Interaction between Electron Donor and Acceptor Groups in Some Trisubstituted Benzenes. Part 1. Relative Reactivities of 4-Substituted 1,2-Dinitrobenzenes towards Sodium Methoxide

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In an effort to study the effects of 'through conjugation' on the properties of some 1,2,4-trisubstituted benzenes, the rates of reaction of a series of four 4-substituted 1,2-dinitrobenzenes with sodium methoxide in methanol have been studied. Although reactivities at the 2-position were qualitatively in the order to be expected from inductive effects, those at the 1-position were highly sensitive to the influence of mesomeric donor action of the 4-substituent. Relatively large effects were seen for the 4-alkyl derivatives; and C–H hyperconjugation appeared to be stronger than C–C hyperconjugation.

Almost all the extensive quantitative work on the effects of substituents on the properties of aromatic compounds has employed monosubstituted or disubstituted derivatives, with the aromatic ring system itself or one of the substituents serving as the probe group.[1–5] Although the interpretation of these effects in terms of the constituent factors and the relative importance of the latter in each type of measurement have been the subject of many studies, uncertainties have remained.[4,6–11] *p*-Disubstituted benzenes in which there is conjugative interaction between the substituents across the benzene ring, *i.e.* systems having 'through conjugation,' have always been troublesome in dual parameter analysis of substituent effects in the linear free energy relationship (LFER) approximation.[4,12,13] The problem of the variation of the nature of the response of donor groups with the strength of the interacting acceptor group has remained, in spite of the adoption of a variety of σ_R scales.[4,14,15] A recent example is the anomalous increase in ν_{16} vibrational band intensities for *p*-disubstituted benzenes with donor–acceptor type of combination of substituents.[16–18] The correlation between absorbance and the square of the difference of σ_R values, which has satisfactorily described the behaviour of other such disubstituted derivatives, did not work in these cases, and the interpretation of the additional terms that appeared to be present was ambiguous.

In a series of investigations now to be reported, we have examined a number of properties of selected series of 1,2,4-trisubstituted benzenes having acceptor groups in the positions 1 and 2 and donor groups in the 4-position, in the hope that the results would give further useful information on the nature of the interaction between the donor and the acceptor groups. Techniques used include kinetic, spectroscopic, and electrochemical. The presence of steric effects in the type of substrate chosen does not necessarily lead to greater complication in the consideration of every aspect of their electronic interaction. In fact, it will be seen in due course that the steric interaction actually helps to bring into sharper focus the effects of donor–acceptor interaction. We present in this initial account the results of a kinetic study of the relative reactivities of a set of 4-substituted 1,2-dinitrobenzenes towards sodium methoxide in methanol, which illustrates the remarkable sensitivity of this system to conjugative interaction. Some preliminary indication of this sensitivity is available in the known difference in reactivity between the nitro groups of 4-chloro-1,2-dinitrobenzene,[19] which must have its origin in mesomeric electronic release from the chloro group. Electron release from alkyl groups in this mode is known to be weaker and the strength of such release, *i.e.* the importance of hyperconjugation, has been a matter of controversy.[20,21] In the present context, therefore, the behaviour of the alkyl derivatives appeared particularly interesting. Thus, the series of substrates studied includes methoxy, methyl, and t-butyl derivatives in addition to 1,2-dinitrobenzene itself. Since the early work of Holleman and others,[19] which included only halogen derivatives, no further kinetic study of substituent effects on the reactivity of these systems towards nucleophiles seems to have been performed.

Experimental

Materials and Methods.—1,2-Dinitrobenzene (B.D.H. reagent grade) was used after recrystallization from ethanol (m.p. 118 °C). 4-Methyl-1,2-dinitrobenzene was prepared from 4-methylaniline *via* the 2-nitro derivative, using the method of Hodgson *et al.*[22] for replacement of the amino group. The methoxy analogue was prepared from 4-methoxy-2-nitroaniline by the same procedure. Both these derivatives were purified first by chromatography on a short alumina column and then by repeated crystallizations from ethanol (m.p.s 61 and 70 °C, respectively). The t-butyl derivative was prepared by nitration of 1-nitro-3-t-butylbenzene as reported,[23] and purified by distillation (b.p. 170 °C at 2 mmHg).

