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NORMAL *vs* CINE-SUBSTITUTION OF A NITRO GROUP IN 6,7-DINITROQUINOXALINE WITH PIPERIDINE

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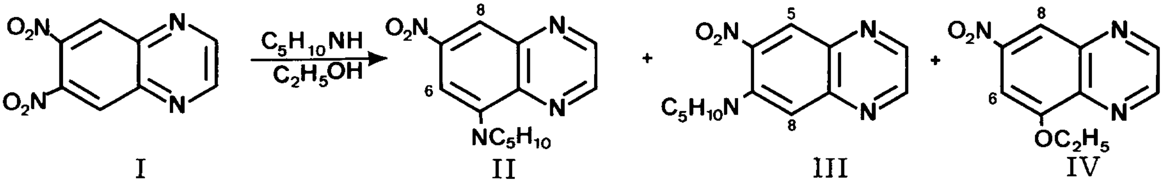
2,3-Dinitronaphthalene is known to give rise essentially to cine-substitution with alkoxides and amines(1). The extension of these reactions to 6,7-dinitroquinoxaline (I) gave unexpected results which we report here.

Whereas I undergoes almost quantitative normal substitution with sodium methoxide to give 6-methoxy-7-nitroquinoxaline [m.p. 195-197°; NMR signals at δ(DMSOd_6) 9,04(d,1H), 8,95(d,1H), 8,64(s,1H), 7,82(s,1H), 4,32(s,3H)ppm], reactions with ammonia in ethanol or methanol lead to mixtures of 5-amino-7-nitro- and 6-amino-7-nitroquinoxalines in variable proportions. We felt that this variability deserved some attention and the influence of nucleophile concentration was investigated in the case of piperidine in ethanol. The isomeric nitro-piperidinoquinoxalines were identified by their NMR ($CDCl_3$) spectra ; II[m.p. 147-148°] had H_6 at 7,84 ppm (d) and H_8 at 8,48 ppm (d) with $J_{6,8}$ = 2,5 Hz; III[m.p. 88-89°] showed H_5 at 8,31 ppm (s) and H_8 at 7,53 ppm (s).

The table summarizes the data for several runs where the nucleophile-to-substrate molar ratio was always 10, but with various total concentrations. The cine/normal ratios where determined by integration of the relevant NMR peaks. The amount of cine-substitution steadily increases with rising concentration. Another fact worth noticing is the presence of 5-ethoxy-7-nitroquinoxaline [IV; m.p. 185-187° ; H_6 at 7,85 ppm (d,1H) and H_8 at 8,75 ppm (d,1H) with $J_{6,8}$ = 2,5 Hz] also a cine-substitution product, whose yield increases at higher dilution ; the ratio III/IV is essentially concentration independent.



I II III IV

yield : 90 - 95%

$[I]$ M.l^{-1}	0,13	0,07	0,057	0,029	0,015	0,007
$[NHC_5H_{10}]$ M.l^{-1}	1,30	0,70	0,57	0,29	0,15	0,07
II %	91	83	78,5	62	49	37,2
III %	4,3	8,7	11	20	28	31,1
IV %	5	8,3	10,5	18	23	31,6
II/III + IV	9,8	4,9	3,6	1,6	0,96	0,59
III/IV	0,86	1,05	1,05	1,1	1,2	0,98

Reaction of I (0,66g, 3mmol) with piperidine (3ml, 30 mmol) in ethanol (20-400 ml) at 80°C. II and III are not interconverted in these conditions.

These findings can be rationalized in terms of different rate equations for the three reactions. If one assumes, in analogy with what has been found for 2,3-dinitronaphtalene(1), that the cine-substitution by piperidine is second order in nucleophile, i.e.

$$v(\text{cine}) = k_c\,[I]\,[NHC_5H_{10}]^2, \qquad (1)$$

that the normal substitution is first order in amine, as is found in the case of o-dinitrobenzene(2), i.e.

$$v(\text{normal}) = k_n\,[I][NHC_5H_{10}], \qquad (2)$$

and that cine-ethoxylation requires one molecule of piperidine

$$v(\text{ethoxy}) = k_{EtO}\,[I][NHC_5H_{10}], \qquad (3)$$

one sees that (provided piperidine is in fair excess over substrate, which is the case here), [cine] / [normal]+[EtO] increases linearly with the concentration of nucleophile, whereas [normal]/[EtO] is concentration independent. Although the linearity suggested by equations (1) (2) and (3) is not strictly obeyed, we feel safe in assuming that the concentration of the amine plays a major role in determining the ratio of cine to normal substitution. It might be of interest to enquire whether other examples of cine-substitution reported in the literature show a similar concentration dependence.

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Notes and References

All new compounds gave satisfactory analytical data

1) G. Guanti, S. Thea & C. Dell'Erba, Tetrah. Lett. 461 (1976).
2) F. Pietra & D. Vitali, J. Chem. Soc. Perk. II, 385 (1972).