

Registry No.—Phenylacetic acid, 103-82-2; *p*-methoxyphenylacetic acid, 104-01-8; *p*-tolylacetic acid, 622-47-9; *m*-tolylacetic acid, 621-36-3; *p*-chlorophenylacetic acid, 1878-66-6; *m*-chlorophenylacetic acid, 1878-65-5; benzyl acetate, 140-11-4; *p*-methoxybenzyl acetate, 104-21-2; *p*-methylbenzyl acetate 2216-45-7; *m*-methylbenzyl acetate 17369-57-2; *p*-chlorobenzyl acetate, 5406-33-7; *m*-chlorobenzyl acetate, 21388-93-2; phenylbutyric acid, 1821-12-1; cobaltic acetate, 917-69-1.

References and Notes

- Reviewed by L. Ebersson in "The Chemistry of Carboxylic Acids and Esters", S. Patai, Ed., Interscience, New York, N.Y., 1969, p 53; J. P. Coleman and L. Ebersson, *Chem. Commun.*, 1300 (1971).
- A. A. Clifford and W. A. Waters, *J. Chem. Soc.*, 2796 (1965); P. R. Sharan, P. Smith, and W. A. Waters, *J. Chem. Soc. B*, 1322 (1968); S. S. Lande and J. K. Kochi, *J. Am. Chem. Soc.*, **90**, 5196 (1968).
- J. K. Kochi, *J. Am. Chem. Soc.*, **87**, 3609 (1965); J. D. Bacha and J. K. Kochi, *J. Org. Chem.*, **33**, 83 (1968); J. K. Kochi, J. D. Bacha, and T. W. Bethea, III, *J. Am. Chem. Soc.*, **89**, 6538 (1967); J. K. Kochi and T. W. Bethea, III, *J. Org. Chem.*, **33**, 75 (1968); R. A. Sheldon and J. K. Kochi, *J. Am. Chem. Soc.*, **90**, 6688 (1968); J. M. Anderson and J. K. Kochi, *ibid.*, **92**, 1651, 2450 (1970); J. M. Anderson and J. K. Kochi, *J. Org. Chem.*, **35**, 986 (1970).
- R. A. Sheldon and J. K. Kochi, *Org. React.*, **19**, 279 (1972); J. K. Kochi in "Free Radicals", Vol. 1, Wiley, New York, N.Y., 1973, pp 651-655.
- W. S. Trahanovsky, J. Cramer, and D. W. Brixlus, *J. Am. Chem. Soc.*, **96**, 1077 (1974).
- E. I. Heiba, R. M. Dessau, and W. J. Koehl, Jr., *J. Am. Chem. Soc.*, **91**, 6830 (1969).
- J. P. Coleman and L. Ebersson, *Chem. Commun.*, 1300 (1971); J. P. Coleman, J. H. Putley, and B. C. L. Weedon, *ibid.*, 438 (1971); J. P. Coleman, R. Lines, J. H. Putley, and B. C. L. Weedon, *J. Chem. Soc., Perkin Trans. 2*, 1064 (1974).
- Cobaltic acetate was formed by the ozonolysis of cobaltous acetate in acetic acid.
- D. D. Tanner and S. A. A. Osman, *J. Am. Chem. Soc.*, **90**, 6572 (1968).
- P. D. Bartlett and C. Ruchardt, *J. Am. Chem. Soc.*, **82**, 1756 (1960).
- R. O. C. Norman, P. M. Storey, and P. R. West, *J. Chem. Soc. B*, 1087 (1970).
- R. M. Dessau, S. Shih, and E. I. Heiba, *J. Am. Chem. Soc.*, **92**, 412 (1970).
- E. I. Heiba, R. M. Dessau, and W. J. Koehl, Jr., *J. Am. Chem. Soc.*, **90**, 1082, 2706 (1968).
- The low yield of lactone produced by hydrogen abstraction was further dramatically reduced in the presence of 0.2 M cupric acetate, which simultaneously converted all of the propylbenzene to allylbenzene by oxidation of the intermediate 3-phenylpropyl radical.
- The data of ref 5, contrary to the conclusions stated therein, suggest that a similar mechanism is indeed operative in the case of ceric ion. The ρ value reported there, -2.9, is quite consistent with those we observed in the oxidation reactions of cobaltic ion. The high rate reported for the ceric oxidation of *p*-methoxyphenylacetic acid, which must have been extremely difficult to measure accurately by NMR, is just about what would have been expected for a reaction with such a large ρ . The high reactivity of the *m*-methoxy compound, which definitely does not fit the Hammett correlation (which we also found in our system, it being only slightly less reactive than *p*-tolylacetic acid), is exactly what would be expected on the basis of aromatic radical cation formation and the ease of electron transfer from anisole and its derivatives. On the basis of molecular orbital theory, it is clear that the symmetry of the highest occupied molecular orbital of the radical cation of *m*-methoxyphenylacetic acid differs from all the other derivatives in terms of electronic symmetry relative to the carboxymethylene group. Consequently, a *m*-methoxy substituent is not a minor perturbation of the aromatic ring and should not fit a Hammett plot.

