Hyperconjugation. V. Relative Rates of Bromination of t-Alkylbenzen

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In previous investigations it has been shown that the relative rates of bromination of primary and secondary alkylbenzenes depend on the number and positions of the hydrogen atoms in the alkyl group, with *alpha* hydrogens exerting the greatest influence.[1,2] The importance of the hydrogen atoms is thought to lie in their participation in carbon–hydrogen hyperconjugation, which makes the aromatic nucleus more susceptible to an electrophilic attack. Hyperconjugation of the carbon–carbon bonds did not play a noticeable part in the reactivities of the primary and secondary alkylbenzenes. However, the observation that t-amylbenzene is brominated appreciably faster than t-butylbenzene suggested that in those hydrocarbons which do not possess *alpha* hydrogen atoms, hyperconjugation involving the carbon–carbon bonds might become the decisive factor in determining the relative rates of bromination.[1] It therefore seemed of interest to study a number of tertiary alkylbenzenes. The present investigation is such a study; it also concludes the work on the bromination of alkylbenzenes in acetic acid solution.

Experimental

PREPARATION AND PROPERTIES OF t-ALKYLBENZENES

Hydrocarbon	Boiling point °C.	Mm.	n^{25}D
t-Butylbenzene[a]	168–168.4	763	1.4902
t-Amylbenzene[b]	189.4–189.9	754	1.4915
2-Phenyl-2,3-dimethylbutane[c]	205.8–206.6	755	1.4931
3-Phenyl-3-methylpentane[d]	209.9–211.2	755	1.4931
2-Phenyl-2-methylhexane[e]	225.6–226.6	752	1.4892
3-Phenyl-3-ethylpentane[f]	226.8–227.6	756	1.4928
4-Phenyl-4-methylheptane[c]	241.7–242.2	757	1.4898
3-Phenyl-3-methylheptane[c]	242.4–243.2	755	1.4899
4-Phenyl-2,4-dimethylhexane[c]	237.4–237.8	757	1.4895
2-Phenyl-2,4-dimethylhexane[c]	237.2–237.4	751	1.4899
3-Phenyl-3-ethylhexane[c]	241.6–242.5	751	1.4909
4-Phenyl-4-ethylheptane[c]	252.6	754	1.4870

[a] Prepared and purified as described before.[1] [b] Prepared according to Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., New York, 1941, p. 179, from t-amyl chloride and benzene. [c] This sample was generously supplied to us by Professor R. C. Huston, Michigan State College, East Lansing, Michigan. It was repeatedly treated with ice-cold concentrated sulfuric acid as described previously.[1] It is not thought that the treatment with ice-cold sulfuric acid caused any isomerization of the alkylbenzenes. [d] Prepared in 41% average yield (b. p. 207–211°) from 0.5 mole of methyl-diethylcarbinol, 2.5 moles of thiophene-free benzene and 0.25 mole of aluminum chloride according to the procedure of Huston, Fox and Binder, J. Org. Chem., 3, 251 (1938). After repeated treatment of the crude product with portions of ice-cold concentrated sulfuric acid, the acid layer was still somewhat yellow-green in color; the

(1) Berliner and Berliner, THIS JOURNAL, 71, 1195 (1949).

(2) Berliner and Berliner, ibid., 72, 222 (1950).

sample was therefore agitated for 20 hours with aqueous potassium permanganate. No reduction of the permanganate was observed. The organic material was separated, washed and resubjected to treatment with cold concd. sulfuric acid, giving the same pale yellow-green color in the acid layer. The hydrocarbon was washed, dried, refluxed for one hour over metallic sodium and fractionated twice from sodium affording a sample with the physical constants recorded in the table. Part of this sample was refluxed over potassium hydroxide for one hour and fractionated from potassium hydroxide, b. p. 210–211° at 755 mm., n^{25}D 1.4933. Both samples behaved in the same way in the bromination reactions. [e] Prepared in 44% yield of crude product (b. p. 225°) from 0.4 mole of dimethyl-n-butylcarbinol and benzene according to the procedure of Huston, Fox and Binder, op. cit. [f] Prepared in 50% yield of crude product (b. p. 227–229°) from 0.5 mole of triethylcarbinol (Huston, Fox and Binder, op. cit.).

