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Competition between Reduction, Hydroxylation, and Cyclization in Copper(I)-Promoted Aryldiazonium Ion Reactions

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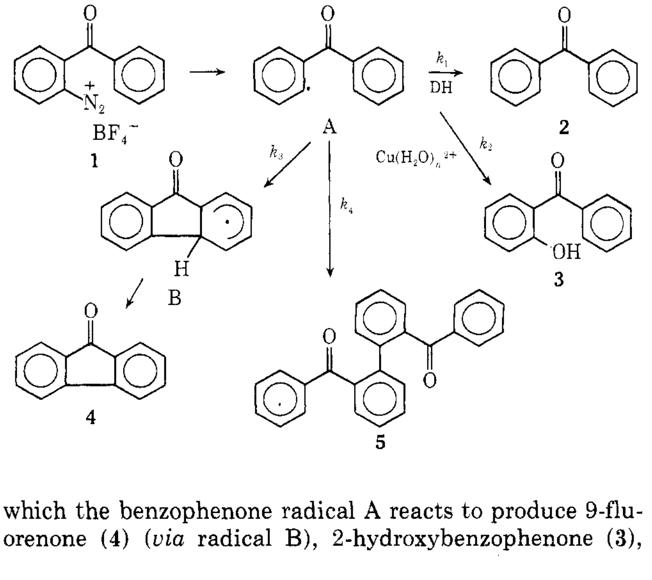
The relative rate constants for reduction, phenol formation, and cyclization of the radical produced in the copper(I)-promoted decomposition of 2-diazobenzophenone tetrafluoroborate are 4, 2, and 1, respectively. In solutions containing 15% or more dioxane, however, the rate constant for phenol formation is drastically reduced by micelle formation. A pH-dependent competition between dimerization and cyclization is reported.

Although copper-promoted aryldiazonium ion decompositions had traditionally been utilized largely in the Sandmeyer, Pschorr, and Meerwein reactions, it has been shown that products other than those traditional ones can be made to predominate by choice of the appropriate reaction conditions. Thus, it has recently been reported that biaryls and azoarenes are produced when excess copper(I) is used in the decomposition of *p*-nitrobenzenediazonium tetrafluoroborate in acetone[2] and high yields of biaryl are obtained at high copper(I) to diazonium salt ratios in the decomposition of 2-diazobenzophenone tetrafluoroborate in water.[3] Previously it had been shown that good yields of phenol can be obtained, even in systems prone to Pschorr cyclization, in the presence of a large excess of cupric ions[4] and that reduction products predominate if hydrogen donors, such as dioxane, are present.[4] The advantage of carrying out Sandmeyer reactions in the presence of excess cupric ion and excess ligand has also been pointed out.[5] We had become interested in examining the relative rates and competitions between these various pathways and had selected the 2-diazobenzophenone system for study, owing to the extensive information available on it.[3,4,6]

Results and Discussion

Scheme I
Reaction Pathways in the Copper(I)-Promoted Decomposition of 2-Diazobenzophenone Tetrafluoroborate



In considering the copper(I)-promoted decomposition of 2-diazobenzophenone tetrafluoroborate as represented in Scheme I, we wished to evaluate the relative rates by which the benzophenone radical A reacts to produce 9-fluorenone (4) (*via* radical B), 2-hydroxybenzophenone (3), and benzophenone (2). The rate expression for the rearrangement of radical A to radical B unquestionably can be formulated as

$$\frac{d[B]}{dt} = k_3[A] \tag{1}$$

and since this reaction is most likely irreversible, the rate of formation of 9-fluorenone can be expressed in the same way.

$$\frac{d[\mathbf{4}]}{dt} = k_3[A] \tag{2}$$

It has been shown[3,4] that the major pathway to the formation of benzophenone is *via* the abstraction of a hydrogen atom from a hydrogen donor; therefore the rate of formation of benzophenone is expressed by

$$\frac{d[\mathbf{2}]}{dt} = k[A][DH] \tag{3}$$

No rate expression can be written, with any degree of certainty, for dimer formation, because the reaction pathway is presently unknown. The biphenyl may be formed by radical coupling,[3] free-radical arylation of benzophenone,[7] and/or arylcopper coupling.[2]

