Calcd for $C_{10}H_{10}F_2$ *m/e* 168.0745, Found *m/e* 168.0745; *m/e* 168 (M^+, 24), 151 (16), 150 (86), 149 (25), 140 (42), 135 (14), 133 (14), 127 (22), 122 (100), 109 (90). Product **11**: F NMR δ −101.25 ppm (broad singlet); H NMR δ 1.75 (m, 4 H), 2.25 (m, 4 H), 6.3 ppm (broad singlet, 2 H); mass spectrum, Calcd for $C_{10}H_{10}F_2$ *m/e* 168.0745, Found *m/e* 168.0750; *m/e* 168 (M^+, 53), 151 (19), 150 (87), 149 (26), 140 (72), 135 (20), 133 (21), 127 (28), 122 (100), 109 (84).

Acknowledgment. We thank Professor J. Slivnik for the xenon difluoride, Professor J. Marsel for providing facilities, and the Boris Kidrič Foundation for financial assistance.

Registry No.—**1**, 496-11-7; **2**, 37530-82-8; **3**, 64683-00-7; **4**, 95-47-6; **5**, 452-64-2; **6**, 443-82-3; **7**, 119-64-2; **8**, 2840-40-6; **9**, 700-45-8; **10**, 64683-01-8; **11**, 64683-02-9; XeF_2, 13709-36-9.

References and Notes

(1) Presented in part at the 6th European Symposium on Fluorine Chemistry, Dortmund, March 1977.
(2) W. H. Mills and I. G. Nixon, *J. Chem. Soc.*, 2510 (1930).
(3) For reviews of the Mills–Nixon effect, see (a) Hückel, "Theoretische Grundlagen der Organischen Chemie", Vol. II, Akademische Verlagsgesellschaft Geest u. Portig K. G., Leipzig, 1957, p 691; M. J. S. Dewar, "The Electronic Theory of Organic Chemistry", Oxford University Press, London, 1949, p 197.
(4) M. A. Dolliver, T. L. Gresham, G. B. Kistiakowsky, and W. E. Vaughan, *J. Am. Chem. Soc.*, **59**, 831 (1937).
(5) J. W. Baker and W. S. Nathan, *J. Chem. Soc.*, 1844 (1935).
(6) M. Zupan and A. Pollak, *J. Chem. Soc., Chem. Commun.*, 845 (1973); *Tetrahedron Lett.*, 1015 (1974); *J. Org. Chem.*, **39**, 2646 (1974); **40**, 3794 (1975); *J. Fluorine Chem.*, **7**, 443, 445 (1976); *J. Org. Chem.*, **41**, 4002 (1976); *J. Fluorine Chem.*, **8**, 275 (1976); M. Zupan, *ibid.*, **8**, 305 (1976); *Chimia*, **30**, 305 (1976).
(7) R. T. Arnold, V. J. Webers, and R. M. Dodson, *J. Am. Chem. Soc.*, **74**, 368 (1952), and earlier papers.
(8) J. Vaughan, G. J. Welch, and G. J. Wright, *Tetrahedron*, **21**, 1665 (1965).
(9) (a) K. Jones and E. F. Mooney, "Annual Reports in NMR Spectroscopy", Vol. 3, E. F. Mooney, Ed.; Academic Press, London, 1970, p 261; (b) W. Adcock, P. D. Bettess, and S. Q. A. Rizvi, *Aust. J. Chem.*, **23**, 1921 (1970); (c) W. Adcock, B. D. Gupta, T. C. Khor, D. Doddrell, D. Jordan, and W. Kitching, *J. Am. Chem. Soc.*, **96**, 1595 (1974).
(10) M. J. Shaw, J. A. Weil, H. H. Hyman, and R. Filler, *J. Am. Chem. Soc.*, **92**, 5096 (1970); M. J. Shaw, H. H. Hyman, and R. Filler, *J. Am. Chem. Soc.*, **92**, 6498 (1970); *J. Org. Chem.*, **36**, 2917 (1971); S. P. Anand, L. A. Quarterman, H. H. Hyman, K. G. Migliorese, and R. Filler, *J. Org. Chem.*, **40**, 807 (1975); S. P. Anand, L. A. Quarterman, P. A. Christian, H. H. Hyman, and R. Filler, *J. Org. Chem.*, **40**, 3796 (1975).
(11) A. Weissberger, Ed., "Technique of Organic Chemistry", Vol. V11, Interscience, New York, N.Y., 1955.
(12) S. M. Williamson, *Inorg. Synth.*, **11**, 147 (1968).

Products and Kinetics of Decarboxylation of Activated and Unactivated Aromatic Cuprous Carboxylates in Pyridine and in Quinoline[1a]

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Received August 15, 1977

Aromatic cuprous carboxylates can be prepared in a state suitable for kinetic and product studies of their decarboxylations in quinoline and pyridine by reducing the cupric salt with copper in the decarboxylation solvent. The results were indistinguishable from those obtained from the same salts prepared by treatment of the acids with cuprous *tert*-butoxide, a more tedious procedure. The major neutral product, besides carbon dioxide, for the decarboxylation of $ArCO_2Cu$ is ArH except in the case of cuprous *o*-nitrobenzoate in which it is Ar_2. The hydrogen which replaces the carboxyl group appears to be derived largely from the solvent and is released during the substitution of aryl groups into solvent molecules and the coupling of solvent molecules. In quinoline, the latter type of product consists mainly of biquinolyls and some oxybiquinolyls. Since approximately the same composition of solvent-derived products is obtained from the decarboxylations of all of the aromatic salts and by heating pentafluorophenylcopper in quinoline, it is believed that arylcopper and quinolylcopper intermediates are involved; this is the first evidence for such intermediates in the case of nonactivated cuprous carboxylates. Such intermediates, the clean first-order kinetics, evidence against a radical process, and the similarity with respect to substituent, solvent, and ligand effects between this reaction and the Ullmann biaryl coupling as well as copper-induced exchange processes lead to a new mechanistic suggestion which involves an oxidative addition of the carboxyl C–C bond to the copper(I) followed by loss of carbon dioxide. An efficient method of preparation of 2-deuterioquinoline is presented, as is a nearly complete analysis of the 250-MHz spectrum of 2,2′-difluorobenzophenone.

Introduction

The decarboxylation of aromatic carboxylic acids by heating them in quinoline solution in the presence of copper metal or copper salts (the copper–quinoline decarboxylation) has been widely used[2] since its discovery in 1930 by Shepard, Winslow, and Johnson.[3] Previous work in this laboratory indicates that cuprous and cupric salts decarboxylate at approximately the same rate, but that the latter are converted to the former under the reaction conditions.[4,5] For preparative purposes, the reaction is most easily performed by heating the acid in quinoline under an inert atmosphere in the presence of cuprous oxide.[4,6]

The work of Nilsson and co-workers provided early evidence that in the decarboxylations of *o*-nitrobenzoic, 2-furoic, 2-thenoic, and 3,4,5-trichloro-2-thenoic acids or their copper(I) salts arylcopper intermediates are involved.[6,7] The intermediates are capable of condensing with aryl iodides present in the quinoline to form mixed biaryls. Furthermore, the first of these yielded some 2,2′-dinitrobiphenyl, a product expected from self-coupling of *o*-nitrophenylcopper. In the case of the chlorinated thenoic acid, the quenching with hydrochloric acid of samples withdrawn during the course of the reaction revealed a protonatable intermediate.[8]

This conclusion was confirmed by an experiment reported by Cairncross, Roland, Henderson, and Sheppard, who were able to isolate the relatively stable pentafluorophenylcopper from the low temperature decarboxylation of cuprous pentafluorobenzoate.[9] However, these workers provided evidence that *o*-nitrophenylcopper does not accumulate in the quinoline during the decarboxylation of cuprous *o*-nitrobenzoate, although its presence was demonstrated by the Nilsson method of trapping the intermediate with aryl iodide and by its self-coupling to form biaryl.

Our own work[4] and that of Cairncross et al.[9] demonstrated that the rate of reaction is greater the better the ability of the solvent or additive to complex cuprous ion; it was found,[4] for example, that 2,2′-bipyridyl and 1,10-phenanthroline are rather good catalysts. Furthermore, the cupric salts of the saturated acids, adamantane-1-carboxylic acid and dodecanoic acid, failed to decarboxylate under conditions that caused rapid decarboxylation of a number of cupric salts of aromatic acids;[4,10] Cairncross et al.[9] took advantage of such relative reactivities to selectively monodecarboxylate a dicarboxylic acid possessing both aromatic and unconjugated carboxyl groups. It has been pointed out[4] that a radical intermediate is unlikely in view of the very predominant retention of configuration which occurs in the decarboxylation of geometrically isomeric α,β-unsaturated carboxylic acids[11] and the corresponding copper(I) and copper(II) carboxylates.[4]

An investigation of the kinetics of decarboxylation of several copper(I) and copper(II) carboxylates in quinoline revealed that the reactions are first order in the salts and, as stated above, that the rate constants are essentially the same for copper(I) and copper(II) salts.[4] The rate of decarboxylation of excess carboxylic acid in the presence of varying amounts of cuprous oxide was directly proportional to both the concentration of the acid and the quantity of cuprous oxide added. Furthermore, the cuprous and cupric carboxylates can behave as catalysts for the decarboxylation of excess acid.[4]

Chodowska-Palicka and Nilsson[12] have studied the kinetics of decarboxylation of the very activated (toward decarboxylation) salt copper(I) *o*-nitrobenzoate and the moderately active copper(I) *p*-nitrobenzoate in quinoline. In the former case, although good first-order rate constants were observed in individual runs, the rate constants varied in unexpected ways with changes in initial concentration of the salts. Thus, increasing the concentration of pure cuprous salt caused a *decrease* in the rate constant. On the other hand, when free carboxylic acid was present, an increase in the concentration of cuprous salt resulted in a large increase in the rate constant. Finally, apparent catalysis by copper metal was noted.

All of the previous evidence for organocopper intermediates in copper–quinoline decarboxylations have involved "activated" acids such as *o*-nitro-, *p*-nitro-, or pentafluorobenzoic acids. Indeed, all product studies of the decarboxylation of pure cuprous carboxylates have involved such activated compounds. Other product studies have involved the presence of contaminants which are generated during the in situ preparation of the cuprous salt; for example, water is formed by the reaction of cuprous oxide with carboxylic acids and oxidized quinolines are formed[4,5] when cupric carboxylates are reduced to the cuprous salts.[5] Our earlier kinetic studies[4] suffer from the same shortcoming; those of Nilsson[12] involve only activated cuprous carboxylates and the effects of concentration appear to negate the conclusion that the decarboxylation is first order in cuprous carboxylate. In the present paper, we report product and kinetic studies of the decarboxylation of a variety of pure cuprous carboxylates in pyridine and quinoline; a number of new types of products are reported and our kinetic results for cuprous *o*-nitrobenzoate are shown not to be in agreement with published conclusions. We also comment on the ease of various preparative methods for cuprous carboxylates and the suitability of these methods for product and kinetic studies.

Results

Acquisition of Kinetic Data. The decarboxylations were generally performed by heating the reactants in the dry solvent under nitrogen ebullition. The carbon dioxide evolution was monitored by passing the effluent gas stream through a drying tube and then through tubes filled with Ascarite, which absorbed the carbon dioxide. Two Ascarite tubes were used so that one could be weighed while the other continued to absorb carbon dioxide. The increase in weight of the Ascarite tubes was determined as a function of time and was a direct measure of the amount of carbon dioxide produced for a given time interval. The computations required for the analysis of the data were carried out on a PDP-10 time-sharing computer equipped with a Calcomp plotter. The mass data were transformed, appropriate to first-order kinetics, to $\log A/(A - X)$, where A is the ultimate mass of carbon dioxide released during complete reaction and X is the amount at a given time, and plotted vs. time. A straight line was fitted to the middle third of the ordered data. Using the parameters of this preliminary fit, 95% confidence limits were computed for all other points. All observed pairs of data which lay within these limits were used in fitting a new straight line to the data. This process of fitting and testing was continued so long as data pairs were included or discarded from the data set. The unrepresentative points which were eliminated constituted less than 5% of the data and they occurred almost exclusively in the early parts of the runs when the carbon dioxide had not yet completely displaced the nitrogen in the apparatus. Once self-consistency was obtained, the retained points and the kinetic parameters were plotted on a labeled graph. In all instances in which the kinetic data were acceptable, the correlation coefficient for the straight line was at least 0.99.

