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Synthese und Reaktionsmechanismen in der Farbstoffchemie

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3. Internationale Farbensymposium

statt. Alle an dieser Arbeitstagung gehaltenen Vorträge waren dem obengenannten Thema gewidmet. Vier der Hauptvorträge wurden am 19. Mai für ein erweitertes Auditorium gehalten. Sie finden sich nachfolgend abgedruckt. Für die übrigen Vorträge sei auf das demnächst im Verlag Sauerländer erscheinende Supplementum zum Band 22 der *Chimia* hingewiesen: *3. Internationales Farbensymposium. Synthese und Reaktionsmechanismen in der Farbstoffchemie.* Es enthält alle am Symposium vorgetragenen Arbeiten, teils *in extenso*, teils in gekürzter Form. Das Supplementum kann direkt beim Verlag oder durch den Buchhandel bezogen werden.

Substitution Reactions in Aromatic Systems

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Summary

Quantitative aspects of recent developments in theories of electrophilic aromatic substitution are reviewed, and it is shown how better understanding of these theories can help to predict with greater accuracy, optimum conditions for maximum yield of a required product in a given substitution.

Particular reference is made to the acid-catalysed hydrogen-exchange reaction as a tool for diagnosing new electronic effects, and to its usefulness in predicting isomer product ratios in other substitutions. In relation to this, new quantitative work on the electrophilic substitution of some derivatives of naphthalene is described in some detail.

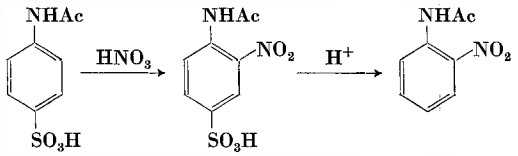
Some recently elucidated factors which affect the *ortho: para*-ratios are described and the need to consider strain as a factor in controlling isomer ratios in substitution of aromatics possessing cyclic side-chains is emphasized.

The broad aims of a preparative organic chemist can perhaps be summarized as the production of (i) new compounds, (ii) previously known compounds with improved purity, and (iii) previously known compounds by easier and more economic routes. Theories of electrophilic substitution are useful to the preparative chemist primarily if they help to fulfil these aims. Recent theoretical developments which bear on these requirements concern the Hammett equation, the *ortho:para*-ratio, and strain effects, and may be conveniently considered under these headings.

Electrophilic substitution reactions of aromatic compounds may be conveniently subdivided into the following four categories,[1] and in each of these a substituent in the ring is replaced by another and leaves without the electrons which formerly bonded it to the ring:

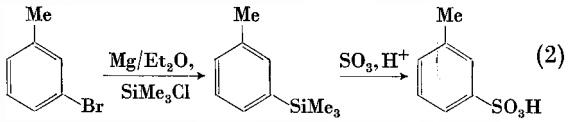
(i) Reactions in which hydrogen is replaced by some other substituent, e.g. in nitration, halogenation, and sulphonation. These reactions are the best known for they are still the most useful from the preparative viewpoint.

(ii) Reactions in which hydrogen replaces some other substituent. These are less well known but have considerable synthetic usefulness, particularly in that a group used for blocking a given site in the aromatic ring can subsequently be removed e.g. in protodesulphonation (1).



(1)

(iii) Reactions in which one substituent replaces another and neither is hydrogen. These are the subject of more recent studies in electrophilic aromatic substitution and sulphodisilyation (2) is an example of their preparative usefulness.[2]



(2)

[1] R.O.C. Norman and R. Taylor, *Electrophilic Substitution in Benzenoid Compounds*, Elsevier, Amsterdam 1965.

[2] C. Eaborn and T. Hashimoto, *Chem. & Ind. 1961*, 1081; R. W. Bott, C. Eaborn and T. Hashimoto, *J. Chem. Soc. 1963*, 3906.

The product *m*-methylbenzenesulphonic acid is otherwise difficult to obtain.

(iv) Reactions in which hydrogen replaces hydrogen. The kinetics of these hydrogen-exchange reactions are followed by using hydrogen in isotopic forms and following changes in the deuterium or (more usually nowadays) the tritium content of the aromatic by means of infra-red or scintillation counting techniques, respectively. These reactions are apparently synthetically useless and have therefore received less attention than they deserve, for in fact studies of these reactions can lead to very useful information and some of the recent developments in electrophilic substitution are described below with particular reference to the hydrogen-exchange reaction.

