Kinetics and Mechanism of the Thalliation of Benzene and Toluene by Thallium(III) Acetate Catalysed by Perchloric and Sulphuric Acid in Aqueous Acetic Acid

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The thalliation of benzene and toluene by thallium(III) acetate in 4:1 (w/w) acetic acid–water is catalysed by both perchloric and sulphuric acid. The catalysis can be explained by the acid-base interaction with thallium(III) acetate to produce $Tl(OAc)_2X$, $Tl(OAc)X_2$. and TlX_3 (X = ClO_4 or HSO_4) which on ionization yield more reactive electrophiles than does $Tl(OAc)_3$. Equilibrium constants have been determined for the formation of $Tl(OAc)_2X$. Isomer distributions, and the relative reactivity of toluene to benzene indicate that thalliation is a typical electrophilic aromatic substitution. The reaction shows a primary hydrogen isotope effect, $k_H/k_D = 2\cdot4$. The products from toluene isomerise under the reaction conditions. Thalliation is mechanistically similar to mercuration by mercury(II) salts.

ELECTROPHILIC substitution of metals for hydrogen in aromatic compounds has been observed in only a few instances.[1] Aromatic derivatives of the following species have been prepared in this way: mercury(II), thallium(III), gold(III), platinum(II), palladium(II), lead-(IV), and boron. The mechanistic details of mercurations in aqueous solution,[2] and in acetic acid solution,[3,4]

[1] J. M. Davidson and C. Triggs, *J. Chem. Soc.* (*A*), 1968, 1324, and references therein.
[2] C. Perrin and F. H. Westheimer, *J. Amer. Chem. Soc.*, 1963, 85, 2773.
[3] A. J. Kresge, M. Dubeck, and H. C. Brown, *J. Org. Chem.*, 1967, 32, 745.
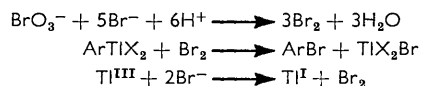[4] A. J. Kresge and J. F. Brennan, *J. Org. Chem.*, 1967, 32, 752.

have been thoroughly investigated. Information concerning the other metallations is primarily of a preparative nature. Thalliation reactions, although known for many years,[5] have received little attention until quite recently.[6-9] We now report a kinetic study which allows a comparison to be made between thalliation by thallium(III) according to equation (1) and mercuration by mercury(II) salts.

$$TlX_3 + ArH \longrightarrow ArTlX_2 + HX \qquad (1)$$

EXPERIMENTAL

Materials.—Acetic acid was dried by azeotropic distillation with benzene, a fraction m.p. >16·5° being collected. Analytical grade benzene and toluene were fractionally distilled from calcium hydride and had b.p. 80 and 110·5°, respectively. Hexadeuteriobenzene, (Merck) the bromotoluenes (Koch–Light; isomer free), and *p*-nitroaniline (Aldrich; Hammett indicator) were used without further purification. Thallium(III) acetate was prepared by dissolving thallium(III) oxide in hot glacial acetic acid. The product was recrystallised from acetic acid, and had m.p. 180°. The 4 : 1 (w/w) acetic acid–water solvent was made up by weight using purified acetic acid and laboratory distilled water. Stock solutions of sulphuric acid in acetic acid–water were prepared making due allowance for the water content of the concentrated acid. Stock solutions of perchloric acid were prepared by carefully treating the aqueous acid with the calculated amount of redistilled acetic anhydride to give the required solvent composition.

Kinetic Procedure.—Reactions were performed in volumetric flasks. Thallium(III) acetate was weighed directly into the flask, solvent was added, and the flask and contents were allowed to reach the thermostat temperature. The reaction was initiated by adding a suitable, known volume of aromatic compound. Solutions were always 0·05M in thallium(III) acetate, and ⩾0·5M in aromatic compound to maintain conditions for the observation of pseudo-first-order rate constants. Samples (4 ml) were withdrawn at appropriate intervals and quenched on crushed ice. Potassium bromide–bromate reagent (5 ml of a solution equivalent to *ca.* 0·01M-bromine) followed by concentrated hydrochloric acid (1 ml) were added. The liberated bromine was estimated by the addition of an excess of potassium iodide followed by titration against sodium thiosulphate solution. Starch could not be used as indicator because its colour change was masked by the dense yellow precipitate formed in the solution. The end-point was obtained using carbon tetrachloride method.[10] The analysis depends on the following sequence of reactions:

$$BrO_3^- + 5Br^- + 6H^+ \longrightarrow 3Br_2 + 3H_2O$$
$$ArTlX_2 + Br_2 \longrightarrow ArBr + TlX_2Br$$
$$Tl^{III} + 2Br^- \longrightarrow Tl^I + Br_2$$

