

Decomposition of Azobisisobutyronitrile in the Presence of Cupric Salts. Oxidation of α -Cyanoalkyl Radicals

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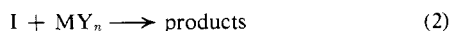
The decomposition of azobisisobutyronitrile in the presence of copper salts at 80° has been studied. It is shown that in glacial acetic acid the 2-cyano-2-propyl radical is readily oxidized by cupric chloride while cupric acetate is ineffective. The effect of water and acetonitrile as solvents on the oxidation of the 2-cyano-2-propyl radical by cupric chloride and acetate has also been studied. The results of these experiments are interpreted with reference to the electron-withdrawing effect of the α -cyano group in electron transfer and ligand transfer oxidation of alkyl radicals by metal salts.

Introduction

The oxidation of organic carbon radicals by metal salts is generally a facile process. Simple alkyl radicals are oxidized by a variety of cupric salts¹; the polymerization of vinyl monomers² and the autoxidation of aralkanes³ are effectively inhibited by cupric and ferric halides. However, little is known about the relationship between structure and reactivity of free radicals toward metal salt oxidants.

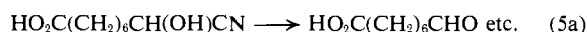
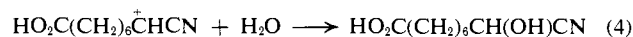
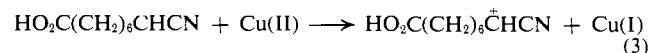
It has been postulated⁴ that the oxidation of free radicals proceeds by at least two mechanisms: electron transfer⁵ and ligand transfer.⁶ In the transition state of the former reaction path, oxidation is accompanied by a development of a positive charge on the carbon moiety, whereas the charge requirements for the ligand transfer process are more akin to atom transfer reactions of free radicals.

Telomerization reactions of various vinyl monomers with 5-(methoxycarbonyl)pentyl radical in the presence of metal salts was interpreted on this basis.⁷ It was

$$\text{CH}_3\text{O}_2\text{C}(\text{CH}_2)_4\text{CH}_2\cdot + \text{CH}_2=\text{CHX} \longrightarrow \text{CH}_3\text{O}_2\text{C}(\text{CH}_2)_4\text{CH}_2\text{CH}_2\text{CHX} \quad (1)$$


found that when X (in eq. 1) was an electron-withdrawing group such as halogen, carbonyl, or cyano, oxidation of the adduct radical I by electron transfer oxidants such as cupric acetate and perchlorate was slow, but rapid with ligand transfer reagents such as

cupric and ferric chloride. Minisci⁸ has recently reported conflicting results which indicated that the oxidation of I (X = CN) by cupric salts was independent of the anion. Cupric acetate, sulfate, and nitrate were reported to oxidize the adduct radical to suberic acid.



Related studies on the effect of metal salts on the inhibition of the polymerization of acrylonitrile, however, reveal a high selectivity of the growing α -cyanoalkyl radical II, $\sim\text{CH}_2\text{CHCN}$, toward oxidation by various metal salts. For example, Monteiro⁹ has shown that the initiated polymerization of acrylonitrile is effectively inhibited by cupric chloride. Watanabe and Kuichi¹⁰ have corroborated these results and shown further that cupric sulfate, nitrate, and acetate actually increased the rate of polymerization (probably due to the catalytic decomposition of the persulfate initiator). Entwistle¹¹ has found a similarly large variation in the effectiveness with which various ferric salts inhibit the polymerization of the related methacrylate monomer.

The effect of several metal salts on the rate of polymerization of styrene has received considerable attention.¹² The extant literature on this monomer can also be interpreted in terms of the varying reactivity of the growing benzylic radical III, $\sim\text{CH}_2\text{—CH—C}_6\text{H}_5$, toward various metal salts.⁶

In order to resolve the question of the effect of an α -cyano group on the oxidizability of alkyl radicals by various metal salts, we sought to generate these radicals in an unequivocal manner and subject them to oxidation by various metal salts. The thermolysis of azobisisobutyronitrile (ABN) is known to produce 2-cyano-2-propyl radicals, IV, and it has been shown^{6c} that in the presence of cupric chloride α -chloroisobutyronitrile is formed in 53% yield. In this paper we wish to describe studies directed toward the oxidation of this radical by metal salts. The decomposition of azobisisobutyronitrile in the presence of copper salts in a variety of solvents represents a means of directly studying the effect of the α -cyano group on the oxidation of alkyl free radicals by metal salts.

(1) H. E. De La Mare, J. K. Kochi, and F. F. Rust, *J. Am. Chem. Soc.*, **85**, 1437 (1963).

(2) C. H. Bamford, A. Jenkins, and R. Johnston, *Trans. Faraday Soc.*, **55**, 418 (1959); **58**, 1212 (1962); A. Chermick, E. Collinson, F. S. Dainton, and E. Meaburn, *Proc. Chem. Soc.*, 54 (1958).

(3) G. S. Hammond, L. R. Mahoney, and U. S. Nandi, *J. Am. Chem. Soc.*, **85**, 737 (1963).

(4) (a) J. K. Kochi, *Tetrahedron*, **18**, 483 (1962); (b) C. H. Bamford, A. Jenkins, and R. Johnston, *Trans. Faraday Soc.*, **59**, 530 (1963); (c) R. M. Haines, and W. A. Waters, *J. Chem. Soc.*, 4256 (1955).

(5) E. Collinson, F. S. Dainton, B. Mile, S. Tazuke, and D. R. Smith, *Nature*, **198**, 26 (1963); *Discussions Faraday Soc.*, **29**, 188 (1960).

(6) (a) C. H. Bamford, A. Jenkins, and R. Johnston, *Proc. Roy. Soc. (London)*, **A239**, 214 (1957); (b) J. K. Kochi, *J. Am. Chem. Soc.*, **78**, 4815 (1956); **79**, 2942 (1957); **84**, 2124 (1962); (c) J. Kumamoto, H. De La Mare, and F. F. Rust, *ibid.*, **82**, 1935 (1960).

