197. *The Associating Effect of the Hydrogen Atom. Part III. Further Examples of Steric Interference between Vicinal Groups.*

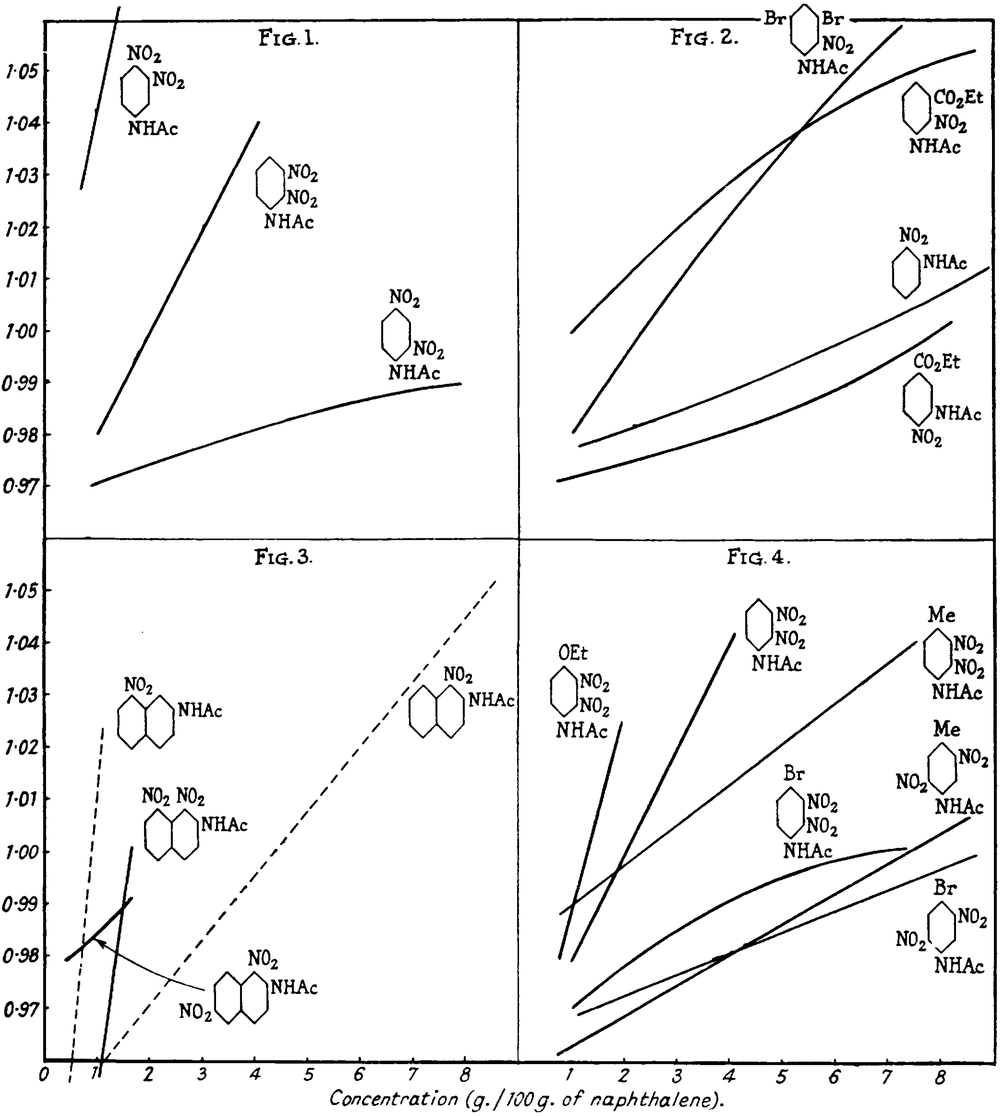
By Hubert O. Chaplin and Louis Hunter.

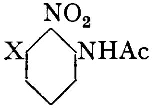
A marked diminution of properties dependent upon chelation is brought about by the introduction of a substituent into *o*-nitroacetanilide in the 3-position. This fact is interpreted as evidence of a restricting effect by the new substituent on the nitro-group, which is rotated into a position no longer co-planar with the benzene nucleus. By a comparison of the behaviour of 2 : 3-dinitroacetanilide (V; X = H) with its 4-substituted derivatives (V), evidence is obtained of a transmission of steric effects along the four adjacent groups, provided the substituent in position 4 is sufficiently large (Br, CH_3). The properties compared are wet melting-point depression and cryoscopic behaviour in naphthalene solution.