The Hammett Equation

The Hammett Equation (3) has been successfully applied to electrophilic substitution by H.C. BROWN and his co-workers,[3]

$$\log \frac{k}{k_0} = \varrho\sigma \qquad (3)$$

by employing modified sigma values (derived from the S_N1 solvolysis of *t*-cumyl chlorides, $ArCMe_2Cl$) and designated σ^+, which take account or resonance interactions which are virtually absent in the standard reaction, ionisation of benzoic acids. They are applicable to reactions which have electron-deficient (i.e. positively-charged) transition states.

The modified equation can, like the original, be separated into two forms appropriate for *meta*- and *para*-substitutions:

$$\log f_p = \varrho\sigma_p^+ \qquad (4)$$

$$\log f_m = \varrho\sigma_m^+ \qquad (5)$$

where f_p and f_m are the partial-rate factors for *para*- and *meta*-substitution, respectively. Eq. (4) – eq. (5) gives eq. (6) and hence eq. (7),

$$\log f_p - \log f_m = \varrho\,(\sigma_p^+ - \sigma_m^+) \qquad (6)$$

$$\log \frac{f_p}{f_m} = \varrho \times \text{constant} \qquad (7)$$

from which it follows that if the same products can be obtained by reaction with electrophiles of differing reactivity, in order to obtain the maximum amount of any one product (the *para* say) one requires f_p/f_m and hence ϱ to be at a maximum which corresponds to the use of the least reactive electrophile and the lowest temperatures. This is illustrated in Table 1 by the data for hydrogen-exchange of toluene under various conditions.

[3] H.C. BROWN and L.M. STOCK in *Advances in Physical Organic Chemistry*, Ed. V. GOLD, Academic Press, London 1963, p. 35.

Table 1. Hydrogen-exchange of Toluene

A*	Conditions	$-\varrho$	Ref.
2	aq. H_2SO_4, 25°	~ 7.7	[4]
1.3	CF_3COOH, 70°	~ 8.5	[5]
0.13	liquid HBr, 25°	~11.5	[6]

* Percentage of hydrogen-exchange at the *meta*- and *para*-positions which occurs at the *meta*-position.

The percentage of *meta*-substitution clearly decreases as the ϱ-factor for the reaction increases. This is obviously important for reactions of preparative importance in view of the difficulty of separating *meta*- and *para*-compounds from each other. The data[7] in Table 2 shows how the percentage of *meta*-derivative can be minimised by choice of reagent in chlorination of toluene.

Table 2. Chlorination of Toluene

% *meta* in *meta*, *para*-mixture	Conditions	$-\varrho$
5	Cl^+	~ 6.0
0.6	Cl_2/HOAc	~ 9.5
0.09	Cl_2/$MeNO_2$	~13.0

By similar reasoning, in the absence of secondary resonance, or steric effects, one should be able to manipulate the reaction conditions in order to obtain the optimum *ortho*:*para*-ratio in benzene derivates or the optimum α:β-ratio in naphthalene derivatives. The data in Table 3 shows how the percentage of reaction at the β-position in hydrogen-exchange of naphthalene can be altered by varying the reagent.

Table 3. Hydrogen-exchange of Naphthalene

% reaction occurring at the β-position	Conditions	$-\varrho$	Ref.
14.4	aq. $HClO_4$/CF_3COOH, 25°	~ 8.0	[8]
11.5	CF_3COOH, 70°	~ 8.5	[9]
2.9	liquid HBr, 25°	~11.5	[6]

Recent data[10,11] for nitration of naphthalene by nitric acid in acetic acid (Table 4), shows that this technique can be applied to reactions of preparative importance. In this example the reactivity of the electrophile is decreased by lowering the temperature.

[4] C. EABORN and R. TAYLOR, *J. Chem. Soc. 1960*, 3301.
[5] R. BAKER, C. EABORN and R. TAYLOR, *J. Chem. Soc. 1961*, 4927; K.C.C. BANCROFT, Ph. D. thesis, University of Leicester, 1963.
[6] E.N. YURIGINA *et al.*, *Zh. Fiz. Khim. 34* (1960) 587.
[7] Ref. [1], p. 134.
[8] C. EABORN and R. TAYLOR, *J. Chem. Soc. 1961*, 1012.
[9] R. BAKER, Ph. D. thesis, University of Leicester, 1962.
[10] A. STREITWIESER and R.C. FAHEY, *J. Org. Chem. 27* (1962) 2352.
[11] P.G.E. ALCORN and P.R. WELLS, *Austr. J. Chem. 18* (1965) 1377.