Preparation of Cuprous Carboxylates and the Kinetics of Their Decarboxylation. At the time that this research was begun, two methods appeared appropriate for the preparation of aromatic cuprous carboxylates. The first (method A), which was used previously[14] in this laboratory, involves heating the carboxylic acid and cuprous oxide in xylene with continuous removal of the water by azeotropic distillation; this method was found not to be general, failing for quinaldic, *o*-fluorobenzoic, and *o*-chlorobenzoic acids, and was thus used in only one experiment which was designed to compare the product mixtures obtained upon decarboxylation of cuprous benzoate prepared by different methods. The second, which was advocated recently,[9] involves the reaction between *m*-(trifluoromethyl)phenylcopper and the carboxylic acid; this method has the disadvantage for kinetic work that the arylcopper slowly undergoes self-coupling at room temperature and is therefore contaminated with varying amounts of biaryl and copper metal, a fact which makes it difficult to determine the stoichiometric quantities and which may lead to contamination of the salt with the metal.

An alternative general method, which does not have this disadvantage, was therefore developed. It consisted of the reaction of pure, freshly sublimed, cuprous *tert*-butoxide[15] with the carboxylic acid; this procedure is designated method B. Cuprous benzoate, prepared in this way, had the same color and infrared spectrum as that prepared by the azeotropic distillation method and the products of its decarboxylation were the same (see below). Cuprous *o*-nitrobenzoate, which was prepared by method B, gave excellent first-order kinetics upon decarboxylation in pyridine and in quinoline. More significantly, the rate constants in both solvents were identical within experimental error with those exhibited by the same salts prepared by the redox method (D) described below (Table I). The rate constants for the decomposition of this salt prepared by methods B and D at various concentrations and in the presence of various additives are recorded in Table I. Several other cuprous carboxylates prepared by the cuprous *tert*-butoxide method also gave good first-order kinetics upon decarboxylation (Table II).

However, the satisfactory results obtained by the use of method B came at a great expense in time; the cuprous *tert*-butoxide is very sensitive to air and moisture and must be handled in an efficiently operating glove box. For this reason, two in situ methods for the preparation of cuprous carboxylates were examined. The first (method C), which had been employed earlier for the production in high yield of 2,2′-di-

Table I. Rates of Decarboxylation of Cuprous *o*-Nitrobenzoate in Pyridine and Quinoline

Concn, M	Prep[a]	Solvent[b]	Temp, °C	Additive (concn, M)	$k \times 10^4$, s^{-1}
0.60	B	Q	122		1.97 ± 0.05
0.75	D	Q	122		2.00 ± 0.08
0.22	C	Q	137		2.2 ± 0.2[c]
0.65	B	P	116		3.07 ± 0.05
0.18	D	P	116		3.03 ± 0.03
0.37	D	P	116		3.1
0.75	D	P	116		3.13 ± 0.03
0.75	D	P	116	bis(cyclohexene)copper(I) triflate (0.16)	3.16
0.75	D	P	116	cuprous iodide (0.75)	3.2
0.75	D	P	116	benzoic acid (0.35)	3.5

[a] Method of preparation: B, acid + cuprous *tert*-butoxide; C, in situ preparation from anhydride + cuprous oxide; D, in situ preparation from cupric salt + copper metal. [b] P = pyridine; Q = quinoline. [c] Rate-determining step is not decarboxylation; see text.

Table II. Rate Constants for the Decarboxylation of Cuprous Salts in Quinoline[a]

Registry no.	Cuprous salt[b]	Prep[c]	Temp, °C	$k \times 10^4$, s^{-1}
35425-38-8	*p*-Nitrobenzoate	D[d]	197	14.9 ± 0.4
64508-51-6	3-Methyl-4-nitrobenzoate	D[d]	197	8.5 ± 0.2
64508-52-7	Picolinate	D[d]	233	2.76
64508-53-8	Quinaldate	D[d]	197	3.02 ± 0.11
14604-51-4	Benzoate	D[d]	197	0.45 ± 0.01
	Benzoate[e]	D[d]	197	0.42
	Benzoate	D[d]	200	0.88 ± 0.03
	Benzoate	D[d]	203	0.99 ± 0.04
	Benzoate	D[f]	216	1.84 ± 0.04
64508-54-9	*o*-Methylbenzoate	D[d]	197	1.76 ± 0.08
	o-Methylbenzoate	D[c]	200	3.2 ± 0.10
	o-Methylbenzoate	D[f]	200	3.2 ± 0.1
64508-55-0	1-Naphthoate	D[d]	197	2.71 ± 0.11
64508-56-1	2-*tert*-Butylbenzoate	D[d]	197	2.05
64508-57-2	2,6-Dimethylbenzoate	D[d]	197	0.97 ± 0.2
446-25-3	*o*-Fluorobenzoate	D[d]	178	0.73 ± 0.01
	o-Fluorobenzoate[g]	D[d]	178	0.76
	o-Fluorobenzoate	D[d]	192	2.7 ± 0.05
	o-Fluorobenzoate	D[d]	197	3.7 ± 0.1
	o-Fluorobenzoate[h]	D[d]	197	3.7
	o-Fluorobenzoate	D[d]	200	4.01 ± 0.07
27269-44-9	*o*-Nitrobenzoate	B	122	1.97 ± 0.05
64508-58-3	3-Methyl-2-nitrobenzoate	B	122	0.201 ± 0.003
27269-45-0	6-Chloro-2-nitrobenzoate	B	122	5.78
64508-59-4	6-Methyl-2-nitrobenzoate	B	157	2.15

[a] The yields of carbon dioxide were generally over 90%, but never below 85%. [b] Concentrations range from 0.59 to 0.75 M except for next to last entry (0.32 M) and last entry (1.5 M). [c] Method of preparation; see footnotes to Table I. [d] The copper–cupric salt mixture was heated at 130 °C for 30 min prior to raising the temperature to that indicated. [e] Fivefold excess of copper metal. [f] The reactants were added to quinoline at the temperature indicated. [g] Tetrakisacetonitrilecopper(I) perchlorate (0.36 M) present. [h] Cuprous iodide present.

nitrobiphenyl from cuprous *o*-nitrobenzoate,[4] involves the treatment of the carboxylic anhydride with cuprous oxide in the heterocyclic solvent which is to be used for the decarboxylation; however, it was found that in the case of *o*-nitrobenzoic anhydride a significantly higher temperature was required in order to attain the same rate of carbon dioxide evolution as that exhibited by the preformed cuprous carboxylate (Table I), indicating that cleavage of the anhydride rather than decarboxylation was rate determining and therefore method C was used only for product studies for which it proved quite convenient (see below).

The second in situ method (D) consisted of reduction of the cupric carboxylate with copper metal in quinoline solution.[16a] An electron spin resonance spectrum of a quinoline solution of cupric *o*-nitrobenzoate containing suspended copper, recorded at room temperature under nitrogen, exhibited a broad asymmetric signal typical of the cupric ion. After the solution had been heated at 55 °C for 3 min, the signal intensity decreased to <0.1% of the original value, indicating that the copper(II) had been reduced to the diamagnetic copper(I). The physical appearance of the solution obtained by heating the cupric *o*-nitrobenzoate and copper metal in quinoline under nitrogen was the same as that of a solution of cuprous *o*-nitrobenzoate and quinoline obtained by method B; i.e., the solution was homogeneous and red-orange in color. When the experiment was repeated in the absence of copper metal the solution remained dark blue and the asymmetric cupric signal at 55 °C was not diminished after 30 min of heating. It should be noted that this redox reaction proceeds rapidly at a temperature far below that at which decarboxylation occurs at a measurable rate; furthermore, the decarboxylation of cuprous *o*-nitrobenzoate occurs at the lowest temperature of all of the salts studied. It may be seen (Table I) that the copper–cupric couple method (D), which generates the cuprous salt in situ, produces the same rate constants as those obtained from the cuprous salt which is preformed by the cuprous *tert*-butoxide method (B) in the case of cuprous *o*-nitrobenzoate.[16b] Furthermore, as indicated below, the products are the same as

Table III. Product Yields in Decarboxylation of Cuprous Carboxylates in Quinoline

Cuprous salt (method)[a]	Concn, M	Temp, °C	% CO_2	% ArH	% Ar_2	% Ar_2CO	% QAr[b,c]	% QCOAr[b,d]	% ($Q_2 + Q_2O$)[e]
Benzoate (C)	2.5	220[f]	67.2 ± 0.4[g]	63.6 ± 1.4[g]	*h*	*i*	*h*	>6	–[j,k]
Benzoate (C)[l]	2.5	220[f]	67.5	51.5[m]	–	–	–	–	–
Benzoate (A)	2.5	220[n]	76.1	*o*	*i*	*o*	*o*	*o*	–
Benzoate (B)	0.75	220[n]	65.8	53.8	–	–	–	–	–
Benzoate (D)	0.75	200	85	*o*	*o*	*o*	*h*	*o*	17
o-Nitrobenzoate (D)	0.75	122	91	23	62	*h*	7.3	*h*	0.4
p-Nitrobenzoate (D)	1.00	197	93	74	*h*	*h*	14	*h*	51
p-Nitrobenzoate (C)	2.5	200	91	*p*	*h*	*h*	*p*	*h*	–
o-Fluorobenzoate (D)	0.75	197	96	*p*	10	*p*	–	–	–
o-Fluorobenzoate (C)	2.5	195	66	*p*	*p*	>13	*p*	*q*	*p*
3-Methyl-2-nitrobenzoate (C)	0.59	122	87	74	14	*h*	*p*	*h*	–
1-Naphthoate (D)	0.75	197	93	71	*h*	–	–	–	*p*
o-Methoxybenzoate (C)	2.5	215	58[q,r]	*p*	*h*	*p*	*h*	*p*	–

[a] Method of preparation; see text. [b] See ref 19 for yield basis. [c] Isomeric arylquinoline mixture. [d] Acylquinoline. In the benzoate case, it is 2-benzoylquinoline; in other cases, the structure was not determined. In some cases more than one isomer was detected. [e] Yield based on eq 5. [f] Anhydride and Cu_2O added at temperature of decarboxylation. [g] Average of three runs. [h] None detected. [i] Trace product. [j] Dash indicates that presence was not determined. [k] *N*-(2-Quinolyl)-2-quinolone detected as minor product. [l] Conducted in 2-deuterioquinoline (81% monodeuterated). [m] 13% monodeuterated. [n] Reactants mixed at 25 °C. [o] Semiquantitative analysis only; the order of yields was the same as that for the first run. [p] Present, but yield not determined. [q] Present as minor product. [r] Reaction might not have been brought to completion.

those obtained via methods A–C. Therefore, this method has been used for most of the kinetic runs and for much of the product study.

All of the decarboxylations studied generated excellent first-order kinetics and the rate constants were unaffected by the presence of cuprous ion, supplied as bis(cyclohexene)copper(I) triflate,[17] cuprous iodide, or tetrakisacetonitrilecopper(I) perchlorate,[18] or of benzoic acid (Tables I and II). In the case of cuprous *o*-nitrobenzoate, the first-order kinetics are verified by the insensitivity of the rate constants to concentration (Table I); this result appears to conflict with those of an earlier study.[12]

Products. The products were of two types: those derived only from the cuprous carboxylate and those derived from the solvent (the latter type was investigated only for the cases in which quinoline was the solvent). The most prominent members of the former category were carbon dioxide, a major product in all cases, and arene (the product of replacement of the cuprocarboxyl group with a hydrogen atom), which was always a major product even when no obvious "active proton" source was present. In most of the cases in which the arene yield was determined, it was over 50% (Table III); only in the case of cuprous *o*-nitrobenzoate was the yield (18–23%) of arene less and in that case another aryl-containing product, 2,2′-dinitrobiphenyl (biaryl), was formed in 63% yield. The only other salts which produced biaryl in noticeable yield were cuprous 3-methyl-2-nitrobenzoate and *o*-fluorobenzoate, in which cases the yields were 14 and 10%, respectively.

The only other type of product in this category which was formed in significant yield was diaryl ketone. A 13% yield of 2,2′-difluorobenzophenone was isolated from the decarboxylation product of cuprous *o*-fluorobenzoate generated from the reaction of the anhydride and cuprous oxide; a major factor in the structural proof of this ketone is its 250-MHz NMR spectrum, which is analyzed in the Appendix. The corresponding ketones also appeared (by gas chromatography) to be products of comparable significance in the decarboxylation of cuprous *o*-nitrobenzoate, pentafluorobenzoate, and *o*-methoxybenzoate. The decarboxylations of cuprous benzoate, generated by all four methods, produced trace amounts of benzophenone and the decarboxylation of cuprous *p*-methoxybenzoate produced trace amounts of the corresponding ketone. That of *p*-nitrobenzoate yielded no detectable quantity of the ketone.