In so far as steric restriction is concerned, there is presumably complete freedom of rotation about the single bond between nitrogen and the nucleus in the molecule of acetanilide. Evidence was adduced in Part II (this vol., p. 375) that suitably constituted *o*-substituents can, by chelating with the anilide hydrogen atom, so fix the position of the groups that their constituent atoms are more or less accurately coplanar with the benzene nucleus. It was further shown that substitution of a group in the second ortho (or 6)-position may so interfere with the acetamido-group as to rotate it into a position transverse to the plane of the benzene nucleus, with a consequent diminution of properties dependent upon chelation.

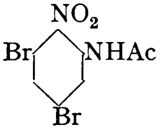
It is now shown that the rotation of the nitro-group in nitrobenzene about the

N–nuclear bond can be similarly restricted by introducing groups into the *o*- and the *o′*-position. Evidence of this effect is based on a comparison of the cryoscopic and wet melting-point behaviour (see Part II) of *o*-nitroacetanilide (I; X = H) with that of 2 : 3-dinitroacetanilide (I; X = NO_2), 2-nitroaceto-*m*-toluidide (I; X = CH_3), *ethyl* *2-nitro-3-acetamidobenzoate* (I; X = CO_2Et), and 3 : 5-dibromo-2-nitroacetanilide (II). As a check, comparison was also made with as many isomers as possible in which the





(I.)



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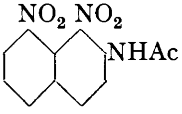

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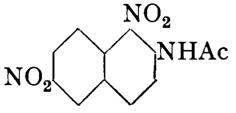

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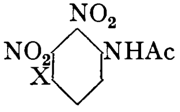


(V.)

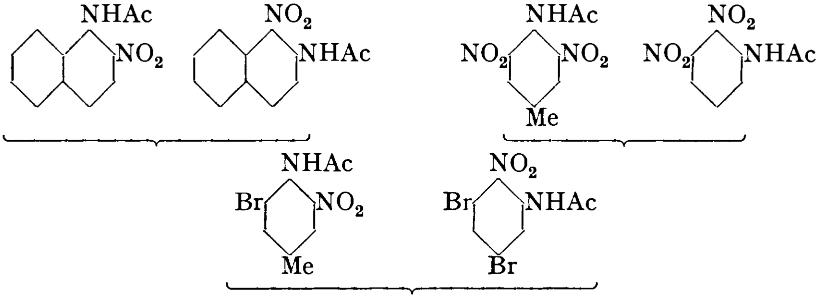
effect would not be expected. The results show that substitution of a group in the 3-position of *o*-nitroacetanilide markedly decreases its chelating and increases its associating tendencies. Reference to the association–concentration curves (Fig. 1) will show that, whilst 2 : 4-dinitroacetanilide is unassociated (as indicated by a flat curve), and 3 : 4-dinitroacetanilide is associated (as indicated by a steep curve), the vicinal 2 : 3-isomer (I; $X = NO_2$) shows a curve of intermediate slope. The same tendencies are borne out in the wet melting-point data shown in the following table, 2 : 3- resembling the non-chelate 3 : 4- rather than the chelate 2 : 4-dinitroacetanilide.

	M. p.	Wet m. p.	Δ.	
o-Nitroacetanilide	92°	82°	10°	Unassociated.
2 : 4-Dinitroacetanilide	121	110	11	Unassociated.
3 : 4-Dinitroacetanilide	144—145	112	32—33	Associated.
2 : 3-Dinitroacetanilide	186—187	156	30—31	Associated.

The same effect (Fig. 2) has also been detected in substances where group X in (I) is methyl, carbethoxy, or bromine (as in II), and in each case the properties of the vicinal compound (I) lie intermediate between those of the chelate isomer and those typical of a normal anilide (see Part I, J., 1937, 1114). It would appear that the substitution of a group in the 3-position of *o*-nitroacetanilide has the effect of rotating the nitro-group into a position non-coplanar with the benzene nucleus. This removes the nitro-oxygen atom too far from the amide hydrogen atom to permit of chelation, so that the molecular association usual in amides (see Part I) reasserts itself.

The comparison of 1 : 8-dinitroaceto-2-naphthalide (III) with its 1 : 6-isomer (IV) is rendered difficult by their sparing solubility in naphthalene, but the slopes of the association–concentration curves (Fig. 3) are in the expected order, showing the former to be less chelated than the latter. On the other hand, from previous measurements on 1-nitroaceto-2-naphthalide (see Part II, p. 378, Fig. 5), it would appear that a nitro-group substituted in the α-position in the naphthalene nucleus itself suffers some steric restriction from the *peri*-CH group. This fact would tend to diminish any observed differences in chelate character between (III) and (IV).