(7) J. K. Kochi and F. F. Rust, *ibid.*, **84**, 3946 (1962); D. M. Mog and J. K. Kochi, *Chim. Ind. (Milan)*, **46**, 342 (1964).

(8) F. Minisci and R. Galli, *ibid.*, **45**, 448 (1963).

(9) H. Monteiro, *J. chim. phys.*, **59**, 2 (1962); J. Parrod and H. Monteiro, *Compt. rend.*, **251**, 2026 (1960).

(10) M. Watanabe and H. Kuichi, *J. Polymer Sci.*, **58**, 103 (1962).

(11) E. R. Entwistle, *Trans. Faraday Soc.*, **56**, 284 (1960).

(12) J. Betts, F. S. Dainton, and K. J. Ivin, *ibid.*, **58**, 1203 (1962); M. E. Mullier, *J. Polymer Sci.*, **58**, 1009 (1962); E. Collinson, *et al.*, *J. chim. phys.*, **52**, 565 (1955); M. Lefort, *ibid.*, **52**, 566 (1955).

Experimental

Materials. Metal Salts. Cupric acetate hydrate ($\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$), cupric chloride ($\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$), cupric bromide (CuBr_2), cuprous chloride (CuCl), lithium chloride (LiCl), and lithium bromide (LiBr) (analytical reagent) were obtained from Mallinckrodt Chemical Works; ferric chloride (anhydrous, FeCl_3) was from Fisher Scientific Co.; ferric bromide (FeBr_3) was obtained from City Chemical Corp.; cupric acetate (anhydrous, $\text{Cu}(\text{OAc})_2$) was from McGean Chemical Co. Anhydrous cupric chloride was prepared by heating the hydrate under vacuum. Cuprous acetate (purity 92%) was prepared from cuprous oxide in acetic acid.¹³ Azobisisobutyronitrile, from the Aldrich Chemical Co., was purified by recrystallization from methanol.

Solvents. Glacial acetic acid (99.7%) was DuPont reagent; acetonitrile, Matheson Coleman and Bell industrial grade, was purified by distillation from phosphorus pentoxide and sodium carbonate; dimethylformamide was from Rohm and Haas Co.

Benzonitrile (practical grade), valerionitrile, *n*-butyl acetate, and *sec*-butyl acetate were from Eastman Organic Chemical Co.; isobutyryl chloride was obtained from Trubek Laboratories; methacrylonitrile was from Borden Chemical Co.; pyridine (reagent grade), distilled from potassium hydroxide, and acetone cyanohydrin were from Rohm and Haas Co.; isobutyronitrile was from Eastman Chemical Products, Inc.; tetramethylsuccinonitrile (m.p. 165–167°), acetone, and methyl ethyl ketone were purified by distillation from potassium permanganate.

Preparation of Authentic Materials. α -Acetoxyisobutyronitrile was prepared from acetone cyanohydrin and acetyl chloride.¹⁴ The material was distilled through a 2-ft. spiral column, b.p. 181–183°, lit.¹⁴ 180–182° at 760 mm., $n_D^{24} - 1.4071$.

α -Chloroisobutyronitrile was prepared from isobutyronitrile and phosphorus pentachloride.¹⁵ The material was distilled using a 1-ft. Vigreux column, b.p. 115–117°, lit.¹⁵ 114–116° at 760 mm., $n_D^{26} - 1.4055$.

Isobutyramide was prepared by adding isobutyryl chloride to cold, concentrated NH_4OH , and filtering off the crude product.¹⁶ The crude material had a melting point of 125–129°, lit.¹⁶ 129°.

Kinetic Method. The first-order rate constant for the decomposition of AIBN was determined by following the rate of nitrogen evolution. All decompositions were carried out in a thermostat at $79.9 \pm 0.1^\circ$. Rate constants were determined graphically by plotting $\log (v_8 - v)$ vs. time. Good linear plots were obtained in all cases and the reproducibility of the results was better than 2%.

Decomposition of Azobisisobutyronitrile (ABN). The general procedure used in the decomposition of ABN under varying conditions can be summarized as follows. Recrystallized ABN (0.02–0.6 g.) and the metal salts (0.02–1.2 g.) were weighed into a dry 50-ml. reaction

flask fitted with a side arm, and 30–50 ml. of solvent was added. Final solution volumes, required for quantitative product analyses, were obtained either by dilution to known volume in a volumetric flask or by direct measurement of the residual volume to the nearest 0.5 ml. using a graduated container. The reaction flask and its contents were then connected to the gas collecting apparatus. A stream of nitrogen was bubbled through the solution by means of a glass capillary inserted through the side arm of the flask. After deaeration for 15–30 min., the glass capillary was removed, and the side arm was simultaneously capped with a rubber serum cap. Complete flushing of the system, to remove the oxygen above the solution, was achieved by inserting a syringe needle through the serum cap and passing a flow of nitrogen over the solution, through the system, and exhausting through a bubbler at the outlet, thus keeping the system closed to the atmosphere. The reaction vessel was placed into a thermostated bath and the contents were rapidly stirred magnetically to break the surface of the solution.

Product Identification and Analysis by Gas Chromatography. All gas chromatographic work was done using an Aerograph Hy-Fi Model 600 flame ionization detector chromatograph in conjunction with a Sargent Model SR recorder. The column used was a 5 ft. \times $\frac{3}{16}$ in. piece of stainless steel tubing filled with 20% Carbowax-4 M terephthalic acid on Chromosorb W packing. Nitrogen was used as carrier gas. Since the products of the reactions were expected to be fairly well defined, product identification was made on the basis of retention times. In some cases authentic materials were added to the reaction mixtures, and the occurrence of a single peak before and after the addition was taken as identification. Quantitative analyses of the following products was achieved by an internal standard method: tetramethylsuccinonitrile (TMSN), isobutyronitrile, α -chloroisobutyronitrile, and acetone. TMSN was standardized against benzonitrile. *n*-Valeronitrile was used as a standard for both isobutyronitrile and α -chloroisobutyronitrile, while acetone was standardized against methyl ethyl ketone. The yields of products represent an average of at least duplicate determinations which were commonly reproducible to within 1–2% and maximally to within 4%.

