toluene (**12**), 9.0 min; and 3-nitro-2,4,6-tri-*t*-butyltoluene (**13**), 11.1 min.

3-Nitro-2,4,6-tri-*t*-butyltoluene (13) was isolated by trituration of the crude reaction product with hot methanol followed by filtration. The residue collected (0.85 g) was recrystallized from toluene–ethanol with poor recovery yielding 0.19 g, mp 253–255°. The nmr spectrum showed three *t*-butyl absorption lines at 1.33 (9 H), 1.49 (9 H), and 1.55 (9 H), an aromatic methyl at 2.67 (3 H), and an aromatic proton at 7.66 (1 H).

Anal. Calcd for $C_{19}H_{31}NO_2$: C, 75.66; H, 9.84; N, 4.41. Found: C, 75.29; H, 10.06; N, 4.49.

4-Nitro-2,6-di-*t*-butyltoluene (12) was isolated in pure form by preparative glpc of the concentrated mother liquor. Crystallization of the 500 mg isolated, from 3 ml of absolute ethanol, yielded 320 mg of faintly yellow silken spars, mp 119–120°. The nmr spectrum showed only one *t*-butyl absorption line at 1.54 (18 H), an aromatic methyl absorption at 2.76 (3 H), and one aromatic absorption at 8.31 (2 H).

Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.61. Found: C, 72.49; H, 9.57; N, 5.89.

2-Nitro-4,6-di-*t*-butyltoluene (11) was also isolated by preparative glpc.[38] The nmr spectrum showed two *t*-butyl absorption lines at 1.32 (9 H) and 1.50 (9 H), an aromatic methyl at 2.51 (3 H), and an AB (J = 2 Hz) aromatic quartet with doublet lines centered at 7.50 (1 H) and 8.70 (1 H) indicating nonequivalent *meta*-oriented aromatic protons.

Product Distributions in Nitration of 1-CH_3 and 1-CH_3-d_2. Three milliliters of a precooled solution of nitric acid in nitromethane (3:7) was added to flasks containing 3.00 ml of stock solutions of **1**-CH_3 or **1**-CH_3-d_2 (1.5×10^{-2} M in nitromethane) which were held at 0° in a large dewar. A noticeable brown color developed in all of the reaction solutions upon addition of the colorless nitrating solution, and this color disappeared as the reaction proceeded. After a 1-hr reaction period, the contents of each flask were poured into about 50 ml of water, and nitration products were extracted with 5.00 ml of purified toluene. Residual nitromethane was removed by extraction of the toluene solutions with dilute aqueous ammonia and the dried toluene solutions, after concentration, were subjected to glpc analysis.

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(38) Column chromatography over alumina with pentane elution gave fair separation of the isomers, **11** being eluted shortly before **12**.

Reactions of Cyclohexadienyl Cations. Aromatic Acetoxylation Accompanying Halogenation[1]

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Abstract: Halogenation of 1,3,5-tri-*t*-butylbenzene and other alkylbenzenes with positive halogenating agents in acetic acid solvent results in the formation of aryl acetate products. Yields of aryl acetates increase upon addition of sodium acetate to the solvent. Data derived from studies of product distributions, kinetic isotope effects, and structural effects indicate that acetoxylation accompanying halogenation occurs by addition–elimination.

Some time ago we reported that the silver ion induced bromination of 1,3,5-tri-*t*-butylbenzene proceeds with a slow proton transfer from aromatic carbon.[3] This result represented one of the first observations of a rate-limiting proton transfer in aromatic bromination of a benzene system, and it was suggested at that time that the change-over in rate-limiting step was due to the large steric repulsion effects imposed around the reaction site by the *t*-butyl substituents. This view seems amply supported by subsequent studies of aromatic bromination of this and related systems and also by studies of other aromatic substitution reactions.[4,5]

During this interval we have attempted to examine the effects of changing the concentration of solvent acid–base species on the isotope effect in bromination of 1,3,5-tri-*t*-butylbenzene. These and supporting studies have shown that bromination of this hydrocarbon is considerably more complex than originally proposed. Of perhaps greatest interest is the observation that significant quantities of acetoxylation product accompany aromatic halogenation in acetic acid solutions containing added acetate ion. In this report we describe product distribution and kinetic isotope effect studies in the bromination and chlorination of 1,3,5-tri-*t*-butylbenzene and some related compounds, and discuss the attending acetoxylation reaction in terms of the long-discarded but recently revitalized addition–elimination mechanism of aromatic substitution.

(1) Presented in part at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965.

(2) (a) Petroleum Research Fund Undergraduate Research Participant; (b) National Science Foundation Undergraduate Research Participant.

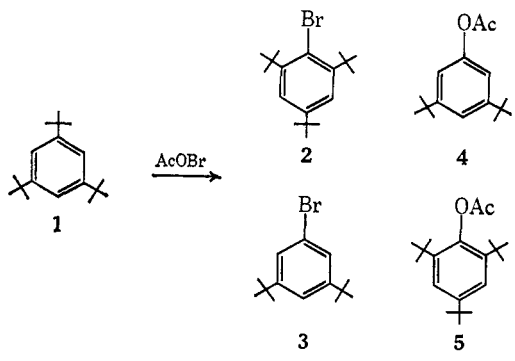
(3) P. C. Myhre, *Acta Chem. Scand.*, **14**, 219 (1960).

(4) (a) E. Baciocchi, G. Illuminati, G. Sleiter, and F. Stegel, *J. Am. Chem. Soc.*, **89**, 125 (1967); (b) M. Christen and H. Zollinger, *Helv. Chim. Acta*, **45**, 2066 (1962); (c) E. Helgstrand, *Acta Chem. Scand.*, **18**, 1616 (1964); **19**, 1583 (1965); (d) E. Helgstrand and Å. Nilsson, *ibid.*, **20**, 1463 (1966); (e) Å. Nilsson, *ibid.*, **21**, 2423 (1967).

(5) The occurrence of rate-limiting proton transfers in aromatic nitration of benzene derivatives has also been attributed to increasing steric effects; see P. C. Myhre, M. Beug, and L. James, *J. Am. Chem. Soc.*, **90**, 2105 (1968).

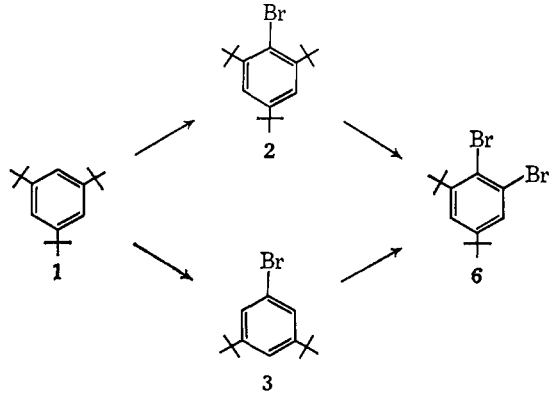
Results

Bromination of 1,3,5-tri-*t*-butylbenzene (**1**) in acetic acid solvent with molecular bromine and silver salts or with preformed acetyl hypobromite results in the initial formation of not only 2,4,6-tri-*t*-butylbromobenzene (**2**) and 3,5-di-*t*-butylbromobenzene (**3**), but also variable amounts of 3,5-di-*t*-butylphenyl acetate (**4**) and 2,4,6-tri-*t*-butylphenyl acetate (**5**).



All of these products are subject to further halogenation. Both products **2** and **3** are subsequently halogenated to yield 1,2-dibromo-3,5-di-*t*-butylbenzene (**6**). The phenyl acetates yield a number of bromination products which have not been fully characterized.