The glacial acetic acid, bromine and sodium acetate used in these experiments have been previously described.[1]

General Procedure.—The twelve t-alkylbenzenes were brominated at 25 ± 0.05° using 90% aqueous acetic acid (by volume) 0.2 M in sodium acetate as a solvent. The initial reaction mixtures (volume 40 ml.) were 0.10 M in hydrocarbon (2.5-fold excess) and 0.04 M in bromine, prepared by adding 10 ml. of a 0.16 M bromine solution to 30 ml. of a 0.1333 M solution of the hydrocarbon.[3] The further procedure was the same as previously described,[1] except that 0.0800 M sodium thiosulfate was used in the titrations. The per cent. reaction of bromine with each hydrocarbon after 28 hours was established by repeated determinations. Two readings were taken for each reaction mixture prior to the 28-hour reading. A blank run, containing only bromine and the solvent, was made with each set of reactions in order to correct for loss of bromine from the reaction mixtures through evaporation. The blank varied somewhat from day to day, but the variation in the blank after 28 hours never amounted to more than 0.4% of the initial bromine content. The several values for the per cent. reaction of any one hydrocarbon after 28 hours (after correcting for the observed blank) did not differ from one another by as much as 0.4%. A mean of the set of values for each hydrocarbon was taken and rounded off to the nearest 0.05%. This mean value is recorded for each hydrocarbon in Table I, and it is thought to be uncertain by not more than ±0.2%. The hydrocarbons were studied in groups of six, so that before the investigation was concluded every hydrocarbon had been studied simultaneously several times with every other hydrocarbon, and although the per cent. reaction in 28 hours for each hydrocarbon varied slightly from run to run, the relative order of reactivity of the hydrocarbons never varied.

Comparing the amounts of reaction of a series of compounds after a stated time interval (28 hours in this case) is not a preferred method for comparison of the reactivities because it involves comparing reactions in quite different states of progress. However, in the present study it did not seem desirable to determine the time required for 10% reaction of each hydrocarbon, as was done in the previous bromination studies, because of the great length of time required for 10% reaction of some of the slower compounds. The chief result of the method of comparison that was used is that it minimizes the differences in reactivities, and

(3) The low solubilities of the heavier t-alkylbenzenes in aqueous acetic acid prevented the use of the reaction conditions employed in the earlier studies.[1,2]

therefore the recorded differences are smaller than is actually the case.[4]

Results and Discussion

In Table I are listed the hydrocarbons which were brominated and the per cent. reaction of each after 28 hours. The same compounds are arranged into series in Tables II and III for greater ease of comparison. The data in general indicate

TABLE I

BROMINATION OF t-ALKYLBENZENES IN 90% ACETIC ACID AT 25°

t-Alkylbenzene	% Bromination in 28 hours
PhC(CH$_3$)$_3$	5.80
PhC(CH$_3$)$_2$(C$_2$H$_5$)	7.30
PhC(CH$_3$)$_2$(CH(CH$_3$)$_2$)	6.95
PhC(CH$_3$)(C$_2$H$_5$)$_2$	9.00
PhC(CH$_3$)$_2$(CH$_2$CH$_2$CH$_2$CH$_3$)	7.30
PhC(C$_2$H$_5$)$_3$	10.20
PhC(CH$_3$)(CH$_2$CH$_2$CH$_3$)$_2$	9.80
PhC(CH$_3$)(C$_2$H$_5$)(CH$_2$CH$_2$CH$_2$CH$_3$)	10.00
PhC(CH$_3$)(C$_2$H$_5$)(CH$_2$CH(CH$_3$)$_2$)	10.70
PhC(CH$_3$)$_2$(CH$_2$CH(CH$_3$)CH$_2$CH$_3$)	11.50
PhC(C$_2$H$_5$)$_2$(CH$_2$CH$_2$CH$_3$)	11.70
PhC(C$_2$H$_5$)(CH$_2$CH$_2$CH$_3$)$_2$	9.10

TABLE II

t-Alkylbenzene	CH$_3$—C(CH$_3$)(CH$_3$)—Ph	CH$_3$—C(CH$_3$)(C$_2$H$_5$)—Ph
% Reaction in 28 hours	5.80	7.30

	CH$_3$—C(C$_2$H$_5$)(C$_2$H$_5$)—Ph	C$_2$H$_5$—C(C$_2$H$_5$)(C$_2$H$_5$)—Ph
% Reaction in 28 hours	9.00	10.20

a trend toward greater reactivity with an increase in the size and branching of the alkyl group. This is particularly evident in the compounds recorded in Table II, where each successive replacement of a methyl group by an ethyl group increases the rate of bromination. In Series I (Table III) a change from methyl to ethyl causes an increase in rate; replacing the ethyl by an isopropyl group, however, produces a drop, followed by a slight increase with n-butyl and a greater increase with amyl. In Series II there is a steady increase in reactivity as the methyl group is replaced by an ethyl, a n-butyl and an isobutyl group, and similar increases are observed in
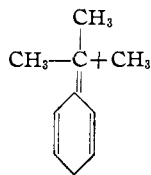
CH$_3$—C(CH$_3$)+CH$_3$

Fig. 1.