It had been shown by Lewin and Cohen that phenol production was favored in aryldiazonium salt decompositions in aqueous acid containing a large excess of cupric ion.[4] The reaction pathway proposed involved the transfer of $H_2O\cdot^+$ from the aquation sphere of cupric ion followed by loss of a proton.[4] The argument was based on two observations: (a) the yield of phenol was unaffected by the addition of excess sodium nitrate and therefore nitrate was not the ligand being transferred; (b) the yield of phenol remained constant in reactions in which the acidity was varied 100-fold and therefore the transfer of OH· from $Cu(OH)(H_2O)_n^+$, which is in equilibrium with aquated copper, was not likely to be the source of phenol.[4] In fact, Lewin and Cohen[4] performed their experiments in 1, 0.1, and 0.01 *N* H_2SO_4 containing an excess (124 mmol) of cupric nitrate, which hydrolyzes and tends to act as a buffer, so that the acidity change is not quite as described. In addition, only decompositions at pH <1.25 could be examined by Lewin and Cohen[4] owing to the insolubility and resulting ineffectiveness of copper(I) oxide in less acidic solutions.[3] We examined the product composition of copper(I)-promoted decompositions of 2-diazobenzophenone tetrafluoroborate as a function of pH in the range 0.45–4.4 using copper(I) oxide at pH <1 and tetrakis(phyridine)copper(I) perchlorate at pH >1[3] (Table I). Since the yield of phenol shows only minor variations while the acidity is changed by a factor of 10^4, the original

Table I
Effect of Increasing Acidity in the Copper(I)-Promoted Decomposition of 2-Diazobenzophenone Tetrafluoroborate (1) in the Presence of Excess Copper(II)[a]

			Product yields, %[d,e]			
No.[b]	pH[c]	Catalyst	Benzophenone (2)	2-Hydroxybenzophenone (3)	9-Fluorenone (4)	2,2′-Dibenzoylbiphenyl (5)
1[b]	3.5	$(py)_4CuClO_4$[f]	1.2	4.1	30.3	64.4
2[b]	0.6	$(py)_4CuClO_4$[f]	1.2	g	63.7	25.1
3	4.4	$(py)_4CuClO_4$[f]	1.8	7.0	22.6	68.6
4	2.5	$(py)_4CuClO_4$[f]	1.9	7.5	22.4	68.2
5	1.6	$(py)_4CuClO_4$[f]	4.8	9.0	40.0	46.2
6	1.3	$(py)_4CuClO_4$[f]	4.9	8.6	38.0	48.5
7	0.95	Cu_2O[h]	3.2	6.9	42.6	47.3
8	0.72	Cu_2O[h]	2.1	7.5	43.1	48.3
9	0.5	$(py)_4CuClO_4$[f]	8.2	9.5	52.2	30.1
10	0.45	Cu_2O[h]	12.9	9.7	36.3	41.1

[a] Reaction of 0.6 mmol of 2-diazobenzophenone tetrafluoroborate in 30 ml of aqueous H_2SO_4 with 5.0 mmol of cupric nitrate. [b] Runs 1 and 2 are without cupric nitrate. [c] The pH was measured before addition of the Cu(I) catalyst. [d] Determined by vpc analysis *vs.* hexadecane as added internal standard. [e] Normalized to 100%; overall recovery was 85–100%. [f] Tetrakis(pyridine)copper(I) perchlorate (1.0 mmol). [g] Present, but less than 1% of the overall reaction products. [h] Ultrapure (99+%) cuprous oxide (0.42 mmol).

