(± 0.002) Å, $b = 17.509$ (± 0.002) Å, $c = 8.833$ (± 0.001) Å, $\beta = 102.78$ $(\pm 0.03)°$, space group, $P2_1/c$, molecules/unit cell, 4, density (calcd) $= 1.289$ g/cm³, and density (measured by flotation) $= 1.32$ g/cm³.

Intensity data were collected by the stationary counter-stationary crystal technique using balanced filters for Cu Kα radiation.[14] The intensities (maximum *two θ* = 100°) were converted to structure factor amplitudes by applying appropriate corrections for absorption, α_1–α_2 splitting, and Lorentz-polarization effects. These data were scaled by Wilson statistics[15] and converted to their respective normalized structure factors.

The phases of the 159 largest normalized structure factors were derived by the application of the Sayre relationships.[16] Electron density and least squares calculations using all the data enabled the atomic coordinates of atoms and the thermal parameters (hydrogens isotropically and others anisotropically) to be refined. The final R index for the observed data was 0.038. A table of

the positional and thermal parameters for the molecule, as well as the F tables, the bond distances, and angles, can be obtained from the authors.

(14) T. F. Furnas and D. Harker, *Rev. Sci. Instrum.*, **26**, 449 (1955).

(15) A. J. C. Wilson, *Nature*, **150**, 152 (1942).

(16) D. Sayre, *Acta. Crystallogr.*, **5**, 60 (1952).

Halogenation with Copper(II) Halides. The Synthesis of Aryl Iodides

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Aryl iodides have been synthesized by a simple, single-step reaction of aromatic compounds with copper salts and an iodide donor. The reaction is capable of application to substituted and unsubstituted aromatic substrates. Iodination fails to occur only with ring systems bearing strongly deactivating substituents or possessing functional groups that deactivate the copper salt through complexation. Iodine may be supplied to the reaction by molecular iodine or by any group I–VIII metallic or nonmetallic iodide. Certain metal iodides exhibit greater reactivity than iodine itself; aluminum and ferrous iodides, in particular, have been found to be potent catalysts for this iodination reaction. The new synthetic method affords several advantages with regard to classical iodination procedures.

Halogenation by molecular halogen is one of the classical reactions of aromatic compounds and has been thoroughly investigated for both its theoretical and synthetic value.[1] The reactions of chlorine, bromine, and iodine with aromatic structures have generated a wealth of physical–organic data that define the structure-reactivity relationships and the steric and electronic factors that control these systems. The general reaction is agreed to involve the electrophilic attack of polarized halogen, or suitable halogen donor, on the aromatic and to proceed through a sequence of π and σ complexes to aryl halide product. The reaction is markedly sensitive to the presence of a catalyst whose principal function is to polarize the halogen source.

In contrast to chlorination and bromination which occur in the absence of catalysts, iodination demands the use of a catalytic agent. The failure of noncatalyzed iodination to occur was originally believed to be indicative of the reduction of aryl iodide product by hydrogen iodide.[2] Rather, the fact is that the role of the catalyst is to convert molecular iodine to a more reactive species, notably the iodonium (I$^+$) ion. Historically, this has *not* been accomplished through the use of conventional Lewis acid metal salts, for the coordination of iodine with these salts is reportedly

weak owing to steric inhibition of orbital overlap.[1] Consequently, the synthesis of aryl iodides has required specialized conditions. These traditional procedures include (1) iodination of active aromatics with iodine in water;[3,4] (2) iodination of benzene and its alkyl homologs in the presence of strong mineral acids,[4-6] oxidizing agents,[4,6] or silver and mercury salts;[4,6,7] (3) decomposition of diazonium salts or arylthallium ditrifluoroacetates[8] with potassium iodide; (4) reaction of iodine with certain arylmercury chlorides.[4]

All of these procedures suffer from one or more deficiencies. The most serious of these are substrate limitations due to reaction conditions and the loss of iodine from the reaction as hydrogen iodide or metallic iodide.

The reaction of olefins with copper halides in various solvent media has been a topic of investigation in these laboratories.[9] During these studies it had been found that olefins react readily with copper(II) chloride and iodine in an inert hydrocarbon diluent to give high yields of chloroiodoalkanes.[10] When this reaction was performed in high-boiling aromatic solvents, the forma-

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(1) For a recent general review of aromatic halogenation, see H. P. Braendlin and E. T. McBee in "Friedel-Crafts and Related Reactions," Vol. III, G. A. Olah, Ed., Wiley, New York, N. Y., 1964, Chapter 46.

(2) J. D. Roberts and M. C. Caserio, "Basic Principles of Organic Chemistry," W. A. Benjamin, New York, N. Y., 1965, p 789.

(3) See ref 1, p 1521.

(4) L. F. Fieser and M. F. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, pp 495–497.

(5) See ref 1, p 790.

(6) W. J. Hickinbottom, "Reactions of Organic Compounds," Longmans, Green and Co., London, England, 1957, p 84.

(7) G. A. Olah and H. W. Quinn, "Friedel-Crafts and Related Reactions," Vol. IV, G. A. Olah, Ed., Wiley, New York, N. Y., 1965, p 263.

(8) A. McKillop, J. S. Fowler, M. J. Zelesko, J. D. Hunt, E. C. Taylor, and G. McGillivray, *Tetrahedron Lett.*, 2427 (1969).

(9) W. C. Baird, Jr., and J. H. Surridge, *J. Org. Chem.*, **35**, 2090 (1970).

