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OXIDATION OF AROMATIC AMINES WITH CHROMYL CHLORIDE—I

OXIDATION OF AROMATIC PRIMARY AMINES

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Abstract—The oxidation of aromatic primary amines with chromyl chloride in carbon tetrachloride or chloroform, results in the formation of intermediate solid adducts (Etard adducts) which, on hydrolysis, give azobenzenes (1), 1,4-benzoquinones (2), anilino-1,4-benzoquinones (3), 1,4-benzoquinone anils (4) and anilino-1,4-benzoquinone anils (5) in yields which depend on the position, nature and degree of substitution of the ring.

Oxidation of aromatic primary amines has attracted the attention of many workers in recent years.[1–12] The nature of the oxidation products formed depends on the type of oxidant used and the reaction conditions employed, i.e. aqueous or non-aqueous medium and pH. The major oxidation products of anilines using common oxidants such as manganese dioxide, dichromate, lead tetra-acetate, copper(II) salts, ferricyanide, etc. are 1,4-benzoquinones, azobenzenes, quinone anils and aniline black. The mechanisms suggested for the oxidation of amines incorporate the formation of either anilino radicals[5,13,14] or anilino cations.[2,3,15,16] However, in spite of much speculation, there is no compelling evidence for or against the involvement of radicals or cations. For reactions from which azobenzenes have been isolated in good yield, anilino radicals have been proposed as major intermediates. When quinone anils are formed in good yield and azobenzenes in small yields, anilino cations have been proposed as major intermediates.

Although the reactions of chromyl chloride with a large variety of organic substrates have been studied, the oxidation of aromatic primary amines using chromyl chloride has not been studied. Oxidation reactions were carried out by adding anilines (in CCl_4) to chromyl chloride in CCl_4 (chromyl chloride–organic substrate, 2 : 1).

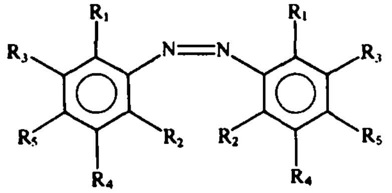
RESULTS AND DISCUSSION

The reaction of anilines with chromyl chloride results in the formation of intermediate solid adducts (Etard adducts) which are deeply coloured, often highly hygroscopic complex co-ordination compounds, similar to the Etard adducts of phenols.[17] Undiluted anilines, in particular liquid anilines, react explosively with neat chromyl chloride, the reaction mixture catching fire instantaneously and giving out thick, dense fumes. These adducts on hydrolysis gave a complex mixture of products usually obtained as reddish violet tarry solids. Chromatographic separation of the tarry solids led to the isolation of azobenzenes (1), 1,4-benzoquinones (2), anilino-1,4-benzoquinones (3), 1,4-benzoquinone anils (4) and anilino-1,4-benzoquinone anils (5).

The oxidation of unsubstituted aniline gave only intractable polymeric material. This was not unexpected as there are several free positions on the ring where oxidation, condensation and polymerization reactions can take place with relative ease.[7] Replacement of the hydrogen atoms in the ring with substituents, especially good blocking groups which are difficult to remove as anions, limit the number of ring sites open to oxidative polymerization. Thus, substituted anilines gave smaller amounts of polymeric material and higher yields of simple identifiable products (Table 1). With substituted anilines, the type of products formed depends on the position, nature and degree of substitution of the ring. Trisubstituted anilines formed higher yields of simple products than mono- or disubstituted anilines.

A significant feature of the oxidation of anilines with chromyl chloride is the formation of low yields of azobenzenes, particularly from substituted anilines. The major products of the oxidation reactions are 1,4-benzoquinones (2) and 1,4-benzoquinone anils (4). The corresponding 1,2-analogues were not isolated and this may be attributed to steric effects operating at the *ortho* position but it is more likely that the *ortho* derivatives are highly unstable and polymerize rapidly under the reaction conditions.[18]

Among the alkyl substituted anilines, those with unsubstituted *para* positions formed higher yields of 1,4-benzoquinones than those with *para* substituents. However, the reverse trend was observed with halo-substituted anilines. Thus, *para* halo-substituted anilines gave higher yields of quinones and quinone anils whereas 3,5- and 2,6-dimethylanilines gave significantly higher yields of quinones than 2,4-dimethyl-, 2,4,5-, 3,4,5- and 2,4,6-trimethylanilines, even though the latter ones might be expected to provide a better attack potential for the oxidant. As far as the yields of quinones are concerned, in terms of the removal of the *para* substituent, the following trend is



