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Cupric Bromide and Alkylbenzenes. Influence of Water on Nuclear Bromination *vs.* Side-Chain Attack[1]

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The course of the cupric bromide–monoalkylbenzene reaction was critically influenced by the presence of water in small quantities. With toluene, ethylbenzene, and cumene, nuclear bromination predominated in rigorously anhydrous systems. When small amounts of water were added, diarylmethanes were the principal products, in addition to benzylic bromides. Mesitylene gave bromomesitylene both in the presence and absence of water. Our results are at variance in several respects with those recently reported by Nonhebel for the toluene–cupric bromide reaction.

Introduction

Although cupric halides are known to halogenate organic compounds, both in the aromatic and aliphatic series, the scope of the reaction has not been clearly defined. From the rather limited amount of previous work, it appears that only the extremely active aromatics undergo halogenation by these reagents. For example, Fort[2] effected bromination of 3,4,5-trimethylanisole and β-naphthol using cupric bromide in methanol. With cupric chloride or cupric bromide, phenol was transformed to *o*- and *p*-halophenols, in addition to more highly halogenated products.[3] By means of these metal halides, Ware and Borchert[4] halogenated various polynuclear hydrocarbons, including naphthalene, anthracene, and pyrene, usually under rather drastic conditions. They provided evidence in support of a polar reaction mechanism. In contrast, Nonhebel[5] favors a free radical sequence for substitution reactions in this series.

In the aliphatic category, there are several literature references to the chlorination of alkanes[6,7] and alkenes[8] by cupric chloride. α-Halogenation of ketones occurs with ease, *e.g.*, acetone with cupric chloride yields chloroacetone.[9] More recently, this method for the halogenation of active C–H groups in ketones has been extended by other investigators.[3a,10–12] Analogously, cupric bromide is reported to react readily with aliphatic aldehydes yielding the α-bromo derivatives.[13]

In view of our continuing interest in the reactions of metal halides with aromatic compounds, and the recent publication by Nonhebel[5] concerning the cupric bromide–toluene reaction, we wished to carry out a detailed investigation of the cupric bromide–alkylbenzene systems.

Results

Toluene.—The course of the toluene–cupric bromide reaction was critically influenced by the presence of water in small quantities. In a rigorously anhydrous system, bromotoluenes were essentially the only organic products. In contrast, addition of water altered the reaction pathway, resulting primarily in the formation of phenyltolylmethanes. Product identification was performed with reaction mixtures obtained from scouting experiments prior to our cognizance of the water effect. The course of the reaction could be followed conveniently by titration of the evolved hydrogen bromide (Tables I and II).

TABLE I

CUPRIC BROMIDE AND ALKYLBENZENES

Aromatic[a]	H_2O, mole	Temp., °C.	Time, hr.	HBr, mole	ArBr, mole	Benzylic bromide,[b] mole	Diarylmethane, mole	Higher boiler,[c] mole	Polymer, g.
Toluene[d]	0	110–116	4	0.46	0.40	...	0.005	...	Trace
Toluene[e]	0.1	110–115	35	.74	.01	0.01	.11	...	20
Ethylbenzene[d]	0	114–116	4	.45	.40	...	.005	Trace	Trace
Ethylbenzene	0.25	112–127	29	.81	.01	Trace	.03	0.015	10.5
Cumene	0	115–120	10	.77	.01	Trace	.034	...	7.5
Cumene	0.25	110	7.5	.47	[f]	.23	[f]	[f]	[f]
Mesitylene	0	111–113	3	.49	0.41	...	...	...	1
Mesitylene	0.25	105–110	1	.43	0.42	...	...	...	1

[a] Aromatic (2 moles) and cupric bromide (1 mole). [b] Decomposition during gas chromatography was noted. [c] Derived from 3 moles of aromatic. [d] Aromatic (3 moles). [e] Toluene (1.5 moles) and cupric bromide (0.5 mole); yields are adjusted to the standard scale. [f] Not determined.

Toluene, distilled from sodium, and cupric bromide, dried at 110°, reacted at reflux to give bromotoluenes in 81% yield. Identification was accomplished by the physical constants, elemental analyses, infrared spectrum, and oxidation to *o*- and *p*-bromobenzoic acids. Infrared analysis provided the isomer distribution, 35% *ortho*, 2% *meta*, and 63% *para*. In addition, a hydrocarbon product was obtained in about 1% yield, which was shown to be phenyltolylmethanes.

When undried cupric bromide, which contained about 10 mole % of water, was allowed to react with toluene, the major product (22% yield) consisted of a mixture of phenyltolylmethanes. The physical constants, elemental analyses, and infrared spectrum were used in characterization. The n.m.r. spectrum indicated a

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[1] Paper XIII, "Reactions of Metal Halides with Organic Compounds," undergraduate thesis of K. E. Davis, Case Institute of Technology, 1963.

[2] A. W. Fort, *J. Org. Chem.*, **26**, 765 (1961).

[3] (a) E. M. Kosower, W. J. Cole, G. S. Wu, D. E. Cardy, and G. Meisters, *ibid.*, **28**, 630 (1963); (b) W. W. Kaeding and R. O. Lindblom, U. S. Patent 2,805,263 (1957).

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[5] D. C. Nonhebel, *Proc. Chem. Soc.*, 307 (1961); *J. Chem. Soc.*, 1216 (1963).

[6] H. T. Tizard, D. L. Chapman, and R. Raylor, British Patent 214,293 (1922).

[7] C. M. Fontana and E. Gorin, U.S. Patent 2,575,167 (1951).

[8] (a) M. De Simo, Canadian Patent 451,379 (1948); (b) R. P. Arganbright and W. F. Yates, *J. Org. Chem.*, **27**, 1205 (1962).

[9] J. K. Kochi, *J. Am. Chem. Soc.*, **77**, 5274 (1955).

