Aromatic Nitro-group Displacement Reactions. Part 1. A Novel Route to Substituted 10-Phenylacridones

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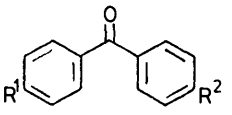
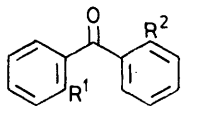
Methoxy-anions in dimethyl sulphoxide initially displace the *para*-nitro-groups from 2,2',4,4'-tetranitrobenzophenone (6). Primary aromatic amines however displace the two *ortho*-nitro-groups to give 10-aryl-3,6-dinitro-9-acridones (15), in which the nitro-groups can be displaced by anionic nucleophiles to give compounds of a previously inaccessible substitution pattern. Enhanced reactivity towards aromatic amines seems to be general in nitro-groups activated by *ortho*-carbonyl. Hydroxydenitration of (6) produces 3,6-dinitroxanthen-9-one (19) and 4-hydroxy-2,2',4'-trinitrobenzophenone (20).

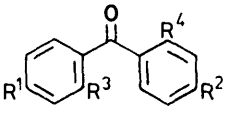
AROMATIC nitro-groups, if sufficiently activated by *ortho*- or *para*-carbonyl groups, are displaced by oxy-anions in dipolar aprotic solvents.[1] Thus, in dimethyl sulphoxide (DMSO), the benzophenones (1), (4), and (6)



(1) $R^1 = R^2 = NO_2$
(2) $R^1 = OMe, R^2 = NO_2$
(3) $R^1 = R^2 = OMe$

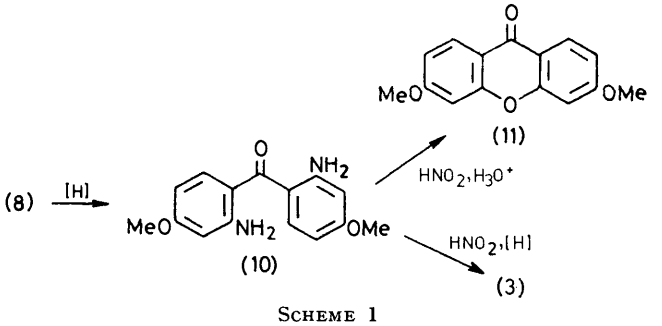


(4) $R^1 = R^2 = NO_2$
(5) $R^1 = OMe, R^2 = NO_2$



(6) $R^1 = R^2 = R^3 = R^4 = NO_2$
(7) $R^1 = OMe, R^2 = R^3 = R^4 = NO_2$
(8) $R^1 = R^2 = OMe, R^3 = R^4 = NO_2$
(9) $R^1 = R^2 = R^3 = OMe, R^4 = NO_2$

reacted with stoicheiometric amounts of methanolic sodium methoxide to yield (3), (5), and (9) *via* isolable intermediates such as (2) and (7). In 2,2',4,4'-tetranitrobenzophenone (6) the *para*-nitro-groups were

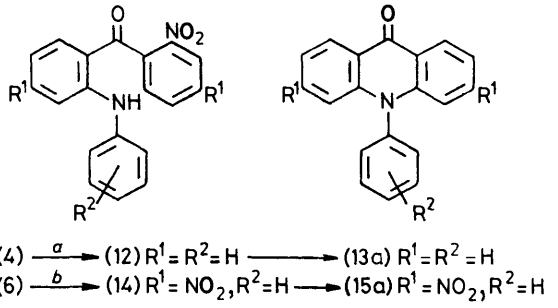


SCHEME 1

preferentially displaced, so that (8) was isolated in yields of >80%. Subsequently one *ortho*-nitro-group was displaced to give (9) but, as with (5),[1] the second *ortho*-nitro-group proved resistant. The structure of (8) was established by ^1H n.m.r. and by the diazonium reactions of the corresponding diamine (10) (Scheme 1).

Displacement of nitro-groups in these benzophenones by primary aromatic amines followed a different pattern. Thus 4,4'-dinitrobenzophenone (1) was substantially unaffected by aniline at its boiling point or at 125 °C in the presence of DMSO or hexamethylphosphoramide,[2] whereas the 2,2'-isomer (4) reacted in refluxing aniline with displacement of one nitro-group (12) but with a consecutive slow intramolecular displacement of the second to give 10-phenyl-9-acridone (13a) (Scheme 2).

The tetranitro-compound (6) reacted readily with an excess of aniline at 125 °C with displacement of both *ortho*-nitro-groups and the formation of 3,6-dinitro-10-phenyl-9-acridone (15a) in yields of *ca.* 80%. This reaction ‡ is fairly general for *meta*- and *para*-substituted



SCHEME 2 *a*, $PhNH_2$, 7 h reflux; *b*, $ArNH_2$, 125 °C

anilines (Table 1), though it proceeds less readily with *o*-toluidine and *o*-fluoroaniline. Base-weakening substituents tend to lower yields and increase reaction time. Optimal yields of 10-aryl-9-acridones are obtained when at least 8 molar equivalents of amine are used for each mole of (6); the orange-yellow product normally crystallises from the highly coloured reaction mixture. DMSO is the best co-solvent and often leads to a cleaner product, though with little increase in yield; it is also effective for recrystallising the resulting 10-aryl-9-acridones. As with (4), the reaction involves two stages (Scheme 2); on heating (6) in aniline (10 mol equiv.) to boiling, a self-sustaining reaction continued for one or two minutes and, on cooling, the mixed product could be

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TABLE 1

(*a*) 10-Aryl-3,6-dinitroacridones (15) prepared from (6) by treatment with aromatic amines (10 mol equiv.) in DMSO [a] at 125—130 °C

