Tetrahedron Letters, Vol.22, No.24, pp 2303 - 2306, 1981
Printed in Great Britain

0040-4039/81/242303-04$02.00/0

NUCLEOPHILIC DISPLACEMENT OF THE NITRO GROUP IN 2- AND 4-NITRONAPHTHALIC-1, 8-ANHYDRIDES AND THEIR DERIVATIVES

By Michael Alexiou, John Tyman*, and (the late) Ian Wilson
(School of Chemistry, Brunel University, Uxbridge, Middlesex, UB8 3PH)

Abstract: The nitro group in 2- and 4-nitronaphthalic-1,8-anhydrides can be substituted by amines in certain cases with retention of the anhydride grouping.

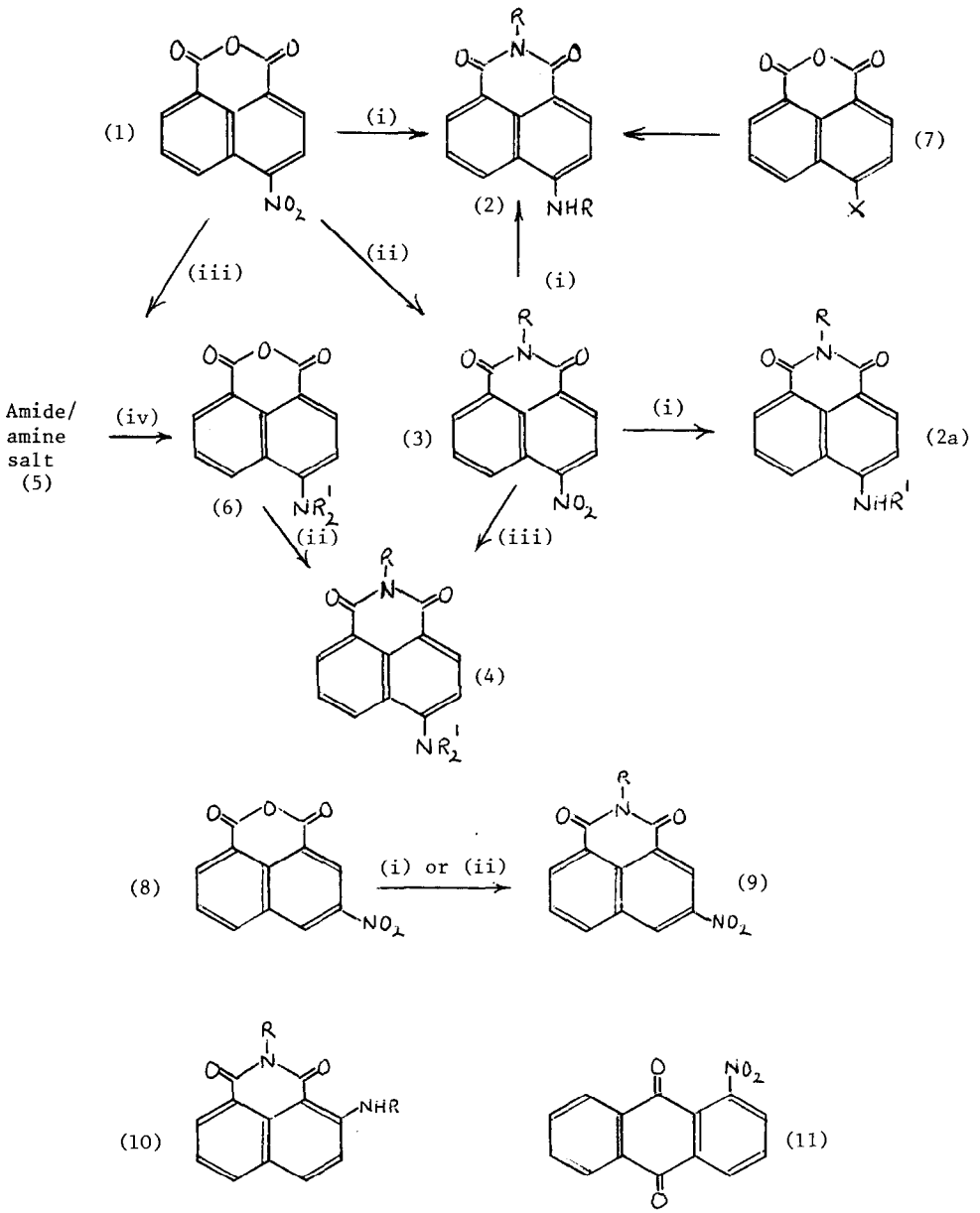
We wish to report the novel displacement of the nitro group in certain nitronaphthalic-1,8-anhydrides by ammonia, primary, secondary and tertiary amines. During an investigation of the reaction of 4-nitronaphthalic anhydride (1) with n-butylamine in hot o-dichlorobenzene, 4-n-butylamino-N-butylnaphthalic-1,8-imide (2;R=nBu) was formed along with many tarry by-products. The yield of (2) was greatly improved with aprotic solvent such as dimethylformanide (DMF), or hexamethylphosphoric triamide (dimethylsulphoxide (DMSO) enabled reaction to proceed at a lower temperature but tended to form by-products) and various compounds having the properties indicated in the Table were synthesised[2] from the amines indicated.