[10] P. B. Sollman and R. M. Dodson, *J. Org. Chem.*, **26**, 4180 (1961).

[11] K. B. Doifode, *ibid.*, **27**, 2665 (1962).

[12] E. R. Glazier, *ibid.*, **27**, 2937, 4397 (1962); E. M. Kosower and G. S. Wu, *ibid.*, **28**, 633 (1963).

[13] C. E. Castro, *ibid.*, **26**, 4183 (1961).

TABLE II

TOLUENE AND CUPRIC BROMIDE: EFFECT OF WATER AND CATALYSTS[a]

Curve, Fig. 1	Procedure[c]	Catalyst	Water, ml.	CuBr, mole	Time, hr.	HBr, meq.	Product, %[b]					
							Br-$C_6H_4CH_3$	Phenyltolylmethane	"Trimer"	$C_6H_5CH_2Br$[d]	$BrC_6H_4CH_3$,[e] % o-	p-
	A[f]	...	...	...	4.5	445	96.5	2	1.5	...	36	64
	A[g]	...	...	...	2.7	465	97	1.5	1.5	...	36	64
	A	$AlCl_3$[h]	...	...	3	470	80	7	13	...	43.5	56.5
	A	$FeCl_3$[i]	...	...	5	460	92	4	4	...	39	61
3	C	...	...	...	1.6	480	100	...	...	...	35	65
8	C[j]	...	0.5	...	3.7	104	83	17	...	Trace	......	
7	C[j]	...	.5[k]	...	2	480	100	Trace	...	...	......	
	C[j]	...	.5	...	23.5	660	27	66	7	Trace	......	
4	B	...	...[l]	...	1.5	484	100	...	...	...	......	
5	B	...	...[m]	...	1.5	474	100	Trace	...	...	......	
2	C	...	...	0.035	1.5	492	100	...	...	...	......	
1	C	...	...	0.25	1.3	486	100	...	...	...	36	64

[a] Toluene, 2 moles; cupric bromide, 1 mole. [b] Based on the product volatilized by g.l.c. [c] General procedure. [d] Decomposition during gas chromatography was noted. [e] By g.l.c.; the *p*-peak also contained the *m*-isomer (about 2%). [f] Cupric bromide from Mallinckrodt. [g] Cupric bromide from Baker. [h] 0.25 g. [i] 0.2 g. [j] Water was added after reaction had begun; see Experimental for details. [k] Added in two portions. [l] Relative humidity 60% at 26°. [m] Relative humidity 80% at 26°

3:2 ratio of methyl:methylene hydrogens, and an isomer distribution consisting of about 60% *para* and 40% *ortho*.[14] Furthermore, chromic acid oxidation afforded *p*-benzoylbenzoic acid and *o*-methylbenzophenone. The original reaction also yielded small amounts of benzyl bromide and bromotoluenes, in addition to an appreciable amount of tar. Similar results were observed when water was added initially to the dried cupric bromide–anhydrous toluene system. The benzyl bromide from this experiment was identified by conversion to the S-benzylthiuronium salt. When an analogous reaction mixture was refluxed with aqueous sodium carbonate, benzaldehyde was formed in low yield. It is conceivable that benzal bromide served as the precursor.

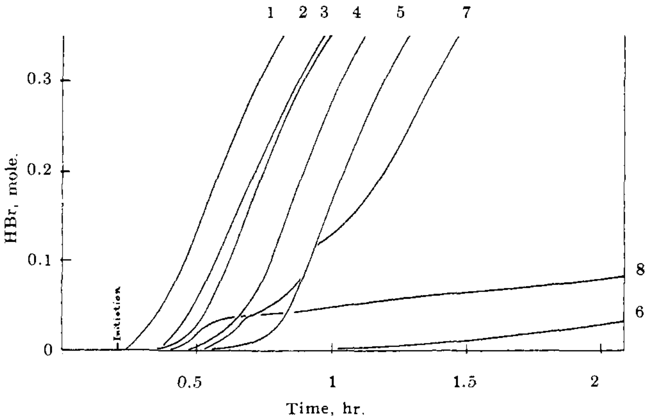

Fig. 1.—Rate of hydrogen bromide evolution in toluene–cupric bromide reactions (Table II): 1, CuBr (0.25 mole); 2, CuBr (0.035 mole); 3, rigorously anhydrous; 4, anhydrous, 60% relative humidity; 5, anhydrous, 80% relative humidity; 6, water (6 mole %); 7, water (0.25 ml. twice); 8, water (0.5 ml.).

Our findings are at variance in several respects with those recently published by Nonhebel[5] for the toluene–cupric bromide reaction. He reported a product mixture composed of bibenzyl, benzyl bromide (traces), cuprous bromide, and hydrogen bromide with no mention of bromotoluene or phenyltolylmethane. Assignment of the bibenzyl structure was based upon comparison with authentic bibenzyl in gas chromatography. Using several types of columns, we were unable to separate bibenzyl and phenyltolylmethane by this technique. The present investigation yielded no indication of the formation of bibenzyl which certainly could not be present in more than very minor amounts. In addition to the data already cited, the characteristic infrared absorption maximum at 13.35 μ for bibenzyl was not evident in the spectrum of our $C_{14}H_{14}$ fraction.

In view of the intimation by our preliminary observations that water[5] may play a critical role, we decided to investigate the influence of this additive in more detail. Figure 1 and Table II summarize these results. The rate of hydrogen bromide evolution provides a reliable indication of the reaction pathway. Under the most rigorous conditions of dryness, gas was produced at the fastest rate entailing the shortest induction period (Fig. 1, curve 3). In this easily reproduced reaction, gas chromatographic analysis revealed that bromotoluenes were essentially the only organic products. When 6 mole % (based on cupric bromide) of water was added, hydrogen bromide was generated at a very slow rate (Fig. 1, curve 6). The relationship was established that increasing amounts of water resulted in decreasing yields of bromotoluenes, increasing yields of phenyltolylmethanes, increasing induction times, and decreasing rates of gas evolution. Furthermore, several experiments were performed in which water was added to an anhydrous mixture which was undergoing rapid nuclear substitution. In every instance, there was an abrupt decrease in the reaction rate. The data indicate that less than 3 mole % of water is sufficient to switch the reaction course from nuclear to side chain. In these cases, product analyses were performed by gas chromatography.

