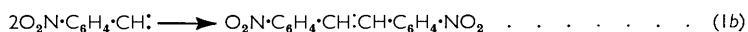
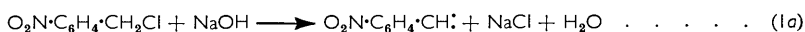


39. The Influence of the Nitro-group upon Side-chain Reactivity.
Part I. The Reaction between 4-Nitrobenzyl Chloride and Alkali.

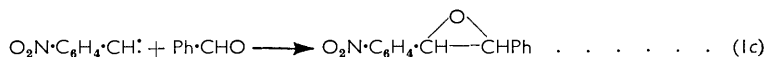
By SAMIR B. HANNA, YOUSSEF ISKANDER, and (in part) YOUSSEF RIAD.

The reaction between 4-nitrobenzyl chloride and alkali in aqueous acetone or aqueous dioxan gives 4,4'-dinitrostilbene. The kinetic form, the effect of added aldehydes, and the effect of deuterium in the starting material have been studied. *p*-Nitrophenylmethylene is accepted as an intermediate.

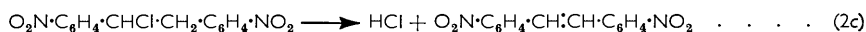
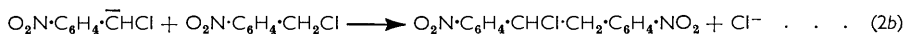
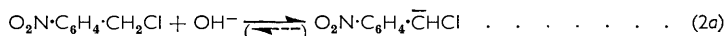
WHEN 4-nitrobenzyl chloride is hydrolysed by alkali in water, it gives the normal product, 4-nitrobenzyl alcohol,¹ but reaction in aqueous alcohol, acetone, or dioxan gives the 4,4'-dinitrostilbene.² This abnormal behaviour was investigated by Bergmann and Hervey,³ who proposed a mechanism involving the free biradical *p*-nitrophenylmethylene:



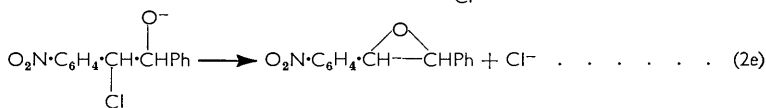
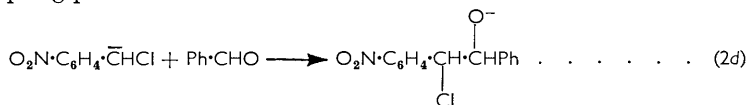
They based their proposal on the fact that in presence of carbonyl compounds the reaction would be diverted to the formation of epoxides, *e.g.*:



Hahn,⁴ and Kleucker,⁵ on the other hand, considered that the reaction involved nucleophilic displacement by a carbanion, thus:



In this case the intercepting process would be:



In an attempt to establish the details, we have examined how the kinetics and products are affected by change in structure, including substitution of deuterium for hydrogen in the side-chain.

¹ Soderbaum and Widman, *Ber.*, 1892, **25**, 3291.

² Walden and Kernbaum, *Ber.*, 1890, **23**, 1959.

³ Bergmann and Hervey, *Ber.*, 1929, **62**, 893.

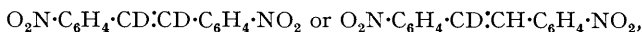
⁴ Hahn, *Ber.*, 1929, **62**, 2485.

⁵ Kleucker, *Ber.*, 1929, **62**, 2587.

EXPERIMENTAL

Benzyl chloride (b. p. 66—67°/16 mm.), 3-nitrobenzyl chloride (m. p. 45·5°), *p*-nitrobenzyl chloride (m. p. 72·5°), 2-nitrobenzyl chloride (m. p. 49·5°), 2,4-dinitrobenzyl chloride (m. p. 34°), *p*-nitrobenzaldehyde (m. p. 106·5°), *p*-methoxybenzaldehyde (b. p. 112°/10 mm.), *trans*-4,4'-dinitrostilbene (m. p. 288°), 4,4'-dinitrostilbene oxide (m. p. 200—201°), 2,4,2'4'-tetranitrostilbene (m. p. 260°), 2,4,4'-trinitrostilbene oxide (m. p. 142°) and 2,4,4'-trinitrostilbene (m. p. 235°) were prepared by standard methods and carefully purified. The solvents, after purification, had b. p.s within 0·1° and were always freshly prepared. An $x\%$ solution of acetone or dioxan was made by mixing x volumes of the organic solvent with $(100 - x)$ volumes of the acid or alkali solution just before the kinetic experiment.

