[1961]

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-4nitrobenzyl 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-4nitrobenzaldehyde 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. C₇H₆ClNO₃ 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	$48 \cdot 8$	$55 \cdot 8$	62.5	70· 4
$10^4 k_1 \text{ (min.}^{-1} \text{)}$	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. H OH OH OH	Temp. 30° 30 30 30 30	Solvent 50% dioxan 50% dioxan 50% acetone 50% dioxan	ОН- (м init.) 0·10 0·11 0·11 0·21	$\begin{array}{c} 10^4 k_1 \\ (\text{min.}^{-1}) \\ 96 \cdot 8 \ ^a \\ 1 \cdot 70 \\ 1 \cdot 99 \\ 3 \cdot 12 \ ^b \end{array}$	3-Subst. OH OMe OH OMe	Temp. 40° 30 60 60	Solvent 50% dioxan 50% dioxan 50% acetone 50% acetone	OH- (M init.) 0·21 0·10 0·00 0·00	$ \begin{array}{r} 10^{4}k_{1} \\ (\min.^{-1}) \\ 9.72^{b} \\ 6.4 \\ (rising) \\ 0.35 \\ 0.51 \end{array} $
^a Ref. 1. ^b Activation energy calc. 21,700 cal./mole.									

¹ Part I, preceding paper.

² Lock, Ber., 1929, 62, 1184.

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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 6.4×10^{-4} min.⁻¹ at 5.5% reaction to 12.0×10^{-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 CH₂Cl 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):



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 ₂ PhCl deriv	Unsubst.	$4-NO_2$	3-HO-4-NO ₂	3-MeOH-4-NO ₂
$10^{5}k_{1} \text{ (min.}^{-1} \text{)} \dots \dots$	46	$4 \cdot 6$	3.6	$5 \cdot 1$

The hydrolysis of benzyl chlorides in neutral medium usually proceeds by the $S_{\rm N}$ 1 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 NO₂ has caused coplanarity of the NO₂ 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 NO₂ 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.

The authors acknowledge their indebtedness to Professor P. B. D. de la Mare, D.Sc., for his interest and suggestions about preparation of the manuscript.

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[Received, May 19th, 1960.]

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