Copper(I)-Induced Reductive Dehalogenation, Hydrolysis, or Coupling of Some Aryl and Vinyl Halides at Room Temperature

Theodore Cohen* and Ioan Cristea

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

Received August 5, 1975

The room temperature reactions of some activated aryl and vinyl halides with acetone solutions of copper(I) trifluoromethanesulfonate, ammonia (aqueous or dry), and various quantities of copper(II) trifluoromethanesulfonate have been studied. Conditions have been found for the following conversions in good yield: *o*-bromonitrobenzene to 2,2'-dinitrobiphenyl, nitrobenzene, or *o*-nitrophenol; methyl *o*-iodobenzoate to methyl salicylate or methyl benzoate; diethyl iodofumarate to *trans,trans*-1,2,3,4-tetracarboxy-1,3-butadiene or diethyl fumarate; diethyl iodomaleate to diethyl maleate. Reductive dehalogenation and phenol formation are favored, respectively, by the presence of ammonium tetrafluoroborate and a substantial quantity of cupric ion. The retention of configuration observed for the protolysis products of the organocopper intermediates derived from the vinyl iodides has been interpreted as ruling out vinyl radicals as intermediates.

It was recently reported from this laboratory that the Ullmann coupling,¹ which is usually performed with copper powder at elevated temperatures, can, in the case of certain activated aryl halides, be performed at room temperature in homogeneous solutions containing copper(I) trifluoromethanesulfonate² (triflate) dissolved in equal volumes of acetone and 5% aqueous ammonia.³ For example, while *p*-nitro- and *o*-fluoroiodobenzene failed to react, *o*-iodonitrobenzene and 2,4-dinitroiodobenzene coupled in a few minutes to form 2,2'-dinitrobiphenyl (2) and 2,2',4,4'-tetraniobiphenyl, respectively. However, with *o*-bromonitrobenzene (1) as substrate, under the same conditions, the reaction took far longer (about 24 hr) and only produced a 15% yield of biaryl (2) in addition to *o*-nitroaniline (5), the other significant product. Methyl *o*-iodobenzoate (6) was about as reactive as *o*-bromonitrobenzene (1) but, under these conditions, it produced mainly methyl anthranilate and no discernible coupling product. We summarize here a survey of reaction conditions for bromide displacement in *o*-bromonitrobenzene (1) and we report satisfactory condi-

tions for the formation of good yields of any of the following products: biaryl (2), *o*-nitrophenol (4), or nitrobenzene (3). Conditions for halide displacement reactions in methyl *o*-iodobenzoate (6), diethyl iodofumarate (10), and diethyl iodomaleate (13) are also reported.

