

in nitrobenzene in the absence of cocatalyst, such as water or alkyl halide, and that in carbon tetrachloride, where the dielectric constant is too low to allow any ion formation, only water is an effective cocatalyst. In 1,2-dichloroethane, however, there is polymerization in the absence of any other added substance due to solvent cocatalysis (1,2-dichloroethane is also an effective cocatalyst in nitrobenzene). Methylene chloride has a dielectric constant (9.08 at 25°) similar to that of 1,2-dichloroethane (10.2 at 25°) and should also be a cocatalytic solvent for cationic polymerization. We believe that the reaction of stannic chloride with cycloheptatriene in methylene chloride proceeds mainly by reaction path 4, and that the generation of diene carbonium ions in cycloheptatriene solutions will always lead to much cationic polymerization in addition to ion formation. This is supported by the observation that conversion of cycloheptatriene to tropylium ion by sulfuric acid<sup>9b</sup> and perchloric acid is accompanied by extensive polymerization of the triene.

The reaction of boron halides with cycloheptatriene goes more rapidly in methylene chloride than in cyclohexane. This might be due to solvent cocatalysis; certainly *t*-butyl chloride appears to act as a cocatalyst with boron chloride.<sup>31</sup> However, the reaction of boron chloride with cycloheptatriene in the presence of *t*-butyl chloride is accompanied by much darkening of the solution and concurrent polymerization of cycloheptatriene. Since neither boron bromide nor chloride produces polymerization or decomposition of cycloheptatriene<sup>32</sup> in

(31) Colclough and Dainton<sup>30</sup> found that *t*-butyl chloride is  $1.43 \times 10^4$  times as effective a cocatalyst as 1,2-dichloroethane for the polymerization of styrene by stannic chloride in nitrobenzene.

(32) These reaction solutions become colored (yellow to red) but this is attributed to the C-T absorptions of tropylium halide<sup>12</sup> rather than to de-

methylene chloride in the absence of cocatalyst, we conclude that the cocatalytic activity of the solvent is negligible, and that the increase in rate of these reactions in going from hydrocarbon to chlorocarbon solvent is caused by a lowering of the energy of the first, ion-forming hydride transfer step by the more polar solvent.

A note should be made of the work of Joy and Lappert<sup>33</sup> who find that refluxing a neat mixture of boron chloride and cycloheptatriene leads to the formation of benzylboron dichloride. Under the conditions of our reactions we find no aromatic product. Since they did not look for tropylium salt products, it cannot be said at this time whether they produced benzylboron dichloride concurrently with, subsequently to, or instead of tropylium chloroborate.

The work reported herein, coupled with studies on triarylmethanes to be reported shortly, establishes the existence of carbon-to-metal hydride transfer reactions as a source of carbonium ions in the reactions of certain hydrocarbons with metal halides, and has laid a foundation for more detailed studies, currently in progress, of the scope, limitations, and mechanisms of such reactions.

**Acknowledgment.**—We wish to thank Dr. Hyp J. Dauben, Jr., who encouraged us in the early stages of this work and jointly developed the mechanistic discussion with us, Drs. L. R. Honnen and M. F. Lappert for discussions and suggestions, and the many students at Harvey Mudd College who have assisted in parts of the work.

composition of cycloheptatriene. Solutions of pure tropylium haloborates in methylene chloride are also colored unless excess boron halide is present to suppress dissociation of the anion.

(33) F. Joy and M. F. Lappert, *Proc. Chem. Soc.*, 353 (1960).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STATE UNIVERSITY OF NEW YORK, STONY BROOK, NEW YORK]

## Stable Free Radicals. I. Isolation and Distillation of 1-Ethyl-4-carbomethoxypyridinyl

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The preparation of the stable free radical, 1-ethyl-4-carbomethoxypyridinyl, by reduction of the corresponding pyridinium iodide with zinc or magnesium and its isolation in pure form by distillation under high vacuum are described. In acetonitrile, the radical has  $\lambda_{\text{max}}$  (m $\mu$ ) 6326 ( $\epsilon$  83), 3950 ( $\epsilon$  4700), 3040 ( $\epsilon$  11,300), and 2080 ( $\epsilon$  concentration dependent). The structure of the radical is proved through the identity of the spectrum with that of radical produced in quantitative electrochemical reduction, by elemental analysis, and by its magnetic properties, including high-resolution e.s.r. spectra and magnetic susceptibility which indicates 93% radical in the pure material at 25°. Infrared and visible spectra demonstrate that the radical at 77°K., a sapphire-blue solid, is identical with the radical at 298°K., an emerald-green liquid. The radical reduces methylviologen dication to the cation radical, abstracts halogen rapidly from such halocarbons as dibromomethane, trichloromethane, and tetrachloromethane, and reacts rapidly with oxygen. Other physical and chemical properties are described. The stability of the radical is attributed to steric hindrance to dimerization and to an intrinsic factor related to delocalization and the presence of electronegative atoms (nitrogen and oxygen) and summarized as decreased "electron availability."

The first stable organic free radical, triphenylmethyl, was prepared by Gomberg in 1900.<sup>3</sup> A modest number of other stable free-radical types have been discovered in the succeeding five decades.<sup>4</sup> In the last 15 years,

(1) Alfred P. Sloan Fellow 1960–1964.

(2) (a) Secretary of the Army Research and Study Fellow 1962–1963.

(b) Support from the Department of Defense through Contract DA-49-083 OSA-2615 is gratefully acknowledged.

(3) M. Gomberg, *J. Am. Chem. Soc.*, **22**, 757 (1900); *Ber.*, **33**, 3150 (1900).

(4) *Cf.*, for example, the list given by G. W. Wheland in "Resonance in

the combination of electron spin resonance (e.s.r.) techniques with careful methods of reduction (or oxidation) has led to an enormous increase in the number and variety of stable free radicals. However, largely because of preparative accessibility, most of the radicals reported have been charged species, either monoanions or monocations. The only reasonably simple *neutral* stable free radicals which have been investigated have

*Organic Chemistry.* John Wiley and Sons, Inc., New York, N. Y., 1955, p. 391.

been phenoxy (e.g., 2,4,6-tri-*t*-butylphenoxy<sup>5,6</sup>) and nitroxy (e.g., di-*t*-butylnitroxy<sup>7</sup>).

The descriptive term "stable" should be taken to mean survival for sufficient time so that the material can be used in another experiment. It is the possibility of use in a variety of experimental conditions, including those widely different from those under which the radical was generated, which makes "stability" a valuable property and which distinguishes stable radicals from those generated in matrices (at either low<sup>8</sup> or high<sup>9</sup> temperatures), in flow systems (e.g., tropy radical<sup>10</sup>), or by irradiation of crystals.<sup>11</sup>

Simple stable pyridinyl radicals were first erroneously reported by Weitz<sup>12</sup> (the products were alkylviologen radical cations<sup>13</sup>), and Wallenfels<sup>14</sup> has claimed that the colored solutions formed by 1-equiv. chromium(II) reduction of several pyridinium ions contain pyridinyl radicals. Dilute solutions of 1-ethyl-4-carbomethoxypyridinyl and 1-ethyl-4-carbamidopyridinyl in acetonitrile have been prepared by controlled potential reduction of the corresponding pyridinium ions.<sup>15,16</sup> The reduction of 1-methylpyridinium and 1-benzylpyridinium ions by sodium amalgam in aqueous solution was reported to yield tetrahydrodipyridyls.<sup>17</sup> In that case, and in other instances of tetrahydrodipyridyl formation (these are pyridinyl radical dimers), there has been no evidence for the occurrence of uncomplexed free radicals as intermediates.

We report in this paper the preparation and isolation by distillation of the simple stable free radical, 1-ethyl-4-carbomethoxypyridinyl. We shall also discuss the physical and chemical properties of this radical. Such simple radicals as the one reported in this work present favorable opportunities for studying many fundamental aspects of the physical and chemical behavior of free radicals.<sup>18</sup>

## Results

**Reduction.**—Electrochemical reduction of pyridinium ions in acetonitrile produces dilute solutions of pyridinyl radicals in the presence of large amounts of tetra-*n*-butylammonium perchlorate.<sup>15,16</sup> It was deemed necessary to develop chemical methods of reduction for the preparation of isolable quantities of radicals. The procedures required the use of high vacuum line techniques in order to avoid reaction of the radicals with oxygen during manipulations.

