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SUBSTITUTION OF THALLIUM WITH HALOGEN IN THE REACTION OF ARYLTHALLIUM(III) COMPOUNDS WITH COPPER HALIDES

S. UEMURA*
Institute for Chemical Research, Kyoto University, Uji, Kyoto, Japan

and

Y. IKEDA and K. ICHIKAWA
Department of Hydrocarbon Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Kyoto, Japan

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Abstract—The reaction of arylthallium(III) compounds with copper(II) and (I) halides was found to afford aromatic hydrocarbons, aromatic halides and aromatic coupling products in various organic solvents. Choice of solvent had a remarkable effect on the yields and the product distributions, dioxane being the solvent of choice for the purpose of preparaing aromatic halides. The aromatic halide formation is explained by an ionic concerted intermolecular mechanism.

THE reaction of phenylmercuric,[1,2] -plumbic,[3] and -stannic[3] compounds with copper(II) chloride has been known to give corresponding organometallic chloride and chlorobenzene (chlorodemetallation). Recently, it was reported that mercury in phenylmercuric salt can be replaced by an anionic group such as OAc^-, N_3^-, Cl^-, NO_2^-, Br^-, CN^-, and SCN^- in the presence of oxidant.[4] As far as these results are concerned, it appears that the attacking reagents have to be oxidant. However, we have shown that the thallium in arylthallium(III) compounds can be replaced by a cyano group in the reaction with copper(I) as well as copper(II) cyanides.[5]

Herein we report that arylthallium(III) compounds, ArTlYZ, react with copper(II) and (I) halides to form Ar–H, Ar–X, and Ar–Ar and that the ratio of these products varied widely depending on the conditions.[6] The main subject of this paper is the formation of Ar–X, and a probable mechanism for this is discussed. Most of the study has been carried out with arylthallium(III) acetate perchlorate, $ArTl(OAc)ClO_4 \cdot H_2O$, since the compounds can be prepared readily.[7]

RESULTS AND DISCUSSION

Arylthallium(III) compounds and copper halides were added to solvents, such as alcohols, tetrahydrofuran, acetonitrile, water, dioxane, pyridine and acetic acid and heated under reflux. Only in the case of acetonitrile (containing LiCl) and acetic acid as solvents, did the reaction mixtures become almost homogeneous under reflux. Refluxing temperatures were required to make the reaction proceed. The organic products were Ar–H, Ar–X and Ar–Ar. Results obtained with $CuCl_2 \cdot 2H_2O$ are shown in Table 1. The products from substituted-phenylthallium compounds show

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* Author to whom correspondence should be addressed.

TABLE 1. RESULTS OF THE REACTION OF ArTlYZ WITH $CuCl_2 \cdot 2H_2O$

ArTlYZ mmol	$CuCl_2 \cdot 2H_2O$ mmol	Additive mmol	Solvent 50 ml	Temp °C	Time hr	Product, yield[a]		
						Ar–H	Ar–Cl	Ar–Ar
I 10	10	—	AcOH	70	5	trace	0	trace
I 10	10	—	AcOH	117	1	4	56	trace
I 10	10	—	AcOH	117	5	4	59	2
I 10	10	—	AcOH	117	10	2	59	trace
I 10	20	—	AcOH	117	5	2	60	trace
I 10	10	NaOAc 10	AcOH	117	5	3	12	9
I 10	10	LiCl 40	AcOH	117	5	1	53	trace
I 10	10	—	MeOH	67	5	7	trace	trace
I 10	10	—	C_4H_8O[b]	67	5	*c*	20	21
I 10	10	LiCl 10	MeCN	81	5	2	28	3
I 10	10	—	H_2O	100	5	0	0	trace
I 10	10	—	$C_4H_8O_2$[d]	102	5	*c*	80	trace
I 10	10	$CH_2{=}CHCN$ 40	$C_4H_8O_2$	102	5	*c*	77	trace
I 5	10	—	C_5H_5N[e]	117	5	*c*	14	0
II 10	10	—	AcOH	117	5	2	67	trace
II 10	1	LiCl 10	MeCN	81	20	2	32	21
III 10	10	—	AcOH	117	5	10[f]	45[f]	trace
IV 10	10	—	AcOH	117	5	5	30	trace
V 10	10	—	AcOH	117	5	19	16	4
VI 20	20	—	AcOH	117	5	18	32[g]	5[h]
VI 10	10	—	AcOH	117	5	13	19[g]	37[h]
VI 10	10	—	AcOH	117	5	40	20[g]	trace
VI 10	10	—	$C_4H_8O_2$	102	5	*c*	59[g]	trace
VII 10	20	—	$C_4H_8O_2$	102	5	trace	83[i]	0
VIII 10	20	—	$C_4H_8O_2$	102	5	8	77[j]	0
IX 10	10	—	AcOH	50	5	30	trace	0
IX 10	10	—	AcOH	117	5	69	2[k]	0
IX 10	20	—	$C_4H_8O_2$	102	5	21	45[k]	0
IX 5	10	—	70% $C_4H_8O_2$[l]	89	5	53	17[k]	0