Thus, at the end of the reaction (*i.e.* all thallium present as ArTlX₂) the bromine generated in solution is equivalent to that produced by the bromide–bromate reagent. This provides a check on the completion of the reaction. At the start (*i.e.* when no ArTlX₂ is present) the titre is equivalent to the bromine liberated by the bromide–bromate reagent plus that derived from the oxidation of bromide ion by thallium(III). Hence the titre at any time, when corrected for the infinity value is directly proportional to the concentration of unchanged thallium(III) in solution. Rate constants were obtained from the slope of plots of the logarithm of the corrected titre *versus* time. Good pseudo-first-order plots were always obtained and rate constants were reproducible to ±4%. The linearity of the first-order plots indicates that disproportion of arylthallium to diarylthallium compounds[9] is not important under the present reaction conditions.

The thalliations were performed in 4 : 1 (w/w) acetic acid–water because the reaction products are not sufficiently soluble in pure acetic acid. Unfortunately, benzene and toluene are not very soluble in aqueous acetic acid and their concentrations could not be increased much beyond 0·5M. At the same time difficulties in determining the end-point of the titrations prevented any appreciable reduction in initial concentration of thallium(III) acetate below 0·05M. Consequently the aromatic substrate concentration could not be reduced below *ca.* 0·5M if pseudo-first-order conditions were to be maintained. Hence we were unable to examine any substantial change in substrate concentration and therefore could not obtain the reaction order in the aromatic species. In what follows we have assumed this order to be unity.

Isomer Distribution in the Reactions with Toluene.—Reaction mixtures were made up as for kinetic runs and placed in the thermostat at 70°. After the appropriate time interval the solution was poured into water and the excess of toluene was removed as the water azeotrope. The calculated amount of bromine (dissolved in acetic acid) was added to the cool mixture to convert all tolythallium species into the corresponding bromotoluenes. The bromotoluenes were extracted into cyclohexane (10 ml total) and analysed quantitatively by i.r. spectroscopy using a Perkin-Elmer 237 spectrophotometer. Bands at 730, 765, and 800 cm⁻¹ were used for estimation of *ortho-*, *meta-*, and *para-*bromotoluene, respectively by comparisons with standard mixtures. Analyses were reproducible to ±1% of the recorded figures (Table 4).

Indicator Measurements.—These were obtained using a Zeiss PMQ II spectrophotometer. Measurements were made at 378 nm with *p*-nitroaniline as the indicator. The temperature was 22 ± 1°. Solutions of *p*-nitroaniline in acetic acid–water are unstable in the presence of thallium-(III) acetate, as shown by the slow decrease in absorbance with time. Measurements were made as soon as practicable after preparation of the solutions. Our results are shown in Table 2.

RESULTS AND DISCUSSION

Catalysis by Perchloric and Sulphuric Acids.—In the absence of added acid there is a spontaneous thalliation whose rate depends on the aromatic substrate (Table 1). The addition of either perchloric or sulphuric acid catalyses this reaction, the catalysis increasing as the

[5] H. Gilman and R. K. Abbott, *J. Amer. Chem. Soc.*, 1943, **65**, 122; V. P. Gluohkova and K. A. Kocheshkov, *Bull. Acad. Sci. U.S.S.R.*, 1957, 1211.

[6] E. C. Taylor and A. McKillop, *Accounts Chem. Res.*, 1970, **3**, 338.

[7] J. M. Davidson and C. Triggs, *Chem. and Ind.*, 1966, 457.

[8] J. M. Briody and R. A. Moore, *Chem. and Ind.*, 1970, 803.

[9] P. M. Henry, *J. Org. Chem.*, 1970, **35**, 3083.