Limits of Detection of α -Acetoxyisobutyronitrile. A lower limit to the concentration of α -acetoxyisobutyronitrile, detectable by the methods employed, was determined by adding approximately 3 mg. of the authentic material to 10 ml. of acetic acid. This mixture was worked up by the usual methods and chromatographed. In this manner it was possible to detect a lower limit of $\sim 0.2\%$ yield of α -acetoxyisobutyronitrile based on the concentrations of starting materials used in the reactions.

Attempts to Find α -Acetoxyisobutyronitrile. ABN was decomposed in acetic acid in the presence of $\text{Cu}(\text{OAc})_2$. Sample aliquots were removed at intervals of 0.5, 1.5, and 2.5 hr. To the aliquots was added 10 ml. of benzonitrile. The benzonitrile extract was washed with water followed by saturated sodium bicarbonate until all of the acid was removed, and then by a final water wash. Gas chromatography of the extracts showed no indication of α -acetoxyisobutyronitrile.

(13) S. Weller, *J. Am. Chem. Soc.*, **75**, 770 (1953).

(14) L. Henry, *Chem. Zentr.* **II**, 661 (1898); *Bull. Acad. Roy. Med. Belg.*, [3] **35**, 173 (Beilstein III, 317).

(15) C. L. Stevens, *J. Am. Chem. Soc.*, **70**, 165 (1948).

(16) R. Shriner, R. Fuson, and D. Curtin, "Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N.Y., 1956, p. 200.

Though α -acetoxyisobutyronitrile reacts slowly in glacial acetic acid (*vide infra*), the rate of reaction is sufficiently slow that had any α -acetoxyisobutyronitrile been found it would have been detected.

Product of the Decomposition of α -Acetoxyisobutyronitrile in Acetic Acid. Authentic α -acetoxyisobutyronitrile (0.66 g.) and $\text{Cu}(\text{OAc})_2$ (0.27 g.) were dissolved in 50 ml. of glacial acetic acid and heated to 80° for 1 week. Removal of solvent yielded a white solid which could be sublimed. The sublimate had a melting point of $106\text{--}108^\circ$. The material had an infrared spectrum with bands characteristic of a primary amide as well as those characteristic of an acetate. The proton magnetic resonance spectrum in water showed two singlets in a 2:1 ratio. These results together with the elemental analysis are indicative that the acetolysis product is α -acetoxyisobutyramide. *Anal.* Calcd. for $\text{C}_6\text{H}_{11}\text{NO}_3$: C, 49.64; H, 7.64; N, 9.65. Found¹⁷: C, 49.42; H, 7.62; N, 9.63.

Determination of Cuprous Salts. The amount of cuprous species present in the reaction mixtures was determined by removing sample aliquots from the reaction mixture with a hypodermic syringe to exclude air. The amount of cuprous salt present was determined by titration with standard ceric sulfate solution (0.021 or 0.084 *N*) according to a standard procedure.¹⁸ Results are reported on the basis of single determinations. A duplicate analysis showed the method to give results which were reproducible to better than $\pm 2\%$.

Reactant and Product Stabilities under Reaction Conditions. The stabilities of the reactants and products were determined under reaction conditions. α -Acetoxyisobutyronitrile was found to be stable in pure acetic acid, but was 60% decomposed only after 24 hr. in the presence of cupric acetate (*vide supra*). Methacrylonitrile in the presence of AIBN and cupric acetate was 70% polymerized after 3.25 hr. Cuprous acetate was found to disproportionate slightly in glacial acetic acid. In the presence of ABN, the cuprous species was quite unstable with only 30% of the material left in the reduced state after 1.5 hr. Cuprous chloride, cupric acetate, tetramethylsuccinonitrile, and α -chloroisobutyronitrile were found to be stable in the acetic acid system.

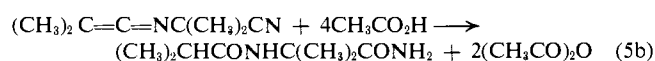
Cupric chloride was found to give some cuprous salt in glacial acetic acid at 80° . Both cupric chloride and cupric acetate were found to give a cuprous titer in systems with acetonitrile or water as solvent. Consequently, each of the values reported for per cent reduction has been maximally corrected for a blank which was determined by repeating each experiment in the absence of AIBN.

Isolation and Determination of the Diamide from the Acetolysis of the Ketenimine. The N-2-cyano-2-propyl-dimethylketenimine derived from the head-to-tail coupling of α -cyano-2-propyl radicals¹⁹ reacted readily with glacial acetic acid and could not be isolated as such. A similar result was obtained in the presence of cupric acetate. The product of acetolysis in both cases was N-isobutyryl- α -aminoisobutyramide ($(\text{CH}_3)_2\text{CHCONHC}(\text{CH}_3)_2\text{CONH}_2$, V), which was isolated by

the removal of the solvent and volatile products on a rotary evaporator. The resulting solid was powdered and subjected to vacuum sublimation at steam bath temperatures. This process removed the TMSN. The weight of the diamide remaining was then used to calculate the percentage yield. In the run with cupric acetate, the weight was first corrected for the presence of cupric acetate. The diamide was isolated by further vacuum sublimation of the crude material admixed with cupric acetate at $150\text{--}170^\circ$. It was obtained as a colorless crystalline sublimate melting at 190° ; lit.¹⁹ $189\text{--}190^\circ$. The infrared spectrum showed characteristic amide bands. The proton magnetic resonance spectrum in water showed a singlet and a doublet in a 1:1 ratio compatible with structure given above. It is undoubtedly the same compound isolated by Talât-Erben and Bywater from the hydrolysis of the ketenimine.¹⁹ *Anal.* Calcd. for $\text{C}_8\text{H}_{16}\text{N}_2\text{O}_2$: C, 55.79; H, 9.36; N, 16.27. Found: C, 55.87; H, 9.22; N, 16.10.