Table II
Product Composition and Relative Rate Constants in the Copper(I) Oxide Promoted Decomposition of 2-Diazobenzophenone Tetrafluoroborate (1)[a] with Added Cupric Nitrate[b]

	Product yields, %[c,d]				
$Cu(NO_3)_2$, mmol	Benzophenone (2)	2-Hydroxybenzophenone (3)	9-Fluorenone (4)	2,2′-Dibenzoylbiphenyl (5)	k_2/k_3,[e] l./mol
0	5.6	f	41.2	53.2	
3.5	3.6	8.1	44.0	44.3	1.56
10.0	2.8	15.3	35.3	46.7	1.29
25.0	1.1	38.6	24.9	35.4	1.86
50.0	0.6	52.2	16.3	30.9	1.92

[a] Reaction of 0.6 mmol of 2-diazobenzophenone tetrafluoroborate and 0.42 mmol of copper(I) oxide (99+% pure) in 30 ml of aqueous sulfuric acid at constant pH. [b] Added as cupric nitrate trihydrate. [c] Determined by vpc analysis *vs.* hexadecane as the added internal standard. [d] Normalized to 100%; overall recovery was 75–110%. [e] Ratio of rate constants for the formation of 2-hydroxybenzophenone (3) and 9-fluorenone (4). [f] Present, but less than 0.5% of the overall reaction products.

Table III
Product Composition and Relative Rate Constants in the Copper(I) Oxide Promoted Decomposition of 2-Diazobenzophenone Tetrafluoroborate (1)[a] with Added Dioxane

		Product yields, %[b,c]				
Dioxane %	Dioxane Mmol	Benzophenone (2)	2-Hydroxybenzophenone (3)	9-Fluorenone (4)	2,2′-Dibenzoylbiphenyl (5)	k_1/k_3,[d] l./mol
0	0	5.6	e	41.2	53.2	
5	18	63.2	e	26.4	10.4	3.63
15	51	84.3	e	14.5	1.2	3.18
45	153	95.5	e	4.5	0	3.90
75	253	97.6	e	2.4	0	4.50
100	340	98.0	e	2.0	0	4.08

[a] Reaction of 0.6 mmol of 2-diazobenzophenone tetrafluoroborate and 0.42 mmol of copper(I) oxide (99+% pure) in 30 ml of solution (dioxane + 0.5 *N* H_2SO_4). [b] Determined by vpc analysis *vs.* hexadecane as the added internal standard. [c] Normalized to 100%; overall recovery was 82–106%. [d] Ratio of rate constants for the formation of benzophenone and 9-fluorenone. The yield of benzophenone was corrected by subtracting the residual yield in the absence of dioxane. [e] Present, but less than 1% of the overall reaction products.

proposal,[4] that $H_2O\cdot^+$ is the ligand being transferred, is confirmed.

The rate expression for phenol formation can, therefore, be formulated as

$$\frac{d[3]}{dt} = k_2[A][Cu(H_2O)_n{}^{2+}] \tag{4}$$

The ratios of the rate constants for the various pathways are

$$\frac{k_2}{k_3} = \frac{[3]}{[4][Cu(H_2O)_n{}^{2+}]} \tag{5}$$

$$\frac{k_1}{k_3} = \frac{[2]}{[4][DH]} \tag{6}$$

When the copper(I) oxide promoted decomposition of 2-diazobenzophenone tetrafluoroborate in aqueous acid was carried out in the presence of increasing amounts of cupric nitrate trihydrate, the yield of 2-hydroxybenzophenone increased, as expected (Table II).[3,4] From these data the ratio of the rate constants for the formation of 2-hydroxybenzophenone and 9-fluorenone was calculated, using eq 5 (Table II).

When the reaction was performed without any cupric nitrate but with increasing amounts of dioxane added, increased yields of benzophenone were obtained, in accord with expectation (Table III).[3,4] The ratio of the rate constants for the formation of benzophenone and 9-fluorenone was then calculated with these data and eq 6 (Table III).[8]

This series of reactions was next carried out in the presence of 50 mmol of cupric nitrate trihydrate. As expected, the yield of benzophenone increased until it was essentially the only product (Table IV). The ratios of the reaction rate constants, k_1/k_2, k_1/k_3, and k_2/k_3, were again calculated and are shown in Table IV.[9] The results show that the ratio of rate constants for the formation of benzophenone and 9-fluorenone (k_1/k_3) remains relatively constant through the series both with and without cupric nitrate (Tables III and IV) with the rate of hydrogen atom abstraction by the benzophenone radical A from dioxane exceeding the rate of its rearrangement to radical B by a

