The Influence of the Nitro-group upon Side-chain Reactivity. Part IV.[1] The Inhibition of α-Proton Extraction from 4-Nitrobenzyl Chloride by the Steric Effect of Methyl Groups in the 3- and 5-Positions

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The fast α-proton extraction from 4-nitrobenzyl chloride by alkali in dioxan, leading to the formation of 4,4′-dinitrostilbene by the α-*E*1*cB* mechanism (the rate-determining step is formation of a carbene intermediate), is greatly retarded by one methyl group in the 3-position and completely inhibited by two methyl groups in the 3- and 5-positions; instead, alcohols and ethers are formed by the S_N2 displacement of the halogen by the alkali and by the formed alkoxides. Kinetic investigations, and evaluation of the Arrhenius parameters, on the chlorides with the alkali in dioxan, alone or in presence of added alkoxides, demonstrate clearly the steric effect of the methyl groups. Infrared and ultraviolet spectra of the chlorides and related structures throw much light on the results.

THE mechanism (α-*E*1*cB*) of the transformation of 4-nitrobenzyl chloride into 4,4′-dinitrostilbene by the action of alkali in aqueous dioxan was discussed in Part I.[2] The formation of the same stilbene from 4-nitrobenzyldimethylsulphonium toluene-*p*-sulphonate and alkali has also been observed,[3] and carbene is assumed to be the intermediate in both reactions. Other related systems, *e.g.*, 9-bromofluorenes, react with alkali by the displacement mechanism to give the corresponding ethylenes.[4] Introduction of a 2-nitro-group in 9-bromofluorene and use of a stronger base makes this system react by the α-elimination mechanism.[5] The introduction of a 3-O^- substituent in 4-nitrobenzyl chloride [6] resulted in very strong inhibition of the influence of the nitro-group on the side-chain owing to the mesomeric binding of the nitro-group with the 3-O^- substituent, which allowed only for a slow S_N2 displacement of the halogen instead of the α-elimination, as with benzyl chloride itself under the same conditions. The effect of the nature of the substituents on the course of the reaction has lately led to a further study to compare their effect on the rates of hydrolysis of ethyl nitrobenzoates.[1]

In this work the alteration of the influence of the *p*-nitro-group on α-proton extraction was studied in 3-methyl- and in 3,5-dimethyl-4-nitrobenzyl chloride. In such compounds it might be expected that the methyl groups *ortho* to the nitro-group would bring about steric inhibition of resonance in the system by forcing the nitro-group out of the plane of the ring, and that the effect would be greater with 3,5-dimethyl- than with 3-methyl-4-nitrobenzyl chloride.

EXPERIMENTAL

The two new chlorides, 3-*methyl*- and 3,5-*dimethyl*-4-*nitrobenzyl chloride* were prepared from 1,3-dimethyl- and 1,3,5-trimethyl-4-nitrobenzene, respectively, through the following steps: (i) chromic–acetic anhydride oxidation of the methyl group *para* to the nitro-group (the one suffering the least steric repulsion and accordingly the most susceptible to the oxidation), yet partial oxidation of two methyl groups was unavoidable; (ii) hydrolysis of the diacetate from (i) to the aldehyde; (iii) reduction of the aldehyde to the alcohol by aluminium isopropoxide in isopropyl alcohol; (iv) transformation of the alcohol into the chloride by phosphorus pentachloride in chloroform.

Most of the compounds in these two series are new, and their structures were verified by reference to the corresponding acids which are already known.

3-*Methyl*-4-*nitrobenzaldehyde*.— 1,3-Dimethyl-4-nitrobenzene (21·7 g.) in glacial acetic acid (228 ml.) and acetic anhydride (228 ml.) was treated with concentrated sulphuric acid (43 ml.), with cooling and stirring, and chromic anhydride (40 g.) was added slowly, at 5—8°. The semisolid obtained by adding water, was washed with 2% aqueous sodium carbonate, and from the washings a small amount of 3-methyl-4-nitrobenzoic acid, m. p. 218—219°, was obtained. The solid residue was crystallised from ethanol, to give 3-methyl-4-nitrobenzaldehyde di-

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[1] Part III, Y. Iskander, R. Tewfik, and S. Wasif, *J. Chem. Soc.* (*B*), 1966, 424.