α -Deutero-4-nitrobenzyl Chloride.—Side-chain chlorination of deuterated toluene⁶ by Kharasch and Brown's method⁷ gave α -deuterobenzyl chloride which on nitration⁸ gave α -deutero-4-nitrobenzyl chloride. This was expected statistically to contain 33% of the non-deuterated material. On treatment with alkali in 50% dioxan, it gave $\alpha\alpha'$ -dideutero-4,4'-dinitrostilbene (expected statistically to be only 33% deuterated). Comparison of the infrared spectra of deuterated and non-deuterated materials showed the presence of the following new absorption bands in the deuterated materials which must be attributed to the presence of the α -CD bond: *p*-O₂N·C₆H₄·CHDCl, 7·7w, 8·3w, 11·0s, 12·7vs, and 13·25s μ ;



10·95s and 12·95m μ .

Kinetic Measurements.—The rates of reaction were determined by following the rate of liberation of chloride by electrometric titration of aliquot parts of the mixture.⁹ Most of the experiments were carried out in duplicate. It was shown that none of the organic materials interfered with the measurements. The following is an example of a typical kinetic run, with 4-nitrobenzyl chloride (0·01M) and sodium hydroxide (0·10M) in 50% aqueous dioxan at 30°:

Time (min.).....	15·05	25·13	38·33	52·63	75·30	110·30	136·00
Reaction (%)	14·05	20·94	29·60	38·00	51·50	65·90	75·50
10 ⁴ k ₁ (min. ⁻¹)	101·0	93·5	94·5	94·6	96·0	96·2	103·2

The following are results for benzyl chloride (0·01M) in 50% aqueous dioxan:

Temp.	30	30	30	35	40
OH ⁻ (M)	0·10	0·15	0·20	0·20	0·20
10 ⁴ k ₁ (min. ⁻¹)	2·8	4·0	5·25	10·6	18·0

Activation energy = 23,500 cal./mole.

Corresponding results for 4-nitrobenzyl chloride are:

Temp.	20	23	30	30	30	30	30
ArCl (M)	0·01	0·01	0·01	0·01	0·01	0·05	0·05
OH ⁻ (M)	0·10	0·10	0·10	0·01	0·02	0·05	0·05
10 ⁴ k ₁ (min. ⁻¹)	38·7	50·7	96·8	—	—	—	—
10 ⁴ k ₂ (l. mole ⁻¹ sec. ⁻¹)	—	—	—	16·9	15·2	16·0	22·7*

* In 70% dioxan.

Activation energy = 16,300 cal./mole.

Added *p*-methoxybenzaldehyde had little effect on the rate. Catalysis by added *p*-nitrobenzaldehyde is shown by the following two tables. Table 1 shows the percentages of reaction of 0·05M-4-nitrobenzyl chloride with 0·05M-sodium hydroxide (*a*) in the absence and (*b*) in the presence of 0·05M-*p*-nitrobenzaldehyde at 30° in 50% dioxan. Similarly, Table 2 shows the percentages of reaction between 0·01M-*p*-nitrobenzyl chloride and 0·1M-sodium hydroxide (*a*) in the absence and (*b*) in the presence of 0·01M-*p*-nitrobenzaldehyde at 30° in 50% dioxan.

For reactions in 50% dioxan at 30°, with 0·01M-ArCl and 0·1M-NaOH, the following values of k_1 were obtained: 2-nitrobenzyl chloride, $13·2 \times 10^{-4}$; 3-nitrobenzyl chloride, $4·35 \times 10^{-4}$.

⁶ Turkevich, McKenzie, Friedman, and Spurr, *J. Amer. Chem. Soc.*, 1949, **71**, 4045.

⁷ Kharasch and Brown, *J. Amer. Chem. Soc.*, 1939, **61**, 2147.

⁸ Alway, *J. Amer. Chem. Soc.*, 1902, **24**, 1062.