The products containing the quinoline nucleus were of two general types, those containing an aryl nucleus as well, such as aryl- and acylquinolines, and those containing only the quinoline nucleus, such as biquinolyls (Q_2) and compounds containing an oxygen in addition to two quinolyl groups (oxybiquinolyls, Q_2O). The decarboxylation of cuprous benzoate, prepared by any of the four methods, yielded 2-benzoylquinoline (**1**). This product was isolated in 6% yield[19] from the reaction of benzoic anhydride with cuprous oxide (method C), but some was undoubtedly lost during the extensive purification procedure; the same product was isolated by preparative high-pressure liquid chromatography from the decarboxylation of cuprous benzoate prepared by the redox method (D). It is worthwhile to note that considering the 67% yield of carbon dioxide formed in the decarboxylation leading to the 6% of **1**, a maximum yield[19] of 33% of the latter is possible.

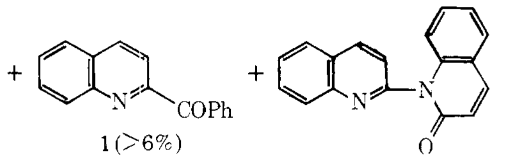
The gas chromatograms of most of the product mixtures (but not of that from cuprous benzoate) exhibited at least two peaks, the combined gas chromatographic mass spectrum of which indicated that they are probably arylquinolines. Some gas chromatographic yields are given in Table III. Only in the case of cuprous *p*-nitrobenzoate could the yield (14%)[19] of arylquinolines be considered substantial.

All of the product mixtures exhibited a number of gas chromatographic peaks, the mass spectra of which suggest that they are biquinolyls and monooxygenated biquinolyls. None of the biquinolyls is 2,2′-biquinoline, a sample of which was in hand. Two of the biquinolyls were isolated in small amounts by HPLC of the products of decarboxylation of cuprous *p*-nitrobenzoate and are labeled biquinolyls 1 and 2 (Q_2-1, and Q_2-2). The first of these (Q_2-1) was also isolated from the cuprous benzoate decarboxylation. Their melting points and mass spectra are described in the Experimental Section. The oxygenated biquinolyls are apparently not phenols, since extracting the mixture with strong aqueous base did not change the appearance of the gas chromatogram. A very minor product of this kind, formed in the cuprous benzoate experiment, was shown to be *N*-2-quinolyl-2-quinolone (**2**) by comparison of its retention time and mass spectrum with those of an authentic sample. The predominant oxybiquinoline isomer, labeled Q_2O-1 in Table IV (see paragraph at end of paper about supplementary material), is presumably

Scheme I

$PhCO_2Cu + C_9H_7N \xrightarrow{\Delta} CO_2 + PhH + Ph_2CO$

67% 64% tr



1(>6%) 2 (minor)

$+ [(C_9H_6N)_2 + (C_9H_6N)_2O]$ (1)

17%

$o\text{-}FC_6H_4CO_2Cu + C_9H_7N \xrightarrow{\Delta} CO_2 + PhF + (FC_6H_4)_2CO$

96% major >13%

$+ (FC_6H_4)_2 + C_9H_6NCOC_6H_4F + [(C_9H_6N)_2 + (C_9H_6N)_2O]$ (2)

10% minor

$o\text{-}NO_2C_6H_4CO_2Cu + C_9H_7N \xrightarrow{\Delta} CO_2 + PhNO_2$

91% 23%

$+ (o\text{-}NO_2C_6H_4)_2 + C_9H_6NC_6H_4NO_2 + [(C_9H_6N)_2 + (C_9H_6N)_2O]$ (3)

62% 0.8% 0.4%

$p\text{-}NO_2C_6H_4CO_2Cu + C_9H_7N \xrightarrow{\Delta} CO_2 + PhNO_2$

93% 74%

$+ C_9H_6NC_6H_4NO_2 + [(C_9H_6N)_2 + (C_9H_6N)_2O]$ (4)

14% 51%

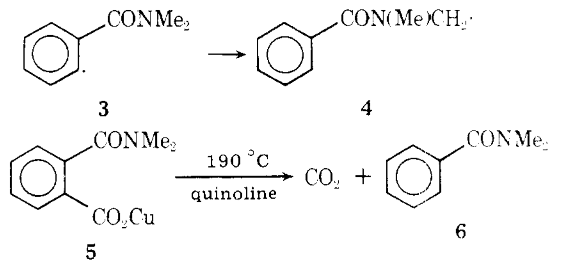
either another N-quinolylquinolone or a diquinolyl ether. Another compound with a somewhat longer retention time than Q_2O-1 did not elute from the gas chromatograph attached to the mass spectrometer and its constitution is unknown; however, judging from its retention time, this material, labeled "unknown" in Table IV, probably contains two quinolyl groups. Finally, a very small quantity of 2-quinolinol was identified and isolated from the cuprous benzoate decarboxylation.

A significant finding is that the relative gas chromatographic peak heights of compounds Q_2-1, Q_2-2, Q_2O-1, and the unknown were remarkably similar in all of the decarboxylation products in which they were measured (Table IV). Furthermore, these same four compounds were observed in approximately the same relative yields when pentafluorophenylcopper was submitted to the reaction conditions (Table IV).

Equations 1–4 (Scheme I), in which information from more than one method is combined, provide a concise overall picture of the types and quantities of products which are formed in some representative examples.

The cuprous salts (formed by the redox method D) of the saturated acids 1-adamantanecarboxylic and dodecanoic acid were found to decarboxylate extremely slowly in quinoline; only about 6% of carbon dioxide was evolved in 3 h at 205 °C. Adamantane was the main neutral product in the former case; in addition, adamantylquinolines were produced and the pattern of biquinolyls and oxybiquinolines was the same as that from the decarboxylations of the aromatic carboxylates. However, in the case of cuprous decanoate, the neutral layer contained about 12 compounds and, although traces of nonylquinolines were formed, the traces of biquinolyls and oxybiquinolines differed gas chromatographically from those obtained from the aromatic carboxylates.

It has previously been shown that the o-N,N-dimethylbenzamido radical (**3**) undergoes an extremely rapid 1,5-hydrogen atom transfer to yield **4**.[20,21] In order to probe the possibility that aryl radicals are intermediates in the copper–quinoline decarboxylation, cuprous N,N-dimethylphthalamate (**5**) was decarboxylated at 190 °C in quinoline; a quantitative yield of carbon dioxide was produced and the only neutral organic product was N,N-dimethylbenzamide (**6**).



3 **4** **5** **6**

The modes of formation of 2,2′-dinitrobiphenyl and especially of nitrobenzene, the major organic products from the decarboxylation of cuprous o-nitrobenzoate, were investigated next. Table V (see paragraph at end of paper about supplementary material) indicates how the yields of these two products vary with concentration and additives. There is a tendency for the yield of biaryl to increase at the expense of that of nitrobenzene as the concentration of reactants increases and as the concentration of external cuprous salts increase. Although the presence of benzoic acid does not change the rate constant for decarboxylation (Table I), the presence of 0.2 M benzoic acid causes a very marked increase in the ratio of nitrobenzene to biaryl produced; carboxy-labeled deuteriobenzoic acid has the same effect but leads to nitrobenzene which is 52% monodeuterated. It thus appears that an intermediate or product is becoming protonated; this is consistent with the earlier finding[4] that the presence of water increases the yield of nitrobenzene relative to that of biaryl. If an arylcopper intermediate has a choice of protonation or self-coupling, then the presence of cupric salts could affect the ratio of arene to biaryl produced, since cupric salts have been shown[22] to increase the rate of self-coupling of arylcopper(I) compounds; however, the presence of 0.75 M cupric chloride during the decarboxylation of cuprous o-fluorobenzoate, p-nitrobenzoate, and 1-naphthoate (all 0.75 M in quinoline solution at 200 °C) did not change the distribution of organic products.

In order to explore the possibility that the species which becomes protonated accumulates in the reaction mixture, samples were withdrawn at 5-min intervals (starting 25 min after the required temperature was reached) and quenched with DCl, and the deuterium incorporation into the nitrobenzene and the ratio of gas chromatographic peak heights of nitrobenzene to those of 2,2-dinitrobiphenyl were determined. The values of the latter at increasing times were found to be as follows: 24, 2.0, 1.5, 1.2, 1.3, 1.1, 1.1, 1.2, 1.3, 1.2; no deuterium was found in the nitrobenzene. In another experiment in which HCl was used for the quench and the first sample withdrawn 5 min earlier, the peak height ratios were 128, 21, 12, 1.3, 1.2, 1.8, 1.4, 0.9, 0.9, 0.9, 1.0.

These experiments imply that the species which is being protonated, presumably an arylcopper, is an intermediate which does not accumulate in the reaction mixture. This is consistent with the finding of Cairncross et al.[9] that a putative arylcopper intermediate could be trapped with iodobenzoate if the latter were present during the decarboxylation of cuprous o-nitrobenzoate in quinoline but not if it were added after gas evolution had ceased.

The quenching experiments also provide a clue as to the origin of at least some of the protons which replace the carboxylate groups. It appears that a small quantity of a proton source is present, probably as a contaminant, in the solvent and that the intermediate is easily protonated as long as the proton source lasts. When pyridine which was 1.25 M in D_2O

was used as the medium, the nitrobenzene (80% yield) formed by decarboxylation was 94% monodeuterated. However, moisture in the solvent could only account for 0.7% of the 18% of nitrobenzene ordinarily produced, since a Karl Fischer titration of the purified quinoline which was used as solvent was found to be 2.5×10^{-3} M in water. Another possible source of protons is the water of hydration of the cupric *o*-nitrobenzoate. When the latter was shaken in D_2O, placed for 12 h in a vacuum desiccator which was evacuated by a mechanical pump, and then decarboxylated, the arene (48% yield) produced by its decarboxylation was found to be deuterated to the extent of 54%. However, cupric *o*-nitrobenzoate which had been heated in an oven for 12 h at ~110 °C prior to being placed in a vacuum desiccator (the usual procedure used in this work) was subjected to elemental analysis and found to be anhydrous within the usual limits of error. The major source of "active protons" in the solution may be water contaminating the copper powder; an analysis performed after the completion of most of the work reported here indicated that this metal contained 0.8% water, enough to account for about 26% of the nitrobenzene produced.

The remainder of the protons appear to be slowly generated during the reaction and it is reasonable to suppose that these protons are released during the various coupling reactions of the quinoline. This supposition was verified by conducting the decarboxylation of cuprous *o*-nitrobenzoate (prepared by method B) in a 1.25 M solution in 2-deuterioquinoline (97 ± 0.7% enriched);[23] 7% of the nitrobenzene formed (20% yield) was monodeuterated. When cuprous benzoate was decarboxylated in 2-deuterioquinoline (81% monodeuterated) a substantial decrease in benzene formation was observed (Table III), probably indicating an isotope effect, and the benzene was 13% monodeuterated. In view of the types of compounds containing quinolyl groups identified in the product mixtures, it is clear that protons are also released from positions other than the 2 position of quinoline and the solvent must thus be considered as a major source of hydrogen.

Two experiments were performed in order to determine if the ketones produced in the decarboxylations could result from attack of an anhydride on an arylcopper. In the first, *m*-(trifluoromethyl)phenylcopper[24] was treated with benzoic anhydride in ether at room temperature; combined GC–MS analysis indicated the presence of 3-(trifluoromethyl)benzophenone, in addition to 3-trifluoromethylphenyl benzoate, ethyl benzoate, and 3,3′-bis(trifluoromethyl)biphenyl, the normal product of self-coupling of the arylcopper.[24,25] In the second experiment, *o*-nitrobenzoic anhydride was heated in quinoline at 140 °C in the presence of an equivalent quantity of cuprous oxide and benzoic anhydride, since the former anhydride readily undergoes decarboxylation under these conditions and the latter decarboxylates slowly even at 200 °C; analysis of the neutral layer by GC–MS indicated the presence of 2-nitrobenzophenone, presumably formed by benzoylation of a reaction intermediate, in addition to nitrobenzene and 2,2′-dinitrobiphenyl.

Discussion

Preparative Methods for Cuprous Carboxylates. An apparently general, albeit tedious, method (B) for preparing cuprous carboxylates is the exchange reaction between carboxylic acids and freshly sublimed cuprous *tert*-butoxide. An in situ method, C, which consists of generation of the cuprous salt by heating the anhydride with cuprous oxide in the quinoline solvent, is satisfactory for product studies but not for studies of the kinetics of decarboxylation. The preferred method, D, appropriate for both types of studies, is the reduction by copper powder of the corresponding cupric salt in quinoline or pyridine.