α -N-Isobutyramidoisobutyronitrile ($(\text{CH}_3)_2\text{CHCO-NHC}(\text{CH}_3)_2\text{CN}$). Acetone cyanohydrin was converted to acetoneaminonitrile with liquid ammonia.²⁰ The aminonitrile (0.5 g.) was treated with isobutyryl chloride (0.5 g.) in 10 ml. of benzene at 70° for 30 min. The reaction mixture was treated with water and the aqueous solution was evaporated. The amide was extracted with *n*-butyl alcohol and yielded colorless material melting at 102° .²¹ It showed the characteristic amide and nitrile bands in the infrared spectrum, and it was distinctly different from the diamide isolated from the decomposition of ABN.

Analysis for Acetic Anhydride. The acetolysis of the ketenimine to the diamide requires that 2 moles of acetic anhydride be formed concomitantly.



Acetic anhydride could not be determined directly, but *n*-butyl alcohol was added and converted to butyl acetate. The ester was determined by gas chromatography using *sec*-butyl acetate as an internal standard. After correction for ester formed in the blank run, the amount of acetic anhydride was estimated to be 70–80% of the diamide isolated (based on a 2:1 stoichiometry). Though admittedly crude, this method of analysis does support eq. 5b.

Unsuccessful Attempts to Separate the Diamide (V) from Cupric Chloride–Lithium Chloride. The diamide (V) could not be determined in the cupric chloride–lithium chloride runs by the sublimation technique used in the cupric acetate oxidations. Removal of solvent always resulted in a gummy brown solid which could not be subjected to vacuum sublimation procedures. This complication was probably due to the presence of hygroscopic lithium chloride. Attempts were made to separate the metal salts from the amide product by passing the reaction solution through a Dowex 50 cation-exchange column. The procedure was successful in removing the copper salts, but in every case the product isolated showed some amide character; however their infrared spectra did not

(17) All analyses by Galbraith Laboratories, Knoxville, Tenn.

(18) J. K. Kochi, *J. Am. Chem. Soc.*, **77**, 5274 (1955).

(19) M. Talat-Erben and S. Bywater, *ibid.*, **77**, 3710, 3712 (1955).

(20) R. A. Jacobson, *ibid.*, **68**, 2628 (1946).

(21) M. Talat-Erben, and A. N. Isfendiyaroglu, *Can. J. Chem.*, **36**, 1156 (1958).

coincide with the spectrum of the authentic material. Attempts to recover authentic diamide from solution using this procedure gave similar results. Apparently the ion-exchange column catalyzed a reaction which altered the characteristics of the product. Similar results were obtained with a mixed anion-cation bed.

Results and Discussion

In Table I is listed the first-order rate constants determined by nitrogen evolution of the thermolysis of azobisisobutyronitrile at 79.9°. First-order kinetics

Table I. Effect of Metal Salts on the Rate of ABN Decomposition^a

Metal salt added	Molarity	First-order rate constant, $k_1 \times 10^4$, sec. ⁻¹	
		Glacial HOAc	Acetonitrile
None	0	1.43 ^b	1.25
Cu(OAc) ₂	0.054	1.45	...
CuOAc	0.0069	1.48	...
CuCl ₂	0.058	1.48	1.24
CuCl	0.049	1.62	...
LiCl	0.07	1.48	...

^a At 79.9°, ABN = 0.040 M to 0.080 μ. ^b $k_1 = 1.5 \times 10^{-4}$ sec.⁻¹ at 82°: L. M. Arnett, *J. Am. Chem. Soc.*, **74**, 2027 (1952); F. M. Lewis and M. S. Matheson, *ibid.*, **71**, 747 (1949).

were generally followed to greater than 80% of the reaction even at relatively high concentrations of added salts. Numerous studies of ABN decompositions have shown that it decomposes by the rate-determining homolysis of the carbon-nitrogen bond(s) to yield a pair of 2-cyano-2-propyl radicals (IV).^{22, 23} Kinetically, the release of nitrogen from azobisisobutyronitrile is concurrent with the production of two 2-cyano-2-propyl radicals.²⁴ Thus the rate of nitrogen evolution equals the rate of radical production. The results given in Table I show that the rate of radical production is independent of the presence of the metal salts studied and that there is no induced decomposition of the ABN molecule. We can conclude that any interactions with the metal salts must involve the 2-cyano-2-propyl radical rather than the ABN molecule. This corroborates earlier studies^{6c} made with cupric chloride.

In inert solvents, the fate of the 2-cyano-2-propyl radicals is disproportionation and recombination to tetramethylsuccinonitrile VI and ketenimine VII.^{19, 22, 23, 25} Disproportionation products, isobutyronitrile, and methacrylonitrile, generally are the minor products.^{22, 26} The reversibility of reaction has been examined.²⁷ In acetic acid this reaction appears not to be reversible,

(22) A. F. Bickel and W. A. Waters, *Rec. trav. chim.*, **69**, 1490 (1950).

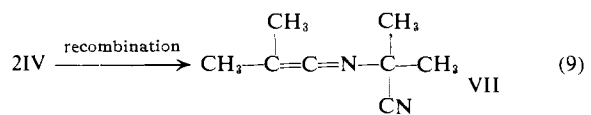
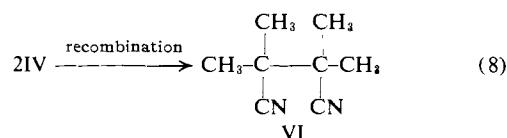
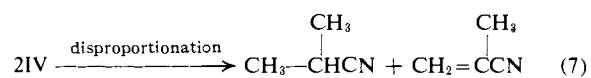
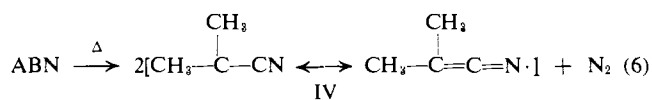
(23) G. S. Hammond, C. S. Wu, and O. D. Trapp, *J. Am. Chem. Soc.*, **82**, 5386 (1960); G. S. Hammond, J. N. Sen, and C. E. Boozer, *ibid.*, **77**, 3244 (1955).

