Molecular Orbital Studies of Aminoanthraquinones

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Both the Hückel and CNDO/2 methods have been used to calculate the charge densities and localisation energies of 1- and 2-aminoanthraquinones. It is found that a reasonably good correlation exists between the calculated and experimentally determined positions of ring substitution as assessed by the halogenation, nitration, and sulphonation of these systems. The experimentally determined substitution patterns obtained for 1- and 2-methylaminoanthraquinone show considerable differences from their amino-analogues suggesting that the methyl group is exerting a considerable steric effect in these reactions.

ALTHOUGH anthraquinone and its amino-derivatives constitute an important part of dyestuff chemistry little attempt has been made to examine the chemistry of these systems in terms of molecular orbital theory. A limited number of calculations have been reported on anthraquinone itself.[1,2] Molecular orbital studies of simple substituted anthraquinone systems such as the 1- and 2-amino-derivatives would be expected to lead to a more fundamental understanding of their behaviour with both heterolytic and homolytic reagents and would provide a deeper insight into the reactions of more complex anthraquinone systems with the same reagents. While the substituent effect of the amino-group present in aminoanthraquinones has been examined by the Hückel method,[3] the studies reported here are an attempt to correlate the observed reactivities of these systems with those predicted theoretically by calculation of charge densities and localisation energies using both the Hückel (HMO) and CNDO/2 methods. Semi-empirical calculations of a similar type to those reported here have been described recently for a number of polycyclic aromatic hydrocarbons [4] and for mono-substituted benzenes.[5]

Theoretical Investigation

Method of Calculation.—(a) *HMO.* The coulomb integrals, α_x, and bond integrals, β_x, of the heteroatoms present in the substituted anthraquinone were expressed in terms of the carbon integrals in the normal way, *i.e.* $\alpha_x = \alpha_c + h\beta_{cc}$ and $\beta_{cx} = k_{cx}\beta_{cc}$.[6] The parameters h and k for individual heteroatoms were calculated by the adoption of a similar procedure to that used by Jaffé for monosubstituted benzenes.[7] In the present treatment, however, variations in h-values for individual heteroatoms present in mono-substituted benzenes were graphically related to the calculated electron density at that centre.[8] The latter, in turn, was assumed to be proportional to the averaged Hammett σ_R° value obtained from i.r.[9] and n.m.r.[10] spectroscopic measurements. By this means it is possible to assess one substituent against another, *e.g.* the amino-group *versus* the carbonyl-group in an aminoanthraquinone. Values of h calculated by this procedure were: $h_{\dot{O}} = h_{\dot{N}\dot{H}_2} = 0{\cdot}6$. In both cases k was kept constant and equal to unity. A standard eigenvalue/eigenvector programme was used for calculation.

HMO localisation energies were calculated in the usual way [6] by taking the difference in π-bonding energy between the aminoanthraquinone and the corresponding cation produced by the removal of two electrons from the π-electron system at specific ring positions to give a new π-system of one less atom and two less electrons. A total of seven possible cations can be produced by this procedure and their relative energies assessed from simple eigenvalue calculations.

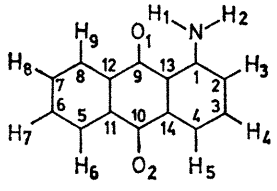
(b) *CNDO/2.* The charge densities and localisation energies of 1- and 2-aminoanthraquinones were evaluated by application of the semi-empirical CNDO/2 all-valence electron SCF method of Pople, Santry, and Segal.[11] Calculations were carried out using Program 141 of Quantum Chemistry Program Exchange.[12] Molecular geometries were treated as empirical quantities and each molecule was assumed to be planar with the normal bond angles associated with each atom in its particular state of hybridisation. Furthermore, using the standard structure approach,[13] each system was generated from two regular hexagons with carbon–carbon bond lengths of 1·40 Å and carbon–hydrogen bond lengths of 1·08 Å. The central carbon–carbon bonds joining each carbonyl group to both aromatic rings were assumed to be of the same length as those found in anthraquinone itself, *i.e.* 1·48 Å.[14] The carbon–oxygen, carbon–nitrogen, and nitrogen–hydrogen bond lengths adopted were those recommended by Pople and Beveridge, *i.e.* 1·22, 1·40, and 1·01 Å respectively.[15] The input data was presented