Compound number	R^2	S.p. (°C) [b] (approx.)	Reaction time (h)	Yield (%)	Solvent for cryst. [c]	Found (%) C	H	N	Formula	Required (%) C	H	N	ν(C=O) (cm^{-1})
(15a)	H	418	1	80 [d]	A	63.2	3.05	11.4	$C_{19}H_{11}N_3O_5$	63.2	3.1	11.6	1 650
(15b)	4-Me	394	2	74	A	63.7	3.6	11.0	$C_{20}H_{13}N_3O_5$	64.0	3.5	11.2	1 650
(15c)	3-Me	349	2	73	A, B	64.2	3.5	11.2	$C_{20}H_{13}N_3O_5$	64.0	3.5	11.2	1 645br
(15d)	2-Me	317	52	38	A	64.1	3.5	11.05	$C_{20}H_{13}N_3O_5$	64.0	3.5	11.2	1 655br
(15e)	3,5-diMe	355	3	80	A	64.9	3.8	10.8	$C_{21}H_{15}N_3O_5$	64.8	3.9	10.8	1 645
(15f)	3-Cl-4-Me	375	14	78	A	58.5	2.8	9.9	$C_{20}H_{12}ClN_3O_5$	58.6	2.95	10.25	1 645br
(15g)	4-Cl	415	6	80	B	57.7	2.45	10.8	$C_{19}H_{10}ClN_3O_5$	57.7	2.55	10.6	1 650
(15h)	2-F	327	48	35	A	60.05	2.6	10.8	$C_{19}H_{10}FN_3O_5$	60.2	2.7	11.1	1 650br
(15i)	4-NHAc	410	2	65	B	60.3	3.4	13.5	$C_{21}H_{14}N_4O_6$	60.3	3.4	13.4	1 650 (1 670)
(15j)	3-NHAc	365	20	>50	B	60.15	3.5	13.2	$C_{21}H_{14}N_4O_6$	60.3	3.4	13.4	1 640 (1 690)
(15k)	4-OMe	350	2 4 [k]	48 61	A	61.45	3.3	10.6	$C_{20}H_{13}N_3O_6$	61.4	3.35	10.7	1 645
(15l)	4-Ph	320	30	60	B	68.7	3.4	9.5	$C_{25}H_{15}N_3O_5$	68.65	3.5	9.6	1 650br
(15m)	4-CN	410	42 95	27 42	B	62.2	2.7	14.4	$C_{20}H_{10}N_4O_5$	62.2	2.6	14.5	1 655br
(15n)	4-SO_2NH_2	310	125	49	C	52.0	3.2	11.7	$C_{19}H_{12}N_4O_7S$, $0.5C_4H_8O_2$	52.1	3.3	11.6	1 650
(15o)	4-NO_2 [e]	420	335	27	A	55.9	2.5	13.7	$C_{19}H_{10}N_4O_7$	56.2	2.5	13.8	1 650

10-Aryl-3,6-dinitroacridones (15) derived from compounds listed in (*a*)

Compound number	R^2	S.p. (°C) [b] (approx.)	Solvent for cryst. [c]	Found (%) C	H	N	Formula	Required (%) C	H	N	ν(C=O) (cm^{-1})
(15p)	4-CO_2H [f]	393	B	59.3	2.6	10.2	$C_{20}H_{11}N_3O_7$ [g]	59.3	2.7	10.4	1 640 (1 730)
				58.6	3.1	11.1	$C_{20}H_{11}N_3O_7$, $0.5C_3H_7NO$	58.4	3.3	11.1	
(15q)	4-$CONH_2$ [h]	370	B	58.3	4.0	14.5	$C_{20}H_{12}N_4O_6$, C_3H_7NO	57.9	4.0	14.7	1 650 (1 675) (1 690sh)
(15r)	4-NH_2 [i]	385	B	60.5	3.2	14.9	$C_{19}H_{12}N_4O_5$	60.6	3.2	14.9	1 650
(15s)	4-OH [j]	395	A	59.1	2.9	10.7	$C_{19}H_{11}N_3O_6$, $0.5H_2O$	59.1	3.1	10.9	1 640

[a] 50% v/v of amine used. [b] These compounds exhibit no true m.p. or decomposition point; the sintering point (s.p.), which is somewhat dependent on the rate of heating, appears to indicate incipient decomposition; in most cases there is considerable sublimation of pure material before this temperature is attained. [c] A = DMSO or DMSO–EtOH; B = DMF–EtOH; C = dioxan. [d] Yields obtained using 7.5, 6, 5, and 1 mol equiv. of aniline were 68, 65, 55, and 23%, irrespective of the amount of DMSO present. [e] Also formed by nitration of (15a) with potassium nitrate in concentrated sulphuric acid at room temperature (24 h). [f] By refluxing (15m) with acetic acid (40 parts) and 60% w/w aqueous sulphuric acid (60 parts) for 33 h. [g] Dried at 120° and 0.01 mmHg. [h] By keeping a solution of (15m) in concentrated sulphuric acid for 160 h at room temperature, then pouring onto ice. [i] By refluxing (15i) for 7 h with acetic acid (20 parts) and 60% w/w aqueous sulphuric acid (10 parts). The yellow amine sulphate was filtered off and suspended overnight in aqueous ammonia. [j] By refluxing (15k) for 12 h with acetic acid (24 parts) and 60% aqueous hydrogen bromide (12 parts). [k] 100 °C.

separated into (6), (15a), and 2-anilino-2′,4,4′-trinitrobenzophenone (14). The intermediate (14) is stable under normal conditions but cyclises to (15a) above its melting point or in DMSO at 100 °C.

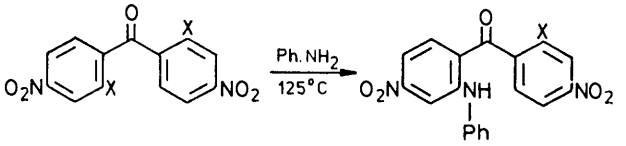
The ready displacement of an *ortho*-nitro-group in (4) and (6) suggests some degree of intramolecular participation by the carbonyl group (the effect sometimes known as ' built-in solvation ' [3]). This might either take the form of simple electrostatic interaction to stabilise the positive ammonium centre of the intermediate complex [3a] or of hydrogen-bonding between the *N*-hydrogen of the aniline and oxygen of the carbonyl group.[3b] That (6) reacts much faster than (4) indicates that further electron-withdrawal from the reaction centre enhances this stabilisation. These concepts are largely derived from nucleophilic halogen displacement reactions in which *ortho* : *para* substitution ratios with amines are normally greater than unity [3] even if finite. For nitro-displacement reactions an anchimeric role has been suggested for the *ortho*-nitro group.[4] A corresponding role for *ortho*-carbonyl may be inferred from the reactivity of 1-nitro-9-acridones towards amines,[5] while the ready displacement by aniline of a 1-nitro-group in anthraquinones [6] has long been familiar. We find also that 1-nitroxanthen-9-one reacts readily with refluxing aniline under conditions in which 1-chloroxanthen-9-one requires an external (copper) catalyst,[7] whereas 3-nitroxanthen-9-one fails to react.

In the benzophenone system the nitro-group is similarly displaced more readily than halogen. With aniline at 125 °C, neat or in DMSO, (16b) [1] and (16c) reacted very slowly. Reaction was faster with the di-iodo compound (16a) which gave (17), but conversion to the 10-aryl-9-acridone (15a) was not observed (Scheme 3).

The reaction of ammonia or primary aliphatic amines with (6) does not lead to 9-acridone or its 10-alkyl derivatives; reaction is rapid but takes a complex course resulting generally in non-crystalline products. The isolation of small yields of the dinitroanilines (18a), (18b), and (18c) (Scheme 4) suggests that attack is directed initially at the carbonyl-group.