Table IV
Product Composition and Relative Rate Constants in the Copper(I) Oxide Promoted Decomposition of 2-Diazobenzophenone Tetrafluoroborate (1)[a] in the Presence of Cupric Nitrate[b] and with Added Dioxane

Dioxane		Product yields, %[c,d]						
%	Mmol	Benzophenone (2)	2-Hydroxy-benzophenone (3)	9-Fluorenone (4)	2,2′-Dibenzoyl-biphenyl (5)	k_1/k_2[e]	k_2/k_3,[f] l./mol	k_1/k_3,[g] l./mol
0	0	0.6	52.2	16.3	30.0			
5	18	35.6	46.9	14.5	3.0	2.09	1.93	4.02
15	51	60.5	24.8	12.5	2.2	2.42	1.18	2.82
45	153	90.5	4.5	5.0	*h*	6.60	0.54	3.54
75	253	96.0	1.2	2.8	*h*	9.42	0.26	4.02

[a] Reaction of 0.6 mmol of 2-diazobenzophenone tetrafluoroborate, 0.42 mmol of copper(I) oxide (99+% pure), and 50 mmol of cupric nitrate trihydrate in 30 ml of solution (dioxane + 0.5 *N* H_2SO_4). [b] $Cu(NO_3)_2 \cdot 3H_2O$ (50 mmol). [c] Determined by vpc *vs.* hexadecane as the added internal standard. [d] Normalized to 100%; overall recovery was 74–88%. [e] Ratio of rate constants for the formation of benzophenone and 2-hydroxybenzophenone; the yield of benzophenone was corrected. [f] Ratio of rate constants for the formation of 2-hydroxybenzophenone and 9-fluorenone. [g] Ratio of rate constants for the formation of benzophenone and 9-fluorenone; the yield of benzophenone was corrected. [h] Present, but less than 1% of the overall reaction products.

factor of *ca.* 4. The ratio of the rate constants for the formation of 2-hydroxybenzophenone and 9-fluorenone (k_2/k_3) also does not change appreciably in the absence of dioxane (Table II). The transfer of the $H_2O\cdot^+$ ligand is seen to proceed at a rate comparable to that of the rearrangement reaction (k_3). Strikingly, however, the combination of cupric nitrate and dioxane causes enormous variations in the values of k_1/k_2 and k_2/k_3 (Table IV). Since the value of k_1/k_3 is relatively constant, it appears that k_2 is misbehaved under these conditions, its value decreasing drastically with the addition of dioxane. This behavior may be accounted for taking into account the following considerations.

Water–dioxane mixtures are miscible in all proportions and the decomposition of 2-diazobenzophenone tetrafluoroborate by copper(I) oxide in this solvent is a homogeneous reaction in contrast to the same reaction in water only, where the organic products that are formed are insoluble. It seems likely that the intermediate benzophenone radical would be hydrophobic; in water–dioxane solvent it would be solvated by dioxane, possibly forming micelles. In order to form 2-hydroxybenzophenone, the ligand transfer species, $Cu(H_2O)_n^{2+}$, which is hydrophilic, must approach the dioxane-solvated benzophenone radical (micelle). As the fraction of dioxane in the dioxane–water solvent mixture increases, it would become more difficult for the hydrophilic species $Cu(H_2O)_n^{2+}$ to approach and/or enter the micelle in order to transfer $H_2O\cdot^+$ to the benzophenone radical and to form 2-hydroxybenzophenone. In accord with this explanation, the calculated value of k_1/k_2 obtained by using k_1/k_3 and k_2/k_3 from Tables III and IV, respectively, which is 2.3, agrees with the experimental value in solutions containing up to 15% dioxane (Table IV). Neither the rearrangement to radical B nor the hydrogen abstraction from dioxane would be affected by micelle formation and therefore the values of k_1 and k_3 remain constant while the value of k_2 decreases.