[1] C. A. Coulson and A. Streitwieser jun., 'Dictionary of π-Electron Calculations,' Pergamon Press, Oxford, 1965, pp. 340—343, and references therein.
[2] K. Nishimoto and L. S. Forster, *Theor. Chim. Acta*, 1966, **4**, 155.
[3] W. Kemula and M. T. Krygowski, *Bull. Acad. polon. Sci., Ser. Sci. chim.*, 1967, **15**(10), 479.
[4] A. Streitwieser, jun., P. C. Mowery, R. G. Jesaitis, and A. Lewis, *J. Amer. Chem. Soc.*, 1970, **92**, 6529.
[5] G. R. Howe, *J. Chem. Soc.* (*B*), 1971, 984.
[6] A. Streitwieser, jun., 'Molecular Orbital Theory for Organic Chemists,' John Wiley and Sons Ltd., New York, 1961.
[7] H. H. Jaffé, *J. Chem. Phys.*, 1952, **20**, 279.
[8] J. O. Morley, unpublished results.
[9] A. R. Katritzky and R. P. Topsom, *Angew. Chem. Internat. Edn.*, 1970, **9**(2), 87.
[10] R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davies, *J. Amer. Chem. Soc.*, 1963, **85**, 709; *ibid.*, 1963, **85**, 3146.
[11] J. A. Pople, D. P. Santry, and G. A. Segal, *J. Chem. Phys.*, 1965, **43**, S129; J. A. Pople and G. A. Segal, *ibid.*, 1965, **43**, S136; 1966, **44**, 3289.
[12] P. A. Dobosh, *CNINDO*, Program 141, Quantum Chemistry Program Exchange, Indiana University.
[13] J. A. Pople and M. Gordon, *J. Amer. Chem. Soc.*, 1967, **89**, 4253.
[14] B. V. R. Murty, *Z. Krist.*, 1960, **113**, 445.
[15] J. A. Pople and D. L. Beveridge, 'Approximate Molecular Orbital Theory,' McGraw Hill, Inc., New York, 1970.

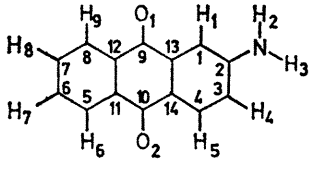
as atomic numbers and cartesian co-ordinates in the usual way [12] and the programme limited to ten iterations only as this was considered to be sufficiently accurate for the purposes of the present investigation.

Localisation energies were calculated by assuming that the Wheland intermediate produced by attack of an electrophile on the aminoanthraquinone system could be represented simply by the addition of a proton to the molecule at the same position. Geometries were derived by addition of a proton to the reacting carbon atom to generate a normal methylene group with a carbon–hydrogen bond length of 1·10 Å and an internal angle of 110°. Each methylene group was assumed to be connected to the aromatic system by carbon–carbon bond lengths of 1·52 Å, with a calculated internal angle of 105° 48′. Calculations were confined to those intermediates generated by electrophilic attack in the most reactive ring of the molecule. Localisation energies, L, were calculated by taking the difference between the binding energy of the aminoanthraquinone and the corresponding Wheland intermediate.

Each molecule was enumerated in the following way:



(1)



(2)

The results of these calculations are shown in Tables 1 and 2.

RESULTS

The complete lack of explicit consideration of electron-repulsion effects in the Hückel theory is undoubtedly a major weakness; nevertheless, the results obtained from these calculations in comparison with those obtained by the CNDO/2 method are sufficient to show that the former method provides a useful indication of the reactivities of the anthraquinone systems considered here. However, though similar charge-density patterns are obtained for 1-aminoanthraquinone by both methods, significant differences are found in the results obtained for 2-aminoanthraquinone. Each molecular system will be discussed in turn.