(10) W. C. Baird, Jr., unpublished results.

tion of by-product aryl iodides was surprisingly observed. The realization that this system represented a new and potentially general synthesis of aryl iodides prompted a detailed study of the reaction of aromatics with copper salt–iodine donor combinations. The remainder of this paper presents the results of the investigation of this new procedure. The scope of this reaction has been defined in terms of the following variables: the copper salt, the iodine source, the nature of the aromatic substrate, the effect of Lewis acid catalysis.

Results and Discussion

The Nature of the Copper Salt.—The reaction of xylene and iodine with copper(I) and copper(II) salts was studied to determine the ability of various copper compounds to participate in the synthesis of aryl iodides. Table I presents the results of these experiments.

TABLE I
COPPER SALTS FOR ARYL IODIDE SYNTHESIS

Copper salt	Time, at reflux hr	Yield of iodoxylene, %
$CuCl_2$	5	85
CuCl	5.5	22
CuF_2	5	42
$CuF_2 \cdot 2H_2O$	5	26
$CuCl_2 \cdot 2H_2O$	6	12
$Cu(OAc)_2$	5.5	<5
$Cu(OAc)_2 \cdot H_2O$	5.5	<5
CuCN	5.5	0

The observed reactivity order for these various copper(I) and copper(II) salts [$CuCl_2$ > CuF_2 > CuCl > $Cu(OOCCH_3)_2$] indicates that these compounds play a dual role in the iodination reaction. The primary function is to promote the iodination reaction *via* Lewis acid catalysis; the other, which is valid only for copper(II) compounds, is to recycle by-product hydrogen iodide to the reaction as iodine *via* a redox reaction. While aromatic iodination has been reported to be insensitive to Lewis acid catalysts,[1] the present results are certainly indicative of and best interpreted by such catalysis. Furthermore, subsequent sections of this report will clearly demonstrate that the reported failure of Lewis acid catalysts to promote aromatic iodination is erroneous.

Both copper(I) and copper(II) halides are known to possess Lewis acid characteristics and have shown mild to moderate activity as Friedel–Crafts catalysts.[11] Copper(II) chloride, in particular, has been effective in chlorination and bromination reactions.[1] It is not especially surprising then that this copper salt has demonstrated the greatest activity in aromatic iodination. In line with the previously proposed dual function of copper(II) salts the reaction based on copper(II) chloride may be considered to involve the sequence illustrated by eq 1–2. In the first step iodination of

$$ArH + I_2 \xrightarrow{(CuCl_2)} ArI + HI \quad (1)$$

$$ArH + HI + 2CuCl_2 \longrightarrow 2HCl + ArI + 2CuCl \quad (2)$$
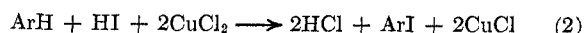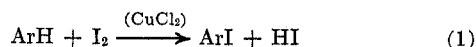
the ring is catalyzed by copper(II) chloride to produce aryl iodide and hydrogen iodide. The latter is subsequently oxidized to iodine or iodine monochloride, a potent iodination reagent,[1] which iodinates a second mole of aromatic under the influence of either copper(I) or copper(II) chloride as a catalyst. The overall stoichiometry of the reaction (eq 3) is in accord with this

$$2ArH + I_2 + 2CuCl_2 \longrightarrow 2ArI + 2HCl + 2CuCl \quad (3)$$
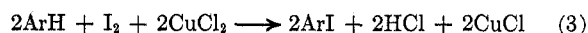
interpretation, and the isolated yields of organic and inorganic products are equally consistent with this reaction path. Whether iodine monochloride plays a transient role in the reaction cannot be definitely stated; that hydrogen iodide is oxidized by copper(II) chloride and can serve as an iodide donor for aromatic iodination has been demonstrated as will be seen subsequently.

The diminished reactivity of copper(II) fluoride is derived from two sources. The salt possesses little Lewis acid activity owing to its highly ionic fluoride type lattice,[11] and the oxidation of hydrogen iodide is complicated by the unstable nature of cuprous fluoride[11] which leads to its conversion to cuprous iodide in the presence of iodine.

Copper(I) chloride possesses mild Friedel–Crafts properties, and the reaction with this salt is solely metal halide catalyzed iodination. The chloride is recovered unchanged from the reaction, and by-product hydrogen iodide is lost from the system. The poor activity exhibited by the hydrates of copper(II) chloride and fluoride, copper acetates, and copper(I) cyanide is best rationalized by the diminished Lewis acid character of these salts. Water is a notorious Lewis acid poison, the available coordination sites of the metal ion being preempted by this ligand. In a similar manner the coordinating ability of the copper ion is destroyed by the strongly bridging acetate and cyanide ions, and the ability of these salts to activate iodine through complexation is lost.

Iodide Donors for the Synthesis of Aryl Iodides — Iodine may be supplied to the synthesis of aryl iodides in a variety of forms. While molecular iodine is a convenient source, it has been shown that virtually any group I–VIII metallic or nonmetallic iodide is satisfactory. The reactivity of certain of these iodide salts permits achieving iodination reactions that fail to occur with elemental iodine. Table II lists various iodides

TABLE II
IODIDE DONORS FOR ARYL IODIDE SYNTHESIS

Iodide donor	Time, at reflux hr	Yield of iodoxylene, %
BaI_2	6	49
BiI_3	7	81
CoI_2	1	62
$FeI_2 \cdot 4H_2O$	2	100
$FeI_2 \cdot 4H_2O$	0.5	54
FeI_2	0.5	26
SnI_4	5	85
LiI	5	36
NH_4I	6	17
HI	5	14
AlI_3	6	13[a]

[a] Reaction yielded condensed aromatic products of undetermined structure. *Anal.* Found: C, 88.36; H, 9.25.