[10] A. I. Vogel, 'Quantitative Inorganic Analysis,' Longmans, London, 1961, 3rd edn., p. 346.

catalyst concentration rises (Table 1, Figure 1). Perchloric acid is the more effective catalyst. Since thalliation occur in the absence of added acid, the

TABLE 1

Thalliation of aromatic substrates by thallium(III) acetate catalysed by added mineral acids in 4 : 1 (w/w) acetic acid–water solution at 70°

$[Tl(OAc)_3]_{initial} = 0.05M$ [Aromatic substrate] $= 0.50M$

(a) Catalysis by sulphuric acid

(i) Benzene

$[H_2SO_4]/M$	0	0·6	0·8	1·0	1·4	1·8	2·0
$10^6 k_{obs}/s^{-1}$	0·35	0·58	0·70	0·73	1·03	1·93	2·77

(ii) Hexadeuteriobenzene

$[H_2SO_4]/M$	2·0
$10^6 k_{obs}/s^{-1}$	1·17

(iii) Toluene

$[H_2SO_4]/M$	0	0·2	0·6	1·0	1·4	1·6	1·8	2·0
$10^6 k_{obs}/s^{-1}$	0·65	1·23	2·82	7·70	16·2	20·0	24·7	31·3

(b) Catalysis by perchloric acid

(i) Benzene

$[HClO_4]/M$	0	0·26	1·02	1·79	2·30	2·55
k_{obs}/s^{-1}	0·35	1·37	2·37	4·60	14·3	20·1

(ii) Toluene

$[HClO_4]/M$	0	0·25	0·76	1·26	1·51	1·89	2·20	2·37
k_{obs}/s^{-1}	0·65	14·8	25·7	49·2	66·6	83·0	133	213

$[HClO_4]/M$	2·52
k_{obs}/s^{-1}	311

catalyst could operate simply by increasing the concentration of the electrophilic species responsible for the spontaneous reaction. This would imply a constant relative reactivity of benzene compared with toluene at all acid concentrations. Such constancy is observed for neither catalyst. Significantly different electrophiles are, therefore, likely to exist in the presence of the catalyst.

The catalyst could be accounted for qualitatively by considering the acid–base equilibria (2)—(4). The replacement of acetate by perchlorate (or bisulphate) in thallium(III) acetate will lead to a more polar species which are also more likely to ionise [equations (5)—(8)].

$$Tl(OAc)_3 \rightleftharpoons Tl^+(OAc)_2, \overline{O}Ac \rightleftharpoons Tl^+(OAc)_2 + \overline{O}Ac \quad (5)$$

$$K_1 \updownarrow$$

$$Tl(OAc)_2ClO_4 \rightleftharpoons Tl^+(OAc)_2, ClO_4^- \rightleftharpoons Tl^+(OAc)_2 + ClO_4^- \quad (6)$$

$$K_2 \updownarrow$$

$$Tl(OAc)(ClO_4)_2 \rightleftharpoons Tl^{2+}(OAc), 2ClO_4^- \rightleftharpoons Tl^{2+}(OAc) + 2ClO_4^- \quad (7)$$

$$K_3 \updownarrow$$

$$Tl(ClO_4)_3 \rightleftharpoons Tl^{3+}, 3ClO_4^- \rightleftharpoons Tl^{3+} + 3ClO_4^- \quad (8)$$
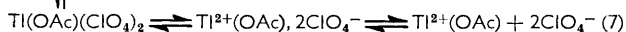
(2), (3), and (4)

Hence a change in electrophile can be envisaged. A full analysis of the catalysis would require a knowledge of the equilibrium constants K_1, K_2, and K_3. An approximate value for K_1 was obtained [11] by observing the protonation of p-nitroaniline by added acid catalyst in the presence, and absence, of thallium(III) acetate. Figure 2 shows plots of the fraction of unprotonated

[11] H. Lemaire and H. J. Lucas, *J. Amer. Chem. Soc.*, 1955, **77**, 939.