It is interesting that a considerable period of induction, about 15 min., exists even when precautions are exercised to maintain an anhydrous system. We found that introduction of cuprous bromide reduced the induction period until, with 25 mole %, it was almost completely eliminated. An analogous result was previously obtained by Oziomek[15] from the addition of cuprous chloride to the mixture of benzene–aluminum chloride–cupric chloride which forms *p*-polyphenyl. The mode of action of cuprous bromide is not known.

Conversely, the course of the toluene–cupric bromide reaction which was proceeding by side-chain attack was altered in the direction of nuclear bromination by the use of small amounts of aluminum chloride or ferric chloride. The catalyst was introduced after only slight amounts of hydrogen bromide had evolved.

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(14) We are grateful to Dr. William M. Ritchey, Sohio Research Laboratory, for obtaining and interpreting the n.m.r. spectrum.

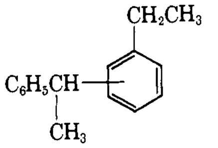
(15) J. Oziomek, unpublished work.

Phenyltolylmethanes and the "trimer" were obtained in much larger amounts than expected.

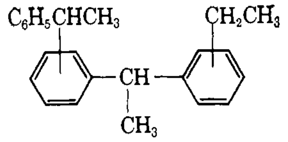
In contrast, there was no evidence of reaction between cupric chloride and toluene after 12 hr. at reflux. Nonhebel[5] found that cupric chloride behaves similarly to the bromide when placed in contact with toluene, but reacts much less rapidly.

Ethylbenzene.—With cupric bromide and ethylbenzene, a similar influence involving water was observed (Table I). In a relatively anhydrous system, the reaction proceeded with formation of bromoethylbenzenes in 80% yield. Physical constants and elemental analyses were used in product identification. From gas chromatographic analysis, an isomer distribution of 31% *ortho* and 69% *para* was obtained. The *p*-peak probably contains the small amount of *m*-isomer indicated by the infrared spectrum. *p*-Bromobenzoic acid was isolated from the oxidation products formed by treatment with alkaline permanganate. In addition, the original reaction yielded a small amount of an oily mixture which contained 1-(ethylphenyl)-1-phenylethanes (I). There was no evidence from gas chromatography for the presence of *meso*-2,3-diphenylbutane.

When the reaction was carried out with added water, gas chromatographic analysis revealed the presence of about thirty products. The principal one, b.p. 114–117° at 2 mm., was shown to be an isomeric mixture of 1-(ethylphenyl)-1-phenylethanes (I). The structural designation was based upon elemental analyses, physical constants, infrared spectrum, and oxidation to *p*-benzoylbenzoic acid This hydrocarbon product was essentially identical with authentic material which had been prepared previously from ethylbenzene–ferric chloride,[16] ethylbenzene–antimony pentachloride,[17] and ethylbenzene–styrene–aluminum chloride.[16]



I



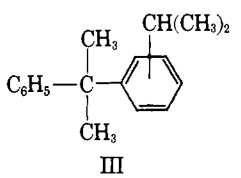
II

The second most abundant product, b.p. 180–190° at 2 mm., purified by chromatography on alumina, possessed an infrared spectrum almost identical with that of 1-(ethylphenyl)-1-phenylethanes. From the elemental analyses and molecular weight, the empirical fromula $C_{24}H_{26}$ was deduced. On the basis of this evidence, together with oxidation to *p*-benzoylbenzoic acid, the product was assigned the structure 1-(ethylphenyl)-1-[1′-phenyl-(ethylphenyl)]-ethanes (II). This material was previously reported from ethylbenzene–ferric chloride and ethylbenzene–styrene–aluminum chloride.[16]

Side-chain bromination was further indicated by the evolution of hydrogen bromide during distillation and the presence of tar in large amounts. In addition, bromoethylbenzenes were found in low yield. More detailed investigations of the water effect were not made in this system.

Cumene.—As expected, the behavior of cumene was in keeping with that of the lower homologs (Table I). When special precautions were taken to obtain anhydrous conditions, cupric bromide and cumene gave predominantly bromocumenes (40–50% yield). The identity was established by infrared and gas chromatographic analysis. Gas chromatography also indicated the presence of 2-(isopropylphenyl)-2-phenylpropanes (III), diisopropylbenzenes, and bromobenzene.

When less stringent conditions were taken to preclude water, an extremely lacrymatory reaction mixture resulted. The principal product was a hydrocarbon mixture believed to contain 2-(isopropylphenyl)-2-phenylpropanes.



III

In addition to elemental analyses and physical properties, structural evidence was provided by comparison with material prepared from cumene–ferric chloride,[16] cumene–antimony pentachloride,[17] cumene–α-methylstyrene–aluminum chloride,[16] and 2,2-diphenylpropane–isopropyl chloride–aluminum chloride.[17] Distillation during work-up produced copious quantities of hydrogen bromide, presumably from decomposition of cumyl bromide. A low-boiling fraction proved to be bromocumenes. In addition, bicumyl was apparently present in trace amounts.

After the initial addition of water in another experiment, an aliquot of the subsequent reaction mixture was treated with alcoholic silver nitrate. Quantitative analysis of the precipitated silver bromide indicated the presence of active bromide, probably cumyl bromide, in 46% yield.