I = $C_6H_5Tl(OAc)ClO_4 \cdot H_2O$, II = $C_6H_5TlCl_2$, III = $(C_6H_5)_2TlCl$, IV = $C_6H_5Tl(OCOCF_3)_2$ V = $C_6H_5Tl(OAc)_2$, VI = 4-$MeC_6H_4Tl(OAc)ClO_4 \cdot H_2O$, VII = 3,4-$Me_2C_6H_3Tl(OAc)ClO_4 \cdot H_2O$ VIII = 2,4-$Me_2C_6H_3Tl(OAc)ClO_4 \cdot H_2O$, IX = 4-$MeOC_6H_4Tl(OAc)ClO_4 \cdot H_2O$

[a] Based on Tl compounds charged (GLC determination). [b] Tetrahydrofuran. [c] Not determined. [d] Dioxane. [e] Pyridine. [f] It is assumed that 2 mol of each Ar–H and Ar–Cl are formed from 1 mol of III. [g] 4-MeC_6H_4Cl. [h] 4,4′-Dimethylbiphenyl. [i] 3,4-$Me_2C_6H_3Cl$. [j] 2,4-$Me_2C_6H_3Cl$. [k] 4-$MeOC_6H_4Cl$. [l] Dioxane: H_2O = 7:3.

clearly that both chlorination and coupling occurred at the position where thallium was attached to the phenyl ring.

It appears that the solvent has considerable effects on both the reaction rate and the product distribution. For example, the reaction of $C_6H_5Tl(OAc)ClO_4 \cdot H_2O$ (I) was very slow in water, methanol and pyridine and much faster in dioxane and acetic acid. Hydrodethallation to form benzene was the main reaction in methanol and the coupling reaction to form biphenyl proceeded well in acetonitrile (LiCl was added to make the reaction mixture homogeneous) and tetrahydrofuran. In dioxane, chlorodethallation proceeded almost exclusively. The *p*-methoxyphenylthallium compound

(IX) gave large amounts of anisole (hydrodethallation product) in acetic acid and even in dioxane. It is clear that hydrodethallation is accelerated by the presence of electron-releasing group in the phenyl ring and proceeds more rapidly in acetic acid than in dioxane, and in the latter solvent the rate increases with water content. The same tendency was observed in the methyl substituted phenylthallium compounds, VI, VII and VIII. These results suggest that hydrodethallation is the reverse reaction of electrophilic aromatic substitution with thallium(III) salt. It should be noted that three runs with the *p*-tolylthallium compound (VI) in acetic acid under the same conditions produced different product distributions, whilst this was not the case using dioxane as solvent. Although the nature of the coupling reaction is not yet clear, the discrepancies in the reactions in acetic acid may depend on the purity of VI, because control experiments showed that purified I was stable in acetic acid under reflux but unpurified I containing inorganic thallium(III) salt gave non-reproducible results of coupling under the same conditions.