base *versus* perchloric acid concentration. At the higher acid concentrations it is clear that free perchloric acid is removed from the system by addition of thallium-(III) acetate. The curves cross at low acid concentration because lowering of the observed absorbance is mainly due to the Lewis acid-base interaction between thallium-(III) acetate and p-nitroaniline (Table 2) rather than to protonation of the indicator by the acid. To calculate a value for K_1 it is necessary to assume first, that terms equivalent to K_2 and K_3 may be neglected and secondly, since thallium(III) acetate reacts with the
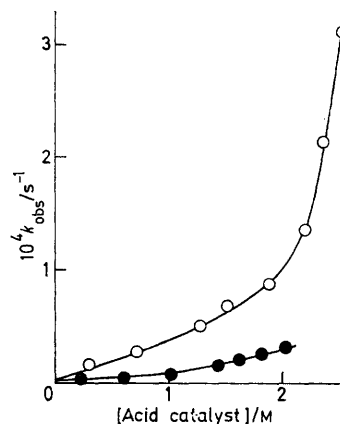

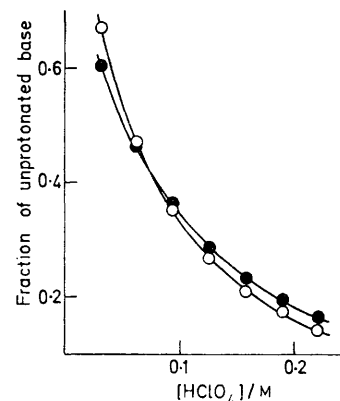FIGURE 1   Catalysis of the thalliation of toluene by perchloric acid (○) and sulphuric acid (●)

FIGURE 2   Protonation of 4-nitroaniline by perchloric acid in the absence (○), and in the presence of thallium(III) acetate (●)

indicator, that $Tl(OAc)_2ClO_4$ [or $Tl(OAc)_2HSO_4$] may also do so. Two sets of calculations were made. In one set it was assumed that $Tl(OAc)_2ClO_4$ would have no effect on the indicator, and in the other set that the effect would equal that for thallium(III) acetate. Over the perchloric acid concentration range 0·05—0·20M a K_1 value between 4·6 and 5·0 l mol⁻¹ satisfactorily reproduces individual points on the experimental curve obtained in the presence of thallium(III) acetate assuming $Tl(OAc)_2ClO_4$ exhibits no Lewis acidity. Assuming constant Lewis acidity for all thallium(III) species

present, the calculated K_1 values rise from 6·0 (at 0·05M perchloric acid) to 8·4 1 mol⁻¹ (at 0·20M) indicating that terms K_2 and K_3 may be important. For sulphuric acid the corresponding values for K_1 range from 5·2 to 8·0 and 7·4 to 16 1 mol⁻¹.

TABLE 2

Effect of added thallium(III) acetate on the protonation of p-nitroaniline by mineral acids in 4 : 1 (w/w) acetic acid–water solution

Absorbance at 378 nm in the absence of added acid or Tl(OAc) = 0·780

(a) Effect of Tl(OAc)₃ in the absence of added acid

10[Tl(OAc)₃]/ M	0·147	0·313	0·528	0·723	0·912	1·13
Absorbance	0·734	0·698	0·667	0·640	0·615	0·591

(b) Effect of sulphuric acid in the absence and presence of 0·104M-Tl(OAc)₃

10[H₂SO₄]/M	0·401	0·802	1·20	1·60	2·00	2·41
Absorbance	0·446	0·279	0·199	0·140	0·110	0·094
Absorbance Tl(OAc)₃ present	0·430	0·297	0·221	0·172	0·135	0·109

(c) Effect of perchloric acid in the absence and presence of 0·104M-Tl(OAc)₃

10[H₂SO₄]/M	0·316	0·632	0·948	1·26	1·58	1·89	2·21
Absorbance	0·522	0·365	0·214	0·209	0·164	0·139	0·112
Absorbance Tl(OAc)₃ present	0·470	0·358	0·284	0·222	0·180	0·150	0·126