(a) 1-*Aminoanthraquinone*.—The charge-density indices calculated by each method for ring substitution clearly show that the greatest negative values occur at the 2- and 4-positions of the molecule with the major charge concentrated at the former position. However, while the HMO localisation energies indicate that the intermediate produced by attack (protonation) at the 2-position is favoured, the more accurate CNDO/2 method indicates that the intermediate produced by attack at the 4-position is slightly preferred.

It follows therefore, that the charge-density index predicts that electrophilic attack is likely to produce mainly the 2-derivative whereas the CNDO/2 localisation energies predict that attack is likely to produce mainly the 4-derivative.

(b) 2-*Aminoanthraquinone*.—In this case, the charge density indices calculated by each method for ring substitution show that the greatest negative values occur at the 1- and 3-positions of the molecule. However, the HMO results give the greatest charge concentration at the 3-position while the more accurate CNDO/2 method gives roughly equal charge at both activated positions. However, the localisation energies, calculated by the two methods show that the intermediate produced by attack (protonation) at the 1-position is favoured. The CNDO/2 charge densities therefore predict that electrophilic attack is likely to give rise to approximately equal amounts of the 1- and 3-substituted products, while the localisation energies predict that attack is likely to produce mainly the 1-substituted product.

The results presented in Tables 1 and 2 show the π-electron charges at positions of ring substitution are polarised in the opposite way to the σ-electron core. While the classical concept of the mesomeric effect of the amino-group is confirmed for these cases it is noticeable that the inductive effect of the same group is only relayed over a distance of two carbon atoms. Similar results have been reported recently for mono-substituted benzenes.[5]

Experimental Investigation

While a large volume of qualitative information has been published on the substitution reactions of simple anthraquinone systems such as the ones considered here,[16] quantitative assessments of the isomer ratios produced during these reactions are not available owing to the absence of reliable analytical techniques, such as thin layer chromatography, at the time of experimentation. For this reason, therefore, a re-investigation of the reactivities of these simple systems has been conducted in order to assess the predictions of the molecular orbital studies discussed above. The substitution patterns examined were those obtained from the halogenation, nitration, and sulphonation of 1- and 2-aminoanthraquinones. Furthermore, the reactivities of 1- and 2-methylaminoanthraquinones were also studied in order to examine the extent of reported steric factors in these reactions.[16] In theory, the methyl-amino-compounds would be expected to show similar, though not identical charge distribution patterns to their amino-analogues in view of the close similarity between the substituent constant values σ_R°, of the amino- and methylamino-groups.[9]

In all the reactions described here, only 30% of the calculated quantity of electrophilic reagent necessary to

[16] See, for example, S. Coffey and J. Van Alphen, ' Chemistry of Carbon Compounds,' ed. E. H. Rodd, Elsevier, Amsterdam, 1956, vol. III, p. 1393, and references therein; F. B. Stilmar and M. A. Perkins, ' The Chemistry of Synthetic Dyes and Pigments,' ed. H. A. Lubs, Reinhold, New York, 1955, p. 345, and references therein.

TABLE 1

Calculated molecular orbital parameters for 1-aminoanthraquinone

Molecular position	CNDO/2 Total charge density	CNDO/2 σ Charge density	CNDO/2 π Charge density	Localisation energies × 10 (a.u.)	HMO π Charge density	HMO Localisation energies (β)
C_1	+0·1809	+0·0764	+0·1045		+0·0871	
C_2	−0·0494	+0·0217	−0·0711	−1·513	−0·0428	2·063
C_3	+0·0469	−0·0108	+0·0577	−2·074	+0·0265	2·611
C_4	−0·0163	+0·0232	−0·0395	−1·499	−0·0131	2·116
C_5	+0·0207	−0·0005	+0·0212		+0·0390	2·502
C_6	+0·0206	0·0000	+0·0206		+0·0219	2·550
C_7	+0·0191	+0·0042	+0·0149		+0·0266	2·566
C_8	+0·0266	−0·0010	+0·0236		+0·0342	2·488
C_9	+0·2178	+0·0678	+0·1500		+0·1632	
C_{10}	+0·1970	+0·0711	+0·1259		+0·1831	
C_{11}	−0·0345	−0·0255	−0·0090		+0·0040	
C_{12}	−0·0389	−0·0263	−0·0126		+0·0091	
C_{13}	−0·1078	+0·0017	−0·1095		−0·0932	
C_{14}	−0·0112	−0·0334	+0·0222		+0·0041	
H_1	+0·1510	+0·1510				
H_2	+0·1047	+0·1047				
H_3	+0·0025	+0·0025				
H_4	−0·0041	−0·0041				
H_5	+0·0061	+0·0061				
H_6	+0·0082	+0·0082				
H_7	−0·0017	−0·0017				
H_8	−0·0018	−0·0018				
H_9	+0·0077	+0·0077				
N	−0·2628	−0·3793	+0·1165		+0·3299	
O_1	−0·2561	−0·0191	−0·2370		−0·4287	
O_2	−0·2214	−0·0393	−0·1821		−0·3512	

