base formed short colorless prismatic needles, m. p. 144° (cor.).

Anal. Calcd. for $C_6H_6N_2Br_2$: C, 27.09; H, 2.27; N, 10.53; Br, 60.10. Found: C, 27.31; H, 2.33; N, 10.63; Br, 59.93.

5-Bromo-6-methyl-2-pyridone.—A solution of 8.4 g. of 2-amino-5-bromo-6-methylpyridine in 40 g. of ice-cold 20% sulfuric acid was diazotized below 10° by adding dropwise a solution of 3.3 g. of sodium nitrite in 7 ml. of water. The sulfate of the pyridone separated during the reaction. The paste was diluted with 30 ml. of water and the suspension heated on the steam-bath for five minutes. A solution of 9 g. of potassium carbonate in 15 ml. of water was added with stirring and the yellow suspension heated to boiling, then allowed to stand in the icebox. The yield of tan needles was 6.9 g. (82%). The compound was recrystallized from 95% ethanol, then from benzene to form colorless needles, m. p. 204° (cor.). The analytical sample was prepared by vacuum-sublimation.

Anal. Calcd. for C_6H_6ONBr: N, 7.45; Br, 42.50. Found: N, 7.28; Br, 42.50.

3,5-Dibromo-6-methyl-2-pyridone.—A warm solution of 13.3 g. of 2-amino-3,5-dibromo-6-methylpyridine in 54 g. of 20% sulfuric acid was cooled rapidly in an ice-salt bath with efficient stirring to cause separation of very small crystals, then diazotized by adding dropwise a solution of 3.7 g. of sodium nitrite in 10 ml. of water. The mixture became pasty as the sulfate of the pyridone separated. The suspension obtained by adding 300 ml. of water was heated to boiling and made alkaline by adding slowly with stirring a solution of 13 g. of potassium carbonate in 50 ml. of water. The yield of colorless crystals was 12.9 g. (97%). After recrystallization from ethanol-benzene and then from 95% ethanol, colorless needles, m. p. 254–255° (cor.), resulted. Errera[13] reported m. p. 238–239°.

Summary

1. In order to devise methods by which cytisine might be synthesized, a further knowledge of the activity of a 6-methyl group in 1-substituted 2-pyridones was required. It has been shown that the 6-methyl group in 1,6-dimethyl-2-pyridone condenses readily with ethyl oxalate in presence of potassium or sodium ethoxide to give the corresponding pyruvate. The same is true of the 4-methyl group in 1,4-dimethyl-2-pyridone.

2. These pyruvic esters were saponified to the corresponding acids and these by means of alkali and hydrogen peroxide degraded to the corresponding 1-methyl-2-pyridone-6(or 4)-acetic acids. The 6-pyruvic ester was converted directly in one step to the 6-acetic acid with alkali and hydrogen peroxide. Its potassium salt, however, by treatment with hydrogen peroxide, gave 1-methyl-2-pyridone-6-carboxylic acid.

3. Pyrolysis of 1-methyl-2-pyridone-6-(α-oximino)-propionic acid, obtained by reaction of the 6-pyruvic acid and hydroxylamine or by hydrolysis of the oximino ester, gave the 6-acetonitrile which could be alkylated with alkyl halides in the presence of sodium ethoxide. In the same way the 6-acetic ester, obtained from the acid, was alkylated with benzyl chloride and *n*-butyl iodide and acylated with acetyl chloride, the resulting products saponified and the corresponding acids decarboxylated by pyrolysis. 1-Methyl-6-phenethyl-2-pyridone, 6-*n*-amyl-1-methyl-2-pyridone and 6-acetonyl-1-methyl-2-pyridone were thus obtained.

4. 1,6-Dimethyl-2-pyridone condensed with *m*-nitrobenzaldehyde in presence of acetic anhydride to give a very low yield of 1-methyl-6-*m*-nitrostyryl-2-pyridone.

5. 2-Acetamido-6(or 4)-methylpyridine condensed with benzaldehyde to give 2-acetamido-6(or 4)-stilbazole, from which by saponification of the acetyl group and diazotization, 6- or 4-styryl-2-pyridone resulted.

6. 6-Methyl-2-pyridone condensed with acrylonitrile in presence of alkaline catalysts to give 6-methyl-2-pyridone-1-β-propionitrile, which was hydrolyzed to the corresponding acid. 6-Methyl-2-pyridone sodium condensed with bromoacetic ester to give ethyl 6-methyl-2-pyridone-1-acetate which in turn condensed with ethyl oxalate to form a pyruvate.