Mesitylene and Other Aromatics.—The mesitylene reaction was also investigated under anhydrous conditions and with added water (Table I). It is interesting that, in both cases, cupric bromide gave bromomesitylene as the major product. The absence of side-chain attack can be attributed to the extreme ease with which the mesitylene nucleus undergoes electrophilic substitution.[18]

There was no evidence for the reaction of cupric bromide with either benzene or chlorobenzene. Apparently, only the more reactive aromatics are susceptible to nuclear bromination by cupric bromide. Halogenation of benzene by bromine in the presence of copper is known to occur.[19]

Discussion

The over-all equation for nuclear bromination may be written as

$$\mathrm{ArH} + 2\mathrm{CuBr_2} \longrightarrow \mathrm{ArBr} + 2\mathrm{CuBr} + \mathrm{HBr} \qquad (1)$$

Cuprous bromide was isolated from one of the reaction mixtures and characterized.

The predominant *ortho–para* orientation in toluene and ethylbenzene (Table III) indicates that the reaction proceeds by electrophilic substitution. Catalysis by strong Lewis acids, such as aluminum chloride and ferric chloride, provides additional support for this hypothesis.

Since cupric bromide is known to undergo dissociation at the reaction temperature, free bromine may

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(16) P. Kovacic, C. Wu, and R. W. Stewart, *J. Am. Chem. Soc.*, **82**, 1917 (1960).

(17) P. Kovacic and A. K. Sparks, *J. Org. Chem.*, **28**, 972 (1963).

(18) K. L. Nelson and H. C. Brown in "The Chemistry of Petroleum Hydrocarbons," Vol. 3, Reinhold Publishing Corp., New York, N. Y., 1955, Chapter 56.

(19) B. V. Tronov and L. A. Pershina, *J. Gen. Chem. USSR*, **24**, 1593 (1954).

actually be involved in the nuclear halogenation.

$$2CuBr_2 \rightleftarrows 2CuBr + Br_2 \qquad (2)$$

One might then visualize undissociated cupric bromide as the catalyst for subsequent bromination. The close correspondence in the orientation (Table III) derived from cupric bromide to that from bromine–ferric bromide adds appeal to the proposal. However, cupric bromide undergoes decomposition[20] at 110° to only a slight extent, corresponding to an equilibrium pressure of bromine of about 0.2 mm. (obtained by a small extrapolation of literature data[21]). Nevertheless, it may be that irreversible removal of bromine *via* nuclear substitution facilitates dissociation by shifting the equilibrium.

TABLE III

BROMINATION OF TOLUENE AND ETHYLBENZENE

C_6H_5R, R =	Brominating agent	Temp., °C.	BrC_6H_4R *o*	BrC_6H_4R *p*
CH_3	$CuBr_2$	110	35	63
CH_3	$CuBr_2$–$FeCl_3$	110	39	61
CH_3	$CuBr_2$–$AlCl_3$	110	44	56
CH_3[a]	Br_2–$FeBr_3$	50	37	63
CH_3[b]	Br_2	45	42	58[c]
C_2H_5	$CuBr_2$	115	31	69
C_2H_5[b]	Br_2	45	18	82[c]

[a] F. van der Laan, *Rec. trav. chim.*, **26**, 1 (1907). [b] I. N. Nazarov and A. V. Semenovskii, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 840 (1957). [c] The isomer distribution was determined by an oxidative method which would probably be less accurate that the generally used infrared and gas chromatographic techniques.

Previous work has shown that ferric chloride[16] and antimony pentachloride[22] can effect electrophilic aromatic substitution without prior degradation to free chlorine. By analogy, cupric bromide may function in the intact form[5b] wherein the attacking species might conceivably consist of a dimer complex.

One criterion for an acceptable mechanism is that it must account for the inhibiting effect of water on nuclear bromination. It is reasonable to designate water as a poisoner of the bromination catalyst. Since the inhibitor is effective even when added in minor amounts, the active promoter is apparently present in small quantities. An attractive interpretation spotlights hydrogen bromide, which should be present initially in trace amounts, as a crucial component for the nuclear reaction. From previous work, it is known that hydrogen bromide accelerates the halogenation of benzene with bromine. Furthermore, water, acetic acid and sodium carbonate, which can inactivate the hydrogen bromide by neutralization or complex formation, inhibit the reaction.[19] In the case of toluene and bromine, benzyl bromide (56%) and bromotoluene (44%) were formed in the absence of additives. With added water, benzyl bromide was essentially the only product formed.[19] Hydrogen bromide would presumably play the role of cocatalyst in the present case. Several earlier investigations provide evidence for cocatalysis by Brönsted acids in the alkylation of benzene with alkyl halides and ethers in the presence of boron trifluoride catalyst.[23,24]

Inhibition of nuclear bromination permits the predominance of a slower competing reaction involving the side chain. The presence of benzylic halides suggests that these serve as intermediates for formation of diarylmethanes.

$$C_6H_5CH_3 \xrightarrow{CuBr_2} C_6H_5CH_2Br \xrightarrow[C_6H_5CH_3]{CuBr_2} C_6H_5CH_2C_6H_4CH_3 \qquad (3)$$

Side-chain attack in alkylbenzenes is known to occur with other metal halides, *e.g.*, ferric chloride[16] and antimony pentachloride.[17] An analogous relationship between product composition and reagent purity was previously observed in the cumene–antimony pentachloride reaction.[17]