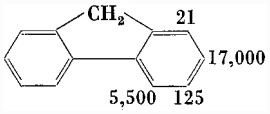
Table 4. Nitration of Naphthalene

% β-nitration	Temperature °C
7.5	100
6.0	50
4.5	25

Eq. (4) ÷ eq. (5) gives eq. (8),

$$\frac{\log f_p}{\log f_m} = \frac{\sigma_p^+}{\sigma_m^+} \qquad (8)$$

i.e. the ratio of the logarithms of the partial-rate factors is independent of the particular reaction. It follows from this that from the results obtained in any particular reaction such as hydrogen-exchange, we can predict the effects of substituents in another reaction. It follows also that in the absence of complicating factors we should be able to apply the equation to *ortho*-positions and to the α- and β-positions of naphthalene as well.



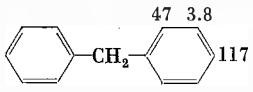
(9)

An example of the use of the hydrogen-exchange reaction in predicting isomer ratios in other electrophilic substitutions comes from the detritiation of fluorene by anhydrous trifluoroacetic acid at 70°. Partial rate factors[12] are shown (9). From the relative ϱ-factors for hydrogen exchange and nitration (0.67) we can predict the percentage of products expected in the latter reaction which are compared in Table 5 with the observed values,[13] for nitration by nitric acid in acetic anhydride.

Table 5. Nitration of Fluorene

Position	Predicted product	Observed product
1	0.7 %	0 %
2	65.9	67.6
3	2.5	1.9
4	30.9	30.5

The detritiation results suggest that a repeat study of fluorene nitration using v.p.c. analysis would probably detect a small amount of 1-nitration.



(10)

A second example involves diphenylmethane, for which the detritiation partial-rate factors[12] are shown (10), and the predicted and observed[13] isomer distribution for nitration by nitric acid in acetic anhydride is given in Table 6.

[12] K.C.C. Bancroft, R.W. Bott and C. Eaborn, *J. Chem. Soc. 1964*, 4806.
[13] M.J.S. Dewar and D.S. Urch, *J. Chem. Soc. 1958*, 3079.

Table 6. Nitration of Diphenylmethane

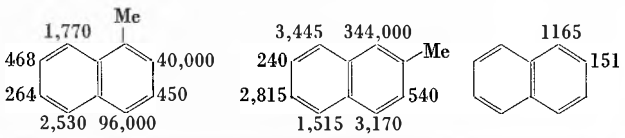
Position	Predicted product	Observed product
2	47.0 %	45 %
3	8.9	0
4	44.1	55

The lack of *meta*-isomer in the preparative reaction suggested a re-examination of nitration of diphenylmethane using more modern analytical techniques would be useful. This proved to be the case and a recently obtained[14] more accurate (v.p.c.) isomer distribution is: *ortho*, 41.5%; *meta*, 6.5% and *para*, 52%. The discrepancy which remains can reasonably be attributed to the steric hindrance to *ortho*-substitution in nitration, whereas hydrogen-exchange is apparently free of primary steric effects (see below).

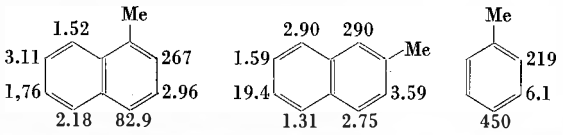
It is becoming clear therefore that use of the modified Hammett equation together with a model reaction such as hydrogen-exchange enables one to predict substituent effects and hence isomer distribution, with considerable accuracy in other electrophilic substitutions, and to suggest where existing data in the literature may be in error. Agreement cannot, of course, be truly quantitative not only because of differing steric effects but because of the different demands for resonance stabilisation of the transition states in each reaction and which is neglected in this treatment because our knowledge of these effects is inadequate at present. Another interesting recent example of the application of data obtained from the hydrogen-exchange reaction to other electrophilic substitutions comes from detritiation of a number of naphthalene derivatives by anhydrous trifluoroacetic acid at 70°. Partial-rate factors (relative to benzene) for the detritiation of methylnaphthalenes and naphthalene, together with derived partial-rate factors for the effect of a methyl group in naphthalene and in benzene,[15] are shown in Table 7.

Table 7

Partial-rate factors relative to benzene



Partial-rate factors for the effect of a methyl substituent in naphthalene and in benzene



[14] R. Taylor, unpublished work.
[15] P. Golborn, D. Phil. thesis, University of Sussex, 1967.

From these results one can predict that electrophilic substitution of 1-methylnaphthalene should give products in the following decreasing quantities:

$$4 > 2 > 5 > 8 > 7 > 3 > 6$$

Recently, quantitative studies have been made of the nitration of methylnaphthalenes under various conditions,[11] and apart from the fact that no 6- or 7-isomer was detected, this order was approximately followed for 1-methylnaphthalene. For example, with nitric acid in acetic anhydride the order was:

$$4 > 2 > 8 > 5 > 3$$

Under other conditions rather less 2-nitro derivative was formed but this can be attributed to the different steric requirements of the nitrating species, whereas hydrogen-exchange is apparently free from steric effects. The lack of 6- or 7-nitration is attributable to the difficult nature of vapour phase chromatography analysis in the nitration work whereby it is necessary to find a column which will resolve all seven isomers. The column used in the nitration work was not shown to be capable of this hence it is almost certain that the 6- and 7-isomers were not resolved from other isomers since the detritiation study indicates that significant 6- and 7-nitration should occur.