Competitive bromination of mixtures of **2** and **3**, utilizing reaction conditions which result in only minor formation of acetate products ("neutral" solutions of acetic acid and dioxane), indicate that bromode-*t*-butylation of **2** is more rapid than bromodeprotonation of **3**, $k_{6\leftarrow 2}/k_{6\leftarrow 3} = 1.45$. The ratio of rates of formation of **2** and **3** from **1**, k_2/k_3, has been found to decrease as the acidity of the reaction mixture increases. In the limiting case, bromination with Friedel–Crafts catalysts such as ferric halides, no 2,4,6-tri-*t*-butylbromobenzene is detected.[6,7]



The occurrence of the dibromination of both **2** and **3** (eq 1) necessitated a different approach to the measurement of the hydrogen isotope effect in the formation of 2,4,6-tri-*t*-butylbromobenzene from 1,3,5-tri-*t*-butylbenzene.[8] Of the several alternatives, a comparison of the product distributions upon parallel, partial bromination (~5% conversion) of 1,3,5-tri-t-butylbenzene (**1**) and 1,3,5-tri-*t*-butylbenzene-2,4,6-d_3 (**1**-d_3) was selected.

These studies, conducted in acetic acid solvent mixtures containing variable amounts of added perchloric acid or sodium acetate, revealed that striking changes in the distribution of products could be effected by variation of the hydrogen ion or acetate ion concentration as well as by introduction of deuterium in the reactant hydrocarbon. The resulting product distribution data are presented in Table I.

Most of the data (Table I) was obtained by addition of bromine to solutions of the hydrocarbon and silver perchlorate; however, some runs were also made with preformed acetyl hypobromite, produced by the reaction of bromine with silver acetate in carbon tetrachloride solution. The results observed with both methods are substantially the same.

The data show that the distributions are extremely sensitive to changes in hydrogen ion concentration, particularly near the "neutral" point. Since the stoichiometry of the silver ion induced bromination is such that hydrogen ion is formed together with the bromination product, equimolar amounts of bromine and sodium acetate were added dropwise to the reaction mixture containing the specified amount of added perchloric acid or sodium acetate so that acid formed by the reaction would be neutralized by added acetate.[9]

The structures of the phenyl acetate products were established by isolation of these products from larger scale runs and subsequent spectral analysis. Finally, these products were compared with authentic samples of phenyl acetates synthesized by independent methods.

Control studies demonstrated that product aryl halides are not converted to aryl acetates, that acetate formation is insensitive to the presence of free-radical initiators or inhibitors, and that direct acetoxylation by the action of peracetic acid and metal ions or lead tetraacetate (in the absence of molecular halogen) is not realized, even when more prolonged reaction times and higher temperatures are employed.

By contrast with bromination, silver-induced chlorination of 1,3,5-tri-*t*-butylbenzene in acetic acid solvent yields primarily 2,4,6-tri-*t*-butylchlorobenzene (**7**). However, chlorination in acetic acid and acetic acid solutions containing added acetate ion results in small, but measurable, amounts of the two acetate products, **4** and **5**. Some data obtained from parallel chlorinations of **1** and **1**-d_3 are presented in Table II.

Finally, a brief survey of the products of silver ion induced halogenation of other alkylbenzenes shows that acetoxylation attending halogenation is not unique to **1**. Yields of acetate products observed in partial halogenations of several alkylbenzenes are shown in Table III.

(6) P. D. Bartlett, M. Roha, and R. M. Stiles, *J. Am. Chem. Soc.*, **76**, 2349 (1954).

(7) The existence of a facile protodebromination of **2** in strongly acidic media is one of several factors which complicate the interpretation of this trend; see P. C. Myhre, *Acta Chem. Scand.*, **14**, 947 (1960).

(8) The method used initially involved preparative bromination of tritium-labeled 1,3,5-tri-*t*-butylbenzene and determination of tritium in the product, **2**.[3] The problems introduced by the subsequent reaction of **2** could, in principle, be eliminated by determining the tritium content of the unconsumed reactant. However, preliminary experiments directed toward this end were complicated by experimental difficulty in isolating pure samples of unconsumed reactant (by preparative glpc) which had not undergone some hydrogen exchange. The alternate procedure used appeared to yield equivalent or more detailed information with considerable economy of time.

(9) This is, of course, only an approximate technique, since not all of the added bromine undergoes a substitution reaction in which a proton is released. Bromodealkylation liberates an alkyl fragment which is capable of accepting bromine. In addition some bromine is consumed by silver salt decarboxylation.

Table I. Product Distributions in Partial Bromination of 1,3,5-Tri-*t*-butylbenzene (**1**) and 1,3,5-Tri-*t*-butylbenzene-2,4,6-d_3 (**1**-d_3) in Acetic Acid Solutions at 25°

Reactant[a]	Added, mol × 10^{-3}, l.$^{-1}$ $HClO_4$	NaOAc	Mole % prodt[b] **2**	**3**	**4**	**5**
			Glacial Acetic Acid			
1	100		81.8	14.5	1.8	1.9
1-d_3			54.8	35.2	5.0	5.0
1	50		84.0	13.0	1.6	1.4
1-d_3			58.3	31.2	5.0	5.4
1	25		87.8	9.3	1.6	1.3
1-d_3			63.0	26.6	4.9	5.5
1	10		89.6	7.1	1.6	1.7
1-d_3			67.9	20.9	5.0	6.2
1	...	...	89.8	6.6	1.8	1.8
1-d_3			70.5	19.1	4.2	6.2
1		10	75.5	3.8	8.4	11.3
1-d_3			46.5	8.0	18.6	26.9
1		25	58.8	1.1	15.9	24.2
1-d_3			28.3	1.6	26.6	43.5
1		50	53.3	0.5	19.0	27.2
1-d_3			26.9	0.9	28.8	43.4
1		100	51.8	0.2	19.2	28.8
1-d_3			25.6	0.3	29.4	44.7
			97% Acetic Acid[c]			
1	100		70.0	18.5	4.9	6.6
1-d_3			39.8	37.6	9.4	13.2
1	25		70.8	16.4	4.0	8.8
1-d_3			39.5	35.5	10.2	14.8
1	5		72.0	16.2	3.8	8.0
1-d_3			44.0	31.5	8.2	16.2
1	...	...	71.7	15.6	3.8	7.9
1-d_3			44.9	28.9	8.0	18.2
1		5	64.6	12.8	8.7	13.9
1-d_3			36.6	25.1	14.8	23.5
1		10	61.0	8.0	11.7	19.3
1-d_3			33.2	13.2	21.5	32.1
1		20	55.4	4.3	15.0	25.3
1-d_3			28.1	5.7	25.8	40.5
1		25	55.0	3.5	16.5	25.0
1-d_3			28.9	5.4	25.7	40.0
1		100	55.4	0.7	17.5	26.5
1-d_3			25.0	1.5	29.2	44.3
			Acetic Acid and Dioxane (6:1 by volume)[d]			
1	50		87.4	9.7		2.9
1-d_3			67.3	25.3		7.4
1	...	...	91.7	6.4		1.9
1-d_3			72.9	19.5		7.6
1		50	59.0	9.3		31.7
1-d_3			30.5	17.3		52.3
			Acetyl Hypobromite in Acetic Acid and Carbon Tetrachloride (4:1 by volume)			
1			99	0.3	0.3	0.7
1-d_3	...	...	96	0.9	0.9	2.2
1		10	56.2	19.7		24.1
1-d_3			36.6	30.1		33.3

[a] Reactant hydrocarbon and silver perchlorate concentrations were 0.050 and 0.010 *M*, respectively; 0.1 equiv of bromine, with respect to the hydrocarbon, was added to the stirred reaction solution. [b] Product analyses were made by glpc with the use of an SE 30 column. Areas under curves were measured with the use of a Disc Instruments integrator and corrected for relative response with the use of data obtained from synthetic mixtures. The mole per cent values reported are the average of at least three chromatographic determinations. The average deviation from the mean values reported were approximately ±1% or less for the larger values and ±0.5% or less for the smaller values. [c] An additional and as yet unidentified product was found in variable amount in studies conducted in 97% acetic acid. The yield of this product is largest in solutions of highest acidity and when **1**-d_3 is the reactant (maximum yield 20%) and decreases when the acidity is reduced or unlabeled reactant is used. Characterization of this product has proved elusive, since large-scale "preparative" runs showed no or, at best, trace amounts of this material. [d] Chromatographic conditions in this series did not permit resolution of the peaks representing **3** and **4**.