(24) For a discussion of this question see: G. S. Hammond and R. C. Neuman, Jr., *ibid.*, **85**, 1500 (1963); H. C. Ramsperger, *ibid.*, **50**, 714 (1928); J. C. Roy, J. R. Nash, R. R. Williams, and W. H. Hamill, *ibid.*, **78**, 514 (1956); P. Smith and S. Carbone, *ibid.*, **81**, 6174 (1959).

(25) O. D. Trapp and G. S. Hammond, *ibid.*, **81**, 4877 (1959); C. S. Wu, G. S. Hammond, and J. M. Wright, *ibid.*, **82**, 5386 (1960).

(26) O. H. Grant and N. Grassie, *J. Polymer Sci.*, **42**, 587 (1960); P. W. Allen, G. Ayrey, and C. G. Moore, *ibid.*, **86**, 55 (1959).

(27) G. S. Hammond, O. D. Trapp, R. T. Keys, and D. L. Neff, *J. Am. Chem. Soc.*, **81**, 4879 (1959); P. Smith, N. Muller, and W. C. Tosch, *J. Polymer Sci.*, **57**, 823 (1962); J. C. Bevington and H. G. Troth, *Trans. Faraday Soc.*, **58**, 186 (1962).

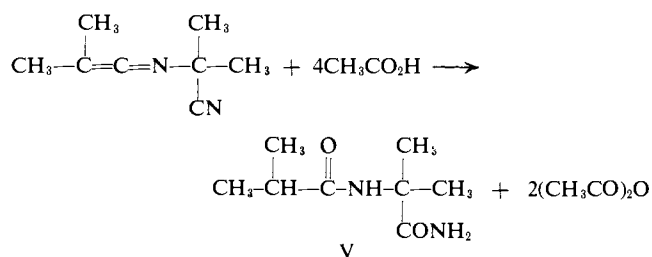


since reaction with solvent is faster than dissociation; and the acetolysis product (V) can be isolated in good yields as shown in Table II.

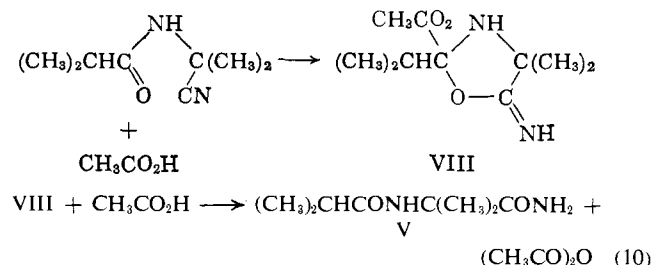
Table II. Products from the Thermolysis of ABN in Glacial Acetic Acid^a

Reactants, M			Products, %		
ABN	Cu(OAc) ₂	TMSN	Diamide	IBN + ^(b) MAN	Acetone ^c
0.30	0	42 ± 1	48	3 ± 0.5	1
0.30	0	41	..	2	..
0.45	0.080	43	47	3	2
0.11	0.040	43	..	3	..

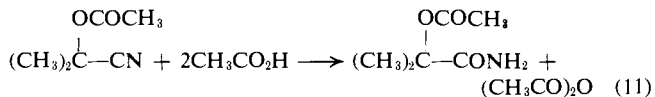
^a At 79.9°. ^b Combined yields of isobutyronitrile and methacrylonitrile. ^c Estimated yield from gas chromatography. These small amounts of acetone probably arise from the reaction of the radicals with oxygen remaining in the system after deaeration with nitrogen (see ref. 42).



The yield of by-product, acetic anhydride, was determined to be present in approximately the amount required by the stoichiometry of the acetolysis. It is interesting to note that the expected cyanoamide²¹ ((CH₃)₂CHCONHC(CH₃)₂CN) was not isolated but reacted further with acetic acid to the diamide V. Nitriles generally are not converted to amides under these mild conditions and it is possible that there is anchimeric assistance from the neighboring carbonyl group, perhaps by an intermediate such as VIII.



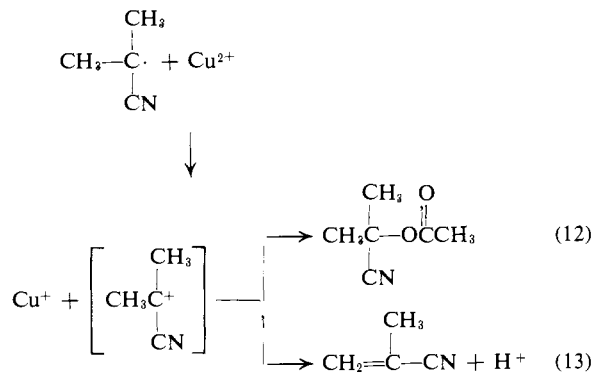
A similar product of acetolysis is obtained with α -acetoxisobutyronitrile in the presence of cupric salts under slightly more vigorous conditions.^{28a}



An assistance by a neighboring carbonyl group has also been reported in the base-catalyzed hydrolysis of a similarly constituted nitrile.^{28b}

As shown in Table II the product distribution from the decomposition of ABN in glacial acetic acid in the presence of cupric acetate is the same as that in its absence. This composition was invariant with ABN/Cu(OAc)₂ mole ratios of 6:1 and 3:1. Titration for cuprous acetate indicated that less than 1% was present.

The results in Table II indicate that cupric acetate does not participate in the decomposition of ABN or react with the radicals formed therefrom. The oxidation of 2-cyano-2-propyl radicals by cupric acetate in acetic acid *via* electron transfer²⁹ would be expected to follow the reaction sequence shown in eq. 12 and 13.



