# Intramolecular Nucleophilic Aromatic Substitution Reactions Involving the Novel Displacement of Hydride Ion by Cyanobenzyl Carbanions

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*Summary* α-(*N*-Substituted-*N*-3,5-dinitrobenzoylamino)-, α-(*N*-substituted-*N*-2-chloro-3,5-dinitrobenzoylamino)-, and α-(*N*-substituted-*N*-3-nitrobenzoylamino)phenylacetonitriles (1) and (2) undergo base-catalysed cyclisation with displacement of hydride ion or chloride ion to afford the corresponding isoindolin-1-ones (3), (4), and (5).

HYDRIDE ion displacement[1] is comparatively rare in nucleophilic aromatic substitution reactions. Intramolecular processes of this type do not appear to have been reported hitherto. Recently, we described[2] examples of the intramolecular nucleophilic displacement of aromatic nitro-groups by carbanions. We now report cyclisation reactions of nitrobenzene derivatives involving the analogous displacement of hydride ion by cyanobenzyl carbanions.†

Heating compound (1a) under reflux with aqueous 1N sodium carbonate gave a mixture, chromatography of which afforded the compound (3a) (20%), m.p. 228°, which showed characteristic[2] i.r. carbonyl absorption at 1720 cm$^{-1}$ and $^1$H n.m.r. absorption at $\tau$ ($CF_3{\cdot}CO_2H$) 0·56 [1H, d, H(5) or H(7)] and 0·73 [1H, d, H(7) or H(5)], and was identical with the dinitroisoindolinone prepared (95%) by cyclising[2] (1d) in hot aqueous ethanolic sodium acetate.

The formation of compound (3a) from (1a) is readily explained in terms of the formal intramolecular displacement of hydride ion by cyanobenzyl carbanion generated in the side-chain (*cf.* Scheme). Concomitant reduction of the substrate and/or product by the liberated hydride ion [or by the intermediate adduct (7)] then accounts for the low yield of (3a) and the formation of by-products. In support of these contentions, compound (3a), was obtained in quantitative yield when the sodium acetate catalysed cyclisation of (1a) was carried out in the presence of a mild oxidising agent such as *p*-benzoquinone to scaveng ethe hydride ion formed [or alternatively to oxidise the intermediate (7) into (3a)]. Similar cyclisation of the amides (1b and c) in the presence of *p*-benzoquinone gave quantitative yields of the compounds (3b), m.p. 179°, and (3c), m.p. 134° which were identical with the isoindolinones

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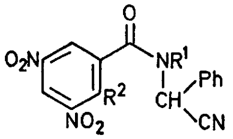
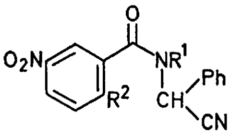
† Satisfactory analyses were obtained for all new compounds.

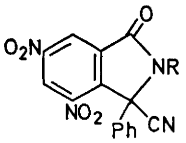
formed by the sodium acetate catalysed cyclisation of compounds (1e) and (1f).



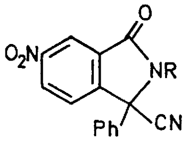
| (1) | $R^1$ | $R^2$ |
|---|---|---|
| a; | Ph | H |
| b; | $CH_2Ph$ | H |
| c; | Me | H |
| d; | Ph | Cl |
| e; | $CH_2Ph$ | Cl |
| f; | Me | Cl |



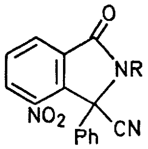
| (2) | $R^1$ | $R^2$ |
|---|---|---|
| a; | Ph | H |
| b; | $CH_2Ph$ | H |
| c; | $CH_2Ph$ | Cl |



| (3) | R |
|---|---|
| a; | Ph |
| b; | $CH_2Ph$ |
| c; | Me |



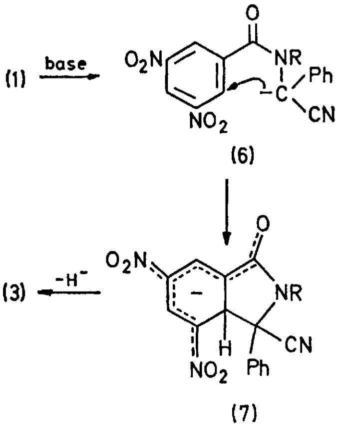
(4)



(5)

| | R |
|---|---|
| a; | Ph |
| b; | $CH_2Ph$ |

A single nitro-group provides sufficient activation for cyclisation with hydride displacement. Thus, heating the (2a) under reflux with aqueous ethanolic sodium carbonate gave the known[2] compound (4a) (30%), m.p. 225°, $\tau$ ($CF_3$$\cdot$$CO_2H$) 1$\cdot$00 [1H, d, H(7)], 1$\cdot$26 [1H, q, H(5)], and 2$\cdot$19 [1H, d, H(4)], together with the compound (5a) (2%), m.p. 214°, $\tau$ ($CF_3$$\cdot$$CO_2H$) 1$\cdot$25 [1H, dd, H(5) or H(7)], 1$\cdot$42 [1H, dd, [H(7) or H(5)], and 1$\cdot$87 [1H, t, H(6)], demonstrating competing nucleophilic attack *ortho* and *para* to the nitro-group. Similar cyclisation of (2b) in the presence of *p*-benzoquinone again occurred in higher yield to afford a readily separated mixture of the isomeric compounds (4b) (62%), m.p. 158° [identical with an authentic sample prepared (92%) by cyclising (2c) in hot aqueous ethanolic sodium carbonate] and (5b) (8%), m.p. 148°.



SCHEME

The ease of hydride displacement by the side-chain carbanion in the amides (1a—c) and (2a and b) is remarkable and may be due at least in part to the favourable steric situation. In contrast, the intermolecular substitution[3] of nitrobenzenes by cyanobenzyl carbanions appears to require more extreme conditions and yields products (quinone oximes, nitrones, azoxy-compounds) derived from nitrosobenzene intermediates formed by the predominant expulsion of hydroxide ion (as opposed to hydride ion) from initial carbanion adducts [*cf.* (7)].

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[1] T. J. de Boer and I. P. Dirk in 'The Chemistry of the Nitro and Nitroso Groups,' ed. H. Feuer, Interscience-Wiley, New York, 1969, Part I, p. 554.

[2] T. W. M. Spence and G. Tennant, *J.C.S. Perkin I*, 1972, 835.

[3] M. Jawdosiuk, B. Ostrowska, and M. Makosza, *Chem. Comm.*, 1971, 548; M. Makosza and M. Jawdosiuk, *ibid.*, 1970, 648; R. B. Davis, L. C. Pizzini, and J. D. Begnini, *J. Amer. Chem. Soc.*, 1960, **82**, 2913.