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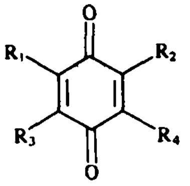

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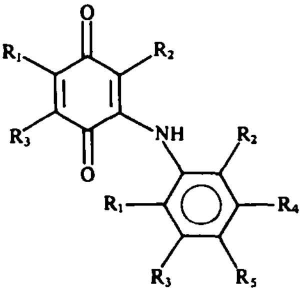

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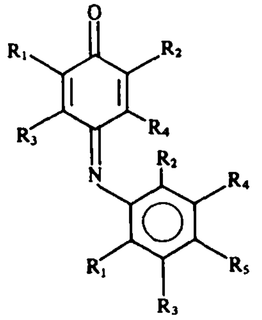

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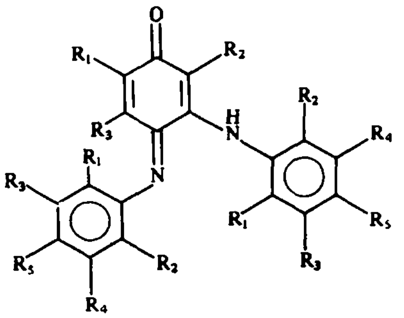


5

(R_1–R_5 = H,Cl,Br,F and CH_3 as appropriate)

observed: Br > Cl > H > Me. The non-formation of fluoroquinone may be due to the highly electronegative nature of the fluorine atom which reduces the electron density at the α-carbon significantly, thus inhibiting attack of the oxidant.

Most of the halo-substituted anilines formed quinone anils in substantial yields whereas, among the alkyl substituted anilines, only 2,6-dimethyl- and 2,4,6-trimethylanilines formed quinone anils. However, highest yields of quinone anils were obtained from

Table 1. The percentage yields (based on anilines) of various products for a 2 : 1 ratio of oxidant to anilines

Aniline	Azo compound (%)	M.p. (°)	Quinone (%)	M.p. (°)	Quinone anil (%)	M.p. (°)	Anilino quinone anil (%)	M.p. (°)
Aniline	—	—	—	—	—	—	—	—
2-Chloro-	12.2	190	14.7	57	—	—	—	—
4-Chloro-	12.0	188	18.0	116	20.0	84	14.0	98
2,4-Dichloro-	14.1	163	23.0	57	17.2	73	16.8	85
2,5-Dichloro-	13.6	224	19.2	160	15.6	114	23.5	121
2,6-Dichloro-	13.0	104	13.0	121	25.0	139	16.0	123
2,4,5-Trichloro-	11.1	167	11.2	160	49.7	151	—	—
2,4,6-Trichloro-	11.3	188	11.6	121	42.0 (23.0)[a]	162(115)	—	—
2,4,6-Trifluoro-	24.0	158	—	—	15.0 (32.0)[a]	134(112)	—	—
2-Bromo-	12.5	188	14.3	563	—	—	—	—
4-Bromo-	12.0	203	21.0	116	24.0	103	—	—
2,4-Dibromo-	14.3	178	24.0	565	16.4	114	13.5	99
2,5-Dibromo-	13.2	246	18.7	189	17.0	144	22.5	151
2,6-Dibromo-	12.0	141	15.0	131	28.0	155	—	—
2,4,6-Tribromo-	11.2	213	11.6 (24.5)[b]	132(154)	39.0	185	—	—
2-Methyl-	12.0	55	22.5	69	—	—	—	—
4-Methyl-	—	—	17.0	116	—	—	—	—
2,4-Dimethyl-	—	—	20.0	69	—	—	—	—
2,5-Dimethyl-	—	—	28.0	125	—	—	—	—
2,6-Dimethyl-	—	—	27.5(32.0)[b]	72(176)	36.0	81	—	—
3,4-Dimethyl-	—	—	16.0	69	—	—	—	—
3,5-Dimethyl-	—	—	43.0	71	—	—	—	—
2,4,5-Trimethyl-	12.0	177	18.2	125	—	—	—	—
2,4,6-Trimethyl-	—	—	7.2	172	73.5	96.5	—	—
3,4,5-Trimethyl-	11.5	192	—	—	—	—	—	—

[a] Quinone anil formed by *para* group migration.