In contrast to the case with $CuCl_2 \cdot 2H_2O$, the reaction of I with anhydrous copper(II) chloride in acetic acid gave non-reproducible results, e.g. chlorobenzene (19–20% yield) and biphenyl (6–66% yield), and further studies were discontinued.

It must be added that chlorodemercuration of phenylmercuric compounds with $CuCl_2 \cdot 2H_2O$ proceeded rather smoothly compared with cyanodemercuration with $Cu(CN)_2$.[5] The reactions of phenylmercuric acetate (10 mmol) with 10 and 20 mmol of $CuCl_2 \cdot 2H_2O$ in acetic acid gave 18 and 63% yields of chlorobenzene under reflux for 1 hr (compared with 56 and 60% yields with thallium compounds) and 41% of chlorobenzene was obtained from the reaction of phenylmercuric chloride (5 mmol) with $CuCl_2 \cdot 2H_2O$ (5 mmol) in dioxane under reflux for 5 hr.

TABLE 2. RESULTS OF THE REACTION OF ArTlYZ WITH $CuBr_2$

Substrate mmol	$CuBr_2$ mmol	Solvent ml	Temp °C	Time hr	Product, yield %[a]	
					Ar–Br	Ar–Ar
I 5	10	MeOH 50	67	1	13	43
I 5	10	EtOH 100	78	1	59	14
I 5	10	$C_4H_8O_2$[b] 50	102	1	94	6
VI 5	10	MeOH 100	67	1	26[c]	14[d]
VI 5	10	$C_4H_8O_2$[b] 50	102	1	58[c]	0
VII 5	10	MeOH 100	67	1	16[e]	46[f]
IX 5	5	MeOH 100	20	24	trace[g]	0

[a] Based on Tl compounds charged (GLC determination). [b] Dioxane. [c] 4-Methylbromobenzene. [d] 4,4'-Dimethylbiphenyl. [e] 3,4-Dimethylbromobenzene. [f] 3,3',4,4'-Tetramethylbiphenyl. [g] Anisole was obtained in 13% yield.

With copper(II) bromide, arylthallium(III) compounds reacted as in the case of copper(II) chloride, refluxing temperatures again being required. Dioxane again was the solvent of choice for bromodethallation. In methanol and ethanol, bromodethallation accompanied the coupling reaction (Table 2).

A possibility of bromine formation from copper(II) bromide has been a subject of discussion in several types of reaction.[8] To investigate the possibility of this occurring in the present reaction, the following experiment was performed. Reaction of I (10 mmol) with copper(II) bromide (10 mmol) in dioxane (100 ml) containing phenol (10 mmol) gave bromobenzene (8·26 mmol, 82·6% yield) under reflux for 1 hr. Neither bromophenol nor dibromobenzene could be detected. If bromine formed from copper(II) bromide ($2CuBr_2 \rightarrow Cu_2Br_2 + Br_2$) is the reacting species, the formation of bromophenol should have been observed. Therefore, this possibility can be excluded.

In order to determine whether the attacking reagent has to be oxidant or not, the reaction of I with copper(I) halides was studied. The results are shown in Table 3.

TABLE 3. RESULTS OF THE REACTION OF I WITH COPPER(I) HALIDES

Substrate I mmol	Cu_2X_2 mmol	Solvent 50 ml	Temp °C	Time hr	Product (%)[a] C_6H_5X
20	Cu_2Cl_2 10	AcOH	117	5	42
20	Cu_2Cl_2 20	AcOH	117	5	43
5	Cu_2Cl_2 5	$C_4H_8O_2$[b]	102	5	24
5	Cu_2Br_2 10	$C_4H_8O_2$	102	1	4
5	Cu_2Br_2 10	C_5H_5N[c]	114	5	23
5	Cu_2I_2 5	$C_4H_8O_2$	102	1	22
5	Cu_2I_2 5	$C_4H_8O_2$	20	1	3
5	Cu_2I_2 5	H_2O	20	1	1

[a] Based on I charged (GLC determination). Trace amount of biphenyl detected in all cases. [b] Dioxane. [c] Pyridine.