Certain reactions of (6) which did not lead to 10-aryl-9-acridones, such as that with 3-aminopyridine, gave low

yields of the previously unknown 3,6-dinitroxanthen-9-one (19) (Scheme 5), identified by reduction to the known 3,6-diaminoxanthen-9-one [8] and by methoxy-denitration to (11).[9]

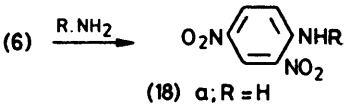


(16) a; X = I
b; X = Br
c; X = Cl

(17) X = I

SCHEME 3

We find that (19) is produced from (6) by a variety of reagents, either by an ionic route, *e.g.* OH^- or ONO^- [10] in DMSO, or by what appears to be a Nef-type [11] hydroxydenitration proceeding through an anion-radical

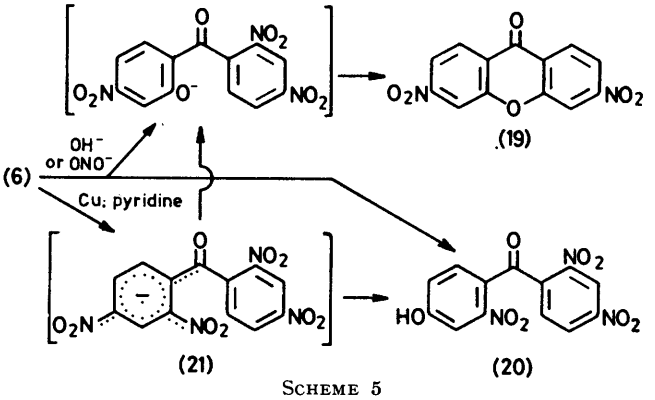


(18) a; R = H
b; R = $[CH_2]_2NEt_2$
c; R = C_6H_{11}

SCHEME 4

(21), *e.g.* copper in pyridine,[12] potassium cyanide in DMSO.[13] In most cases the phenol (20) [also obtained by demethylation of (7)] is formed in approximately equal amount. The anion-radical (21) might be expected to yield equivalent amounts of (19) and (20) but the ionic route, if similar to attack by OMe^-, would be expected to yield mainly (20). This difference in behaviour between OMe^- and OH^- (ONO^-) is open to several interpretations which will be discussed in a later publication.

In the reaction of (6) with substituted anilines (Scheme 2), liberated nitrite ion (acting as ONO^-) seems not to produce (19) and (20) even when only 1 mol of amine is used. Evolution of nitrogen normally occurs,



SCHEME 5

and in one instance at least there is evidence for normal diazotisation and coupling with excess of amine. In the reaction of (6) with *m*-toluidine, after filtration of crystalline product (15c), the basic residue was freed from any nitrite ion; acidification then gave the insoluble hydrochloride of the azo-compound (22).[14]

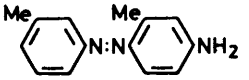
TABLE 2

10-Aryl-3,6-disubstituted 9-acridones (13) prepared from compounds (15) listed in Table 1 by nitro-group displacement

Compound	R^2	R^1	Starting compound	Yield (%)	M.p. [g] (°C)	Solvent for cryst. [a]	Found (%) C	H	N	Formula	Required (%) C	H	N
(13e)	H	OMe	(15a)	98	208—209	A	76.0	5.2	4.1	$C_{21}H_{17}NO_3$	76.1	5.2	4.2
(13f)	H	OPh	(15a)	83	243—244	B	81.5	4.7	2.95	$C_{31}H_{21}NO_3$	81.7	4.65	3.1
(13g)	H	S·C_5H_4N (2)	(15a)	79	189—191	C	71.0	3.8	8.3	$C_{29}H_{19}N_3OS_2$	71.1	3.9	8.6
(13h)	H	O·$[CH_2]_2$·NEt_2	(15a)	79	108—109	A	74.3	7.9	8.1	$C_{31}H_{39}N_3O_3$	74.2	7.8	8.4
		b			*ca.* 270 [e]	D	64.2	7.3	6.9	$C_{31}H_{39}N_3O_3$,2HCl, $0.5H_2O$	63.8	7.3	7.2
(13i)	H	O·$[CH_2]_2$·$N(CH_2)_5$	(15a)	82	138—139	A	75.5	7.7	7.9	$C_{33}H_{39}N_3O_3$	75.4	7.5	8.0
		c			*ca.* 290 [e]	D	54.8	6.1	5.6	$C_{33}H_{39}N_3O_3$,2HBr,$2H_2O$	54.8	6.3	5.8
(13j)	H	O·CH_2·CMe_2·NMe_2	(15a)	69	224—225	A	71.9	7.75	7.9	$C_{31}H_{39}N_3O_3,H_2O$	71.65	7.95	8.1
(13k)	H	S·$[CH_2]_2$·NMe_2	(15a)	56	130—131	A	66.5	6.55	8.4	$C_{27}H_{31}N_3OS_2$, $0.5H_2O$	66.6	6.6	8.6
	H	*b*			255—256	E	56.1	6.3	6.9	$C_{27}H_{31}N_3OS_2$,2HCl, $1.5H_2O$	56.1	6.3	7.3
(13l)	4-Me	OMe	(15b)	96	221—222	A	76.5	5.7	3.9	$C_{22}H_{19}NO_3$	76.5	5.5	4.05
(13m)	4-Me	O·$[CH_2]_2$·NEt_2	(15b)	90	98—99	A	74.3	8.1	8.0	$C_{32}H_{41}N_3O_3$	74.5	8.0	8.15
		b			*ca.* 265 [e]	D	64.3	7.4	6.9	$C_{32}H_{41}N_3O_3$,2HCl, $0.5H_2O$	64.3	7.4	7.0
(13n)	4-Cl	OMe	(15g)	95	258—259	A	68.9	4.4	3.65	$C_{21}H_{16}ClNO_3$	68.9	4.4	3.8
(13o)	4-Cl	O·$[CH_2]_2$·NEt_2	(15g)	71	145—146	A	69.4	7.3	7.6	$C_{31}H_{38}ClN_3O_3$	69.45	7.1	7.8
(13p)	2-OMe	OMe	(15h) [f]	65	184—185	A	73.1	5.3	3.8	$C_{22}H_{19}NO_4$	73.1	5.3	3.9
(13q)	4-OMe	OMe	(15k)	86	198—199	A	72.9	5.1	3.7	$C_{22}H_{19}NO_4$	73.1	5.3	3.9
(13r)	4-OMe	O·$[CH_2]_2$·NEt_2	(15k)	47	70—72	F	72.2	7.9	7.9	$C_{32}H_{41}N_3O_4$	72.3	7.8	7.9
		b			*ca.* 265 [e]	D	61.4	7.3	6.5	$C_{32}H_{41}N_3O_4$,2HCl,H_2O	61.7	7.3	6.75
(13s)	4-Ph	O·$[CH_2]_2$·NEt_2	(15l)	77	105—106	A	74.6	7.5	7.0	$C_{37}H_{43}N_3O_3,H_2O$	74.6	7.6	7.05
		d			210—211	D	59.1	6.6	5.2	$C_{37}H_{43}N_3O_3$,$2CH_4O_3S$, H_2O	59.4	6.8	5.3
(13t)	4-SO_2NH_2	OMe	(15n)	83	298—300	A	61.6	4.4	6.7	$C_{21}H_{18}N_2O_5S$	61.4	4.4	6.8

[a] A = EtOH or EtOH–H_2O; B = dioxan–EtOH; C = DMF–EtOH–H_2O; D = EtOH–Et_2O; E = EtOH–Me_2CO; F = light petroleum (b.p. 60—80°). [b] Hydrochloride salt. [c] Hydrobromide salt. [d] Methanesulphonate salt. [e] With decomp. [f] With concurrent displacement of fluorine. [g] $\nu_{max.}$ 1 630—1 640 cm^{-1} (C=O).