[2] S. B. Hanna, Y. Iskander, and Y. Riad, *J. Chem. Soc.*, 1961, 217.

[3] C. G. Swain and E. R. Thornton, *J. Amer. Chem. Soc.*, 1961, **83**, 4033.

[4] D. Bethell, *J. Chem. Soc.*, 1963, 666.

[5] D. Bethell and A. F. Cockerill, *Proc. Chem. Soc.*, 1964, 283.

[6] S. B. Hanna, Y. Iskander, and A. Salama, *J. Chem. Soc.*, 1961, 221.

acetate, yellow needles (11·4 g.), m. p. 86·5—88·5° (lit.,[7] 80—82°). From the mother-liquors, *1,3-diformyl-4-nitrobenzene tetra-acetate* was isolated as yellow prisms, m. p. 104—105° (Found: C, 50·1; H, 4·6; N, 3·7. $C_{16}H_{17}NO_{10}$ requires C, 50·1; H, 4·4; N, 3·7%). This, on hydrolysis with sulphuric acid in aqueous alcohol, gave *1,3-diformyl-4-nitrobenzene*, m. p. 98·5—100° (from petroleum) (Found: C, 53·9; H, 3·3; N, 7·9. $C_8H_5NO_4$ requires C, 53·6; H, 2·8; N, 7·8%). *3-Methyl-4-nitrobenzaldehyde* was obtained from the corresponding diacetate (6·78 g.) by refluxing it with water (20 ml.), ethanol (20 ml.), and concentrated sulphuric acid (2·2 ml.) for 30 min. It crystallised from light petroleum as pale yellow prisms, m. p. 66—68° (lit.,[7] 64°).

3-Methyl-4-nitrobenzyl Alcohol.—This was prepared from the corresponding aldehyde (17·6 g.) by reduction with aluminium isopropoxide in isopropyl alcohol. The pure *alcohol* (7·6 g.) separated from carbon tetrachloride as pale yellow needles, m. p. 60—62·5° (Found: C, 58·2; H, 5·8; N, 8·4. $C_8H_9NO_3$ requires C, 57·5; H, 5·4; N, 8·4%).

3-Methyl-4-nitrobenzyl Chloride.—The alcohol (13 g.) in chloroform (300 ml., previously treated with phosphorus pentachloride until no more hydrogen chloride was evolved) was treated with phosphorus pentachloride (20 g.) in small portions. After refluxing for 20 min., cooling, and treating with ice (300 g.), it was washed with water and sodium hydrogen carbonate solution. Removal of the chloroform gave the chloride (13 g.), b. p. 104—107°/0·4 mm., m. p. 15° (Found: C, 52·1; H, 4·4; N, 7·7. $C_8H_8ClNO_2$ requires C, 51·8; H, 4·3; N, 7·5%).

3,5-Dimethyl-4-nitrobenzaldehyde.— Nitromesitylene (59·4 g.), by the chromic–acetic anhydride method, gave *3,5-dimethyl-4-nitrobenzaldehyde diacetate* (34 g.), prisms, m. p. 128—130° (from ethanol) (Found: C, 55·7; H, 5·8; N, 5·4. $C_{13}H_{15}NO_6$ requires C, 55·5; H, 5·3; N, 5·0%). The diacetate (30·2 g.) gave the *aldehyde* (15·3 g.) by the method described above, as light straw-coloured prisms, m. p. 52—54° (from petroleum) (Found: C, 59·7; H, 5·3; N, 8·1. $C_9H_9NO_3$ requires C, 60·3; H, 5·0; N, 7·8%). The diacetate mother-liquor of crystallisation contained *1,5-diformyl-3-methyl-2-nitrobenzene tetra-acetate*, prisms, m. p. 101—102° (from ethanol) (Found: C, 51·2; H, 4·8; N, 3·8. $C_{17}H_{19}NO_{10}$ requires C, 51·4; H, 4·8; N, 3·5%), which on hydrolysis as above gave *1,5-diformyl-3-methyl-2-nitrobenzene*, pale yellow prisms, m. p. 84—85° (from petroleum) (Found: C, 55·8; H, 3·7; N, 7·3. $C_9H_7NO_4$ requires C, 56·0; H, 3·6; N, 7·3%).