The Question of an Aryl Radical Intermediate. The argument of Cohen and Schambach[4] against a radical intermediate on the basis of the high stereoselectivity in geometrically isomeric vinyl systems is supported by the production of only *N*,*N*-dimethylbenzamide (**6**) from the decarboxylation of the cuprous salt (**5**) of *N*,*N*-dimethylphthalamic acid, since the formation of the aryl radical **3** would be expected to yield products derived from the radical **4**; the 1,5-hydrogen shift which converts **3** to **4** is detectable even in the presence of a large concentration of cupric chloride,[20,21] which is capable of transferring a chlorine atom to an organic radical at a rate approaching that of a diffusion-controlled process.[26] Thus radical **3** could only be involved if some unknown reaction which yields **6** from the aryl radical is faster than this exceedingly rapid hydrogen transfer.

The Question of an Arylcopper Intermediate. Prior to the initiation of the present work, the evidence for an organocopper intermediate in the copper–quinoline decarboxylation consisted of trapping of the intermediate by aryl iodides and by protons, self-coupling to form biaryls, and, in one case, isolation of an aryl copper. However, all of these demonstrations have occurred with arenecarboxylates which are activated toward decarboxylation, usually by the presence of strong electron-withdrawing groups. No self-coupling was observed in the present work except with *o*-fluoro and *o*-nitro substituents. Attempted trapping of an intermediate with aryl iodides in the case of nonactivated cuprous carboxylates would be impractical, since cuprous carboxylates themselves react rapidly with aryl iodides to form aryl carboxylates at the temperatures required for decarboxylation.[14]

However, an important indication that organocoppers may also be present in the decarboxylations of nonactivated cuprous carboxylates is that four biquinolyl and oxybiquinolyl products were formed in similar proportions in the decarboxylations of all of the aromatic cuprous carboxylates in quinoline but not when cuprous decanoate, which hardly decarboxylates under the usual conditions, was heated in quinoline solution. The same four products were formed in similar proportions during the decarboxylation of cuprous pentafluorobenzoate, a reaction which has been shown to produce an isolable organocopper, and, most importantly, during the heating of an authentic sample of pentafluorophenylcopper in quinoline at the temperature at which the majority of the decarboxylations were performed (Table IV). It is thus likely that an organocopper is somehow involved in the production of these four compounds. It may be that organocoppers formed in the decarboxylation of unactivated acids metalate the quinoline to produce quinolylcoppers faster than they self-couple and the quinolylcoppers may then couple or undergo further reaction; a mechanism for quinoline metalation is suggested below.

The identification of ketone products in which an acyl group has replaced the carboxyl group can be readily explained on the basis of acylation of an arylcopper by an anhydride. 2-Nitrobenzophenone was formed when benzoic anhydride was present during the decarboxylation of cuprous *o*-nitrobenzoate in quinoline. Furthermore, *m*-(trifluoromethyl)phenylcopper was successfully benzoylated with the same anhydride.

However, the absence of self-coupling in a number of cases must cause some reservations about the possibility of organocoppers as major intermediates. It has been shown by Lewin and Cohen[8] that the copper-induced coupling of *p*-iodotoluene in quinoline produces an intermediate, thought to be an organocopper, which is capable of self-coupling or protonation by an acid. In the present work, the decarboxylation of cuprous *p*-toluate gave no bitolyl; this was true even when Ullmann reaction conditions were simulated by adding copper metal and cuprous iodide to the reaction mixture. Nevertheless, this evidence against organocopper intermediates in nonactivated cases should not be considered definitive, since the behavior of the organocopper intermediate in these reactions may be decisively controlled by the oxidation state of the metal and the nature of the ligands as the intermediate is produced.[27]

Source of Protons. The major product formed in the decarboxylation of most of the cuprous carboxylates is one in which the carboxyl group has been replaced by a proton. As indicated above, a portion of the protons which replace the carboxyl group is probably derived from traces of water in the reagents, particularly the copper metal. Much of the remainder presumably must be derived from the hydrogen atoms of the quinoline. This is indicated by the experiments in which 2-deuterioquinoline was used as solvent. The yield of benzene from cuprous benzoate was significantly decreased (Table III), presumably due to an isotope effect, and the benzene formed was partially monodeuterated; similarly, the nitrobenzene from cuprous *o*-nitrobenzoate was partially monodeuterated. Since all of the substitution is not at the 2 position in the quinoline-containing products, it is clear that protons from unlabeled positions of the 2-deuterioquinoline must also be released. Assuming that all of the protons released from the quinoline (QH) are utilized in the replacement of carboxyl groups, the stoichiometry indicated in the equations

$$2ArCO_2Cu + QH \rightarrow ArH + QCOAr + CO_2 + Cu_2O \quad (5)$$

$$2ArCO_2Cu + QH \rightarrow ArH + QAr + 2CO_2 + 2Cu \quad (6)$$

$$2ArCO_2Cu + 2QH \rightarrow 2ArH + Q_2 + 2CO_2 + 2Cu \quad (7)$$

$$4ArCO_2Cu + 2QH \rightarrow 2ArH + Q_2O + (ArCO)_2O + 2CO_2 + 4Cu \quad (8)$$

appears likely for the production of acyl- and arylquinolines (QCOAr and QAr), biquinolyls (Q_2), and oxybiquinolyls (Q_2O), respectively. In the case of the last equation, the anhydride could react with Cu_2O from eq 5 to regenerate cuprous carboxylate, it could react with traces of water to yield carboxylic acid and thence arene and CO_2, or it could be used to acylate a quinolylcopper (see below).[31]

The reaction of an arylcopper(I) compound with quinoline has also been noted recently by Lewin.[32] She has found that 1-naphthylcopper reacts at 160 °C with quinoline to give ~50% naphthalene, 1,1′-binaphthyl, two isomers of 1-naphthylquinoline, and small quantities of biquinolyls. Essentially the same results were obtained when 1-iodonaphthalene was heated in quinoline with copper under the same conditions.

$$ArCu + QH \rightarrow QAr + QQ + ArH$$

It is thus clear that arylcopper(I) compounds can react with quinoline. At the present state of knowledge of transition metal organometallics, reasonable mechanisms can be put forth for the results reported here.

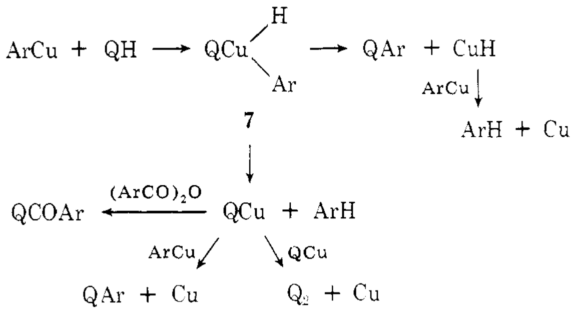
Oxidative addition of aromatic CH bonds to transition metals in low oxidation states is a recognized process.[33] Such an oxidative addition of a CH bond of quinoline to the copper of an arylcopper(I) reactant or intermediate would lead to the organocopper(III) 7 (Scheme II).[28] This key intermediate could undergo reductive elimination in either of two directions. One of these leads to an arylquinoline and cuprous hydride; the latter would be capable of reacting with an arylcopper to yield arene and copper metal.[34] The other direction leads to an arene and a quinolylcopper; the latter could become acylated, as demonstrated in the Results section, by a molecule of anhydride (formed by eq 8 or by the reverse of the reaction of cuprous oxide with anhydride to produce cuprous carboxylate by method C), it could couple with arylcopper to yield an arylquinoline, or it could couple with another quinolylcopper to produce a biquinolyl.

Table VI. Relationship of Yields of Arenes and Quinoline-Containing Products[a]

Cuprous salt	% yield of arene	% yield of ($QAr + QCOAr + Q_2 + Q_2O$)
o-Nitrobenzoate	23	7.7
Benzoate	54–64	23
p-Nitrobenzoate	74	65

[a] Data from Table III.

Scheme II



An apparently analogous replacement of a copper(I) attached to an sp[2] carbon atom by hydrogen (presumably derived from solvent) was observed by van Koten and Noltes[35] when the organocopper compound was heated in quinoline to 200 °C. Another analogy, possibly occurring by the same type of mechanism, is the exchange of the proton at the 2 position of acrylonitrile for a deuteron when the former is treated with a copper(I)–isonitrile complex and Me_3COD.[36]

If, indeed, some of the arene is produced by adventitious proton sources present in the reactants and the remainder by the hydrogens released from the quinoline, the yields of quinoline-containing products should be a sensitive function of the yield of arene. This, in fact, appears to be true for the three cases in which the yields of the basic products were determined (Table VI).

Kinetic Order. The kinetics are clearly first order in the cuprous carboxylate in all cases. In the case of cuprous *o*-nitrobenzoate, this order is confirmed by the invariance of the rate with concentration over the limited range studied (Table I)[37] and its insensitivity to the presence of soluble cuprous salts. Since the cuprous carboxylate consists of two parts, a cation and an anion, the first-order kinetics could be indicative that: (1) the cuprous carboxylate behaves as a single unit; (2) the reaction is first order in carboxylate and zero order in cuprous ion; or (3) the reaction is first order in cuprous ion and zero order in the carboxylate ion. The second possibility may be excluded by a study involving cupric *o*-nitrobenzoate, which was shown to decarboxylate 100 times slower than the cuprous salt; cuprous ion is thus required for the decarboxylation.[38] The third possibility is excluded by the results presented in Tables I and II; added cuprous salts are shown not to influence the rate of decarboxylation of the cuprous carboxylate. It therefore appears that the cuprous carboxylate is acting as a unit and the reaction is first order in this unit. This behavior by the cuprous carboxylate could be explained as the result of ion pairing, which would certainly be expected in a solvent of such low polarity.

Substituent Effects. The relative rates for the decarboxylation of substituted cuprous benzoates in quinoline at 197 °C are (Table II): *p*-nitro, 33; 3-methyl-4-nitro, 20; *o*-fluoro, 8.8; *o-tert*-butyl, 4.9; *o*-methyl, 4.2; 2,6-dimethyl, 2.3; unsubstituted, 1.0. Only the *o*-nitro group has a very substantial effect, allowing a comparable rate at 122 °C. When the 2-nitro group is twisted out of the plane of the ring by an *o*-methyl group (cuprous 3-methyl-2-nitrobenzoate), the rate decreases by a factor of 10. When a methyl group is placed ortho to the carboxylate function in cuprous *o*-nitrobenzoate, a large decrease in rate is also noted.

The *p*-nitro substituent moderately accelerates the reaction (Table II). Twisting the nitro group out of the plane of the ring, as in the case of cuprous 3-methyl-4-nitrobenzoate, decreases the influence of this group. The *o*-fluoro substituent also mildly accelerates the reaction. *o-tert*-Butyl and *o*-methyl groups weakly accelerate the reaction. The substitution of a second *o*-methyl group decreases the rate slightly. An *o*-methyl group introduced in addition to an *o*-nitro group already present greatly slows the rate of the reaction (Table II). The nitrogen of the pyridine ring in the 2 position is very much less effective than an *o*-nitro substituent at facilitating the decarboxylation.

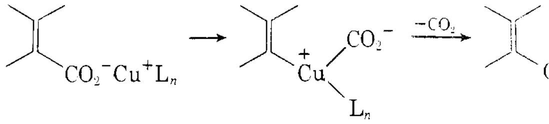
Solvent Effects. This study represents the first reported instance in which pyridine was used as the solvent for the decarboxylation reaction of cuprous salts. From the work of Cohen and Schambach[4] and of Cairncross, Roland, Henderson, and Sheppard[9] it is seen that the rate of the decarboxylation is enhanced by the presence of complexing agents for cuprous ions, and the better the complexing ability of the agent the more effective it is in promoting the reaction. The rate enhancement by 2,2′-bipyridyl was reported to be greater than that by 2,2′-biquinoline.[4] This same sort of relationship seems to hold in the present study. The rate constant found for the decarboxylation of cuprous *o*-nitrobenzoate in quinoline at 122 °C is $1.96 \times 10^{-4}\ \mathrm{s}^{-1}$, while that for the decarboxylation of the same salt in pyridine at 116 °C is $(3.13 \pm 0.03) \times 10^{-4}\ \mathrm{s}^{-1}$. The faster rate in pyridine may be due to less steric hindrance to complexation of the cuprous ion by the smaller pyridine molecule.