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[CONTRIBUTION FROM THE MARION EDWARDS PARK LABORATORY OF BRYN MAWR COLLEGE]

Hyperconjugation. III. Relative Rates of Bromination of Twelve Monoalkylbenzenes

BY ERNST BERLINER AND FRANCES BERLINER

The relative rates of bromination of toluene, ethylbenzene, *i*-propylbenzene and *t*-butylbenzene in aqueous acetic acid at 25° are 100, 76, 44 and 23, respectively.[1] A competitive bromination study of toluene and *t*-butylbenzene has confirmed the order for the latter two compounds.[2] These results have been explained by hyperconjugation involving the hydrogen atoms on the carbon atom alpha to the benzene ring.[1,2,3] In the work presented here the above order of reactivity is confirmed and investigation of the relative rates of bromination of monoalkylbenzenes is extended to include both propylbenzenes, all four butylbenzenes, and four of the eight amylbenzenes. The results are considered in the light of hyperconjugation.

Method. The procedure adopted for measuring the relative rates of bromination was similar to that used by De la Mare and Robertson.[1] The relative rates were calculated by comparing the times necessary for ten per cent. reaction of bro-

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[1] De la Mare and Robertson, *J. Chem. Soc.*, 279 (1943).

[2] Berliner and Bondhus, THIS JOURNAL, 68, 2355 (1946).

[3] Baker and Nathan, *J. Chem. Soc.*, 1844 (1935).

mine with the hydrocarbon. However, in the present investigation the reactions were conducted with a ten-fold excess of hydrocarbon and in the presence of excess sodium acetate. Sodium acetate increased the rates considerably and made it possible to conclude the reactions in a much shorter time.[4] In view of the work of Robertson, De la Mare and Johnston[1,5] it has seemed justified to assume that the order of the reaction with respect to bromine is the same for all monoalkylbenzenes.[6]

Experimental Part

Preparation of Materials

Glacial Acetic Acid.—C. P. acetic acid ("Niacet") was purified according to the method of Orton and Bradfield,[7] m. p. 16.4–16.5°. The "85% acetic acid" was prepared by adding 15 parts by volume of water from a buret to 85 parts of the above acetic acid, measured in a volumetric flask. The stock solution was kept in an amber bottle.

Bromine.—C. P. bromine was used without purification.

Sodium Acetate.—J. T. Baker C. P. Analyzed anhydrous sodium acetate was used without purification. The 0.15 *M* solution contained 6.1530 g. of sodium acetate in 85% acetic acid made up to volume in a 500-ml. flask.

Table I records the monoalkylbenzenes which were prepared for this study, their properties and the methods of synthesis.

TABLE I

PREPARATION AND PROPERTIES OF MONOALKYLBENZENES

Hydrocarbon	Boiling point °C.	Mm.	$n^{25}D$	Acetamino derivatives,[a] m. p., °C.
Toluene[b]	109.8–110.1	750	1.4930	
Ethylbenzene[b]	135.9–136.9	760	1.4930	
n-Propylbenzene[c]	158.9–159.2	766	1.4893	Mono 97.3–97.8 Di 206.7–207.7
i-Propylbenzene[b]	151.9–152	754	1.4885	Mono 105–106
n-Butylbenzene[d,e]	183–183.1 182–183	766[d] 764[e]	1.4872[d] 1.4872[e]	Mono 104–104.8 Di 216.4–217.4
i-Butylbenzene[f]	171.8–172	759	1.4840	Mono 130.8–131.5 Di 210.3–211.3
s-Butylbenzene[g]	172.2–172.3	751	1.4877	Mono 123.7–124.3
t-Butylbenzene[h]	168–168.4	763	1.4901	Mono 170.8–171.8
n-Amylbenzene[i]	203.5–203.8	753	1.4859	Mono 101.6–102.2
Neopentylbenzene[j]	185.5–185.8	755	1.4850	Mono 164.5–165.5 Di 245.9–246.9
2-Methyl-3-phenylbutane[k]	189–190	755		Mono 147.3–147.9
t-Amylbenzene[l]	188–189.5	755	1.4909	