3,5-Dimethyl-4-nitrobenzyl Alcohol.—This was prepared from the aldehyde (16·5 g.) by the reduction method described above (7 hr.). The pure *alcohol* (8·5 g.) separated from petroleum as pale straw-coloured prisms, m. p. 49·5—51·5° (Found: C, 59·8; H, 6·0; N, 7·7. $C_9H_{11}NO_3$ requires C, 59·7; H, 6·1; N, 7·7%).

3,5-Dimethyl-4-nitrobenzyl Chloride.—The alcohol (13·9 g.), on treatment with phosphorus pentachloride in chloroform, gave the *chloride* (14·8 g.), b. p. 108°/0·65 mm., m. p. 35—36° (Found: C, 54·2; H, 5·0; N, 7·0. $C_9H_{10}ClNO_2$ requires C, 54·1; H, 5·1; N, 7·1%).

α-(*3-Methyl-4-nitrobenzylthio*)*acetic Acid.*—This was prepared by refluxing the chloride (1·16 g.) and mercaptoacetic acid (0·6 g.) in a mixture of ethanol (25 ml.) and water (25 ml.) with the addition of a solution of sodium hydrogen carbonate (1·25 g.) in water (4 ml.). After 75 min. the solution was diluted with water and the turbidity removed by ether. Acidification gave the required *acid* (1 g.), needles (from carbon tetrachloride), m. p. 67·5—68·5° (Found: C, 49·8; H, 4·7; N, 5·2. $C_{10}H_{11}NO_4S$ requires C, 49·8; H, 4·5; N, 5·8%). The acid, on boiling with alkali (5 min.), gave a brown-red precipitate,[8] and the filtrate gave hydrogen sulphide on acidification, showing that carbon–sulphur fission had occurred.

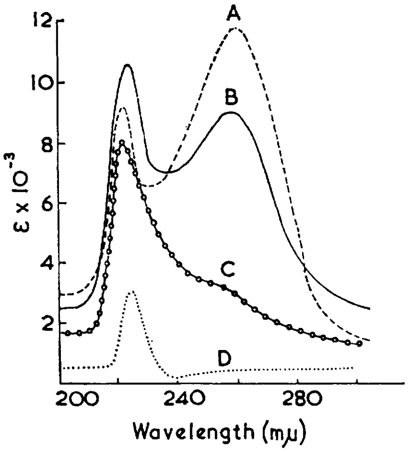
α-(*3,5-Dimethyl-4-nitrobenzylthio*)*acetic Acid.*—This, prepared from the chloride and mercaptoacetic acid as above, separated as *prisms*, m. p. 97—99°, from carbon tetrachloride (Found: C, 51·4; H, 5·2; N, 5·5. $C_{11}H_{13}NO_4S$ requires C, 51·8; H, 5·1; N, 5·5%). The acid was recovered unchanged after boiling with alkali for 5 min.

α-(*3-Methyl-4-nitrobenzylthio*)-*αα-diphenylacetic Acid.*—This, prepared from the chloride and diphenylmercaptoacetic acid as above, came down as pale yellow *prisms* from ethanol, m. p. 173—174° (Found: C, 66·8; H, 5·0; N, 3·6. $C_{22}H_{19}NO_4S$ requires C, 67·2; H, 4·8; N, 3·6%). The acid, on boiling with alkali (5 min.) gave a brown-red precipitate,[8] showing that carbon–sulphur fission had occurred.

TABLE 1

Ultraviolet spectra

	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$
(A)	221	9220	259	11,800
(B)	223	10,600	257	9080
(C)	222	8350	259	3010
(D)	224	3020	259	345



Ultraviolet spectra, in cyclohexane, of (A) 4-nitrobenzyl chloride, (B) 3-methyl-4-nitrobenzyl chloride, (C) 3,5-dimethyl-4-nitrobenzyl chloride, and (D) benzyl chloride

Spectral Investigations.—(*a*) The ultraviolet spectra (Figure, Table 1) of four chlorides were determined.