(5) C. D. Cook, D. A. Kuhn, and P. Fianu, *J. Am. Chem. Soc.*, **78**, 2002 (1956).

(6) E. Müller and K. Ley, *Chem. Ber.*, **88**, 601 (1955).

(7) A. K. Hoffman and A. T. Henderson, *J. Am. Chem. Soc.*, **83**, 4671 (1961).

(8) Cf. G. C. Pimentel in "Formation and Trapping of Free Radicals," A. M. Bass and H. P. Broida, Ed., Academic Press, Inc., New York, N. Y., 1960.

(9) P. Goldberg, *J. Chem. Phys.*, **40**, 427 (1964).

(10) A. Carrington, personal communication.

(11) H. M. McConnell, C. Heller, T. Cole, and R. W. Fessenden, *J. Am. Chem. Soc.*, **82**, 766 (1960).

(12) E. Weitz, A. Roth, and A. Nelken, *Ann.*, **425**, 161 (1921); E. Weitz and A. Nelken, *ibid.*, **425**, 187 (1921).

(13) Cf. the following paper: E. M. Kosower and J. Cotter, *J. Am. Chem. Soc.*, **86**, 5524 (1964).

(14) K. Wallenfels and M. Gellrich, *Chem. Ber.*, **92**, 1406 (1959); *Ann.*, **621**, 198 (1959).

(15) W. M. Schwarz, E. M. Kosower, and I. Shain, *J. Am. Chem. Soc.*, **83**, 2013 (1961).

(16) W. M. Schwarz, Ph.D. Thesis, University of Wisconsin, 1961.

(17) A. W. Hoffman, *Ber.*, **14**, 1503 (1881).

(18) A preliminary report of this work has appeared: E. M. Kosower and E. J. Poziomek, *J. Am. Chem. Soc.*, **85**, 2035 (1963). Other details were presented at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963; Abstracts, p. 382.

The first successful method was a classical one involving the use of an alkali metal to reduce a halide.<sup>19</sup> A mixture of powdered sodium (prepared from sodium dispersion) and 1-ethyl-4-carbomethoxypyridinium iodide (m.p. 111–112°<sup>20</sup>) was heated in an evacuated flask to about 100°. A vigorous, apparently exothermic reaction ensued and a blue-green substance was collected on a condenser cooled by liquid nitrogen. Comparison of the spectrum of the product with that of authentic radical<sup>15,16,21</sup> indicated that impure 1-ethyl-4-carbomethoxypyridinyl had distilled. This experiment demonstrated that the desired radical was volatile and reasonably stable at elevated temperatures.

Granular magnesium dissolves in the molten pyridinium iodide, a deep red liquid,<sup>22</sup> in a spectacular experiment which yields reasonably pure radical, collected by condensation at 77°K. as a blue solid. Powdered aluminum reacts less rapidly with molten pyridinium iodide, and requires a temperature of 170° for an adequate reaction rate. Even in the most favorable case, that of magnesium, the "thermal" method always produces some by-products, and has therefore been used only in preliminary studies on new halides.

Magnesium metal also dissolves rapidly in a degassed acetonitrile solution of 1-ethyl-4-carbomethoxypyridinium iodide, even at 0°, forming a deep purple solution. Although such solutions show strong e.s.r. signals, it has not been possible to extract or distil more than negligible quantities of radical from them. Since it was likely that iodide ion was important to the stability of the radical-magnesium iodide complex, we attempted to reduce 1-methyl-4-carbomethoxypyridinium *p*-toluenesulfonate (tosylate) with magnesium in acetonitrile. To our surprise, the reaction was exceedingly slow, suggesting that iodide ion played an important role in the reduction process itself. This notion was confirmed by the finding that addition of potassium iodide to the mixture of tosylate salt and magnesium resulted in a more rapid reaction than that observed without the catalyst. Radical may be recovered from reduction mixtures containing potassium iodide by extraction with *n*-heptane, suggesting that complexation between the radical and magnesium tosylate is weak. The yield of radical obtained by extraction of a reaction mixture after a standard procedure varies in a striking way with the amount of potassium iodide added, as shown in Fig. 1. Other consequences of radical-metal salt complexation will be reported elsewhere.<sup>23a</sup>

The best procedure for the preparation of the radical from the point of view of purity, convenience, and yield involves the use of zinc. Zinc powder dissolves in a degassed acetonitrile solution of 1-ethyl-4-carbomethoxypyridinium iodide (1) within a few hours to form a deep blue solution. After removal of the solvent, the radical 2 may be recovered by extraction with *n*-heptane or by distillation directly from the residue (eq. 1). The yield varies from 2 to 15%. Pyridine can also be used as solvent in place of aceto-

(19) Berzelius reduced potassium zirconium fluoride to zirconium with potassium. Cf. "Extrait d'une Lettre de M. Berzelius à M. Dulong," *Ann. chim. phys.*, [2] **26**, 43 (1824).

(20) E. M. Kosower, *J. Am. Chem. Soc.*, **80**, 3253 (1958).

(21) We thank Dr. W. M. Schwarz for making these spectra available.

(22) Light absorption in the visible region is attributed to iodide-pyridinium ion charge-transfer transitions (ref. 20).

(23) (a) E. J. Poziomek, unpublished results; (b) cf. discussion on p. 305, ref. 26.

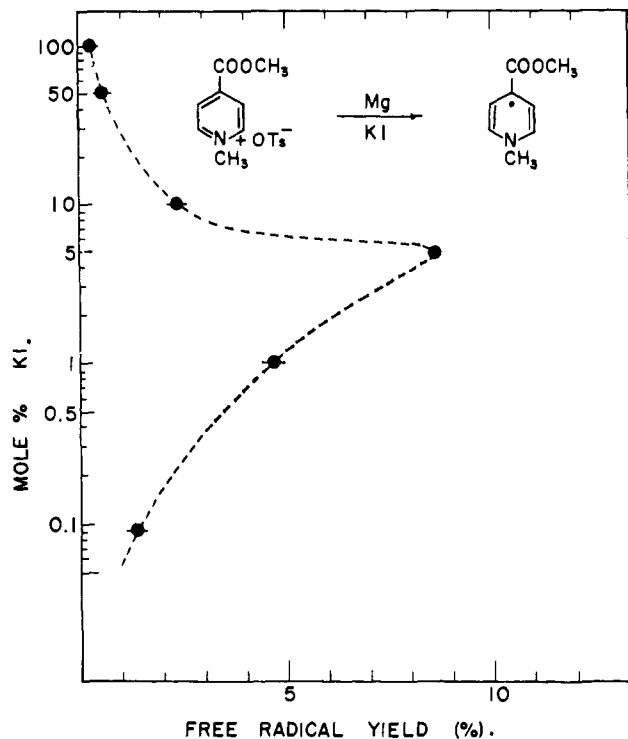
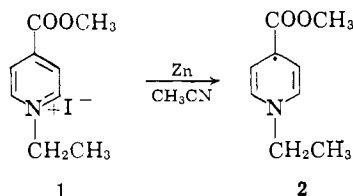


Fig. 1.—Yield of 1-ethyl-4-carbomethoxy-pyridinyl obtained in a standard procedure in the presence of different amounts of potassium iodide.

nitrile, and led to a yield of 35% in one experiment. However, acetonitrile is preferred since it is troublesome to remove the last traces of pyridine from the product.



Relatively little effort has been devoted to improving the yield of the radical **2** and distillations and extractions were normally terminated before all of **2** had been removed so as to avoid the possibility of contamination by other products.

**Proof of Structure.**—The structure of the radical **2** is proved through its spectroscopic identity with radical produced electrochemically, its elemental analysis, and its magnetic properties.