[a] Ipatieff and Schmerling, THIS JOURNAL, 59, 1056 (1937); 60, 1476 (1938); 65, 2470 (1943). The melting points of the derivatives must be taken as indications of the identity rather than the purity of the hydrocarbons. [b] A C. P. chemical grade was purified with cold concentrated sulfuric acid according to Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Company, Boston, 1941, p. 364. [c] Prepared in 79% yield (b. p. 158–160° (758 mm.)) from 0.6 mole of propiophenone by a Wolff–Kishner reduction as modified by Huang-Minlon, THIS JOURNAL, 68, 2487 (1946). [d] Prepared in 78% yield by a Clemmensen reduction (with stirring) of butyrophenone. [e] Prepared by a Wurtz reaction of bromobenzene and *n*-butyl bromide ("Organic Syntheses," 25, 11(1945)). [f] Prepared in 79% yield (b. p. 170–172°) from 189 g. of *i*-butyrophenone, see ref. in (*c*). The *i*-butyrophenone was prepared in 81% yield (b. p. 66–67 (2 mm.)) from 300 g. of aluminum chloride suspended in 1200 ml. of thiophene-free benzene and 168 g. of *i*-butyryl chloride in 200 ml. of thiophene-free benzene at ice-bath temperature (Schmidt, Hopp and Schoeller, *Ber.*, 72, 1893 (1939); Hennion and Auspos, THIS JOURNAL, 65, 1603 (1943)); m. p. dinitrophenylhydrazone 161.3–162.8°. [g] Prepared according to Price and Lund, THIS JOURNAL, 62, 3105 (1940), using three times their amounts and letting the reaction mixture stand overnight, yield 70% (b. p. 170–173°). [h] Prepared as previously described, see ref. 2. [i] Prepared in 80% yield (b. p. 202–203° (750 mm.)) from 0.8 mole of *n*-valerophenone, see ref. in (*c*); $n^{20}D$ 1.4878 for the pure sample. The valerophenone was prepared as described for *i*-butyrophenone in 77.5% yield (b. p. 81.2° (2 mm.)); m. p. dinitrophenylhydrazone 166–167°. [j] Prepared by the method of Bygden, *Ber.*, 45, 3479 (1912), from benzylmagnesium chloride and *t*-butyl chloride. The yield was raised from 39 to 57.5% by adding benzene to the reaction mixture and refluxing it for several hours, b. p. 185.1–185.9° (755 mm.), $n^{25}D$ 1.4855, $n^{20}D$ 1.4875, m. p. monoacetamino derivative 164.9–165.8°. The diacetamino derivative melted between 236° and 242° after three crystallizations and was not pure. This sample was later found to contain small amounts of *p*-*t*-butyltoluene (see last paragraph of the experimental part) and was repurified in the following manner. Thirty-five milliliters of the hydrocarbon was treated with 10% of bromine in a brown bottle in the presence of a catalytic amount of iodine; after three days a trace of iron was added and the reaction mixture was heated briefly to 50° to complete the bromination. The product was washed and fractonally distilled affording the sample of neopentylbenzene recorded in the table, $n^{20}D$ 1.4870. [k] Prepared by catalytic reduction of 2-methyl-3-phenylbutene-2 in the presence of Adams catalyst at room temperature. The reduction proceeded slowly and never exceeded 75% of the theoretical. The olefin was prepared in about 45% yields from 0.5 mole of acetophenone and *i*-propylmagnesium chloride (Ipatieff, Pines and Schmerling, THIS JOURNAL, 60, 353 (1938); Klages, *Ber.*, 36, 3688 (1903)). [l] Prepared in 60% yield from 2 moles of *t*-amyl alcohol and 10 moles of thiophene-free benzene by the method of Huston, Fox and Binder, *J. Org. Chem.*, 3, 252 (1938), $n^{20}D$ of pure sample 1.4928.

All of the samples recorded in Table I were purified with cold concentrated sulfuric acid, or with aqueous potassium permanganate (agitated overnight at room temperature) followed by sulfuric acid, prior to final fractionations from metallic sodium. The ice-cold concentrated sulfuric acid extracted acid-darkening material from the reaction products regardless of the method of synthesis, and whereas it alone is effective in removing rapidly brominated impurities from the hydrocarbons, treatment with permanganate had to be followed by washing with sulfuric acid. It is believed that the ice-cold sulfuric acid did not cause any rearrangement. Of all of the compounds described above, only the purity of the 2-methyl-3-phenylbutane is questionable. Bromination of several samples was erratic, and there was never a sufficient amount available for rigorous purification.

The following samples were generously supplied by the Sun Oil Company, Norwood, Pennsylvania, the Phillips

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(4) The increase in rate produced by sodium acetate may be due to the formation of a more active brominating agent or may be connected with the removal of a proton from the activated complex by the acetate ion, the strongest base in the system. See also Bennett, Brand, James, Saunders and Williams, *J. Chem. Soc.*, 474 (1947).