[b] Anilino quinone.

Table 2

Organic substrate–oxidant	Quinone anil (%)	Quinone (%)
1:1.5	57.1	6.8
1:2	73.5	7.2
1:3	52.8	23.7
1:4	41.2	30.4
1:10	31.7	26.7

trisubstituted anilines. 2,4,6-Trimethylaniline gave good yields of quinone anil despite the fact that the *para* position is occupied by a methyl group which is not a good leaving group. The formation of quinone anils by such anilines could be explained by the mediation of a quinone methide intermediate analogous to the mechanism proposed for the oxidation of 2,4,6-trimethylaniline by peroxidase.[7] The variation in the yields of quinone anils between 2,5- and 2,6-dihaloanilines is more apparent than real. If the anilinoquinone anils (5) are produced via 1,4-addition of aniline and quinone di-imine, the difference in the yields of quinone anils, arises as a result of the secondary reaction rather than the primary reaction. The non-formation of anilinoquinone anils and anilinoquinones by the majority of the anilines studied seems likely to be due to the rapid precipitation of quinone imines thus preventing the 1,4-addition leading to such products.

In addition to the quinone anils formed by loss of the *para* substituent, 2,4,6-trifluoro- and trichloroanilines also formed quinone anils with migration of the *para* substituent. However, none of the alkyl substituted anilines formed such products, although the products have been isolated in the oxidation of anilines with peroxidase.[7]

Oxidation of 2,4,6-trimethylaniline was chosen to study the effect of varying the molar ratio of organic substrate to oxidant, as this gave good yields of identifiable products. The results are presented in Table 2. It is apparent from Table 2 that, as the concentration of the oxidant is increased, the yield of the quinone anil decreases and that of the quinone increases, up to a ratio of 4:1 (oxidant–organic substrate). When the concentration of the oxidant is increased 10-fold, the yields of both the quinone and the quinone anil decrease. This suggests that chromyl chloride in excess of a certain amount reacts further with the oxidation products giving intractable polymeric products.

A situation involving some of the competitive pathways in the oxidation reaction is illustrated in the oxidation of a mixture of 2,4,6-trichloro- and trimethylanilines. In addition to the expected products (i.e. the products formed in the individual oxidation), 2,2′,4,4′,6,6′-hexamethylazobenzene and the cross condensed quinone anil, 2,6-dimethyl-1,4-benzoquinone-2,4,6-trichloroanil were also isolated. The formation of azocompounds from both anilines indicates that anilino radicals are formed in the initial stages of the reaction. Hexamethylazobenzene was not formed by the oxidation of 2,4,6-trimethylaniline. This indicates that, in the presence of 2,4,6-trichloroaniline, the alkyl anilino radicals undergo (N–N) coupling. Furthermore, the formation of cross condensed quinone anil and the non-formation of the mixed azobenzene indicates that alkyl anilino radicals are formed well ahead of the chloro analogue and that quinone anils are not formed by the coupling of the anilino radicals. This clearly suggests that quinone anils are formed via anilino cations.