A thorough search for α -acetoxisobutyronitrile using a procedure which had been shown to be capable of detecting a 0.5% yield of product gave negative results.³⁰ This fact along with the excellent material balance (95%) shows that it is not formed, and that, furthermore, the 2-cyano-2-propyl radical is not oxidized by cupric acetate under these conditions.

In sharp contrast to these observations are the results of studies carried out in glacial acetic acid with ABN in the presence of cupric chloride. Oxidation of the 2-cyano-2-propyl radical by cupric chloride occurs by a ligand transfer mechanism⁶ to yield α -chloroisobutyronitrile and cuprous chloride (eq. 14).³¹

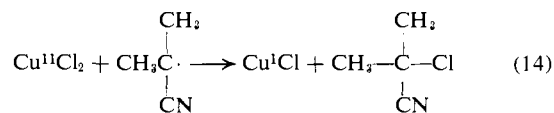
In addition to oxidation, the radicals can undergo dimerization to yield TMSN (VI) and the ketenimine

(28) (a) It is possible but improbable that the amide is the isomeric *N*-acetyl- α -hydroxyisobutyramide. Insolubility in aprotic solvents which will not obscure the hydrogen-bonded hydroxyl resonance prevented examination of the n.m.r. spectrum; (b) J. P. Freeman and G. B. Lucas, *J. Am. Chem. Soc.*, **77**, 2334 (1955).

(29) H. E. DeLaMare, J. K. Kochi, and F. F. Rust, *ibid.*, **85**, 1437 (1963); J. K. Kochi, *ibid.*, **85**, 1958 (1963).

(30) Though α -acetoxisobutyronitrile is slowly acetolyzed (*vide supra*) in the presence of cupric acetate, the rate is sufficiently slow that had any been found it would have been detected.

(31) The resonance-stabilized 2-cyano-2-propyl radical IV is shown in eq. 6 with the unpaired electron on carbon. The possibility of ligand transfer oxidation at the nitrogen site was investigated. It was found not to occur, probably for the same reason that copper salts do not oxidize thyl or alkoxy radicals.⁴⁹ Both the oxidation potential (N = 14.6 v. and C = 11.3) as well as the strengths of the N-Cl bond (47.7 kcal./mole) compared to the C-Cl bond (78.5 kcal./mole) disfavor attack at the nitrogen site (L. Pauling "Nature of the Chemical Bond" 3rd Ed., Cornell University Press, Ithaca, N. Y., 1960, pp. 57, 85).



intermediate VII which would react with solvent to yield diamide V. The yields of α -chloroisobutyronitrile (α -CIBN) and tetramethylsuccinonitrile together with the estimated yield of diamide constitute an excellent material balance in each case. These yields are shown in Table III as a function of the initial cupric

Table III. Products from ABN in the Presence of Cupric Chloride^a

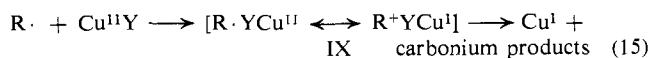
ABN	M		%			
	CuCl ₂	LiCl	CuCl ₂ /ABN	α -Cl-BN	TMSN	Diamide ^b
0.024	0.050	0.19	2.1	54	20	23
0.0085	0.056	0.28	6.6	61	17	20
0.0034	0.11	0.38	35	65	15	17

^a In glacial acetic acid at 79.9°. ^b Diamide yields were estimated assuming that the diamide-to-TMSN ratio is the same as that obtained in the absence of cupric chloride. Difficulty encountered in isolating diamide (see Experimental) precluded a more quantitative determination of this compound.

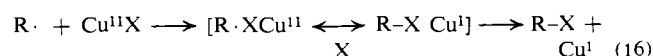
chloride-to-ABN ratio. The stoichiometry requires 2 moles of cupric chloride per mole of ABN decomposed and 1 equiv. of cuprous chloride for each α -chloroisobutyronitrile formed. However, cupric chloride reacts slowly with glacial acetic acid under these conditions,¹⁸ and the cuprous chloride formed was generally 10–15% greater than the yield of α -chloroisobutyronitrile.

The rapidity of the ligand transfer process is brought out by the fact that increasing the CuCl₂/ABN ratio 17-fold only increased the yield of oxidation product from 54 to 65%. The significant yield of TMSN in the presence of high concentrations of cupric chloride is an indication of the importance of the cage effect in the decomposition of azo compounds.³² The yield of TMSN dimer can be used to compare the ability of various metal salts to act as free-radical traps. Thus we found that CuCl₂ \cong CuBr₂ < FeCl₃ < FeBr₃. These results are in agreement with the order predicted from other studies.^{4-6,9-12}

The observed rapid oxidation of the 2-cyano-2-propyl radical by cupric and ferric bromide and chloride and the inertness of this radical with respect to oxidation by cupric acetate support our earlier contention⁷ with regard to the relative ease of oxidation of an α -cyanoalkyl radical by electron transfer and ligand transfer processes. In such a formulation oxidation by electron transfer proceeds through a transition state such as IX (eq. 15) which places a positive charge on the carbon moiety.



In a ligand transfer process the direct transference of an atom or radical from the metal oxidant to the carbon radical moderates the development of charges in the transition state such as X (eq. 16). The inability



(32) H. P. Waits and G. S. Hammond, *J. Am. Chem. Soc.*, **86**, 1911 (1964).

of the carbon moiety to accommodate a positive charge is thus a less severe limitation in ligand transfer processes.³³ The formation of carbonium ions are unfavored by electron-withdrawing substituents in the α -position⁷ and this effect is manifested by the more difficult oxidation of such radicals by electron transfer oxidants compared to ligand transfer oxidants.

Table IV gives the results of experiments carried out on ABN in the presence of cupric acetate in various solvents at 80°. In each case 1.45 mmoles of ABN and 5.5 mmoles of Cu(OAc)₂ were dissolved in 40 ml. of solvent.