Pure, dry methanol for use as solvent was prepared from the commercial material according to the method of Lund and Bjerrum.[24]

Products.—The reaction with sodium methoxide gave single products from two of the four derivatives studied. Thus, 1,2-dinitrobenzene and its 4-methoxy derivative gave, respectively, 2-nitroanisole and 5-methoxy-2-nitroanisole as sole products. However, for the methyl and t-butyl derivatives, the products were found to be simple two-component mixtures with the help of their n.m.r. spectra.† The dominant reaction was the displacement of the nitro group *meta* to the alkyl group. Since separation of these product mixtures into their components by chromatography was not easy, the identities of minor products were established by independent syntheses and comparison of the aromatic regions of their n.m.r. spectra with those for the product mixtures. The proportions of displacement of *para* nitro groups were ascertained to be about 14 and 23% respectively, and remained roughly constant within the accuracy of n.m.r. intensity measurements for all kinetic runs in

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† The susceptibility of 4-methyl-1,2-dinitrobenzene to nucleophilic attack at both 1- and 2-positions has been known for some time.[25] With sodium methoxide formation of stilbene derivatives is a possibility.[25a] However, with the low concentrations involved in our experiments this reaction was not observed.

the narrow temperature range (30—50 °C) over which rate measurements were made. The aryl methyl signals of the products from the methyl derivative and the methoxy signals of the products from the t-butyl derivative proved convenient for determining product ratios. The aryl methyl signals of 3-methyl-6-nitroanisole and 4-methyl-6-nitroanisole occurred at δ 2.41 and 2.33. The corresponding t-butyl derivatives showed methoxy absorptions at δ 3.96 and 3.91. For the stronger signals, errors in the intensity measurements were about 2%. The accuracies obtainable for the weaker signals were much lower. No attempt was therefore made in this study to measure the variation of relative reactivities at the two positions with temperature within the small range employed.

Rate Measurements.—All rate measurements were made in pure methanol as solvent. The concentrations of sodium methoxide and dinitro compounds were varied between 0.03 and 0.04M for the former and 0.03 and 0.2M for the latter. For each individual run, the reagent concentrations within these limits were chosen so as to obtain an amount of reaction which would assure reasonable accuracy of measurement. Reaction temperatures could be regulated to within ±0.05 °C.

The reactions were followed by titration with HCl. Samples were quenched in an excess of ice-cold distilled water in titration flasks kept in crushed ice, and titrated against standard acid.* Since the substrate nitro compounds were insoluble in water, this procedure was very effective. In experiments with the methyl and t-butyl derivatives, the products were extracted, along with unchanged substrate, from the titrated samples using chloroform. The extracts were dried, concentrated, and examined by n.m.r. The resulting product ratios were used for evaluation of k_p and k_m, the specific reaction rates for the 1- and 2-positions. Clean second-order kinetics were obtained in all cases. The details of a set of individual experiments are shown in Table 1. Each experiment was repeated at least five times so that consistency could be checked. When three or more consistent values were obtained their average was taken as the correct rate constant (Table 2).

Arrhenius parameters were obtained from the rate constants of Table 2 from plots of log k *vs.* T^{-1}.

Results and Discussion

The rate constants in Table 2 show that reactivity decreases in the order OMe > H > Me > Bu^t. Except for the methoxy derivative, these figures represent the sums of reactivities at two positions. However, for a meaningful discussion, we require the partial reaction rates involved. The partial rates for the alkyl derivatives were obtained as mentioned earlier, and those for 50 °C are presented in Table 3 along with corresponding values for the others. These proved adequate for our purposes.

The rate constants for the displacement of the nitro group *meta* to the substituent groups are qualitatively in the order expected from their inductive effects (σ_m: OMe +0.11; Me −0.07; Bu^t −0.10),[26a] the electron-withdrawing group increasing the reactivity and the alkyl groups acting in an opposite sense. Any secondary effect on the reactivity at the 2-position arising from conjugative interaction between the 4-substituent and the 1-nitro group with resulting change in conformation is apparently not large enough to disturb the inductive order seriously.

However, the reactivity pattern for the nitro group *para* to the substituent, *i.e.* at the 1-position, is quite different. The order is H > Bu^t > Me > OMe. For both the alkyl derivatives, the reactivity is sharply reduced, and, for the methoxy compound, it is totally suppressed. The enhancement of nucleophilic reactivity for the 2-position in the 4-methoxy derivative and the total lack of reactivity for the 1-position are in general agreement with expectations. We have already noted that even for the chloro derivative (for which one might ordinarily expect the effect of inductive electron withdrawal to be more than that of mesomeric electron donation) the reactivity at the 1-position is negligible in comparison with that at the 2-position. For the methoxy derivative, where there is a large net donor effect, the observed behaviour is therefore not surprising. However, the data for the alkyl derivatives are more interesting since mesomeric effects here are known to be weaker than for the chloro derivative. We have already noted that the relative magnitudes of the decrease in reactivity at the 2-positions in these derivatives are roughly in the order expected from inductive effects, although they may be influenced to a smaller