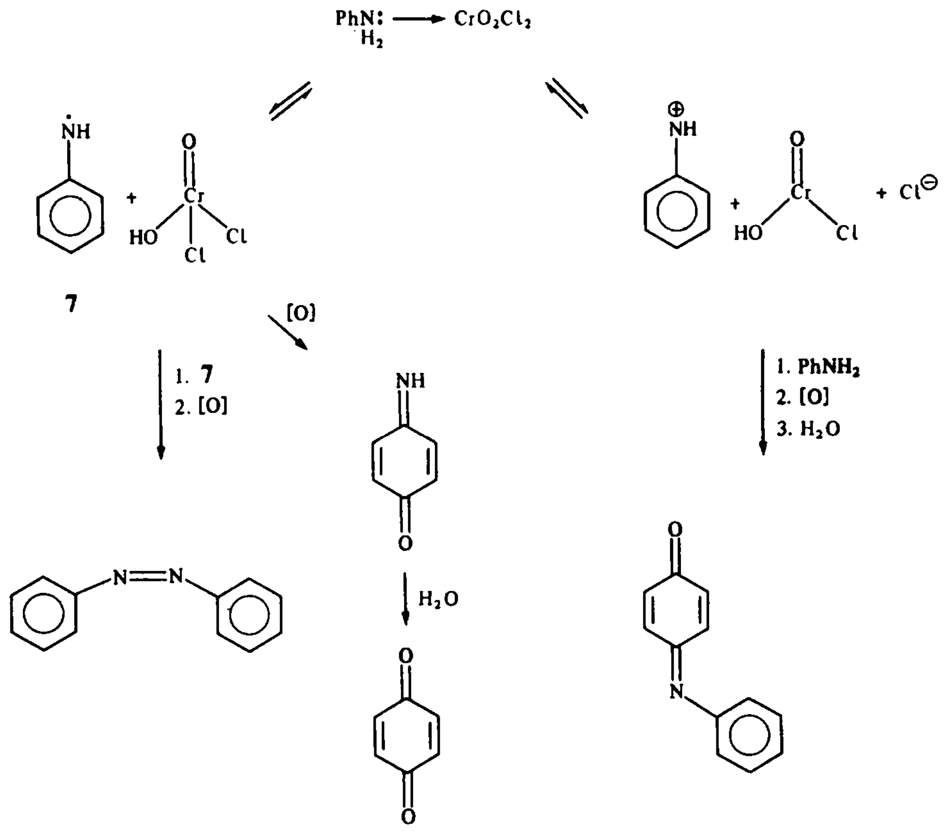
A number of different mechanisms have been proposed for the Etard reaction.[19,20] It is by no means certain that all the chromium atoms are present in the same oxidation state in the adduct. All evidence suggests that the adduct contains reduced chromium species. Although some workers have implied that hydrolysis of the adduct is a major part of the oxidation reaction, it has been shown that the hydrolysis stage is merely a ligand exchange process which releases the co-ordinated oxidized species.[21,22]

The product distribution in our study indicates that anilino radicals and cations are formed as reactive intermediates at an early stage of the reaction. Anilines with electron withdrawing groups were found to react more slowly with chromyl chloride than those with electron releasing substituents. Furthermore, *N*-acetyl- and *N*-benzoylanilines were found to be non-reactive with chromyl chloride. This suggests that the first stage in the oxidation reaction is a co-ordination process arising from the electron donor nature of aniline and the electron acceptor nature of the oxidant.[23–25]

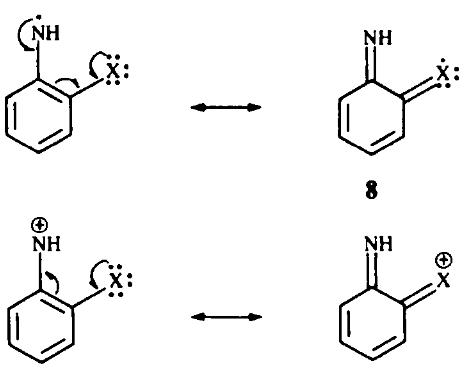
$$\mathrm{Ph\ddot{N}H_2 + CrO_2Cl_2 \rightleftharpoons Ph\ddot{N}:H_2 \rightarrow CrO_2Cl_2}.$$

The anilino radicals and cations could then be formed by the oxidation of the co-ordinated aniline. If anilino radicals were the only intermediates formed at the initial stages of the reaction then the yields of azobenzene should be high.[9] However, the yields of azobenzene are low. This clearly indicates that the radical coupling to form azobenzene is in competition with further oxidation of the anilino radicals. In view of the excess oxidant present, the latter is more likely. Such a reaction between anilino radicals and the oxidant is much more likely to yield quinones. It is conceivable that azobenzene is formed initially in good yields but undergoes further reaction with the oxidant. Azobenzene was, however, found to be practically non-reactive with chromyl chloride under the reaction conditions employed.

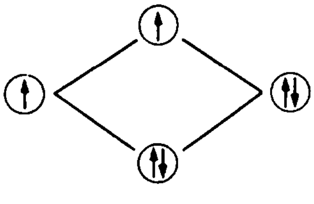
The formation of quinone anil should clearly involve the attack of a second molecule of aniline on an intermediate formed in the initial stages of the reaction. The intermediate must be more reactive towards aniline than it is with the oxidant which is present in excess. Given that aniline is an electron donor and the oxidant an electron acceptor, it is most likely that the reactive intermediate is also an electron acceptor. Thus, it is most likely that quinone anils are formed via anilino cations rather than anilino radicals. The proposed mechanism for the oxidation of anilines with chromyl chloride is represented in Scheme 1. The formation of the cations will be favoured by stronger bases while the formation of radicals will be favoured by weaker ones. Within the halo-substituted anilines, the formation of the cation will be favoured although they are weaker bases than the corresponding alkyl-substituted anilines, since the cation is more stabilized than the radical (Scheme 2). The resonance hybrid for the radical involves structure **8** where the halo atom has more than eight electrons in the valence shell. However, such structures are possible but they involve the participation of antibonding orbitals (Fig. 1), hence, less



Scheme 1.