We have found that in the case of *o*-bromonitrobenzene far better yields of biaryl can be obtained by using a smaller volume of more concentrated aqueous ammonia. The yields can be further enhanced by the presence of a small quantity of copper(II) triflate. On the other hand, the presence of a much larger quantity of copper(II) triflate leads to a 74.6% yield of *o*-nitrophenol (4). A selection of our re-

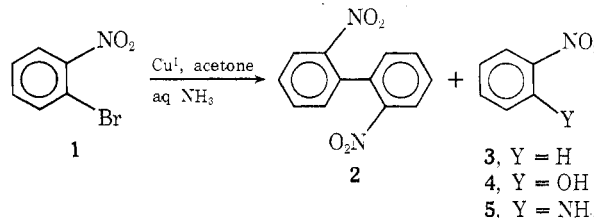


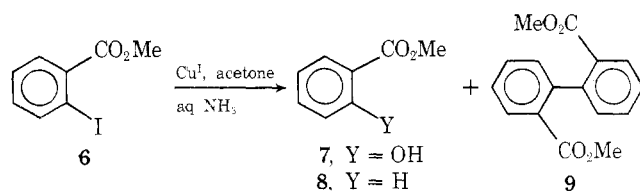
Table I
Reaction of *o*-Bromonitrobenzene with Copper(I) Triflate
in Acetone Containing Aqueous Ammonia^a

ml 20% aq NH ₃	mmol Cu ^{II}	Yields ^{b-d}			
		Ar ₂ (2)	ArH (3)	ArOH (4)	ArNH ₂ (5)
25	0.20	17.5	56.0	2.5	20.5
5	0.20	70.0	9.2	18.3	3.2
4	0.20	80.7	6.4	9.7	2.6
2	0.20	62.6	0.8	32.9	
5	0.42	89.8	7.8	1.2	0.7
4	3.46	21.6	2.6	74.6	
4	5.19	18.2 ^e	2.8 ^e	50.8 ^e	
4	11.1	10.2 ^f	3.4 ^f	4.1 ^f	
5 ^g	0.20	40.1	7.2	50.2	1.2
5 ^h	0.42	16.4	80.4	<i>i</i>	0.9

^aIn all runs, 25 ml of acetone and 1.25 ml of acetonitrile were used and, unless otherwise stated, the reactions were run for 24 hr at room temperature; for other reaction conditions, see text. ^bAr = *o*-nitrophenyl. ^cGas chromatographic yields. ^dUnless otherwise indicated, not more than 1% of *o*-bromonitrobenzene remained unreacted. ^e28% of unreacted aryl bromide remained. ^f82.3% of unreacted aryl bromide remained. ^gFive hours at reflux. ^h2.0 mmol of NH₄BF₄ was present; ref 5. ⁱNot determined.

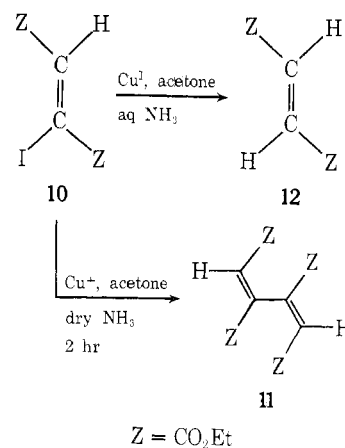
sults utilizing different quantities of 20% aqueous ammonia and of cupric triflate is shown in Table I; in all cases the copper(I) triflate was prepared by reducing 2.70 mmol of copper(II) triflate hydrate with 2.50 mmol of copper powder in a refluxing mixture of 25 ml of acetone and 1.25 ml of acetonitrile [which is required in order for the production of copper(I) to proceed], the aqueous ammonia, any extra copper(II) triflate, and the aryl bromide (0.250 mmol) were then added and, unless otherwise stated, the solution was stirred for 24 hr. Similar yields of biaryl could be obtained by using the optimum conditions of Table I [5 ml of ammonia water and 0.42 mmol of copper(II)] but replacing the acetone with 2-propanol or diglyme. A mechanistic study of the present reaction has revealed that, as in the heterogeneous Ullmann coupling,^{1,4} there is an organocopper intermediate which is capturable by protonation;⁵ thus, the presence of only 2.0 mmol of ammonium tetrafluoroborate causes the production of nitrobenzene in 80% yield⁵ (last entry in Table I). Finally, in a preparative run, starting with a 20-fold greater quantity of *o*-bromonitrobenzene, a 90% crude yield and a 79% yield of recrystallized 2,2'-dinitrobiaryl were obtained.