Formerly such compounds have been derived[3] from 4-chloro or 4-bromonaphthalic anhydride[4] (7;X=Br) with primary amines in dichlorobenzene or nitrobenzene[5] or from sodium 4-sulphonaphthalic anhydride (7;X=SO_3Na) in aqueous pressurised media although no details[7] have appeared of this last method. 4-Nitronaphthalic-1,8-anhydride has been reacted in methanolic solution with a variety of lower alkylamines but surprisingly the displacement of the 4-nitro group was not observed and simply formation of the N-alkylimide (3)[8]. (Scheme).

We have found it more convenient to carry out this reaction in an aprotic solvent (DMF) at 0-10° to give (3) which under more drastic conditions with primary amine or secondary amine furnished respectively (2), (2a) or (4). Direct reaction of 4-nitronaphthalic anhydride with a secondary amine gave a 4-dialkyamino compound as an amide/amine salt (5) by anhydride ring opening together with (6). Acidic and thermal treatment converted the former into (6). With certain cyclic secondary amines such as piperidine, exclusive formation of (6) appeared to occur possibly due to the greater steric hindrance of the anhydride group towards substitution. Reaction of (6) with a primary amine afforded an alternative synthesis of (4). With tertiary amines, 4-nitronaphthalic anhydride in dimethylformanide underwent a more complex product to give salt-like products in which, from uv and ir spectral evidence, the nitro group had been displaced

In general the rate of nucleophilic substitution with alkylamines occurred in the order, $RNH_2 > R_2NH > R_3N$, and with the primary amines higher members reacted faster, ammonia itself being the least reactive nucleophile. Arylamines react slowly and displacement of the nitro group required in these cases an activated $-NH_2$ group. The nitrite ion was readily detected in the products of reaction of alkylamines. 2-Nitronaphthalic-1:8-anhydride[9] underwent interaction

Scheme



Reagents: (i) NH_3, RNH_2, or R^1NH_2, DMF (120°), (or HMPT, hot); (ii) NH_3 or RNH_2, DMF, cold (0-10°); (iii) NR^1_2, DMF, (120°); (iv) $H^{\oplus}$, heat.

Reaction of Amines with Nitronaphthalic-1,8-anhydrides

Structure†	Route	m.p. (°C)	yield (%)	Reaction time (h)	medium* and conditions	λ(max) nm	$\varepsilon/10^{-3}$	R_f§
2, R=H	(i)	250	51	48	EtOH, NH_3, sealed tube	243	14.4	-
2, R=Me	"	260-261	63	16	$MeNH_2$, H_2O sealed tube	258	24.5	0.30
2,R=Et	"	188-189	80	16	$EtNH_2$ sealed tube	259	22.8	-
2,R=n-Pr	"	170-172	46	8	n-$PrNH_2$ reflux, DMF	266	24.6	-
2,R=n-Bu	"	123-124	58	4	n-$BuNH_2$, DMF 120°	266	25.3	0.78
2,R=n-Am	"	104-105	67	3	n-$C_5H_{11}NH_2$, DMF 120°	266	26.0	-
2,R=n-Hex	"	84-85	65	4	n-$C_6H_{13}NH_2$, DMF, 120°	266	26.6	0.83
2,R=n-Oct	"	88-89	64	4	n-$C_8H_{17}NH_2$ DMF, 120°	266	28.8	-
2,R=n-Dec	"	94-95	53	5	n-$C_{10}H_{21}NH_2$ DMSO, Ambient	265	23.4	0.86
2,R=$(CH_2)_2OH$	"	224-225	10	1	$HOCH_2CH_2NH_2$, DMF, 100°	264	15.8	0.00
2a R=H (via 3)	(ii) NH_3 R^1=n-Bu (i)n-$BuNH_2$	237-239	18	5	0-10°, DMF, NH_3 100°, n-$BuNH_2$	285	20.0	0.19
2a R=n-Bu (via 3)	(ii) $BuNH_2$ R^1=n-Dec (i)n-$DecNH_2$	109-110	50	5	0-10°, DMF, $BuNH_2$ 100°, $C_{10}H_{21}NH_2$	265	23.5	-
4 R=n-Bu (via 3)	(ii)n-$BuNH_2$ R^1=Et (iii)Et_2NH	oil	30	5	0-10°, DMF, $BuNH_2$ 100°, Et_2NH	266	16.6	0.89
4 R=H (via 3)	(ii) NH_3 R^1=Et (iii)Et_2NH	249-251	22	5	0-10°, DMF, NH_3 100°, Et_2NH	283	14.3	0.21
10 R=n-Bu	(i)	88-89	29	6	DMF 120°, n-$BuNH_2$	269	39.1	0.77
6 R^1=Et	(iii)Et_2NH (iv)	118-120	28	4	DMF 120°, Et_2NH	287	14.2	0.77
6 $(R^1)_2$=	(iii) (iv)	179-180	17	4	DMF, 120°	279	14.9	0.79

