was added. A solution of 43 mmol of **2**, 4.3 equiv of $(C_6F_5Cu)_4$, and 50 ml of quinoline was heated for 2 hr at 213–215° giving a 98% yield of gas and 71.5% yield (81.7% crude) of pure 5-(trifluoromethoxy)-3-indolepropionic acid, **4**: mp 87–87.6°; $\lambda_{\max}^{\mathrm{EtOH}}$ 226, 247, and 286 nm (ϵ 57,000; 9500; 10,700). Similarly **1** decarboxylated easily at 185–205° to give 98% yield of gas and 63.7% yield of pure 5-(trifluoromethoxy)-3-indoleacetic acid, **3**, mp 117–118.5°.

In conclusion, organocopper compounds easily react with carboxylic acids to form cuprous carboxylates. In turn some cuprous carboxylates decarboxylate to give useful organocopper intermediates. *o*-Nitrophenylcopper has not been generated any other way. These two reactions together are the basis of an organocopper-catalyzed decarboxylation.

Allan Cairncross, John R. Roland
Rosetta M. Henderson, William A. Sheppard
Contribution No. 1662, Central Research Department
Experimental Station, E. I. du Pont de Nemours and Company
Wilmington, Delaware 19898
Received December 31, 1969

The Copper–Quinoline Decarboxylation[1]

Sir:

To our knowledge, a mechanism for the loss of carbon dioxide in the widely used copper–quinoline decarboxylation[2] has never been suggested. The reaction is usually performed by heating an aromatic carboxylic acid in quinoline solution with copper powder, although copper salts are sometimes used. We have found that the copper metal procedure is much slower than that involving the cupric[3] or cuprous (acid plus cuprous oxide) salt of the carboxylic acid (180–200°) and that the yields are excellent provided that a nitrogen atmosphere is maintained. Cuprous salts have recently been utilized in studies by Nilsson, who has provided evidence that organocopper compounds are intermediates in the reaction.[4] Our own results confirm this conclusion and, in addition, provide a variety of new observations and a basis for suggesting a mechanism for the loss of carbon dioxide. Pertinent results are as follows. (1) The loss of carbon dioxide is first order in cuprous or cupric carboxylate. (2) Cupric and cuprous salts decarboxylate at nearly the same rate. (3) Either type of salt behaves as a catalyst for the decomposition of excess carboxylic acid and the reactions are pseudo-first-order in the metal ions. (4) Certain chelating agents such as 1,10-phenanthroline and 2,2′-bipyridyl considerably increase the rate of decarboxylation of both types of salt. The latter reagent, which is less effective but far less expensive, increases the rate by a factor of 17 when used in a tenmolar excess. (5) Whereas neither cuprous nor cupric benzoate decarboxylates at a noticeable rate in a solvent such as 1-methylnaphthalene at 200°, and aromatic cupric carboxylates undergo an entirely different type of reaction at higher temperatures in noncomplexing solvents,[5] cupric benzoate does undergo smooth decarboxylation in 1-methylnaphthalene provided that some 2,2′-bipyridyl is present. (6) All substituents on cupric benzoate increase the rate. The salts of the isomeric 2,3-diphenylpropenoic acids and of α-naphthoic acid decarboxylate very much faster than those of benzoic acid, the latter by a factor of 87 at 200°. (7) The cupric salts of the saturated acids adamantane-1-carboxylic acid and dodecanoic acid do not decarboxylate under the same reaction conditions. (8) Decarboxylation products, arenes and substituted arenes, can be obtained in high yield in most cases. However, in the case of the cupric salt of *o*-methoxybenzoic acid, a 5% yield of 2,2′-dimethoxybiphenyl was also isolated and in the case of the cuprous salt of *o*-nitrobenzoic acid (prepared under anhydrous conditions from the anhydride and cuprous oxide) 2,2′-dinitrobiphenyl was obtained in 78% yield. (9) Decarboxylation of the cupric salts of pure *cis*- and *trans*-2,3-diphenylpropenoic acids proceeds with 94 and 99% retention of configuration, respectively. These figures are unchanged when the reaction is performed in the presence of a large excess of 2,2′-bipyridyl and the degree of retention is only slightly different for the corresponding cuprous salts. (10) In the absence of copper salts, the rates of decarboxylation of the acids were either negligible or far slower.