Methyl *o*-iodobenzoate (6), which previously yielded methyl anthranilate in the presence of 5% ammonia,³ was found to provide mainly methyl salicylate (7), along with some dimethyl diphenate (9), in the presence of 20% aqueous ammonia. When the same reaction was performed in the presence of 3.46 mmol of copper(II) triflate (in 31.25 ml of solvent), this phenol was essentially the only product and was formed in 94% yield (GLC). In the absence of excess copper(II) triflate, but in the presence of 10.0 mmol of ammonium tetrafluoroborate, the product was entirely methyl benzoate (8), formed in 98% yield (GLC).

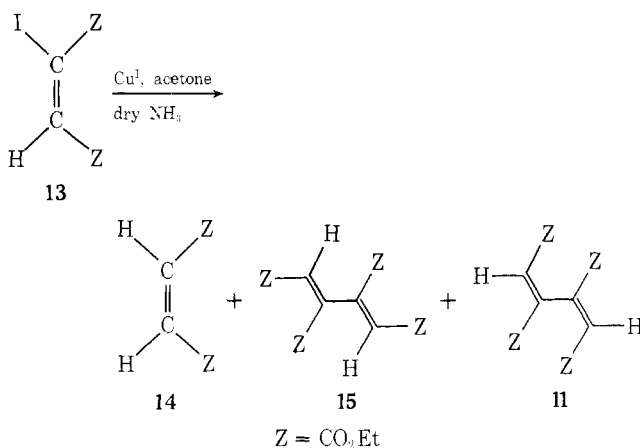


It has been shown recently that diethyl iodofumarate (10) couples to form the *trans,trans* tetraester 11 in good yield when heated with copper powder for 12 hr at 100°.⁶

Under the optimum conditions for coupling of *o*-bromonitrobenzene (fifth entry of Table I), 10 gives very little coupling product (11); the overwhelming product was diethyl fumarate (12). However, when the 25 ml of acetone and 5 ml of 20% aqueous ammonia was replaced with 20 ml of acetone and 5 ml of acetone saturated with ammonia gas, a 95% yield (GLC) of *trans,trans*-1,2,3,4-tetracarboethoxy-1,3-butadiene (11) was formed in 2 hr. From a scale-up run, this ester was isolated in 90% crude yield, from which 80% of pure crystalline material could be obtained. The crude material contained none of the geometrically isomeric dienes.⁶



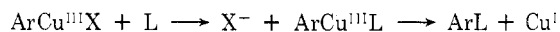
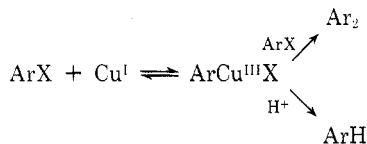
When diethyl iodomaleate (13) was subjected to the successful coupling conditions used for the iodofumarate ester (dry ammonia) for 20 hr, 54.5% of 13 remained unreacted and 30% of diethyl maleate (14) was produced along with 8.6% of *cis,cis*-tetracarboethoxy-1,3-butadiene (15) and 2.1% of the *trans,trans* ester (11). When the same experiment



was performed for 10 hr at 40°, reaction was complete to yield 86% (GLC) of diethyl maleate (14). It is of interest that the reactivity sequence (*trans* > *cis*) and the stereoselectivity of the coupling process are rather comparable to those of the corresponding heterogeneous Ullmann coupling of these iodoesters.⁶

Our recent mechanistic study⁵ of the homogeneous Ullmann coupling of *o*-bromonitrobenzene revealed that an arylcopper(III) intermediate, which is reversibly produced by oxidative addition of the CBr bond to copper(I), is capable of reacting with another aryl bromide molecule to form biaryl or of competitively becoming protonated by the medium. If these two processes are slow, it seems likely that a ligand (L) such as water or ammonia could displace the bromide in the intermediate to give another copper(III) compound which would undergo reductive elimination of copper(I) to produce the protonated phenol or aniline

(ArL). This reductive elimination is analogous to the reverse of the first step and such processes appear to be common in the mechanisms of the displacements of aryl and vinyl halides with the anions of copper(I) salts.⁷ More work will obviously be required before reliable predictions can be made concerning the different reaction paths of the intermediate in an unstudied case.