Although it is impossible, in view of the semi-quantitative nature of the results summarised above, to give them any exact interpretation, it seems justifiable to conclude that in passing from *o*-nitroacetanilide to derivatives of formula (I) there is a reduction in the proportion of chelated molecules. It is probably more accurate to represent the molecular condition of *o*-nitroacetanilide as an equilibrium between molecules possessing intra- and those with inter-molecular hydrogen bonds; such an equilibrium can be conveniently expressed, chelate molecules $\rightleftharpoons$ associated molecules. The time spent by an individual molecule in the chelate condition is profoundly influenced by the substitution of groups in the 3- or the 6-position. Thus, the above equilibrium is displaced to the right by the substitution of a group ortho to the acetamido-group (for examples, see Part II) or to the nitro-group (present paper). That the steric effect on these two groups of an ortho-substituent will not be identical in magnitude would be expected on geometrical grounds, and it is confirmed experimentally that steric interference between a given ortho-substituent and the large acetamido-group is more pronounced than that suffered by the smaller nitro-group. Thus, in the preceding pairs of *o*-nitroacetamido-compounds, those in which the acetamido-group is situated between two substituents (the first of each pair) are markedly less chelate than those in which the acetamido-group is the extreme substituent of a vicinal trio (the second of each pair).



	Concn.	*M.*	α.	M. p.	Wet m. p.	Δ.
Fig. 1.						
3 : 4-Dinitroacetanilide (225)	0·73	231·1	1·03	144—145°	112°	32—33°
	2·15	248·5	1·105			
	3·18	266·6	1·185			
	4·27	280·6	1·25			
2 : 3-Dinitroacetanilide (V; X = H)	1·00	220·1	0·98	186—187	156	30—31
	2·01	225·6	1·00			
	3·08	229·6	1·02			
	4·03*	234·7	1·04			
2 : 4-Dinitroacetanilide	0·89	219·0	0·97	121	110	11
	2·15	219·5	0·975			
	3·78	219·9	0·98			
	5·87	220·6	0·98			
	7·86	222·5	0·99			
FIG. 2.						
o-Nitroacetanilide (180) (cf. Auwers and Pelzer, *Z. physikal. Chem.*, 1897, **23**, 449)	1·44	176·6	0·98	92	82	10
	3·69	176·8	0·98			
	5·96	179·5	1·00			
	8·42	181·9	1·01			
	10·15	183·6	1·02			
3 : 5-Dibromo-2-nitroacetanilide (338) (II)	1·04	332·1	0·98	184—185	156	28—29
	2·515	338·3	1·00			
	4·46	348·4	1·03			
	7·63	357·2	1·06			
Ethyl 2-*nitro*-3-*acetamidobenzoate* (252) (I; X = CO_2Et)	0·99	253·0	1·00	133	113	20
	2·23	256·1	1·02			
	4·04	257·1	1·02			
	6·43	262·5	1·04			
	8·61	265·8	1·055			
Ethyl 4-*nitro*-3-*acetamidobenzoate*	0·94	244·5	0·97	92	81	11
	2·12	248·0	0·98			
	4·02	247·7	0·98			
	6·31	248·9	0·99			
	8·145	251·7	1·00			
2-Nitroaceto-*m*-toluidide (I; X = CH_3)	(Not measured)			126	104	22
Fig. 3.						
1 : 8-Dinitroaceto-2-naphthalide (275) (III)	0·78	260·3	0·94	235	196	39
	1·24	267·2	0·97			
	1·67*	275·6	1·00			
1 : 6-Dinitroaceto-2-naphthalide (IV)	0·52	269·7	0·98	224	192	32
	1·03	270·2	0·98			
	1·50*	272·7	0·99			
Fig. 4.						
2 : 3-Dinitroaceto-*p*-phenetidide (269) (V; X = OEt)	0·83	263·5	0·98	210	175	35
	1·42	272·6	1·01			
	1·94*	275·4	1·02			
4-Bromo-2 : 3-dinitroacetanilide (304) (V; X = Br)	1·07	296·3	0·97	188	161	27
	2·22	299·3	0·98			
	5·415	304·4	1·00			
	7·385	303·6	1·00			
4-Bromo-2 : 5-dinitroacetanilide	1·15	294·5	0·97	152	139	13
	2·74	297·0	0·98			
	4·33	296·2	0·97			
	6·82	301·1	0·99			
	8·53	302·7	1·00			
2 : 3-Dinitroaceto-*p*-toluidide (239) (V; X = CH_3)	0·72	235·5	0·99	173	147	26
	2·10	237·7	0·995			
	3·75	241·0	1·01			
	5·635	245·0	1·025			
	7·38	248·2	1·04			
2 : 5-Dinitroaceto-*p*-toluidide	0·845	229·4	0·96	122	112	10
	2·04	231·8	0·97			
	3·63	233·2	0·98			
	5·545	235·8	0·99			
	8·28	240·1	1·005			
2 : 3-Dinitroaceto-*p*-anisidide (V; X = OMe)	(Too insoluble for measurement)			222	189	33
3 : 5-Dinitroaceto-*p*-anisidide				157	115	42