⁹ Best, *J. Agric. Sci.*, 1929, **19**, 533; Snyder, *Soil Sci.*, 1933, **35**, 43; Janz and Taniguichi, *Chem. Rev.*, 1953, **53**, 397; MacInnes and Beattie, *J. Amer. Chem. Soc.*, 1920, **42**, 1117; Smith, *J. Res. Nat. Bur. Standards*, 1929, **2**, 1137; Hine and Lee, *J. Amer. Chem. Soc.*, 1951, **73**, 22.

The reaction of 0.01M-2,4-dinitrobenzyl chloride with 0.01M-NaOH in 50% dioxan at 20° was 95% complete after 1 min.

TABLE 1.

Time (min.)	20	30	60	61	110	150	170	210	270
Reaction (%)	(a)	—	12.8	21.8	—	34.8	42.4	—	50.0	56.3
	(b)	17.6	—	—	34.7	45.5	—	52.7	55.8	—

TABLE 2.

Time (min.)	5	15	15.05	25.0	25.13	35	38.33	75.30
Reaction (%)	(a)	—	—	14.05	—	20.94	—	29.60	51.50
	(b)	20.5	50.3	—	66.5	—	76.0	—	—

Tracer Experiments.—4-Nitrobenzyl chloride (0.04M) and sodium hydroxide (0.04M) in dioxan-deuterium oxide (99.8%) (4:1 v/v) at 30° were allowed to react for 100 min.; about 38% of the chloride should have reacted. The unhydrolysed chloride was recovered; its infrared spectrum was determined and compared with that of the prepared sample, which is considered to be 66% deuterated. From the ratios of the heights of the absorption bands at 12.7 and at 6.1 μ , it can be calculated that the product is 42% deuterated. The infrared spectrum of 4,4'-dinitrostilbene isolated from the reaction showed the deuterium bands at 10.9 and 12.9 μ .

Deuterated 4-nitrobenzyl chloride (0.01M; 66% deuterium in the side-chain) reacted with alkali (0.1M) in 50% aqueous dioxan at 30° at a rate ($k_1 = 75 \times 10^{-4} \text{ min.}^{-1}$) slower by a factor of 1.28 than that ($90 \times 10^{-4} \text{ min.}^{-1}$) observed under the same conditions for the undeuterated material.

Reaction in Aqueous Acetone.—The following is a summary of kinetic measurements in aqueous acetone:

Benzyl chloride (0.013M), NaOH (0.13M), at 30° in 50% acetone, $k_1 = 3.1 \times 10^{-4} \text{ min.}^{-1}$.

4-Nitrobenzyl chloride at 30°:

	ArCl (M)	OH ⁻ (M)	$10^4 k_1$ (min. ⁻¹)	$10^4 k_2$ (l. mole ⁻¹ sec. ⁻¹)
In 50% acetone	0.01	0.10	191	—
	0.05	0.05	—	32.4
In 70% acetone	0.05	0.05	—	69.0

Products.—Under the conditions of the kinetic investigation, 4-nitrobenzyl chloride (0.01—0.05M) with alkali (0.01—0.1M) in aqueous ethanol, acetone, or dioxan gave almost quantitatively 4,4'-dinitrostilbene (*trans*-isomer, m. p. 288°; a little of the *cis*-isomer, m. p. 185°, was obtained from the mother-liquors).

The product was unchanged when the reaction was carried out in the presence of 4-nitrobenzyl alcohol or *p*-methoxybenzaldehyde. When it was carried out in the presence of *p*-nitrobenzaldehyde, 4,4'-dinitrostilbene oxide (m. p. and mixed m. p. 200—201°) was isolated.

2,4-Dinitrobenzyl chloride similarly gave 2,4,2',4'-tetranitrostilbene, m. p. and mixed m. p. 260°, and, in the presence of *p*-nitrobenzaldehyde and anhydrous potassium carbonate in methanol gave the corresponding stilbene oxide, m. p. 142°, which with potassium iodide in glacial acetic acid gave 2,4,4'-trinitrostilbene, m. p. and mixed m. p. 235°.