Series III and IV with each substitution of a larger group. Series V and VI do not follow this pattern, but in both of these series the irregularity is caused by the same compound (di-n-propyl-ethylcarbinylbenzene); we do not know whether this is significant, or if perhaps the compound contained an impurity that could not be removed. The only other irregularity involves either the ethyl or isopropyl compound of Series I; one of the two is out of line. In spite of the observed irregularities, the general tendency is definitely in the direction of an increase in rate with an increase in the size of the t-alkyl group. This behavior is quite the opposite of that observed for alkylbenzenes which have *alpha* hydrogens. For example, if in the compounds in Table II, one methyl group is replaced by a hydrogen, the order of reactivity is exactly reversed, PhCH(CH$_3$)$_2$ > PhCH(CH$_3$)(C$_2$H$_5$) > PhCH-(C$_2$H$_5$)$_2$. It is also noteworthy that the order of reactivities of the t-alkylbenzenes is quite the contrary of what might have been expected from a blocking of the *ortho* positions by classical steric hindrance or from a diminution of resonance due to a lack of coplanarity. These facts lend support to our previous statement,[1] that steric effects of the above nature are not decisive in the primary and secondary alkylbenzenes.[5,6]

Since the order of reactivity of tertiary alkyl-benzenes is so different from that of alkylbenzenes with *alpha* hydrogens, a somewhat different interpretation must be sought. Several interpretations suggest themselves. A transition state involving carbon–carbon hyperconjugation, as suggested before, is one possibility (Fig. 1). Carbon–carbon hyperconjugation is considered to be less important than hyperconjugation involving only carbon–hydrogen bonds, and in the case of the alkylbenzenes where the latter is possible, carbon–carbon hyperconjugation—whether or not it occurs—did not have to be used. In the absence of *alpha* hydrogens, contributions from structures of the type shown in Fig. 1 may become important and decisive. These structures will account for the increase in rate of the compounds in Table II and the regular increase from methyl to ethyl in the other series, because an ethyl group must contribute more to the resonance stabilization than a methyl group. The isopropyl compound in Series I (Table III) should then be faster than the ethyl compound and is out of line, although it is faster than the methyl compound. The n-butyl compound is as fast as the ethyl compound in Series I, but faster in Series II. The n-propyl (Series IV) and isobutyl groups (Series II) also increase the reactivi-

(5) Baddeley, Chadwick and Rawlinson, *Nature*, **164**, 833 (1949). have suggested that steric inhibition of resonance is the decisive factor.

(6) Of all of the compounds studied, toluene is the fastest and t-butylbenzene the slowest; the former because toluene has three *alpha* hydrogens, the latter because t-butylbenzene is the t-alkylbenzene with the smallest alkyl group.

(4) The importance of the fact that energies and entropies of activation were not determined, and that the differences in reactivities are in part small, has been discussed previously, ref. 2.

TABLE III
% Reaction in 28 Hours

R	Series I $R-\overset{CH_3}{\underset{CH_3}{C}}-Ph$	Series II $R-\overset{C_2H_5}{\underset{CH_3}{C}}-Ph$	Series III $R-\overset{(CH_3)_2CH}{\underset{CH_3}{C}}-Ph$	Series IV $R-\overset{C_2H_5}{\underset{C_2H_5}{C}}-Ph$	Series V $R-\overset{CH_2CHCH_3}{\underset{C_2H_5}{C}}-Ph$	Series VI $R-\overset{CH_2CH_2CH_3}{\underset{CH_2CH_2CH_3}{C}}-Ph$
CH_3	5.80	7.30	7.30	9.00		9.80
C_2H_5	7.30	9.00	10.00	10.20	11.70	9.10
$CH_3CH_2CH_2$				11.70	9.10	
$(CH_3)_2CH$	6.95					
$CH_3CH_2CH_2CH_2$	7.30	10.00				
$(CH_3)_2CHCH_2$		10.70				
$CH_3CH_2CH(CH_3)CH_2$	11.50					

ties over those of the ethyl compounds. Whether or not the *n*-propyl and *n*-butyl groups should be stabilized more than the ethyl group is undecided,[7] but taking *all possible* structures into consideration, it would seem that the resonance contribution should increase as the charge is spread out over a wider arrangement of atoms, *i. e.*, it should increase with size and branching of the alkyl group. A similar view was taken by Butler and Polanyi.[8]