TABLE 2

Calculated molecular orbital parameters for 2-aminoanthraquinone

Molecular position	CNDO/2 Total charge density	CNDO/2 σ Charge density	CNDO/2 π Charge density	Localisation energy × 10 (a.u.)	HMO π Charge density	HMO Localisation energy (β)
C_1	−0·0449	+0·0220	−0·0669	−1·924	−0·0305	2·003
C_2	+0·1757	+0·0799	+0·0958		+0·0762	
C_3	−0·0480	+0·0224	−0·0704	−1·974	−0·0777	2·068
C_4	+0·0468	−0·0112	+0·0580		+0·0399	2·552
C_5	+0·0209	−0·0006	+0·0215		+0·0352	2·490
C_6	+0·0196	−0·0001	+0·0197		+0·0274	2·568
C_7	+0·0186	+0·0010	+0·0176		+0·0227	2·549
C_8	+0·0211	−0·0007	+0·0218		+0·0400	2·508
C_9	+0·1985	+0·0708	+0·1277		+0·1875	
C_{10}	+0·2057	+0·0700	+0·1351		+0·1675	
C_{11}	−0·0357	−0·0279	−0·0078		+0·0099	
C_{12}	−0·0359	−0·0235	−0·0124		+0·0048	
C_{13}	−0·0108	−0·0341	+0·0233		+0·0095	
C_{14}	−0·0741	−0·0005	−0·0736		−0·0778	
H_1	+0·0116	+0·0116				
H_2	+0·1102	+0·1102				
H_3	+0·1097	+0·1097				
H_4	+0·0023	+0·0023				
H_5	+0·0068	+0·0068				
H_6	+0·0082	+0·0082				
H_7	−0·0023	−0·0023				
H_8	−0·0023	−0·0023				
H_9	+0·0072	+0·0072				
N	−0·2443	−0·3485	+0·1042		+0·3189	
O_1	−0·2247	−0·0397	−0·1842		−0·3398	
O_2	−0·2400	−0·0315	−0·2085		−0·4138	

effect monosubstitution was employed in order to minimise the formation of disubstituted products. Where possible, reactions were carried out in neutral solvent systems rather than strong acids as the latter are known to protonate aromatic amines, reduce their reactivity, and under some circumstances change the substitution pattern.[17] As the ultraviolet spectrum of 1-aminoanthraquinone in acetic acid is similar to that reported in ethanol and different from that of its conjugate acid in methanol,[18] it is concluded that protonation

[17] J. March, 'Advanced Organic Chemistry: Reactions, Mechanisms and Structure,' McGraw Hill, Inc., New York, 1968, p. 397.

[18] K. Hirayama, 'Handbook of Ultraviolet and Visible Absorption Spectra of Organic Compounds,' Plenum Press, New York, 1967, p. 284.

of the amino-group does not occur to any appreciable extent in the former solvent. Consequently, all halogenation reactions were carried out in acetic acid as this provides a suitable solvent for both the substrate and halogenating reagent. Both chlorination and bromination proceed easily at room temperature to give halogeno-derivatives, but iodination requires the addition of a silver salt to promote reaction and give the corresponding iodo-derivatives. Silver-assisted iodination reactions of a similar type have been reported also for other aromatic systems.[19a] The chlorination and bromination reactions of 1-aminoanthraquinone were also examined separately in both nitromethane and carbon tetrachloride in order to assess the effect of solvent on the substitution pattern.

