40. *The Influence of the Nitro-group upon Side-chain Reactivity. Part II.*[1] *The Inhibition of the Influence of the Nitro-group upon α-Proton-extraction from 4-Nitrobenzyl Chloride.*

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The rates of liberation of chloride ion from 3-hydroxy- and 3-methoxy-4-nitrobenzyl chloride have been measured in initially neutral and in alkaline aqueous acetone and aqueous dioxan. In alkaline media, the formation of derivatives of 4,4′-dinitrostilbene was inhibited by the presence of the O^- substituent *ortho* to the nitro-group, and the rate of reaction was similar to that of the alkaline hydrolysis of benzyl chloride. An *o*-methoxyl group was less effective. It is suggested that the electron-withdrawing power of the nitro-group is reduced by mesomeric interaction with adjacent OMe and especially O^- substituents.

The nitro-group has been shown [1] to promote the formation of the appropriate derivative of stilbene from *p*-nitrobenzyl chloride in its reaction with nucleophilic reagents. In the present work, the influence of methoxyl and hydroxyl groups *ortho* to the nitro-group has been examined in acid and in alkaline media, to determine whether the methoxyl, hydroxyl, and O^- substituents modify the activating power of the nitro-group for this reaction.

Experimental

3-Hydroxy-4-nitrobenzyl alcohol, m. p. 97° (lit.,[2] 97°), was prepared from 3-hydroxy-4-nitrobenzaldehyde by reduction with isopropyl alcohol and aluminium isopropoxide. 3-*Hydroxy*-4-*nitrobenzyl chloride* was prepared from the alcohol (3 g.) in benzene (30 ml.), phosphorus pentachloride (3·7 g.) being added in small portions with constant shaking. The mixture was warmed for a few minutes, then cooled and poured into ice-cold water. The benzene layer contained a viscous residue which crystallised from light petroleum in yellow needles, m. p. 48° (2 g.) (Found: C, 44·9; H, 3·2; N, 8·0; Cl, 18·9. $C_7H_6ClNO_3$ requires C, 44·8; H, 3·2; N, 7·5; Cl, 18·9%).

3-*Methoxy*-4-*nitrobenzyl alcohol*, prepared similarly, crystallised from benzene–light petroleum in colourless needles, m. p. 96° (Found: C, 52·9; H, 4·9; N, 7·7. $C_8H_9O_4N$ requires C, 52·5; H, 4·9; N, 7·7%). It was converted by phosphorus pentachloride into the *chloride* that crystallised from light petroleum in colourless needles, m. p. 68° (Found: C, 47·6; H, 4·1; N, 6·9; Cl, 17·6. $C_8H_8O_3NCl$ requires C, 47·6; H, 4·0; N, 6·9; Cl, 17·6%).

Kinetics.—The reactions in alkaline media were followed as described in the previous paper. The reactions in initially neutral solution were very slow at 30°; measurements were made for runs at 60° in sealed ampoules. Most of the experiments were carried out in duplicate. The following is an example of a typical kinetic run, for 3-methoxybenzyl chloride (0·01M) and OH^- (0·10M) in 50% dioxan at 30°:

Time (hr.)	10	25	40	50	60	75
Reaction (%)	14·9	33·9	48·8	55·8	62·5	70·4
10^4k_1 (min.$^{-1}$)	2·69	2·77	2·78	2·73	2·74	2·71

The annexed Table summarises the results.

Rates of reaction of 3-*substituted* 4-*nitrobenzyl chlorides, initially* 0·01M.

3-Subst.	Temp.	Solvent	OH^- (M init.)	10^4k_1 (min.$^{-1}$)
H	30°	50% dioxan	0·10	96·8 [a]
OH	30	50% dioxan	0·11	1·70
OH	30	50% acetone	0·11	1·99
OH	30	50% dioxan	0·21	3·12 [b]
OH	40°	50% dioxan	0·21	9·72 [b]
OMe	30	50% dioxan	0·10	6·4 (rising)
OH	60	50% acetone	0·00	0·35
OMe	60	50% acetone	0·00	0·51

[a] Ref. 1. [b] Activation energy calc. 21,700 cal./mole.