Nonhebel[5] advanced a free radical mechanism for side-chain attack. If the homolytic aspect is correct, the preference for diarylmethanes and benzylic bromides, instead of a bibenzyl-type product, leads to the conclusion that the benzyl radical, rather than dimerizing, selectively interacts with cupric bromide or bromine. Kochi[25] found that photolysis of cupric chloride in toluene yielded benzyl chloride, together with trace amounts of bibenzyl and chlorotoluene. The sequence 4–7 was proposed. There is also evidence for halogen abstraction from cupric halides by other free radicals.[26–30] The paramagnetic nature of cupric bromide may be an important factor.[31]

$$CuX_2 \rightleftarrows CuX + X\cdot \qquad (4)$$

$$C_6H_5CH_3 + X\cdot \longrightarrow C_6H_5CH_2\cdot + HX \qquad (5)$$

$$2C_6H_5CH_2\cdot \longrightarrow C_6H_5CH_2CH_2C_6H_5 \qquad (6)$$

$$C_6H_5CH_2\cdot + CuX_2 \longrightarrow C_6H_5CH_2X + CuX, \text{ or} \qquad (7)$$

$$C_6H_5CH_2\cdot + X_2 \longrightarrow C_6H_5CH_2X + X\cdot \qquad (8)$$

Another possible mechanism entails cocatalytic abstraction of α-hydride with concomitant reduction of cupric bromide. This approach is consistent with the observation that aluminum chloride and ferric chloride catalyze not only nuclear bromination, but also side-chain attack. Of relevance is the recent report pointing to an electrophilic mechanism in certain side-chain halogenations.[32]

Whereas toluene underwent exclusive nuclear bromination in a rigorously anhydrous system, cumene, under similar conditions, gave a considerable amount of product arising from side-chain attack. These results are reasonable since the usual order of reactivity in side-chain reactions at the α-position is: $C_6H_5CH(CH_3)_2 > C_6H_5CH_2CH_3 > C_6H_5CH_3$.

Experimental[33]

Materials.—Benzene and toluene (Mallinckrodt Chemical Works), ethylbenzene (Eastman Kodak Co.), cumene (Phillips Petroleum Co.), and mesitylene (Matheson Coleman and Bell) were dried and distilled over sodium. Chlorobenzene (Fisher Scientific Co.) was used directly. Cupric bromide (Mallinckrodt Chemical Works or Baker Chemical Co.) was dried at 110° for at least 24 hr., or used directly where indicated.

General Procedure.—The alkylbenzene–cupric bromide reactions were carried out under nitrogen with efficient agitation by a paddle stirrer. Evolution of hydrogen bromide was followed by titration with standard caustic. When the reaction was complete, the mixture was cooled and filtered. The filtrate was washed first with hydrochloric acid, then with water, dried, and distilled.

Reactions were performed according to one of the following three methods. Unless otherwise indicated, the standard procedure was used. A. Standard: Cupric bromide was dried and

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[20] C. G. Jackson, *J. Chem. Soc.*, **99**, 1066 (1911).

[21] P. Barret and N. Guenebaut-Thevenot, *Bull. soc. chim. France*, 409 (1957).

[22] P. Kovacic and A. K. Sparks, *J. Am. Chem. Soc.*, **82**, 5740 (1960).

[23] G. F. Hennion and R. A. Kurtz, *ibid.*, **65**, 1001 (1943).

[24] R. L. Burwell and L. M. Elkin, *ibid.*, **73**, 502 (1951).

[25] J. K. Kochi, *ibid.*, **84**, 2121 (1962).

[26] J. Kumanoto, H. E. De La Mare, and F. F. Rust, *ibid.*, **82**, 1935 (1960).

[27] H. E. De La Mare, J. K. Kochi, and F. F. Rust, *ibid.*, **85**, 1437 (1963).

[28] J. K. Kochi, *ibid.*, **78**, 4815 (1956).

[29] J. K. Kochi, *ibid.*, **79**, 2942 (1957).

[30] J. K. Kochi, *ibid.*, **84**, 2785 (1962).

[31] S. S. Shaffer and N. W. Taylor, *ibid.*, **48**, 843 (1926).

[32] E. Baciocchi and G. Illuminati, *Tetrahedron Letters*, 637 (1962).

[33] Melting points and boiling points are uncorrected. Elemental analyses were performed by Drs. Weiler and Strauss, Oxford, England. Molecular weights were determined by the Rast method.

then weighed in air; the aromatic reactant was distilled from sodium and stored over sodium. B. Anhydrous: Cupric bromide as in A; the aromatic was distilled from sodium immediately before use. C. Rigorously anhydrous: The aromatic as in B; the cupric bromide, redried for at least 4 hr. after being weighed, was added to the aromatic in the reaction flask through a closed system, so that exposure to the atmosphere was minimal. Initially, the reaction flask was heated (mantle) to an air temperature of >100° for at least 1 hr. in a stream of nitrogen. The flask was cooled to room temperature before the reactants were added. In B and C, the H_2SO_4–NaOH–Na_2SO_4 train used for drying the nitrogen was recharged after several runs to ensure effectiveness.

Toluene and Cupric Bromide. 1.—A mixture of toluene (3 moles) and anhydrous cupric bromide (1 mole) was allowed to react at reflux for 21 hr. Hydrogen bromide (0.46 mole) was evolved mainly during the first 4 hr. Distillation yielded bromotoluenes (69 g.), b.p. 179–182°, $n^{25}D$ 1.5506; lit.[34,35] for the *o*-isomer, b.p. 180.3°, $n^{25}D$ 1.5537; for the *p*-isomer, b.p. 183.6°, $n^{25}D$ 1.5486. The infrared spectrum was essentially identical with that of a mixture of *o*- and *p*-bromotoluene. Quantitative infrared analysis[36] gave the isomer distribution, 35% *ortho*, 2% *meta*, 63% *para*.

Anal. Calcd. for C_7H_7Br: C, 49.15; H, 4.10; Br, 46.75; mol. wt., 171. Found: C, 49.05; H, 4.39; Br, 47.00; mol. wt., 173.

Oxidation with alkaline permanganate provided a mixture of acids which was fractionally sublimed. The impure *o*-bromobenzoic acid was converted to the ester with ethereal diazomethane, and then characterized by comparison with the authentic ester in gas chromatographic analysis. The residual *p*-bromobenzoic acid melted at 251–253°; mixture melting point with the authentic material was undepressed.

Further distillation of the original product gave a yellow liquid (1 g.), b.p. 279° at 747 mm., in addition to a trace amount of black residue. The infrared spectrum indicated an isomeric mixture of phenyltolylmethanes.