The nitric acid nitration of the aminoanthraquinones does not proceed in acetic acid alone, but reaction does occur in a mixture of acetic and sulphuric acids at 0° to give a mixture of mononitroaminoanthraquinones along with small amounts of oxidised material; some dinitro-derivatives are also formed. It is assumed in this reaction that the free amino-compound is attacked rather than its conjugate acid as it is likely that the reactivity of the former is considerably greater than that of the latter.

Attempts to sulphonate the anthraquinone systems in either acetic acid or dioxan with sulphur trioxide, sulphuric acid, oleum, or chlorosulphonic acid were unsuccessful. Sulphonation does occur, however, with chlorosulphonic acid in sulphuric acid at elevated temperatures. It is not possible to say in these reactions whether the free amine or its conjugate acid is attacked as the protonation equilibrium was not studied.

The results of these experiments are shown in Table 3.

TABLE 3

Isomer ratios obtained from the reaction of aminoanthraquinones with electrophilic reagents

Substrate	Product composition %	Reaction type: Chlorination [a]	Chlorination [b]	Chlorination [c]	Bromination [a]	Bromination [b]	Bromination [c]	Iodination [d]	Nitration [e]	Sulphonation [f]
1-Amino-	2-Isomer	28·4	17·3	41·3	90·6	77·4	94·6	91·0	77·1	83·4
anthraquinone	4-Isomer	71·6	82·7	58·7	9·4	22·6	5·4	9·0	22·9	16·6
2-Amino-	1-Isomer	99·0			54·9			32·6	43·7	
anthraquinone	3-Isomer	1·0			45·1			67·4	56·3	
1-Methylamino-	2-Isomer	34·5			14·8			1·4		1·0
anthraquinone	4-Isomer	65·5			85·2			98·6		99·0
2-Methylamino-	1-Isomer	98·8			34·3			7·8		
anthraquinone	3-Isomer	1·2			65·7			92·2		

[a] Reactions carried out at 25° with elemental halogen in acetic acid. [b] As *a* but in nitromethane. [c] As *a* but in carbon tetrachloride. [d] As *a* except silver acetate was added to the solvent. [e] Reactions carried out with nitric acid at 0° in a mixture of acetic acid and sulphuric acid. [f] Reactions carried out with chlorosulphonic acid in sulphuric acid at 100°.

DISCUSSION

It has been clearly demonstrated in the sulphonation and nitration reactions of toluene with aqueous sulphuric acid and aqueous nitric/acetic acids respectively that the attacking reagents display only a low substrate and positional selectivity.[20] The transition state of highest energy in these reactions therefore, occurs fairly early in the passage along the reaction co-ordinate and resembles the unperturbed starting materials rather than the Wheland intermediate.[21] By analogy, it seems likely that the selectivity of the attacking species in the nitration and sulphonation reactions described here (Table 3) are similar to, though not identical with, those produced in the corresponding reactions of toluene. The substitution patterns observed for 1- and 2-aminoanthraquinone, therefore, are more likely to show a correlation with the charge densities than the localisation energies. The results shown in Tables 1 and 2 are fully consistent with this view, with nitration and sulphonation occurring mainly at the 2-position in the former case, and at both positions in the latter.

The halogenation results presented here, however, are more difficult to rationalise. Kinetic studies have shown that the reactions of phenolic ether and anilides with chlorine or bromine in acetic acid proceed by attack of molecular halogen on the respective substrate.[20] Furthermore, the latter reagents show a high substrate and positional selectivity in their reactions with toluene under similar conditions.[20] The transition state in these reactions occurs further along the reaction co-ordinate than in the corresponding nitration or sulphonation reaction, and is believed to show a structural resemblance to the Wheland intermediate.[22]

It is probable that all the chlorination and bromination reactions described here also proceed by attack of molecular halogen on the respective aminoanthraquinone. It follows on the basis of the preceding discussion that the localisation energies are likely to give a better measure of the substitution pattern than the charge densities for aromatic molecular halogenation. The chlorination results shown for 1- and 2-aminoanthraquinone fully support this argument and show that the substitution pattern observed is related to the stabilities of the Wheland intermediates as expressed by the

[19] P. B. D. De La Mare and J. H. Ridd, 'Aromatic Substitution, Nitration and Halogenation,' Butterwirths, London, 1959; (*a*) p. 111; (*b*) p. 131.

