Aromatic Detritiation. Part IV.[1] 1,3,5-Triphenylbenzene: A Possible Example of Steric Hindrance to Hydrogen Exchange

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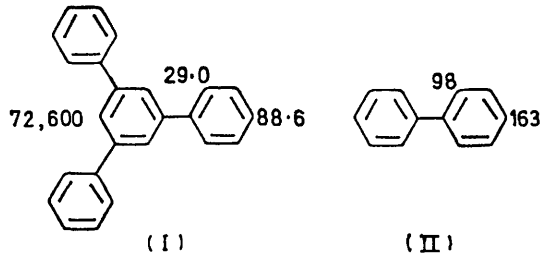
Rates of protiodetritiation of 1,3,5-triphenylbenzene have been measured in anhydrous trifluoroacetic acid at temperatures between 70 and 130 °C and lead to the following partial rate factors: 72,600 (2-position); 88 (4'-position); 29 (2'-position). This quantitative determination of the electrophilic reactivity of the molecule shows that the isomer distributions obtained in all previous electrophilic substitutions of it are affected by steric hindrance to 2- and 2'-substitution, and further, by comparison with detritiation data for biphenyl, that even in hydrogen exchange the 2- and 2'-positions are probably slightly hindered; this being so, it constitutes the first example of steric hindrance to acid-catalysed hydrogen exchange. The data for nitration of triphenylbenzene by nitric acid in acetic anhydride is at variance with the prediction of the hydrogen exchange reaction indicating the nitration pattern to be anomalous as is that for nitration of biphenyl under these conditions.

Conjugation between the phenyl rings appears to be the same as in biphenyl, consequently the angles between the rings must be closely similar for both molecules in trifluoroacetic acid.

1,3,5-TRIPHENYLBENZENE (I) is an interesting aromatic molecule because of the possibilities for extreme steric hindrance to substitution on the central ring, and for deformation of the outer rings out of the plane of the central ring thereby leading to abnormal substitution patterns.



FIGURE

Relatively few electrophilic substitutions of the molecule have been carried out [2-8] and only one, nitration, has been quantitative leading to partial rate factors [4,8] which were: f_2, 672; $f_{2'}$, 125; $f_{4'}$, 163. Furthermore, the qualitative data show very considerable disagreement as shown in Table 1. The result for acetylation led Lewis [5] to suggest that severe steric hindrance is encountered in this molecule. As a

TABLE 1

Electrophilic substitution of 1,3,5-triphenylbenzene

Reaction	% Substitution at 2-Position	2'-Position	4'-Position	Ref.
Bromination by Br_2 in CS_2	91, 96, 79—100			2
Nitration by HNO_3 in HOAc	70			3
Nitration by HNO_3 in Ac_2O	62	23	15	4
Acetylation by Ac_2O in $PhNO_2$, CS_2, and $C_2H_4Cl_2$	0	0	100	4, 5
Benzoylation by PhCOCl in CS_2	75, 90,[a] 98			5, 6
Iodine-catalysed chlorination by Cl_2 in CCl_4	76			7

[a] Solvent not recorded (ref. 2).

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consequence it is probable that the remaining data do not accurately describe the true positional reactivities. In particular it is now well established that nitration may be an unsatisfactory model for electrophilic substitution due to the problems of encounter and mixing control,[9,10] and in addition, nitration by nitric acid in acetic anhydride of biphenyl (and probably therefore its derivatives) produce results anomalous in terms of normal substituent effects;[11] hence it is unlikely that the nitration data describe the true electrophilic reactivity of the molecule. By contrast, hydrogen exchange is now the electrophilic substitution for which there is the greatest accumulation of kinetic data,[12] the data are certainly more accurate than in most other electrophilic substitutions, and the results without question the most meaningful because steric effects are minimal in the reaction (indeed none have previously been detected). Whilst the latter fact makes the reaction pre-eminent for theoretical analysis, the simplicity and symmetry of the transition state additionally recommends the reaction in this respect. With these facts in mind we have sought to determine the true electrophilic reactivity of 1,3,5-triphenylbenzene.