Nevertheless, some synthetically useful generalizations have apparently been established. The replacement of halogen by hydrogen can be readily accomplished at room temperature by performing the reaction in the presence of ammonium ion, although in some cases this additive is not necessary; furthermore, in the case of the isomeric vinyl iodides studied, the reductive dehalogenation occurs with complete retention of configuration. Phenol production is encouraged by the presence of a fairly high concentration of copper(II). Finally, in the absence of these additives, except for a small quantity of copper(II), reductive coupling can be accomplished at room temperature in some cases, but, at least under the conditions we have investigated, not in others.

These results also provide valuable mechanistic information. Our recent mechanistic study provided strong evidence that the *o*-nitrophenyl radical is not an intermediate in the homogeneous Ullmann coupling of *o*-bromonitrobenzene.⁵ The stereospecific reductive dehalogenation of the iodofumarate and iodomaleate esters under the same conditions constitutes completely independent evidence for the absence of radical intermediates since vinyl radicals are extremely unstable stereochemically.^{6,8} The same stereochemical result obtains in the reductive dehalogenation of these esters by copper metal at elevated temperatures in the presence of benzoic acid.⁶ Finally, an organocopper species has been shown to be an intermediate, not only in biaryl formation, as was demonstrated in our mechanistic study,⁵ but also in phenol formation; this follows from its diversion to methyl benzoate by ammonium ion in the case of **6** which ordinarily gives mostly phenol **7**. However, the role of copper(II) in phenol formation has not yet been clarified.

Experimental Section⁹

Preparation of Solutions of Copper(I) Triflate. The procedure was the same in each case. The quantities of ingredients used in preparative experiments are specified under each preparation. The quantities that were used in gas chromatographic analytical experiments are included in the following description. A magnetically stirred mixture of copper(II) triflate (the light blue salt, $\text{Cu}(\text{CF}_3\text{SO}_3)_2 \cdot 5.5\text{H}_2\text{O}$,³ obtained by drying the freshly prepared hydrate² for 1 hr at room temperature in a vacuum desiccator, 1.24 g, 2.70 mmol) and copper powder (0.159 g, 2.50 mmol) in 25 ml of acetone (except for the experiments using anhydrous ammonia, in which 20 ml of acetone was used) and 1.25 ml of acetonitrile was heated at reflux for 1 hr under a nitrogen atmosphere. The light blue mixture, which had become homogeneous, was then cooled to room temperature.

Analytical (Nonpreparative) Experiments. In all the experi-

ments summarized in Table I, *o*-bromonitrobenzene (0.0506 g, 0.250 mmol, Eastman), the gas chromatographic standard 4,4'-dinitrobiphenyl (0.035 g, 0.125 mmol), and appropriate quantities of 20% aqueous ammonia and $\text{Cu}(\text{CF}_3\text{SO}_3)_2 \cdot 5.5\text{H}_2\text{O}$ were added to the solution of cuprous triflate and, unless otherwise specified in Table I, the solution was stirred under nitrogen for 24 hr at room temperature. In the other analytical experiments, methyl *o*-iodobenzoate (0.117 g, 0.500 mmol), diethyl iodofumarate (0.25 g, 0.80 mmol), or diethyl iodomaleate (0.25 g, 0.80 mmol), copper(II) triflate (0.10 g, 0.22 mmol or 1.50 g, 3.26 mmol, as specified in the Results section), and 5.0 ml of either 20% aqueous ammonia or acetone saturated with gaseous ammonia were added and the solution was allowed to stir under nitrogen for the specified time.

The solution was separated into ether-soluble and aqueous phases by a thorough extraction procedure and the ether extracts were dried (magnesium sulfate), the solvent removed, and the residue dissolved in acetone. The acetone solution was submitted to gas chromatographic analysis on a 10 ft \times 0.125 in. column packed with 3% OV-17 on Gas-Chrom Q 100/120 with a program of 50–300° at 10°/min; the relative flame ionization detector response of the standard and products had been previously determined utilizing an electronic integrator. The products were identified by comparing their gas chromatographic behavior (by coinjection) with that of authentic samples. The products in the case of experiments with diethyl iodofumarate and iodomaleate were available from the previous study.⁶ Other ester products were either commercially available or readily prepared by esterification (CH_3OH , HCl) of the commercially available acids.