The hydrogen-exchange results predict that electrophilic substitution of 2-methylnaphthalene should give products in the following decreasing quantities:

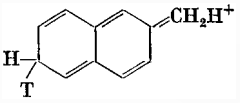
$$1 \gg 8 > 4 > 6 > 5 > 3 > 7$$

The recent nitration data gives very good agreement. No 7-product was determined under any condition, the detritiation data predicting that the amount should be very small, and the order generally obtained was:

$$1 \gg 8 > 4 > 5 > 6 > 3$$

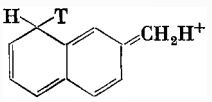
though in two cases the reactivities of the 4- and 8-positions were slightly reversed; significantly the hydrogen-exchange data predicts these reactivities to be very close. The greater reactivity of the 6-position than the 5-position in hydrogen-exchange relative to nitration can probably be attributed to the greater demand for resonance stabilisation of the transition state in the former reaction, the 6-position being conjugated with the 2-position.

An interesting feature which emerges from the detritiation data is the very strong activating effect of a methyl group across the 1,2-bond. In view of the fact that the naphthalene system is very much more reactive than the benzene system, the effect of a methyl group in stabilising the transition state for substitution should be smaller—as indicated by the partial-rate factors for *meta*- and *para*-substitution in toluene and 1-methylnaphthalene. The effect of an *ortho*-methyl substituent across the 1,2-bond is much greater however and this may be attributed to the high bond order of this bond (1.756) relative to that (1.667) for a bond in benzene. By contrast however, the effect of an *ortho*-methyl across the 2,3-bond is very small which is again consistent with its low bond order (1.570). Another feature is the strong interaction between the 2- and the 6-positions in 2-methylnaphthalene, whereas there is no similar interaction between the conjugated 2- and 8-positions. Calculations do not predict this difference though it is significant that the model for the transition state for substitution at the 6-position involves a *p*-quinonoid structure (11) and a



(11)

corresponding quinone has been isolated, whereas substitution at the 8-position would involve the structure (12) and the corresponding quinone has not been isolated.

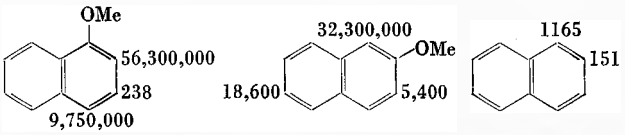


(12)

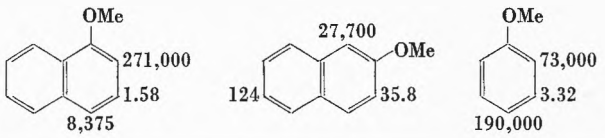
Detritiation of methoxynaphthalenes has recently been carried out[15] and Table 8 gives the relevant data:

Table 8

Partial-rate factors relative to benzene



Partial-rate factors for the effect of a methoxy substituent in naphthalene and benzene



The effect of the methoxy substituent parallels that for the methyl substituent but the agreement with recently obtained data[16] is less satisfactory. Only three isomers were detected in each case in nitration which may mean that the observed isomer distributions are to some extent in error, but a factor which probably contributes more significantly is the larger steric requirement of the methoxy substituent which would adversely affect nitration. It is not surprising therefore that nitration of 1-methoxynaphthalene yielded more of the 4- than the 2-isomer, and 2-methoxynaphthalene yielded

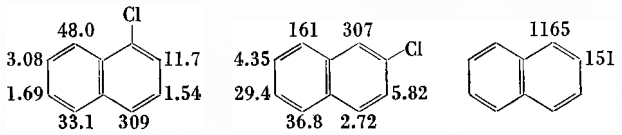
[16] P.G.E. Alcorn and P.R. Wells, *Austr. J. Chem. 18* (1965) 1399.

rather less of the 1-isomer than predicted from the hydrogen-exchange data.

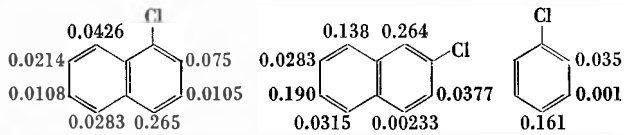
Much data is now available for the detritiation of all of the halogenonaphthalenes[15] and for the chloronaphthalenes the results are complete as shown in Table 9.

