the expected straightforward substitution product. Dealkylations are also observed in the reactions with isopropylcyclohexylamine and dicyclohexylamine. A carbanionic mechanism is proposed.

As part of a study on steric effects on ANS started several years ago[1], the reaction of 2,4-dinitrofluorobenzene (DNF) with di-isopropylamine (DIPA) in benzene was studied. But, N-(2,4-dinitrophenyl)-isopropylamine ( 1 in Scheme I) was produced instead of the expected straigthforward substitution product: N-(2,4-dinitrophenyl)-di-isopropylamine ( 3 ) of which none was obtained under the reaction conditions. An even more striking result is the second in importance reaction product: N-(2,4-dinitrophenyl)-n-propylamine ( 2 ).



Scheme I

Analogous results were obtained in the reactions of 2,4-dinitrochloro- and 2,4-dinitrobromobenzene, the quantitative yields are set forth in the Table. Similar results were observed at 80°.

The reaction of DNF with DIPA was also performed in methanol. In this solvent the basic dissociation of the amine ($pK_B$ of di-isopropylamine in methanol is 5.50[2] determined by an spectrophotometric[3] and by an independent kinetic method[4]) produces methoxide ion which also reacts with DNF, but the main amino-defluorination product was again 1 and only traces of 3 were obtained. A similar result was observed in DMSO, the amount of 3 being slightly greater.

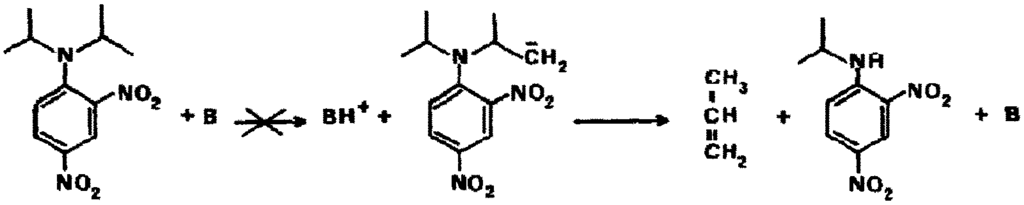
TABLE

Reaction of 2,4-dinitrohalobenzenes with DIPA in benzene at 60° [a,b]

| COMPOUND | X = F[c]<br>% Yield | X = Cl[c]<br>% Yield | X = Br[c]<br>% Yield |
|---|---|---|---|
| N-(2,4-dinitrophenyl)--isopropylamine | 81.7 | 85.4 | 82.6 |
| N-(2,4-dinitrophenyl)--n-propylamine | 15.8 | 12.6 | 14.7 |
| N-(2,4-dinitrophenyl)--di-isopropylamine | - | 1.9 | 1.7 |

[a] Yield calculated over the total of peaks found in g.l.p.c. (assuming response unity for the unidentified peaks). [b] [2,4-dinitrohalobenzene] = 4.2 x $10^{-4}$M. [c] [DIPA] = 0.28M.

The formation of 1 could, in principle, be explained by an isopropyl group elimination in 3 promoted by an attack of base on the methyl hydrogen, (Scheme II). 3 was then submitted to the same reaction conditions but it was recovered unaltered by g.l.p.c.



3 1

Scheme II

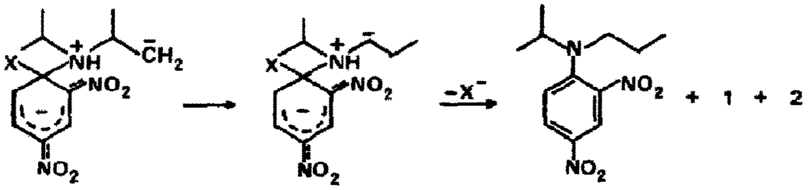
A second possibility could be a similar alkyl elimination in the zwiterionic $\sigma$ complex intermediate. Since propene is difficult to detect, the reaction was studied using isopropylcyclohexylamine. N-(2,4-dinitrophenyl)-cyclohexylamine (4), and 1 (in a ca. 9:1 relation), were the main products but no cyclohexene was found. The reaction was also carried out using di-cyclohexylamine as a nucleophile, 4 was isolated in a 15% yield but no cyclohexene was detected.

Another conceivable mechanism is heterolysis of the intermediate to form an alkyl cation which under the reaction conditions could form an alkyl halide, or even alkylate benzene. However, neither isopropylbromide nor cyclohexylbromide nor cumene were found in the reaction mixture.

A fourth possibility could be that the Meissenheimer complex act as an alkylating agent of the amine forming tri-isopropylamine (TIPA). This amine was synthesized and its limit of detection was determined, but again no TIPA was found in the reaction mixture. Some salts of secondary amines are reported to become dealkylated on heating[5], and, therefore, dealkylation of the DIPA due to the long heating was examined by g.l.p.c. analysis of samples of DIPA heated during 30 days at 80°; no dealkylated nor rearranged products were found.

Compound 2 is obviously a rearrangement product, but, the amine alone or 3 do not suffer rearrangement, then, it must occur in the Meissenheimer intermediate. Inasmuch as the most obvious explanations fail to gain experimental support and inasmuch as it is difficult to conceive of a carbenium ion mechanism, in which an isopropyl cation rearranges to an n-propyl cation, a carbanion mechanism is proposed instead. Attack of base on the Meissenheimer intermediate would produce 5, which by a 1,2-alkyl shift would form 6. Then 6 can result: dehydrofluorinated to form 7 or dealkylfluorinated to form 1 and 2, (Scheme III).

Although 1,2-shifts of alkyl groups from carbon to carbon that are carbanionic in character are very rare, we have found an example in the literature which is the Grovenstein-Zimmerman rearrangement.[6]



5 6 7

Scheme III

If the proposed mechanism is valid, at least traces of 7 could be found. A careful search of the 2,4-dinitrophenylderivatives which are formed in very small amounts was then carried out. The following were identified: N-(2,4-dinitrophenyl)-n-propyl-isopropylamine ( 7 ); N-(2,4-dinitrophenyl)-ethylisopropylamine ( 8 ); N-(2,4-dinitrophenyl)-methyl-n-propylamine ( 9 ); 2,4-dinitrophenylphenyl ether ( 10 ); 2,4-dinitroanisole ( 11 ); 2,4-dinitroaniline ( 12 ) and 2,4-dinitrophenol ( 13 ). Some of the products found gave support to the proposed mechanism: an intermolecular methyl transfer from 5 would produce 8 and reattachment of the methyl group on the dealkylated intermediate complex to 2 would produce 9 .

A kinetic study of the complex reaction performed by a method previously described[7] showed that the aminodehalogenation is slow (the results of each reaction will be given elsewhere) and formation of the ethers could be explained by a competitive reaction with traces of water present in the benzene.[8] The formation of the 2,4-dinitrophenyl ethers and the cleavage of the isopropyl groups could explain, in part, the failure to detect the fate of the isopropyl groups. As far as we know this is the first time that dealkylations and rearrangements are observed in reactions of this type. The reaction of DNF with diethylamine and oth secondary amines[9,10] as well as with primary amines[11] and of other substrates reported in the literature[12] gave the expected straightforward substitution products.

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