Formation of (22) also occurred when (14) cyclised to (15a) in DMSO containing *m*-toluidine. If these examples are representative of the normal fate of



(22)

liberated nitrite it is evident that conversion of (6) to (15) may involve up to 5 mol equiv. of aromatic amine.

The very few 10-aryl-9-acridones reported in the literature [15] have usually been prepared by cyclisation of triphenylamine-2-carboxylic acids, which restricts the attainable substitution patterns. The present route is more versatile in this respect, for the 3,6-dinitro-groups in (15) may be replaced by hydrogen or other groups. 3,6-Diamino-10-aryl-9-acridones are conveniently prepared by hydrogen iodide or tin(II) chloride reduction and undergo normal diazotisation reactions. Thus (15a) gave 3,6-diamino-10-phenylacridone (13b; $R^1 = NH_2$, $R^2 = H$) and hence 10-phenyl-9-acridone (13a) [15a] and its 3,6-dihydroxy-derivative (13c; $R^1 = OH$, $R^2 = H$). Similarly (15i) gave, on reduction and hydrolysis, the triamine (13d; $R^1 = NH_2$, $R^2 = 4\text{-}NH_2$). Since in (15) the nitro-groups are carbonyl-activated they may be displaced in dipolar aprotic solvents by alkoxide or phenoxide anions and very readily by their thio-analogues (Table 2). In particular a series of basic ethers and thioethers * was obtained by treatment of (15) with basic alcohols or thioalcohols in DMSO in the presence of potassium hydroxide pellets. In Table 3 are shown typical ^1H n.m.r. data for compounds listed in Table 2. H-1 and H-8 resonate at a relatively low field owing to the deshielding effect of the *ortho* cyclic carbonyl function; [16] the high-field signal for H-4 and H-5 indicates a strong shielding effect by the 10-aryl nucleus.

Some of the basic ethers, *e.g.* (13h), showed marked activity against taeniasis in dogs, but host toxicity proved to be unacceptably high.[17]

* B.P. Appl. 48,419/1974.

TABLE 3

^1H N.m.r. data for some 10-aryl-3,6-disubstituted acridones (13)

Compound	Chemical shift [a] H-1(8) (d)	H-2(7) (dd)	H-4(5) (d)	Other
(13e)	8.28	6.92	6.01	3.65 (s, OMe)
	(8.6) [b]	(8.8, 2.3)	(2.3)	
(13p)	8.28	6.93	6.03	3.66 (s, OMe), 3.69 (s, OMe)
	(8.8)	(8.8, 2.3)	(2.3)	
(13q)	8.27	6.92	6.07	3.67 (s, OMe), 3.92 (s, OMe)
	(9.0)	(8.9, 2.4)	(2.3)	
(13h)	8.26	6.85	6.01	3.89 (t, CH_2), 2.65 (t, CH_2), 2.44 (q, CH_2), 0.89 (t, Me)
	(8.8)	(8.9, 2.3)	(2.3)	(6.2) (6.3) (7.2) (7.1)
(13j)	8.28	6.96	6.02	3.73 (s, CH_2), 1.01 (s, Me), 2.17 (s, Me)
	(8.9)	(9.0, 2.3)	(2.2)	
(13k)	8.22	7.19	6.45	~2.91 (m, CH_2), ~2.37 (m, CH_2), 2.08 (s, Me)
	(8.4)	(8.4, 1.7)	(1.5)	

[a] In p.p.m., in solution in [$^2H_6$]DMSO at 60 °C from internal Me_4Si; concentration 60 mg ml^{-1}, except for (13k) which was 45 mg ml^{-1}. [b] In parentheses, coupling constant J in Hz.

EXPERIMENTAL

M.p.s up to 300 °C were determined on an Electrothermal melting point apparatus; a Mel-Temp apparatus was used above 300 °. Infrared spectra, which were recorded for all products using a Perkin-Elmer 157G spectrometer (KBr), were utilised in identifications and comparisons but the absorptions were unexceptional and are reported only sparingly. Instruments used for the recording of ^1H n.m.r., u.v., and mass spectra were Bruker HX-90, Beckmann Acta CV, and A.E.I. MS 902 (at 70 eV), respectively. Nitrogen was confirmed as a reaction product using a Spex Raman spectrometer with argon ion laser, excitation at 5 145 Å (N≡N stretching vibration at $\nu_{max.}$ 2 330 cm^{-1}).

The following were prepared by standard methods: 4,4′-dinitrobenzophenone (1),[18] 2,2′-dinitrobenzophenone (4),[19] 2,2′,4,4′-tetranitrobenzophenone (6),[20] 1-nitroxanthen-9-one,[8b] and 3-nitroxanthen-9-one.[8b]

Methoxydenitration of 4,4′-Dinitrobenzophenone (1).—To a solution of (1) (2.72 g, 10 mmol) in DMSO (60 ml) at room temperature was added 1M-sodium methoxide in methanol (10.3 ml) with rapid agitation. Colour changes, intense green ⟶ olive brown, occurred in the first 10 min. After 3½ h, water was added and the product recovered and dried. Two crystallisations from acetic acid–methanol gave 4-methoxy-4′-nitrobenzophenone (2) (1.71 g, 67%), m.p. 121—123° (lit.,[21] 121—123°), identical with authentic material.

Methoxydenitrations of 2,2′,4,4′-Tetranitrobenzophenone (6).—(*a*) To a solution of (6) (3.62 g, 10 mmol) in DMSO (25 ml) was added 1M-methanolic sodium methoxide (11 ml). After 4 h, dilution with water gave *4-methoxy-2,2′,4′-trinitrobenzophenone* (7) which, after alternate crystallisations from acetic acid and DMF–ethanol gave crystals, m.p. 164—165°, $\nu_{max.}$ 1 680 cm^{-1} (C=O) (Found: C, 48.5; H, 2.6; N, 11.7. $C_{14}H_9N_3O_8$ requires C, 48.4; H, 2.6; N, 12.1%).