Table II. Product Distribution in Partial Chlorination of 1,3,5-Tri-*t*-butylbenzene (**1**) and 1,3,5-Tri-*t*-butylbenzene-2,4,6-d_3 (**1**-d_3) in Acetic Acid Containing Sodium Acetate, 0.10 *M*

Reactant	% Conversion	Products, % **7**	**4**	**5**
1	8	90.8 ± 0.3	2.4 ± 0.2	6.8 ± 0.2
1-d_3		88.6 ± 0.2	3.5 ± 0.1	7.9 ± 0.3
1	17	91.5 ± 0.2	2.2 ± 0.1	6.3 ± 0.2
1-d_3		89.5 ± 0.2	3.2 ± 0.1	7.3 ± 0.1
1	22	91.5 ± 0.2	2.2 ± 0.1	6.3 ± 0.1
1-d_3		89.5 ± 0.1	3.3 ± 0.1	7.2 ± 0.1

Table III. Yields of Aryl Acetate Products Formed in the Silver Ion Induced Halogenation of Some Alkylbenzenes in Acetic Acid Solvent

Reactant	Acetate product, % Bromination "neutral"	Bromination 0.1 *M* NaOAc	Chlorination "neutral"	Chlorination 0.1 *M* NaOAc
Mesitylene	...	0.3	...	1
Durene	...	13	...	7
1,4-Diisopropyl-*p*-xylene	...	30	32	48
1,3,5-Tri-*t*-butylbenzene	3.5	48	6	9

Discussion

The data unquestionably show that formation of 2,4,6-tri-*t*-butylbromobenzene by silver ion induced bromination of 1,3,5-tri-*t*-butylbenzene proceeds with a rate-limiting proton transfer; that acetoxylation which accompanies halogenation can become a major reaction path when sodium acetate is added to the acetic acid solvent; and that the yield of aryl acetate products in the silver-induced halogenation of alkylbenzenes is markedly dependent upon the structure of the aromatic reactant. An interpretation of these observations is required.

The absence of any evidence indicating a facile, direct path of acetoxylation of **1** independent of halogenation, by default, implies that aryl halides and aryl acetates stem from common reactants or intermediates. Further, the marked dependence of the yield of aryl acetate products on the concentration of added sodium acetate (see Figure 1) is most consistent with a two-step process in which the relative yield of aryl acetate and aryl halide depends upon the rate at which a common intermediate reacts with acetate ion. An elaboration of the usual mechanism of aromatic electrophilic substitution in which the competitive paths of decomposition of the cyclohexadienyl cation intermediate are proton loss and nucleophilic addition of acetate would provide a possible explanation of the observations. Such a scheme, applicable to the bromination of **1**, is shown in Chart I. As written the scheme represents a partitioning of the intermediate cation between the normal path of aromatic electrophilic substitution and a path frequently called addition–elimination.

Addition–elimination represents one of the earlier mechanistic formulations of the aromatic substitution reaction.[10] As a generally applicable mechanism, it has been rightly discarded, but the operative character

(10) See L. F. Fieser in "Organic Chemistry," Vol. 1, 2nd ed, G. Gilman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p 174.

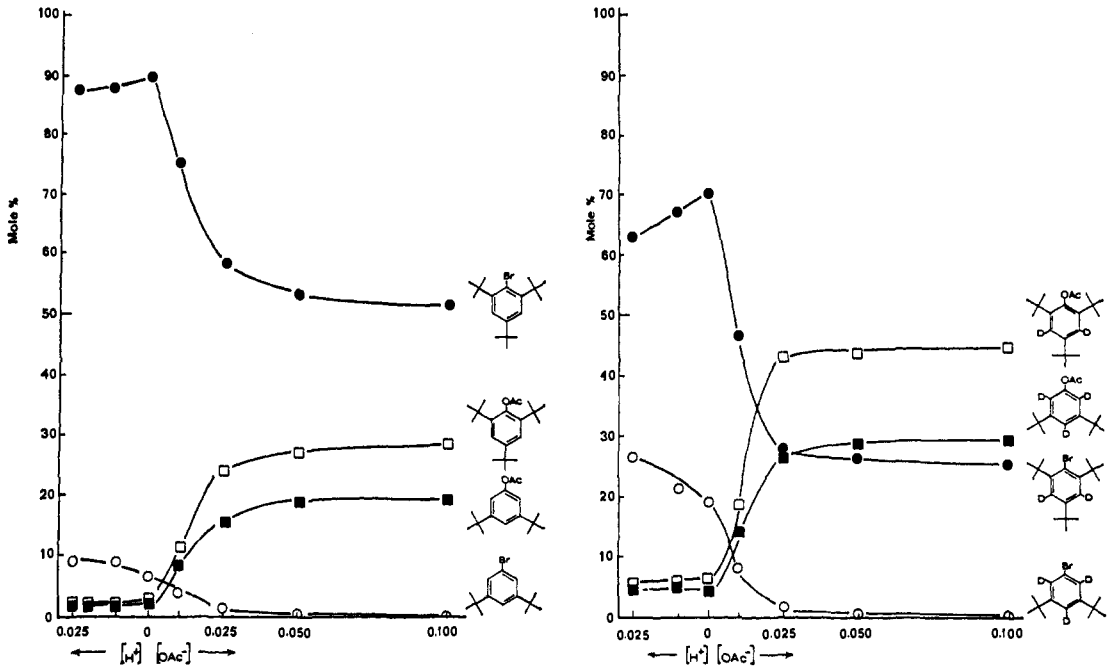
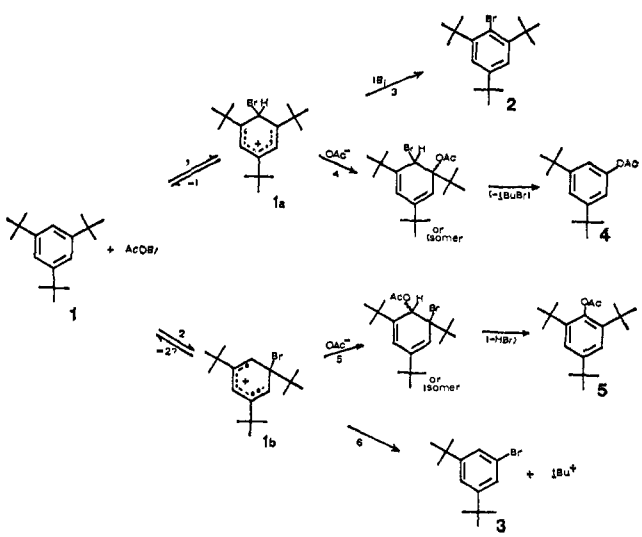


Figure 1. Profiles of product distributions observed in partial bromination of **1** and **1**-d_3 in glacial acetic acid containing added perchloric acid or sodium acetate.

of this mechanism in reactions of polycyclic aromatic compounds has been established by the investigations of several groups.[11] The studies of de la Mare and coworkers, in particular, demonstrate the complexities which can attend this reaction path.[11e,12] In recent years, several unusual reactions including the amination of monocyclic aromatic compounds by the action of chloramine and aluminum chloride[13] and the acetoxylation of alkylbenzenes attending nitration in acetic anhydride media[14] have (or could be) explained in terms of an addition–elimination scheme.