Table 1. Rate constants for the reaction of 4-substituted 1,2-dinitrobenzenes with sodium methoxide at various temperatures and concentrations

Subst.	Concentrations of reagents: Alkali molarity	Substrate molarity	t/°C	k/l mol^{-1} h^{-1}
OMe	0.122	0.067	30	0.652
OMe	0.125	0.050	35	1.067
OMe	0.080	0.050	40	1.960
OMe	0.046	0.050	45	3.961
OMe	0.036	0.050	50	7.424
H	0.200	0.100	30	0.312
H	0.137	0.083	35	0.786
H	0.093	0.067	40	1.110
H	0.037	0.067	45	1.980
H	0.060	0.033	50	4.571
Me	0.033	0.200	30	0.128
Me	0.166	0.083	35	0.255
Me	0.139	0.067	40	0.450
Me	0.110	0.067	45	0.897
Me	0.036	0.050	50	2.010
Bu^t	0.398	0.200	30	0.101
Bu^t	0.139	0.100	35	0.247
Bu^t	0.115	0.067	40	0.388
Bu^t	0.124	0.071	45	0.743
Bu^t	0.039	0.050	50	0.679

Table 2. Rate constants (k/l mol^{-1} h^{-1}) for the reaction of 4-substituted 1,2-dinitrobenzenes with sodium methoxide at various temperatures

Subst.	T/°C: 30	35	40	45	50
OMe	0.608	1.155	1.964	4.062	7.472
H	0.326	0.787	1.137	2.016	4.571
Me	0.124	0.255	0.462	0.833	1.981
CMe$_3$	0.105	0.233	0.368	0.744	1.669

Table 3. Partial rate constants for the reaction of 4-substituted 1,2-dinitrobenzenes with sodium methoxide at 50 °C

Subst.	k/l mol^{-1} h^{-1}	K_p	K_m
OMe	7.472	0.00	7.472
H	4.571	2.285	2.285
Me	1.981	0.277	1.704
Bu^t	1.669	0.384	1.285

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* The usually preferred procedure of quenching in an excess of acid and titrating against alkali was not practicable in this case. The displaced group was nitrite ion, and the instability of nitrous acid that would be formed in acid solution would result in an acid-consuming decomposition.

extent by resonance effects as well. Since the reactivity of the 1-nitro group would be susceptible to mesomeric interaction in full strength, a further decrease of reactivity is to be expected. However, it is remarkable that the observed lowering is much more for the methyl derivative than for the t-butyl derivative. The rate for the former is only about 70% of the latter. This reactivity difference cannot be be attributed to any steric effect. The nucleophilic displacement involved is presumably a two-stage process where the first stage is the formation of a Meisenheimer-type adduct and the second its decomposition. The observed effects of the substituents on the reactivity at the 2-position clearly indicate that the first stage is rate-determining. The difference between affinities of methoxide and nitrite ions for electron-deficient sites is so large that there cannot be any doubt about the relative ease of decomposition of the intermediate in the forward and reverse directions. The expected effects of any steric hindrance to reagent approach or solvation of the anionic transition state would therefore be in the opposite direction for either of the two positions. We conclude that the substrate system here is highly susceptible to the effects of mesomeric electron donor action of the substituent and that such action is undoubtedly more for the methyl group.

It is useful to consider the significance of the k_p/k_m values in the light of the Taft–Lewis-type relations (1) and (2) for relative reactivities, which have been found to describe satisfactorily the behaviour of several series of reactions.[12] The quantity log

$$\log\,(k_m/k_o) = \rho(\sigma_{\mathrm{I}} + \alpha\sigma_{\mathrm{R}}) \qquad (1)$$

$$\log\,(k_p/k_o) = \rho(\sigma_{\mathrm{I}} + \sigma_{\mathrm{R}}) \qquad (2)$$

$$\therefore\ \log\,(k_p/k_m) = \rho\sigma_{\mathrm{R}}(1 - \alpha)$$

(k_p/k_m) may be conveniently used for comparison of resonance effects of substituents in a given series, since ρ and α are constants for the series. The log (k_p/k_m) values for the methyl and t-butyl derivatives are -0.79 and -0.52, respectively. This implies that the value for the methyl group exceeds that for the t-butyl group by an unusually large factor. The assumption implied in the Taft–Lewis relations that the effects of 'induction', whatever they are, are the same for the *meta* and *para* positions may be questioned. However, so long as such effects are larger for the t-butyl group than for the methyl, our qualitative conclusions will not be altered. It is of interest that, in the $\sigma_{\mathrm{R}}^{\mathrm{BA}}$ scale, the value for the methyl group exceeds that for the t-butyl group by less than 10%.[26b] The experimental data here appear in better accord with σ_p^+ values (Me -0.31; Bu^t -0.26),[26a] although the electron-deficient ground state, which is the prime determinant of activation energy, is uncharged. For comparison we recall that in the σ_{R}^0 scale, the order of electron release for the alkyl groups is reversed, the value for the methyl group being smaller than that for the t-butyl group by at least 20%.[27]