(*b*) A solution as in (*a*) was treated with 1M-NaOMe/MeOH (21 ml). After 1.5 h, hexagonal plates of *4,4′-dimethoxy-2,2′-dinitrobenzophenone* (8) (1.86 g, 56%) separated, which crystallised from acetic acid–ethanol; m.p. 163—164°, $\nu_{max.}$ 1 665 cm^{-1} (C=O) (Found: C, 54.0; H, 3.7; N, 8.4. $C_{15}H_{12}N_2O_7$ requires C, 54.2; H, 3.6; N, 8.4%). Crystallisation of material obtained from the filtrate brought the yield to >80%. ^1H N.m.r. in [$^2H_6$]DMSO (~40 mg ml^{-1}) at 24 °C (chemical-shift reference: [$^2H_5$]-

DMSO at 2.50 p.p.m.) δ 3.93 (s, OMe), 7.67 (d, *J* 2.4 Hz, H-3), 7.31 (dd, *J* 8.5 Hz and 2.4 Hz, H-5), and 7.58 (d, *J* 8.5 Hz, H-6).

(*c*) Unrecrystallised dimethoxy-compound (8) (3.32 g) in DMSO (30 ml) was left for 24 h with an excess of 1M-NaOMe–MeOH (25 ml). Dilution with water gave *2,4,4′-trimethoxy-2′-nitrobenzophenone* (9) which, from ethanol, gave yellow prisms, m.p. 126—127°, $\nu_{max.}$ 1 630 cm^{-1} (C=O) (Found: C, 60.75; H, 4.7; N, 4.4. $C_{16}H_{15}NO_6$ requires C, 60.6; H, 4.8; N, 4.4%).

2,2′-Diamino-4,4′-dimethoxybenzophenone (10).—4,4′-Dimethoxy-2,2′-dinitrobenzophenone (8) was reduced in ethanol–acetic acid–concentrated hydrochloric acid with tin(II) chloride. The *diamine* (10), obtained on addition of an excess of sodium hydroxide, formed large crystals, m.p. 137—138° (from ethanol) (Found: C, 66.25; H, 5.7; N, 10.2. $C_{15}H_{16}N_2O_3$ requires C, 66.2; H, 5.9; N, 10.3%).

The base (10) was diazotised in acetic acid–4% sulphuric acid. Addition of 50% hypophosphorous acid and warming at 100 °C caused the separation of 4,4′-dimethoxybenzophenone (3), m.p. 141—143° (from ethanol).

The solution of diazonium compound from (10) was poured into an excess of boiling water which, after cooling, was made alkaline and filtered; the resulting solid, sublimed at 205° and 0.1 mmHg, gave 3,6-dimethoxyxanthone (11) (22%), m.p. 187—188° (lit.,[9] 187°), $\nu_{max.}$ 1 655 cm^{-1} (C=O).

Both compounds were identified by comparison with authentic material.[1,9]

Reaction of 2,2′-Dinitrobenzophenone (4) *with Aniline.*—A solution of (4) (2.94 g) in aniline (25 ml) was refluxed for 7 h, then poured into dilute aqueous hydrochloric acid. When the precipitated tarry material had hardened (*ca.* 2 days) it was recovered, dried, and shaken with benzene. The solution was passed through a column of activated alumina ('Camag' M.F.C.) (40 g) collecting 400 ml. Evaporation of solvent and crystallisation from acetic acid gave *2-anilino-2′-nitrobenzophenone* (12) (1.8 g, 52%) which formed yellow needles from aqueous ethanol, m.p. 123—124°, $\nu_{max.}$ 1 630 (C=O) and 3 290 (NH) cm^{-1} (Found: C, 71.4; H, 4.4; N, 8.65. $C_{19}H_{14}N_2O_3$ requires C, 71.7; H, 4.4; N, 8.8%). Elution of the alumina with warm benzene (200 ml) and concentration of the acetic acid mother-liquor gave a mixture of (4) and 10-phenylacridone (13a), identical with synthetic material.[15a] When (12) was heated at 300—320 °C at ordinary pressure a sublimate of 10-phenylacridone (13a) was obtained, m.p. 276—277° (lit.,[15a] 276°), $\nu_{max.}$ 1 635 cm^{-1} (C=O), *m/e* 271 (M^+) (Found: C, 84.0; H, 5.0; N, 5.2. Calc. for $C_{19}H_{13}NO$: C, 84.1; H, 4.8; N, 5.0%).

2-Anilino-2′,4,4′-trinitrobenzophenone (14).—A suspension of (6) in aniline (4.7 g, 10 mol equiv.) was heated over a free flame to the boiling point. A somewhat vigorous reaction ensued, with evolution of nitrogen; heating was discontinued. The reaction moderated (1—2 min) and was left to stand. A crystalline crop was obtained (*ca.* 0.8 g) consisting of a mixture of (6) and 3,6-dinitro-10-phenylacridone (15a). On dilution with ethanol the filtrate gave a solid (*ca.* 0.7 g) which was further crystallised from dioxan–ethanol, yielding the *anilino-compound* (14) as orange-red rhombs, m.p. 201—202° (decomp.) with resolidification (*ca.* 220°) and remelting at *ca.* 350° (orange sublimate) (Found: C, 55.85; H, 3.1; N, 13.75. $C_{19}H_{12}N_4O_7$ requires C, 55.9; H, 3.0; N, 13.7%), $\lambda_{max.}$(EtOH) 225 (ε 26 160), 260 (25 880), 278 (21 140), and 444 nm (5 740) (suggesting a planar molecule); $\nu_{max.}$ 1 650 (C=O) and 3 300 (NH) cm^{-1} (no indication of hydrogen bonding); *m/e* 408 (27%, M^+) and 361 [6%, $M^+ - NO_2H$] (loss supported by a metastable); ^1H n.m.r. in [$^2H_6$]DMSO is temperature-dependent from 60—100 °C suggesting a high-energy barrier to rotation,[22] prior to cyclisation. A solution in DMF was orange, but crimson on addition of sodium hydroxide. The product formed on heating above the m.p. gave (15a) on crystallisation from DMSO.

Cyclisation of 2-Anilino-2′,4,4′-trinitrobenzophenone (14) *in the Presence of* m-*Toluidine.*—A solution of (14) (40 mg) in DMSO (2 ml) with *m*-toluidine (20 mg, 2 mol equiv.) was held at 125 °C for 2 h. Ethanol was added to the cooled solution. Filtration gave *3,6-dinitro-10-phenyl-9-acridone* (15a) (32 mg, 89%). The filtrate was concentrated and aqueous sodium hydroxide added. Extraction with ether gave a yellow oil which, on treatment with aqueous hydrochloric acid in ethanol, gave steel-blue crystals (2.5 mg, 10%) converted by pyridine–aqueous ammonia to orange needles, m.p. 82—83°, identical with 4-amino-2,3′-dimethylazobenzene described below.