A second possibility is suggested by the similarity in relative rates of bromination of *t*-alkylbenzenes and relative rates of solvolysis of *t*-alkyl halides.[9,10] Brown and Fletcher[10] attribute the increase in rate of first order solvolysis of *t*-alkyl chlorides with an increase in the size and branching of the *t*-alkyl group to an increase in strain in the molecule which promotes ionization to a *t*-alkyl carbonium ion that is planar and therefore strain-free. While the *very* highly branched compounds corresponding to those of Brown and Fletcher were not available, those of our compounds which do have the corresponding *t*-alkyl group show a striking similarity in order of reactivity (including the falling off of the dimethylisopropylcarbinyl compound). The two reactions are obviously quite different, notably because in the bromination of the alkylbenzenes the alkyl

(7) See for instance Remick, "Electronic Interpretations of Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 2nd ed., 1949, pp. 158-159.

(8) Butler and Polanyi, *Trans. Far. Soc.*, **39**, 19 (1943). The order of resonance energies of alkyl *free radicals* as calculated by Baughan, Evans and Polanyi, *ibid.*, **37**, 377 (1941), is isopropyl > isobutyl > *n*-propyl > ethyl > methyl. According to the authors similar resonance energies must be expected for the alkyl free radicals and corresponding carbonium ions. If this is the case, one could expect a similarity between the order of stabilization of these simple alkyl groups—as calculated and as found from the decomposition of alkyl iodides—and that of the tertiary alkylbenzenes where the same alkyl groups are the only variables. Except for the isopropyl group, this order corresponds to the one found in the present study.

(9) Hughes and MacNulty, *J. Chem. Soc.*, 1283 (1937); Shorter and Hinshelwood, *ibid.*, 2412 (1949); Bartlett and Knox, THIS JOURNAL, **61**, 3184 (1939); Benfey, *ibid.*, **70**, 2163 (1948).

(10) Brown and Fletcher, *ibid.*, **71**, 1845 (1949).

group is far removed from the seat of reaction, and the reaction involves no ionization to a *t*-alkyl carbonium ion. But in both types of reactions the reactant passes through an electron deficient transition state, and it would seem economical to look for similar interpretations. In an attempt to make the picture of the alkylbenzenes closely analogous to that of the alkyl halides, one would have to assume for the former a transition state of the type shown in Fig. 2.
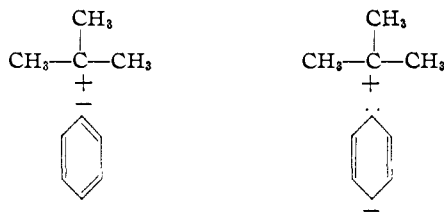

Fig. 2.

Unlike in the alkyl chlorides the "carbonium ion" in Fig. 2 is part of a contributing resonance structure. Such structures would have a certain *a priori* probability independent of any strain, but in adopting the strain hypothesis, one would have to add that the flattening out of the *t*-alkyl group with a consequent release of the strain is an inherent part of the picture. There remains a conflict between such a picture and the requirement that the atomic nuclei must not be moved too far from their average positions if a resonance structure is to contribute. The moving of the atoms is implicit in the whole steric strain concept, but it may be assumed that this is not too serious a limitation. The structures in Fig. 2 must be stabilized by further hyperconjugation within the alkyl group, and this stabilization would increase with the size of the *t*-alkyl group. Thus the structures shown in Fig. 2 would contribute to the right order of reactivity even without considering the strain involved in the molecules. Whether or not steric strain is as *decisive* a factor in the reactions of *t*-alkylbenzenes as it

appears to be in those of *t*-alkyl halides therefore cannot be decided on the basis of the present experiments.