(*b*) Only the differences in the infrared spectra of the three chlorides A—C containing the nitro-group are in Table 2. By reference to the important C–D vibrational frequencies in the spectrum of $4\text{-}NO_2\cdot C_6H_4\cdot CHDCl$[2] (910, 790, and 750 cm.$^{-1}$), the corresponding frequencies of the C–H bond (those of the C–D multiplied by 1·41) should be 1280, 1110, and 1060, respectively. The actual values in 4-nitrobenzyl chloride are 1270, 1106, and 1020 cm.$^{-1}$, and a strong band at 800 cm.$^{-1}$. The 1270 cm.$^{-1}$ band is

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[7] H. Suida, *Monatsh.*, 1912, **33**, 1281.

[8] Y. Iskander and Y. Riad, *J. Chem. Soc.*, 1961, 2397, and previous Papers quoted.

probably the out-of-plane (wag) bending vibration usually observed at ~1300 cm.$^{-1}$, and the remaining three are probably due to the other bending modes of the C–H bond. These and those in the 1600 cm.$^{-1}$ region (the stretching vibration of the aromatic C=C) and at 840—860 cm.$^{-1}$ (the stretching vibration of the C–N bond in aromatic nitro-compounds) involve some variations on the introduction of methyl groups in the 3- and 5-positions:

TABLE 2

Infrared spectra

(A)	1620s [a] 1610m	1270s	1106s	1020s	870s 860s	800s [e]
(B)	1620s [b] 1590s	1270m	1080w	1040m	840s	Absent
(C)	1610m [c]	1270w	1100w	1040m	840s	Absent

[a] The medium band is fused with the strong sharp one at about its half-length, with a clear peak head. In all other derivatives of 4-nitrobenzyl chloride (A), 4-nitrotoluene, 4-nitrobenzyl alcohol, 4,4′-dinitrostilbene (*trans*), 4,4′-dinitrostilbene oxide, (*cis* and *trans*) and di-4-nitrobenzyl ether, this band is a single sharp strong one. [b] Similarly, in all derivatives of 3-methyl-4-nitrobenzyl chloride (B), 1,3-dimethyl-4-nitrobenzene, 3-methyl-4-nitrobenzyl alcohol, and their corresponding stilbene, stilbene oxides, and ether, and even 2-nitrotoluene, twin bands 20—35 cm.$^{-1}$ apart are always found in this region. [c] Similarly, in all the derivatives of 3,5-dimethyl-4-nitrobenzyl chloride (C), nitromesitylene, 3,5-dimethyl-4-nitrobenzyl alcohol, its symmetrical ether, and its 4-nitrobenzyl ether, this band is always single and sharp with medium strength. [d] This splitting, found in (A) and its derivatives disappears in (B) and (C) and their derivatives. [e] This band is found also in 2-nitrotoluene, 2,4-dinitrotoluene, and in all the derivatives of (A) as under *a* above, but disappears in (B) and (C) and all their derivatives as under *b* and *c* above.

The Products of the Reactions of the Chlorides with Alkali under the Kinetic Conditions.—Changes in concentrations of alkali (0·05—0·01M) in 50% v/v aqueous dioxan at 30° have no effect on the nature of the products.