Reaction of 2,2′,4,4′-Tetranitrobenzophenone (6) *with* m-*Toluidine.*—A suspension of (6) (3.62 g) in *m*-toluidine (10.7 g, 10 mol equiv.) was heated at the boiling point for 4—5 min. DMSO (15 ml) was added, and the mixture left overnight. Filtration gave *3,6-dinitro-10-(3-tolyl)-9-acridone* (15c) (2.34 g, 62%). The filtrate was diluted with ether and washed thoroughly with dilute aqueous sodium hydroxide and with water. The ethereal solution was then concentrated and, to the residue, was added an excess of 4M-hydrochloric acid. The dark precipitate (2.8 g) consisted mainly of the hydrochloride of 4-amino-2,3′-dimethylazobenzene, which formed steel-blue crystals from ethanol, m.p. 209—210° (Found: C, 63.8; H, 6.3; N, 15.8. Calc. for $C_{14}H_{15}N_3$,HCl: C, 64.2; H, 6.2; N, 16.05%), converted by pyridine–aqueous ammonia to the free base, m.p. 82—83° (from ethanol) (lit.,[14] 80°). Both base and hydrochloride were identical with authentic material.[14]

3,6-Diamino-10-phenyl-9-acridone (13b).—(*a*) Reduction of (15a) (2.7 g) with tin(II) chloride in acetic acid–concentrated hydrochloric acid proceeded slowly at 100 °C owing to low solubility. After 12 h the solution was filtered and the residual (15a) washed with ethanol. Addition of an excess of aqueous sodium hydroxide to the filtrate gave the *diamine* (13b). This crystallised from DMF in yellow hydrated needles (*ca.* 65%), m.p. *ca.* 300°, which, on drying at 120° and 0.01 mmHg, had m.p. *ca.* 330° (Found: C, 75.4; H, 5.2; N, 13.7. $C_{19}H_{15}N_3O$ requires C, 75.7; H, 5.0; N, 13.9%).

(*b*) Reduction of (15a) (3.6 g) in a refluxing mixture of 55% aqueous hydrogen iodide (45 ml) and acetic acid (10 ml) was complete in 4 h. Treatment with sodium hydrogen sulphite in hydrochloric acid and with sodium hydroxide gave 3,6-diamino-10-phenyl-9-acridone (13b) in *ca.* 65% yield (after crystallisation).

The diamine (13b), diazotised in dilute sulphuric acid and treated with hypophosphorous acid at 90—100 °C, gave 10-phenyl-9-acridone (13a).[15a]

From diazotised (13b), on pouring into boiling water, was obtained *3,6-dihydroxy-10-phenyl-9-acridone* (13c), which sublimed up to 350° and 0.01 mmHg, and from aqueous ethanol gave yellow crystals, m.p. *ca.* 383° (decomp.) (Found: C, 75.4; H, 4.4; N, 4.8. $C_{19}H_{13}NO_3$ requires C, 75.2; H, 4.3; N, 4.6%).

3,6-Diamino-10-(4-aminophenyl)-9-acridone (13d).—10-(4-Acetamidophenyl)-3,6-dinitro-9-acridone (15i) was re-

duced and deacetylated under the foregoing conditions with 55% hydrogen iodide–acetic acid. The *triamine* (13d) (*ca.* 85%) was obtained by precipitation from its solution in dilute aqueous hydrochloric acid as a hemihydrate, m.p. *ca.* 338° (Found: C, 70.5; H, 5.2; N, 17.0. $C_{19}H_{16}N_4O,0.5H_2O$ requires C, 70.1; H, 5.3; N, 17.2%), and formed a hydrated *trismethanesulphonate*, m.p. *ca.* 305° (decomp.) (from acetone–ethanol–ether) (Found: C, 42.35; H, 4.7; N, 8.8. $C_{19}H_{16}N_4O,3CH_4O_3S,H_2O$ requires C, 42.4; H, 4.9; N, 9.0%).

As with (13b), the base (13d) gave 10-phenyl-9-acridone (13a) [15a] on reduction of its diazonium derivative.

Nitro-group Displacement Reactions of 10-*Aryl*-3,6-*dinitro*-9-*acridones* (15).—The compounds listed in Table 2 were prepared by fairly standardised procedures; the examples quoted below are generally applicable.

(a) 3,6-*Dimethoxy*-10-*phenyl*-9-*acridone* (13e). To (15a) (1.81 g) dissolved by heating in dry DMSO (50 ml) was added 1M-sodium methoxide in methanol (12 ml, 20% excess). Colour changes (orange → brown → light red) occurred initially, and the solution was left for 1 h at 90—100 °C. The *compound* (13e), obtained on dilution with water was once recrystallised.

N.B. In the preparation of (13p), an excess (over 3 mol equiv.) of methoxide was added to (15h).

(b) 3,6-*Diphenoxy*-10-*phenyl*-9-*acridone* (13f). Phenol (2.05 g, 22 mmol) in methanol was evaporated to dryness with 1M-sodium methoxide in methanol (22 ml, 22 mmol). 3,6-Dinitro-10-phenyl-9-acridone (15a) (3.61 g, 10 mmol) was added to the phenate, with dry DMSO (50 ml), and the mixture heated at 125—130° for 12 h. Dilution with aqueous sodium hydroxide gave the *product* (13f) which was recrystallised.

The use of 2-mercaptopyridine under similar conditions gave rise to 10-*phenyl*-3,6-*bis*(2-*pyridylthio*)-9-*acridone* (13g).

(c) 3,6-*Bis*(2-*diethylaminoethoxy*)-10-*phenyl*-9-*acridone* (13h). 3,6-Dinitro-10-phenyl-9-acridone (15a) (36.1 g, 0.1 mol), 2-diethylaminoethanol (28 g, 20% excess over 0.2 mol), and potassium hydroxide pellets (16 g, 40% excess over 0.2 mol) in DMSO (135 ml) were stirred together at 90—95 °C for 4 h, then the solution was diluted to 1 l with water and filtered. The product was dissolved in warm hydrochloric acid, treated with charcoal, and filtered into dilute aqueous sodium hydroxide. The *base* (13h) separated as a crystalline solid which could be converted into its *dihydrochloride* by treatment with ethanolic hydrochloric acid and precipitation with ether.

The reaction gave an almost quantitative yield when sodium hydride was used instead of potassium hydroxide, the mixture being shaken for 6 h at room temperature; (15a) needed, however, to be initially dissolved in the DMSO by heating in order to avoid the persistence of difficultly soluble crystals.