Table IV. Solvent Effects on Reduction by Cupric Acetate^a

Solvent ^b	Products, %		
	Cu ^{+c}	TMSN	Acetone
HOAc	0	42	2
CH ₃ CN	4		
7:1 CH ₃ CN/DMF	20	66	
3:1 HOAc/H ₂ O	~1	40	4
1:1 HOAc/H ₂ O	<1		
1:3 CH ₃ CN/HOAc	3		
1:1 CH ₃ CN/HOAc	6		
3:1 CH ₃ CN/HOAc	13	48	
3:1 CH ₃ CN/H ₂ O ^{d,e}	15	40	10
1:1 CH ₃ CN/H ₂ O ^{d,e}	20		8
1:3 CH ₃ CN/H ₂ O ^d	6		

^a At 79.9°, ABN = 0.036 M; Cu(OAc)₂ = 0.137 M. ^b Solvent ratios are vol./vol. ^c Cupric to cuprous, based on radicals. ^d Five milliliters of HOAc added. ^e Heterogeneous.

Table V shows the results of experiments carried out on ABN in the presence of cupric chloride–lithium chloride in various solvents at 80°. In each case 0.6 mmole of ABN and 7.4 mmoles of cupric chloride were dissolved in 40 ml. of solvent.

Table V. Solvent Effects on Reduction by Cupric Chloride^a

Solvent	%	
	TMSN	α -CIBN
3:1 HOAc/H ₂ O	22	44
1:1 HOAc/H ₂ O	28	42
1:3 HOAc/H ₂ O	..	25
1:1 CH ₃ CN/HOAc	10	82
1:1 CH ₃ CN/H ₂ O	20	43
CH ₃ CN ^b	9	84

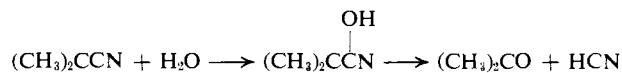
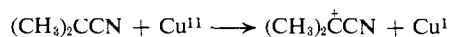
^a At 79.9°, ABN = 0.015 M; CuCl₂ = 0.185 M; LiCl = 0.59 M. ^b A run in acetonitrile with a slight excess of CuCl₂ gave the same results to within the experimental error.

The results shown in Table IV indicate that the 2-cyano-2-propyl radical can be oxidized by electron transfer in the presence of acetonitrile as solvent,³⁴ albeit in low efficiency. Acetone, arising from acetone cyanohydrin, would be an expected oxidation product in aqueous systems. The yields of acetone noted in Table IV bear this out. The occurrence of oxidation

(33) This does not imply that no positive charges on the carbon fragment was developed in the ligand transfer oxidation. Further studies will elaborate on this point.

(34) Although oxidation of the 2-cyano-2-propyl radical occurs in systems containing acetonitrile and acetic acid, contrary to Minisci's results⁸ no evidence for α -acetoxyisobutyronitrile could be found. The oxidation products are presumably methacrylonitrile and (for systems containing water) methacrylonitrile and acetone cyanohydrin; the latter yields acetone.

in the presence of acetonitrile is most likely due to a change in the Cu⁺/Cu²⁺ oxidation potential brought about by the stabilization of the cuprous species by acetonitrile.³⁵ Because of its ability to solvate ions,



aqueous systems are also beneficial to electron transfer oxidation. The results in Table IV indicate that this effect is much less pronounced than that produced by the stabilization of the cuprous species.

The addition of water to acetonitrile decreases the extent of reduction.³⁶ This may be due to the stabilization of the cupric ion as the aquo species³⁷ which makes it a less potent oxidant, and a concomitant destabilization of the cuprous salt. In all cases, the changes of solvent composition do not materially affect the results obtained in glacial acetic acid. That oxidation of α -cyano-2-propyl radicals by electron transfer occurs in acetonitrile–water solvent helps to explain Minisci's observations.⁸ He reported oxidation of radicals in the polymerization of acrylonitrile in an aqueous system. As we have shown, under these conditions the electron transfer process is slightly favored by the presence of acrylonitrile which would be expected to stabilize the cuprous species in the same manner that acetonitrile does. Thus, the discrepancies in the studies involving acrylonitrile systems probably stem from differences in experimental conditions.

The results shown in Table V indicate that the addition of water to acetic acid decreases the amount of ligand transfer oxidation of the 2-cyano-2-propyl radical to α -chloroisobutyronitrile. The effect here is 2-fold. The ligand transfer reaction is slower in water than the more weakly solvating acetic acid.³⁸ In addition, water promotes dissociation of the complex chlorocupric species (CuCl_n⁺²⁻ⁿ) into the lower aquochlorocupric species,³⁹ which may be less effective as ligand transfer oxidants.

The results in Table V also indicate that ligand transfer oxidation, like electron transfer, is significantly favored by the addition of acetonitrile as solvent. The tremendous ability of cupric chloride in acetonitrile to act as a radical trap is demonstrated by the fact that in the presence of a 5% excess of CuCl₂ an 85% yield of α -chloroisobutyronitrile is observed and less than a 10% yield of TMSN results.⁴⁰ This is quite significant in view of the fact that in the presence of many very good radical traps 20% yields of TMSN

(35) G. Morgan and F. Burnstall, *J. Chem. Soc.*, 143 (1928); R. C. Larson and R. T. Iwamoto, *J. Am. Chem. Soc.*, **82**, 3239, 3526 (1960); I. M. Kolthoff and J. F. Coetzee, *ibid.*, **79**, 870, 1825 (1957).

(36) This effect is large since cupric acetate is largely dimerized in nonaqueous solutions: R. L. Martin and A. Whitley, *J. Chem. Soc.*, 1394 (1958). It is the monomeric cupric species which is the oxidant: unpublished results, R. V. Subramanian.

(37) I. V. Nelson, R. C. Larson, and R. T. Iwamoto, *J. Inorg. Nucl. Chem.*, **22**, 279 (1961); I. V. Nelson and R. T. Iwamoto, *J. Inorg. Chem.*, **1**, 151 (1962).