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[1] Part I, preceding paper.

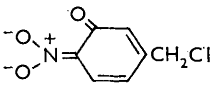
[2] Lock, *Ber.*, 1929, **62**, 1184.

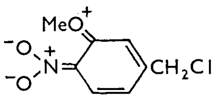
The product from the reaction of 3-hydroxy-4-nitrobenzyl chloride with alkali was shown to be the alcohol; 3-methoxy-4-nitrobenzyl chloride did not give the alcohol; it gave material, m. p. 150° (Found: C, 55·5; H, 4·0; N, 8·0%), probably the impure stilbene; in this experiment, the integrated rate coefficients, k_1, determined through the course of the reaction, rose from $6{\cdot}4 \times 10^{-4}$ min.$^{-1}$ at 5·5% reaction to $12{\cdot}0 \times 10^{-4}$ at 67·5% reaction.

Discussion

It was shown in the previous paper that reaction of 4-nitrobenzyl chloride with alkali in aqueous acetone or aqueous dioxan is very much more rapid than of benzyl chloride and gives the stilbene. The similar reaction of 3-hydroxy-4-nitrobenzyl chloride has a rate similar to that of benzyl or 3-methoxybenzyl chloride and gives the alcohol. The activation energies bear the expected relationship. Under these experimental conditions, the hydroxyl group must be converted into O^-; it is clear that the negatively charged oxygen atom *ortho* to the nitro-group has prevented extraction of a proton from the CH_2Cl group, so that the reaction no longer gives a stilbene derivative. It is suggested that the O^- substituent prevents the nitro-group from exerting its strong electron-withdrawing influence by mesomerism involving structure (I):

(I)





(II)

For 3-methoxy-4-nitrobenzyl chloride, reaction is complicated and does not lead to a simple kinetic equation; perhaps hydrolysis and α-proton-extraction occur side by side at different rates. The initial rate of reaction is, however, notably more rapid than that of benzyl chloride, but much less than that of 4-nitrobenzyl chloride; probably some resonance interaction (structure II) reduces the effectiveness of the nitro-group and diminishes the relay of electrons from the side-chain.

The following are the rate coefficients for hydrolyses of substituted benzyl halides (0·01M) in 50% aqueous acetone at 60°, the solutions being initially neutral:

CH_2PhCl deriv.	Unsubst.	4-NO_2	3-HO-4-NO_2	3-MeOH-4-NO_2
10^5k_1 (min.$^{-1}$)	46	4·6	3·6	5·1

The hydrolysis of benzyl chlorides in neutral medium usually proceeds by the S_N1 mechanism.[3] The *p*-nitro-group, attached alone to the nucleus, reduces the rate considerably (from 46×10^{-5} to $4{\cdot}6 \times 10^{-5}$ min.$^{-1}$), by its $-T$ and $-I$ effects. The influence of *m*-hydroxyl or *m*-methoxyl on the electron-attracting influence of the *p*-nitro-group, although very slight, yet seems to be observable. The *m*-hydroxyl reduced the rate still further to $3{\cdot}6 \times 10^{-5}$ min.$^{-1}$ (contributing with its $-I$ effect; probably also the hydrogen bonding between OH and NO_2 has caused coplanarity of the NO_2 with the ring, thus increasing its attraction of electrons from the side-chain). *m*-Methoxyl, on the other hand, increased the rate slightly (to $5{\cdot}1 \times 10^{-5}$ min.$^{-1}$): it should have contributed also with its $-I$ effect (no hydrogen bonding in this case). Therefore the slight increase in the rate may be due to interaction between the NO_2 and the OMe group, which has counterbalanced the $-I$ effect and also decreased to a slight extent the attraction of electrons from the side-chain.

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[3] Olivier, *Rec. Trav. chim.*, 1922, **41**, 646; 1923, **42**, 775.