(5) Robertson, De la Mare and Johnston, *J. Chem. Soc.*, 276 (1943); De la Mare and Robertson, *ibid.*, 100 (1948).

(6) In the bromination of aromatic compounds in acetic acid the order with respect to bromine is dependent on the temperature, the dilution and the type of compound. In the present case it is probably between two and three (see ref. 1 and 5). The bromination of benzene in benzene as a solvent is also kinetically of a higher order with respect to bromine. Bruner, *Z. physik. Chem.*, 41, 513 (1902); Price, THIS JOURNAL, 58, 2101 (1936).

(7) Orton and Bradfield, *J. Chem. Soc.*, 983 (1927).

Petroleum Company, Bartlesville, Oklahoma, and the Universal Oil Products Company, Riverside, Illinois: toluene, 99.7% pure; ethylbenzene, 99.82%; ethylbenzene, 99.3%; *n*-propylbenzene 99.0%; *i*-propylbenzene, 98%; *n*-butylbenzene 99.5%; *i*-butylbenzene, 99.8%; *s*-butylbenzene, 99.2%; *s*-butylbenzene, 98%; *s*-butylbenzene; *t*-butylbenzene, 99.9%; *t*-butylbenzene, 99.76%; *t*-butylbenzene, 98%. Each sample was redistilled from metallic sodium immediately before use.

All samples of hydrocarbons used in the bromination study were stored in amber bottles over sodium wire.

General Procedure

The bromination experiments were conducted as follows in a room provided with black curtains and lighted with a red lamp. To 20 ml. of an 85% acetic acid solution, 0.4 *M* in hydrocarbon and 0.15 *M* in sodium acetate, contained in a blackened bottle and brought to 25 ± 0.05° in a thermostat, was added 20 ml. of an 85% acetic acid solution, 0.04 *M* in bromine and 0.15 *M* in sodium acetate.[8] The solutions were mixed and a 5-ml. portion was immediately withdrawn and analyzed for bromine iodimetrically with 0.04 *M* sodium thiosulfate, contained in a microburet graduated to 0.01 ml., using starch as an indicator. This reading was taken as the zero point. The thiosulfate solution was prepared for each run from a 0.1000 *M* stock solution. A freshly prepared 6% solution of potassium iodide was used for each titration. A blank was run simultaneously with each reaction in order to provide corrections for loss of bromine by evaporation. The loss occurred only during sampling and became rather large and irregular after four or five samples had been withdrawn. In order to reduce to a minimum the corrections for loss of bromine by evaporation, preliminary studies were made for each monoalkylbenzene in which six to eight readings were taken in order to establish the approximate time for 10% reaction of bromine. Then subsequent runs were made for each compound in which only four readings were taken, one to establish the zero point, two shortly before 10% reaction, and one shortly after 10% reaction, in order to determine accurately the 10% reaction time. The error, introduced chiefly through the uncertainty of the blank, was about ±1% of the final reaction time. The results were well reproducible. Due to the volatility of the bromine the initial concentration usually deviated slightly from 0.02 *M*, but corrections for this deviation were applied to the final results and never amounted to more than a few minutes. A large number of check runs was made for each monoalkylbenzene and all samples listed above were used, although some were found to contain small amounts of rapidly brominated impurities. Results obtained with such samples were discarded. A rapidly brominated impurity was easily recognized by the large deviation of the initial titer from the blank. Small amounts of impurities which are brominated more slowly than the hydrocarbons would not have affected the rates. All compounds were studied independently by each investigator; a total of about 200 runs was made. Some results of a typical study (*n*-propylbenzene) are listed below. (The blanks found were on the average 0.15, 0.25, 0.35 for each successive opening.)

Sample I (synthetic)

Time	Sodium thiosulfate, ml. of 0.04 *M*	Reaction, %
0	4.951	...
240′	4.598	6.83
325′	4.507	8.46
420′	4.420	10.02

10%, 419 minutes

0	4.972	...
340′	4.510	8.99
390′	4.469	9.61
440′	4.422	10.36

10%, 416 minutes

Sample II (99.0% pure)