Cuprous bromide from a toluene–cupric bromide reaction (procedure B) was washed with ether, hydrochloric acid, water, acetone, and finally ether. The slightly off-white powder was dried under vacuum at 100°. The X-ray powder pattern, obtained with a Norelco camera (copper Kα radiation, 1 hr.), gave *d*-spacings of 3.58, 3.15, 3.09, 2.27, 2.24, 1.69, 1.68, 1.52, and 1.505 Å. Authentic cuprous bromide provided essentially the same *d*-spacings.

2. **With Water.**—(1) From drying experiments, it was estimated that the commercial cupric bromide contained about 10 mole % of water. The reaction of dry toluene (1.5 moles) and commercial cupric bromide (0.5 mole) carried out at 110–116° for 35 hr., produced 0.37 mole of hydrogen bromide. In the work-up, removal of toluene by distillation through an 8-in., helix-packed column gave a black, viscous residue. Fractionation through an 18-in. by 6-mm. spinning band column yielded a light yellow liquid (1 g.), b.p. 48° at 4.5 mm., which appeared to be a mixture of bromotoluenes and benzyl bromide by comparison of the infrared spectrum with those of the authentic materials.

In addition, a yellow oil (10 g.) was collected at 118–130° at 5 mm., b.p. 280° at 747 mm., $n^{20}D$ 1.5713; lit.[37] for phenyltolylmethanes: *o*-isomer, b.p. 280.5° at 760 mm., $n^{20}D$ 1.5763; *m*-isomer, b.p. 279° at 760 mm., $n^{20}D$ 1.5712; *p*-isomer, b.p. 282° at 760 mm., $n^{20}D$ 1.5692. The infrared spectrum indicated the presence of *o*- and *p*-isomers.

Anal. Calcd. for $C_{14}H_{14}$: C, 92.26; H, 7.74; mol. wt., 182. Found: C, 91.94; H, 7.76; mol. wt., 184.

Oxidation with chromic acid gave *p*-benzoylbenzoic acid, m.p. 196–197°; the mixture melting point with authentic material was not depressed. A small amount of liquid was also obtained, whose 2,4-dinitrophenylhydrazone melted at 191–193°; the mixture melting point with the 2,4-dinitrophenylhydrazone of authentic 2-methylbenzophenone was not depressed.

A mixture of the phenyltolylmethane fraction and authentic bibenzyl was investigated by gas chromatography. No separation was obtained with the columns: silicone rubber, 6 ft.; Apiezon L, 9 ft.; or polydiethyleneglycol succinate, 15 ft.

The residue from distillation of the reaction mixture consisted of black solid, 10 g.

(2) A similar experiment was performed with toluene (0.75 mole), anhydrous cupric bromide (0.25 mole), and water (1.1 g.). A light colored liquid (1 g.) was obtained by distillation. Infrared and gas chromatographic analyses indicated the presence of bromotoluenes and benzyl bromide. Treatment of this fraction with ethanolic thiourea yielded S-benzylthiuronium bromide, m.p. 156–157° from ethanol–ether; the mixture melting point with authentic material was undepressed.

(3) In another experiment under these conditions, aqueous sodium carbonate was added when the reaction was near completion. After an additional 3 hr. at reflux, work-up yielded a small amount of benzaldehyde. The gas chromatogram and infrared spectrum were essentially identical with those of authentic benzaldehyde. In addition, bromotoluenes and phenyltolylmethanes were isolated during gas chromatography, and characterized by retention time and infrared analysis.

(4) In curves 7 and 8 in Fig. 1, water was added when the hydrogen bromide evolution became vigorous (generally after 25 meq. had evolved). In curve 7, the rate decreased after 0.25 ml. (0.014 mole) of water was added. After a short time the rate increased. When 100 meq. had evolved, an additional 0.25 ml. of water was added with similar results. In curve 8, 0.5 ml. (0.028 mole) of water was added; the rate decreased and remained at a low level. In the reactions shown in Fig. 1 and Table II, semiquantitative analysis of the products was performed by gas chromatography (silicone gum rubber columns). Isomer distributions were determined with a 12-ft. Carbowax column at 100°; complete separation of the *o*- and *p*-bromotoluenes was effected. In Fig. 1, the "initiation" time, *i.e.*, the time at which acid gas was first detected, was essentially the same in all cases except for curve 6 (much longer time).

Toluene–Cupric Bromide–Catalyst.—The catalyst was added to a mixture which was undergoing reaction at the side chain (slow rate) until a vigorous reaction ensued: ferric chloride, 0.2 g. (0.00125 mole); aluminum chloride, 0.25 g. (0.002 mole) (Table III).

Toluene–Cupric Bromide–Cuprous Bromide.—Dry cuprous bromide was added initially to the reaction mixture (procedure C); 5 g. (0.035 mole), curve 2 in Fig. 1; 35 g. (0.25 mole), curve 1.

Ethylbenzene and Cupric Bromide. 1.—Hydrogen bromide (0.45 mole) was evolved from the reaction of ethylbenzene (3 moles) with anhydrous cupric bromide (1 mole) at 114–116° for 4 hr. After the recovery of unchanged ethylbenzene, bromoethylbenzenes (75 g.) were obtained at 200–203°, $n^{25}D$ 1.5433; lit.[38] for bromoethylbenzenes: *ortho*, b.p. 201.5°, $n^{25}D$ 1.5463; *para*, b.p. 205°, $n^{25}D$ 1.5423. The infrared spectrum was essentially identical with that of a mixture of authentic *o*- and *p*-bromoethylbenzenes (Aldrich Chemical Co.). The isomer distribution ascertained by gas chromatography was 31% *ortho* and 69% *para*.

Anal. Calcd. for C_8H_9Br: C, 51.91; H, 4.91; Br, 43.18. Found: C, 52.09; H, 4.93; Br, 43.30.