(1) 3-*Methyl*-4-*nitrobenzyl chloride and sodium hydroxide* (0·05M each) *in* 50% *aqueous dioxan*. The chloride (0·928 g.) in dioxan (50 ml.) was treated with aqueous sodium hydroxide solution (50 ml.; 0·1M) and the mixture kept at 30° for 25 days. Four compounds were isolated. (i) A yellow precipitate (0·20 g.) which gave yellow rosettes, m. p. 190—191° (from acetone), of trans-3,3′-*dimethyl*-4,4′-*dinitrostilbene oxide* (Found: C, 60·8; H, 4·6; N, 8·9. $C_{16}H_{14}N_2O_5$ requires C, 61·1; H, 4·5; N, 8·9%). (ii) On dilution of the mother-liquor with water to 2 l. and cooling to 7° for 2 days, a pale yellow solid (0·13 g.) was obtained. This separated from ethanol (6 ml.) as colourless branched needles (0·1 g.), m. p. 129—130°, of cis-3,3′-*dimethyl*-4,4′-*dinitrostilbene oxide* (Found: C, 61·0; H, 4·5; N, 9·1%). (iii) The ethanol mother-liquor (6 ml.), concentrated to 2 ml., gave on cooling *di*-(3-*methyl*-4-*nitrobenzyl*) *ether* (0·015 g.) as rosette-shaped isles, m. p. 96—98° (Found: C, 60·8; H, 5·2; N, 8·8. $C_{16}H_{16}N_2O_5$ requires C, 60·8; H, 5·1; N, 8·9%). It gives a strong band at 1100 cm.$^{-1}$ characteristic of aliphatic ethers. (iv) The turbid aqueous mother-liquor from (ii) was extracted chloroform (3 × 300 ml.). Distillation of the chloroform left 3-methyl-4-nitrobenzyl alcohol (0·50 g.) which separated from carbon tetrachloride as pale yellow needles, m. p. and mixed m. p. 60—62·5°. The two stilbene oxides isolated in (i) and (ii) are identical with those obtained from the chloride and the corresponding aldehyde in 50% aqueous dioxan (cf. the followingPaper).

The corresponding stilbene (as occurs with 4-nitrobenzyl chloride [2]) was not formed under the kinetic conditions, even when the concentrations of the reactants reached 0·2M each in 50% aqueous dioxan; but at 1·2M each in 95% dioxan–water mixture a small yield of 3,3′-*dimethyl*-4,4′-*dinitrostilbene* (E) was obtained as fine bright yellow needles, m. p. 260° (from alcohol–acetone) (Found: C, 64·2; H, 4·7; N, 9·2. $C_{16}H_{14}N_2O_4$ requires C, 64·4; H, 4·7; N, 9·4%). Table 3 summarises the ultraviolet absorption data for this stilbene (E) with those for 4,4′-dinitrostilbene (F) in chloroform.

TABLE 3

Ultraviolet spectra

	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$
(E) *trans* ...	240	11,300	355	30,200
(F) *trans* ...	303 *	13,000	335 *	14,600

* These two (broad) bands merge to give the appearance of a single very broad band.

(2) 3,5-*Dimethyl*-4-*nitrobenzyl chloride and sodium hydroxide* (0·025M each) *in* 50% *aqueous dioxan*. The chloride (1·5 g.) in dioxan (150 ml.) was treated with aqueous sodium hydroxide solution (150 ml.; 0·05M) and the mixture kept at 30° for 60 days. Two compounds were isolated. (i) A crystalline solid (0·16 g.), *di*-(3,5-*dimethyl*-4-*nitrobenzyl*) *ether*, separated from ethanol as straw-coloured rods, m. p. 165—166·5° (Found: C, 62·5; H, 6·0; N, 8·1. $C_{18}H_{20}N_2O_5$ requires C, 62·7; H, 5·9; N, 8·1%). It gives a strong band at 1100 cm.$^{-1}$ characteristic of aliphatic ethers. (ii) The mother-liquor was diluted with water to 2 l., and extracted with chloroform (3 × 300 ml.). Distillation of the chloroform left 3,5-dimethyl-4-nitrobenzyl alcohol (1·2 g.) which separated from carbon tetrachloride as pale straw-coloured prisms, m. p. and mixed m. p. 49·5—51·5°.

When the chloride was allowed to react with an added equivalent of 4-nitrobenzyl alcohol in the presence of the alkali under the kinetic conditions of Table 5, 3,5-*dimethyl*-4-*nitrobenzyl* 4-*nitrobenzyl ether*, m. p. 91—92° (from ethanol), was obtained (Found: C, 60·7; H, 5·1; N, 8·9. $C_{16}H_{16}N_2O_5$ requires C, 60·8; H, 5·1; N, 8·9%). It gives two strong bands at 1100 and 1120 cm.$^{-1}$ characteristic of aliphatic ethers.

No epoxide was formed when the reaction was carried out in the presence of *p*-nitrobenzaldehyde.