Schwarz has demonstrated a highly specific one-electron reduction of 1-ethyl-4-carbomethoxy-pyridinium perchlorate in acetonitrile to the radical **2** by means of polarography and cyclic triangular wave voltammetry. Solutions of **2** obtained by macro-scale electrochemical reduction contained about 100% of the expected amount of free radical as shown by a comparison of the strength of the e.s.r. signal with that from a solution of ethylviologen cation radical. The success of electrochemical reoxidation of **2** to the pyridinium ion by cyclic triangular wave voltammetry indicated that dimerization was either very slow or negligible in the concentration range between 0.4 and  $1.4 \times 10^{-3}$  M. The absorption spectrum of **2** was measured in the visible and ultraviolet ranges.<sup>15,16</sup>

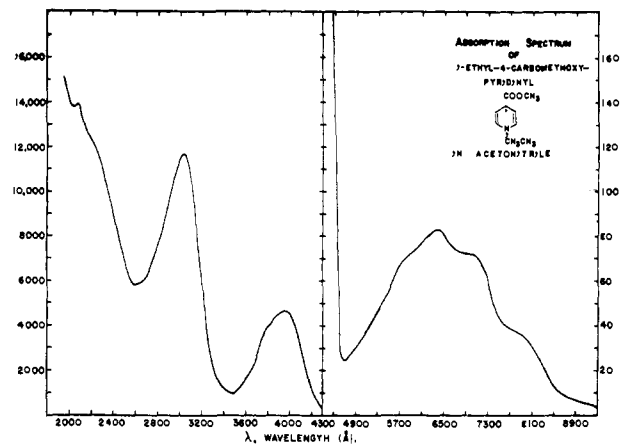


Fig. 2.—The ultraviolet and visible absorption spectrum of 1-ethyl-4-carbomethoxy-pyridinyl in acetonitrile. Note that the left-hand scale is 100 times that of the right-hand scale.

Solutions of the radical prepared by zinc reduction of the pyridinium ion had visible and ultraviolet absorption spectra almost identical with the spectra reported by Schwarz.<sup>21</sup> In addition, the visible absorption band varied linearly with concentration over the range  $1 \times 10^{-4}$  to 0.02 M. The elemental analysis is in reasonably good agreement with that expected for **2**.

The high resolution e.s.r. spectrum of a very dilute solution of the radical **2** has 143 lines within a region of 31.25 gauss. The appearance of the wings suggests different coupling constants for the two methylene hydrogens attached to the nitrogen, with magnitudes 0.40 and 0.25 gauss. Although it may be tentatively concluded that the nitrogen coupling constant is of the same order of magnitude as the constants for the 2- and 6-hydrogens, there are no obvious regularities in the spectrum which could assist in the interpretation. A relatively low nitrogen coupling constant implies a low spin density on nitrogen. An  $A_N$  of ca. 5.0 gauss would imply a spin density of about 0.2 from the relationship  $A_N = Q_N \rho_N$ .<sup>23b</sup> Since free spin on the nitrogen should be associated with a positive charge and therefore a dipole moment, the physical properties (see below) of the radical **2** as a reasonably nonpolar molecule are in agreement with a low spin density on nitrogen. The width of the e.s.r. spectrum implies some negative spin densities, probably at the 3- and 5-positions.

The number of lines found may be accounted for if the 2- and 6-hydrogens have somewhat different coupling constants, thus implying a rotation of the carbomethoxy group which is slower than the time scale of the e.s.r. measurement. If the coupling constants for the 3- and 5-hydrogens do not differ much, one should observe  $2(2\text{-H}) \times 2(6\text{-H}) \times 3(3,5\text{-H}_2) \times 3(\text{N}) \times 4(\text{different H of CH}_2) = 144$  lines.

Some of these points could be resolved through a study of deuterated radicals.

Pure **2** is essentially pure radical as shown by its magnetic susceptibility of  $1082 \times 10^{-6}$  c.g.s., corresponding to 93% radical, and its failure to give an observable n.m.r. spectrum.

The ultraviolet and visible absorption spectrum is shown in Fig. 2 and an e.s.r. spectrum of a dilute

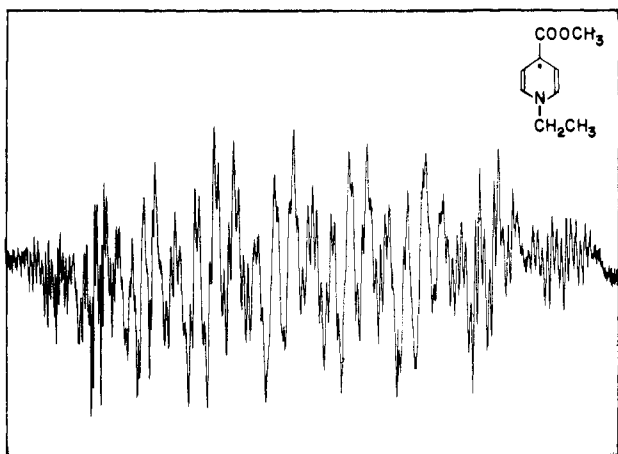


Fig. 3.—The e.s.r. spectrum of 1-ethyl-4-carbomethoxypyridinyl in acetonitrile at 25°.

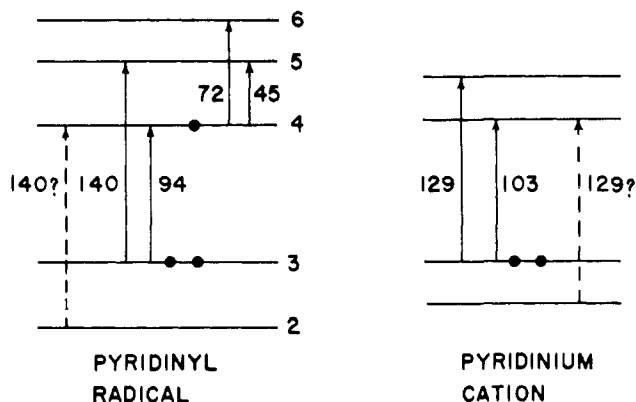


Fig. 4.—Electronic transitions of 1-ethyl-4-carbomethoxypyridinyl and 1-ethyl-4-carbomethoxypyridinium ion.

solution of **2** (not that of the highest resolution) is given in Fig. 3.

**Physical Properties.**—Pure radical **2** is an emerald-green oil,  $d^{25}_4$  0.85, which solidifies to a sapphire-blue solid at *ca.*  $-10^\circ$ . The color transition occurs even in solution somewhat below  $0^\circ$ . However, infrared and visible spectra of the pure radical at  $77^\circ\text{K}$ . (blue) and at  $25^\circ\text{C}$ . (green) indicate that there is no fundamental change in chemical constitution involved.

The volatility of the radical **2** is remarkable (as well as useful in purification). Pure **2** is readily distillable at *ca.*  $40^\circ$  at  $10^{-6}$  to  $10^{-7}$  mm. Dilute solutions of **2** may be prepared by distillation of acetonitrile solution maintained at  $25^\circ$  into a receiver held at  $0^\circ$ . From the known vapor pressure of acetonitrile and Raoult's law, the vapor pressure of **2** at  $25^\circ$  may be estimated as  $0.85 \times 10^{-4}$  mm.

The radical **2** is apparently not very polar, since it is soluble in *n*-heptane (up to *ca.*  $0.02 M$ ) as well as acetonitrile, dimethylformamide, pyridine, alcohols, and water. (The solutions of **2** in the latter solvents are not stable; see below.)

The conductivity of the radical **2** at  $77^\circ\text{K}$ . and at  $25^\circ\text{C}$ . was too low to measure with the apparatus used. At  $130^\circ$ , the specific conductivity was found to be  $3.1 \times 10^{-5}$  ohm $^{-1}$  cm $^{-1}$ . No visible change occurred during the brief period during which the radical was heated, and upon cooling to room temperature the conductivity again dropped below that which could be measured. Further work on the conductivity is in progress.