Oxidation with alkaline permanganate provided a crude acid which, after sublimation, melted at 249.5–250°. The mixture melting point with authentic *p*-bromobenzoic acid was undepressed.

The original reaction mixture also yielded a yellow oil (2 g.), b.p. 106–120° at 2 mm. Gas chromatography demonstrated the presence of a gross mixture from which the major component was separated. Infrared and gas chromatographic analysis indicated that this material was essentially identical with authentic 1-(ethylphenyl)-1-phenylethanes.[16,17]

2. **With Water.**—The interaction of ethylbenzene (2 moles), anhydrous cupric bromide (1 mole), and water (0.25 mole) at 112–127° for 29 hr. generated 0.82 mole of hydrogen bromide. Distillation of unchanged ethylbenzene (copious hydrogen bromide evolution) yielded a black viscous residue which on fractionation (hydrogen bromide evolution in the early stages) gave three main portions: A, 1 g., b.p. 45–46° at 2 mm.; B, 5.4 g., b.p. 114–117° at 2 mm.; C, 3.7 g., b.p. 180–190° at 2 mm. The residue consisted of black solid (10.5 g.).

By infrared and gas chromatographic analysis, fraction A was shown to be an isomeric mixture of bromoethylbenzenes.

Fraction B, a yellow oil, was purified by gas chromatography, $n^{25}D$ 1.5600; reported[39] for 1-(ethylphenyl)-1-phenylethanes: *p*-isomer, b.p. 170° at 20 mm., $n^{25}D$ 1.5605; *o*-isomer, b.p. 165° at 20 mm., $n^{20}D$ 1.5650. The infrared spectrum was identical with that of 1-(ethylphenyl)-1-phenylethanes[16,17,39] except for relative band intensities. Absorption maxima were present at: 7.30 (m), 8.46 (w), 8.94 (w), 9.47 (w), 9.73 (m), 9.82 (m), 10.25 (w), 10.40 (w), 11.04 (w), 11.17 (w), 12.00 (s), 12.55 (w), 13.23 (m), and 14.36 (s) μ.

Anal. Calcd. for $C_{16}H_{18}$: C, 91.43; H, 8.57. Found: C, 91.17; H, 8.55.

Oxidation of B with chromic acid in acetic acid yielded *p*-benzoylbenzoic acid, m.p. 193.5–194°; the mixture melting point with authentic material was undepressed.

Gas chromatographic analysis revealed the absence of *meso*-2,3-diphenylbutane in B and the preceding intermediate fraction.

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Fraction C was a viscous yellow oil, $n^{25}\mathrm{D}$ 1.6144, whose infrared spectrum was similar to that of fraction B except for an additional band at 14.88 μ. Purification was accomplished by passage through an alumina column (pentane solvent) in order to remove higher boiling material.

Anal. Calcd. for $C_{24}H_{26}$: C, 91.67; H, 8.33; mol. wt., 314. Found: C, 91.75; H, 8.40; mol. wt., 320.

Oxidation with chromic acid in acetic acid gave a crude, brown product which, on vacuum sublimation, yielded *p*-benzoylbenzoic acid, m.p. 193–194°; the mixture melting point with authentic material was undepressed.

Cumene and Cupric Bromide. 1.—Cumene (2 moles) and anhydrous cupric bromide (1 mole) were allowed to react for 8 hr. at 115–120°. When the hydrogen bromide evolution decreased, the mixture was heated at 149° for 2 hr. A total of 0.77 mole of hydrogen bromide resulted. During work-up of the black lacrymatory mixture, removal of unchanged cumene by distillation was accompanied by hydrogen bromide evolution which continued during most of the subsequent distillation.

The products were collected in three main fractions: (A), wt. 2.8 g., b.p. 45–64° at 3 mm.; (B), 3.4 g. b.p. 65–85° at 3 mm.; (C), 7.2 g., b.p. 115–125° at 3 mm.; (D), a small amount of yellow solid, b.p. 125° at 3 mm.; (E), 7.5 g. of black solid residue. Fraction B was shown by gas chromatography to be a gross mixture and was not further investigated.

Fraction A, which was very lacrymatory, turned dark after a short time. Gas chromatographic analysis, with authentic *p*-bromocumene as the reference, indicated the presence of bromocumenes. Except for the occurrence of *ortho* bands at 12.75, 14.04, and 14.20 μ, the infrared spectrum was identical with that of *p*-bromocumene. Oxidation of A with chromic acid in acetic acid gave a crude product which was purified by sublimation, m.p. 249–250°. The mixture melting point with authentic *p*-bromobenzoic acid was undepressed.

Fraction C, a yellow liquid which also was very lacrymatory, was chromatographed in part through an alumina column in order to remove cumyl bromide. The recovered material, only slightly colored, $n^{25}\mathrm{D}$ 1.5578, possessed the same retention time in gas chromatography as did 2-(isopropylphenyl)-2-phenylpropane,[16,40] $n^{25}\mathrm{D}$ 1.5582. The infrared spectrum was essentially identical with that of the authentic material, with absorption bands present at 7.31 (m), 7.36 (m), 7.63 (m), 8.31 (w), 8.67 (w), 9.09 (w), 9.31 (w), 9.49 (w), 9.76 (m), 10.69 (w), 12.04 (w), 12.48 (w), 13.26 (s), and 14.34 (s) μ.

Anal. Calcd. for $C_{18}H_{22}$: C, 90.75; H, 9.25; mol. wt., 238. Found: C, 90.60; H, 9.35; mol. wt., 236.

Gas chromatography of the crude reaction product also revealed trace amounts of a component whose retention time was identical with that of bicumyl.

The solid product D, m.p. 170–180° from acetone–water, possessed infrared bands at 9.39 (w), 9.80 (w), 10.00 (w), 11.98 (m), 13.39 (s), and 14.46 (s) μ. It was not further characterized.

