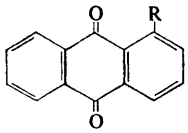
Reactions in *NN*-Dimethylformamide. Part II.[1] Halogen Replacement in the Anthraquinone Series

By **W. M. Lord** and **A. T. Peters,*** School of Colour Chemistry and Colour Technology, The University, Bradford 7

In the condensation of 1-chloroanthraquinone with arylamines, the use of *NN*-dimethylformamide as solvent can lead to the formation of 1-arylaminoanthraquinone, 1-alkylaminoanthraquinone, or mixtures thereof depending on the basicity of the arylamine. 1-Chloroanthraquinone reacted with *NN*-dimethylformamide with initial formation of 1-dimethylaminoanthraquinone; prolonged reaction resulted in demethylation and ultimate formation of 1-methylaminoanthraquinone. A similar replacement was observed with 2-chloro- and 1,2-, 1,4-, 1,5-, and 1,8-dichloroanthraquinones. Dealkylation of 1-dimethylaminoanthraquinone occurs in other dipolar aprotic solvents, *e.g.* dimethyl sulphoxide, but none occurs in comparatively high-boiling basic (*e.g.* β-picoline and pyridine) or neutral (*e.g.* ethylene glycol monomethyl ether) solvents.

REPLACEMENT of α-halogeno-groups by both substituted and unsubstituted amino-groups [2-5] is a well known method of preparing intermediates and dyestuffs in the anthraquinone series; several solvents have been used [2,4-9] but the use of *NN*-dimethylformamide (DMF) has not been described.

Small quantities of DMF or hexamethylphosphoramide accelerate the formation of diphenylamines [10] from arylamines and *p*-chloronitrobenzene, and the preparation of nitrodiphenylamine dyes by condensation of various nitrochlorobenzenes with arylamines in DMF can lead to [1,11] anomalous replacement of the halogeno-group by the dimethylamino-group. We have also noted [1] the reaction of 1-chloroanthraquinone in DMF to give 1-dimethylaminoanthraquinone (I) and an unidentified product; this is now shown to be 1-methylaminoanthraquinone (II).



(I) R = Me_2N

(II) R = MeNH

During the preparation of a series of 1-arylaminoanthraquinones from 1-chloroanthraquinone and arylamines, we used DMF as a reaction solvent in some cases and observed a further anomalous replacement of the halogen atom. With *p*-anisidine, only 1-*p*-methoxyanilinoanthraquinone was formed; with amino-α-trifluorotoluenes, the appropriate 1-(trifluoromethylanilino)-anthraquinone was formed together with (II); with *p*-methylsulphonylaniline, aniline carboxamides, and amino-pyridines only (II) was formed. These results led us to investigate the reaction between halogenoanthraquinones and DMF more fully. All halogeno-derivatives were pure, and fresh samples of DMF were used for each condensation to minimise the known formation of dimethylamine.[12] Compounds (I) and (II) were readily distinguished by t.l.c. (on Eastman Chromagram sheets type K301R) on silica gel with benzene as solvent [(I) had R_F 0·27, (II) had R_F 0·67] and by i.r. spectra [NH stretching frequency of (II) at 3300 cm.$^{-1}$ (lit.,[13] 3300 cm.$^{-1}$), absent in spectrum of (I)].

1-Chloroanthraquinone, when heated under reflux in an excess of DMF for up to 32 hr. gave a bright red material which contained (I) and (II); with reaction times greater than 32 hr., the product contained only traces of (I). A partial dealkylation of (II) to 1-aminoanthraquinone in boiling nitrobenzene has been previously noted.[14]

2-Chloroanthraquinone similarly gave 2-dimethylaminoanthraquinone only; even after prolonged reaction (105 hr.) no dealkylation to 2-methylaminoanthraquinone was observed.