Chart I. Addition–Elimination Scheme of Aryl Acetate Formation



A preliminary examination of the anticipated features of this mechanism will be useful. In this examination, as well as the discussion which follows, attention will be focused on the cyclohexadienyl cation intermediate (in the present case, **1a** and **1b**) which, given free although short-lived existence, can choose among several reactions paths: return to reactant by loss of the attacking electrophile, formation of substitution product by expulsion of a cation (normally a proton), or interception by a nucleophile to form, transiently, a cyclohexadiene derivative. The latter reaction clearly should be favored when proton loss is relatively slow and when the concentration of nucleophile in the reaction system is relatively large. Both factors should be important in determining the amount of normal substitution product *vs.* addition–elimination product.

It is also important to recognize that the situation can exist where the cyclohexadienyl cation, once formed, does not lose its particular counterion to the solvent shell before addition. Thus, *cis* addition or collapse of a tightly associated ion pair could yield a cyclohexadiene derivative without the establishment of a fair competition between proton loss and nucleophilic addition. The chlorinations of naphthalene and phenanthrene in acetic acid provide examples of the possible importance of this further elaboration of the mechanistic scheme.[11e] We will refer hereafter to this as one-step addition, in contrast with the two-step process.

The possible reactions of the cyclohexadiene intermediates formed are also the subject of concern. Stepwise or concerted elimination to yield rearomatized acetate product, as shown in Chart II, should be facile. But several other paths including continued addition or

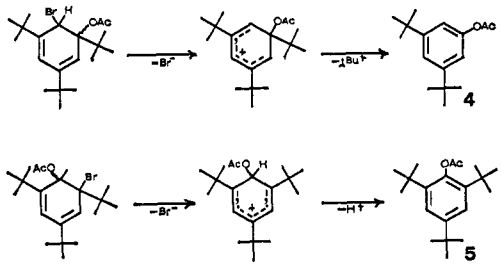
(11) (a) C. C. Price, *J. Am. Chem. Soc.*, **58**, 2101 (1936); (b) C. C. Price and C. E. Arntizen, *ibid.*, **60**, 2835 (1938); C. C. Price, *Chem. Rev.*, **29**, 37 (1941); (c) F. R. Mayo and W. B. Hardy, *J. Am. Chem. Soc.*, **74**, 911 (1952); (d) P. B. D. de la Mare, N. V. Klassen, and R. Koenigsberger, *J. Chem. Soc.*, 5285 (1961); (e) P. B. D. de la Mare, M. D. Johnson, J. S. Lomas, and V. Sanchez del Olmo, *ibid.*, *B*, 837 (1966), and related work cited therein; (f) L. Altschuler and E. Berliner, *J. Am. Chem. Soc.*, **88**, 5837 (1966).

(12) P. B. D. de la Mare and R. Bolton, "Electrophilic Addition to Unsaturated Systems," Elsevier Publishing Co., New York, N. Y., 1966, p 240 ff.

(13) P. Kovacic, J. A. Levisky, and C. T. Goralski, *J. Am. Chem. Soc.*, **88**, 100 (1966), and related papers.

(14) A. Fischer, J. Packer, J. Vaughan, and G. J. Wright, *J. Chem. Soc.*, 3687, 3691 (1964).

Chart II. Possible Paths of Stepwise Elimination



reversal (loss of acetate) could be competitive. In addition one can devise reactions, such as neighboring group migration, that could result in crossover from one reaction path to the other. Little information concerning these added complexities is available from the present data. In testing the merits and deficiencies of the proposed scheme, it will be necessary to make the simplifying assumptions that aromatization by elimination is the predominant mode of reaction of the cyclohexadiene intermediates and that the rate-limiting step in aryl acetate formation precedes the final loss of a proton or a *t*-butyl group (see Chart II).

Rate Studies. A recent investigation of the bromination of benzene and several simple alkylbenzenes by the action of molecular bromine and mercuric acetate in acetic acid solvent has implicated acetyl hypobromite as the brominating species.[15] In the present studies, the similarity of products obtained when either molecular bromine and silver salts or preformed acetyl hypobromite is used implies that the brominating agent is acetyl hypobromite or, possibly, a reagent derived therefrom. The very rapid rate of these brominations is also in accord with the results of Keefer and Andrews, who found that only benzene underwent bromination with acetyl hypobromite at a slow enough rate to permit direct kinetic measurements. The kinetic data available in this study are limited to relative rates derived from product distribution studies. However, the scheme shown in Chart I can be tested in part with the aid of these kinetic data.

The scheme predicts the observed sharp increases in yields of aryl acetates upon addition of sodium acetate to the reaction solution. Further, it is anticipated that proton transfer from **1a** to yield **2** would be subject to general base catalysis, while the loss of a *t*-butyl group from **1b** to yield **3** might be more reasonably approximated as a unimolecular ionization, occurring at a rate independent of solvent base concentration. Assuming this, one could express the ratios of product **2** with respect to **4**, and **3** with respect to **5**, as shown in eq 1 and 2.[16]

$$\frac{2}{4} = \frac{k_3[B] + k_3[OAc^-]}{k_4[OAc^-]} \quad (1)$$

$$\frac{3}{5} = \frac{k_6}{k_5[OAc^-]} \quad (2)$$

Equation 2 predicts that the yield of **3** should tend toward zero at high acetate ion concentrations. This is the effect that is experimentally observed. Equation 1 predicts that the yield of **4** with respect to **2** should increase as the acetate ion concentration increases and then level off if the term, $k_3[OAc^-]$, becomes sufficiently large to dominate the numerator. This effect is also observed experimentally; see Figure 1.

A more crucial test, plots of the yield ratio of products **2** and **4** *vs.* the reciprocal of the acetate ion concentration (eq 1), cannot be considered decisive. Fair linear plots are obtained with slopes that indicate that $k_4 \cdot [OAc^-] >> k_3[B]$ and intercepts that imply that $k_4 \cdot [OAc^-] \approx k_3[OAc^-]$. However, several considerations (*vide infra*) as well as the variation in ionic strength from run to run make further discussion unwarranted at the present time.

It should be noted that the yields of aryl acetates do not decrease to zero in acidic solutions. Rather, the yields decrease to small values in neutral solutions of acetic acid and remain essentially constant as the acidity is increased by addition of perchloric acid. Acetate formation in neutral and acidic acetic acid solutions can be attributed to either reaction of the cyclohexadienyl cation intermediate with acetic acid, the intrusion of another mode of acetoxylation, or a one-step addition. Any or a combination of these processes might account for the formation of a small and essentially constant fraction of the total product.

Isotope Effects. In order to interpret the kinetic isotope effect data it is important to consider the possible modes of formation of products. Clearly, if all four products resulting from the bromination of **1** were formed by independent paths (all branching starts at the hydrocarbon reactant), and the rates of formation of **3, 4,** and **5** are not appreciably affected by deuterium substitution, then the over-all isotope effect in the formation of 2,4,6-tri-*t*-butylbromobenzene, $(k_H/k_D)_2$, can be obtained from combinations of product ratios from parallel brominations of **1** and **1**-d_3 (eq 3).[17]

$$(k_H/k_D)_2 = \frac{[2]_H[3]_D}{[3]_H[2]_D} = \frac{[2]_H[4]_D}{[4]_H[2]_D} = \frac{[2]_H[5]_D}{[5]_H[2]_D} \quad (3)$$

The combinations of product ratios shown in eq 3 will not necessarily yield the over-all isotope effect if the reaction paths shown in Chart I are operative. The critical question concerns the relative rates of steps -1 and 4 with respect to step 3. Thus, by the scheme in Chart I, eq 4 and 5 may be obtained if it is assumed that **1a** and **1b** are steady-state intermediates and that the rates of formation of **3, 4,** and **5** are not affected by deuterium substitution.[18,19]

$$\frac{[2]_H[4]_D}{[4]_H[2]_D} = \frac{k_3^H[B] + k_3^H[OAc^-]}{k_3^D[B] + k^D[OAc^-]} = \frac{k'^H_3}{k'^D_3} \quad (4)$$

(15) Y. Hatanaka, R. M. Keefer, and L. J. Andrews, *J. Am. Chem. Soc.*, 87, 4280 (1965).