[20] L. M. Stock and H. C. Brown, 'Advances in Physical Organic Chemistry', ed. V. Gold, Academic Press, London, 1963, vol. I, p. 35, and references therein.

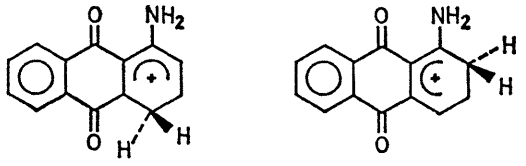
[21] See, for example, R. O. C. Norman and R. Taylor, in 'Electrophilic Substitution in Benzenoid Compounds,' ed. C. Eaborn, Elsevier, London, 1965, p. 283, and references therein.

[22] S. F. Mason, *Progr. Org. Chem.*, 1964, **6**, 214.

calculated localisation energies. However, the bromination results are in some disagreement with this argument as the substitution patterns observed do not correlate well with the localisation energies in spite of the greater substrate and positional selectivity of molecular bromine over that of chlorine in acetic acid.[20] A similar change of the substitution pattern has been observed in the reactions of toluene with bromine on chlorine. Molecular bromination in acetic acid produces an *ortho* : *para* ratio of 32·9 : 66·8 compared with a ratio of 59·8 : 39·7 for the corresponding chlorination reaction under similar conditions.[20] The *ortho* : *para* ratio for the molecular chlorination of toluene however, varies considerably with the nature of the solvent but does not relate either to changes in the absolute rate of reaction or to the dielectric constant of the medium. It has been suggested that this variation arises because the effective halogenating species consists of a complex between solvent and reagent and that the selectivity of this species depends on the nature of the solvent.[23]

Although no kinetic studies were carried out during the present work, the effect of solvent on the substitution pattern obtained from the reaction of 1-aminoanthraquinone with either chlorine or bromine was examined. The results shown in Table 3 clearly demonstrate that the substitution pattern observed is significantly effected by the solvent in the transition from protonic to aprotic media. The pattern observed is similar therefore to the pattern obtained from the related reactions of toluene.[23] Furthermore, it has been shown that the reagent involved in the chlorination of toluene in nitromethane displays a considerably higher substrate and positional selectivity (kt/kb 2445, *Sf* 2·9471) than the reagent involved in the corresponding chlorination in acetic acid (kt/kb 344, *Sf* 2·219).[20,21] It follows by analogy that the substitution pattern of 1-aminoanthraquinone observed in nitromethane is likely to be more related to the stabilities of the Wheland intermediates than the corresponding reaction in acetic acid, as the transition state has now been displaced further along the reaction co-ordinate because of the increase in reagent selectivity in the former solvent. The bromination results, however, are still difficult to rationalise even on this basis.

It is suggested therefore that the bromination results are best interpreted as a reflection of steric interactions between the carbonyl group and the reagent experienced during the formation of the transition state. Such an effect will be of lesser importance in chlorination reactions and of greater importance in iodination reactions when the attacking reagent is molecular in nature. This argument is supported to some extent by the isomer patterns obtained from the uncatalysed halogenation of 3-hydroxybenzaldehyde in chloroform or carbon tetrachloride. It has been claimed that molecular chlorination produces a mixture of 2- and 6-chloro-derivatives, whereas molecular bromination produces a mixture of 4- and 6-bromo-derivatives.[24] The larger bromine molecule, therefore, preferentially attacks at those ring positions where steric effects are small. The protonated models originally chosen as representations of the Wheland intermediates (shown below for 1-aminoanthraquinone), therefore, will no longer be suitable guides to the general substitution patterns in these systems as the calculated localisation energies do not include steric effects of this kind.