0	4.900	...
325′	4.459	8.70
400′	4.395	9.80
440′	4.353	10.45

10%, 412 minutes

0	4.902	...
290′	4.501	7.87
370′	4.422	9.28
440′	4.357	10.40

10%, 415 minutes

The sample of neopentylbenzene, prepared by the method of Bygden (Table I, ref. *j*) was found kinetically to contain a by-product, although the impurity was not brominated rapidly enough to show a deviation of the initial titer from the blank. The sample showed a 10% reaction time of about 400 minutes, almost identical with *n*-propylbenzene (415 minutes). A comparison of the time/% reaction curves for the two compounds up to 15% reaction showed, however, that they were not identical in shape. The neopentyl curve rose more rapidly and slowed down appreciably after 10%, suggesting that the sample contained an impurity, present to the extent of about 1%, which was brominated more rapidly than neopentylbenzene. A 5-ml. sample of the impure neopentylbenzene was oxidized with potassium permanganate[9] in aqueous pyridine and afforded a small amount of *p*-*t*-butylbenzoic acid, m. p. after crystallization from dilute alcohol 165–166°. Mixed melting point with an authentic sample of *p*-*t*-butylbenzoic acid[10] showed no depression. The formation of *p*-*t*-butyltoluene from benzylmagnesium chloride and *t*-butyl chloride is similar to the recently reported formation of *p*-ethyltoluene from benzylmagnesium chloride and ethyl sulfate.[11]

Results and Discussion

In Table II are recorded the compounds that were brominated and the times required for 10% reaction of each. Table III summarizes some of the pertinent relative rates.

The members of Series I (first column of Table III) fall in an order demanded by the Baker–Nathan effect and identical with that obtained by De la Mare and Robertson.[1] Under the present experimental conditions the differences in relative rates of bromination of the four compounds (100:70:40:18) are larger than those obtained by the latter investigators (100:76:44:23). That the solvent composition (the presence of sodium acetate) should influence the spacing of the rates is not unreasonable and was discussed in a previous communication.[12] The relative rates of bro-

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[8] The amylbenzenes required more dilute solutions since they were not sufficiently soluble for the preparation of 0.4 *M* solutions in 85% acetic acid. The bromine solution was therefore concentrated accordingly so that after mixing the concentrations of bromine and hydrocarbon were still 0.02 and 0.2 *M*, respectively.

(9) Nightingale, Radford and Shanholtzer, THIS JOURNAL, **64**, 1662 (1942).

(10) Prepared by Mrs. Lucille Altschul.

(11) Burtle and Shriner, THIS JOURNAL, **69**, 2059 (1947). It is possible that the rearrangement which occurred during the preparation of neopentylbenzene was due to the higher temperature employed through the use of benzene, and does not occur when ether is used.

(12) Berliner and Bondhus, *ibid.*, **70**, 854 (1948).

TABLE II

TEN PER CENT. REACTION TIMES FOR BROMINATION OF MONOALKYLBENZENES

Alkylbenzene	Time in minutes for 10% reaction
Toluene	230
Ethylbenzene	330
n-Propylbenzene	415
i-Propylbenzene	570
n-Butylbenzene	390
i-Butylbenzene	620
s-Butylbenzene	710
t-Butylbenzene	1300
n-Amylbenzene	440
Neopentylbenzene	1110
2-Methyl-3-phenylbutane	(800)
t-Amylbenzene	1000

TABLE III

RELATIVE RATES OF BROMINATION OF MONOALKYLBENZENES

R	Series I Ph–R	Series II $PhCH_2$–R	Series III $PhCHRCH_3$
Methyl	100	100	100
Ethyl	70	80	80
i-Propyl	40	53	(71)
t-Butyl	18	30	

mination of the two propylbenzenes and the four butylbenzenes also follow the general pattern of the Baker–Nathan effect, *i. e.*, are dependent on the number of hydrogen atoms available on the alpha carbon atom for conjugation with the benzene ring. Thus *n*-propylbenzene with two alpha hydrogen atoms is brominated faster than *i*-propylbenzene with only one (100:73). The four butylbenzenes fall in the order *n*-butyl > *i*-butyl > *s*-butyl > *t*-butyl (100:63:55:30). The difference between *i*-butyl and *s*-butylbenzene, although in accord with the theory, is not very large. On the other hand, the difference between the normal and the iso compound seems quite pronounced, where on the basis of the Baker–Nathan effect *per se* no statement could have been made regarding a difference as both compounds carry the same number of hydrogen atoms on the carbon atom alpha to the ring and have, moreover, identical molecular weights. Series II (second column of Table III) affords a more comprehensive example of the same type. This series corresponds to Series I with a methylene group placed between the ring and the variable alkyl group. The rates of bromination decrease in the order R = methyl > ethyl > *i*-propyl > *t*-butyl, *i. e.*, the order of reactivity corresponds to that for Series I, although the relative rates can no longer be accounted for by the Baker–Nathan effect. A similar situation exists for Series III (last column of Table III).[13]