With dichloroanthraquinones, reaction with DMF was more complex and the nature of the products varied with the reaction time. 1,2-Dichloroanthraquinone was converted into a mixture of unchanged starting material, 2-chloro-1-methylaminoanthraquinone, and (II); 1,4-dichloroanthraquinone gave unchanged chloro-compound, 1-chloro-4-methylaminoanthraquinone, and (II). The formation of relatively large amounts of (II) was not due to contamination of the dichloroanthraquinones with 1-chloroanthraquinone; its formation is thus an example of the well known halogen elimination [15,16] in the anthraquinone series. The elimination was observed only for dichloroanthraquinones in which both chlorine atoms were in the same phenyl ring; *viz.* not with 1,5- and 1,8-dichloroanthraquinones.

1,5-Dichloroanthraquinone, after 21 hr. under reflux in DMF, gave a dark red material from which were isolated 1-chloro-5-dimethylamino- and 1-chloro-5-methylamino-anthraquinones. Longer reaction (74 hr.) gave these products together with 1,5-bisdimethylaminoanthraquinone and even more prolonged reaction (250

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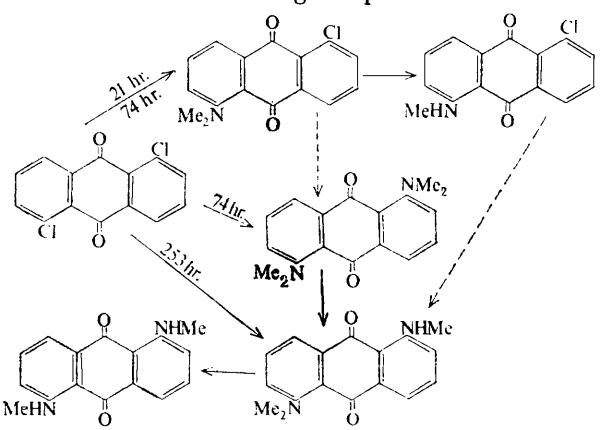
hr.) gave 5-dimethylamino-1-methylamino and 1,5-bis-(methylamino)-anthraquinone (see Scheme). 1,8-Dichloroanthraquinone and DMF gave similar products (see Experimental section).

With 1,4,5,8-tetrachloroanthraquinone, a more complex reaction occured, and the formation of numerous red, red-violet, blue-violet, and blue compounds was observed (column chromatography); these probably arose from the replacement of each of the four chlorine atoms singly and in combination.

Whilst dealkylation of 1,4-dialkylaminoanthraquinones in concentrated sulphuric acid at 150° and in concentrated sulphuric acid and boric acid at 130° has been noted,[17] dealkylation in DMF has not been previously recorded. The formation of (II) from (I) during the above condensations was confirmed by heating pure (I) under reflux in DMF; thin-layer chromatography control tests showed the gradual and eventually complete conversion into (II). No dealkylation was observed in high-boiling basic solvents (pyridine and β-picoline) or neutral solvents (ethylene glycol monomethyl ether), but in other dipolar aprotic solvents (dimethyl sulphoxide and dimethyl sulphone) (I) was converted into (II) very readily. Several reactions involving replacement of halogeno-groups with DMF as solvent have been reported, *e.g.*, by cyano-[18] and nitro-groups;[19] we found no evidence of anomalous replacement in these cases.

Brompentafluorobenzene, when heated in DMF in the presence of cuprous cyanide, gives[20] 4-dimethylamino-2,3,5,6-tetrafluorobenzonitrile. 1-Chloroanthraquinone, when similarly treated, gave a bluish-red material which was shown to contain 1-cyanoanthraquinone and (II); this reaction thus affords examples of normal and anomalous halogen replacements.



SCHEME

Products isolated from the reaction between 1,5-dichloroanthraquinone and DMF.

The difficulties previously reported with the use of DMF as solvent in the preparation of nitrodiphenylamine dyes[1,11] are thus shown to be equally pertinent in reactions involving chloroanthraquinones. The mechanism of the reaction is not yet clear. We have found evidence of similar reactions between halogenoanthraquinones and other *N*-substituted formamides and these may prove helpful in clarifying the mechanism of this novel reaction.