(11) G. A. Olah, "Friedel-Crafts and Related Reactions," Vol. I, G. A. Olah, Ed., Wiley, New York, N. Y., 1963, pp 215–216.

that have been tested in this reaction. The reactions occurred with the general overall stoichiometry illustrated by eq 4; at the conclusion of the reaction the

$$MI_n + 2nCuCl_2 + nArH \longrightarrow$$
$$nArI + nHCl + 2nCuCl + MCl_n \quad (4)$$
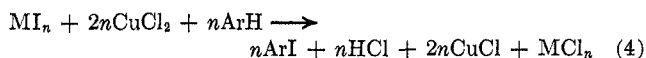
metal iodide had been completely transformed to the corresponding metal chloride. All of these reactions proceeded with the release of elemental iodine in the early stages of the reaction period. The generally better performance of the more covalent iodides relative to the ionic iodides is attributed to a more facile generation of iodine in the former reactions and to the Lewis acid properties of the metals involved.

The impact of Lewis acid character is apparent from the data of Table II, for optimum yields of iodoxylene were produced under more moderate conditions in those reactions that generated strong Friedel–Crafts catalysts. The reactions utilizing the iodides of cobalt, bismuth, iron, tin, and aluminum in general required shorter reaction periods, lower temperatures, and gave better yields. The active "catalyst" in these reactions is probably a blend of copper(I) chloride and other metal halide. The two metal salts operating in concert appear to exert a synergistic effect on the reaction although the exact mechanism of this influence is vague.

It is interesting to note that the use of a hydrated metal iodide does not inhibit the reaction as does the use of hydrated copper(II) chloride. One of the most active iodide salts, iron(II) iodide, is supplied to the reaction as the tetrahydrate without deleterious effect. The absence of serious inhibition in the latter case may be ascribed to unusual features of the iron(II) iodide–copper(II) chloride reaction. One of these is the release of water of hydration from the metal ions during the iodide to iodine oxidation. The resultant metal chlorides possess a degree of reactivity that surpasses that encountered in the reaction with anhydrous iron(II) iodide. The reasons for this distinction are not wholly apparent.

The reactivity of the aluminum(III) iodide and iron(II) iodide systems permits the iodination of aromatics that fail to experience reaction with iodine and copper(II) chloride. This technique is most applicable to aromatics bearing deactivating groups and to benzene and its alkyl homologs that either react sluggishly or not at all. While this topic is more completely discussed in the following section, a few comments are relevant at this point. The high activity of the aluminum(III) iodide–copper(II) chloride couple leads to undesirable side reactions when alkyl benzenes serve as the aromatic substrate. This is in large part due to the production of aluminum chloride as the reaction proceeds. Xylenes not only experience nuclear iodination, but are also converted to arylmethanes, biaryls, and disproportionated and polymerized materials.[12] *tert*-Butylbenzene does not undergo iodination with this couple, but is totally disproportionated to benzene and *m*- and *p*-di-*tert*-butylbenzenes. For these reasons the use of aluminum iodide is restricted to the reactions of benzene, toluene, and halobenzenes. Iron(II) iodide, which does not induce the destruction of the aromatic

compound by any of the cited side reactions, is consequently a preferred iodide donor.

Synthesis of Aryl Iodides —This section describes the iodination of various aromatic structures by copper(II) chloride–iodine donor combinations. Iodine was selected as the primary iodine donor; other more reactive iodine sources were employed where necessary as noted subsequently. Table III summarizes the aromatic substrates that yielded aryl iodides.

Benzene is not iodinated by copper(II) chloride in combination with iodine or iron(II) iodide but is converted to iodobenzene in the presence of aluminum(III) iodide. The reaction is completely free of the polyphenyls obtained by treatment of benzene with aluminum and copper(II) chlorides.[12] The absence of these benzene polymers is ascribed to the destruction of the requisite copper(II) chloride by the oxidation of aluminum iodide to iodine and aluminum chloride. While the latter may initiate polymerization of the aromatic, the copper(II) salt is required for propagation of the reaction.

Toluene is converted to iodotoluenes in 25% yield by iodine–copper(II) chloride. The ortho/para ratio, 41:59, is reminiscent of that observed during the iron(III) bromide catalyzed bromination of this aromatic (ortho/para = 37:63).[13] An 81% yield of iodotoluenes is realized with iron(II) iodide under milder conditions (3 hr at reflux *vs.* 7 hr); in this case the ortho/para distribution is shifted to 53:47. It is not clear whether this change in substitution pattern is indicative of a smaller steric requirement of the attacking complex in the latter reaction; it is conceivable that the greater degree of reactivity of this iodinating system renders it less selective. The antimony(V) chloride catalyzed chlorination of toluene exhibited a threefold preference for ortho attack while iron(III) chloride catalysis gave an ortho/para distribution of 64:32.[14] This distinction has been attributed to a smaller steric factor in the antimony reaction; it is of interest to note, however, that antimony(V) chloride is a more reactive chlorinating agent than iron(III) chloride. Postisomerization of the iodotoluenes is not likely, for halogenation reactions are not reversible at temperatures below 150° and generally become significant only in the range 200–400°.[1] The presence of strong Lewis acid metal halides seems to have little bearing on this point.