* Solute separates at higher concentrations.

A further important difference is that the transverse positioning of the acetamido-group in the former type should lead in the extreme case to optical activity, a conclusion which has been experimentally realised in a related substance by Mills and Kelham (J., 1937, 274), whilst the symmetry of the nitro-group would preclude this in the latter type.

In view of the evidence cited above of mutual steric interference between vicinal groups, it seemed desirable to examine the effect of four groups occupying adjacent positions in the benzene nucleus. For this purpose 2 : 3-dinitroacetanilide (I; X = NO_2) was compared with derivatives having a substituent in the 4-position (V). Unfortunately, compounds of this complexity are usually only sparingly soluble in naphthalene, but among the few substances examined some showed a slight but definite increase of chelate character compared with 2 : 3-dinitroacetanilide. The suggestion is made that in (V) the group X, if sufficiently large, can orientate the adjacent nitro-group transverse to the plane of the benzene nucleus; this facilitates the assumption by the 2-nitro-group of a mean position more nearly coplanar with the nucleus, it being then more favourably situated to achieve chelation with the neighbouring acetamido-group. This transmission of steric effects from group to group must be considered to affect the time spent by individual molecules in the chelate, as opposed to the associated, condition, with a consequent change in the balance of the chelate $\rightleftharpoons$ associated equilibrium. The magnitude of the effect will depend upon the character, and particularly the size, of the group X (V). From a comparison of the slope of the association–concentration curves (Fig. 4) it is clear that the most marked steric effect is produced by the large bromine atom (*i.e.*, in 4-bromo-2 : 3-dinitroacetanilide; V, X = Br), and to a less extent by the smaller methyl group (*i.e.*, in 2 : 3-dinitroaceto-*p*-toluidide; V, X = CH_3). Evidently the ethoxy-group in 2 : 3-dinitroaceto-*p*-phenetidide (V; X = OEt), owing perhaps to the angular distribution of the oxygen valencies, is not effective in producing a steric effect, there being little or no difference in slope between the curve due to this substance and that of 2 : 3-dinitroacetanilide. Although the wet melting-point data are not opposed to this view, the depressions do not differ sufficiently to be of significance.

In the preceding tables and for the curves, the apparent molecular weight, M, and the association factor, α, have been calculated, as in the previous parts of this series, according to the ideal-solution laws. The concentrations are given as g./100 g. of naphthalene, and Δ is the depression of melting point in the presence of water. Melting points and wet melting points were taken with the same thermometer throughout and are uncorrected. Figures in parentheses indicate the normal molecular weight. The broken curves in Fig. 3 are taken from Part II.

EXPERIMENTAL.

Molecular weights were measured cryoscopically in naphthalene. The following new compounds were prepared in the course of the investigation.

Ethyl 2-*nitro*-3-*acetamidobenzoate* was prepared from the corresponding acid (Kaiser, *Ber.*, 1885, **18**, 2946) by conversion into the silver salt and subsequent interaction with ethyl iodide in benzene suspension. The product crystallised from alcohol in white needles, m. p. 133° (Found: N, 11·0. $C_{11}H_{12}O_5N_2$ requires N, 11·1%). *Ethyl* 4-*nitro*-3-*acetamidobenzoate*, prepared similarly, formed bright yellow needles, m. p. 92° (Found: N, 11·3%).

An attempt to esterify 2-nitro-3-acetamidobenzoic acid by the Fischer–Speier method yielded a mixture of the expected ethyl ester with a substance crystallising in bright yellow needles, m. p. 48—49°, which proved to be *ethyl* 2-*nitro*-3-*aminobenzoate* (Found: N, 13·15. $C_9H_{10}O_4N_2$ requires N, 13·3%), since acetylation converted it into ethyl 2-nitro-3-acetamidobenzoate.

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