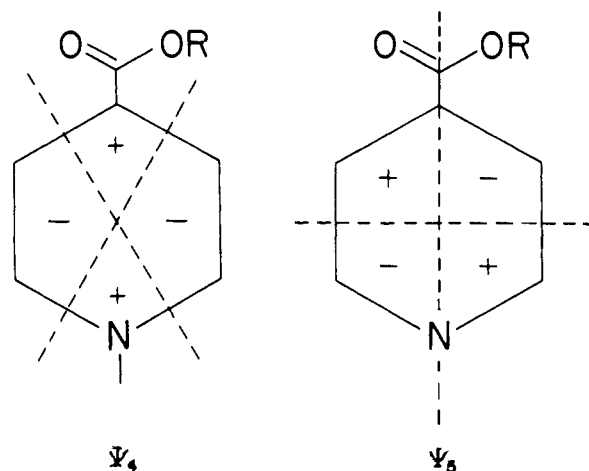
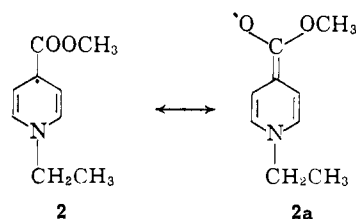


Fig. 5.—An m.o. description for the lowest empty and highest filled  $\pi$ -orbitals of the 1-ethyl-4-carbomethoxypyridinyl radical.

Discharge from a Tesla coil into a stream of radical vapor caused a white emission which usually ended before the cold trap. Under the same conditions, **2** condenses in the cold trap as a blue solid. No scintillations were observed at  $-12^\circ$  (*i.e.*, there were no emissions between 3000 and 6000 Å.) in the presence of  $\text{C}^{14}\text{O}_2$ .<sup>24</sup>

The visible and ultraviolet light absorption may be rationalized in terms of the transitions depicted in Fig. 4. The radical is even alternant, and the transitions resemble those expected for a radical cation.<sup>25</sup> According to the tentative assignment shown, the transitions which occur at 103 and 129 kcal./mole in the pyridinium ion are found at 94 and 140 kcal./mole in the pyridinyl radical. If the molecular orbitals,  $\Psi_4$  and  $\Psi_5$  (Fig. 5), were exactly like those in benzene, a transition between them would be formally forbidden. They are split by the nitrogen and a weakly allowed transition ( $\epsilon$  83) is observed. The lowest orbital may be assigned on the basis of the infrared spectrum, which exhibits a marked shift in carbonyl frequency,  $\nu_{\text{C}=\text{O}}$  1642  $\text{cm}^{-1}$ , in comparison with that for 1-ethyl-4-carbomethoxypyridinium iodide,  $\nu_{\text{C}=\text{O}}$  1730  $\text{cm}^{-1}$ , and methyl isonicotinate,  $\nu_{\text{C}=\text{O}}$  1736  $\text{cm}^{-1}$ . Strong overlap (**2**  $\leftrightarrow$  **2a**) between the substituent and the ring is possible and permits some insight into one source of the stability of **2**. The situation for the pyridinyl radical is thus very similar to that for benzene radical anion



derivatives, in which an electron-attracting substituent favors overlap (*i.e.*,  $\Psi_4$ ).<sup>26</sup>

The visible absorption band shows a small sensitivity to solvent polarity, the maximum shifting from 6450 Å. in *n*-heptane ( $Z$  60.1) to 6326 Å. in acetonitrile ( $Z$  71.3) to 6190 Å. in methanol ( $Z$  83.6).<sup>20</sup> The ab-

(24) We thank Dr. D. Christman, Chemistry Dept., Brookhaven National Laboratory, for his cooperation.

(25) J. N. Murrell, "The Theory of the Electronic Spectra of Organic Molecules," John Wiley and Sons, Inc., New York, N. Y., 1963, p. 259.

(26) M. C. R. Symons in "Advances in Physical Organic Chemistry," Vol. 1, Ed. V. Gold, Academic Press, Inc., New York, N. Y., 1963, p. 301.

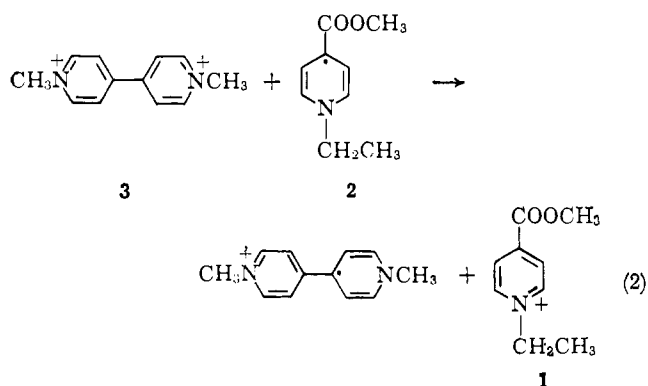
sorption maximum of the blue radical at 77°K. is 6350 Å., but the band is appreciably narrower, accounting for the change in color from green at 25°.

**Chemical Properties.**—Although **2** is a highly reactive species, it is stable in a number of solvents (heptane, acetonitrile, dimethylformamide, pyridine) and in the pure form for a reasonable time. The half-life for the disappearance of the radical in 0.01 *M* acetonitrile solution at 75° is greater than 12 days, and there is good reason to believe that this figure is a minimum.<sup>27a</sup> Pure radical is less stable. Although samples of **2** appear unchanged at room temperature for many hours, the characteristic green color changes markedly after a day or two at room temperature or after several hours heating at 100°. Nevertheless, it is clear that **2** is stable enough for use in many other experiments under conditions quite different from those under which it was prepared.<sup>27</sup>

The chemical behavior of **2** can be considered under three categories: (a) reaction with oxidizing agents, (b) reaction with electrophiles, and (c) complexation with metal ions. Most of the chemical studies have been preliminary, but the reaction with halocarbons has been studied in detail and is described in the third article in this series.<sup>27a</sup>

Radical **2**, unlike di-*t*-butylnitroxyl,<sup>7</sup> reacts rapidly with oxygen. The product, after treatment with acid, has essentially the spectrum of the 1-ethyl-4-carbomethoxy pyridinium ion with a maximum at 2700 Å. and strong absorption below 2270 Å. Presumably the other product is hydrogen peroxide.<sup>28</sup>

The bismethyl quaternary salt of 4,4'-dipyridyl, methylviologen (**3**), is reduced very rapidly by **2** to the corresponding radical cation, a result readily comprehensible in terms of the relative reduction potentials for the two ions: **1**, -0.93 v., and **3**, -0.57 v., both with respect to the aqueous saturated calomel electrode<sup>15</sup> (eq. 2).

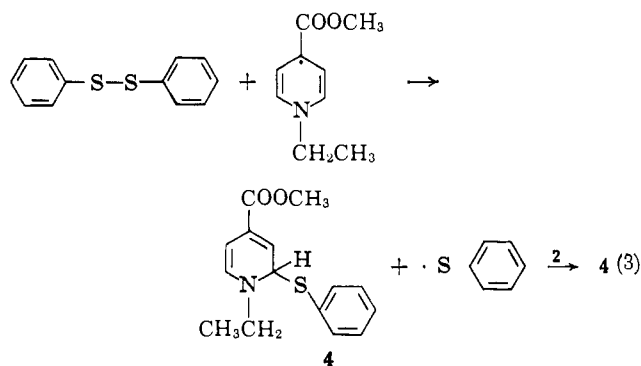


Both dibenzyl disulfide and diphenyl disulfide react with **2**, with rate of the latter reaction about twenty-five times as great as that for the former. Preliminary studies indicate that the product from diphenyl disulfide might be **4** or a derivative of **4** (eq. 3).<sup>29</sup>

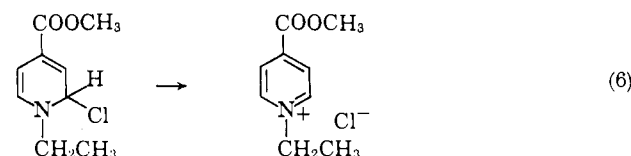
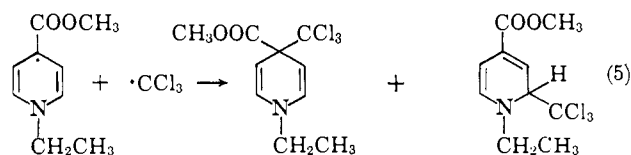
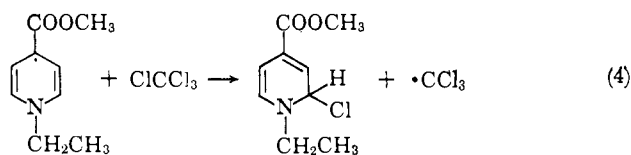
(27) (a) E. M. Kosower and I. Schwager, *J. Am. Chem. Soc.*, **86**, 5528 (1964). (b) Schwarz (ref. 16, p. 129) has noted that solutions of **2** in acetonitrile containing tetra-*n*-butylammonium perchlorate can be stored for several months with little change in their electrochemical properties (*cf.* ref. 28).