(38) Unpublished observations, R. V. Subramanian.

(39) J. K. Kochi, *J. Am. Chem. Soc.*, **84**, 2121 (1962).

(40) The higher yields of α -chloroisobutyronitrile in acetonitrile compared with acetic acid may be due to the dissociation of the ketenimine VII in the aprotic solvent to regenerate 2-cyano-2-propyl radicals. Under these circumstances no diamide is expected.

are observed.⁴¹ As a radical trap, cupric chloride in acetonitrile is as good or better than molecular oxygen which reportedly⁴² is able to trap 85% of the radicals produced in benzene solution. The product appeared mainly as acetone cyanohydrin, though in *p*-xylene a 46% yield of 2-cyano-2-propyl hydroperoxide was isolated. The scavenging efficiencies toward the 2-cyano-2-propyl radical of a number of effective scav-

(41) G. S. Hammond, E. S. Wu, and O. D. Trapp, *J. Am. Chem. Soc.*, in press.

(42) Talat-Erben and N. Onal, *Can. J. Chem.*, **38**, 1154, 1157 (1960).

engers, among which are iodine,²² galvinoxyl,⁴³ mercaptans,^{22c} and diphenylpicrylhydrazyl,⁴¹ have been studied. Present results⁴⁴ are encouraging enough to pursue these efficiencies with metal salt inhibitors.

Acknowledgment. We wish to thank the National Science Foundation for a generous grant which supported the work.

(43) P. D. Bartlett and T. Funabashi, *J. Am. Chem. Soc.*, **84**, 2596 (1962).

(44) Until actual competition experiments are conducted, relative efficiencies are not relevant since radical-pair production may vary substantially in different solvents.

The Diazapentalene System.

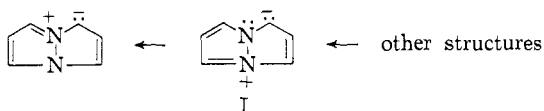
1-Benzoyl-2-phenylpyrazolo [1,2-*a*]pyrazole Derivatives

T. W. G. Solomons, F. W. Fowler,¹ and J. Calderazzo

Contribution from the Chemistry Department, University of South Florida, Tampa, Florida. Received August 7, 1964

Pyrazole has been converted to 1,2-diphenacylpyrazolium salts by reaction with 2 moles of phenacyl bromide, *p*-bromo-, *p*-chloro-, and *m*-nitrophenacyl bromide. The salts undergo cyclization to 1-benzoyl-2-phenylpyrazolo-[1,2-*a*]pyrazole derivatives (IV) when heated with aqueous sodium bicarbonate. Heating one of these derivatives ($X = H$) with concentrated hydrochloric acid has been found to result in cleavage of the benzoyl group.

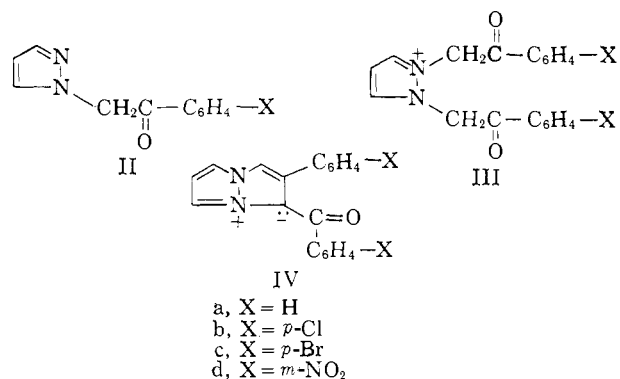
The pyrazolo[1,2-*a*]pyrazole (I) ring system has been of interest to us because of the steric and electronic analogies that can be drawn between it, pentalene,² and naphthalene. Our interest in this system was increased by the synthesis of the pentalene dianion,³ a structure with which I is isosteric and isoelectronic.



In an earlier communication⁴ we reported the synthesis of 1-phenyl-2-benzoylpyrazolo[1,2-*a*]pyrazole. We now record the details of that synthesis and report an extension of it to three other phenyl-substituted derivatives.

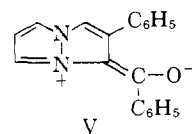
Pyrazole reacted with phenacyl bromide in 1,2-dimethoxyethane to give a salt which on treatment with aqueous ammonia gave 1-phenacylpyrazole (IIa) in 48% yield. Alkylation of compound IIa by a second mole of phenacyl bromide in dimethylformamide produced 1,2-diphenacylpyrazolium bromide (IIIa)

in 86% yield. This dialkylated salt was a colorless water-soluble substance; its infrared spectrum was lacking in N-H absorption and showed a strong carbonyl band at 5.90 μ .



The salt IIIa was treated with 10% aqueous sodium bicarbonate and heated to 50°. After a few minutes yellow crystals began to deposit, and after 3 hr. a 98% yield of compound IVa was obtained.

The infrared and n.m.r. data are in accordance with our structure for IVa. No N-H, O-H, or aliphatic C-H bonds are indicated in the infrared; indeed, in this region the only peaks that appear are those normally assigned to aromatic C-H. A strong absorption at 6.58 μ is assigned to the carbonyl group and suggests that such canonical forms as V are important. The n.m.r. spectrum shows a complex series of peaks in the region τ 2.4–3.3 only.



(5) These are the conditions used in the Chichibabin pyrrocoline synthesis; cf. A. E. Chichibabin, *Ber.*, **60**, 1607 (1927).

(1) National Science Foundation Undergraduate Participant (1962–1963); American Chemical Society–Petroleum Research Fund Scholar (1963–1964).

(2) For a review see the chapters by E. D. Bergmann and D. Craig in "Non-Benzenoid Aromatic Compounds," D. Ginsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959.

(3) T. J. Katz, M. Rosenberger, and R. K. O'Hara, *J. Am. Chem. Soc.*, **86**, 249 (1964).

(4) T. W. G. Solomons and F. W. Fowler, *Chem. Ind* (London), 1462 (1963).