RESULTS AND DISCUSSION

Rate coefficients obtained at the indicated temperatures are given in Table 2; some of the values are averages of a number of runs. Values italicised were obtained by extrapolation from the other temperatures. The data for the 2′- and 4′-compounds gave excellent Arrhenius plots and the extrapolated rates cannot therefore be significantly in error; the activation energies are in good agreement with those previously obtained in this medium for compounds more reactive than benzene,[13] and the partial rate factors together with those for biphenyl [14] are shown in the Figure.

Since the partial rate factors for substitution at the *ortho*- and *para*-positions in the peripheral ring are closely similar to those for biphenyl, the different $f_o : f_p$ value of 0·33 (*cf.* 0·60 for biphenyl) may not be attributed to a difference in the position of the transition state along the reaction co-ordinate.*

Nor may it be attributed to the differential electronic effect of the *meta*-phenyl groups upon the *ortho*- and *para*-positions in the other ring, for in a subsequent publication we shall show that even an *ortho*-fluoro-substituent produces less than 10% difference in deactivation between the *ortho*- and *para*-positions of the other ring. For a *meta*-substituent this difference would be even less since the distance between the sites is greater, and for a phenyl substituent (which has a much smaller polar effect than a fluoro-substituent) this difference will be insignificant. It is very probable then that the lower ratio in 1,3,5-triphenylbenzene derives from the most likely alternative namely steric hindrance to *ortho*-substitution in the peripheral rings in which case this constitutes the first example of steric hindrance to hydrogen exchange. The amount of hindrance is obviously very small in contrast to the results obtained with other reactions (described below), so that this at the same time confirms the very small steric requirement of the electrophile in hydrogen exchange.

TABLE 2

Protiodetritiation of tritiated 1,3,5-triphenylbenzene

Isomer	t/°C	$10^7 k$/s^{-1}	Partial rate factor	E_a/kcal mol^{-1}
1,3,5-[2-^{3}H]Triphenylbenzene	70	6900	72,600	
1,3,5-[2′-^{3}H]Triphenylbenzene	70	*2·75*	29·0	21·6
	90	15·95		
	100	34·8		
	110	75·3		
	120	151·5		
	130	309		
1,3,5-[4′-^{3}H]Triphenylbenzene	70	*8·415*	88·6	20·2
	90	43·9		
	100	90·2		
	110	188·5		
	120	379		
	125	536		

It is instructive to compare the partial rate factors for the peripheral ring with those calculated. The 4′-position is activated by a *p*-phenyl substituent which itself is substituted by two *meta*-phenyl groups. Now in hydrogen exchange in a medium which gives a slightly smaller spread of partial rate factors, f_m^{Ph} was 0·7, so that correction for the difference in reaction ρ-factors leads to an expected value of 0·66 for the present medium. However the effect of this substituent on the peripheral ring will be diminished by the intervening (central) phenyl group, this having shown to be the case (for other substituents) in hydrogen exchange [16] and correction of the partial rate factor according to the difference in ρ-factors for exchange in biphenyls and benzenes, brings this value to 0·91. Consequently we can confidently state that the true effect of the *meta*-phenyl substituents lies between the *extreme* limits of 0·65 and 1·00, and the activation of the 4′-position can be predicted as between 163 × 1·0 × 1·0 (163) and 163 × 0·65 × 0·65 (69). The observed value of 88 is in

* A 60-fold change in partial rate factor for exchange of biphenyl in different acids produces a reduction of 0·81 in the $o : p$ ratio.[15] For a 2-fold change in rate factor the predicted change in the ratio would be only *ca.* 0·02, and therefore insignificant.

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excellent agreement, so clearly non-coplanarity effects are unimportant here in the sense that the angles between the phenyl rings must be closely similar in biphenyl and 1,3,5-triphenylbenzene; for the latter an angle of 38° has been quoted [17] but this will undoubtedly depend on the medium involved.