The result that cuprous and cupric salts behave in identical fashion, with regard to both rates and stereochemistry, is rendered understandable by the finding that the esr signal of cupric benzoate disappears in a few minutes under the reaction conditions. It is evident that the quinoline is capable of reducing cupric ion to cuprous ion at a very rapid rate.[6] The destruction of cupric ion before the loss of carbon dioxide, the rate dependence on the concentration of cuprous ion, and the large rate changes caused by the presence of complexing agents for cuprous ion clearly implicate the latter as the active catalyst in this decarboxylation.

The stereochemical results probably rule out mechanisms involving homolytic C–C bond cleavage[7] and allow one involving electrophilic attack of cuprous ion at the carbon atom bearing the carboxyl group only if the subsequent loss of carbon dioxide is much faster than rotation about the resulting C–C single bond. The necessity for unsaturation in the substrate acid, the rate increase with increased polarizability, and the π-complexing ability of cuprous ion[8] suggest the following mechanism in which a π-bonded cuprous ion inductively stabilizes the negative charge which develops as the carbon dioxide is lost.

The replacement of the carboxylate ligand by the "softer" and more electron-accepting (by backbonding)

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[1] This investigation was supported by Grant No. GP 7262 from the National Science Foundation; taken from the Ph.D. Thesis of Robert A. Schambach, University of Pittsburgh, Pittsburgh, Pa., 1969.

[2] A. F. Shepard, N. R. Winslow, and J. R. Johnson, *J. Amer. Chem. Soc.*, 52, 2083 (1930); P. H. Leake, *Chem. Rev.*, **56**, 27 (1956), and references cited therein; L. F. Fieser and M. Fieser, "Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1956, p 549.

[3] We thank Mr. Mordecai Treblow and Mr. Edward Slusser for carrying out the rate comparison between the use of the metal and the cupric salt.

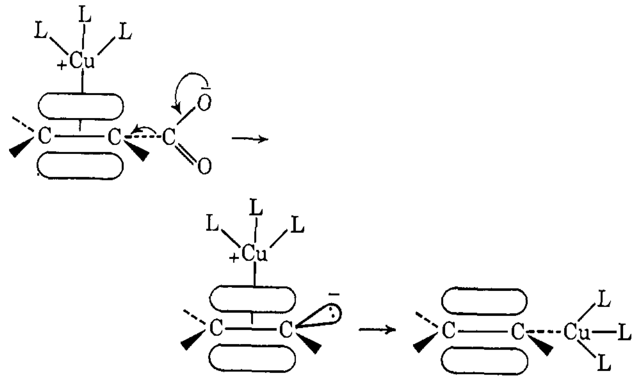
[4] M. Nilsson, *Acta Chem. Scand.*, **20**, 423 (1966); C. Björklund and M. Nilsson, *ibid.*, 22, 2585 (1968).

[5] W. W. Kaeding, H. O. Kerlinger, and G. R. Collins, *J. Org. Chem.*, **30**, 3754 (1965), and references cited therein.

[6] The quinoline appears to be converted mainly to 2-oxygenated quinolines: unpublished observations of F. J. Rattay.

[7] The resulting 1,2-diphenylethenyl radicals undergo rapid stereochemical equilibration: L. A. Singer and N. P. Kong, *J. Amer. Chem. Soc.*, **88**, 5213 (1966); J. A. Kampmeier and R. M. Fantazier, *ibid.*, **88**, 1959 (1966).

[8] R. N. Keller, *Chem. Rev.*, **28**, 229 (1941); M. A. Bennett, *ibid.*, **62**, 611 (1962); R. Jones, *ibid.*, **68**, 785 (1968).