Xylene, mesitylene, and durene are all readily iodinated by copper(II) chloride and iodine. As anticipated, the degree of reactivity increased with increasing alkylation of the ring indicating that the reaction is abetted by high aromatic basicity. The observed order of xylene reactivity (meta > ortho ≅ para) is in accord with the basicity of the xylene isomers toward electrophiles.[15]

Chloro- and bromobenzene were inert toward iodine–copper(II) chloride, but aluminum(III) iodide and iron(II) iodide did effect the iodination of these halobenzenes. Bromobenzene experienced exclusively para substitution, a manifestation of steric control rather than electronic. Chlorobenzene yielded chloroiodobenzenes in which the ortho/para distribution was 18:82. The degree of ortho substitution is higher than

(12) P. Kovacic, "Friedel–Crafts and Related Reactions," Vol. IV, G. A. Olah, Ed, Wiley, New York, N. Y., 1965, Chapter 48.

(13) F. Van der Laan, *Recl. Trav. Chim. Pays-Bas*, **26**, 1 (1907).

(14) P. Kovacic and A. K. Sparks, *J. Amer. Chem. Soc.*, **82**, 5740 (1960).

(15) D. A. McCaulay, "Friedel–Crafts and Related Reactions," Vol. II, G. A. Olah, Ed, Wiley, New York, N. Y., 1964, pp 1050–1054.

TABLE III

SYNTHESIS OF ARYL IODIDES

Aromatic ml or g (mol)	Solvent[a]	Iodine source g (mol)	Copper salt g (mol)	Reaction conditions Time, hr	Temp, °C	Product	Yield, %	Isomeric distribution
Benzene 75 ml		AlI₃ 8.1 (0.02)	CuCl₂ 16.1 (0.12)	5	80	Iodobenzene	65	
Toluene 70 ml		I₂ 13.0 (0.05)	CuCl₂ 13.3 (0.10)	7	110	Iodotoluene	25	2-Iodo 41% 4-Iodo 59%
Toluene 100 ml		FeI₂·4H₂O 9.5 (0.025)	CuCl₂ 16.1 (0.12)	3	110	Iodotoluene	81	2-Iodo 53% 4-Iodo 47%
m-Xylene 75 ml		I₂ 12.7 (0.05)	CuCl₂ 13.3 (0.10)	7	145	Iodoxylene	63	1,3-Dimethyl-4-iodo 86% 1,3-Dimethyl-2-iodo 14%
o-Xylene 75 ml		I₂ 12.7 (0.05)	CuCl₂ 13.4 (0.10)	7	145	Iodoxylene	13	1,2-Dimethyl-4-iodo 75% 1,2-Dimethyl-3-iodo 25%
p-Xylene 75 ml		I₂ 12.7 (0.05)	CuCl₂ 13.4 (0.10)	7	145	Iodoxylene	34	1,4-Dimethyl-3-iodo
Mesitylene 50 ml		I₂ 12.7 (0.05)	CuCl₂ 13.4 (0.10)	0.5	150	Iodomesitylene	86	
Durene 26.8 (0.20)	50 ml C₆H₅Cl 10 ml C₆H₆	I₂ 12.7 (0.05)	CuCl₂ 13.4 (0.10)	20	115	Iododurene	100	
tert-Butylben- zene 50 ml		FeI₂·4H₂O 9.6 (0.025)	CuCl₂ 16.8 (0.13)	5	150	p-Iodo-tert-butyl- benzene	76	
Chlorobenzene 75 ml		AlI₃ 8.1 (0.02)	CuCl₂ 16.1 (0.12)	5	80	Chloroiodobenzene	29	1-Chloro-4-iodo 82% 1-Chloro-2-iodo 18%
Bromobenzene 75 ml		FeI₂·4H₂O 9.5 (0.025)	CuCl₂ 16.8 (0.13)	11	150	p-Bromoiodo- benzene	33	
Acetanilide 13.5 (0.10)	60 ml C₆H₅Cl 10 ml C₆H₆	I₂ 12.7 (0.05)	CuCl₂ 13.3 (0.10)	28	115	p-Iodoacetanilide	76	
Anisole 50 ml		I₂ 12.7 (0.05)	CuCl₂ 13.3 (0.10)	6	140	p-Iodoanisole	80	
Phenol 9.4 (0.10)	50 ml C₆H₅Cl	I₂ 12.7 (0.05)	CuCl₂ 13.3 (0.10)	29	130	p-Iodophenol	69	
N,N-Dimethyl- aniline 36.0 (0.30)	70 ml C₆H₆	I₂ 12.7 (0.05)	CuCl₂ 13.3 (0.10)	0.5	60	p-Iododimethyl- aniline	47	
Naphthalene 12.8 (0.10)	50 ml C₆H₅Cl 10 ml C₆H₆	I₂ 12.7 (0.05)	CuCl₂ 13.3 (0.10)	21	115	1-Iodonaphthalene	44	
Anthracene 17.8 (0.10)	40 ml C₆H₅Cl 10 ml C₆H₆	I₂ 12.7 (0.05)	CuCl₂ 13.3 (0.10)	20	95	9-Chloroanthracene	92	
Anthracene 8.9 (0.05)	50 ml C₆H₅Cl 10 ml C₆H₆	I₂ 12.7 (0.05)	CuCl 5.9 (0.05)	42	120	9-Chloroanthracene	48	
Anthracene 17.8 (0.10)	80 ml C₆H₅Cl	I₂ 19.0 (0.076)	CuF₂ 5.0 (0.05)	48	132	9-Iodoanthracene	26	
Biphenyl 15.4 (0.10)	20 ml C₆H₅Cl	I₂ 12.7 (0.05)	CuCl₂ 13.3 (0.10)	48	130	p-Iodobiphenyl p,p'-Diiodobi- phenyl	45 14	
Terphenyl 23.0 (0.10)	45 ml C₆H₅Cl	I₂ 12.7 (0.05)	CuCl₂ 13.3 (0.10)	52	130	Iodoterphenyl	30	