(28) Reaction of a bispyridinyl diradical (ref. 30) with oxygen produced bispyridinium ion and hydrogen peroxide in approximately equal amounts. Schwarz (ref. 16, p. 129) has found electrochemical evidence that peroxides are present in solutions of **2** after exposure to small amounts of oxygen.

(29) I. Schwager, unpublished results.



The most interesting reaction of **2** thus far found is that which involves halogen atom transfer from halocarbons, producing a pyridinium halide and dihydropyridines. An extremely rapid reaction with tetrachloromethane may be described as shown in eq. 4, 5, and 6. The kinetics of the reaction with halocarbons are reported in another paper.<sup>27</sup>



Radical **2** appears to function as a nucleophile, reacting at a moderate rate with dimethyl carbonate. The related radical, 1-methyl-4-carbomethoxy pyridinyl (**2M**), reacted fairly rapidly with the same reagent in pyridine and in heptane. The products have not yet been studied, but it is difficult to imagine a first step other than nucleophilic addition to the carbonyl group of the dimethyl carbonate.

Solutions of the radical in water, methanol, ethanol, isopropyl alcohol, and tetrafluoropropanol (TFP<sup>20</sup>) are unstable. In water, the half-life is about 5 min., while in isopropyl alcohol the half-life (at 25°) is about 3 hr. In the more acidic solvent, TFP, the radical seemed to disappear very rapidly. Methanol and ethanol cause the radical to disappear at rates between that of water and isopropyl alcohol.<sup>27a</sup> We conclude that proton transfer to **2** from the alcohol is the rate-determining step. The products have not yet been examined.

Although **2** reacted only to a slight extent with benzaldehyde, irradiation of the solution with a high-pressure mercury vapor lamp through quartz caused the disappearance of the radical. The radical itself does not change under these conditions. Removal of the solvent after photolysis left a red gum with an absorption

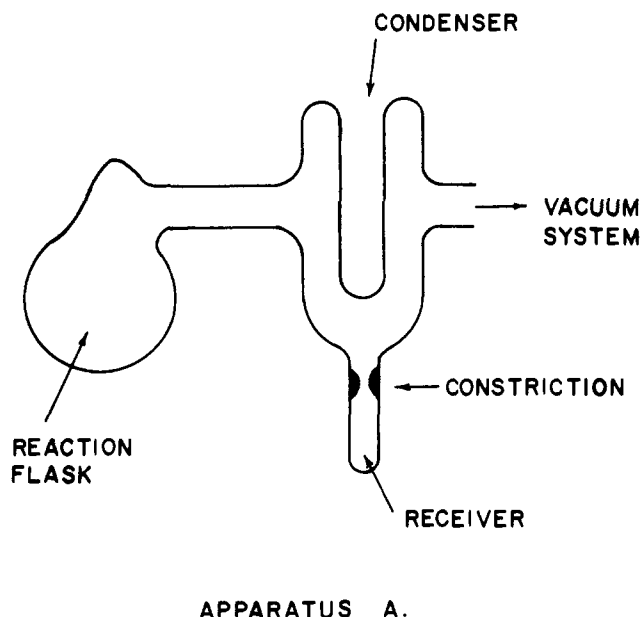


Fig. 6.—A reaction apparatus used in the preparation of 1-ethyl-4-carbomethoxy-pyridinyl (apparatus A). A bulb is introduced into the line between the reaction flask and the condenser when the extraction procedure is used (apparatus A').

maximum at 5300 Å. that did not change upon exposure of the material to air. Assuming that all of the pyridinyl radical had combined with benzaldehyde, 90% of the material was derived from the benzaldehyde. The slight odor of benzaldehyde became very strong upon treatment with dilute acid. Thus the radical **2** may have induced polymerization of benzaldehyde under the influence of light.

Radical **2** forms complexes with magnesium iodide and zinc iodide. Although the nature of these complexes is still under investigation,<sup>23a</sup> it can be stated that they differ somewhat from **2** itself in both spectroscopic and chemical properties. It is necessary to take into account possible complexation when designing preparative procedures for **2** or similar radicals. We have sought for but have not found a complex of magnesium iodide and methylviologen cation radical and believe therefore that the carbomethoxy substituent is important in complexation.

### Discussion

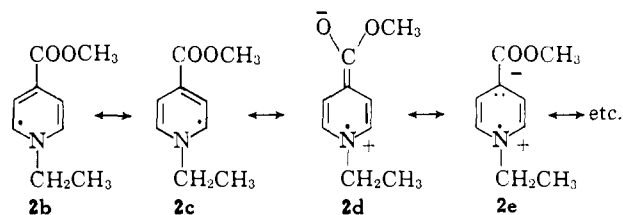
The significance of the present work lies in two areas: (a) in the demonstration that simple and convenient procedures can be utilized for the preparation and isolation of simple free radicals and (b) in the fact that stable free radicals may be found for much simpler systems than heretofore imagined. Clearly, the factors which control the stability and reactivity of free radicals may be examined in greater detail with stable radicals, since the experimental conditions may be varied over a wide range and are not limited to those under which the radical was generated. Both the physical and chemical properties of *neutral stable free radicals*, which one may regard as the organic analogs of metals, will be of much general interest.

The preparative methods described above are perhaps not as controllable as electrochemical methods with respect to the applied potential for reduction. However, these methods seem to us more convenient for use on the scale required for isolation and adaptable

to a large variety of heterocyclic salts. In particular, the use of distillation in the purification procedure shortens and simplifies the isolation, since distillation is easier to perform than recrystallization and filtration on a vacuum line.

Free radicals may be isolated if they possess sufficient *intrinsic stability* and sufficient *steric hindrance to dimerization*. The former seems to depend upon "electron availability" and increases with delocalization and the presence of electronegative atoms, like nitrogen and oxygen.

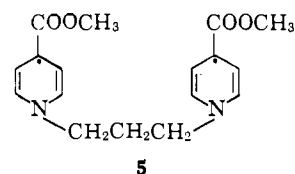
In the case of **2**, the intrinsic stability depends both upon resonance stabilization and the presence of nitrogen and oxygen. In addition to the resonance forms already cited ( $2 \leftrightarrow 2a$ ), a number of other ones may be written ( $2b \leftrightarrow 2c \leftrightarrow 2d \leftrightarrow 2e$ , etc.). Since the solubility of the radical **2** in *n*-heptane precludes a



high dipole moment, forms like **2d** and **2e** cannot make a large contribution to radical stability. From models, steric hindrance to the dimerization of **2** through the 4-position is readily apparent. However, for reasons which are none too clear, dimerization through the 2-position does not occur although 2,2'-dimers have been claimed to arise from the more reactive 1-(2,6-dichlorobenzyl)-3-carbamidopyridinyl radical.<sup>14</sup>

It seems likely that the position of the charge-transfer band for quaternary heterocyclic iodides will provide a valuable clue to whether or not one might expect to isolate a stable free radical from a particular system. There is a linear relationship between the reduction potential of pyridinium ions<sup>15</sup> and the position of the charge-transfer bands of pyridinium iodides in non-polar solvents. This is reasonable since the excited state of the pyridinium iodide produced by the charge-transfer transition is a pyridinyl radical-iodine atom pair.