Reaction of 1-*Nitroxanthen*-9-*one with Aniline*.—1-Nitroxanthen-9-one (4.8 g, 0.02 mol) was refluxed with aniline (15 g, 0.16 mol) for 4 h. The precipitate obtained on addition to dilute aqueous hydrochloric acid was collected and crystallised from aqueous ethanol (charcoal) to give 1-anilinoxanthen-9-one (3.3 g, 58%) as gold laminae, m.p. 131—132° (lit.,[7] 120—125°), $\nu_{max.}$ 1 630 cm^{-1} (C=O) (Found: C, 79.4; H, 4.55; N, 5.0. Calc. for $C_{19}H_{13}NO_2$: C, 79.4; H, 4.6; N, 4.9%). 3-Nitroxanthen-9-one was recovered unchanged after exposure to these conditions.

2,2′-*Dihalogeno*-4,4′-*dinitrobenzophenones* (16).—(*a*) Bis-(2-iodo-4-nitrophenyl)methane [23] in acetic acid was oxidised with chromium(VI) oxide at 100 °C; 2,2′-*di-iodo*-4,4′-*dinitrobenzophenone* (16a) was obtained on addition of water, and formed yellow needles, m.p. 177—178°, $\nu_{max.}$ 1 690 cm^{-1} (C=O) (from ethanol) (Found: C, 29.6; H, 1.2; N, 5.2; I, 48.3. $C_{13}H_6I_2N_2O_5$ requires C, 29.8; H, 1.15; N, 5.35; I, 48.4%).

(*b*) The 2,2′-dibromo-analogue [1] (16b), prepared similarly, had m.p. 185—186°, $\nu_{max.}$ 1 675 cm^{-1} (C=O) (Found: C, 36.6; H, 1.4; Br, 37.4. Calc. for $C_{13}H_6Br_2N_2O_5$: C, 36.3; H, 1.4; Br, 37.2).

(*c*) From bis(2-chloro-4-nitrophenyl)methane [24] was similarly obtained 2,2′-*dichloro*-4,4′-*dinitrobenzophenone* (16c), m.p. 155—156°, $\nu_{max.}$ 1 670 cm^{-1} (C=O) (from aqueous ethanol) (Found: C, 45.45; H, 1.6; N, 8.2. $C_{13}H_6Cl_2N_2O_5$ requires C, 45.8; H, 1.8; N, 8.2%).

2-*Anilino*-2′-*iodo*-4,4′-*dinitrobenzophenone* (17).—2,2′-Diiodo-4,4′-dinitrobenzophenone (16a) (0.103 g) in aniline (2 ml) and DMSO (0.5 ml) was held at 125—130 °C for 7 h, then poured into dilute hydrochloric acid. Warming the precipitated solid in ethanol gave (17) (0.057 g, 59%), while unchanged (16a) (>10%) passed into solution. Crystallisation from DMF–ethanol gave the *anilino-compound* (17) as red crystals, m.p. 204—206°, $\nu_{max.}$ 1 635 (C=O) and 3 270 (NH) cm^{-1} (Found: C, 46.7; H, 2.6; N, 8.4; I, 26.0. $C_{19}H_{12}IN_3O_5$ requires C, 46.65; H, 2.5; N, 8.6; I, 25.9%). When heated in pyridine (125 °C for 13 h) (17) remained unchanged.

Reactions of 2,2′,4,4′-*Tetranitrobenzophenone* (6).—(a) *With ethanolic ammonia*. To a suspension of (6) (3.62 g) in DMSO (25 ml) was added 8.5% ethanolic ammonia (30 ml). The initial violet colour changed to red within 15 min. The mixture was kept at room temperature for 6 days with occasional agitation, until no solid remained. Dilution with water and partial neutralisation yielded 2,4-dinitroaniline (18a) (0.43 g, 23%), m.p. 182—183° (from ethanol) (Found: C, 39.6; H, 2.8; N, 23.1. Calc. for $C_6H_5N_3O_4$: C, 39.35; H, 2.75; N, 22.95%), identical with authentic material. From the filtrate, only polymeric material could be obtained.

(b) *With* 2-*diethylaminoethylamine*. To (6) (0.905 g) was added redistilled base (5 ml, *ca.* 20 mol equiv.) and the mixture shaken for 9 h, the initial red solution becoming dark brown. It was diluted with water, brought to pH 6 with acetic acid, and a polymeric solid filtered off. Extraction of the filtrate at pH 10 with ether gave an orange gum (0.23 g) which crystallised. From aqueous ethanol this gave *N*-2-diethylaminoethyl-2,4-dinitroaniline (18b) (0.04 g), m.p. 93—94° (lit.,[25] 93—94°) (Found: C, 51.1; H, 6.4; N, 20.0. Calc. for $C_{12}H_{18}N_4O_4$: C, 51.1; H, 6.4; N, 19.9%), identical with authentic material.[25]

(c) *With cyclohexylamine*. To (6) (0.18 g) in warm DMSO (0.6 ml) was added cyclohexylamine (0.29 ml, 5 mol equiv.); an initial intense purple colour changed to red. The mixture was left at ambient temperature for 70 h, diluted with water, and extracted with ether. The residue obtained on evaporation of the dried ethereal solution was sublimed up to 160° and 0.01 mmHg. The sublimate crystallised from aqueous ethanol to give *N*-cyclohexyl-2,4-dinitroaniline (18c) (0.01 g), m.p. 155—156° (lit.,[26] 156°) unchanged by admixture with authentic material.[26]

Hydroxydenitration of 2,2′,4,4′-*Tetranitrobenzophenone* (6).—(a) *With potassium hydroxide*. A suspension of (6) (0.362 g, 1 mmol) in dry DMSO (15 ml) and one pellet of potassium hydroxide (0.09 g, >1 mmol) was stirred rapidly

while slowly raising the temperature from 55 °C. An initial green colour changed to orange, which became very intense at 105 °C. Stirring was continued at 100—105 °C for 2 h, then the mixture was allowed to cool slowly and was added to dilute aqueous ammonia. The precipitate of *3,6-dinitroxanthen-9-one* (19) (0.11 g, 38%) was recovered, and purified by sublimation at 280° and 0.01 mmHg and crystallisation from DMSO–ethanol. It formed yellow needles, m.p. 278—279°, $\nu_{max.}$ 1 680 cm^{-1} (C=O) (Found: C, 54.3; H, 2.1; N, 9.9%). $C_{13}H_6N_2O_6$ requires C, 54.55; H, 2.1; N, 9.8%). The ammoniacal filtrate gave, with dilute hydrochloric acid, a precipitate of *4-hydroxy-2,2′,4′-trinitrobenzophenone* (20) (0.135 g, 40%) which crystallised from aqueous ethanol in needles, m.p. 239—241°, $\nu_{max.}$ 1 680 (C=O) and 3 340 (OH) cm^{-1} (Found: C, 47.2; H, 2.1; N, 12.2. $C_{13}H_7N_3O_8$ requires C, 46.9; H, 2.1; N, 12.6%). An identical compound was prepared from 4-methoxy-2,2′,4′-trinitrobenzophenone (7) by demethylation in refluxing acetic acid–60% aqueous hydrogen bromide.