Catalysis cannot be due only to the equilibrium K_1 since at the higher catalyst concentrations almost all the thallium(III) acetate will be converted into Tl(OAc)₂ClO₄ and the rate should tend to a maximum. [Assuming a value $K_1 = 5$ 1 mol⁻¹ and an initial thallium-(III) acetate concentration of 0·05M there would be 70% conversion at 0·5M catalyst and 92% at 2·0M.] Hence, equilibrium K_2, and perhaps K_3, must be included to account for the shape of the catalytic curve. In the absence of values for K_2 and K_3 a quantitative account of the catalysis is impossible. Further complications arise when the exact nature of the electrophilic species is considered. Thallium(III) acetate (0·05M) in the acetic acid–water solvent has 10% of the conductivity of perchloric acid at the same concentration. Ionisation and dissociation [equations (5)—(8)] will be greater for the other species in equilibria [equations (1)—(3)] since perchloric and sulphuric acids are strong acids even in pure acetic acid.[12] Thalliation could occur through either the ion pair or free ion involved in equilibria such as (5)—(8). However, since perchloric acid (or sulphuric) will be more dissociated than its salts,[12] and is also present in large excess the dissociation steps in (5)—(8) will be suppressed by a common-ion effect. For pure acetic acid where even the strongest electrolytes (e.g. perchloric acid) have dissociation constants of less than 10⁻⁵ it would be fair to assume that thalliation occurred very largely via the ion pairs. However, in the aqueous acetic acid solvent used here the possibility of some contribution from the free ions should not be overlooked.

Perchloric acid catalysis of aromatic mercuration in acetic acid solution has also been interpreted along the lines now suggested for thalliation. There are fewer equilibria involved for the mercurations and a quantitative account of the catalysis was obtained.[3]

The Effect of Temperature.—Table 3 records the effect

TABLE 3

Effects of temperature under various catalytic conditions

(a) Catalysis by sulphuric acid

	[H₂SO₄]/ M	t/°C	$10^6 k_{obs}$/ s⁻¹	E_a/kcal mol⁻¹	ΔS^*/cal mol⁻¹ K⁻¹
	0·40	69·50	0·51	61	88
	0·40	84·95	24·0		
Benzene	1·00	69·50	0·73	61	86
	1·00	84·95	34·6		
	1·80	69·50	1·93	49	55
	1·80	84·95	44·6		
	0·40	69·50	1·60	42	33
Toluene	0·40	84·95	24·6		
	1·80	69·50	24·7	23	−17
	1·80	84·95	107		

(b) Catalysis by perchloric acid

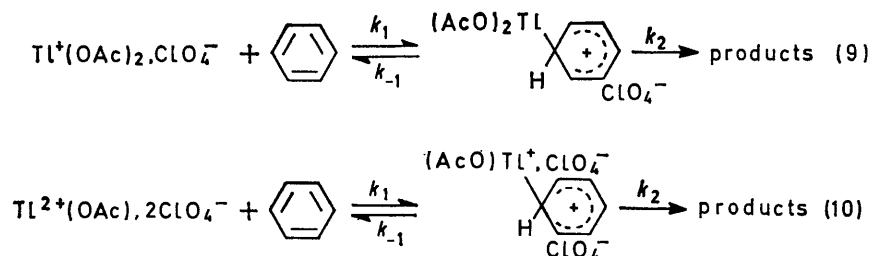|	[H₂SO₄]/ M	t/°C	$10^6 k_{obs}$/ s⁻¹	E_a/kcal mol⁻¹	ΔS^*/cal mol⁻¹ K⁻¹
	0·51	69·50	0·176	44	43
	0·51	84·95	3·39		
Benzene	1·28	69·50	0·250	41	32
	1·28	84·95	4·00		
	2·55	69·50	2·01	20	−26
	2·55	84·95	7·75		
	0·51	69·50	2·00	39	30
	0·51	80·50	14·0		
Toluene	1·28	69·50	4·92	36	23
	1·28	80·50	27·2		
	2·55	69·50	31·1	10	−50
	2·55	80·50	48·3		

of temperature on the observed rate at varying acid concentrations. The Arrhenius activation energy (E_a) and the entropy of activation (ΔS^*) were calculated from these results. There is a marked variation in E_a and ΔS^* with catalyst concentration which supports the view that more than one electrophile is involved. At low catalyst concentrations the reaction is characterised by a high energy of activation and a large positive entropy of activation. At high concentrations, where catalysis is most effective, there is a considerable lowering in E_a, but this is compensated to a large extent by a decrease in ΔS^*. The net result is that increasing the catalyst concentrations is relatively less effective at high than at low temperatures. Such large changes in the activation parameters with catalyst concentration implies significant changes in mechanistic detail.