Since the relative reactivities of the members of Series II (and Series III) cannot be accounted for on the basis of the number of hydrogen atoms on the carbon atom next to the benzene ring, as all four compounds have two such hydrogen atoms, the determining factor might conceivably be the extent of carbon–carbon hyperconjugation, the electrostatic inductive effect, or the size and polarizabilities of the four alkyl groups. Neopentylbenzene in all cases then should react the most rapidly,[14] ethylbenzene the least, and the total order of reactivity for the series should be exactly the reverse of the order actually obtained. Increasing steric hindrance in the *ortho* positions with increasing size of the alkyl group *might* account for the observed order and therefore merits consideration. Moreover, there has been a recent demonstration that the rates of propylation of alkylbenzenes can be accounted for by such an hypothesis.[15]

Toluene, on bromination in excess toluene as a solvent, yields 60.3% *para* and 39.7% *ortho* product.[16] That the ratio will not be appreciably changed in another solvent can be assumed and is borne out by experiments of Ingold, *et al.*[17] If one assumes the least favorable case, that *t*-butylbenzene affords *no ortho* substitution, a comparison of only the *para* positions shows that toluene reacts $5.7 \times 60/100 = 3.42$ times faster than *t*-butylbenzene in the *para* position.[18] Thus steric hindrance can account for only a fraction of the difference in rates of bromination of the two sterically extreme members of Series I. It must therefore contribute even less to the other relative rates of the series.[19]

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[13] These series are not the only cases in which the number of hydrogen atoms alpha to the ring is not the decisive factor. *i*-Butylbenzene (two hydrogens) clearly reacts slower than *i*-propylbenzene (one hydrogen), and neopentylbenzene is brominated appreciably slower than *t*-amylbenzene, in spite of a difference of two hydrogen atoms.

[14] If carbon–carbon hyperconjugation were the determining factor, contributions like $ArCH_2{\ominus}{\oplus}C(CH_3)_3$ would make neopentylbenzene the most reactive.

[15] Condon, THIS JOURNAL, **70**, 2265 (1948).

[16] Holleman, *Chem. Rev.*, **1**, 187 (1924–1925).

[17] Ingold, Lapworth, Rothstein and Ward, *J. Chem. Soc.*, 1959 (1931); Bird and Ingold, *ibid.*, 918 (1938).

[18] Actually some *ortho* substitution in bromination of *t*-butylbenzene does occur. Kozak (*Bull. Akad. Sci. Cracow*, 407 (1906); *Chem. Zentr.*, **78**, I, 1787 (1907)) prepared *o*-*t*-butyltoluene by a Wurtz–Fittig reaction of the bromination product of *t*-butylbenzene. The rate of bromination of toluene in the *para* position relative to that of *t*-butylbenzene is therefore greater than 3.42. In the nitration of *t*-butylbenzene 23% *ortho* and 77% *para* substitution has been reported (Craig, THIS JOURNAL, **57**, 195 (1935)).

[19] Schramm (*Ber.*, **18**, 1272 (1885); *Monatsh.*, **9**, 842 (1888)) has demonstrated the formation of *ortho* products in the bromination of ethylbenzene and cumene. However, the only existent numerical data for *ortho–para* ratios of ethylbenzene, cumene and *t*-butylbenzene were obtained in preparative nitration (see data quoted by Le Fevre (*J. Chem. Soc.*, 980 (1933)) and see also Sterling and Bogert (*J. Org. Chem.*, **4**, 20 (1939)), Mayes and Turner (*J. Chem. Soc.*, 500 (1929)) and Craig (ref. 18). The data show qualitatively that *para* substitution increases successively in the four compounds of Series I as *ortho* substitution decreases. Since bromination affords more *para* substitution in general than nitration (about 20% for toluene), one can tentatively assign to the four compounds, on the basis of the nitration data, the *ortho–para* ratios 40/60, 30/70, 20/80, and 10/90 in bromination. Using these data the relative reactivities for the four compounds in the *para* positions become 100:81:54:27 as compared with the original 100:70:40:18. These corrected relative rates are numerically very close to the relative rates obtained in Series II (100:80:53:30) and Series III (100:80:(71)). However, as the *ortho–para* ratios assigned to the members of Series I are only approximate, one cannot attach great significance to the similarity of the numerical values for the relative rates in the three series.