[a] C₆H₆ = benzene; C₆H₅Cl = chlorobenzene.

expected, for electronegative chlorine is known to de- activate the ortho position more effectively than the para. The result may be rationalized by coordination between the copper–aluminum chloride catalyst and the ring chlorine that facilitates iodination in the ortho position.[16]

The other benzene derivatives listed in Table III were converted to the corresponding p-iodo products by reaction with iodine–copper(II) chloride; the iodina- tion of tert-butylbenzene was best accomplished by iron(II) iodide. The observed substitution pattern was that anticipated on the basis of steric and electronic control. The reaction of phenol was free of chloro- cyclohexenones which are generally produced upon treatment of this aromatic with copper(II) chloride.[17] The absence of this side reaction is indicative of a pref- erential interaction of copper(II) chloride with iodine. Biphenyl and p-terphenyl were also iodinated by these reagents; the exact structure of the iodoterphenyl was not established owing to difficult separation and purification problems. Naphthalene yielded 1-iodo- naphthalene, the normal product of Lewis acid catalyzed halogenation of this condensed ring system.[18] No isomerization to the 2 isomer was apparent.
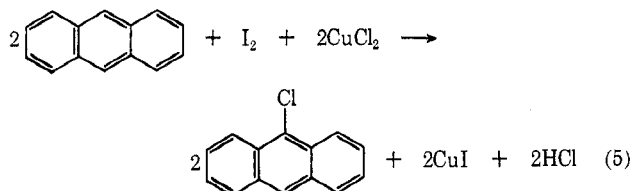
The reaction of anthracene with copper(II) chloride and iodine did not yield any isolable iodoanthracene, but 9-chloroanthracene was recovered from the reaction

(16) Reference 12, pp 113–114.

(17) L. Deniville and R. Fort, *Bull. Soc. Chim. Fr.*, 392 (1959).
(18) Reference 1, p 1552.

in >90% yield. The reaction occurred in accord with the stoichiometry and the products illustrated by eq 5.

$$2 \quad + \quad I_2 \quad + \quad 2CuCl_2 \quad \longrightarrow$$

$$2 \quad + \quad 2CuI \quad + \quad 2HCl \quad (5)$$

While anthracene is halogenated by copper(II) halides in aromatic and aryl halide solvents,[19] the chemistry of this reaction is inconsistent with that observed in the iodine–copper(II) chloride reaction. A rationale for the observed reaction was suggested by a reaction sequence in which anthracene experienced normal iodination and the 9-iodoanthracene subsequently underwent halogen exchange with copper(I) chloride to form the isolated product. This proposed scheme appeared reasonable in the light of other organic iodide–copper(I) halide exchange reactions.[20]

In order to test this proposal, a sample of 9-iodoanthracene was required. This compound was ultimately synthesized by the iodination of anthracene with iodine–copper(II) fluoride; the success of this reaction lay in the inability of copper(II) and -(I) fluorides to participate in halide exchange reactions,[20b] and any exchange with copper(I) iodide would be inconsequential. Treatment of 9-iodoanthracene with copper(I) chloride in refluxing chlorobenzene failed to produce any 9-chloro compound. Reaction of 9-iodoanthracene with excess (10:1) copper(II) chloride in refluxing chlorobenzene resulted in the destruction of the iodide as evidenced by the appearance of iodine vapor in the reaction. From this reaction was isolated a 74% yield of 9,10-dichloroanthracene. The dichloride is generated by the initially formed monochloro compound being further chlorinated by excess copper(II) chloride; the latter reaction has been previously described.[20b]

The key distinction then between the reaction of anthracene and that of other aromatics is the exchange reaction that occurs between 9-iodoanthracene and copper(II) chloride. The mechanism of this exchange is obscure and open to speculation. It is quite reasonable to presume that the π-complexing affinity of the anthracene nucleus for copper(II) chloride[19] is a critical factor.