Solvent effects were different from those in the case of copper(II) halides, and the yield of chlorobenzene was better in acetic acid than in dioxane. The yield of halobenzene increased in the order chloride > iodide > bromide in dioxane solvent. This order appears to have resulted from the combined effects of reactivity and solubility factors.

Several experiments on fluorodethallation of I (25 mmol) with copper(II) fluoride hydrate (50 mmol) in acetic acid (100 ml) under reflux for 5 hr were unsuccessful. The colour of the mixture turned from blue (heterogeneous) to blackish blue accompanied by a slight formation of hydrogen fluoride. Fluorobenzene was not formed and benzene (2·33 mmol), phenylacetate (0·6 mmol) and biphenyl (1·58 mmol) were found to be the products. The reactions in pyridine as solvent were also unsuccessful for fluorodethallation. The reaction of I with copper(II) tetrafluoroborate gave no fluorobenzene.

To consider the reaction mechanism of halodethallation of arylthallium(III) compounds with copper(I) and (II) halides, the following observations should be noted. The reaction does not appear to involve radicals as reactions of I with

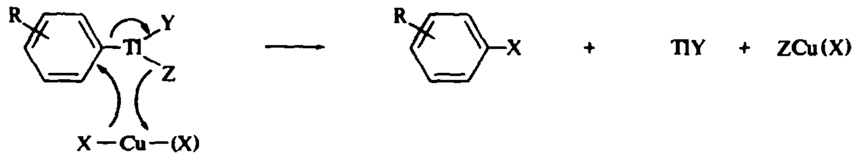
$CuCl_2 \cdot 2H_2O$ and Cu_2Cl_2 in dioxane in the presence of $CH_2{=}CHCN$ gave neither polyacrylonitrile nor arylated acrylonitrile, even though the yields of chlorobenzene were not affected. Reaction of I (10 mmol) with copper(II) acetate (10 mmol) in acetic acid containing lithium chloride (20 mmol) gave only benzene (1·2 mmol, 12% yield) and biphenyl (0·16 mmol, 3·2% yield) after 5 hr duration, demonstrating that the chlorine in chlorodethallation comes from copper(II) or (I) chloride itself and not from free chloride. Reactions of phenylthallium(III) halides with copper(II) halides containing different kinds of halogen ligand revealed that not only the halogen involved in copper(II) halide but also the halogen which is the ligand of thallium compound enter into the halodethallation reaction (Table 4). Furthermore, reaction of phenylthallium(III) dichloride (10 mmol) with $CuCl_2 \cdot 2H_2O$ (1 mmol) gave 3·2 mmol of chlorobenzene in acetonitrile under reflux for 20 hr (see Table 1). These facts show that halogen exchange assisted with copper between phenylthallium(III) halides and copper(II) halides occurs, because phenylthallium(III) halides itself gave no halobenzenes under same conditions without copper salt (Table 4).

TABLE 4. RESULTS OF THE REACTION OF PHENYLTHALLIUM(III) HALIDES WITH COPPER(II) HALIDES IN DIOXANE (50 ml) AT 102° FOR 5 hr

Substrate mmol	CuX$_2$ mmol	Product, yield, %[a]	
		PhCl	PhBr
$PhTlCl_2$ 10	$CuBr_2$ 2·5	48	24
$PhTlCl_2$[b] 5	—	0	—
Ph_2TlBr 5	$CuCl_2 \cdot 2H_2O$ 5	36[c]	15[c]
Ph_2TlBr 5	$CuCl_2 \cdot 2H_2O$ 2·5	11[c]	10[c]
Ph_2TlBr 2·5	—	—	0

[a] Based on Tl compounds charged (GLC determination). [b] $PhTlCl_2$ and Ph_2TlCl gave no PhCl in acetic acid and acetonitrile under reflux for 5 hr. [c] It is assumed that 2 mole of PhX are formed from 1 mol of Tl compounds charged.