As expected [13] for an electrophilic substitution reaction which involves the formation of a weak bond to the aromatic nucleus thalliation shows a primary hydrogen isotope effect (Table 1, $k_H/k_D = 2·4$; and results for reactions in trifluoroacetic acid [8]). The rate-limiting step for the reaction therefore corresponds to decomposition [K_2 in equations (9) or (10)] of the Wheland intermediate. The observed rate constant

[12] I. M. Kolthoff and S. Bruckenstein, in ' Treatise on Analytical Chemistry,' Vol. 1, Part I, I. M. Kolthoff and P. J. Elving, ed., J. Wiley, New York, 1959, pp. 499—518.
[13] E. Berliner, *Progr. Phys. Org. Chem.*, 1964, **2**, 253.

will be influenced by factors which affect the steady state concentration of the intermediate and its rate of decomposition. Two distinct situations may be compared. Thalliation due to electrophiles produced by equilibria (5) and (6), predominating at low catalyst concentrations, leads to a Wheland intermediate which

in the entropy of activation must be considered speculative.

Isomer Distribution.—The thalliation of toluene shows evidence of product isomerisation (Table 4) under the reaction conditions. Also the more strongly catalysed reactions are associated with a lower *ortho* : *para* ratio,

$$TL^{+}(OAc)_2.ClO_4^- + \langle\!\!\langle / \;\;\rangle\!\!\rangle \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \overset{(AcO)_2TL}{\underset{H}{\times}}\!\!\!\langle\!\!\langle\, + \,\rangle\!\!\rangle \overset{k_2}{\underset{ClO_4^-}{\longrightarrow}} products \quad (9)$$

$$TL^{2+}(OAc).2ClO_4^- + \langle\!\!\langle / \;\;\rangle\!\!\rangle \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \overset{(AcO)TL^+.ClO_4^-}{\underset{H}{\times}}\!\!\!\langle\!\!\langle\, + \,\rangle\!\!\rangle \overset{k_2}{\underset{ClO_4^-}{\longrightarrow}} products \quad (10)$$

bears a positive charge on the nucleus. However, thalliation by a more electrophilic species from equilibria such as (7) and (8), predominating at high catalyst concentrations, yields an intermediate [equation (8)] which also has a positive charge on the thallium atom. The value of k_1 will be higher for the multiply charged electrophiles and electronic interactions (inductive and field effect) will destabilise the Wheland resulting in increased values for k_{-1} and k_2. While these rationalisations are consistent with the observed catalysis and a reduced activation energy at the higher catalyst concentrations, it is not clear that there is any mechanistic difference which could lead to the very large changes in ΔS^* which are observed.

If the formation of product *via* (10) involves collapse of ion pairing in the intermediate, so that it now resembles the intermediate in equation (9), there would be an unfavourable entropy change. The enhanced reaction rate in equation (10) compared with equation (9) would then be due to an increase in k_1. The effects on k_{-1} and k_2 would be smaller. However, in view of the difficulties in the interpretation of entropies of activation, and the commonplace observation of compensation,[14] the above explanation for the large variation

[14] L. L. Schaleger and F. A. Long, *Adv. Phys. Org. Chem.*, 1963, **1**, 1.

and a greater relative reactivity of toluene to benzene (Table 1). These effects are similar to those observed for catalysed and uncatalysed mercuration in acetic acid.[15] Toluene reacts *ca.* 11 times faster than benzene with 2M-sulphuric acid as catalyst so that thalliation

Isomer distribution

[H$_2$SO$_4$]/M	Reaction time/ day	Product composition (%)		
		o	*m*	*p*
0·4	1	37·6	3·4	59·0
0·4	4	53·1	4·3	42·7
2·0	1	18·7	6·4	75·0
2·0	4	42·7	6·8	50·5

In 2M-sulphuric acid the reaction is complete within one day whereas at 0·4M the reaction is only 30% completed in the same time.

of toluene fits Brown's reactivity selectivity relationship [16] ($S_f = 1·37$, $\log P_f = 1·69$). Thalliation of toluene is, therefore, a typical electrophilic aromatic substitution with many features in common with mercuration. The major difference is the greater facility of mercuration reactions.

[15] H. C. Brown and C. W. McGary, *J. Amer. Chem. Soc.*, 1955, **77**, 2300 and 2306.
[16] L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, 1963, **1**, 35.