Thermodynamic Parameters. Decarboxylations of two of the salts in quinoline at several temperatures (Table II) has allowed the computation[39] of the following thermodynamic quantities of activation: cuprous benzoate, $\Delta H^{\ddagger} = 33$ kcal/mol and $\Delta S^{\ddagger} = -7.3$ cal/deg-mol; cuprous *o*-fluorobenzoate, $\Delta H^{\ddagger} = 39$ kcal/mol and $\Delta S^{\ddagger}$ +9.9 cal/deg-mol.

The Role of Copper in the Loss of Carbon Dioxide. Cohen and Schambach[4] have proposed that the copper(I) ion, with its heterocyclic ligands, forms a π complex with the aromatic ring of the carboxylate anion. Loss of carbon dioxide from the complex yields a σ carbanion stabilized by the π-complexed metal ion. This species then collapses to an arylcopper(I) compound. The present results are consistent with this mechanism in that one cuprous ion and one carboxylate are involved, electron withdrawing groups increase the rate, and ortho substituents, which are expected to cause steric strain which is relieved in the transition state for loss of carbon dioxide, generally increase the rate. The attenuation of this rate increase with the introduction of a second ortho substituent could be due to steric hindrance to π-complex formation which could occur near the vacant ortho site when a single ortho substituent is present. The ortho nitro group, in addition to having steric bulk and being electron withdrawing, may complex with the copper(I) during the π complexation of the latter.

However, the kinetic results reported here suggest a close mechanistic relationship between the cuprous carboxylate decarboxylation, the Ullmann biaryl coupling,[40–42] and the exchange reaction of aryl and vinyl halides with the anions of copper(I) salts.[20,41,43–49] In all three types of reaction, substituent effects on the rate are extremely modest, nearly all substituents increase the rate, and nitro groups are activating in both ortho and para positions but the ortho effect is far more pronounced. Extensive kinetic studies on the exchange reaction have established that it is first order in copper(I); whereas such studies are precluded in the usual heterogeneous biaryl coupling, the recently discovered homogeneous Ullmann biaryl coupling (which under some conditions is accompanied by an exchange process) was also found to be first order in copper(I).[30] In all three cases, a reaction intermediate, presumed to be an organocopper, can be protonated in the presence of acids.[4,7,8,14,20,30,50,51] In all three reactions, vinyl derivatives react with high degrees of retention of configuration,[4,11b,50,54] a fact which is believed to support a nonradical process; other evidence against a radical mechanism in these reactions is also found in the present results and in ref 20, 30 and 53.

In view of these similarities, it is tempting to suggest a similar mode of participation by copper(I) in these processes. An oxidative addition of the aryl or vinyl halide to the copper(I) appears to be indicated in the Ullmann biaryl reaction[30] and in the exchange reactions.[20,52] Application to the decarboxylation reaction would involve insertion of the copper(I), with associated ligands, into the carbon–carbon bond of the carboxylate (possibly after forming a π complex with the aromatic ring) to form a copper(III) intermediate which would be capable of rapid conversion to a copper(I) compound by loss of carbon dioxide.



The suggested process is analogous to the oxidative addition of aromatic CH groups to various transition metals.[33] In view of the fact that CH and CCO_2^- often behave analogously (one has been termed a carboxylogue of the other[55]), it does not seem unreasonable to suggest such a mechanism.

The small substituent effects are well accounted for by such a mechanism, since a substantial charge never gets dispersed into the ring. On the other hand, the carbon atom bearing the carboxylate group decreases its oxidation number during the substitution by the metal and this accounts for the accelerating effect of electron-withdrawing groups; rather similar substituent effects have been noted in the oxidative addition of aromatic CH groups to transition metal complexes.[33,56] The role of the *o*-nitro group in coordinating with the metal during the process is also understandable.

Conclusions

Cuprous carboxylates for decarboxylation studies can be prepared generally by treatment of carboxylic acids with sublimed cuprous *tert*-butoxide or more readily by reduction of a cupric carboxylate with copper metal in the pyridine or quinoline that is to be used as a solvent.

The coupling to a biaryl found with cuprous *o*-nitrobenzoate is not a general reaction. Unactivated cuprous carboxylates decompose in quinoline to form arene and a variety of other products, most of them derived from the solvent; the protons that replace the carboxyl group appear to be derived largely from the solvent. The pattern of products containing two quinoline nuclei is the same for all of the aromatic decarboxylations studied and for the products of reaction of an authentic arylcopper with quinoline, and this is the main evidence for an arylcopper intermediate in the case of unactivated carboxylates. The rich variety of products formed in most cases makes it unlikely that the decarboxylation of pure cuprous carboxylates in heterocyclic solvents will be a generally useful synthetic procedure.

The kinetics and especially the substituent effects are consistent either with a mechanism in which a cuprous ion, π complexed to the aromatic ring, stabilizes the developing negative charge as the carbon dioxide is lost or one in which the carboxyl carbon–carbon bond oxidatively adds to the metal ion (which may be similarly π-complexed), followed by loss of the carbon dioxide ligand from the resulting copper(III) species.

Experimental Section

Melting points (mp) are corrected. Infrared (IR) spectra were recorded on a Beckman IR-8 spectrophotometer. Proton magnetic resonance (^{1}H NMR) spectra at 60 MHz were taken on Varian A-60D and T-60 spectrometers and those at 250 MHz were taken on a custom built spectrometer utilizing a supercooled solanoid; chemical shift data are reported in units of δ (ppm) relative to internal tetramethylsilane. Mass spectra (MS) were recorded at an ionizing voltage of 70 eV, unless otherwise specified, on an LKB-9000 combined gas chromatograph–mass spectrometer; the *m/e* values are followed in parentheses by the intensity as a percentage of the base peak and the assignment, if known. The combined GLC–mass spectra of all arenes and of the arylquinolines of unknown isomeric structure are recorded in the supplementary material (see paragraph at the end of the paper). High-resolution mass spectra were taken on an AEI MS-9 spectrometer. Gas-liquid chromatographic (GLC) analyses were performed on a Hewlett-Packard 5750 gas chromatograph equipped with a Disc integrator or a Hewlett-Packard electronic integrator. Yields were calculated from peak areas using internal standard techniques. High-pressure liquid chromatography was performed on a DuPont 600 instrument.

Decarboxylation Procedure. Most of the kinetic runs were replicated at least three times; the error limits given in the tables are average deviations for the three or more runs. The reproducibility was always excellent and in a few cases only one decarboxylation was performed; no error limits are listed for those cases.

A. Apparatus. The glassware was dried in an oven at 110 °C for 24 h, assembled while hot, and purged with nitrogen for 30 min. A three-neck (four-neck, when samples were to be withdrawn) round-bottom flask fitted with a condenser, thermometer, and gas inlet tube and containing a magnetic stirring bar was used. During reaction, the evolved carbon dioxide was swept with a stream of nitrogen through the condenser and a cold trap cooled by a mixture of dry ice and isopropyl alcohol and finally through two Ascarite tubes which absorbed the carbon dioxide. The reaction temperature was maintained either by an electric mantle or a sand bath (Tecam, Techne, L and D., Duxford, England) controlled within ±0.5 °C by a Thermowatch (I^{2}R, model L-6, Cheltenham, Pa.).

B. Method B. The cuprous salt, prepared (see below) by metalation of the appropriate acid with cuprous *tert*-butoxide, was charged into the flask which was contained in a dry and oxygen-free atmosphere in a glove box. After the apparatus had been removed from the glovebox, the freshly distilled solvent was injected through a serum cap into the flask. A thermometer was substituted for the serum cap, the system was purged with nitrogen until the Ascarite tubes reached a constant weight, the flask was heated to the desired temperature, and the weighings commenced; the experiment was terminated when carbon dioxide evolution ceased.

C. Method C. A mixture of the solvent and cuprous oxide under a nitrogen purge was heated at the reaction temperature until the weights of the Ascarite tubes had stabilized, the anhydride was quickly added, and the tube weighings were started.

D. Method D. A mixture of the cupric salt (prepared as described below), an equivalent quantity of copper powder, and the solvent was heated to 70 °C for 30 min in the case of cupric salts containing *o*-nitro groups and to 130 °C in the case of other cupric salts. The Ascarite tubes were weighed, the flask was heated to the decarboxylation temperature, and the weighings were started.

E. Analysis of Products. (1) General Procedure. In most cases the qualitative and/or quantitative analyses of a reaction mixture or sample were performed using gas-liquid chromatography (GLC). The columns used are indicated in each case and the nitrogen flow rate was 60 mL/min; the initial column temperature was 80 °C with a programmed rise of 8 or 10°/min to 300 °C, where the temperature was maintained for 10 min. Combined GLC–mass spectrometric analyses were conducted on columns of 1.5% SE-30, 3% OV-17, or 2.0% Dexsil; the column temperature was slowly increased from 80 °C to the column limit and maintained at that temperature.

In order to prepare the product mixtures for qualitative and semiquantitative analysis approximately half of the mixture was dissolved in ether, and this solution was extracted with 1 N hydrochloric acid, washed with water, dried over anhydrous magnesium sulfate, and concentrated to provide the neutral fraction; the acid extract was neutralized with sodium bicarbonate, made slightly basic with concentrated ammonium hydroxide, extracted with ether, and dried over anhydrous magnesium sulfate to give the basic fraction. When the neutral fraction was to be analyzed quantitatively, the internal standard, *n*-octadecane, was added to the entire reaction mixture, which was then treated in the manner described above. When the basic fraction was to be analyzed quantitatively, the quinoline solvent was first removed by vacuum distillation and the internal standard, durene, was then added.

(2) Cuprous *o*-Nitrobenzoate (Methods B, C, and D, Pyridine and Quinoline). Regardless of the method of preparation, the neutral fraction, analyzed on a 3% OV-17 column, contained the following products [compound, retention time, mass spectrum *m/e* (rel intensity, assignment)]: nitrobenzene, 5.9 min; 2,2′-dinitrobiphenyl, 22 min, 199 (14.6), 198 (100, P − NO_2), 168 (16, P − NO_2 − NO), 140 (11), 139 (41), 116 (10), 115 (27), 63 (14) (no parent peak was evident even at 12.5 eV). The mass spectra were similar to those of authentic samples and the identities were further confirmed by coinjection on both the OV-17 and 1% OV-1 columns. Further confirmation was obtained when 2,2′-dinitrobiphenyl was isolated in 69% yield by distillation from a pyridine run; its melting point, 127.5–128.0 °C, was identical with that of the authentic sample (Aldrich).

The basic fractions from pyridine runs contained only traces of material, the mass spectra of which indicated that they may be 2-nitrodiphenylamine and an isomer of *o*-nitrophenylpyridine. The basic fractions from the quinoline runs analyzed by GLC–MS as follows: isomer of *o*-nitrophenylquinoline, 18 min; isomer of *o*-nitrophenylquinoline, 20.2 min; isomer of *o*-nitrophenylquinoline, 20.4 min; isomer of biquinoline, hereafter referred to as biquinolyl 1 (Q_2-1), 22 min, 257 (19.2, P + 1), 256 (96, P), 255 (100, P − H), 254 (13.3), 229 (5.5), 228 (8.2), 227 (8.2), 200 (4.5), 201 (4.5), 128 (12.6, quinolyl$^+$), 127 (4.5), 101 (10, quinolyl$^+$ − HCN); isomer of diquinolyl ether, hereafter referred to as oxybiquinolyl 1 (Q_2O-1), 22.5 min, 273 (6.8, P + 1), 272 (24.6, P), 271 (100, P − H), 243 (11), 231 (6), 136 (9), 128 (13, quinolyl$^+$), 101 (12, quinolyl$^+$ − HCN), 77 (6). The coinjection of 2,2′-biquinoline and the reaction mixture containing biquinolyl isomer 1 on 3% OV-17 indicated that the biquinolyl isomer 1 is not 2,2′-biquinoline. The coinjection of the reaction mixture and 2,2′-diquinolyl ether[57a] produced an increase in the peak height of the diquinolyl ether isomer 1 relative to the other peaks, and peaks foreign to the reaction mixture did not appear; unfortunately, this is not an unambiguous identification, since a second column satisfactory for coinjection could not be found and the melting point of this material (see below) involves an ambiguity.