DISCUSSION

The results show that the reaction of benzyl and of 4-nitrobenzyl chloride in the presence of alkali is of the second order:

$$d[\text{Cl}^-]/dt = k_2[\text{ArCl}][\text{OH}^-]$$

4-Nitrobenzyl chloride reacts faster (60 times in acetone, and 35 times in dioxan) than benzyl chloride. Such a result would not be expected if both compounds reacted by S_N2 displacement of halide; for the results of Olivier¹⁰ and of Simonetta and Favini¹¹ show that, in such solvents, quite powerfully electron-withdrawing groups have little effect on the rate of the reaction. Thus the following relative rates were obtained for

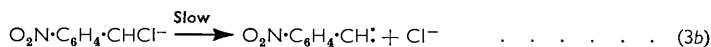
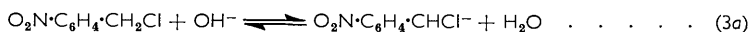
¹⁰ Olivier, *Rec. Trav. chim.*, 1930, **49**, 697, 996.

¹¹ Simonetta and Favini, *J.*, 1954, 1480.

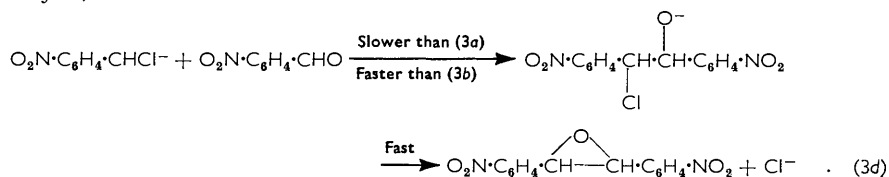
substituted benzyl chlorides (*p*-R·C₆H₄·CH₂Cl; 0.01M) and hydroxide ion at 30.4° in 50% aqueous acetone: ¹²

R.....	Me	H	CN		Me	H	CN
Rel. rate (OH ⁻ = 0.05M)...	2.2	1	1.3	(OH ⁻ = 0.10M).....	3.2	1.8	2.5

The S_N2 mechanism dominates the reaction where R = CN or H, but much less where R = Me. The considerable reactivity of 4-nitrobenzyl chloride suggests that the first stage in its reaction with alkali is removal of a proton, which is shown to be reversible since 4-nitrobenzyl chloride recovered after partial reaction in dioxan-D₂O contains deuterium. Stage 2*a* of Hahn's mechanism is therefore not rate-determining; nor is stage 2*b*, since this would require that the reaction have the kinetic form $d[\text{Cl}^-]/dt = k[\text{ArCl}]^2[\text{OH}^-]$. The following modification, designated α -E1cB, is therefore suggested:



Since *p*-nitrobenzaldehyde diverts the reaction to form an epoxide, with increase in the rate of liberation of chloride ion (the rate does not change in presence of the less reactive *p*-methoxybenzaldehyde and the product is the dinitrostilbene and not an epoxide), it is suggested that this process involves reaction between the intermediate ion O₂N·C₆H₄·CHCl⁻ and the aldehyde, thus:



This mechanism differs from Bergmann and Hervey's ³ in that it is considered that it is not the biradical but the conjugate base which reacts with the intercepting aldehyde.

If the rates of the forward and the backward reaction of (3*a*) are about the same and much greater than that of (3*b*), then α -deutero-4-nitrobenzyl chloride would be substantially converted into 4-nitrobenzyl chloride before hydrolysis by alkali in aqueous dioxan, and no deuterium isotope effect could be observed. The observation of a small effect ($k_{\text{H}}/k_{\text{D}} = 1.28$) suggests, therefore, that the *back-reaction* of (3*a*) is of a rate similar to that of (3*b*). The rate of the backward reaction (3*a*) is the same for both the deuterated and the non-deuterated material, since the same anion is formed by deuterium-extraction. Similarly, the rate of reaction (3*b*) is the same for both materials. The only variable is that of the forward reaction (3*a*), a proton- or a deuterium-extraction. The equilibrium constant (K_a) for (3*a*) will therefore vary according to whether the material is deuterated or not. The overall rate constant of the reaction [$K_a \times$ rate constant of the slow (3*b*) step] will consequently vary.

In the reaction of 2,4-dinitrobenzyl chloride, the overall rate of the reaction is much greater; the intermediate conjugate base must have been formed very easily under the influence of the two nitro-groups, and is clearly very reactive, readily losing halide ion or reacting with added aldehyde to form epoxide.

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CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE,
ALEXANDRIA UNIVERSITY, U.A.R.

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