If steric hindrance is not decisive in Series I, it cannot be decisive in Series II where the branching occurs on a carbon atom once removed from the benzene ring.[20] The contributions from steric factors to the reactivities of the compounds of series II can, as a first approximation, be assumed to be the same. The relevant data in the literature are not very extensive, but the data that exist point toward little difference in the *ortho–para* ratios for the members of this series.[21] In the alpha-methyl series (III) steric hindrance also probably has an insignificant effect on the relative rates. The data on the third compound of Series III, however, are less accurate than those for all other compounds and this series will not be considered further.

One is, therefore, left with a situation in which neither steric effects, first-order hyperconjugation of the carbon–hydrogen bonds, carbon–carbon hyperconjugation nor the electrostatic inductive effect can account for the observed decrease in rates of Series II. The experimental facts, apart from any theories, demonstrate the following. The four alkyl groups methyl, ethyl, *i*-propyl, *t*-butyl, attached directly to the benzene ring, release electrons into the ring (or accommodate a positive charge in the transition state) in the order methyl > ethyl > etc. If a methylene group is placed between the alkyl group and the benzene ring, the effect of these alkyl groups passes through the methylene group in the same order. It is reasonable to assume that whatever causes the four alkyl groups to act as they do in Series I is also responsible for the relative rates in Series II and that this effect is transmitted through the saturated methylene group, contrary to accepted views. If it is correct that the differences in rate in the first series are due to hyperconjugation of the carbon–hydrogen bonds, and there seem to be enough indications that this is the case, one is forced to conclude that the second series is also affected by a similar type of hyperconjugation and that the relative rates depend on the number of hydrogen atoms on the beta carbon atom. A second-order hyperconjugation involving the beta hydrogens as is shown in Fig. 1 is therefore tentatively suggested to account for the relative rates of bromination of the compounds of Series II. The structures would clearly account for the experimentally observed facts, provided that only the number of hydrogen atoms on the *beta* carbon atom determines the stability of the transition state (when the number of *alpha* hydrogen atoms is constant). This type of hyperconjugation must be less important than hyperconjugation involving *alpha* hydrogens, for otherwise ethylbenzene would be brominated faster than toluene and isopropylbenzene would be brominated faster than *n*-propylbenzene, whereas the reverse is true. On the other hand, *n*-butylbenzene with two *beta* hydrogen atoms is brominated faster than isobutylbenzene with only one as previously pointed out, and the difference may be attributed at least in part to a difference in hyperconjugation involving the beta hydrogens. Although it is true that second-order hyperconjugation is supposed to be insignificant (although ever present),[22] it is, in this case, enhanced by conjugation with the benzene ring. Similar forms have been suggested for bibenzyl (where two rings are available for conjugation) and for geranylamine hydrochloride (where a single bond is flanked by two double bonds) to account for the shortening of the central carbon–carbon bond.[23] In looking for other possible explanations the following suggest themselves. There is the possibility of structures of type ArCH$_2^{\oplus}$ $\ominus$R which would withdraw electrons from the ring and account for the order, but such a possibility is not supported by any other evidence. Steric inhibition of resonance due to a lack of coplanarity is not expected to be a decisive factor, nor is it assumed that the observed order is due to a change in mechanism of the substitution by bromine. However, none of these factors can be ruled out completely on the basis of the available experimental evidence.

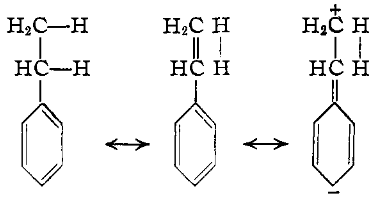

Fig. 1.

It is noteworthy that the order of the rates of bromination of the alkylbenzenes of Series II is identical with that of S_N1 displacement reactions on the corresponding halides (ethyl bromide, *n*-propyl bromide, etc.).[24,25] The order for the S_N1 reactions has been ascribed by Benfey[25] to hyperconjugation of the hydrogen atoms on the beta carbon atoms. S_N1 reactions, like aromatic substitution, are electron demanding and go through a positively charged transition state. Although the reactions of the alkyl halides are different from

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[20] Note the related case of "classical" steric hindrance in 2,4,6-trimethylbenzoic acid and its esters, and the absence of steric hindrance in the corresponding phenylacetic acid: Meyer and Sudborough, *Ber.*, **27**, 1580 (1894); Watson, "Modern Theories of Organic Chemistry," Oxford University Press, 2nd ed., 1941, pp. 246 ff.