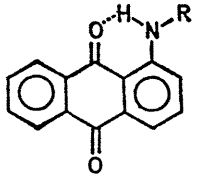
It follows that the localisation energies calculated for simple protonated models such as those illustrated will be meaningful *only* in those cases where steric effects are small or negligible.

The iodination results shown in Table 3 are difficult to interpret mainly because the effective attacking species has not been identified under these conditions. However, while molecular halogen is believed to be the attacking species in the iodination reactions of *p*-nitrophenol and aniline,[25] the reactions described here are more complex and do not proceed in the absence of a silver catalyst: this may mean that as iodination proceeds a very unfavourable equilibrium, involving possibly a positive iodine compound, is shifted to completion by precipitation of silver halide or that the silver salt functions only after the halogen and the aminoanthraquinone have reacted to form an intermediate. If a positive species is involved, the transition state is likely to occur early along the reaction co-ordinate and the substitution pattern observed will be related to the charge densities of the substrate. On the other hand, if a molecular species is involved, the transition state is likely to occur further along the reaction co-ordinate and the substitution pattern observed will then be related to the relative stabilities of the Wheland intermediates. In the latter case, however, steric factors are likely to be prominent as in the bromination reaction discussed above. Consequently, no firm conclusions can be drawn from the iodination data until such time as the selectivity of the attacking reagent has been definitely established in this type of reaction.

The detailed structure of the aminoanthraquinone systems has been examined recently by *X*-ray crystallography,[26] ultraviolet spectroscopy[27,28] and by both

[23] L. M. Stock and A. Himoe, *Tetrahedron Letters*, 1960, **13**, 9.
[24] H. H. Hodgson and H. G. Beard, *J. Chem. Soc.*, 1925, **127**, 876; *ibid.*, 1926, 148.
[25] E. Berliner, *J. Chem. Ed.*, 1966, **43**(3), 124.
[26] K. Ogawa and H. Kobayashai, *Sci. Rep. Osaka Univ.*, 1968, **17**(1), 15.
[27] N. A. Shcheglova, D. N. Shigorin, and N. S. Dokunikhin, *Zhur. fiz. Khim.*, 1968, **42**(11), 2724.
[28] Z. Yoshida and F. Takabayashi, *Tetrahedron*, 1967, **24**(2), 933.

solid-phase infrared spectroscopy and *X*-ray diffraction studies.[29] The results obtained in the solid state show that one hydrogen atom of the amino-group present in 1-aminoanthraquinone is intramolecularly hydrogen bonded to the adjacent carbonyl oxygen atom and the other intermolecularly hydrogen bonded to the free carbonyl oxygen atom on a glide related molecule.[29] These results are supported, in part, by the CNDO/2 calculations (Table 1) which show that the amino-hydrogen atom (H_1) adjacent to the carbonyl group is considerably more acidic than the other (H_2). In solution, the energy of intramolecular hydrogen bonding has been estimated to be 13·8 kJ/mol [27] and there is little evidence for intermolecular hydrogen bonding with the solvent.[28] It is probable, therefore, that both 1-aminoanthraquinone (R = H) and 1-methylaminoanthraquinone (R = CH_3) have the following structure in solution:



Furthermore, molecular models show that the methylamino-group, unlike the amino-group present in 1-substituted anthraquinones, is restricted in its mode of rotation around the nitrogen–aryl axis. It is concluded that the molecule has the conformation shown and that the methyl group impedes attack at the 2-position. It follows, therefore, that the larger the size of the attacking reagent, the greater the steric effect in the transition state and the smaller the proportion of substitution at the 2-position. Steric effects of a related kind have been reported for the halogenation of toluene and t-butylbenzene where it is found that the proportion of *ortho*-substitution decreases with increasing substituent and reagent size.[19b] The results obtained indicate that the methyl group exerts a larger steric effect in the transition state for 2-substitution than the carbonyl-group does for 4-substitution since reaction here occurs mainly at the latter position. The chlorination results, however, are similar to those obtained for 1-aminoanthraquinone and support the suggestion that the size of the attacking reagent is of great importance in these particular reactions.