Kinetic Measurements.—The rates of reaction were determined by following the rate of liberation of chloride by the electrometric method.[2] Typical runs are given in Tables 4 and 5.

TABLE 4

Reaction of 3-methyl-4-nitrobenzyl chloride (0·05M) and sodium hydroxide (0·05M) in 50% aqueous dioxan at 30°

Time (hr.)	6	12	24	36	48	72
Reaction (%)	9·3	18·0	37	50	69·7	70·3
10^4k_2 (l. mole^{-1} sec.$^{-1}$)	0·95	1·01	1·36	1·56	1·71	1·78

k_2 rising as the reaction proceeds. The initial value (obtained by plotting k_2 against % reaction) is 0·78 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

The rate constants (k_1 or k_2) with this chloride at the different ratios of concentration of the alkali and the dioxan–water mixture rose as the reaction proceeded. The initial values of k (before the occurrence of the subsequent complications) were determined by plotting the k values against percentage reaction. The plots always yielded remarkably straight lines even at the different experimental temperatures used. These lines were extrapolated to meet the k-axis where the initial k values were given. In the presence of 4-nitrobenzyl alcohol or its 3-methyl derivatives, however, the rate was constant up to about 70% of the reaction, and then increased as the concentration of the alcohol rose.

TABLE 5

Same as in Table 4 but in the presence of 3-methyl-4-nitrobenzyl alcohol (0·05M) (etherification reaction)

Time (hr.)	3	6	9	21	25	31	45	50
Reaction (%)	9·47	17·75	24·4	42·4	47·5	53·8	65·3	69·0
10^4k_2 (l. mole^{-1} sec.$^{-1}$)	1·93	1·99	1·99	1·95	2·01	2·08	2·31	2·47

k_2 (constant up to *ca.* 60% of the reaction) = $2{\cdot}02 \times 10^4$ l. mole^{-1} sec.$^{-1}$.

With benzyl chloride or 3,5-dimethyl-4-nitrobenzyl chloride, the k_1 or k_2 values are always very constant. Table 6 compares the results of the reaction of the three chlorides, 3-methyl-4-nitrobenzyl chloride (B), 3,5-dimethyl-4-nitrobenzyl chloride (C), and benzyl chloride (D), with alkali in the absence and in the presence of the corresponding alcohol, or of 4-nitrobenzyl alcohol under different conditions.

TABLE 6

Reactions of benzyl chlorides (B), (C), and (D) with alkali or alkoxides

	$t°$	(D)	(B)	(C)
Arrhenius parameters ([RCl] = 0·01M; [OH$^-$] = 0·1M)				
10^4k_1 (sec.$^{-1}$) in 50% aqueous dioxan	30	0·045	0·063 [a]	0·037
	30		0·0725 [b]	0·0695 [b]
	40	—	0·180 [a]	0·0995
	50	—	0·527 [a]	0·272
E_a (kcal./mole)		23·50 [2]	20·82	19·36
$\log_{10} A$ *		11·59	9·81	8·53
A/A_{unsub}		1	0·016	0·0008
$\Delta S^\ddagger$ (cal./mole deg.) †		−5·5	−13·7	−19·5

* $\log_{10} A = \log_{10} k + E_a/2{\cdot}303\boldsymbol{R}T$.

† $\Delta S^\ddagger/4{\cdot}576 = \log_{10} k - 10{\cdot}318 - \log_{10} T + E_a/4{\cdot}576T$.

	$t°$	(D)	(B)	(C)
Solvent effect ([RCl] = [OH$^-$] = 0·05M)				
10^4k_2 (l. mole^{-1} sec.$^{-1}$)				
in 50% aq. dioxan	30	0·50	0·78 [a]	0·44
in 70% aq. dioxan	30	—	0·68 [a]	0·295
Etherification in 50% aqueous dioxan ([RCl] = [R′OH] = [OH$^-$] = 0·05M)				
10^4k_2 (l. mole^{-1} sec.$^{-1}$)				
R = R′	30	0·505	2·02	—
R′OH is 4-$NO_2{\cdot}C_6H_4{\cdot}CH_2{\cdot}OH$	30	0·82	3·00	0·76

[a] The initial value obtained by plotting k against % reaction. [b] Calculated by the use of the Hammett equation.