Table 9

Partial-rate factors relative to benzene



Partial-rate factors for the effect of a chlorine substituent in naphthalene and benzene



From this data we can predict that substitution of 1-chloronapthalene should give isomers in the following decreasing quantities:

$$4 \gg 8 > 5 > 2 > 7 > 6 > 3$$

Very little quantitative data is so far available for other substitutions, but the limited results are in good agreement with the prediction. Nitration gives the distribution: $4 > 8 > 5$, and no other isomers were detected.[17]

Sulphonation gives principally the 4-isomer[18] as does chlorination and bromination.[19]

Substitution in 2-chloronaphthalene should give isomers in the following decreasing quantities:

$$1 > 8 > 5 > 6 > 2 > 7 > 4$$

Here steric hindrance in preparative reactions might reduce the amount of 1-substitution relative to 8-substitution. This seems to be the case in nitration and halogenation of 2-chloro and 2-bromo-naphthalene which give mostly 8-substitution[20]. Significantly, nitration of 2-fluoronaphthalene where steric hindrance would be smaller gives mainly the 1-isomer, whereas sulphonation of 2-fluoronaphthalene (greater steric hindrance) gives mainly the 8-isomer[21].

[17] P. Ferrero and C. Caflisch, *Helv. Chim. Acta 11* (1928) 795.
[18] P. Ferrero and G. Bolliger, *Helv. Chim. Acta 11* (1928) 1144; E. H. Huntress and F. H. Carter, *J. Amer. Chem. Soc. 62* (1940) 511.
[19] P. B. D. de la Mare and P. W. Robertson, *J. Chem. Soc. 1948*, 100.
[20] H. E. Armstrong and F. P. Wynne, *Proc. Chem. Soc. 1889*, 71.
[21] G. Schiemann, W. Gueffroy and W. Winkelmuller, *Ann. Chem. 487* (1931) 270.

The *Ortho : Para*-Ratio

Until recently, the factors affecting the variation in the *ortho:para*-ratio in electrophilic substitution were difficult to interpret especially since substituent-reagent interaction, electronic, and solvent effects were likely to be substantially masked by steric hindrance or steric acceleration.[21] One especially baffling observation was that the more deactivating a substituent (as indicated by a large $\frac{1}{2}m:p$ value), the higher the $\frac{1}{2}o:p$ value,[23] Table 10.

Table 10. Isomer ratios for nitration

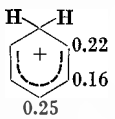
Substituent	$\frac{1}{2}o:p$	$\frac{1}{2}m:p$
NO_2	10.7	155
COOH	7.1	31
CN	4.3	20
COOEt	4.3	10
CHO	1.0	4

Studies with the hydrogen-exchange reaction have helped to solve the reason for this variation. Consider the data[24] for hydrogen-exchange of toluene, *t*-butylbenzene and biphenyl given in Table 11.

Table 11. ½ *ortho : para*-ratios

f_p^{Me}	Toluene	*t*-Butylbenzene	Biphenyl	Conditions
250	1.0	0.95		aq. H_2SO_4, 25°
313	1.05	1.01	1.0	aq. $HClO_4/CF_3COOH$, 25°
347	0.67			aq. H_2SO_4/CF_3COOH, 25°
450	0.49	0.45	0.6	CF_3COOH, 70°
	0.39	0.37	0.43	C_3F_7COOH, 70°
3,800	0.28		0.19	HBr, 25°

It is clear from this data that there is a marked variation in the *ortho:para*-ratio with reaction conditions and this variation is not due to a steric effect since the ratios for toluene, *t*-butylbenzene, and biphenyl parallel each other. (This also indicates the low steric requirement of hydrogen-exchange.) The reason for the variation may be derived from the recent observation that the proton shifts observed in the n.m.r. of the pentamethylcyclohexadienyl cation[25] indicate a distribution of positive charge in the Wheland intermediate for hydrogen-exchange as in (13).



(13)

[22] Ref. [1], p. 301.
[23] P. B. D. de la Mare and J. H. Ridd, *Aromatic Substitution*, Butterworths, London 1959, p. 83; Ref. [1], p. 306.
[24] Data taken from ref. [1], p. 208 and 217.
[25] C. Maclean and E. L. Mackor, *Mol. Phys. 4* (1961) 241; J. P. Colpa, C. Maclean and E. L. Mackor, *Tetrahedron 19* (Suppl. 2) (1963) 65.