The structures represented by Figs. 1 and 2 will both account for the observed order of reactivity of *t*-alkylbenzenes,[11] but the former are perhaps preferable because they have one more bond than those of Fig. 2[12]; in addition, the greater stability of the benzyl group than that of the phenyl group should be reflected in the relative contributions of 1 and 2. Structures 1 are more nearly like those suggested for alkylbenzenes which possess *alpha* hydrogens, for which structures of type 2 could not have been decisive.

If the *t*-alkylbenzenes are strained, one could give up a detailed picture and take refuge in the statement that strain in general increases the polarizability of molecules and that this effect alone can account for the data. The inductive effect of alkyl groups also predicts the right order of reactivity. Both statements may be perfectly true, but neither explanation brings us any closer to a real understanding of the effects of *t*-alkyl groups. On the other hand, hypercon-

(11) For the similar case of the trifluoromethyl group see Roberts, Webb and McElhill, This Journal, **72**, 408 (1950).

(12) Wheland, "The Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 16.

jugation, or perhaps a judicious combination of hyperconjugation and steric strain, probably presents a more fruitful approach.

Summary

The per cent. bromination of twelve *t*-alkylbenzenes in 90% acetic acid in 28 hours has been found to be *t*-butylbenzene, 5.80, *t*-amylbenzene 7.30, dimethyl-*i*-propylcarbinylbenzene 6.95, methyldiethylcarbinylbenzene 9.00, dimethyl-*n*-butylcarbinylbenzene 7.30, triethylcarbinylbenzene 10.20, methyldi-*n*-propylcarbinylbenzene 9.80, methylethyl-*n*-butylcarbinylbenzene 10.00, methylethyl-*i*-butylcarbinylbenzene 10.70, dimethyl-2-methylbutylcarbinylbenzene 11.50, diethyl-*n*-propylcarbinylbenzene 11.70, ethyl-di-*n*-propylcarbinylbenzene 9.10.

The above order of reactivity has been considered in terms of hyperconjugation and steric strain.

Studies in the Sulfone Series. VII. The Preparation of 2,8-Diaminophenoxathiin-5-dioxide and Bis-(2-hydroxy-4-aminophenyl) Sulfone

BY E. D. AMSTUTZ

Previous studies in this series of possible antitubercular compounds have dealt with the synthesis of derivatives of bis-(4-aminophenyl) sulfone which possess a direct union of the 2,2'-positions (dibenzothiophene), a carbonyl bridge in the 2,2'-positions (thiaxanthone) and an –NH bridge in the same positions (phenothiazine).[1] The present paper describes a very simple and satisfactory route to the corresponding oxygen bridged structure.

Since the customary substituting agents attack the phenoxathiin system at the position(s) para to the oxygen,[2] our effects have been directed toward those methods dependent upon ring closures. Of the several possible routes to the desired 2,8-disubstituted ring system the only one which proved satisfactory and which was at all thoroughly investigated, involved the dehydrohalogenation of a substituted 2-hydroxy-2'-iododiphenyl sulfide. The following reaction sequence illustrates the reactions employed and the yields obtained.

The benzyl ether of 2-bromo-5-nitrophenol,

(1) Michels and Amstutz, This Journal, **72**, 888 (1950).

(2) Suter, McKenzie and Maxwell, ibid., **58**, 717 (1936).

prepared in the usual manner[3] in 80% yield, was converted to 2-benzyloxy-5-nitrothiophenol (II) in 70% yield by treatment with sodium disulfide in alcohol.[4] Refluxing for six hours with 3,4-diiodonitrobenzene and potassium carbonate in ethanol afforded an almost quantitative yield of 2-benzyloxy-2'-iodo-4,4'-dinitrodiphenyl sulfide (III). The benzyl group was removed by refluxing with 48% hydrobromic acid in glacial acetic acid to give the corresponding phenol, IV, in 72% yield. Precipitation of the potassium salt of the phenol was carried out by addition of strong potassium hydroxide solution to a dilute aqueous solution of the salt. The ring-closure step was found to give no difficulty if performed in a sealed tube in the absence of oxygen since the dry salt is quite unstable in air above 100°, particularly in the presence of a small amount of potassium hydroxide. The 2,8-dinitrophenoxathiin was oxidized to the 5-dioxide with 30% hydrogen peroxide in glacial acetic acid after which the nitro groups were reduced with stannous chloride in acetic acid.

(3) Powell and Adams, ibid., **42**, 646 (1920).

(4) Price and Stacy, ibid., **68**, 498 (1946).