L = ligand

heterocyclic amine could promote the reaction by (1) stabilizing the π complex ("soft" ligands tend to flock together[9]) and/or (2) increasing the electron-withdrawing ability of the cuprous ion. The intermediacy of a σ-bonded organocopper intermediate[10] is suggested by the trapping experiments of Nilsson,[4] the coupling results reported above,[12] and the fact that in the case of cuprous *o*-nitrobenzoate, the presence of water (0.5 mol/mol of salt) greatly increases the extent of nitrobenzene formation at the expense of symmetrical biaryl.[13]

The novel concept that a metallic ion may be capable of stabilizing the transition state of a reaction in which a negative charge is being generated on an atom whose p orbital is involved in π-bond formation with the metal ion has a number of possible implications, some of which we hope to investigate.

Of immediate practical application are the findings: (1) that this reaction can be very conveniently executed by utilizing the free carboxylic acid in the presence of cuprous oxide which behaves as a catalyst, (2) that nitrogen heterocyclic chelating agents are capable of considerably increasing the rate constant or of allowing a lower reaction temperature when quinoline is used as the solvent, and (3) that the reaction can be conducted in noncomplexing solvents, provided that complexing agents are present. Finally, there are preliminary indications that it is important to maintain a nitrogen atmosphere during the reaction, since the presence of oxygen sharply decreases the cuprous ion concentration and increases that of cupric ion, which causes an oxidative decarboxylation[5] (phenyl benzoate is produced from cupric benzoate). The partiality shown in the literature for the use of copper rather than its salts[14] can very likely be traced to this last factor since inert atmospheres have not generally been used.

Acknowledgment. We thank the National Institutes of Health for providing the LKB 9000 combined gas chromatograph–mass spectrometer which was used for product identification. We also thank Mr. John Naworal for recording the mass spectra and Dr. David Pratt for recording the electron spin resonance spectra.

Theodore Cohen, Robert A. Schambach
Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15213
Received December 31, 1969

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[10] Vinyl copper compounds have considerable stereochemical stability[11] although this has not been tested under the high-temperature conditions of our reaction.

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Kinetic Isotope Effects in the Aqueous Ethanolysis of Deuterated Cyclopentyl Brosylates[1]

Sir:

Several papers have appeared in the literature which have dealt with the solvolysis of cycloalkyl brosylates and tosylates in various solvent systems, *e.g.*, acetolysis of deuterated cyclopentyl tosylates,[2] aqueous ethanolysis of deuterated *cis*-4-*t*-butylcyclohexyl brosylates,[3] aqueous ethanolysis of deuterated *trans*-4-*t*-butylcyclohexyl brosylates,[4] and acetolysis of deuterated cyclohexyl tosylates.[5] Comparison of these papers revealed differences between the two ring systems. The cyclopentyl system tended to show isotope effects that were cumulative in nature, whereas in the cyclohexyl system they were noncumulative in nature. Also for the cyclopentyl system it was observed that the *cis* isotope effect was greater than that of the *trans* isomer which was opposite to that observed for the cyclohexyl system. Because of these differences a reinvestigation of the cyclopentyl system was undertaken.

Cyclopentanol-1-d_1 was prepared by reducing cyclopentanone with lithium aluminum deuteride.[2] *cis*-Cyclopentanol-2-d_1 was prepared by deuterioboration of cyclopentene which was a modification of the Brown[6,7] method in which diborane-d_6 is generated *in situ* from boron trifluoride and lithium aluminum deuteride.[8] *trans*-Cyclopentanol-2-d_1 was prepared by the action of lithium aluminum deuteride on cyclopentene epoxide.[2] Cyclopentanol-2,2,5,5-d_4 was prepared by repeated exchanges of cyclopentanone with weakly basic D_2O followed by reduction of this ketone with lithium aluminum hydride.[2] The brosylates of the various alcohols were prepared by the usual Tipson procedure.[9] These were analyzed[10] by combustion, and the per cent deuterium was obtained by the falling drop technique. The brosylates were chosen rather than the tosylates used in Streitwieser's work because it was more convenient to handle the higher melting compound. Also, the solvolyzing media was changed from acetic acid to 70 vol % ethanol in order that the rates of solvolysis could be monitored by a conductance method. It is felt that despite these minor changes a comparison of the data can still be made.

Results of product analysis of the solvolysis mixture by gas chromatography are given in Table I.

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