(16) The term, $k_3[B]$, represents the proton loss step yielding **2** which is catalyzed by other solvent bases, and should strictly be taken as a sum of base concentration and rate coefficient terms.

(17) The over-all isotope effect in the formation of **2** takes into account all of the steps directly involved. Thus

$$(k_H/k_D)_2 = \left(\frac{k_1k_3'[B]}{k_{-1} + k_3'[B]}\right)_H \left(\frac{k_{-1} + k_3'[B]}{(k_1k_3'[B]}\right)_D$$

This may be contrasted with a partitioning isotope effect which measures the isotope effect in a branching reaction of the intermediate.

(18) This implies that the rate-controlling step in the formation of the aryl acetate **5** precedes the necessary proton loss.

(19) In eq 4 and 5, the term representing the rate of step 3 catalyzed by different bases is reduced for simplicity to the expression k_3'. It is understood that this "rate constant," like others in these formulations, represents a composite of rate constant and base concentration terms, and that valid comparisons of the "k's" can only be made between runs conducted in the same medium.

$$\frac{[2]_H[3]_D}{[3]_H[2]_D} = \frac{[2]_H[5]_D}{[5]_H[2]_D} = \frac{k'_3{}^H(k_{-1} + k'_3{}^D + k_4[OAc^-])}{k'_3{}^D(k_{-1} + k'_3{}^H + k_4[OAc^-])} \quad (5)$$

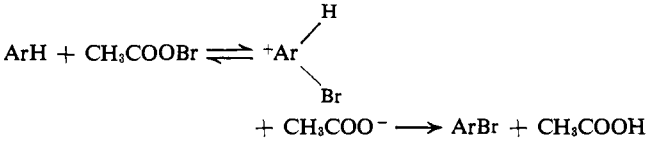
Combinations of the ratios of products **2** with respect to **4** resulting from parallel brominations of **1** and **1**-d_3 (eq 4) will measure the isotope effect in partitioning of the intermediate **1a** and should yield a value for the maximum observable isotope effect in this reaction, since this product ratio is independent of steps -1 and 4. The other product ratios (eq 5) yield rate constant composites which include steps -1 and 4. The isotope effects obtained by application of eq 5 will only be equivalent to those obtained from eq 4 when step 3 is much smaller than the sum of steps -1 and 4.

The data in Table IV show a comparison of isotope effects obtained from various product ratio combinations under various reaction conditions. Within the limits of error there appear to be no significant differences in the values of the various isotope effects so obtained. In terms of the reaction scheme shown in Chart I, this implies that under all conditions of acidity and basicity of the acetic acid solvent, step 3 is slower than the sum of steps -1 and 4.[20]

Table IV. Isotope Effects in Bromination of **1** and **1**-d_3[a,e]

Added $HClO_4$ or NaOAc, *M*	Glacial acetic acid			—97% acetic acid—		
	b	*c*	*d*	*b*	*c*	*d*
0.10 H^+	3.6	4	4	3.6	3.4	3.5
0.05	3.5					
0.025	4.1			3.9	4.5	3.0
0.01	3.9			3.2	3.5	3.3
...	3.7	3	4	3.0	2.7	3.7
0.01 OAc^-	3.4	3.6	3.9	3.5	3.0	3.0
0.025	3	3.5	3.7	2.8	3.0	3.0
0.05	3	3.0	3.3			
0.10		3.1	3.1		3.7	3.7

[a] Values given are not corrected for 5% aromatic protium in **1**-d_3. [b] $(2/3)_H(3/2)_D$. [c] $(2/4)_H(4/2)_D$. [d] $(2/5)_H(5/2)_D$. [e] The errors in isotope effects, based on maximum deviations of repetitive distribution analyses by glpc, are about ±10%. This estimate applies to the more favorable cases where the product pairs compared are all formed in yields greater than about 10%.



The isotope effect studies of the bromination of **1** and **1**-d_3 can be interpreted in terms of the partitioning scheme shown in Chart I. However, the data, by themselves, do not permit a discrimination between this scheme and one in which all four products are formed by totally independent paths. The chlorination of 1,3,5-tri-*t*-butylbenzene, however, appeared to provide a possible means of discrimination.

Previous intermolecular competitive rate studies have shown that chlorination of 1,3,5-tri-*t*-butylbenzene does not proceed with a significant kinetic isotope effect, $k_H/k_D = 1.15$.[21] However, acetoxylation does accompany chlorination with the formation of small amounts of both 3,5-di-*t*-butylphenyl acetate (**4**) and 2,4,6-tri-*t*-butylphenyl acetate (**5**). If the scheme shown for bromination (Chart I) also applies to chlorination, then eq 4 and 5 should also apply with the substitution of 2,4,6-tri-*t*-butylchlorobenzene (**7**) for the corresponding aryl bromide (**2**). Given this, the anticipated results are the following. A comparison of the ratios of products **7** and **4**, from parallel chlorinations of **1** and **1**-d_3, should reveal a full isotope effect, since the resulting ratio of rate constants (eq 4) does not depend upon the rate-limiting step in the formation of 2,4,6-tri-*t*-butylchlorobenzene (**7**). However, a comparison of the ratios of products **7** and **5** will yield a rate constant ratio which will depend on the rate-limiting step in the formation of **7** (eq 5). Since previous independent data indicate that the attack of positive chlorine is rate limiting, the rate constant ratio derived from a comparison of products **7** and **5** should be close to unity. The observed values for the several runs are found to be: $([7]/[4])_H([4]/[7])_D = 1.5 \pm 0.1$ and $([7]/[5])_H([5]/[7])_D = 1.2 \pm 0.1$ (see Table II).

The anticipated effect is observed; the difference in the two partition isotope effects is beyond rather pessimistic error limits. But this difference is certainly much smaller than would be expected if Chart I completely described the chlorination and concomitant acetoxylation of 1,3,5-tri-*t*-butylbenzene. It should be noted in this connection that the increase in total yield of aryl acetate products from chlorination in neutral *vs.* 0.1 *M* sodium acetate solutions of acetic acid is fairly small, from 6.2 to 8.9%. In contrast, the corresponding change in total yield of aryl acetates in bromination is over tenfold (from 3.5 to 48%; see Table III).

A convenient way to explain both the acetate yield and partition isotope effect anomalies in chlorination would be to assume that they reflect the increasing importance of another mode of acetoxylation. While several alternatives appear possible, we presently consider concerted or one-step addition as the most reasonable. If this assumption can be fairly made, only a portion of **5** which forms by chlorination of **1** in acetic acid solutions containing added sodium acetate would originate by a true partitioning of an intermediate cation between two reaction paths. One-step addition would have to be considered as an independent path originating with reactants, and products formed by this path would not reflect an isotope effect unless the rate-limiting step in the formation of **7** is proton loss. Thus, a correction for one-step addition would be required before the partitioning isotope effect, $([7]/[4])_H([4]/[]7)_D$, could be properly calculated. Such a correction would make the partition isotope effect conform to the expected value of 3–4.

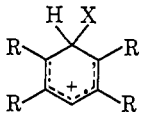
Structural Effects. It has been mentioned earlier that successful competition between the alternate reaction paths of the cyclohexadienyl cation, nucleophilic addition or direct elimination of a cation, should depend not only upon the concentration of nucleophile in the system, but also on the inherent rate of direct rearomatization by cation transfer (proton transfer). Typ-

(20) Acetate catalysis of proton transfer would be expected to greatly increase the rate of step 3; it clearly increases the rate of step 4. However, acetate catalysis of bromine transfer (step -1) must also be operative to maintain the inferred imbalance in rate ratios. Such a conclusion is not inconsistent with the inference that acetyl hypobromite is the active brominating agent.