Scheme 2.



(Filled, half filled configuration, hence stable)

Fig. 1.

stable than the corresponding canonical structure for the cation, which involves only bonding molecular orbitals.

The IR spectra of the adducts and hydrolysis of the adducts using water enriched with heavy oxygen (^{18}O) strongly suggest the presence of quinone imines and di-imines.[16] Thus, hydrolysis of the adduct could be considered as a ligand exchange reaction, followed by hydrolysis of the decomplexed imines and di-imines to form the quinones and quinone anils. During hydrolysis the reduced Cr species can undergo disproportionation to form the chromium(VI) species,

$$3Cr(IV) \rightarrow Cr(VI) + 2Cr(III)$$

$$3Cr(V) \rightarrow 2Cr(VI) + Cr(III)$$

which could effect further oxidation during hydrolysis. However, hydrolysis of the adducts in the presence of Zn dust reveals that this secondary oxidation is insignificant and that oxidation of the organic substrate is essentially complete in the adduct stage.

EXPERIMENTAL

Most of the organic compounds used were of reagent grade purified by redistillation or recrystallization as appropriate. Wherever possible analar reagents were used. CrO_2Cl_2 was purified by room temp distillation at reduced pressure (0.3 Torr) immediately prior to use. CCl_4 was dried over P_2O_5 for several days and, finally, purified by fractional distillation. IR spectra were recorded using a Perkin–Elmer 457 grating spectrometer. Spectra were recorded using Nujol mull, KBr discs or solns in CCl_4. UV–visible spectra were recorded using an SP-800 spectrophotometer for solns in cyclohexane. NMR spectra were recorded on a Perkin–Elmer RIO spectrometer using TMS as internal standard, for solns in either CCl_4 or $CDCl_3$. Mass spectra were recorded using an AEI MS-9 spectrometer, operating at 70 eV with a probe temp of 150–180°. Elemental analyses were performed by Beller microanalytical laboratory (West Germany) and Butterworth microanalytical services (U.K.).

Column chromatography was carried out with Merck silica gel (0.05–0.2 mm) using (400 × 200 mm) columns. Analytical TLC was carried out with silica gel F_{254} (0.25 mm) deposited on plastic sheets. Preparative TLC was performed using silica gel H-type (0.60–0.80 mm) deposited on glass plates (200 × 200 mm). Solvent systems used were petroleum ether (40–60°)–C_6H_6 or petroleum ether (40–60°)–EtOAc.

Typical experimental procedure. Oxidation reactions were carried out by slowly adding the anilines (*ca* 0.02–0.03 mol) in dry CCl_4(100 ml) to a vigorously stirred soln of CrO_2Cl_3 (*ca* 0.04–0.06 mol) in super dry CCl_4(100 ml). The temp was maintained at 0–5° by external cooling. In all reactions a solid pptd after the first few minutes of addition of anilines and after completion of the addition (15–20 min), the mixture was further stirred for 1 h and filtered using an enclosed filter. The solid adduct was washed free of excess CrO_2Cl_2 and dried at room temp under reduced pressure (0.1–0.3 Torr) for 24–48 h.

The adduct filtrate was mixed with excess H_2O (200 ml) and CCl_4 layer was separated, concentrated and dried. The dried CCl_4 layer was concentrated to 2–3 ml and subjected to column chromatography. The adduct filtrate was found to contain mainly azo compounds and unreacted anilines.

The solid adducts were hydrolysed carefully with ice–H_2O (150–200 ml) and the solids (usually deep reddish purple) were extracted with petroleum ether (40–60°) and C_6H_6, respectively. In most cases studied the residues after solvent extraction were deep brown amorphous solids. The solvent extracts were evaporated to dryness and the components were separated by column chromatography or preparative TLC as appropriate, following trial separations by analytical TLC.

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