(3) Cuprous 3-Methyl-2-nitrobenzoate (C, Quinoline). The neutral fraction on 3% OV-17 indicated the presence of: *o*-nitrotoluene, 6.2 min; 3,3′-dimethyl-2,2′-dinitrobiphenyl, 2.3 min, 228 (2.3), 227 (17.9), 226 (100, P − NO_2), 208 (12), 207 (21), 198 (14), 196 (20, P − NO_2 − NO), 195 (22), 183 (12), 180 (11), 170 (11), 165 (18), 115 (24), 104 (11), 91 (11), 89 (15), 77 (32), 75 (18), 74 (11), 65 (22) (no parent peak was present at 20 eV). The identity of *o*-nitrotoluene was confirmed by coinjection with an authentic sample. An authentic sample of the biaryl was not available; however, the fact that the retention time is slightly greater than that of 2,2′-dinitrobiphenyl and the similarity of the fragmentation patterns of the two compounds add credence to its identification.

The following compounds were identified by GLC–MS in the basic fraction: isomer of 3-methyl-2-nitrophenylquinoline, 12.2 min; isomer of 3-methyl-2-nitrophenylquinoline, 16.5 min; isomer of 3-methyl-2-nitrophenylquinoline, 17.4 min.

(4) Cuprous *p*-Nitrobenzoate (D, Quinoline). Nitrobenzene, identified by its retention time and mass spectrum, was the only neutral product. The GLC–MS analysis of the basic fraction revealed the presence of: 2-quinolinol, 16 min, identified by comparison with an authentic sample (Eastman) with respect to melting point, GLC, and MS behavior; isomer of *p*-nitrophenylquinoline, 19 min; isomer of *p*-nitrophenylquinoline, 19.5 min; isomer of *p*-nitrophenylquinoline, 20.7 min; biquinolyl 1, 22.2 min; oxybiquinolyl 1, 22.5 min; unknown (hereafter known as biquinolyl 2, Q_2-2), 23.4 min, 257 (20, P + 1), 256 (100, P), 255 (47), 154 (16), 128 (28, quinolyl$^+$), 97 (9), 85 (10), 82 (10), 71 (15), 69 (12). Biquinolyl 1 and oxybiquinolyl 1 were identified by comparison of their MS with those of the corresponding products from decarboxylation of cuprous *o*-nitrobenzoate and by coinjection of the products from the two reactions.

Three solid compounds were isolated from the basic fraction (after evaporation of the quinoline) by preparative high-pressure liquid chromatography on a Porasil A column (2 ft × 0.35 in.) using a solvent initially composed of 2% isopropyl alcohol, 3% ethyl acetate, and 95% hexane; the eluting power was increased by the addition of methylene chloride or ethyl acetate via a step gradient method and the pressure was increased stepwise during the course of the separation. The first of these was 2-quinolinol: mp 199.5–200.0 °C (lit.[57b] mp 199–200 °C); its GC and MS properties were identical with those of an authentic sample. The second compound, eluted in a trace quantity as a tan solid, mp 97.5–98.5 °C, was identified as biquinolyl 2 on the basis of its mass spectrum and coinjection behavior. A third compound was a white solid, mp 123–124 °C, which was identified as biquinolyl 1 on the basis its GC and MS behavior.

(5) **Cuprous Benzoate (D, Quinoline).** The total product was submitted to GC–MS and, after evaporation of the quinoline, to the high-pressure liquid chromatography procedure described immediately above. The following compounds were isolated: benzophenone, a white solid, mp 49.0–49.5 °C, identical with an authentic sample; 2-benzoylquinoline, a yellow solid, mp 110.5–111.0 °C (lit.[58] mp 110.0–111.0 °C), whose MS and GC (coinjection) behavior was identical with that of an authentic sample prepared by the Friedel–Crafts acylation of benzene[58] with quinaldyl chloride,[59] MS 234 (12.5, P + 1), 233 (73, P), 232 (47), 206 (16), 205 (100, P − CO), 204 (86), 128 (15, quinolyl$^+$), 105 (80, $C_6H_5CO^+$), 101 (13), 77 (83, $C_6H_5^+$); biquinolyl 1, isolated as a white solid, mp 123.0–123.5 °C;[60] oxybiquinolyl 1, mp 176.0–176.5 °C.[63] In addition to these compounds, the following were identified by GC–MS: phenylquinoline isomer; biquinolyl 2; *N*-2-quinolyl-2-quinolone (2), 272 (47, P), 271 (100, P − H), 243 (14), 128 (10, quinolyl$^+$), 101 (10). The MS and GC coinjection behavior of the latter was identical with that of an authentic sample.[57a]

(6) **Cuprous *o*-Fluorobenzoate.** 2,2′-Difluorobenzophenone was isolated in 13% yield as a pale yellow liquid from the neutral fraction of the reaction of the anhydride with cuprous oxide in quinoline (method C) by chromatography on neutral alumina: IR (neat) 3106 (w, CH stretch), 1684 (m) and 1661 (s, carbonyl doublet), 1618 (s), 1580 (m), 1481 (s), 1453 (s), 1305 (s), 1287 (m), 1247 (m), 1224 (s, CF stretch[65a]), 931 (s), 754 (s, br) cm^{-1} (only the carbonyl doublet is recorded in a literature spectrum[66]); MS 218 (25, P), 123 (100, $C_6H_4FCO^+$), 95 (36, $C_6H_4F^+$), 75 (16); high-resolution MS calcd for $C_{13}H_8F_2O$, 218.0543; found, 218.0544.

A complete analysis of the ^1H NMR spectrum is in the appendix.

2,2′-Difluorobiphenyl was isolated by sublimation in 7% yield from the neutral fraction of the decarboxylation mixture of the salt prepared by method D. The white solid had mp 120.0–120.5 °C, whereas a sample from Pierce Chemical Co. had mp 119.5–120.5 °C. The two samples were shown to be identical by coinjection on two columns: MS 191 (13.5, P + 1), 190 (100, P), 189 (19), 188 (18), 170 (10, P − H − F), 74 (30), 59 (50). The gas chromatograms of the products from both decarboxylations showed fluorobenzene as a major product (identified by coinjections on Porapak Q and on 10% Carbowax). The basic fraction was very minor and by GC–MS it showed the presence of three isomers of *o*-fluorophenylquinoline as well as biquinolyl 1.

(7) **Cuprous 1-Naphthoate (D, Quinoline).** Naphthalene was isolated by sublimation from the neutral layer and identified by melting point, coinjection on two columns with an authentic sample, and its mass spectrum. By GC–MS, the basic layer contained Q_2-1, Q_2-2, Q_2O, and the unknown.

(8) **Cuprous 3-Methyl-4-nitrobenzoate (D, Quinoline).** The neutral fraction contained *o*-nitrotoluene and the basic fraction contained the same compounds as that from decarboxylation of cuprous benzoate.

(9) **Cuprous 6-Methyl-2-nitrobenzoate (B, Quinoline).** The neutral layer contained only *m*-nitrotoluene and the basic layer closely resembled that from the decarboxylation of cuprous benzoate.

(10) **Cuprous *o*-Methylbenzoate (D, Quinoline).** The neutral layer contained toluene and no more than 1% of 2,2′-dimethylbiphenyl. The composition of the basic layer closely resembled that from the decarboxylation of cuprous *p*-nitrobenzoate.

(11) **Cuprous Pentafluorobenzoate (D, Quinoline).** The neutral layer contained decafluorobiphenyl: 335 (12.7, P + 1), 334 (100, P), 333 (12), 315 (11, P − F), 294 (23), 272 (12), 265 (28), 259 (11), 198 (13), 197 (69), 167 (14, $C_6F_5^+$), 135 (52), 117 (14). The basic layer contained two isomers of pentafluorophenylquinoline as well as the usual four components containing two quinoline nuclei each; the latter four compounds were identified by coinjection with the basic product of decarboxylation of cuprous *p*-nitrobenzoate.

(12) **Cuprous 2,6-Dimethylbenzoate (D, Quinoline).** The major product in the neutral layer was *m*-xylene. The basic layer contained the usual four products containing two quinoline moieties each.

(13) **Cuprous *o*-*tert*-Butylbenzoate (D, Quinoline).** Only the neutral layer was analyzed by GLC. It contained *tert*-butylbenzene as indicated by coinjection on two columns. In addition, a 45% yield of *tert*-butylbenzene was recovered from the cold trap through which the nitrogen was swept.

(14) **Cuprous α-Picolinate (D, Quinoline).** Analysis of the product by GLC–MS indicated the presence of pyridine, three isomers of pyridylquinoline, and the four isomers containing two quinoline nuclei each.

(15) **Cuprous Quinaldate (D, Quinoline).** The quinoline could not be detected since it was the solvent. The usual other four components were also present.

(16) **Cuprous *N*,*N*-Dimethylphthalamate (D, Quinoline).** The neutral layer contained only *N*,*N*-dimethylbenzamide. The basic layer was not analyzed.

(17) **Cuprous 1-Adamantanecarboxylate (D, Quinoline).** The main component of the neutral layer coinjected with a sample of authentic adamantane: MS 137 (11, P + 1), 136 (100, P), 135 (27), 121 (10), 117 (10), 85 (18), 84 (22), 71 (13), 70 (29), 69 (35), 68 (7), 67 (10). The basic layer contained three compounds with the expected mass spectra of adamantylquinoline isomers in addition to the usual four compounds containing two quinoline nuclei each.

(18) **Cuprous Decanoate (D, Quinoline).** The neutral layer contained about 12 components in comparable quantities. The basic layer contained three compounds which had the molecular weight (272) of oxybiquinolyls, one of the molecular weight (256) of a biquinolyl, and a compound of apparent molecular weight 275.

(19) **Decarboxylation of Cupric *o*-Nitrobenzoate in Refluxing Pyridine.** At the end of a 2-h period, the salt was 5% decarboxylated. After 96 h, the yield of CO_2 was 80 ± 3%.

Reaction of Pentafluorophenylcopper and Quinoline. Approximately 0.2 mmol of pentafluorophenylcopper (Pierce) was heated in quinoline (10 mL) under nitrogen at the temperature which was maintained during the majority of the decarboxylation reactions (197 °C). The basic layer from this reaction was coinjected with the basic layer from the decarboxylation of cuprous pentafluorobenzoate. This indicated that, except for two minor components in the cuprous pentafluorobenzoate product, the basic layers of the two reaction mixtures contained the same compounds. The comparison of the mass spectra of compounds in the basic layer also indicated that at least two of the biquinoline isomers were the same in both reactions. However, it appears that there is somewhat less arylated quinoline product formed in the reaction of pentafluorophenylcopper.

Preparation of Anhydrides. All of the anhydrides with the exception of *o*-fluorobenzoic anhydride were prepared as follows. A benzene solution of the acid and a slight excess of thionyl chloride were heated at reflux for 4 h. The cooled solution was added to a benzene solution containing 1 equiv of the acid and 2 equiv of pyridine. After the solution had been stirred for 10 min, it was washed consecutively with aqueous sodium bicarbonate and with water and evaporated. The anhydrides were recrystallized from benzene–hexane.

***o*-Fluorobenzoic Anhydride.** The acid was dehydrated in 57% yield with acetic anhydride.[67] Recrystallization from benzene–hexane provided white crystals: mp 58.0–59.0 °C; ^1H NMR ($CDCl_3$) δ 8.07 (t of d, 2 H, $J_{6,F} = J_{5,6} = 8$ Hz, $J_{4,6} = 2$ Hz, H-6) and 7.85–6.93 (m, 6 H, aromatic); IR (Nujol) 1783 (s) and 1706 (s, carbonyl), 1616 (m), 1587 (m), 1488 (m), 1305 (m), 1279 (m), 1220 (s, br, carbon fluorine[65a]), 1168 (m), 1157 (m), 1110 (m, br), 1060 (m), 984 (m, br), 773 (m), 760 (s, br), 740 (s), 680 (m, br) cm^{-1}; MS 262 (8, P), 123 (100, $C_6H_4FCO^+$), 95 (24, $C_6H_4F^+$), 75 (13); 15-eV mass spectrum 262 (23, P), 234 (13), 218 (12), 123 (100); high-resolution MS calcd for $C_{14}H_8F_2O_3$, 262.0441; found, 262.0433.

Cuprous *tert*-Butoxide.[15] In a glovebox under an atmosphere of nitrogen which had been deoxygenated by means of hot copper turnings, freshly prepared CuCl[68] was added to a flask containing tetrahydrofuran which had been distilled under nitrogen from $LiAlH_4$. An equivalent amount of the lithium *tert*-butoxide (prepared according to the procedure of Kamienski and Lewis,[69] except that a lithium dispersion in mineral oil was used instead of lithium rod) was slowly added to the stirred solution. After the solution had been subjected to intimate mixing, the tetrahydrofuran was carefully removed by evaporation under reduced pressure. The removal of 20 mL of tetrahydrofuran required approximately 12 h of pumping at 0.5 Torr. The dark yellow crude cuprous *tert*-butoxide was packed in a sublimator which was then removed from the glovebox. The cuprous *tert*-butoxide was sublimed at a pressure of 0.1 Torr and a temperature of 170 °C. The sublimator was thoroughly dried, returned to the drybox, and opened.