† Correct microanalyses were obtained for the compounds examined. Compounds of type 2 possessed characteristic ^1H NMR absorption spectra (R=n-Bu) ($CDCl_3$), 6.70-8.73 (5H, m, HAr), 5.50 (1H,S,NH, exch. D_2O), 4.10-4.33 (2H,t,$CH_2N(CO)_2$), 3.30-3.63 (2H,m,CH_2NHAr), 1.23-1.97 (8H,m,$4CH_2$), 0.77-1.13 (6H,2t,$2CH_3$).

* The reaction conditions consisted of interaction of 2- or 4-nitronapthalic anhydride (0.01m) with the alkylamine (0.05m) in DMF (30-40 cm^3) at 120° for the time indicated followed by recovery of alkylamine and DMF and crystallisation of the residue from isopropanol.

§ $CHCl_3$EtOAc (10:90): (1)0.81, (3)R=n-Bu, 0.87, (10) 0.83, (11) 0.86

progressively as with the 4-nitro compound to give (10) in lower yield than with (2). By contrast 3-nitronaphthalic anhydride (8)[10] reacted only at the anhydride centre to give (9).

With the 2- and 4-nitronaphthalic anhydrides compared with the 3-nitronaphthalic anhydride stable transition states are feasible and a general structural requirement for nucleophilic displacement to occur is a carbonyl group in a 2- or 4-position relative to a nitro group. The reaction pathway is likely to involve substitution and elimination at the same carbon atom rather than attack at C5 and expulsion of $NO_2^{\ominus}$ from C4 such as found[11] in the reaction of 2,3-dinitrophenol with secondary amines to give 2-(N,N-dialkyl)-5-nitrophenol.

A number of examples of replacement of the 1-nitro group in 1-nitroanthraquinone with alkylamines[12], 2-methyl-1-nitroanthraquinone[13], 1-nitroanthraquinone-2-carboxamide[14] and of one nitro group in 1,5-dinitro or 1,8-dinitroanthraquinone[15] are known. Nucleophilic displacement in the present naphthalenic series was less facile than with 1-nitroanthraquinone but easier than with 4-nitro phthalic anhydride. Meisenheimer complex formation in benzenoid and naphthalenic compounds has been compared[16] and nucleophilic displacement of the nitro group in the former series has been reviewed[17].

References

1 Elsevier, Encyclopaedia of Organic Chemistry, Elsevier Publishing Co., Amsterdam, 1949, vol. 12B, p.4773.

2 M.S. Alexiou, P.I. Brittain and J.H.P. Tyman, BP application 43411/78.

3 M. Scalera and A. Joyce, USP 24 15373 (1947).

4 G. Rule and S. Thompson, J. Chem. Soc., 1937, 1964.

5 J.H.P. Tyman and I.H. Wilson, (unpublished work).

6 K. Dziewonski, H. Galitzerowna and A. Kocwa, Bull. internat. Acad. Polonaise, 1926, A, 204; Elsevier, Encyclopaedia of Organic Chemistry, vol. 12B, p.5682.

7 I.G. Farbenind, AG, Fr P753104 (1933); J.H.P. Tyman and M.S. Alexiou, (unpublished work).

8 M. Okazaki, T. Tanaka and S. Taniguchi, Yuki Gosei Kagaku Kyokai Shi, 1956, 14, 344; Chem. Abs., 1951, 51, 8050.

9 G.T. Morgan and H.A. Harrison, J. Soc. Chem. Ind., 1930, 413; P.H. Graysham and A.T. Peters, J. Chem. Soc., (C), 1973, 3600.

10 G. Rule and R. Brown, J. Chem. Soc., 1934, 1710. A. Graebe and N. Briones, Ann., 1903, 327, 84.

11 R.E. Markwell, Chem. Comm., 1979, 428.

12 M.S. Alexiou and J.H.P. Tyman (unpublished work).

13 G.D. Wood and A.T. Peters, J. Chem. Soc., 1962, 3373.

14 T. Hargreaves and A.T. Peters, Nature, 1966, 202, 1209.

15 Ciba-Geigy Ltd., Swiss P 1524729 (1978).

16 J.H. Fendler, E.J. Fendler and C.E. Griffin, J. org. Chem., 1969, 34, 2057.

17 J.R. Beck, Tetrahedron, 1978, 34, 2057.

(Received in UK 30 March 1981)