From this two points follow:

(i) Firstly, substituents should exert a greater stabilising or destabilising effect at the *para*- than at the *ortho*-position, and the differential effect should be larger, the more positively charged the transition state i.e., the nearer it is to the Wheland intermediate. The relative position of the transition state along the reaction coordinate depends largely upon the reactivity of the electrophile, and for reactions involving very reactive electrophiles, the *ortho:para*-ratio should equate with the charge distribution in the unperturbed aromatic molecule, hence for + I substituents such as methyl one would expect an *ortho:para*-ratio greater than unity. As the reactivity of the electrophile decreases (indicated by increasing ϱ- or f_p-values) then the transition state will be nearer to the Wheland intermediate and the ratio will progessively decrease as observed for the data in Table 11.

(ii) Secondly, the differential stabilising or destabilising effect of a substituent at the *ortho*- or *para*-position will be greater the more stabilising or destabilising the substituent. The observations in Table 10 are in complete agreement with this. Electron-withdrawing substituents (as here) will deactivate in the *para*-position more than the *ortho*-position leading to a high *ortho:para*-ratio and the more electron-withdrawing the substituent (as indicated by high *meta:para*-ratios) the larger this ratio should be, as observed.

Strictly speaking of course one should consider changes in $\log f_o : \log f_p$-ratios because if the *ortho:para*-ratio (in the absence of variable electronic effects) is less than unity then it would vary with selectivity even though the $\log f_o : \log f_p$-ratio was constant, and as it would be if a linear free energy relationship existed for substitution at the *ortho*- and *para*-positions. Until recently it has been the custom to consider changes in ½*ortho:para*-ratios as indicative of the presence of steric effects and this can be very misleading. Consider the data in Table 12, for halogenation of toluene under various conditions.[26] The data appears to indicate a widely varying steric effect for the reagents, yet on plotting $\log f_o^{Me}$- *vs.* $\log f_p^{Me}$-values one obtains a smooth curve through all points except those corresponding to the last three conditions in Table 12 and which are slightly below the curve (Fig. 1). This shows that the variation is due mostly to the electronic effect described above and that the ratio is affected by steric hindrance in only three cases.

Table 12

½*o*: *p* for toluene	Condition
0.97	Cl_2/aq. HOAc
0.75	Cl_2/HOAc
0.395	Cl_2/aq. HOAc, 10°
0.407	Cl_2/aq. HOAc, 25°
0.422	Cl_2/aq. HOAc, 35°
0.29	Cl_2/MeCN
0.25	Cl_2/$MeNO_2$
1.63	Cl^+/H_2O
1.29	Br^+/aq. dioxan
0.62	ICl/$ZnCl_2$/HOAc
0.25	Br_2/aq. HOAc
0.11	Br_2/CF_3COOH

[26] Taken from ref. [1], Table 19.

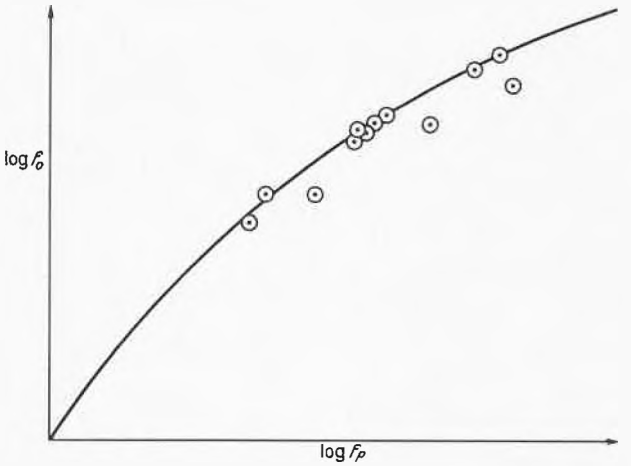
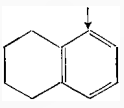


Fig. 1. Plot of $\log f_o^{Me}$ *vs.* $\log f_p^{Me}$ for Halogenation of Toluene

A third consequence arises out of this theory and affects the principle of additivity. If we increase the reactivity of an aromatic substrate, then the $\log f_o : \log f_p$-ratio for a particular electron-supplying substituent should increase because the transition state will be nearer the ground state. Consider the hydrogen-exchange of toluene by anhydrous trifluoroacetic acid at 70°; the $\log f_o^{Me} : \log f_p^{Me}$ is 0.885. We can increase the reactivity of the system by putting in another methyl substituent to give *o*-xylene. The reactivity of the 3-position according to the additivity principle should be $f_o^{Me} \cdot f_m^{Me}$, and that of the 4-position should be $f_p^{Me} \cdot f_m^{Me}$. Hence $\log f_o^{Me} : \log f_p^{Me}$ for *o*-xylene $= \log f_3 - \log f_m^{Me} : \log f_4 - \log f_m^{Me}$ which leads to a value of 0.942.[27] The difference is thus predicted by the theory and although small it is believed to be significant because of the accuracy with which partial-rate factors can be determined in hydrogen-exchange. Further work using other substituents is at present in progress, in order to determine the generality of the breakdown in additivity.