Preparation of Cuprous Carboxylates from Cuprous *tert*-Butoxide. In a glovebox under a purified nitrogen atmosphere, the sublimed cuprous *tert*-butoxide (20 mmol) was added to a solution of the acid (20 mmol) in toluene (40 mL). The mixture was stirred for 5 min and filtered. The recovered finely divided solid was washed with hot toluene in order to dissolve traces of cupric salts, dried, and placed into the reaction vessel used for the decarboxylation.

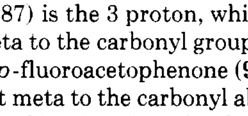
Preparation of Cupric Salts. One method consisted of adding a slight excess of aqueous cupric sulfate solution to a solution of the sodium salt of the acid at 0 °C stirring for 12 h at 25 °C, filtering, and washing the precipitated salt with cold water. A second method consisted of heating a solution of the acid in toluene or xylene at reflux for 24 h with a suspension of the stoichiometric amount of cupric carbonate with removal of the generated water by azeotropic distillation, then removing most of the solvent by distillation, and filtering the salt in a glovebox. Salt prepared by either procedure was dried in an oven at 110 °C for 24 h and stored in a vacuum desiccator for at least 12 h.

2-Deuterioquinoline. A mixture of quinaldic acid and a tenfold excess of D_2O was heated under nitrogen until the acid dissolved. The water was removed utilizing a rotary evaporator and the solid was placed in a vacuum desiccator which was evacuated by an oil pump for a period of 12 h. The above procedure was repeated twice. The solid was then distilled under nitrogen using a short-path condenser to obtain a 95% yield of (97.0 ± 0.7%) monodeuteriated quinoline. The resonance due to the 2 proton in the NMR spectrum of quinoline virtually disappeared in the labeled sample.

Acknowledgments. We thank the National Science Foundation for partial support of this work (Research Grant GP 22955 and Science Development Grant GU 3184). We also wish to thank Dr. Henry Walter for development of the program for the computer and Calcomp plotter and for help with some of the ESR spectra, Drs. Jay Mucha and David Pratt for help with ESR spectra, Messrs. Vance Bell and Richard Montgomery for mass spectra, Mr. Jim Boal for high-resolution mass spectra, Drs. James Carter and George Luther for recording the 250-MHz NMR spectra, Messrs. Paul Schuda, Timmie Governor, and Keith Knopes for technical help, and Dr. Anita Lewin for communicating unpublished results to us.

Appendix A—250-MHz ^{1}H NMR Spectrum of 2,2′-Difluorobenzophenone (8)

Secure assignments could be made for all chemical shifts and coupling constants except $J_{F,4}$, which could be estimated: ($CDCl_3$) δ 7.698 (t of d, 2 H, $J_{5,6} = J_{F,6} = 7.66$ Hz, $J_{4,6} = 1.67$ Hz, H-6), 7.515 (m, 2 H, width 26 Hz, H-4), 7.231 (t of d, 2 H, $J_{4,5} = J_{5,6} = 7.66$ Hz, $J_{3,5} = 1.00$ Hz, H-5), and 7.087 (d of d, 2 H, $J_{F,3} = 10.00$ Hz, $J_{3,4} = 8.33$ Hz, $J_{3,5} \simeq 1$ Hz, H-3).



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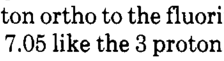

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Several points are noteworthy. The width of the multiplet at δ 7.515 is 26 Hz and was calculated to be 25 Hz, assuming that the coupling constant between the fluorine and the 4 hydrogen is equal to that between the fluorine and 6 hydrogen ($J_{F,6} = 7.66$ Hz). The proton absorbing at highest field (δ 7.087) is the 3 proton, which is ortho to a fluorine atom and meta to the carbonyl group. An analogous situation[65b] occurs in *p*-fluoroacetophenone (**9**). The proton ortho to the fluorine but meta to the carbonyl absorbs at δ 7.05 like the 3 proton in **8**, and its signal is split about equally ($J \simeq 8$ Hz) by the fluorine and the adjacent proton. The proton–fluorine coupling constants as well as the proton–proton coupling constants are consistent with those found in a series of substituted fluorobenzenes.[70]

Furthermore, the ^{1}H NMR spectrum of 2-fluorobenzoic acid, determined in the present study, exhibits a low-field peak for the 6 proton: NMR ($CDCl_3$) δ 12.53 (br s, 1 H, OH), 8.07 (t of d, 1 H, $J_{F,6} = J_{5,6} = 7$ Hz, $J_{4,6} = 2$ Hz, H-6), and 7.84–6.91 (complex, 2 H, aromatic). The 6 proton of *o*-fluorobenzoic anhydride exhibits the same low-field proton signal: NMR ($CDCl_3$) δ 8.07 (t of d, 2 H, $J_{F,6} = J_{5,6} = 8$ Hz, $J_{4,6} = 2$ Hz, H-6), and 7.85–6.93 (complex, 6 H, aromatic).

Appendix B—Calculation of Proton Balance

Presumably, the hydrogen replacing the carboxylate group is supplied, at least in part, from that released in the formation of biquinolyls, oxybiquinolyls, and arylquinolines; in this way we can account for the increase in arene which accompanies an increase in quinoline-containing products (Table VI). In the decarboxylation of cuprous *p*-nitrobenzoate in which 13.9 mmol (93%) of carbon dioxide was released, it can be determined from the yields of quinoline-containing products that their formation would liberate 9.8 mg-atoms of hydrogen, which is 88% of the 11.2 mg-atoms required for the replacement of the carboxylate group by hydrogen during the production of the 11.2 mmol (74%) of nitrobenzene which was formed.

Registry No.—Cuprous *o*-methoxybenzoate, 64508-60-7; pyridine, 110-86-1; quinoline, 91-22-5; *o*-nitrobenzoic acid, 552-16-9; cuprous *tert*-butoxide, 35342-67-7; cuprous oxide, 1317-39-1; *o*-nitrobenzoic acid anhydride, 49619-45-6; cupric *o*-nitrobenzoate, 5819-30-7; nitrobenzene, 98-95-3; 2,2′-dinitrobiphenyl, 2436-96-6; 3-methyl-2-nitrobenzoic acid anhydride, 64508-61-8; 3,3′-dimethyl-2,2′-dinitrobiphenyl, 64508-62-9; *o*-nitrotoluene, 88-72-2; cupric *p*-nitrobenzoate, 5819-29-4; 2-quinolinol, 59-31-4; cupric benzoate, 533-01-7; benzophenone, 119-61-9; 2-benzoylquinoline, 16576-25-3; quinaldyl chloride, 50342-01-3; *N*-(2-quinolyl)-2-quinolone, 10168-37-3; *o*-fluorobenzoic acid anhydride, 64508-63-0; cupric *o*-fluorobenzoate, 50671-56-2; 2,2′-difluorobenzophenone, 342-23-4; 2,2′-difluorobiphenyl, 388-82-9; cupric 1-naphthoate, 14041-38-4; naphthalene, 91-20-3; cupric 3-methyl-4-nitrobenzoate, 64508-41-4; 6-methyl-2-nitrobenzoic acid, 13506-76-8; *m*-nitrotoluene, 99-08-1; cupric *o*-methylbenzoate, 5819-24-9; 2,2′-dimethylbiphenyl, 605-39-0; cuprous pentafluorobenzoate, 27269-46-1; cupric pentafluorobenzoate, 46251-93-8; decafluorobiphenyl, 434-90-2; cupric 2,6-dimethylbenzoate, 64508-42-5; *m*-xylene, 108-38-3; cupric *o*-*tert*-butylbenzoate, 64508-43-6; *tert*-butylbenzene, 98-06-6; cupric α-picolinate, 6955-25-5; cupric quinaldate, 64508-44-7; cupric *N*,*N*-dimethylphthalamate, 64508-45-8; cuprous *N*,*N*-dimethylphthalamate, 64508-46-9; *N*,*N*-dimethylbenzamide, 611-74-5; cuprous 1-adamantanecarboxylate, 64508-47-0; cupric 1-adamantanecarboxylate, 64508-48-1; adamantane, 281-23-2; cupric decanoate, 28567-33-1; cuprous decanoate, 64508-49-2; pentafluorophenylcopper, 18206-43-4; 3-methyl-2-nitrobenzoic acid, 5437-38-7; *o*-fluorobenzoic acid, 445-29-4; CuCl, 7758-89-6; lithium *tert*-butoxide, 1907-33-1; *p*-fluoroacetophenone, 403-42-9; 6-chloro-2-nitrobenzoic acid, 5344-49-0; benzoic anhydride, 93-97-0; benzoic acid, 65-85-0; *p*-nitrobenzoic anhydride, 902-47-6; *o*-methoxybenzoic anhydride, 64508-50-5.

Supplementary Material Available: relative peak heights of the biquinolyls and oxybiquinolyls produced by interaction with the quinoline solvent (Table IV), yields of nitrobenzene and 2,2′-dinitrobiphenyl in the decarboxylation of cuprous *o*-nitrobenzoate under various conditions (Table V), and complete mass spectrometric data, obtained by combined GLC–MS, for all arenes and arylquinolines presented in the order in which they are described in the Experimental Section (4 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) Taken from the Ph.D. Theses of Ronald W. Berninger (1972) and John T. Wood (1974), submitted to the University of Pittsburgh; (b) NDEA and Center of Excellence Research Fellow; (c) Mellon, NDEA, and Stouffer Fellow.

(2) (a) H. G. Rule and F. R. Smith, *J. Chem. Soc.*, 1096 (1937); (b) L. F. Fieser and M. Fieser, "Organic Chemistry", D. C. Heath and Co., Boston, Mass., 1944, p 549; (c) H. R. Snyder, R. G. Handrich, and L. A. Brooks, "Organic Synthesis", Collect. Vol. III, Wiley, New York, N.Y., 1955, p 471; (d) P. H. Leake, *Chem. Rev.*, **56,** 27 (1956), and references cited therein; (e) J. March, *J. Chem. Educ.*, **40,** 212 (1963); (f) N. R. Smith and R. H. Wiley, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 337; (g) M. Fieser and L. F. Fieser, "Reagents for Organic Synthesis", Vol. III, Wiley-Interscience, New York, N.Y., 1972, p 63; (h) H. N. Rydon and J. C. Tweddle, *J. Chem. Soc.*, 3499 (1955); (i) E. Piers and R. K. Brown, *Can. J. Chem.*, **40,** 559 (1962); (j) R. S. Montgomery and E. D. Holly, *Fuel* (*London*), **37,** 181 (1958).

(3) A. F. Shepard, N. R. Winslow, and J. R. Johnson, *J. Am. Chem. Soc.*, **52,** 2083 (1930).

(4) T. Cohen and R. A. Schambach, *J. Am. Chem. Soc.*, **92,** 3189 (1970).

(5) This interesting redox reaction has been studied by F. J. Rattay, M.S. Thesis, University of Pittsburgh, 1970.

(6) (a) M. Nilsson, *Acta Chem. Scand.*, **20,** 423 (1966); (b) M. Nilsson and C. Ullenius, *ibid.*, **22,** 1998 (1968).

(7) (a) M. Nilsson, *Tetrahedron Lett.*, 679 (1966); (b) M. Nilsson and C. Ullenius, *Acta Chem. Scand.*, **25**, 2428 (1971); (c) J. Chodowska-Palicka and M. Nilsson, *ibid.*, **24**, 3353 (1970); (d) C. Björklund and M. Nilsson, *ibid.*, **22**, 2585 (1968).

(8) This technique has been used previously to demonstrate the accumulation of an arylcopper intermediate during the copper-induced Ullmann coupling of *p*-iodotoluene in quinoline: A. H. Lewin and T. Cohen, *Tetrahedron Lett.*, 4531 (1965).

(9) A. Cairncross, J. R. Roland, R. M. Henderson, and W. A. Sheppard, *J. Am. Chem. Soc.*, **92**, 3187 (1970).

(10) Whereas in most copper–quinoline decarboxylations the unsaturation is conjugated with the carboxyl group, Trost and Kinson have recently reported that fluorene-9-carboxylic acid undergoes such decarboxylation: B. M. Trost and P. L. Kinson, *J. Org. Chem.*, **37**, 1273 (1972).