Surprisingly, the results in Table I show that although the yields of phenol and benzophenone are pH insensitive[10] the yield of fluorenone and dimer are pH dependent. Thus it appears that at pH above 2.5 considerably more 2,2′-dibenzoylbiphenyl is formed, at the expense of 9-fluorenone, than at pH <2.5. The extent of dimer formation had been previously related to the concentration of cuprous copper in solution, with high cuprous concentrations favoring dimerization.[3] In the reactions promoted by tetrakis(pyridine)copper(I) perchlorate the concentration of cuprous copper from dissolution of the complex is 0.033 *M*. However, at high acidity (pH <2) it seems rather unlikely that the tetrakis(pyridine)copper(I) cation would survive, owing to extensive protonation of the pyridine, and, since the cuprous state would not be stabilized, disproportionation would immediately take place.[11] Therefore the true cuprous copper concentration would be extremely small and dimerization would diminish. A similar situation would obtain in reactions promoted by copper(I) oxide.

Dimerization, under these reaction conditions, could also be attributed to the intermediacy of organocopper species.[2] Thus, Cohen[2] had found that a threefold excess of added cuprous copper and a tenfold excess of cupric ion led predominately to biaryl. It could, therefore, be argued that with a twofold excess of cuprous copper and an eightfold excess of cupric ion (conditions for the reactions in Table I) the observed yields of biaryl might be produced. The decrease in cuprous copper concentration at high acidities would lead to decreased conversion to arylcopper and consequently to lower biaryl yields.

Conclusions

The proposed[4] transfer of the radical cation of water, $H_2O\cdot^+$, as a ligand, in the formation of phenol from intermediate radicals in the copper(I)-promoted decomposition of aryldiazonium salts, has been confirmed.

The rate constants for reduction and phenol formation have been found to exceed the rate of cyclization for the 2-benzophenone radical by factors of 4 and 2, respectively. The competition between cyclization and dimerization is pH dependent, with the latter predominating at pH >2.5.

Phenol formation is seriously retarded in aqueous solutions containing in excess of 15% dioxane, apparently owing to the formation of micelles.

Experimental Section

Physicial Measurements. pH measurements were read with a Beckman Model 76 expanded-scale pH meter. The meter was standardized with buffer solutions purchased from Fisher Scientific.

Gas chromatographic analyses were carried out as described previously.[3]

Preparation and Decomposition of 2-Diazobenzophenone Tetrafluoroborate. The procedures followed have been described.[3]

Registry No.—**1**, 342-62-1; **2**, 119-61-9; **3**, 117-99-7; **4**, 486-25-9; **5**, 24018-00-6; $(py)_4CuClO_4$, 21465-66-7; Cu_2O, 1317-39-1; $Cu(NO_3)_2$, 3251-23-8.

References and Notes

(1) Taken from the dissertation of R. J. Michl, submitted to the Faculty of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry (1971).

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(3) A. H. Lewin and R. J. Michl, *J. Org. Chem.*, **38**, 1126 (1973).

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(8) The yield of benzophenone was corrected by subtracting the residual amount (5.6%) formed in the absence of dioxane.

(9) The yield of benzophenone was corrected by subtracting the residual yield (0.6%) formed in the absence of dioxane.

(10) Except for the increase in benzophenone at very low pH values.

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

Oxidation of Cyclic Amines with Ruthenium Tetroxide

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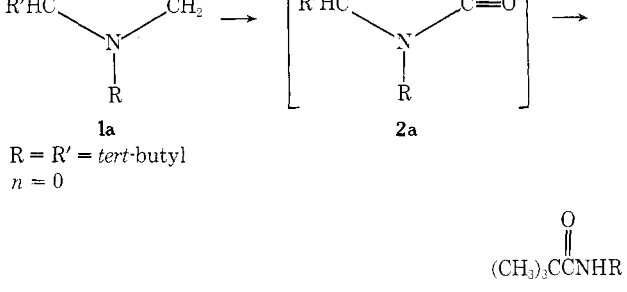
Treatment of 1,2-di-*tert*-butylaziridine with ruthenium tetroxide gave *N*-*tert*-butyl-2,2-dimethylpropionamide. The reaction involves several successive oxidations and intermediates, one of which could be an α-lactam. Treatment of acylated cyclic amines with ruthenium tetroxide gives lactams and/or imides.