DISCUSSION

Interpretations from the Ultraviolet Spectra.—The decreased intensity of the 260 mμ band of the chlorides (B) and (C), which is a measure of the degree of coplanarity of the nitro-group with the ring,[1] shows clearly the steric effect of the 3- and 5-methyl groups. This band has become a mere inflexion in 3,5-dimethyl-4-nitrobenzyl chloride (Table 1). Also, a marked bathochromic shift occurs in the second band of 4,4′-dinitrostilbene on 3,3′-dimethylation (Table 3). Such bathochromic shifts (rather than hypsochromic shifts) due to steric inhibition of resonance have been observed during the last two decades and have more recently been fully explained.[9]

Interpretations from Kinetic Measurements.—The steric effect of two methyl groups in the 3- and 5-positions in 4-nitrobenzyl chloride has stopped completely the α-proton-extraction from 3,5-dimethyl-4-nitrobenzyl chloride (C) by the alkali in 50% aqueous dioxan and caused the return to the S_N2 displacement of the halogen at a rate smaller than that in benzyl chloride itself. Slight etherification (20%) of the chloride by the formed alkoxide ions must have occurred at a rate comparable to that of the hydrolysis by the OH$^-$ ions, as indicated by the constancy of the rate constant throughout the reaction ($k_2 = 0{\cdot}44 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$):

$$\mathrm{RCl + OH^-} \xrightarrow{\text{slow}} \mathrm{ROH + Cl^-} \qquad (1)$$

$$\mathrm{ROH + OH^-} \xrightarrow{\text{fast}} \mathrm{RO^- + H_2O} \qquad (2)$$

$$\mathrm{RO^- + RCl} \xrightarrow[\text{similar to (1)}]{\text{slower or}} \mathrm{ROR + Cl^-} \qquad (3)$$

(R = 3,5-dimethyl-4-nitrobenzyl)

The rate of reaction between the chloride and 4-nitrobenzyl alcohol in the presence of alkali (cf. Table 6) is higher than with the alkali alone ($k_2 = 0{\cdot}76 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$). This confirms step (3), allowing for the fact that RO$^-$ is the more reactive 4-nitrobenzyl alkoxide ion. The same phenomenon is observed with benzyl chloride: k_2 increases from $0{\cdot}505 \times 10^{-4}$ to $0{\cdot}82 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$ on similar manipulation.

The complete inhibition of the α-proton extraction is proved by two facts: (*a*) the non-formation of the corresponding stilbene even by the use of higher concentrations of alkali; (*b*) the non-formation of epoxide when the reaction is carried out in the presence of 4-nitrobenzaldehyde.

α-Proton extraction is not completely inhibited in 3-methyl-4-nitrobenzyl chloride (B), as shown by the following.

(*a*) Although, under the kinetic conditions (dilute alkali in 50% aqueous dioxan), no stilbene is formed, it is obtained in small yield if a higher concentration of alkali is used in 95% dioxan–water. The decreased water content in the reaction mixture, accompanied by the increased alkali concentration, might have shifted the pre-equilibrium (4) to the right and thus given the chance

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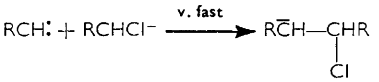
[9] J. N. Murrell, 'The Theory of the Electronic Spectra of Organic Molecules,' Methuen, London, 1963, pp. 238—246.

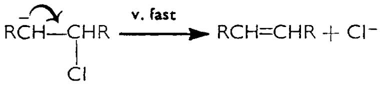
for the formation of the carbanion which changes to the stilbene through carbene intermediate:[2]

$$\mathrm{RCH_2Cl + OH^-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{RCHCl^- + H_2O} \qquad (4)$$

$$\mathrm{RCHCl^-} \xrightarrow[k_2]{} \mathrm{RCH\!:}\ (k_{-1} \gg k_2) \qquad (5)$$