Strain Effects

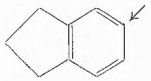
For many years, the reason why tetralin (14) substituted principally in the α-position whereas indane (15)



(14)

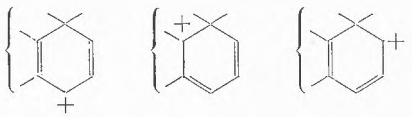
[27] R. Taylor, G. J. Wright and (Miss) A. J. Homes, *J. Chem. Soc.* (B) *1967*, 780.

substituted principally in the β-position,[28] was not understood especially since steric and electronic effects were apparently similar in both systems. Recently it has been suggested that the factor responsible is strain in the side-chain.[29]

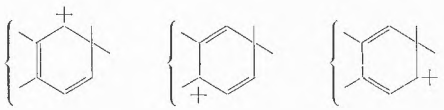


(15)

For substitution at the α-position the principal canonical forms for the resonance hybrid of the transition-state model are, (16), and for β-substitution, (17). In the for-



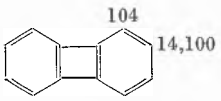
(16)



(17)

mer case two-thirds of the structure have a double-bond common to both rings where as in the latter case one-third of the structures have this. Since the unperturbed molecule has half the structures with a double-bond in this position, going to the transition state for α-substitution involves an increase in strain when the side-chain is a five-membered ring and a decrease in strain when it is a six-membered ring. Hence the favoured orientation follows.

This explanation can now be extended to account for many other previously inexplicable results in electrophilic substitution. For example, biphenylene has for some time been known to substitute predominantly in the β-position,[30] and an exact measure of the difference in reactivity of the α- and β-position is given by the partial-rate factors[31] for detritiation in anhydrous trifluoroacetic acid at 70° (18).

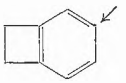


(18)

Since the α- and β-positions may be regarded as *ortho*- × *meta*- and *para*- × *meta*-phenyl, respectively, to a first approximation the β:α-ratio of reactivity (135) should be the same on the *para*:*ortho* ratio in biphenyl (1.6). Clearly this enormous difference can be accounted for by the very large increase in strain that will arise in the four-membered side-chain on going to the transition state for α-substitution.

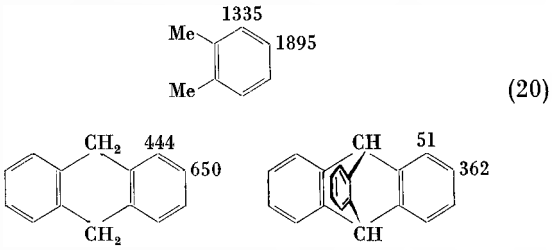
[28] W. H. Mills and I. G. Nixon, *J. Chem. Soc. 1930*, 2510.
[29] J. Vaughan, G. J. Welch and G. J. Wright, *Tetrahedron 21* (1965) 1665.
[30] W. Baker, J. W. Barton and J. F. W. McOmie, *J. Chem. Soc. 1958*, 2666.
[31] J. M. Blatchly and R. Taylor, *J. Chem. Soc. 1964*, 4641.

Likewise substitution is reported[32] to go almost exclusively in the β-position in benzocyclobutene (19)



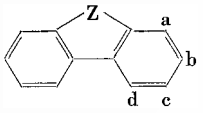
(19)

One further example comes from partial-rate factors[27] for detritiation of triptycene, 9,10-dihydroanthracene, and *ortho*-xylene (20). From the results for *ortho*-xylene and 9,10-dihydroanthracene, the effect of bridging the *ortho*-methyl substituents with a phenyl group



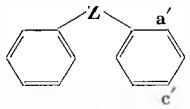
(20)

can be determined, and hence the effect of a second phenyl group (as in triptycene), predicted; the partial-rate factors should thus be 148 and 221, respectively, for the α- and β-positions. The reactivity of the α-position is three times too small and this again can be attributed to the strain in the side-chain ring. It is a corollary of the theory that strain should be decreased on going to the transition-state for β-substitution and the observed reactivity is indeed greater than that predicted.



(21)

Finally, in compounds of the type (21) it has been noted[33,34] that the reactivity of position *a* (an α-position) relative to position *c* (a β-position) is less than expected by comparison with the related compounds (22).