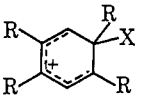
(21) Unpublished work of G. S. Owen.

ically, intermediates in aromatic electrophilic substitution reactions suffer proton loss in kinetically fast steps, sufficiently rapid to overwhelm a competitive addition process. However, the bromination of **1** to yield **2** does proceed with a rate-limiting proton transfer, and the reaction system is also adaptable to a relatively high concentration of the pertinent nucleophile. Thus, both conditions can be fulfilled, and in accordance with expectations, acetoxylation is a major reaction path. In contrast, chlorination proceeds without a significant over-all isotope effect, and one might conclude that the inherent rate of proton transfer is considerably faster than in bromination. As would be expected, the yields of aryl acetates found in chlorination which could be attributed to two-step addition are very much lower than those found in comparable brominations. Similarly, bromination and chlorination of 1,3,5-trimethylbenzene proceed without a significant over-all kinetic isotope effect and yield only trace quantities of aryl acetate.[22]

Aromatic substitution of certain *sym*-tetralkylbenzenes, such as durene and 2,5-diisopropyl-*p*-xylene, yield significant to major quantities of acetoxylation product. This occurs in spite of the fact that chlorination and bromination of durene and the chlorination of 2,5-diisopropyl-*p*-xylene proceed without a rate-limiting proton transfer. The systems, by virtue of the orientation of alkyl groups, can form "blocked" cyclohexadienyl cations (intermediates that cannot rearomatize to products by direct cation elimination). These "blocked" intermediates have stabilities which must be roughly equal to those which can yield substitution product by proton loss (compare **8** and **9**). In addition,



8



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the statistical weighting favors the blocked intermediates. Since these intermediates are not blocked from an addition–elimination reaction, one might anticipate rather large yields of aryl acetate products from hydrocarbon reactants possessing these structural features. Again, the expectation is realized.

Acetoxylation, which accompanies halogenation in acetic acid solutions containing added acetate ion, has been rationalized in terms of an addition–elimination reaction. The major course of acetoxylation in the bromination of **1** appears to be addition by a two-step process (Chart I) although a one-step addition process may also make a minor contribution. Several lines of evidence appear to support this conclusion. Perhaps the most decisive test of the proposed two-step scheme is the observation that product distributions resulting from the chlorination of **1** yield partition isotope effects which are larger than the over-all kinetic isotope effect, but these results are clouded by presumed one-step addition.

The present discussion has been predicated on the assumption that the cyclohexadiene intermediates formed by addition undergo rapid elimination to aromatized products. Within this assumption lie many questions and problems of importance to this particular study as well as the several other unusual aromatic substitutions which have also been explained in terms of an addition–elimination process.

(22) The greater yield of acetate product in chlorination (1%) than bromination (0.3%) of mesitylene may reflect a more rapid rate of one-step addition in chlorination; compare also the yields of acetate product obtained upon chlorination and bromination of **1** in glacial acetic acid.

Experimental Section

Melting points were recorded on a calibrated Fisher-Johns apparatus. Elemental analyses were performed by Mr. C. F. Geiger, Ontario, Calif. Gas–liquid partition chromatograms were obtained with an Aerograph A-90P3 instrument equipped with an SE 30 or a Carbowax 20M column. A Disc Instruments integrator was used to determine area under chromatographic peaks. Nmr spectra were obtained with a Varian A-60 spectrometer. Spectra, unless noted otherwise, were recorded in carbon tetrachloride solution, and chemical shift data are reported in δ values with respect to tetramethylsilane.

Materials. 1,3,5-Tri-*t*-butylbenzene and 1,3,5-tri-*t*-butylbenzene-2,4,6-d_3 were prepared by methods which have been previously described.[5,23] Samples of 2,5-diisopropyl-*p*-xylene (Aldrich, recrystallized four times from methanol), durene (J. B. Hinton Co., zone refined, 99.9% pure), and mesitylene (purified *via* the sulfonic acid[24]) were used in these studies. 2,4,6-Trimethylphenyl acetate and 2,3,5,6-tetramethylphenyl acetate were prepared from commercially available samples of the corresponding phenols by acetylation with acetic anhydride and pyridine. 2,4,6-Tri-*t*-butylphenol was obtained from the Ethyl Corporation and purified by recrystallization from ethanol before use.

Preparative Brominations of 1,3,5-Tri-*t*-butylbenzene (1). A. Friedel–Crafts Conditions. Dropwise addition (20 min) of a solution of bromine (32 g, 0.20 mol) in 20 ml of carbon tetrachloride to a cooled (0–5°), well-stirred mixture of 1,3,5-tri-*t*-butylbenzene (41.8 g, 0.17 mol), ferric chloride (0.34 g, 2.1 mmol), and carbon tetrachloride (175 ml) afforded, after a 2-hr reaction time, 46 g of nonvolatile, oily product.[25] Vacuum distillation yielded a partially crystalline fraction, 36.4 g, bp 115–118° (6 mm). Recrystallization of this fraction from ethanol gave colorless platelets of 3,5-di-*t*-butylbromobenzene, 25.1 g (54%), mp 62.5–63.5° (lit.[6] mp 63–64°). The nmr spectrum showed one *t*-butyl absorption at 1.30 (18 H) and a somewhat broader aromatic singlet at 7.29 (3 H). Strong absorptions in the infrared (Nujol) were observed at 897, 892, 752, and 702 cm^{-1}. The black, oily distillation residue yielded, after chromatography over alumina with *n*-hexane elution, 5.0 g of dense, viscous oil, $n^{25}D$ 1.5535. Repeated molecular distillation (130°, 2 mm) gave a sample, $n^{25}D$ 1.5545, whose nmr spectrum showed two sharp *t*-butyl absorption signals at 1.30 (9 H) and 1.53 (9 H) and an AB (J = 2.5 Hz) aromatic quartet at 7.41 (2 H) indicative of *meta*-oriented protons. Final purification by preparative glpc afforded an analytical sample of 1,2-dibromo-3,5-di-*t*-butylbenzene as a dense oil. Strong absorptions in the infrared (neat) were observed at 1030, 1020, 875, 770, 745, and 718 cm^{-1}.

Anal. Calcd for $C_{14}H_{20}Br_2$: C, 48.30; H, 5.79. Found: C, 48.41; H, 5.94.

B. Silver-Induced Bromination, Acidic Conditions. Bromine (16.0 ml, 0.28 mol) was added dropwise (20 min) to a vigorously stirred solution of 1,3,5-tri-*t*-butylbenzene (50.0 g, 0.20 mol), anhydrous silver pechlorate (60.0 g, 0.29 mol), perchloric acid (70%, 20 ml, 0.2 mol), acetic acid (1 l.), and dioxane (200 ml) which was maintained at 10–15°. After a 3-hr reaction period, the residual bromine was reduced by addition of sodium sulfite; pentane (about 300 ml) was added to dissolve precipitated organic products. Silver salts were collected by suction filtration, and the filter residue was thoroughly triturated with pentane. The combined filtrates were flooded with water, and the separated organic layer was washed with water (two 300-ml portions), 5% sodium hydroxide (two 200-ml portions, red aqueous extract), and water (three 200-ml portions). After being dried over calcium chloride, the pentane was removed by distillation affording a partially crystalline yellow residue. Filtration and trituration with cold ethanol yielded 40 g of crude crystalline product and 21 g of oily filtrate. Two recrystallizations from ethanol–benzene (200 ml, 3:1) gave colorless needles of 2,4,6-

(23) P. C. Myhre, T. Rieger, and J. T. Stone, *J. Org. Chem.*, **31**, 3425 (1966).

(24) L. I. Smith and O. W. Cass, *J. Am. Chem. Soc.*, **54**, 1603 (1932).