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EXPERIMENTAL

Melting points were determined with an electrically heated block and are corrected. Column chromatography was carried out with activated alumina (Spence type H, 100—200 mesh), with benzene as solvent and eluent unless otherwise stated. Microanalyses were performed by Research Laboratorium Dr. C. Janssen, Beerse, Belgium.

1-Dimethylaminoanthraquinone (I), prepared by the method of Bayer [5] and purified by column chromatography, was obtained as crimson needles with a gold reflex, m. p. 139—140° (lit.,[5] 139—141°). A previously reported product,[1] m. p. 113—116°, was shown (t.l.c.) to be a mixture of (I) and (II). 1-Methylaminoanthraquinone (II) was prepared from potassium anthraquinone-1-sulphonate and aqueous methylamine.[21]

Reactions of 1-Chloroanthraquinone with DMF.—1-Chloroanthraquinone (7 g.) and DMF (15 c.c.) were heated under reflux (140—150°) for 24 hr. Addition of the cooled liquor to water gave a deep red solid (6·9 g., 82·8%), m. p. 141—147° (softening at 136°). Chromatography of the crude product (2 g.) gave rise to minor strongly adsorbed dark brown, brick red, yellow, and lilac zones, and, as principal zones, an upper deep bluish-red and a lower deep crimson zone. Unchanged 1-chloroanthraquinone (1·35 g.) was eluted. Extraction of the upper zone with boiling ethanol afforded (I) (0·07 g.), m. p. and mixed m. p. 138—139°. The lower deep crimson zone yielded scarlet needles of (II) (0·13 g.), m. p. 169° (from ethanol) (lit.,[21] 170°). A similar experiment [with 1-chloroanthraquinone (4 g.)] in which the reactants were heated under reflux for 105 hours gave a brownish-black product which when chromatographed (0·27 g. was insoluble) gave unchanged 1-chloroanthraquinone (0·92 g.) and one bright crimson zone which yielded (II) (1·9 g.).

Reactions of 1-Chloroanthraquinone with Arylamines in the Presence of DMF.—1-Chloroanthraquinone (6 g.), *p*-anisidine (6·2 g.), and DMF (50 c.c.) were heated under reflux for 16 hr. The dark red product was slurried with ethanol and acidified with concentrated hydrochloric acid–water (1 : 1) to give a crude product (6·2 g., 74·9%), m. p. 85—106°. This (0·75 g.) when chromatographed gave rise to a black zone (substance strongly adsorbed; rejected) and a principal deep bluish-red zone. Extraction with boiling ethanol gave crimson needles (0·46 g.) of 1-*p*-methoxyanilinoanthraquinone, m. p. 144—145° (lit.,[22] 144°); 1-chloroanthraquinone (0·15 g.) was recovered. No sign of other red compounds was observed.

Similar reactions with other arylamines were noted. (i) 1-Chloroanthraquinone (8 g.), *p*-methylsulphonylaniline (15 g.), and DMF (50 c.c.) when heated under reflux for 20 hr. gave a dark red material (10·3 g., 83%). This (5 g.) when chromatographed gave rise to a single bluish-red zone which when extracted with hot acetone gave cherry-red needles of (II). The expected 1-*p*-methylsulphonylanilinoanthraquinone was not present; 1-chloroanthraquinone

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(1·3 g.) was recovered. (ii) 1-Chloroanthraquinone (7·3 g.), *o*-amino-α-trifluorotoluene (9·7 g.), anhydrous sodium acetate (7 g.), and DMF (50 c.c.), when heated under reflux for 7 hr. gave an orange solid (6·2 g., 57%), m. p. 142—144°. Chromatography gave (II) (1·3 g.), from an upper deep bluish-red zone, and orange-scarlet prisms (4·1 g.) of 1-(2-*trifluoromethylanilino*)*anthraquinone*, m. p. 180—182° (from ethanol), from a lower orange-red zone (Found: F, 15·2; N, 3·9. $C_{21}H_{12}F_3NO_2$ requires F, 15·5; N, 3·8%). *m*-Amino-α-trifluorotoluene under similar conditions gave a deep red product (8·2 g., 75·4%), m. p. 139—140°, which was separated by chromatography (several minor strongly adsorbed black, dark brown, and brownish-purple zones were not investigated) into (II) (2·05 g.), from an upper dark red zone, and, from a lower dark red zone, orange-red needles (2·9 g.) of 1-(3-*trifluoromethylanilino*)*anthraquinone*, m. p. 164—166° (from ethanol) (Found: F, 15·7; N, 3·8%). Unchanged 1-chloroanthraquinone (1·2 g.) was recovered.