Although the explicit estimation of activation energies for reactions at the 1- and 2-positions of the alkyl derivatives has not been possible, and the expected difference in $E^{\ddagger}$ values for the alkyl derivatives is relatively small, it is still of interest to see if the conclusions arrived at from considerations of relative rates of reaction at a single temperature can be confirmed by the Arrhenius parameters now available (Table 4). It can be seen that the larger activation energy values are associated with the larger frequency factors. It is also of interest that the effect of the increase in the frequency factors is never sufficient to offset the effect of increase in activation energy. This situation has its own clear implication for the significance of the difference in k_p values obtained for the alkyl derivatives. However, we would prefer to have more definitive indications.

Table 4. Arrhenius parameters for the reaction of 4-substituted 1,2-dinitrobenzenes with sodium methoxide

Subst.	$E^{\ddagger}$/cal[a]	log PZ
OMe	24 030	17.10
H	24 940	17.20
Me	25 630	17.58
Bu^t	26 080	17.84

[a] 1 cal = 4.184 J.

Fairclough and Hinshelwood observed that for several series of reactions the Arrhenius parameters could be correlated by equations (3),[28–30] where C and M are constants for the series

$$\log PZ = \mathrm{C} - \mathrm{M}/E^{\ddagger\frac{1}{2}} \qquad (3)$$

concerned. A theoretical explanation for this was suggested. A plot of log PZ *vs.* $E^{\ddagger-\frac{1}{2}}$ for the parameters of Table 4 showed that, to a good approximation, the relation of equation (3) holds for the present series also, M and C being 3 124 and 37.145, respectively. If we assume that this single relationship is applicable to reactions at both 1- and 2-positions, it is possible to obtain a very good indication of the difference in activation energies for reactions of the alkyl derivatives at the 1-position, *i.e. para* to the substituent, using our approximate values of k_p/k_m. Since the reactivites at this position for both the alkyl derivatives are only small fractions of the total reactivities, and for a change in reaction rate by a factor *e* we require only a change of 600—640 cal in activation energy in the temperature range of our interest, the actual values of $E_m^{\ddagger}$ will be smaller than the observed weighted averages by only very small amounts. In fact, the difference between $E_m^{\ddagger}$ and $E_p^{\ddagger}$ cannot be very large for either derivative since the reactivities at the 1-positions amount to 14 and 23%, respectively, for the methyl and t-butyl derivatives. From equation (3), equation (4) can be

$$\begin{aligned}\log\,(k_p/k_m &= (\mathrm{M}/E_m^{\ddagger\frac{1}{2}} + E_m^{\ddagger}/2.303\,RT) - \\ &\qquad (\mathrm{M}/E_p^{\ddagger\frac{1}{2}} + E_p^{\ddagger}/2.303RT) \\ &= \mathrm{f}(E_m^{\ddagger}) - \mathrm{f}(E_p^{\ddagger})\end{aligned}$$

$$\text{where } \mathrm{f}(E^{\ddagger}) = \mathrm{M}/E^{\ddagger\frac{1}{2}} + E^{\ddagger}/2.303RT \qquad (4)$$

readily derived. This means that with any given value of k_p/k_m we can obtain likely $E_p^{\ddagger}$ values for $E_m^{\ddagger}$ values anywhere in the range of interest. What is required is only a plot of f($E^{\ddagger}$) against $E^{\ddagger}$ for the range concerned. Since the $E^{\ddagger}$ values for the methyl and t-butyl derivatives shown in Table 4 are approximate $E_m^{\ddagger}$ values, a corresponding set of $E_p^{\ddagger}$ values could be read from this graph. The figures obtained are about 28 100 and 27 700 cal for the methyl and t-butyl derivatives, respectively. The difference of around 400 cal apparently represents mostly the effect of the increase in the strength of conjugative interaction in the ground state in the change from the t-butyl to the methyl derivative. The pronounced sensitivity of the reactivity of the *ortho* dinitro grouping to conjugative interaction is presumably to be attributed to the high electron demand prevailing at the reaction sites.

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