(25) Fractional distillation of the carbon tetrachloride afforded a fraction, bp 72°, characterized as *t*-butyl bromide, one singlet absorption in the nmr at 1.42.

tri-*t*-butylbromobenzene, 30.0 g (45%), mp 174–176° (lit.[26,27] 177–177.5°). Further repeated crystallization from cyclohexane afforded a sample, mp 177–177.5°. The nmr spectrum showed two *t*-butyl absorption lines at 1.31 (9 H) and 1.58 (18 H) and an aromatic singlet at 7.31 (2 H). Infrared spectra (Nujol) showed absorptions at 1012, 926, 882, 773, and 739 cm^{-1}.

Preparative glpc separations of the oily filtrate (SE 30, 10 ft × 3/8 in., 250°, 150 ml min^{-1}) permitted isolation of the four major components: 1,3,5-tri-*t*-butylbenzene (8 min, 18%), 3,5-di-*t*-butylbromobenzene (10.5 min, 33%), 2,4,6-tri-*t*-butylbromobenzene (20.2 min, 8%), and a fourth component (24.5 min, 41%). The fourth component, a colorless, viscous oil, proved to be identical in all respects with 1,2-dibromo-3,5-di-*t*-butylbenzene isolated by bromination of 1,3,5-tri-*t*-butylbenzene with Friedel–Crafts conditions.

C. Silver-Induced Bromination, "Neutral" Conditions. A solution of bromine (8.2 ml, 0.16 mol) and anhydrous sodium acetate (12.3 g, 0.15 mol) in 100 ml of acetic acid was added dropwise (60 min) to a well-stirred solution containing 1,3,5-tri-*t*-butylbenzene (25.0 g, 0.10 mol), silver perchlorate (34.1 g, 0.165 mol), acetic acid (500 ml), and dioxane (100 ml), which was maintained between 10 and 17° during the addition and allowed to rise to room temperature during the 16-hr reaction period. Products were isolated in the manner previously described to yield a yellow partially crystalline product. Glpc analysis indicated the following product distribution: 5.5% unconverted 1,3,5-tri-*t*-butylbenzene, 8.0% 3,5-di-*t*-butylbromobenzene, 58.6% 2,4,6-tri-*t*-butylbromobenzene, and 27.9% 1,2-dibromo-3,5-di-*t*-butylbenzene. Filtration of the product and trituration with cold ethanol afforded 19.6 g of 2,4,6-tri-*t*-butylbromobenzene, mp 172–174.5° (95% pure by glpc, contaminated mainly with the parent hydrocarbon).

Another bromination conducted under "neutral" conditions with the use of reactant hydrocarbon (0.103 mol), bromine (0.105 mol), silver perchlorate (0.11 mol), and sodium acetate (0.115 mol) yielded 31.5 g of crude product. Glpc analysis indicated 21% of unreacted 1,3,5-tri-*t*-butylbenzene, 63% 2,4,6-tri-*t*-butylbromobenzene, 8% 3,5-di-*t*-butylbromobenzene, 3% 1,2-dibromo-3,5-di-*t*-butylbenzene, and about 5% of two previously undetected products, which were identified (see below) as 3,5-di-*t*-butylphenyl acetate and 2,4,6-tri-*t*-butylphenyl acetate.[28]

Isolation and Characterization of 3,5-Di-*t*-butylphenyl Acetate and 2,4,6-Tri-*t*-butylphenyl Acetate. Partial bromination of 1,3,5-tri-*t*-butylbenzene (about 25% conversion) with bromine and silver perchlorate in acetic acid solutions containing added sodium acetate (1 equiv with respect to the hydrocarbon) gave a product mixture which contained significant quantities of two previously unidentified products together with the three identified bromination products. These two products were conveniently separated from reactant and bromination products by column chromatography over alumina. Elution with pentane removed the hydrocarbon and bromination products, and elution with methylene chloride removed the unknown products. Final separation was achieved by preparative glpc to yield a colorless oil and a crystalline product.

The oil was characterized as 3,5-di-*t*-butylphenyl acetate on the basis of its nmr spectrum which showed one *t*-butyl absorption line at 1.32 (18 H), a sharp acetoxyl methyl absorption at 2.38 (3 H), and an aromatic A_2B pattern (J = 2 Hz) with the doublet centered at 6.83 (2 H) and the triplet at 7.20 (1 H); and its infrared spectrum (CCl_4) which showed strong carbonyl absorption at 1770 cm^{-1}, a strong carbon–oxygen band at 1195 cm^{-1}, and a strong absorption at 705 cm^{-1}. 3,5-Di-*t*-butylphenyl acetate was independently synthesized by acetylation of an authentic sample of 3,5-di-*t*-butylphenol with acetic anhydride and pyridine.[29,30] The compounds were identical in all respects.

The crystalline product was characterized as 2,4,6-tri-*t*-butylphenyl acetate on the basis of the nmr spectrum which showed (in CCl_4) a single *t*-butyl absorption line at 1.33 (27 H), an acetoxyl methyl at 2.43 (3 H), and an aromatic singlet at 7.36 (2 H);[31] the infrared spectrum which showed strong carbonyl absorption at 1750 cm^{-1}, and a strong band at 1200 cm^{-1}; and independent synthesis of an identical compound by reaction of sodium tri-*t*-butylphenoxide with acetyl chloride or by diazotization of 2,4,6-tri-*t*-butylaniline in glacial acetic acid, mp 105–106°.

Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59. Found: C, 79.07; H, 10.48.

Competitive Bromination of 2,4,6-Tri-*t*-butylbromobenzene and 3,5-Di-*t*-butylbromobenzene. A solution of bromine (0.15 ml, 3.0 mmol) in 15 ml of glacial acetic acid was added dropwise to a solution of tri-*t*-butylbromobenzene (1.6023 g, 4.98 mmol), 3,5-di-*t*-butylbromobenzene (1.357 g, 5.04 mmol), and anhydrous silver perchlorate (0.69 g, 3.3 mmol) in 150 ml of acetic acid–dioxane (5:1). The temperature of the reaction mixture was maintained at 25°. Products were isolated after a 30-min reaction period, and the resulting product mixture was analyzed by glpc and nmr. Glpc analyses were carried out in the normal fashion. Response data were corrected using standard calibrating mixtures. Nmr analyses were carried out by repetitive (at least six) integrations of the *t*-butyl and aromatic proton regions at a sweep width of 50 Hz. Three well-resolved absorption bands are observed in the *t*-butyl region, corresponding to the *o*-*t*-butyl of 2,4,6-tri-*t*-butylbromobenzene at 1.57, the 3-*t*-butyl protons of 1,2-dibromo-3,5-di-*t*-butylbenzene at 1.53, and the superposition of the *p*-*t*-butyl protons of 2,4,6-tri-*t*-butylbromobenzene, the 5-*t*-butyl protons of 1,2-dibromo-3,5-di-*t*-butylbenzene, and the 3- and 5-*t*-butyl protons of 3,5-di-*t*-butylbromobenzene at 1.30.[32] A similar analysis of the aromatic protons can be made. The distribution data so obtained and the relative rate constant derived from these data are shown in Table V.

Table V. Product Distribution in Competitive Bromination of 2,4,6-Tri-*t*-butylbromobenzene (**2**) and 3,5-Di-*t*-butylbromobenzene (**3**)

Analytical method	Mole % prodt **3**	**2**	**6**	$k_{6\leftarrow 2}/k_{6\leftarrow 3}$
Glpc	42.9	39.0	18.1	1.52
Nmr (aromatic)	41.4	38.7	19.9	1.30
Nmr (*t*-butyl)	42.2	38.8	19.0	1.45

Stability of 2,4,6-Tri-*t*-butylbromobenzene to Reaction with Silver Salts. 2,4,6-Tri-*t*-butylbromobenzene was heated at reflux in acetic acid–dioxane solutions of silver acetate (3 equiv) and, in similar reactions, excess silver perchlorate for periods of 3–4 hr. Glpc analyses of the isolated organic products revealed only unchanged reactant.