Competitive reactions of I (5 mmol) and VI (5 mmol) with $CuCl_2 \cdot 2H_2O$ (10 mmol) (60 min) and $CuBr_2$ (5 mmol) (5 min) in dioxane (50 ml) under reflux gave values of 1·0 and 1·2 for $k\text{-}_{\text{toluene}}/k\text{-}_{\text{benzene}}$ respectively, suggesting the small effect of substituent on the rate of halodethallation.



With consideration of all these results, the most plausible mechanism appears to be expressed by an ionic concerted intermolecular scheme. The driving force of the reaction seems to be the oxidizing power of Tl(III) assisted by copper salts. The oxidizing power of the copper salt is not required as both copper(II) and (I) halides react similarly.

Precise analysis of inorganic products might be very helpful for mechanistic consideration, if possible. Unfortunately, the analysis was rather difficult and could not be accomplished. Possible oxidation of thallium(I) salt by copper(II) salt adds to the difficulty of determination of the nature of the thallium and copper salts which are primary products. Only qualitatively, it was found that the main inorganic product is thallium(I) salt.

EXPERIMENTAL

All organic materials except arylthallium(III) compounds were purified before use by distillation. Commercially available inorganic materials were used without further purification except in the case of copper(I) chloride, where the possible impurity of copper(II) chloride was removed by washing with EtOH and with ether both containing SO_2 and dried under N_2. Commercially available aromatic hydrocarbons and aromatic halides were used as the authentic samples for GLC and spectral measurements. Preparation of arylthallium(III) compounds were described in the previous paper.[5,7] Diphenylthallium chloride and bromide were prepared from phenylboric acid and $TlCl_3 \cdot 4H_2O$ and $TlBr_3 \cdot 4H_2O$ respectively according to the reported method,[9] mp > 320°.

Reaction of arylthallium(III) *compounds with copper halides*

The following example shows a typical experimental procedure: In a 100 ml flask, $CuCl_2 \cdot 2H_2O$(1·70 g, 10 mmol) was added to AcOH (30 ml). The mixture was greenish and not homogeneous at r.t. When heated, the mixture became yellowish green containing brownish solid at 50° and then almost homogeneous and brownish soln at 80°. At this point, a soln of I(4.58 g, 10 mmol) in AcOH(20 ml) was added under stirring, and the mixture turned to greenish blue and almost homogeneous. Upon heating under reflux, a gradual formation of white crystals was observed. After 5 hr, the mixture was cooled down to room temp, filtered from inorganic material (greyish 2·74 g(A) and then green 0·09 g(B) after standing overnight), added with water (300 ml), extracted with ether, washed with satd $NaHCO_3$aq and then with water, and dried over Na_2SO_4. From the ether extract, the solvent was evaporated to give about 20 ml liquid residue. GLC analysis with PEG 6000(25 %)–Chromosorb-W 3 m column showed that the products were benzene, chlorobenzene and biphenyl. Using ethylbenzene (for benzene and chlorobenzene) and diphenylmethane (for biphenyl) as the internal references, the compositions of the three components were determined to be 0·39, 5·85 and 0·12 mmol respectively. Fractional distillation gave a fraction, b.p. 53–55°/53 mmHg, which was identified to be chlorobenzene by spectral(IR and NMR) measurements. The inorganic substance A was washed with hot water to give greyish residue(1·2 g) which was IR(4000–650 cm^{-1}) inactive. Addition of dil HCl to the filtrate gave TlCl(0·90 g). IR spectra of B was identical with that of $Cu(OAc)_2 \cdot 2H_2O$.

Spectral measurements. IR spectra were obtained by means of Hitachi EPI-2 and EPS-3T. NMR spectra were determined by a Varian A-60 spectrometer in $CDCl_3$ using TMS as the internal standard. GLC analysis was carried out on a Shimadzu 5APTF and Hitachi K53 apparatuses, using PEG 6000(25 %)–Chromosorb-W 3 m and Apz-L(30%)–Celite 3 m columns (He as carrier gas).

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