Those aromatic compounds that failed to undergo iodination by copper(II) chloride–iodine donor combinations include methyl benzoate, aniline, thiophene, quinoline, pyridine, cumene, and diphenylmethane. Methyl benzoate was too strongly deactivated to experience reaction. The reactions of cumene and diphenylmethane were complicated by two side reactions that rendered the iodination reaction synthetically useless. The first of these was the sensitivity of the methine and methylene carbons toward halogenation in the presence of metal halides;[21] the second was the coupling of these reactive aryl alkyl halides by copper(I) salts.[20b] The remaining compounds failed to react

owing to the fact that these materials all formed strong complexes with copper(II) chloride. This coordination destroyed both the Lewis acid properties of the copper salt and its oxidizing power. The latter was depleted by the nature of the bonding between copper(II) and these bases, for the strong σ bonding associated with these ligands stabilizes copper(II) relative to copper(I).[22] An interesting distinction was apparent between the behavior of aniline and its N,N-dimethyl derivative. While the former complexed the copper and ultimately underwent condensation and oxidation to aniline dyes, N,N-dimethylaniline was converted to its p-iodo derivative in 47% yield. This difference is ascribed to the poorer complexing ability of the N,N-dimethyl compound toward copper. The adverse steric factors inherent in the formation of the copper complex permit the creation of a dynamic equilibrium, and the iodination of the free amine may proceed in a normal manner.

Lewis Acid Catalysis of Aromatic Iodination — Throughout the preceding discussion reference has frequently been made to Lewis acid catalysis of the addition of iodine to aromatics. Recourse to this interpretation has been predicted on the basis that the experimental observations and results are consistent with this position. The activity of the various copper salts, the poisoning of the reaction by the addition of Lewis bases, and the enhanced reactivity of systems containing known Lewis acid metal ions all support this contention. These facts lead to the conclusion that the historical view that aromatic iodination is insensitive to Lewis acid catalysis is false.[23]

The erroneous nature of this statement is clearly apparent from the successful iodination of aromatics by iodine–copper(II) chloride reactions to which a catalytic quantity of a Lewis acid iodide has been added. The results of such studies are found in Table IV. Iron(II)

TABLE IV
LEWIS ACID CATALYZED SYNTHESIS OF ARYL IODIDES

	Reaction conditions			Aryl iodide, %
Aromatic	Time, hr	Temp, °C	Catalyst (mol of I_2/mol of Cat)	
Xylene	1.5	145		23
Xylene	1.5	145	$FeI_2 \cdot 4H_2O$ (50:1)	87
tert-Butylbenzene	23	170		8
tert-Butylbenzene	5	150	$FeI_2 \cdot 4H_2O$ (50:1)	74

iodide has been utilized exclusively in these reactions; although aluminum(III) iodide would also undoubtedly serve as a potent catalyst, the disproportionation and coupling reactions induced by this salt limit its utility. From the data of Table IV there can be little doubt that the addition of the iron salt has had a profound catalytic effect on the reaction. While the active form of the iron salt is the chloride derived from the redox reaction with copper(II) chloride, the structure of the actual catalytic species is not known. It is likely that the true catalyst is a composite of both iron and copper salts.

In conclusion, a few remarks pertaining to the utility and effectiveness of this new iodination reaction are

(19) D. C. Nonhebel, *J. Chem. Soc.*, 1216 (1963).

(20) For a discussion of the coordination of copper salts with aromatic rings and aryl halides, see (a) ref 19; (b) R. G. R. Bacon and H. A. O. Hill, *ibid.*, 1103 (1964).

(21) Reference 12, pp 114–115.

(22) H. J. Emeléus and J. S. Anderson, "Modern Aspects of Inorganic Chemistry," Rutledge and Kegan Paul Ltd., London, England, 1960, Chapter 6.

(23) Reference 1, p 1531.

TABLE V
COMPARISON OF ARYL IODIDE SYNTHESES

Reagent	Benzene	Toluene	m-Xylene	Mesitylene	Naphthalene	Phenol	Anisole	Chlorobenzene	N,N-Dimethylaniline	Biphenyl
					Yield of aryl iodide, %					
CuCl₂	65	81	63	86	44	69	80	29	47	45
HNO₃ a,b	80	60	56	40	Trace			59		
AgOOCCF₃ c,d	85	88					75	62	41	
Th(OOCCF₃)₃–KI e	96		100	94			75	80		
Na₂S₂O₈ f	70	78	70	83						68
HIO₃ f	83	81			40		40	53		68
AgClO₄ g	80	65			85	80		95		
H₂SO₄–HNO₃ h	80	65						41		64

a R. L. Datta and N. R. Chatterjee, *J. Amer. Chem. Soc.*, **39**, 435 (1917). *b* R. L. Datta and N. R. Chatterjee, *ibid.*, **41**, 292 (1919). *c* A. L. Henne and W. F. Zimmer, *ibid.*, **73**, 1362 (1951). *d* R. N. Haszeldine and A. G. Sharpe, *J. Chem. Soc.*, 993 (1952). *e* Reference 8. *f* H. O. Wirth, D. Königstein, and W. Kern, *Justus Liebigs Ann. Chem.*, **634**, 84 (1960). *g* L. Birckenbach and J. Goubeau, *Ber.*, **65**, 395 (1932). *h* B. V. Tronov and A. N. Novikof, *Izv. Vyssh. Ucheb. Zaved., Khim. Khim. Tekhnol.*, **3**, 872 (1960); *Chem. Abstr.*, **55**, 8348 (1961).

appropriate. The data of Table V illustrate that the new method competes quite satisfactorily with previous synthetic routes to aryl iodides on the basis of product yield. In those instances where reliable isomer distributions are available, no significant variations among these procedures have been noted. The copper(II) halide based system affords some advantages relative to these established methods. These include simplicity of operation and isolation–purification of products; absence of by-product formation; ability to convert all iodine charged; nonreactive environment that does not degrade starting material or product; preparation of reactive intermediates, *e.g.*, diazonium salts, organomercury and thallium salts, not required. Like the other preparative methods, the present case does suffer from some substrate limitations, the nature of which have been reviewed above.