The stability of **2** was great enough to suggest that stable polyradicals containing more than one **2** moiety might be prepared. This supposition was confirmed by the synthesis of the stable diradical, 1,1'-trimethylenebis(4-carbomethoxy-pyridinyl) (**5**).<sup>30</sup>

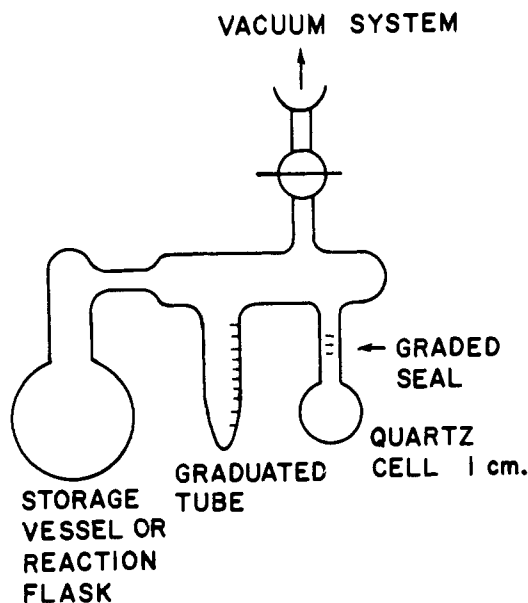


It can be expected that many other simple stable free radicals and polyradicals will be prepared and studied.

### Experimental

**Materials.**—1-Ethyl-4-carbomethoxy-pyridinium iodide, m.p. 111–112° (lit.<sup>20</sup> 111–112°); 1-methyl-4-carbomethoxy-pyridinium

(30) E. M. Kosower and N. R. McFarlane, unpublished results.



APPARATUS B.

Fig. 7.—A reaction apparatus used for the preparation of 1-ethyl-4-carbomethoxypyridinyl and for the preparation of solutions for spectroscopic examination (apparatus B).

*p*-toluenesulfonate (tosylate), m.p. 120°. *Anal.* Calcd. for  $C_{15}H_{17}NO_3S$ : C, 55.71; H, 5.31, N, 4.33. Found: C, 55.72; H, 5.67; N, 3.97. All solvents used were Spectrograde.

**Apparatus and Technique.**—A standard high-vacuum line equipped with a mercury diffusion pump and a McLeod gauge was used in all experiments. Liquid nitrogen was used as coolant for traps and receivers except when a higher temperature was required. Apiezon grease was used on stopcocks and joints. When properly cleaned, pressures of less than  $5 \times 10^{-6}$  mm. were readily obtained in the system.

Solvents were degassed by at least three freezing-pumping cycles, then distilled onto Molecular Sieves (4 A) (small pellets) which had been flame dried under vacuum. Solvents were distilled from the Molecular Sieves into the reaction vessels or other receivers. The chief solvents used were acetonitrile and *n*-heptane. Pyridine was also used in some experiments.

Whenever practical, all-glass systems with only one connection to the vacuum line were constructed. It was noted that radical could be transferred through stopcocks with difficulty, partially because it was hard to heat a stopcock to the appropriate temperature and partly caused by apparent reaction with a contaminant in the grease (oxygen?). In many experiments, however, the characteristic blue color of the radical appeared in the trap of the vacuum line. The two basic types of glass apparatus used in this work are illustrated in Fig. 6 (apparatus A) and Fig. 7 (apparatus B).

**Preparation of 1-Ethyl-4-carbomethoxypyridinyl (2).** "Thermal" Method.—Magnesium (70–80 mesh, 1.0 g.) and 1-ethyl-4-carbomethoxypyridinium iodide (2.86 g.) were thoroughly mixed, ground in a mortar, and placed in the reaction flask of apparatus A (Fig. 6). After sealing (it is important to clean the glass where necessary before any glassblowing), the reaction mixture was heated in an oil bath and liquid nitrogen was placed in the condenser. Pumping was continued throughout the experiment. At about 110–115°, the orange solid melted to a deep red liquid. Above 120° a sapphire-blue solid began to condense on the cold surface. Between 135 and 140° a major proportion of the product collected on the cold surface, and at 145° heating was discontinued. Degassed acetonitrile was distilled onto the condenser, the liquid nitrogen was removed, and the mixture of radical and acetonitrile allowed to flow into the receiver. An absorption spectrum indicated that the radical yield was *ca.* 0.5%, and that the product contained small amounts of material which absorbed below 4000 Å. in regions where the radical was weakly absorbing. (Spectroscopic data are given below.)

**Acetonitrile-Zinc Method.**—Zinc (0.433 g., 0.0066 g. atom), pyridinium iodide (3.89 g., 0.0133 mole), and a stirring bar were

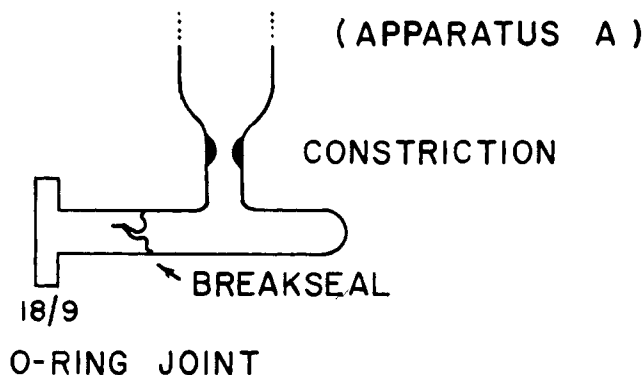


Fig. 8.—A modification of apparatus A suitable for the preparation and use of weighed quantities of 1-ethyl-4-carbomethoxypyridinyl.

sealed into the reaction flask of apparatus A'. After pumping for 1.5 hr., degassed acetonitrile (35 ml.) was distilled in using an ice bath for cooling. The mixture immediately turned bright green. It was stirred for 1.5 hr. at 0–5°, the solvent was removed, and the residue extracted with degassed *n*-heptane. (A' differs from A in having an extra bulb between the reaction flask and the condenser. Extraction is performed by swirling the solvent over the reduction mixture, transferring the solvent to the other bulb, and distilling the solvent back onto the reaction mixture with liquid nitrogen as coolant.) Three extractions were performed with 10 ml. of solvent. The *n*-heptane was removed and the radical distilled by cooling the condenser with liquid nitrogen and warming the bulb containing the extraction residue with a hot air "gun" to 80–90°. (External temperature; distillation can be carried out at much lower temperatures at a lower rate.) The radical condensed as a blue solid. After removal of the liquid nitrogen and warming to *ca.* –10°, the solid melted to an emerald-green oil which flowed into the receiver. (For smaller amounts of radical, it is necessary to use acetonitrile for transfer of the radical to the receiver.) The yield was 61.6 mg. (2.8%).

It is more convenient to distil the radical directly from the residue left after removal of acetonitrile from the reduction mixture. The yield is lower, but the procedure is shortened considerably. A sample of radical prepared in this way was sent for analysis.<sup>31</sup> *Anal.* Calcd. for  $C_9H_{10}O_2N$ : C, 65.03; H, 7.29; O, 19.25; N, 8.43. Found: C, 64.20, 64.41; H, 8.05, 7.84; O, 19.80, 19.34; N, 8.25, 8.52.

Pyridine at room temperature has been used as the solvent for the reduction. After removal of the solvent and distillation of the radical, a 35% yield was measured using the visible absorption band. Some later experiments showed that small amounts of pyridine were difficult to remove from the radical. Further work on this procedure is indicated for large-scale preparations.

**Potassium Iodide Catalysis.**—The experiment which gave the second highest yield is described. The reactants, 1-methyl-4-carbomethoxypyridinium tosylate (322 mg., 0.997 mmole), magnesium (70–80 mesh, 12.3 mg., 0.507 mg. atom), and potassium iodide (granular, Baker Analyzed, 1.63 mg., 0.00982 mmole), were sealed into the reaction flask of apparatus B (Fig. 7). After pumping, acetonitrile (8 ml.) was distilled in, the mixture warmed to room temperature, and the whole stirred for 72 hr. Most of the solvent was removed (enough to permit stirring was left) and the residue extracted by stirring with *n*-heptane for 35 min. The extract was transferred to the absorption cell and the yield calculated on the basis of an optical density of 0.063 at 6350 Å., with *ε ca.* 100, as 4.8%. Figure 1 was constructed on the basis of experiments carried out in this way.