Similar reaction of 1-chloroanthraquinone (3·6 g.) for 6 hr. with *o*-, *m*-, and *p*-aminobenzenecarboxamides (2 g.) (*m*- and *p*-isomers prepared by the method of Laptev and Vysokosova [23]), anhydrous sodium acetate (5 g.), cupric acetate (0·1 g.), and DMF (6 c.c.) gave red materials (*ortho*: 4·4 g., 87·3%, m. p. 130—134°; *meta*: 5·1 g., 100%, m. p. 120—126°; *para*: 4·4 g., 87·3%, m. p. 126—130°) which when chromatographed gave only (II); no evidence for the formation of the expected 1-(carbamoylanilino)anthraquinones was observed. Compound (II) was also the only product isolated from similar reactions between 1-chloroanthraquinone (5 g.), 2-, 3-, and 4-aminopyridines (6 g.), and DMF (50 c.c.) (20 hr. under reflux).

Reactions of 2-*Chloroanthraquinone with DMF*.—2-Chloroanthraquinone (4 g.) and DMF (30 c.c.) were heated under reflux for 20 hr. The crude product (3·8 g., 65·8%) when chromatographed gave rise to an upper principal red zone (A) and a faint lower pink zone which yielded a negligible quantity of pink material. Zone A when extracted with ethanol yielded scarlet needles (1·34 g.) of 2-dimethylaminoanthraquinone, m. p. 180—181° (lit.,[24] 181°; lit.,[14] 185—186°); unchanged 2-chloroanthraquinone (1·98 g.) was eluted.

Condensations similar to the above of halogenoanthraquinones with DMF are listed in the Table.

Halogenoanthraquinone (g.)		DMF (c.c.)	Time (hr.)	Crude product (g.)
2-Chloro-	4·0	30	105	(A) 4·0
1,2-Dichloro-	3·4	20	73	(B) 3·6
1,4-Dichloro-	3·1	20	73	(C) 2·3
1,5-Dichloro-	3·4	20	74	(D) 3·4
1,5-Dichloro-	3·4	20	21	(E) 3·3
1,5-Dichloro-	3·4	20	253	(F) 3·4
1,8-Dichloro-	3·0	20	25	(G) 2·95
1,8-Dichloro-	3·0	20	109	(H) 2·9
1,8-Dichloro-	3·0	20	253	(J) 4·5

The crude reaction products (A)—(J) were chromatographed and afforded the following principal zones, listed in order of decreasing adsorption; all products gave rise to strongly adsorbed minor dark coloured zones which were not investigated.

Product (A) (4 g.): red zone which yielded scarlet needles of 2-dimethylaminoanthraquinone (1·2 g.); 2-chloroanthraquinone (2·1 g.) recovered.

Product (B) (3·3 g.): orange-red zone which yielded (II) (1·7 g.); bluish-red zone which yielded dark red needles (0·5 g.) of 2-*chloro*-1-*dimethylaminoanthraquinone*, m. p. 147—148° (Found: C, 66·7; H, 3·7; Cl, 12·6; N, 5·1. $C_{16}H_{12}ClNO_2$ requires C, 67·3; H, 4·2; Cl, 12·4; N, 4·9%); 1,2-dichloroanthraquinone (0·4 g.) was recovered.

Product (C) (2 g.): deep red zone which gave (II) (0·55 g.); deep crimson zone which gave dark red needles (0·2 g.) of 1-chloro-4-methylaminoanthraquinone, m. p. 154° (from ethanol) (lit.,[25] 169°); 1,4-dichloroanthraquinone (0·5 g.) was recovered.