The corresponding substitution pattern observed for 2-methylaminoanthraquinone shows similarities to its amino-analogue on chlorination and bromination but differences on iodination. Molecular models show that both the amino- and methylamino-substituents can freely rotate without hindrance. The introduction of a bulky substituent such as iodine into the 1-position of 2-methylaminoanthraquinone, however, restricts free rotation and suggests that steric effects are important also in the reaction of this system.

It is concluded that the charge density indices calculated by the CNDO/2 method correlate well with the experimentally determined positions of electrophilic substitution for reagents with low selectivity, such as those produced during nitration and sulphonation, provided that steric effects are small or absent. Furthermore, the localisation energies calculated for protonation by the same method correlate reasonably well with the experimental results obtained for reagents with high selectivity such as chlorine. The correlation falls away for bromination however, and this has been attributed to steric interactions between the bromine molecule and the carbonyl group.

EXPERIMENTAL

AnalaR grade reagents were used throughout the work. The anthraquinone starting materials were purified by column chromatography prior to use. Glass plates coated with 0·5-mm Silica Gel G (Merck Chemicals) were used for t.l.c. analysis and either pyridine–cyclohexane (10 : 90), acetone–toluene (5 : 95), or dioxan–n-butanol–ammonia–water (50 : 25 : 12·5 : 12·5) used as eluant. Each component present in the product mixtures was identified by comparison with an authentic sample (Fine Chemicals, I.C.I. Ltd.). Isomers were separated by t.l.c. and estimated by u.v. spectroscopy in pyridine solution or water on a Unicam SP 700 in the wavelength range 450—550 nm.

Halogenation.—An acetic acid solution (300 ml) of the amino-compound (1·11 g, 5·0 mmol) was treated with an 0·015M-solution of halogen (100 ml) and the resulting solution was agitated at 25° for 30 min. After dilution with water (1 l), the product mixture was filtered off at the pump, washed acid-free with water, and dried (P_4O_{10} *in vacuo*). For the case of iodination, silver acetate (0·25 g, 1·5 mmol) was added to the amino-compound solution prior to the addition of halogen. A number of halogenation experiments were also carried out in nitromethane and carbon tetrachloride. Owing to the lower solubility of 1-aminoanthraquinone in these solvents, the proportion of solvent to amine and halogen was increased by a factor of five. The products in each case were isolated by evaporation of the solvent and direct estimation by t.l.c.

Nitration.—Nitric acid (0·10 g, 1·5 mmol) was added to a solution of the amino-compound (1·11 g, 5·0 mmol) dissolved in a mixture of acetic acid (20 g) and 100% sulphuric acid (80 g) at 0°, and the resulting solution was agitated for 30 min. After dilution with water (1 l), the product mixture was filtered off at the pump, washed acid-free with water, and dried (P_4O_{10} *in vacuo*). Attempts to nitrate the amino-compounds in acetic acid alone were unsuccessful.

Sulphonation.—Chlorosulphonic acid (0·35 g, 3 mmol) was added to a solution of the amino-compound (2·22 g, 10 mmol) in a 100% sulphuric acid (20 g) and the resulting solution was heated at 100° for 3 h with agitation. On cooling, the product mixture was diluted with water and the insoluble starting material was filtered off at the pump and washed with water. The aqueous filtrate and washings were neutralised with aqueous sodium hydroxide and the product composition was estimated directly by t.l.c. Attempts to sulphonate the amino-compound with chloro-

[29] P. D'Antonio, *Diss. Abs.*, *B*, 1967, **28**(5), 1877.

sulphonic acid, sulphuric acid, oleum, or sulphur trioxide (3 mmol in each case) in acetic acid or dioxan were unsuccessful.

In some of the reactions, the products obtained contained small amounts of disubstituted and *N*-substituted products. No allowance has been made for these products in Table 3. There was no evidence to suggest that substitution had occurred at any ring position other than those specified in Table 3.

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