Two additional extractions were performed by distilling the *n*-heptane back into the reaction vessel and stirring for 10 min. The yield of radical was raised to 9.0%. It is assumed that 1-methyl-4-carbomethoxypyridinyl is identical with 1-ethyl-4-carbomethoxypyridinyl in absorption spectrum.

It is important to realize that an experiment carried out in the manner described with 1-ethyl-4-carbomethoxypyridinium iodide and magnesium would have led to an *n*-heptane solution containing almost no radical. Chromium powder in acetonitrile failed to reduce the pyridinium iodide.

(31) Analyses were performed by the Schwarzkopf Microanalytical Laboratories, Woodside 77, N. Y. Samples were transferred in an inert atmosphere.

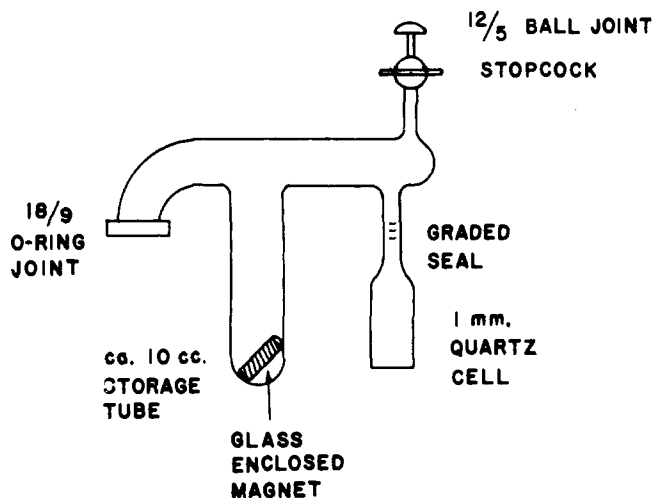


Fig. 9.—An apparatus suitable for use with that shown in Fig. 8 for the transfer and solution of measured quantities of 1-ethyl-4-carbomethoxy-pyridinyl.

**Absorption Coefficients of the Radical.**—It is no small matter to obtain and transfer a sample of material which must be handled completely in the absence of oxygen. We describe here a straightforward technique which would be useful in other cases.

Radical 2 was prepared and allowed to flow into a receiver bearing a breakseal onto which had been sealed an 18/9 O-ring joint<sup>32</sup> as shown in Fig. 8. The receiver was sealed off and weighed (16.04628 g.). The O-ring joint was clamped to the apparatus shown in Fig. 9 through the 18/9 connection, the whole apparatus evacuated and tested for leaks with a high-voltage coil. Exactly 1.8 ml. of acetonitrile was introduced into the storage tube, the seal broken with a magnet, the solution transferred into the 1-mm. cell, and the visible spectrum recorded. Additional measured quantities of acetonitrile were introduced and the spectrum again measured. A plot of optical density against concentration is given in Fig. 10. The blue-green color of the acetonitrile solution was immediately changed to yellow upon the addition of carbon tetrachloride in excess (over 2). The portion of the apparatus shown in Fig. 8 was detached so that no broken glass was lost. Washing was effected with a syringe and acetonitrile as solvent. The apparatus was dried on the vacuum line. Broken glass from the rest of the apparatus was washed into the tube with solvent. The tube was again dried and weighed (15.98465 g.). The weight of the radical 2 was therefore  $61.63 \pm 0.04$  mg.

The absorption coefficient of 2, excluding the highest concentration, at 6326 Å. in acetonitrile at *ca.* 25° is  $83 \pm 4$ . Absorption coefficients in other regions of the spectrum were determined by dilution of solutions with known optical densities at 6326 Å. A summary of the positions and coefficients is: (in acetonitrile, maximum, coefficient) 9250 sh ( $\epsilon \approx 4.5$ ), 7750 sh ( $\epsilon \approx 36$ ), 6900 sh ( $\epsilon \approx 72$ ), 6326 ( $\epsilon \approx 83$ ), 5850 sh ( $\epsilon \approx 36$ ), 3950 ( $\epsilon \approx 4700$ ), 3040 ( $\epsilon \approx 11,300$ , 2280 sh ( $\epsilon$  dependent on concentration), 2080 ( $\epsilon$  dependent on concentration). Schwarz obtained maxima in acetonitrile for radical formed through electrochemical reduction<sup>16,21</sup> as 7750 sh, 6850 sh, 6315 ( $\epsilon \approx 98$ ), 5900 sh, 3940 ( $\epsilon \approx 5200-6000$ ), 3040 ( $\epsilon \approx 10,000-11,700$ ), 2250 sh ( $\epsilon$  dependent on concentration), and 2050 sh ( $\epsilon$  dependent on concentration). The agreement between the two sets of data is excellent.

**Magnetic Susceptibility.**—A sealed sample tube of 2 (later found to contain 85 mg. of radical) gave a positive deflection of 0.40 mg. ( $\pm 5\%$ ) in the field of a permanent magnet (*ca.* 4000 gauss). From similar samples and tubes, Prof. Harry B. Gray estimated the diamagnetic correction. To this was added the correction for molecular diamagnetism derived from the Pascal constants. The resulting molar susceptibility was  $1082 \times 10^{-6}$  c.g.s. units at 295°K., corresponding to 1.61 Bohr magnetons per mole or 93% free radical.

**Electron Spin Resonance Measurements.**—A solution of 2 (*ca.*  $6 \times 10^{-5}$  M) was prepared by distillation of a more concentrated

(32) (a) Delmar Scientific Co., Maywood, Ill. (b) A rounded end on the breakseal would probably have made transfers through the seal more facile. We have used such an end in other radical work and find it convenient (construction of four glassblower, Mr. P. Roman). In the apparatus actually used a standard breakseal was attached.

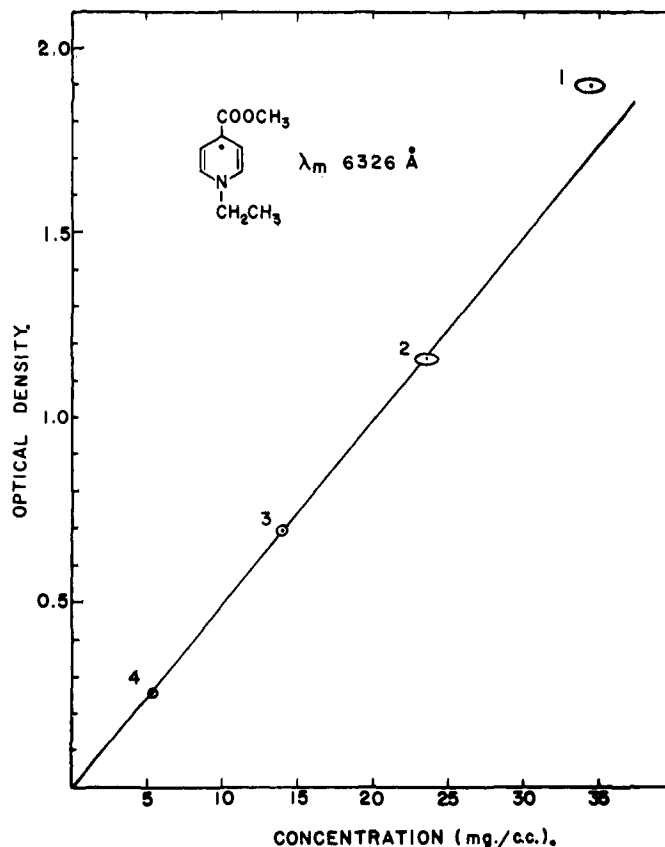


Fig. 10.—A plot of optical density vs. concentration of free radical 2 for the maximum in the visible region. The volumes of acetonitrile ( $\pm 0.05$  ml.) used are: 1, 1.80 ml.; 2, 2.60 ml.; 3, 4.45 ml.; and 4, 12.2 ml.

solution of radical (*ca.* 0.02 M) held at room temperature into a receiver cooled to 0°. The e.s.r. spectrum was measured at a number of scan rates on the instrument of Professor G. Fraenkel, Columbia University.<sup>33</sup> At 0.25 gauss/min., a spectrum 31.25 gauss wide was obtained with 143 lines. The spectrum was symmetrical around line 72. Except for the wings, which suggested different coupling constants for the two methylene hydrogens on the carbon bonded to the nitrogen (0.40 and 0.25 gauss) and, by inference, rather similar coupling constants for the 3- and 5-hydrogens, there were no obvious regularities in the spectrum which could aid in interpretation. Another tentative conclusion was that the nitrogen coupling constant could not be much larger than the coupling constant to the 2- and 6-hydrogens, in accord with the relatively low spin density expected on nitrogen.