Product (D) (3·2 g.): red zone which gave dark red needles (0·14 g.) of 1,5-*bisdimethylaminoanthraquinone*, m. p. 155—157° (Found: C, 73·4; H, 5·8; Cl, 0·0; N, 9·3. $C_{18}H_{18}N_2O_2$ requires C, 73·5; H, 6·1; N, 9·5%); red zone which gave red needles (0·03 g.) of 1-*chloro*-5-*dimethylaminoanthraquinone*, m. p. 144—145° (Found: C, 67·2; H, 4·4; Cl, 12·3; N, 4·5. $C_{16}H_{12}ClNO_2$ requires C, 67·3; H, 4·2; Cl, 12·4; N, 4·9%); bluish-red zone which gave dark red prisms (0·02 g.) of 1,5-*bismethylaminoanthraquinone*, m. p. 218—220° (Found: C, 72·0; H, 5·5; Cl, 0·0; N, 10·2. $C_{16}H_{14}N_2O_2$ requires C, 72·2; H, 5·3; N, 10·5%); orange-red zone which yielded dark red needles (0·05 g.) of 1-*chloro*-5-*methylaminoanthraquinone*, m. p. 196—197° (lit.,[25] 194—196°); unchanged 1,5-dichloroanthraquinone (1·3 g.) was recovered.

Product (E) (3 g.): red zone which gave 1-*chloro*-5-*dimethylaminoanthraquinone* (0·06 g.); red zone which gave 1-chloro-5-methylaminoanthraquinone (0·08 g.); 1,5-dichloroanthraquinone (1·82 g.) was eluted.

Product (F) (2 g.): dark red zone which gave 1,5-*bismethylaminoanthraquinone* (0·29 g.); 1,5-dichloroanthraquinone (1·3 g.) was eluted.

Product (G) (2·9 g.): bluish-red zone which gave red needles (0·14 g.) of 1-*chloro*-8-*dimethylaminoanthraquinone*, m. p. 118—119° (Found: C, 67·5; H, 4·2; Cl, 12·4; N, 4·7. $C_{16}H_{12}ClNO_2$ requires C, 67·3; H, 4·2; Cl, 12·4; N, 4·9%); bluish red zone which gave cherry red needles (1·8 g.) of 1-*chloro*-8-*methylaminoanthraquinone*, m. p. 187° (Found: C, 65·9; H, 3·6; Cl, 13·4; N, 4·95. $C_{15}H_{10}ClNO_2$ requires C, 66·3; H, 3·7; Cl, 13·1; N, 5·2%).

Product (H) (2·9 g.): deep bluish-red zone which gave dark purple needles with a gold reflex (1·2 g.) of 1,8-*bisdimethylaminoanthraquinone*, m. p. 211—215° (Found: C, 72·1; H, 5·4; N, 10·3. $C_{16}H_{15}N_2O_2$ requires C, 72·2; H, 5·3; N, 10·5%); red zone which gave dark red needles (0·44 g.) of 1-*chloro*-8-*methylaminoanthraquinone*, m. p. 187—188°; 1,8-dichloroanthraquinone (0·06 g.) was eluted.

Product (J) (2 g.): cobalt blue zone which gave blue-black needles with a brassy reflex (0·33 g.) of 1,8-bismethylaminoanthraquinone, m. p. 226—227° (lit.,[25] 215—217°); 1,8-dichloroanthraquinone (1·1 g.) was recovered.

1-Chloroanthraquinone (5 g.) cuprous cyanide (1 g.), and DMF (50 c.c.) were heated under reflux for 25 hr. The crude product (2·5 g.) when chromatographed gave rise to a small upper blue-grey zone (not examined), and a pale bluish-purple zone which yielded pale buff plates (from ethanol) of 1-cyanoanthraquinone (0·13 g.), m. p. 249—250° (lit.,[26] 249°), $\nu_{max.}$ 2225 cm.$^{-1}$ (CN stretch). This, when reduced gave the known violet dibenz[*cd*,*g*]indol-6-one;[27] the product isolated from a lower red zone was identified as (I).

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