Isolation of 2,2'-Dinitrobiphenyl. To a solution of copper(I) triflate, prepared from 3.72 g (8.10 mmol) of copper(II) triflate, 0.477 g (7.50 mmol) of copper powder, 75 ml of acetone, and 3.75 ml of acetonitrile, were added 1-bromo-2-nitrobenzene (1.01 g, 5.00 mmol) and 20% aqueous ammonia (15 ml) and the mixture was stirred under nitrogen for 24 hr. The mixture was separated into ether-soluble and aqueous phases by a thorough extraction procedure. Evaporation of the dried (magnesium sulfate) ether extract yielded 0.54 g (90%) of an orange-yellow solid; recrystallization from methanol provided 0.47 g (79%) of 2,2'-dinitrobiphenyl, mp 127.5–128.0° (lit.¹⁰ mp 127–128°).

Isolation of *trans,trans*-1,2,3,4-Tetracarboxy-1,3-butadiene. To a solution of copper(I) triflate prepared from 2.5 g (5.4 mmol) of copper(II) triflate and 0.32 g (5.0 mmol) of copper powder in 35 ml of acetone and 2.5 ml of acetonitrile were added 1.00 g (3.3 mmol) of diethyl iodofumarate and 12 ml of dry acetone which had been saturated with gaseous ammonia. The solution was stirred under a nitrogen atmosphere for 4 hr. Work-up as in the preparation of 2,2'-dinitrobiphenyl yielded 0.51 g of a light yellow oil (89% crude yield); crystallization from hexane yielded 0.46 g (80%) of the *trans,trans* ester, mp 41.5–43.0° (identical with that of an authentic sample⁶). The gas chromatogram of the crude material showed a single peak alone or when coinjected with an authentic sample of the *trans,trans* ester. The NMR spectrum of the crude product was also identical with that of the authentic sample.

Registry No.—1, 577-19-5; 2, 2436-96-6; 3, 98-95-3; 4, 88-75-5; 5, 88-74-4; 6, 610-97-9; 10, 38318-65-9; 11, 38318-64-8; 13, 38318-63-7; copper(I) triflate, 42152-44-3; copper(II) triflate, 34946-82-2; copper, 7440-50-8.

References and Notes

- (1) P. E. Fanta, *Chem. Rev.*, **38**, 139 (1946); **64**, 613 (1964); *Synthesis*, 9 (1974); M. Goshav, O. S. Otroschenko, and A. S. Sadykov, *Russ. Chem. Rev.*, **41**, 1046 (1972); R. G. R. Bacon and H. A. O. Hill, *Q. Rev., Chem. Soc.*, **19**, 95 (1965); E. A. Jukes, *Adv. Organomet. Chem.*, **12**, 215 (1974).
- (2) C. L. Jenkins and J. K. Kochi, *J. Am. Chem. Soc.*, **94**, 843 (1972).
- (3) T. Cohen and J. G. Tirpak, *Tetrahedron Lett.*, 143 (1975).
- (4) A. H. Lewin and T. Cohen, *Tetrahedron Lett.*, 4531 (1965).
- (5) T. Cohen and I. Cristea, *J. Am. Chem. Soc.*, in press.
- (6) T. Cohen and T. Poeth, *J. Am. Chem. Soc.*, **94**, 4363 (1972).
- (7) T. Cohen, J. Wood, and A. G. Dietz, *Tetrahedron Lett.*, 3555 (1974).
- (8) G. M. Whitesides, C. P. Casey, and J. K. Krieger, *J. Am. Chem. Soc.*, **93**, 1379 (1971).
- (9) Melting points are uncorrected.
- (10) "Handbook of Chemistry and Physics", 54th ed, R. C. Weast, Ed., CRC Press, Cleveland, Ohio, 1973–1974, p C-206.