Other Attempts to Acetoxylate Tri-*t*-butylbenzene. A. With Acetyl Hypobromite. Carbon tetrachloride solutions of acetyl hypobromite (~0.1 *M*) were prepared by the method of Levine and Wall.[33] Concentrations of the hypobromite were determined by iodometric titration. The changes in concentration with time could be correlated with the appearance of a new methyl absorption line in the nmr spectrum which had a chemical shift identical with that of methyl bromide.[34] Reaction of this reagent by mixing 2.0 ml of a carbon tetrachloride solution of acetyl hypobromite with 8 ml of a glacial acetic acid solution of tri-*t*-butylbenzene (0.5 mmol) resulted in rapid formation of products.[35] Glpc analyses of the isolated products showed that the principal components of the mixture were 3,5-di-*t*-butylphenyl acetate, 2,4,6-tri-*t*-butylphenyl acetate, and 2,4,6-tri-*t*-butylbromobenzene together with smaller amounts of 3,5-di-*t*-butylbromobenzene. The product distribution varies with variation in the acid–base concentration of the solvent

(26) E. E. Betts and L. R. C. Barclay, *Can. J. Chem.*, **33**, 1768 (1955).

(27) While other products of bromination are readily removed, a number of recrystallizations are required to free the aryl bromide from traces of the parent hydrocarbon.

(28) Higher yields of 2,4,6-tri-*t*-butylbromobenzene are obtained when stoichiometric quantities of brominating agent are used. However, the resulting incomplete conversion of reactant, due to consumption of bromine by other side reactions, presents a difficult problem in separation of reactant from desired product; see ref 27.

(29) The sample of phenol was prepared by diazotization of 3,5-di-*t*-butylaniline which was derived from 3,5-di-*t*-butyltoluene *via* the carboxylic acid. This procedure has been described in detail by Allinger, *et al.*[30]

(30) N. L. Allinger, H. M. Blatter, L. A. Freiberg, and F. M. Karkowski, *J. Am. Chem. Soc.*, **88**, 2999 (1966).

(31) This compound is unique among a number of monosubstituted tri-*t*-butylbenzene derivatives with respect to the coincidental superposition of the *o*- and *p*-*t*-butyl absorption lines. In most cases the *o*-proton absorption is shifted from 4 to 25 Hz downfield.

(32) Three distinct bands are observed at about 1.30 under conditions of maximum resolution, but they cannot be fully resolved.

(33) S. G. Levine and M. E. Wall, *J. Am. Chem. Soc.*, **81**, 2826 (1959).

(34) Rigorously dried reactants gave hypobromite solutions which decomposed to methyl bromide at a much more rapid rate than solutions prepared from less anhydrous reagents.

(35) Attempts to follow the rate of this type of reaction ("neutral" conditions) showed almost complete reaction within the first 3 min.

(see Table I), but the distribution was substantially independent of added radical initiators or inhibitors.

B. With Lead Tetraacetate. A mixture of 1,3,5-tri-*t*-butylbenzene (0.44 g) and freshly recrystallized lead tetraacetate (0.50 g) was heated at reflux in 30 ml of acetic acid for 3 hr and allowed to remain at room temperature overnight. The clear, colorless reaction mixture was flooded with water, and the organic products were extracted with cyclohexane. Glpc analysis revealed only unchanged reactant.

C. With Lead Tetraacetate and Bromine. Bromine (3 mmol) dissolved in acetic acid (3 ml) was added dropwise over a 15-min interval to a stirred solution of 1,3,5-tri-*t*-butylbenzene (0.73 g, 3 mmol), lead tetraacetate (0.68 g, 1.5 mmol), and acetic acid (30 ml). No immediate or rapid reaction was detected. After 2 days some white precipitate, presumably lead bromide, had formed. The reaction mixture was poured into water at this time, and the organic products were extracted with cyclohexane. Glpc of the washed and dried cyclohexane layer indicated about 25% conversion to products: 3,5-di-*t*-butylphenyl acetate (5%), 2,4,6-tri-*t*-butylphenyl acetate (10%), and 2,4,6-tri-*t*-butylbromobenzene (10%).

D. With Lead Tetraacetate and Iodine. A reaction similar in detail to that described above was conducted with the substitution of iodine for bromine. Glpc analysis of the organic products revealed only unchanged starting material.

Studies of Product Distributions in the Silver-Induced Bromination of 1,3,5-Tri-*t*-butylbenzene (1) and 1,3,5-Tri-*t*-butylbenzene-2,4,6-d_3 (1-d_3). Product distribution studies were carried out by addition (micrometer buret) of 0.50 ml of an acetic acid solution containing bromine (0.100 *M*) and sodium acetate (0.100 *M*) to magnetically stirred solutions (final volume 10.0 ml) of 1,3,5-tri-*t*-butylbenzene (5.00×10^{-2} *M*), silver perchlorate (1.00×10^{-2} *M*), and varying quantities of perchloric acid or sodium acetate (0.10 *M* H^+ to 0.10 *M* OAc^-) in acetic acid solvents, maintained at 25 ± 2°.[36] After a 15-min reaction period, the mixture was transferred to a small separatory funnel containing about 25 ml of water, and the organic products were extracted with 5.0 ml of cyclohexane. The organic layer was washed twice with water, once with 5% sodium thiosulfate (to remove suspended silver bromide), and twice with water. After being dried over sodium sulfate and concentrated by rotary evaporation to about 0.5 ml, the cyclohexane solutions were analyzed by glpc. The data resulting from these studies are shown in Table I.

Halogenation of 2,5-Diisopropyl-*p*-xylene. Partial chlorination of this hydrocarbon in neutral acetic acid containing silver perchlorate in the manner described for bromination of **1** afforded five products. The major products were identified by the nmr spectra as 2-chloro-5-isopropyl-*p*-xylene (28%), 2,5-diisopropyl-3,6-dimethylchlorobenzene (39%), and 2,5-diisopropyl-3,6-dimethylphenyl acetate (28%). The minor products were not characterized. Similar chlorination in acetic acid solution containing 0.1 *M* added sodium acetate afforded the same set of products but in different distributions: 12, 32, and 48%, respectively.

The nmr spectrum of the isolated 2,5-diisopropyl-3,6-dimethylphenyl acetate showed two isopropyl groups (superimposed doublets centered at 1.2 and septets at 3.1, J = 7 Hz), two aromatic methyl groups (singlets at 1.95 and 2.32), an acetoxyl methyl (sharp singlet at 2.25), and an aromatic proton at 6.70.

Partial bromination of this hydrocarbon in acetic acid containing 0.1 *M* sodium acetate afforded 67% of 2,5-diisopropyl-3,6-dimethylbromobenzene and 30% of 2,5-diisopropyl-3,6-dimethylphenyl acetate.

Halogenations of Durene and Mesitylene. Partial halogenations at room temperature of these hydrocarbons in acetic acid solvent containing silver perchlorate yielded the corresponding aryl halide and varying amounts of the corresponding phenyl acetate (see Table III).[37,38] 2,3,5,6-Tetramethylphenyl acetate was isolated from product mixtures by column chromatography over alumina with elution of reactant hydrocarbon and aryl halides with *n*-pentane and elution of the aryl acetate with methylene chloride. The product was identical in all respects with an authentic sample of 2,3,5,6-tetramethylphenyl acetate prepared from the corresponding phenol.

Because of the very small yields of 2,4,6-trimethylphenyl acetate upon halogenation of mesitylene, this compound was not isolated. The glpc retention time of an authentic sample matched that of the by-product formed in both silver-induced chlorination and bromination reactions.

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(36) Reaction solutions were normally homogeneous until addition of the bromine–sodium acetate solution; however at the higher concentrations of sodium acetate a precipitate sometimes formed before addition.

(37) Side-chain halogenation products or benzyl acetates were not detected, although several very minor products were not characterized; see ref 38.

(38) E. Baciocchi, A. Ciana, G. Illuminati, and C. Pasini, *J. Am. Chem. Soc.*, 87, 3953 (1965).