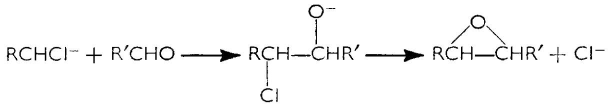
$$\mathrm{RCH\!: + RCHCl^-} \xrightarrow{\text{v. fast}} \mathrm{R\bar{C}H{-}CHR(Cl)} \qquad (6)$$



$$\mathrm{R\bar{C}H{-}CHR(Cl)} \xrightarrow{\text{v. fast}} \mathrm{RCH{=}CHR + Cl^-} \qquad (7)$$

(or the less probable dimerisation of the carbene to the stilbene)
(R = 3-methyl-4-nitrobenzyl)

(*b*) Under the kinetic conditions, by the use of low concentration of alkali, and in the presence of the corresponding aldehyde or 4-nitrobenzaldehyde (cf. the following Paper), epoxides are formed in about quantitative yields. These cannot be formed except through carbanion intermediates, as in (4):



$$\mathrm{RCHCl^- + R'CHO} \longrightarrow \mathrm{RCH(Cl){-}CH(O^-)R'} \longrightarrow \mathrm{RCH{-}CHR'\ (epoxide) + Cl^-}$$

At low concentration of alkali, and in the absence of aldehydes, the main reaction is a normal S_N2 displacement of halogen, but it has been noticed that the rate constant increases gradually as the reaction proceeds. The initial rate constant is $0{\cdot}78 \times 10^{-4}$, increasing to $1{\cdot}78 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$ at *ca.* 70% for the reaction. The reaction, however, proceeded at a constant rate ($k_2 = 2{\cdot}01 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$) right from its beginning if an equivalent amount of alcohol (3-methyl-4-nitrobenzyl alcohol) is added to the reaction mixture, and by a higher rate constant ($k_2 = 3{\cdot}00 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$) if the more reactive 4-nitrobenzyl alcohol is used. These facts are taken as an indication that the formed alkoxide (in the reaction without added alcohol) reacts with the still unreacted chloride to form an ether at a rate higher than that of the S_N2 hydrolysis by alkali [cf. (3) where the OH^- ions are constantly being replaced by the more reactive alkoxide ions].

The great decrease in the *A*-factor of the Arrhenius equation ($k = Ae^{-E_a/RT}$) (which is a good measure of the steric effect as the methyl groups are successively introduced in the 3- and 5-positions) was also significant. Taking benzyl chloride as a reference, we find $A/A_{\text{unsub.}}$ is 0·016 and 0·0008 for the mono- and the di-methyl derivatives, respectively. Similarly, the entropies of activation ($\Delta S^{\ddagger}$) vary considerably from benzyl chloride (−5·5 e.u.) to the monomethyl (−13·7) to the dimethyl derivative (−19·5 e.u.).

It may be recalled that what is being dealt with in the case of 3-methyl-4-nitrobenzyl chloride are initial rates, and that the formation of epoxides encountered here has no direct bearing on the above conclusions. Nevertheless, this unexpected formation of epoxides invites comment and investigation. Only a small amount of ether, relative to the epoxide, was obtained with the major product (the alcohol). This phenomenon of formation of epoxides in the absence of carbonyl intercepting agents, and the difficulty of explaining it, had already been met by previous workers in related reactions.[10-12] None of these workers has pointed to the possible role of alkoxides in this respect. Unpublished results by Iskander and Riad show that the presence of both oxygen and 4-nitrobenzyl alcohol (or even t-butyl alcohol) is necessary for the formation of *cis*- and *trans*-4,4′-dinitrostilbene oxides by the action of alkali on 4-nitrobenzyl chloride in 50% aqueous dioxan, while in the absence of any of these two reagents the epoxides are not formed, but 4,4′-dinitrostilbene is the only product. The mechanism of this reaction, and whether the chloride itself or its derived carbanion or carbene is the reacting species in the presence of the alkoxide and oxygen, is still obscure. But this fact, however, explains why epoxides were formed in the case of the reaction of 3-methyl-4-nitrobenzyl chloride with alkali in 50% aqueous dioxan. The alcohol appears in the reaction, and accordingly alkoxide ion and oxygen co-operate in the transformation of the chloride to the epoxides. In the case of 4-nitrobenzyl chloride itself, the alcohol is not formed at all in the reaction.

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