[21] *Nitration* of *n*-propylbenzene affords the *ortho* isomer to about the same extent as ethylbenzene (Baddeley and Kenner, *J. Chem. Soc.*, 303 (1935)). The presence of the *ortho* isomer in the *bromination* of the former has been demonstrated through oxidation to *o*-bromobenzoic acid (Schramm, Ref. 19). Furthermore, all normal alkylbenzenes afford a dinitro product with great ease (*o/p*), and with the amylbenzenes having two hydrogen atoms next to the ring, including neopentylbenzene, appreciable *ortho* substitution occurs (Ipatieff and Schmerling, Table I, ref. *a*).

[22] Wheland, "The Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, pp. 86–87.

[23] Jeffrey, *Proc. Roy. Soc.* (*London*), **A183**, 388 (1945); **A188**, 222 (1947); Bateman and Jeffrey, *J. Chem. Soc.*, 211 (1945); Robertson, *Ann. Reports*, **42**, 54 (1946).

[24] Dostrovsky and Hughes, *J. Chem. Soc.*, 157 (1946), and following papers.

[25] Benfey, THIS JOURNAL, **70**, 2163 (1948).

those of the alkylbenzenes, in that in the latter the alkyl groups are far removed from the seat of the reaction, it would seem plausible that alkyl groups exhibit the same electronic effect in both alkyl halides and alkylbenzenes. Granted the similarity, it is then perhaps no coincidence that *t*-amylbenzene is brominated faster than *t*-butylbenzene where *t*-amyl chloride is hydrolyzed faster than *t*-butyl chloride.[26] In the case of the two tertiary alkylbenzenes it may mean that in the complete absence of alpha hydrogen atoms carbon–carbon hyperconjugation takes precedence—an hypothesis which will be further tested.

n-Butylbenzene is brominated faster than *n*-propylbenzene to a small but definite extent. The result, tested on two different samples, indicates an apparent anomaly, particularly in view of the fact that *n*-amylbenzene is brominated slower than *n*-propylbenzene.[27] This anomality of the *n*-butyl group is manifested in other reactions and equilibria such as the strengths of aliphatic acids[28] and amines,[29] the enolization of phenyl alkyl ketones[30] and the basic dissociation constants of *p*-alkyldimethylanilines and their reactions with methyl iodide.[31] In the last two cases the order is methyl > ethyl > *n*-butyl > *n*-propyl > *i*-butyl. The anomalous effect has variously been attributed to a field effect,[31,32] or chelation and hydrogen bonding[28,30] resulting from the interaction of the terminal hydrogen atoms with the functional group. In the case of *n*-butylbenzene (and higher alkylbenzenes) chelation, if it occurs, might be pictured in terms of hyperconjugation structures as shown in Fig. 2. Such additional hyperconjugation should increase the rate of bromination and the amount of meta product.[33]

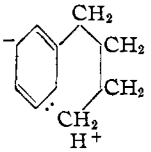

Fig. 2.

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Summary

The relative rates of bromination of twelve monoalkylbenzenes are toluene 100, ethylbenzene 70, *n*-propylbenzene 55, *i*-propylbenzene 40, *n*-butylbenzene 59, *i*-butylbenzene 37, *s*-butylbenzene 32, *t*-butylbenzene 18, *n*-amylbenzene 52, neopentylbenzene 21, 2-methyl-3-phenylbutane 29, *t*-amylbenzene 23. A second-order hyperconjugation involving beta hydrogen atoms is suggested to account for part of this order of relative rates.

Neopentylbenzene prepared from benzylmagnesium chloride and *t*-butyl chloride contains some *p*-*t*-butyltoluene.

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[26] Hughes and MacNulty, *J. Chem. Soc.*, 1283 (1937).

[27] The relative rates of bromination of the normal alkyl series, toluene, ethylbenzene, *n*-propylbenzene, *n*-butylbenzene and *n*-amylbenzene, are 100, 70, 55, 59 and 52, respectively.

[28] Dippy, *Chem. Rev.*, **25**, 189 (1939); *J. Chem. Soc.*, 1222 (1938).

[29] Hall and Sprinkle, THIS JOURNAL, **54**, 3469 (1932).

[30] Evans, *J. Chem. Soc.*, 785 (1936); Evans and Gordon, *ibid.*, 1434 (1938).

[31] Davies, *ibid.*, 1865 (1938). The author assigns the anomality to the *n*-propyl rather than the *n*-butyl group: also ref. 32.

[32] Ayling, *ibid.*, 1014 (1938).

[33] The possibility of accounting for the anomalous effect of the *n*-butyl group by hyperconjugation structures of the above type was suggested by one of the Referees of this paper, who proposed structures involving second-order hyperconjugation throughout the *n*-butyl group.