A spectrum recorded at a higher scan rate is shown in Fig. 3.

An attempt was made to measure the n.m.r. spectrum of a sample of pure radical with an A-60. No absorption whatsoever was observed.

**Infrared Spectrum.**—Radical 2 was prepared in the usual way and distilled onto a potassium bromide disk cemented to a cold finger cooled by liquid nitrogen. The cold finger was rotated 90° so as to line up the disk with two potassium bromide windows. Infrared spectra were measured at 77°K. with a Perkin-Elmer Model 521 infrared spectrophotometer, and calibrated with polystyrene. The visible absorption of the radical was measured with a DK-2A Beckman spectrophotometer. The infrared spectra of 1-ethyl-4-carbomethoxy-pyridinium iodide (Nujol mull) and methyl isonicotinate (CCl<sub>4</sub> solution) were measured at room temperature with the Model 521. The infrared spectrum of 2 at 77°K. is given in Fig. 11 and a comparison of the carbonyl regions for the radical, the pyridinium iodide, and methyl isonicotinate is shown in Fig. 12.

**Other Physical Properties.**—Distillation of a radical solution at 25° (*ca.* 0.01 M) into a receiver at 0–5° yielded a solution of 2 with a concentration of  $1.7 \times 10^{-5}$  M (O.D. 0.08 at 3940 Å. at which  $\epsilon = 4700$ ). Since the vapor pressure of acetonitrile at 25°

(33) Cf. ref. 24, 25 in P. H. Rieger, I. Bernal, W. H. Reinmuth, and G. K. Fraenkel, *J. Am. Chem. Soc.*, **85**, 684 (1963).



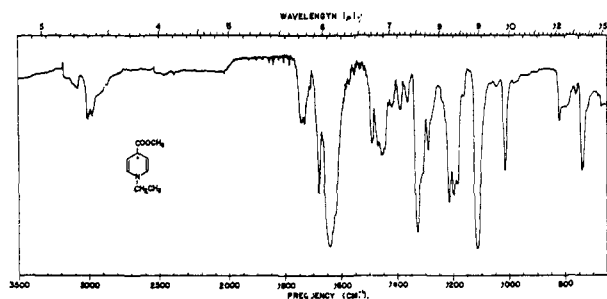


Fig. 11.—The infrared spectrum of 1-ethyl-4-carbomethoxypyridinyl.

is 100 mm., application of Raoult's law gave a vapor pressure of  $0.85 \times 10^{-4}$  mm. at  $25^\circ$  for 2. The ease with which the radical distilled during the preparative work was a direct indication of its high volatility.

It was found that the 85 mg. of radical used in the magnetic susceptibility experiment occupied a volume of 0.100 cc. ( $\pm 5\%$ ), and that the  $d^{26}_4$  was 0.85.

**Chemical Properties. Oxygen.**—In an experiment in which an air leak occurred on sealing off, the oxidized product was extracted with dilute sulfuric acid, yielding a solution with a maximum at  $2700 \text{ \AA}$ . and strong absorption below  $2270 \text{ \AA}$ . In all cases in which radical 2 or a solution of radical 2 was exposed to oxygen, extremely rapid loss of the typical blue-green color of the radical indicated that the reaction was rapid.

**Methylviologen Chloride.**—The vapor of radical 2 reacted with solid methylviologen chloride (the bismethyl quaternary chloride of 4,4'-dipyridyl) to yield a violet material. In acetonitrile, the spectrum of the violet (or blue-violet) solution was identical with that of authentic methylviologen cation radical.<sup>13</sup>

**Carbon Tetrachloride.**—Introduction of carbon tetrachloride into a solution of 2 or even condensation of carbon tetrachloride on solid radical at  $77^\circ\text{K}$ . resulted in extremely rapid disappearance of the visible absorption. The products have been examined, (cf. ref. 27).

The radical reacts at a reasonably low rate with ethyl iodide ( $t_{1/2}$  ca. 6 hr. with 4 M ethyl iodide) with the disappearance of all of the visible absorption. Later work with methyl iodide<sup>27</sup> confirmed that visible absorption disappears in such a reaction, indicating that all of the radical is consumed in the presence of excess alkyl iodide.

**Water.**—The maxima characteristic of the radical 2 disappeared fairly rapidly in a solution in water ( $t_{1/2}$  ca. 4 min.). The product(s) had maxima at  $2640$  and  $2190 \text{ \AA}$ . These maxima shifted to  $2710$  and  $2205 \text{ \AA}$ . in dilute sulfuric acid and back to the original maxima with the addition of sodium hydroxide.

**Alcohols.**—Methanol, ethanol isopropyl alcohol, and 2,2,3,3-tetrafluoropropanol (TFP) all caused the disappearance of radical 2 at rates which seemed parallel<sup>27</sup> to their acidity. TFP abolished the visible absorption of the radical so rapidly that it was not possible to obtain a spectrum.

**Other Reactions.**—Radical 2 reacted with dimethyl carbonate and with benzaldehyde under the influence of light. Our information on these reactions was summarized in the text.

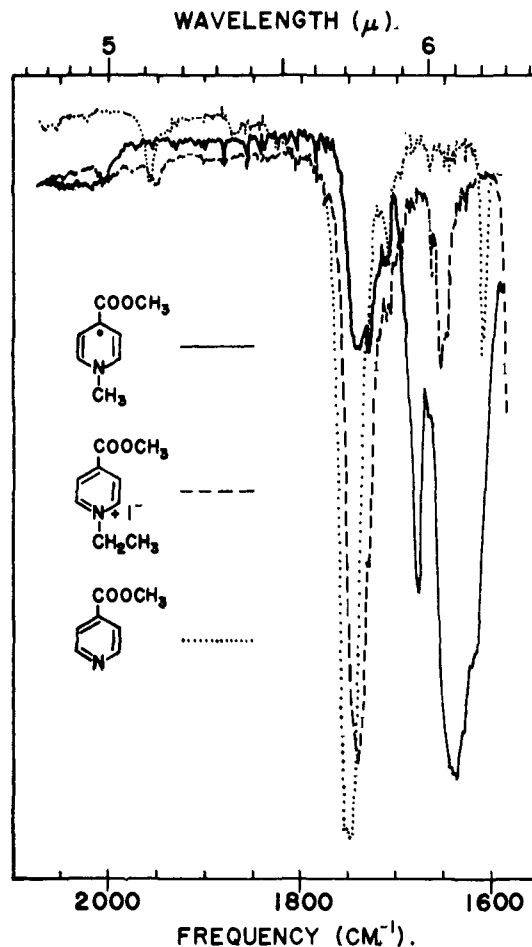


Fig. 12.—The carbonyl region of the infrared spectrum for 1-ethyl-4-carbomethoxypyridinyl, 1-ethyl-4-carbomethoxypyridinium iodide, and methyl isonicotinate.

**Acknowledgment.**—We should like to thank Professors George K. Fraenkel, Harry B. Gray, and William D. Closson, Dr. James R. Bolton and Mr. William Miller, of the Department of Chemistry, Columbia University, for their help and cooperation on the e.s.r. and magnetic susceptibility measurements. We have received much advice from Professor Sei Sujishi, Department of Chemistry, State University of New York, Stony Brook, and from Dr. James Burton, Melpar, Inc., on infrared apparatus and technique. The low temperature infrared and visible absorption studies were carried out at Edgewood Arsenal, Md.