2. **With Water.**—A mixture of cumene (2 moles), anhydrous cupric bromide (1 mole), and water (0.25 mole) evolved 0.47 mole of hydrogen bromide during 7.5 hr. at 110°. After work-up, the pale yellow organic solution was treated with alcoholic silver nitrate, yielding about 0.23 mole of silver bromide. Gas chromatography of the reaction mixture indicated a large number of products.

3. **Procedure C.**—Cumene (2 moles), dried twice over calcium hydride and once over sodium, and cupric bromide (1 mole) were allowed to react at 110° for 5.5 hr.; 0.31 mole of hydrogen bromide was evolved. The reaction mixture was light yellow in color and was not lacrymatory.

Gas chromatography indicated a mixture of products, the major ones being bromocumenes according to gas chromatographic and infrared spectral comparison with authentic *p*-bromocumene. A semiquantitative gas chromatographic analysis gave the composition: bromobenzene, 10%; isomeric diisopropylbenzenes, 5%; bromocumenes, 45%; 2-(isopropylphenyl)-2-phenylpropanes, 30%; and others, 10%.

Mesitylene and Cupric Bromide. 1.—Reaction of mesitylene (2 moles) with anhydrous cupric bromide (1 mole) for 3 hr. at 111–112° resulted in the evolution of 0.49 mole of hydrogen bromide. Work-up yielded 2-bromomesitylene (82 g.), b.p. 221°, $n^{25}\mathrm{D}$ 1.5509; lit.[41] b.p. 226.5–227°, $n^{20}\mathrm{D}$ 1.5527. The infrared spectrum was identical with that of the authentic material.

A small amount of higher boiling material and 1 g. of distillation residue were also obtained.

2. **With Water.**—A mixture of mesitylene (2 moles), cupric bromide (1 mole), and water (0.25 mole) yielded 0.43 mole of hydrogen bromide during 1 hr. at 105–110°. During the product distillation, 2-bromomesitylene (81 g.) was collected at 221°, $n^{25}\mathrm{D}$ 1.5500. The infrared spectrum was identical with that of the authentic material.

Benzene and Cupric Bromide.—A mixture of benzene (1 mole) and anhydrous cupric bromide (0.5 mole) was heated at reflux for 24 hr. There was no evidence of hydrogen bromide evolution. Distillation gave unchanged benzene and a trace of black residue.

Chlorobenzene and Cupric Bromide.—Heating a mixture of chlorobenzene (1 mole) and anhydrous cupric bromide (0.5 mole) at reflux resulted in evolution of a small amount of bromine. While the reaction mixture was maintained at 110° for 24 hr., elimination of small quantities of bromine continued. There was no appreciable formation of hydrogen bromide. In the work-up, distillation yielded unchanged chlorobenzene and a trace of black residue.

***o*-Methylbenzophenone.**—After a mixture of *o*-toluic acid (10 g.) and excess thionyl chloride had been heated at reflux for 0.5 hr., excess thionyl chloride was removed at the aspirator. Following the addition of benzene (40 ml.) and aluminum chloride (30 g.), the mixture was refluxed for 1 hr., and then mixed with hydrochloric acid and ice. The organic layer was washed with base, acid, and water, then dried and distilled, yielding *o*-methylbenzophenone, b.p. 133–135° at 3 mm., $n^{20}\mathrm{D}$ 1.5957; lit.[42] b.p. 128–130° at 2 mm., $n^{20}\mathrm{D}$ 1.5965.

Anal. Calcd. for $C_{14}H_{12}O$: C, 85.71; H, 6.12. Found: C, 85.59; H, 6.33.

The 2,4-dinitrophenylhydrazone derivative melted at 193–194° from ethanol; lit. m.p., 183–184°,[43] 184–190°,[44] 198.5–199.5°.[45]

S-Benzylthiuronium Bromide.—A mixture of benzyl bromide (5 g.), thiourea (2.2 g.), and ethanol (10 ml.) was refluxed gently for 0.5 hr. Addition of ether to the cooled mixture resulted in precipitation of the salt, m.p. 156–157° from ethanol–ether, lit.[46] m.p. 157°.

Anal. Calcd. for $C_8H_{11}BrN_2S$: C, 38.88; H, 4.48; Br, 32.33; N, 11.33; S, 12.97. Found: C, 38.98; H, 4.48; Br, 32.05; N, 11.42; S, 12.98.

A previous preparation was reported[47] to melt at 129°. Before thorough drying, our product was observed to melt in this same region.

***meso*-2,3-Diphenylbutane.**[48]—The Grignard reagent was prepared from (1-bromoethyl)-benzene (15 g.) and magnesium (2.1 g.) in anhydrous ether. After addition of anhydrous cupric chloride, the mixture was refluxed for 3 hr. Work-up yielded *meso*-2,3-diphenylbutane, m.p. 124.5–125° from methanol, lit.[48] m.p. 126°. A small liquid fraction was presumably the crude *dl*-isomer.

2,3-Dimethyl-2,3-diphenylbutane.—The reaction was performed according to the method of Farmer and Moore.[49] A mixture of cumene (26 g.) and di-*t*-butyl peroxide (12.2 g.) was heated at reflux for 60 hr. After removal of volatile materials at the aspirator, the residue was crystallized from methanol, m.p. 117°; lit.[48] for 2,3-dimethyl-2,3-diphenylbutane, m.p. 118–119°.

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(40) Analysis by n.m.r. of the cumene "dimer" from cumene–antimony pentachloride[17] indicated the presence of about 20% impurity which may possibly be the corresponding dehydro derivative (α-methylstyrene structure). This result casts uncertainty upon the purity of the supposed 2-(isopropylphenyl)-2-phenylpropane prepared by the cumene–metal halide routes. We are grateful to Dr. Donald P. Hollis, Varian Associates, for obtaining the n.m.r. spectrum and assisting in the interpretation.

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