For the 2′-position the calculated partial rate factor lies in the range $98 \times 1{\cdot}0 \times 1{\cdot}0$ (98) and $98 \times 0{\cdot}65 \times 0{\cdot}65$ (42); the lower experimental value again points to the existence of steric hindrance, and further shows that this decreases the reactivity by a factor of *ca.* 2.

The predicted partial rate factor for the 2-position is $163 \times 98 \times 98 = 1{\cdot}56 \times 10^6$ so that the experimental value is 20 times less. Part of this is likely to arise from steric hindrance which must be greater than at the 2′-position, and we can therefore reasonably stipulate that this accounts for a factor of not less than 4—5. Furthermore the activation by all three phenyl groups will certainly be less than when acting alone since the transition state here will be shifted towards the ground state. We are left then with at most a very small factor unaccounted for and which could be attributed to differences in non-coplanarity between biphenyl and 1,3,5-triphenylbenzene so again this shows that the angles between the rings must be very similar in both systems.

It is instructive to compare the present results with the data for preparative electrophilic substitutions. Assuming that a linear free-energy relationship holds for all positions in the molecule (errors in this assumption are unlikely to significantly affect our conclusions) we can predict that the percentages of substitution for a reaction of ρ-factor 6 will be 2-, 99%; 2′-, 0·3%; 4′-, 0·7% and for a reaction of ρ-factor 12, 2-, 100% with insignificant substitution at the other positions. The former isomer distribution then is that which we would approximately expect in acylation and nitration. The results for acetylation are therefore confirmed as being anomalous and clearly derive from the marked steric hindrance to acetylation (which is greater than for any other electrophilic substitution), and to substitution on the central ring. The results for benzoylation are closer to that which we would expect and this corresponds to the smaller steric hindrance to this reaction.[5,15]

The result for nitration is confirmed as being very clearly anomalous so that this provides further evidence that great caution is needed in using nitration as a model for studying electrophilic substituent effects.

It is instructive to analyse further the partial rate factors obtained in nitration. From the data of Simamura and Mizuno [18] we can predict the factor for 2-substitution as $41 \times 41 \times 38 = 64{,}000$. The observed value is 100-fold smaller and the discrepancy is much greater than in hydrogen exchange (and even more than indicated by comparison of the numerical discrepancies in view of the differing ρ-factors), so that we may safely conclude that nitration is much more sterically hindered (as indicated by other work, *e.g.* nitration of toluene and t-butylbenzene [19]). The greater steric hindrance therefore facilitates substitution in the peripheral ring (this statement implies of course that the isomer distribution recorded for nitration in Table 1 could be different if obtained under competition conditions). However from the hydrogen exchange data we would expect a much lower $o : p$ ratio especially in view of the greater hindrance to nitration, and the failure to observe this indicates that favoured *ortho*-substitution occurs with 1,3,5-triphenylbenzene as it does with biphenyl [11] and arises from the same cause. Because of the greater nucleophilicity of the central ring, any mechanism which favours *ortho*-substitution and which requires nucleophilic assistance of (say) polarisation of NO_2-X bonds will be more dominant in the present case.

Halogenation should produce the isomer distribution for a ρ-factor of −12. The result for molecular bromination is clearly approaching this quite closely, in contrast to that for chlorination which suggests that the iodine polarising the chlorine–chlorine bond must be sufficiently close to cause an appreciable steric effect.

EXPERIMENTAL

The general kinetic procedure has been described,[1] but because of the very low solubility of triphenylbenzene in trifluoroacetic acid, kinetic runs were each performed with only *ca.* 0·1 mg of compound. As a consequence, where possible the tritiated isomers were prepared with a relatively high specific activity (*ca.* 4 mCi/g); the activity of the 2′-isomer was somewhat lower as inactive material had to be added during the several stages of its preparation.