(b) *With sodium nitrite.* To (6) (0.362 g, 1 mmol) in dry DMSO (4 ml) was added dry powdered sodium nitrite (0.09 g, 1.3 mmol). On heating at 120 °C the initial blue colour changed to brown, and oxides of nitrogen were evolved. After 1.5 h the mixture was added to aqueous sodium hydroxide. Filtration gave (19), purified by sublimation (0.09 g, 31%); the alkaline filtrate on acidification gave (20) (*ca.* 35%).

(c) *With copper in pyridine.* To (6) (0.362 g, 1 mmol) in dry pyridine (6 ml) was added copper bronze (Kahlbaum) (0.32 g, 5 mmol); the mixture was refluxed for 35 min, oxides of nitrogen being initially evolved. Dilute nitric acid was added and the solid material collected. This was extracted with DMF, and the filtrate added to aqueous ammonia. Filtration gave (19), purified by sublimation (0.043 g, 15%); acidification of the ammoniacal filtrate gave (20) (17%).

Reactions of 3,6-*Dinitroxanthen-9-one* (19).—(a) *Methoxydenitration.* To a solution of (19) in DMSO was added an excess of 1M-sodium methoxide in methanol. Dilution with water after 20 h gave 3,6-dimethoxyxanthen-9-one, m.p. 187—188° (from ethanol), identical with (11) and with authentic material.[9]

(b) *Reduction.* When (19) was added to tin(II) chloride in concentrated hydrochloric acid, reduction proceeded normally at 90—100 °C. Addition of an excess of aqueous sodium hydroxide gave 3,6-diaminoxanthen-9-one, purified by sublimation at 280° and 0.01 mmHg, m.p. 322—325° (lit.,[8] 324—326°), identical with authentic material.[8]

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REFERENCES

[1] J. H. Gorvin, *Chem. and Ind.*, 1967, 1525.
[2] H. Suhr, *Chem. Ber.*, 1964, **97**, 3277.
[3] (*a*) J. F. Bunnett and R. J. Morath, *J. Amer. Chem. Soc.*, 1955, **77**, 5051; J. F. Bunnett, R. J. Morath, and T. Okamoto, *ibid.*, p. 5055; (*b*) R. R. Bishop, E. A. S. Cavell, and N. B. Chapman, *J. Chem. Soc.*, 1952, 437; W. Greizerstein and J. A. Brieux, *J. Amer. Chem. Soc.*, 1962, **84**, 1032; S. D. Ross and M. Finkelstein, *ibid.*, 1963, **85**, 2603; N. E. Sbarbati, *J. Org. Chem.*, 1965, **30**, 3365; F. Pietra, D. Vitali, F. Del Cima, and G. Cardinali, *J. Chem. Soc.* (*B*), 1970, 1659; C. F. Bernasconi and R. H. de Rossi, *J. Org. Chem.*, 1976, **41**, 44; (*c*) J. F. Bunnett, *Quart. Rev.*, 1958, **12**, 1; J. Miller, 'Aromatic Nucleophilic Substitution,' Elsevier, Amsterdam, 1968, pp. 100—114.
[4] R. E. Parker and T. O. Reed, *J. Chem. Soc.*, 1962, 3149; J. I. G. Cadogan and D. T. Eastlick, *J. Chem. Soc.* (*B*), 1970, 1314.
[5] H. B. Nisbet and A. B. Goodlet, *J. Chem. Soc.*, 1932, 2772; H. B. Nisbet, *ibid.*, 1933, 1372.
[6] W. M. Lord and A. T. Peters, *J.C.S. Perkin I*, 1973, 2305.
[7] S. N. Dhar, *J. Chem. Soc.*, 1920, **117**, 1053.
[8] (*a*) M. Julia and G. Tchernoff, *Bull. Soc. chim. France*, 1952, 546; (*b*) A. A. Goldberg and H. A. Walker, *J. Chem. Soc.*, 1953, 1348.
[9] P. K. Grover, G. D. Shah, and R. C. Shah, *J. Chem. Soc.*, 1955, 3982; S. Geiger, M. Joannic, M. Pesson, H. Techer, E. Lagrange, and M. Aurousseau, *Chim. Ther.*, 1966, 425.
[10] D. H. Rosenblatt, W. H. Dennis, jun., and R. D. Goodin, *J. Amer. Chem. Soc.*, 1973, **95**, 2133; T. J. Broxton, D. M. Muir, and A. J. Parker, *J. Org. Chem.*, 1975, **40**, 2037, 3230; M. Kobayashi, T. Sakai, and H. Minato, *Chem. Letters*, 1975, 1253.
[11] R. B. Chapas, R. D. Knudsen, R. F. Nystrom, and H. R. Snyder, *J. Org. Chem.*, 1975, **40**, 3746.
[12] C. Björklund and R. Wahren, *Acta Chem. Scand.*, 1976, **B30**, 576.
[13] J. H. Gorvin, *J.C.S. Chem. Comm.*, 1976, 972.
[14] R. Nietzki, *Ber.*, 1877, **10**, 1155.
[15] (*a*) I. Goldberg and M. Nimerovsky, *Ber.*, 1907, **40**, 2448; D. Hellwinkel and M. Melan, *Chem. Ber.*, 1971, **104**, 1001; (*b*) R. Weiss, J. L. Katz, W. Handl, and J. L. Melzer, *Monatsh.*, 1928, **50**, 109; G. M. Kosolapoff and C. S. Schoepfle, *J. Amer. Chem. Soc.*, 1954, **76**, 1276.
[16] R. H. Martin, N. Defay, F. Geerts-Evrard, P. H. Given, J. R. Jones, and R. W. Wedel, *Tetrahedron*, 1965, **21**, 1833.
[17] P. A. Kingsbury, unpublished results.
[18] W. Staedel, *Annalen*, 1894, **283**, 168.
[19] W. Theilacker and O. Korndörfer, *Tetrahedron Letters*, 1959, **18**, 5.
[20] J. M. Gulland and R. Robinson, *J. Chem. Soc.*, 1925, **127**, 1499; K. Matsumura, *J. Amer. Chem. Soc.*, 1929, **51**, 818.
[21] R. B. Davis, L. C. Pizzini, and J. D. Benigni, *J. Amer. Chem. Soc.*, 1960, **82**, 2913.
[22] J. C. Schmidt, H. D. Benson, R. S. Macomber, B. Weiner, and H. Zimmer, *J. Org. Chem.*, 1977, **42**, 2003.
[23] Hwang Wen-kuei, *Sci. Sinica*, 1957, **6**, 123.
[24] J. H. Gorvin, *J. Chem. Soc.*, 1955, 83.
[25] H. Hippchen, *Chem. Ber.*, 1947, **80**, 263.
[26] M. Busch and F. Gebelein, *Z. prakt. Chem.*, 1927, **115**, 111.