Experimental Section

Nmr spectra were determined on a Varian Associates A-60 spectrometer using tetramethylsilane as an internal standard. Infrared spectra were recorded on a Beckman IR-5A spectrophotometer. Vapor phase chromatography (vpc) was performed on a Perkin-Elmer Model 226 chromatograph, a Perkin-Elmer Model 154D fractometer, and a Varian Aerograph Autoprep Model A-700 equipped with analytical columns. Preparative scale vpc was carried out on the latter instrument equipped with preparative columns. Melting points and boiling points are not corrected. All reagents were obtained from commercial sources and used as received.

Copper Salts for Aryl Iodide Synthesis.—In a typical experiment a 500-ml flask was equipped with a Teflon paddle stirrer and a reflux condenser. Into the flask were placed 70 ml of xylene, 13.0 g (0.05 mol) of iodine, and 13.3 g (0.1 mol) of copper(II) chloride. The reaction was stirred at 140° for 5 hr. The reaction mixture was cooled and filtered, and the filtrate was washed with 100 ml of 20% sodium thiosulfate solution to discharge any residual iodine. The filtrate was dried over magnesium sulfate, the solution was filtered, and the excess xylene removed on a rotary evaporator at 60° (13 mm). The crude product (22.8 g) was distilled to give 19.8 g (85%) of iodoxylenes, bp 65–72° (0.2 mm). *Anal.* Calcd for C₈H₉I: C, 41.40; H, 3.91; I, 54.68; mol wt, 232. Found: C, 41.75; H, 3.95; I, 54.3; mol wt, 260. Vpc analysis (2 m × 0.25 in. 20% DC-200 column, 150°, 105 ml/min) showed two product peaks at 16 min (93%) and 19 min (7%) from air. The nmr spectrum (neat) showed a methyl proton/aromatic proton ratio of 2:1 consistent with iodoxylene.

The reactivity of other copper salts was evaluated by an identical procedure; xylene was the aromatic substrate in all cases. The experimental results are summarized by Table I.

Iodide Donors for Aryl Iodide Synthesis.—In a typical experiment 5.7 g (0.03 mol) of copper(I) iodide, 8.0 g (0.06 mol)

of copper(II) chloride, and 45 ml of xylene were stirred at reflux for 6 hr. A strong iodine color developed in the reaction as the temperature approached reflux. The reaction mixture was cooled and filtered to give 8.6 g of copper(I) chloride (theory 8.9 g). The filtrate was washed with 10% sodium thiosulfate solution and was dried over magnesium sulfate. The excess xylene was removed on a rotary evaporator at 60° (15 mm) to give 5.8 g of crude product. Analysis by vpc (2 m × 0.25 in. DC-550 column, 150°, 105 ml/min) showed the product to contain 83% iodoxylene, which corresponded to a ~70% yield.

The activity of other iodide donors was evaluated by a similar procedure; xylene was the aromatic substrate in all cases. The results of these experiments are tabulated in Table II. The stoichiometries were balanced according to eq 4.

Synthesis of Aryl Iodides.—The synthesis of aryl iodides from various aromatic substrates was carried out by a procedure identical with that described above for the preparation of iodoxylene. The reagent quantities, reaction conditions, yield, and isomeric distribution are presented in Table III.

Reactions of liquid aromatics were performed with an excess of the aromatic serving as the reaction diluent. Solid aromatic substrates were reacted in chlorobenzene, which is a reasonably inert solvent. A small amount of benzene was added to reactions carried out in chlorobenzene in order to facilitate the return of sublimed iodine from the cooler portions of the reactor to the liquid phase. The use of chlorobenzene as a diluent decreased the reaction rate markedly so that long reaction periods were required; this was frequently the case even when reactive aromatics were being iodinated. This effect is attributed partially to solvent–copper(II) complexation.[19]

The reactions were worked up by removal of the inorganic salts by filtration and the washing of the filtrates with 10–20% sodium thiosulfate solution. The decolorized aryl iodide solutions were dried over magnesium sulfate, and the excess hydrocarbon or the solvent was removed on a rotary evaporator [60–80° (14–20 mm)]. Liquid products were purified by distillation; solid aryl iodides were recrystallized or sublimed. Fractional sublimation was employed in some cases (naphthalene, anthracene) to separate unreacted starting material. Product purification in some cases was extremely difficult owing to the mutual solubility or insolubility of starting material and products. Yield data in these cases were obtained by vpc analysis using internal standards. Highly insoluble aryl iodides were extracted from the filter cake with acetone when necessary.

The aryl iodides were identified by conventional nmr and vpc techniques,[24] comparison of physical properties with those of authentic samples, and elemental analysis.

Reaction of 9-Iodoanthracene with Copper(I) and Copper(II) Chlorides.—A 3 g (0.01 mol) sample of 9-iodoanthracene was stirred with 5 g (0.049 mol) of copper(I) chloride in refluxing chlorobenzene for 9 hr. At the conclusion of this period vpc analysis indicated that no halogen exchange had occurred. A few crystals of iodine were added as a potential catalyst, and the

(24) In addition to the vpc columns previously mentioned, the following were also useful for analysis of aryl iodides: 2 ft × 0.25 in. 10% silanized polypropylene glycol on Haloport F; 300 ft × 0.01 in. silicone (DC-550); 3 ft × 0.25 in. 3% Dowfax on Chromosorb W.

reaction was refluxed for 2 hr. No 9-chloroanthracene was detected by vpc analysis.