1,3,5-*Triphenyl*[2-^{3}H]*benzene*.— 1,3,5-Triphenylbenzene (33 g, 0·11 mol) was brominated by the method of Kohler and Blanchard [2] and recrystallisation of the crude product from ethanol–toluene (1 : 2 by volume) gave 2-bromo-1,3,5-triphenylbenzene (11·7 g, 28%), m.p. 129—130° (lit.,[2] 129—130°). Much larger amounts of product remained in the mother liquors but were not required for our purposes. 2-Bromo-1,3,5-triphenylbenzene (10 g, 0·26 mol) was converted into the corresponding Grignard reagent by the method of Kohler and Blanchard and hydrolysed with tritiated water (0·2 ml of 160 mCi/ml activity) to give after normal work-up and recrystallisation from ethanol–toluene (7 : 3 by volume), 1,3,5-*triphenyl*[2-^{3}H]-*benzene* (6·2 g, 78%), m.p. 170—171° (lit.,[20] 172°).

1,3,5-[4′-^{3}H]*Triphenylbenzene*.—The general technique [20,21] for the preparation of substituted 1,3,5-triphenylbenzenes from acetophenones was employed to prepare 4′,4″,4‴-tribromo-1,3,5-triphenylbenzene. Potassium pyrosulphate (6·5 g, prepared by dehydration by flame heating of potassium hydrogen sulphate contained in a boiling tube) was finely crushed and mixed with 4-bromoacetophenone (5 g, 0·025 mol) and concentrated sulphuric acid (0·33 g). The mixture was stirred with heating at 130—140° during 6 h; it was then heated under reflux with

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ethanol (25 ml) during 1 h. The mixture was filtered thereby removing unchanged 4-bromoacetophenone, and the filtrate was washed with water (50 ml) to remove inorganic material, Recrystallisation from benzene gave orange crystals of 1,3,5-*tris*-(4-*bromophenyl*)*benzene* (2·55 g, 51%), m.p. 277°, *m/e* 537, 539, 541, 543. This compound (0·1 g) was dissolved in cyclohexane and treated with 4 ml of a 1·5 M-solution of n-butyl-lithium in hexane with heating to 60° to complete reaction. Hydrolysis was affected with tritiated water (0·01 ml of 160 mCi/ml activity). Work up as before gave 1,3,5-[4′-^{3}H]*triphenylbenzene* (0·02 g, 34%), m.p. 171—172°. Note that the very low concentration of tritium in the tritiated water means that in any one molecule the chance of containing *two* tritium atoms is negligible and in any case this occurrence would still give the same kinetic results.

1,3,5-[2′-^{3}H]*Triphenylbenzene*.—Initial attempts to obtain this compound by the above route using 2-bromoacetophenone (obtained by the usual route from 2-nitroacetophenone) were unsuccessful presumably due to steric hindrance to the condensation and the following route was adopted. 1,2-Dibromobenzene was converted [22] into bromo[2-^{3}H]benzene and inactive bromobenzene was added during work up. Bromo[2-^{3}H]benzene (4·44 g, 0·028 mol) was converted into the corresponding Grignard reagent and reacted with an excess of acetaldehyde. Work-up and fractional distillation gave 1-[2-^{3}H]*phenylethanol* (1·80 g, 52%), b.p. 94—96°/15 mm (lit.,[23] 94°/12 mm). This compound was heated under reflux during 2 days with aluminium t-butoxide (7 g), acetone (150 ml), and benzene (150 ml).[24] The ethanol was removed by washing with water and the inorganic material by filtration; solvent was removed from the filtrate to give after fractional distillation and addition of inactive acetophenone, [2′-^{3}H]-*acetophenone* (2·55 g), b.p. 84—85°/16 mm (lit.,[25] 88·5°/16 mm). This compound (1·5 g, 0·0125 mol) was converted into 1,3,5-[2′-^{3}H]*triphenylbenzene* (0·35 g, 27%), m.p. 174°, by the general condensation method used for the 4′-compound.

[1/1470 *Received*, 16*th August*, 1971]

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