(11) (a) T. W. J. Taylor and C. E. J. Crawford, *J. Chem. Soc.*, 1130 (1934); (b) J. Klein and E. Shekhori, *Isr. J. Chem.*, **6**, 701 (1968).

(12) J. Chodowska-Palicka and M. Nilsson, *Acta Chem. Scand.*, **25**, 3451 (1971).

(13) D. A. Edwards and R. Richards, *J. Chem. Soc., Dalton Trans.*, 2463 (1973).

(14) T. Cohen and A. H. Lewin, *J. Am. Chem. Soc.*, **88**, 4521 (1966).

(15) T. Tsuda, T. Hashimoto, and T. Saegusa, *J. Am. Chem. Soc.*, **94**, 658 (1972). After our work was complete, a report appeared describing the preparation of cuprous cyanoacetate by the use of cuprous *tert*-butoxide: T. Tsuda, T. Nakatsuka, T. Hirayama, and T. Saegusa, *J. Chem. Soc., Chem. Commun.*, 557 (1974).

(16) (a) After much of the work reported here was completed, there appeared a report[13] describing the preparation of several copper(I) carboxylates by reduction of the cupric carboxylates with copper metal in acetonitrile solution. (b) When a 0.37 M pyridine solution of cupric *o*-nitrobenzoate, in the absence of copper metal, was heated at 116 °C the apparent first-order rate constant for decarboxylation was about 100 times less than that for cuprous benzoate; see Experimental Section.

(17) R. G. Salomon and J. K. Kochi, *J. Am. Chem. Soc.*, **95**, 1889 (1973).

(18) B. J. Hathaway, D. G. Holah, and J. D. Postlethwaite, *J. Chem. Soc.*, 3215 (1961); M. Kubota and D. L. Johnson, *J. Inorg. Nucl. Chem.*, **29**, 769 (1967).

(19) These yields assume that one carboxylate ion can produce one acyl- or arylquinoline. However, it may be at least as reasonable to assume that two carboxylate ions are required for the production of each molecule of acyl- or arylquinoline, according to the following equations:

$$2ArCO_2Cu + C_9H_7N \rightarrow C_9H_6NCOAr + ArH + Cu_2O + CO_2$$
$$2ArCO_2Cu + C_9H_7N \rightarrow C_9H_6NAr + ArH + 2Cu + 2CO_2$$

However, if these equations are used in yield calculations, confusion may arise in the calculation of material balances of aryl groups.

(20) T. Cohen, J. Wood, and A. G. Dietz, Jr., *Tetrahedron Lett.*, 3555 (1974), and references cited therein.

(21) T. Cohen, K. W. Smith, and M. D. Swerdloff, *J. Am. Chem. Soc.*, **93**, 4303 (1971); A. H. Lewin, A. H. Dinwoodie, and T. Cohen, *Tetrahedron* **22**, 1527 (1966).

(22) A. Cairncross and W. A. Shepphard, *J. Am. Chem. Soc.*, **90**, 2186 (1968); G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Bashe, and H. O. House, *ibid.*, **91**, 4871 (1969).

(23) The labeled quinoline was produced by an efficient procedure consisting of the pyrolysis under nitrogen of carboxy-labeled deuterioquinaldic acid; the mechanism of this decarboxylation has been studied by B. R. Brown and D. L. Hammick, *J. Chem. Soc.*, 173, 659 (1949). 2-Deuteriopyridine has been prepared in a similar manner: A. J. Zoltewicz, C. L. Smith, and J. D. Meyer, *Tetrahedron*, **24**, 2269 (1968). 2-Deuterioquinoline has previously been prepared by reduction of 2-chloroquinoline by tin in DCl: J. Metzger, H. Larive, E. Vincent, and R. Dennilauler, *Bull. Soc. Chim. Fr.*, 46 (1967).

(24) A. Cairncross and W. A. Sheppard, *J. Am. Chem. Soc.*, **93**, 247 (1971).

(25) T. Cohen and M. D. Treblow, *J. Org. Chem.*, **41**, 1986 (1976).

(26) J. K. Kochi in "Free Radicals", Vol. I, J. K. Kochi, Ed., Wiley-Interscience, New York, N.Y., 1973, Chapter 11.

(27) For example, any tolylcopper(I) produced in the first stage of the Ullmann coupling many readily undergo oxidative addition by an iodotoluene molecule to produce the copper(III) species Ar_2CuI[28,29] (quinoline could also be involved as a ligand) which could be the organocopper precursor of biaryl detected in the reaction of *p*-iodotoluene with copper in quinoline solvents.[8] In the present case such a route is unavailable to arylcopper(I) intermediates and reaction with solvent may be the course taken.

(28) (a) For discussions of the formation of copper(III) compounds by oxidative additions to arylcopper(I) compounds and extensive references, see ref 20 and 30; (b) a similar oxidative addition of C–H to copper(I) has been suggested to account for the hydrogen removal from ether solvents by arylcopper intermediates.[25]

(29) T. Cohen, R. J. Lewarchik, and J. Z. Tarino, *J. Am. Chem. Soc.*, **96**, 7753 (1974).

(30) T. Cohen and I. Cristea, *J. Am. Chem. Soc.*, **98**, 748 (1976).

(31) An apparently analogous arylation of a nitrogen heterocycle has been reported by P. G. Cookson and G. B. Deacon, *J. Organomet. Chem.*, **33**, C38 (1971); the decarboxylation of nickel fluoroarenecarboxylates bearing a 1,10-phenanthroline ligand yielded aryl-substituted phenanthrolines.

(32) Private communication from Dr. A. H. Lewin, Research Triangle Institute.

(33) G. W. Parshall, *Acc. Chem. Res.*, **8**, 113 (1975).

(34) G. M. Whitesides, E. R. Stedronsky, C. P. Casey, and J. San Filippo, Jr., *J. Am. Chem. Soc.*, **92**, 1426 (1970).

(35) G. van Koten and J. G. Noltes, *J. Chem. Soc., Chem. Commun.*, 59 (1972).

(36) T. Saegusa, Y. Ito, H. Kinoshita, and S. Tomita, *Bull. Chem. Soc. Jpn.*, **43**, 877 (1970).

(37) Chodowska-Palicka and Nilsson[12] studied the kinetics of decarboxylation of this salt over a greater concentration range and reported an increase in rate constant with decreasing concentration which was not very far outside the error limits of their data.

(38) The apparent decarboxylation of cupric *o*-nitrobenzoate in pyridine may be due to reduction of cupric ion by the solvent as was shown to occur in quinoline.[4,5]

(39) K. B. Wiberg, "Physical Organic Chemistry", Wiley, New York, N.Y., 1964, p 378.

(40) P. E. Fanta, *Chem. Rev.*, **38**, 139 (1946); **64**, 613 (1964); *Synthesis*, 9 (1974); M. Goshaev, O. S. Otroshchenko, and A. S. Sadykov, *Russ. Chem. Rev.*, **41**, 1046 (1972).

(41) R. G. R. Bacon and H. A. O. Hill, *Q. Rev., Chem. Soc.*, **19**, 95 (1965).

(42) A. E. Jukes, *Adv. Organomet. Chem.*, **12**, 215 (1974).

(43) V. A. Nefedov and L. K. Tarygina, *J. Org. Chem. USSR*, **12**, 1730 (1976); A. Bruggink and A. McKillop, *Tetrahedron*, **31**, 2607 (1975).

(44) G. van Koten, J. T. B. H. Jastrzebski, and J. G. Noltes, *Tetrahedron Lett.*, 223 (1976); A. Commercon, J. Normant, and J. Villieras, *J. Organomet. Chem.*, **93**, 415 (1975).

(45) (a) B. Liedholm, *Acta Chem. Scand. B*, **30**, 141 (1976); (b) B. Liedholm, *Acta Chem. Scand.*, **23**, 3175 (1969).

(46) T. Ito and K. Watanabe, *Bull. Chem. Soc. Japan*, **41**, 419 (1968); H. Weingarten, *J. Org. Chem.*, **29**, 977, 3624 (1964); A. L. Williams, R. E. Kinney, and R. F. Bridger, *ibid.*, **32**, 2501 (1967).

(47) M. Sato, I. Motoyama, and K. Hata, *Bull. Chem. Soc. Jpn.*, **43**, 1860, 2213 (1970).

(48) R. G. R. Bacon and H. A. O. Hill, *J. Chem. Soc.*, 1097 (1964).

(49) C. E. Castro, R. Havlin, V. K. Honwad, A. Malte, and S. Mojé, *J. Am. Chem. Soc.*, **91**, 6464 (1969).

(50) T. Cohen and T. Poeth, *J. Am. Chem. Soc.*, **94**, 4363 (1972).

(51) Whereas the evidence[8,50] for an organocopper intermediate in the Ullmann biaryl coupling has been generally accepted[40,42] and an organocopper(III) intermediate is widely believed to be involved in the exchange reaction of aryl and vinyl halides with organocopper(I) compounds,[52] there has been considerable resistance[44,45a] to the suggestion[14,20] that other exchange reactions involving copper(I) proceed by an organometallic intermediate. This skepticism is based mainly on the fact that biaryl coupling occurs as a side reaction only occasionally[14,47] in such reactions. However, the suggested mechanism[20] readily accounts for this fact; no coupling of the organocopper derivative will occur when its rate of coupling is substantially slower than its rate of oxidation by the copper(II) salt. Failure in some cases to trap the organocopper with proton sources could have a similar explanation.

(52) G. H. Posner, *Org. React.*, **22**, 253 (1975). See also: P. Vermeer, J. Meijer, and L. Brandsma, *Recl. Trav. Chim. Pays-Bas*, **95**, 113 (1975); R. G. Pearson and C. D. Gregory, *J. Am. Chem. Soc.*, **98**, 4098 (1976).

(53) A. G. Dietz, Jr., Ph.D. Thesis, University of Pittsburgh, 1975.

(54) R. Lapouyade, M. Daney, M. Lapenue, and H. Bouas-Laurent, *Bull. Soc. Chim. Fr.*, 720 (1973); J. Jennen, *Bull. Soc. Chim. Belg.*, **46**, 199 (1937).

(55) T. Cohen and I. H. Song, *J. Org. Chem.*, **31**, 3058 (1966); T. Cohen, I. H. Song, and J. H. Fager, and G. L. Deets, *J. Am. Chem. Soc.*, **89**, 4968 (1967).

(56) Similar substituent effects were also observed during the oxidative addition of aryl halides to a palladium(0) complex: P. Fitton and E. A. Rick, *J. Organomet. Chem.*, **28**, 287 (1971).

(57) (a) F. J. Rattay, M.S. Thesis, University of Pittsburgh, 1970, p 27; (b) *ibid.*, p 21.

(58) E. Besthorn, *Ber.*, **41**, 2001 (1908).

(59) E. Besthorn and J. Ibele, *Ber.*, **39**, 2329 (1906); J. W. Davis, Jr., *J. Org. Chem.*, **24**, 1691 (1959).

(60) Of the 28 possible biquinolyls, 21 have been reported. Two of these have melting points which correspond to those of biquinolyls 1 and 2: 4,6′-biquinoline, mp 122 °C,[61] and 6,8′-biquinoline, mp 107–108 °C.[62]

(61) W. Koenigs and J. U. Nef, *Ber.*, **20**, 632 (1887).

(62) F. H. Case and A. Idelson, *J. Org. Chem.*, **27**, 4651 (1962).

(63) Of the 28 possible diquinolyl ethers, 16 have been reported. The literature[64] melting point (175 °C) of 2,8′-diquinolyl ether is very close to that of oxybiquinolyl 1.

(64) P. Cohn, *Monatsh. Chem.*, **17**, 667 (1896).

(65) (a) R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds", 2nd ed, Wiley, New York, N.Y., 1967, p 102; (b) *ibid.*, 1st ed, p 143.

(66) E. J. Moriconi, W. F. O'Connor, and W. F. Forbes, *J. Am. Chem. Soc.*, **84**, 3928 (1962).

(67) A modification of literature procedures was used: W. Autenrieth and G. Thomae, *Ber.*, **57**, 423 (1924); E. Berliner and L. H. Altschul, *J. Am. Chem. Soc.*, **74**, 4110 (1952).

(68) R. N. Keller and H. D. Wycoff, *Inorg. Synth.*, **2**, 1 (1946).

(69) C. W. Kamienski and D. H. Lewis, *J. Org. Chem.*, **30**, 3498 (1965).

(70) J. E. Loemker, J. M. Read, Jr., and J. H. Goldstein, *J. Phys. Chem.*, **72**, 991 (1968).