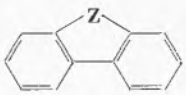
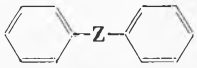


(22)

Calculations on the other hand[14] predict that closing the five-membered ring should increase the reactivity of position *a* relative to position c. It is reasonable therefore attribute this difference to strain in the five-membered ring and the data[34] in Table 13 support this.

[32] J. B. F. Lloyd and P. A. Ongley, *Tetrahedron 30* (1964) 2185.
[33] C. Eaborn and J. A. Sperry, *J. Chem. Soc. 1961*, 4821; R. Baker, R. W. Bott and C. Eaborn, *J. Chem. Soc. 1963*, 2136; P. B. D. de la Mare, O. D. H. el Dusouqui and E. A. Johnson, *J. Chem. Soc.* (B) *1966*, 531.
[34] R. Baker and C. Eaborn, *J. Chem. Soc. 1961*, 5877; K. C. C. Bancroft, R. W. Bott and C. Eaborn, *J. Chem. Soc. 1964*, 4806.

Table 13. Ratios of partial-rate factors in detritiation (anhydrous trifluoroacetic acid, 70°)

Z	$\log f_a : \log f_c$ in 	$\log f_o : \log f_p$ in 
CH_2	0.63	0.81
O	0.62	0.79
S	0.79	0.88

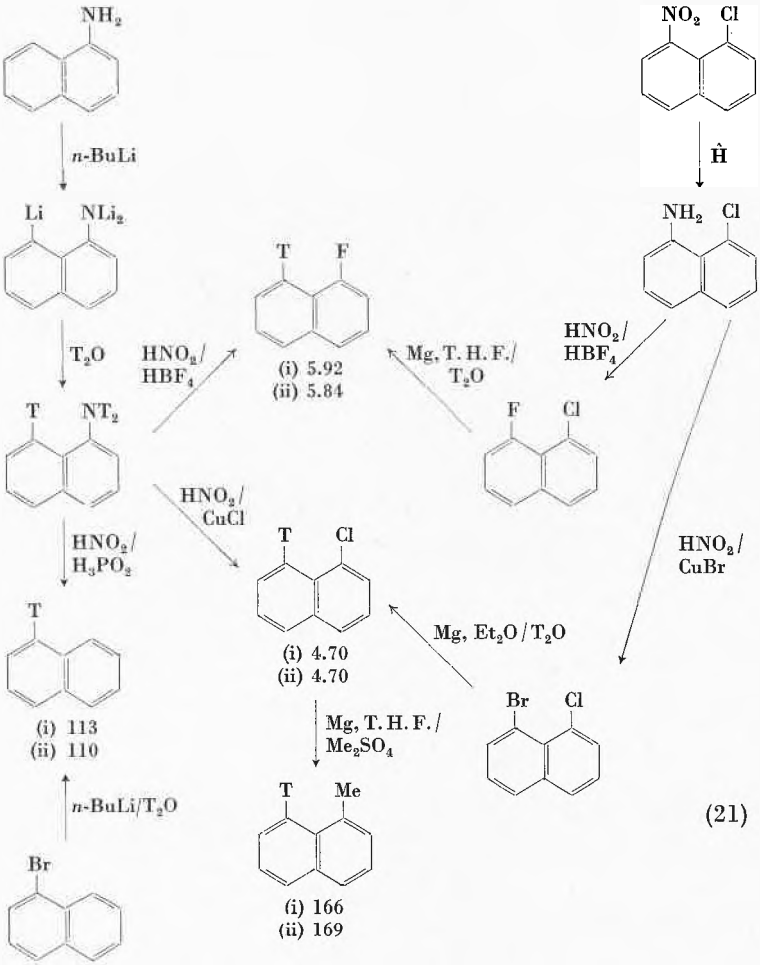
The ring containing sulphur is far less strained than that containing oxygen or methylene and significantly the decrease in the ratio on closing the ring for the sulphur compound is considerably less than for the other two compounds.

Determination of positions of substitution

Hydrogen-exchange can be useful not only in elucidating electronic factors which affect substitution patterns, but also, through kinetic studies, new substitution paths can be discovered. For example in the lithiation of 1-aminonaphthalene, substitution took place in the 8-position[35] and not in the 2-position as expected from the lithiation of aniline. This was shown through the reaction scheme (21) where the values (i) are the rate constants for compounds derived from 1-aminonaphthalene and the values (ii) are the rate constants for compounds derived by the alternative routes shown.

The similarity of the rate constants and the linearity of the kinetic plots showed conclusively not only that substitution occurred in the 8-position, but that no substitution occurred elsewhere.

[35] C. Eaborn, P. Golborn and R. Taylor, *J. Organometal. Chem. 10* (1967) 171.



Numerals denote $10^7 k$, sec^{-1} rate constants (see text)