A mixture of 2 ml of chlorobenzene, 0.5 g (0.0016 mol) of 9-iodoanthracene, and 2.0 g (0.015 mol) of copper(II) chloride was refluxed and stirred for 2 hr. Within 30 min a strong iodine color developed in the reaction. At the end of the reaction period no 9-iodoanthracene remained; vpc analysis (3 ft × 0.25 in. 3% Dowfax, 215°, 100 ml/min) showed two product peaks at 4.9 min (71%) and 14.8 min (29%). Work-up of the reaction mixture gave 0.3 g of yellow-green crystals (74%). Recrystallization from ethanol and subsequently from acetone gave yellow needles: mp 211–213° (lit. 209–210°);[20b] retention time, 4.9 min. *Anal.* Calcd for $C_{14}H_8Cl_2$: C, 68.04; H, 3.26; Cl, 28.70. Found: C, 66.36; H, 3.38; Cl, 28.20.

Catalysts for the Synthesis of Aryl Iodides.—Into 70 ml of xylene were placed 12.7 g (0.05 mol) of iodine, 14.7 g (0.11 mol) of copper(II) chloride, and 0.38 g (0.001 mol) of iron(II) iodide tetrahydrate. The reaction was stirred and refluxed for 1.5 hr. After the normal work-up, an 87% yield of iodoxylene was isolated. A control experiment containing no iron(II) iodide gave a 23% yield under identical conditions.

Synthesis of Two Benzothiacyclanones *via* a Novel Two-Carbon Ring Expansion of Thiolactones with Vinyllithium
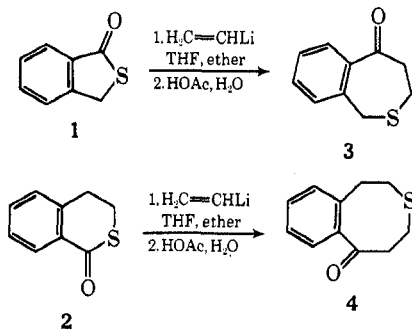
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The thiolactones thiophthalide (1) and 2-thiochroman-1-one (2) react with 1 equiv of vinyllithium in ether–tetrahydrofuran followed by acetic acid to form, respectively, seven- and eight-membered ring γ-keto sulfides by a novel two-carbon ring expansion. This method is an improvement on existing, inefficient Friedel–Craft acylation routes to such ketones. Syntheses of 2-thiochroman-1-one and a much improved synthesis of thianapthen-2-one are reported.

In the course of our studies of organic sulfur chemistry, we required pure samples of 4,5,6,7-tetrahydro-2H-benzo[c]thiepin-5-one (3) and 3,4,7,8-tetrahydro-2H-benzo[e]thiocin-4-one (4), These ketones had pre-


viously been obtained as impure oils in low yield by the AlCl₃-catalyzed cyclization of acid chlorides 5a and b, respectively.[1] We decided to attempt the addition of 1
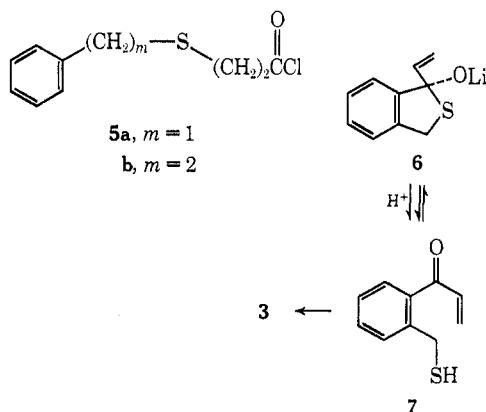
equiv of vinyllithium to the readily available thiophthalide (1), in anticipation that the initial tetrahedral adduct 6 might be stable toward vinyllithium, but ring open to the vinyl ketone 7 upon hydrolysis. The latter should then cyclize by conjugate addition of the mercaptan to form 3. As expected, a 51% yield of crystalline 3 was obtained from treatment of a cold ether solution of 1 with a 2 *M* solution of vinyllithium in tetrahydrofuran, followed by acidification with glacial acetic acid, vacuum distillation, and sublimation. Analogous reaction of thiolactone 2 at −70° gave 19% crystalline 4.

The crude ketones 3 and 4 were contaminated with polymeric material, variable amounts of recovered starting material, and a volatile, pungent oil which has not been identified.

Recovery of thiolactones implies that they undergo either enolate formation or competing addition of 2 equiv of vinyllithium to form divinylcarbinols, which may be responsible for polymer formation. Enolate formation was the predominant reaction between vinyllithium and thianaphthen-2-one (8), at 25 to
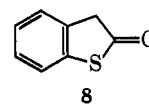
−78°, as evidenced by recovery of 84–95% of this material after treatment with vinyllithium followed by work-up with glacial acetic acid.

Several attempts to synthesize the previously unreported 2-thiochroman-1-one (2) by reaction of derivatives of *o*-(2-hydroxyethyl)benzoic acid with sulfur nucleophiles gave only 2-chroman-1-one (9). It was found, after considerable experimentation, that lactone 9 reacted with sodium benzylmercaptide in dimethylformamide at reflux to give the carboxylic acid 10 in

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(1) P. Cagniant and D. Cagniant, *Bull. Soc. Chim. Fr.*, 1998 (1959).