Acetamide as the *N*-Methylaminating Reagent. The Reaction of Halogenonitrobenzenes with Acetamide

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During an attempt to develop a new method for the synthesis of nitrobenzoxazoles, required for pharmacological work, from halogenonitrobenzenes and acetamide, we came across an interesting reaction which indicates the possible use of acetamide as a *N*-methylaminating reagent, a use which has not been reported hitherto. It has been found that when halogenonitrobenzenes are heated under reflux in the presence of copper sulphate, the halogen activated by the nitro groups is replaced by a methylamino group, thus yielding nitro-*N*-methylanilines.

The compound obtained by treating 1-chloro-2, 4-dinitrobenzene (I) with acetamide by this method was found to be homogeneous by thin-layer chromatography (Silica gel G, activated at 110°C for 24 hr.) using a benzene-ethanol mixture (1 : 1, v/v) which had been purified before use by standard methods. Its structure has been identified as 2, 4-dinitro-*N*-methylaniline, as it exhibits bands at 1515 cm^{-1} and 1351 cm^{-1} corresponding to asymmetric and symmetric stretching valence vibrations of the NO_2-group, and bands at 3350 cm^{-1} and 1645 cm^{-1} corresponding to N–H stretching and deformation vibrations of the secondary amino group. Moreover, it has been found to be identical with the product obtained by treating 2, 4-dinitrochlorobenzene with methylamine.[1)]

The reaction was further studied with 3-chloro-1-iodo-(II), 3-chloro-1-bromo-2, 6-dinitro-4-methylbenzene (III) and with some other halogenonitrobenzenes (IV—VI).

Both the halogen atoms in compounds II and III are likely to be reactive, as they have two nitro groups, either in both the ortho positions or in the ortho and para positions. Neither of them, however, is replaced in this reaction. The products obtained in both cases are identical and invariably contain chlorine, indicating that in this reaction only halogen at position 1 is substituted.

This preferential replacement of the halogen atom can be explained by considering the spatial details of the halogen atom at position 3. The spatial consideration reveals that the NO_2 group at position 2 in compounds II and III is effectively held out of the plane of the ring by the bulky halogen atoms. Moreover, the "H" atoms of the methyl group are tetrahedrally placed. Therefore, the approach of the attacking reagent at position 3 is inhibited due to the *nonbonded interaction* of the tetrahedrally-placed "H" atoms of the methyl group on the side and the "O" atom of the twisted nitro group on the other side; hence, its replacement by the $NH–CH_3$ group is inhibited.

A detailed investigation of the mechanism of this reaction is in progress; it will be communicated separately in the near future.

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1) P. Leymann., *Ber.*, **15**, 1234 (1882).

TABLE I

S. No.	Halo-nitrobenzenes used	*N*-Methylaniline formed $R_1=-NH\cdot CH_3$	Time reflux hr.	Yield %	Colour	M. p.* °C	Formula	N% Found	N% Calcd.
1.	$R_1=Cl$; $R_2=H$; $R_3=CH_3$, $R_4=R_5=NO_2$	$R_2=H$; $R_3=CH_3$ $R_4=R_5=NO_2$	13	51	Yellow	172[3]	$C_8H_9N_3O_4$	19.50	19.90
2.	$R_1=Cl$; $R_3=R_4=H$; $R_2=R_5=NO_2$	$R_3=R_4=H$; $R_2=R_5=NO_2$	13	52	Orange	105[4]	$C_7H_7N_3O_4$	21.02	21.31
3.	$R_1=Cl$; $R_2=F$; $R_3=H$; $R_4=R_5=NO_2$	$R_2=F$; $R_3=H$; $R_4=R_5=NO_2$	10	62	Dirty yellow	126[5]	$C_7H_6FN_3O_4$	19.31	19.53
4.	$R_1=Br$; $R_3=Cl$; $R_4=CH_3$ $R_2=R_5=NO_2$	$R_3=Cl$; $R_4=CH_3$; $R_2=R_5=NO_2$	14	55	Orange	159[6]	$C_8H_8ClN_3O_4$	16.86	17.10
5.	$R_1=I$; $R_3=Cl$; $R_4=CH_3$ $R_2=R_5=NO_2$	$R_3=Cl$; $R_4=CH_3$; $R_2=R_5=NO_2$	13	56	Orange	159[6]	$C_8H_8ClN_3O_4$	16.89	17.10

* Lit. m. p. 173, 106—107, 128, 160 and 160°C respectively.

Experimental

2, 4-Dinitro-*N*-methylaniline.[2]—A mixture of 1 chloro-2,4-dinitrobenzene (2.0 g., 0.01 mol.), copper sulphate (0.1 g., 0.004 mol.) and acetamide (8.0 g.) was refluxed with stirring for about 10 hr. The melt was then poured into ice cold water (ca. 30 ml.). The solid thus separated was filtered and extracted with ethanol. The residue obtained after evaporating the ethanol was crystallised by water in the form of yellow crystals, m. p. 175°C (Found: C, 42.34; H, 3.51; N, 20.98. Calcd. for $C_7H_7O_4N_3$: C, 42.64; H, 3.55; N, 21.31%). (Lit.[2] m. p. 176°C, undepressed on admixture with the the sample obtained above.)

Following the above procedure, a few halogenonitrobenzenes were successfully converted into the respective *N*-methylanilines[3-6] (Table I). In a few cases the product was isolated by extracting the diluted reaction mixture with benzene.

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5) D. S. Deorha and H. L. Sharma, *J. Indian Chem. Soc.*, **40**, 973 (1963).

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