The use of ruthenium tetroxide in the oxidation of organic compounds is becoming increasingly more popular. It has been used primarily in the oxidation of alkenes to aldehydes, acids, or ketones,[1] alkynes to α-diketones,[2] primary alcohols to acids,[1,3] secondary alcohols to ketones,[1,4] acyclic ethers to esters, and cyclic ethers to lactones.[1] Ruthenium tetroxide readily oxidizes aromatic systems, but is unreactive toward hydrocarbons.[1,5] Unusual oxidation insertion reactions have been reported in the oxidation of osuloses[6] and in the oxidation of a sterically hindered cyclopropanol to a β-lactone in low yield.[7]

Berkowitz and Rylander[1] applied ruthenium tetroxide oxidations to nitrogen-containing compounds. Unsubstituted amines produced only intractable mixtures under the reaction condition. Acyclic and cyclic amides were oxidized to imides in good yield. Prompted by these workers, we treated a series of cyclic amines from aziridine to piperidine with ruthenium tetroxide. Essentially similar results were obtained as those reported.[1]

Since ruthenium tetroxide does not oxidize the nitrogen atom directly, it should be possible to influence the oxidation of amines by suitable substitution on nitrogen.

The results of N-alkylation were first determined. Treatment of **1a** with 1 equiv of ruthenium tetroxide gave a low yield (10%) of *N*-*tert*-butyl-2,2-dimethylpropionamide (**3**). It appeared that several successive oxidations were occurring and this was confirmed when a higher yield of **3** was obtained with 4 equiv of oxidant.



1a
R = R′ = *tert*-butyl
n = 0

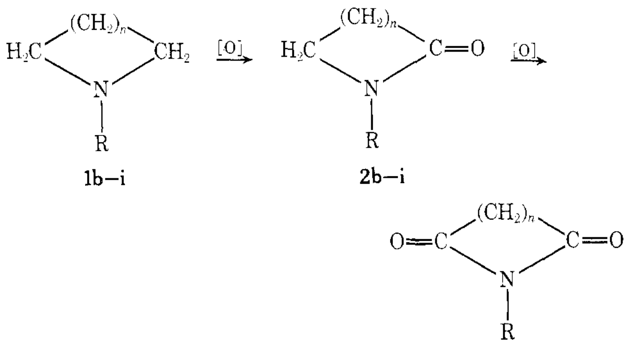
2a

3

A carbon atom is lost during the reaction. Carbon dioxide can be detected as a by-product of the oxidation. Carbon monoxide is oxidized by ruthenium tetroxide only very slowly and in very low yield, indicating that the carbon atom of the aziridine is lost as carbon dioxide.

A possible intermediate in the oxidation of aziridine **1a** is 1,3-di-*tert*-butylaziridinone (**2a**). When compound **2a** was treated with 1 equiv of RuO_4, an 11% yield of amide **3** was obtained. This yield is increased to 77% with 4 equiv of oxidant. Carbon dioxide was isolated in 91% yield. Thus it appears that the α-lactam **2a** is an intermediate in the oxidation of aziridine **1a**.

The effects of N-acylation and N-sulfonation were determined next. The results are shown in Table I for the following reaction.



1b–i **2b–i**

5d,e only

The reaction is more likely to succeed the larger the ring size and seems to be effected by the electronegativity of the N substituent. It was also noted that the rate of reaction decreases as ring size decreases and electronegativity increases.

Different classes of compounds were oxidized preferably in a single-phase rather than a double-phase system. The single-phase system requires stoichiometric amounts of the oxidant. The major disadvantage of this procedure is that a large amount of solid ruthenium dioxide must be filtered from the solution and the desired product may become occluded in the solid, thereby decreasing the