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1-Alkyl-2-(carbomethoxy)pyridinyl Radicals: Monomers and Dimers Defined through Chemical and Photochemical Properties and Electron Paramagnetic Resonance

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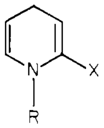
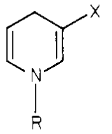
Abstract: 1-Methyl-2-(carbomethoxy)pyridinium ion (**2^+**) is reduced to the radical dimer (**2-2**) which is in equilibrium with a small amount of 1-methyl-2-(carbomethoxy)pyridinyl radical (**2·**). Distillation of the dimer leads to thin films (at 77 K) of the radical **2·**, which dimerizes in solution. Chemical properties and EPR spectra of dimer solutions reflect the presence of the monomeric radical in equilibrium with the dimer; **2^+** polarography also indicates a monomer–dimer equilibrium. Laser pulse dissociation of the dimer in solution gives the monomer reversibly, with k_{assoc} of ca. 10^6 M^{-1} s^{-1}. The dimerization constant, K_a (titration method), is 4×10^5 M^{-1}; electrochemical techniques lead to a K_a value of at least 7×10^4 M^{-1}, a k_{assoc} value of ca. 1–4 $\times 10^4$ M^{-1} s^{-1}, and a k_{dissoc} value of 1 s^{-1}. The activation energy for dimer dissociation (from EPR spectral broadening) is 7.7 kcal/mol (CH_3CN) or 9.4 kcal/mol (2-MTHF). The 1-methyl-2-acetylpyridinyl radical [(CH_3CO)**2·**] is easily prepared and distilled and has a stability similar to that of the 1-methyl-4-(carbomethoxy)pyridinyl radical (**4·**). EPR spectra of the 2-acetyl and 2-(carbomethoxy)pyridinyls are presented and analyzed. A convenient electrochemical cell for the generation and analysis of air-sensitive one-electron reduced species (such as the pyridinyl radicals or unstable pyridinyl radical dimers) is described.

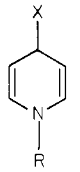
Pyridinyl radicals, the one-electron reduction product of pyridinium ions, have stabilities that are quite dependent on the position and nature of the ring substituent. The 1-alkyl-4-(carbomethoxy)pyridinyl radicals (**4·**) are distillable and reasonably stable in the absence of oxygen.[2] The 1-alkyl-3-carbamidopyridinyl radicals (**3·**), possible intermediates in the biochemical reactions of the coenzymes NAD^+ and $NADP^+$,[3] have been examined only as very reactive intermediates generated by pulse radiolysis.[4,5]



2·



3·



4·

X = $COOCH_3$, except where specifically noted as (X)n·

Some spectroscopic properties of the 1-methyl-2-carbamidopyridinyl radical [($CONH_2$)**2·**] (generated by pulse radiolysis) were known.[6] The 1-methyl-2-(carbomethoxy)pyridinyl radical (**2·**) was reported by Watanabe et al.,[7] but the properties of the **2·** radical solutions were at variance with those expected in both spectra and chemistry. A thorough investigation was then undertaken and has been successful in defining the chemistry and behavior of **2·**. An extremely useful and versatile apparatus devised to carry out some of the spectroscopic studies is described in the following article in this issue.[8]

Results

Reduction of 1-Alkyl-2-(carbomethoxy)pyridinium Ions. Treatment of 1-methyl-2-(carbomethoxy)pyridinium (**2^+**) iodide in acetonitrile with sodium amalgam in the absence of oxygen at 0 °C for about 0.5 h, solvent removal without warming, and 2-methyltetrahydrofuran (2-MTHF) or isopentane extraction and distillation onto a 77 K surface gives a blue film resembling those produced by the same procedure carried out on **4^+** iodide[9] (eq 1).

$$2^+I^- \xrightarrow[CH_3CN]{Na(Hg)} 2\cdot \qquad (1)$$

1-Ethyl- and 1-isopropyl-2-(carbomethoxy)pyridinium iodides also yield blue films.

An acetonitrile solution of the blue film showed an ultraviolet absorption spectrum (λ_{max} 332 nm) distinctly different from that expected [1-methyl-2-carbamidopyridinyl radical generated through pulse radiolysis (λ_{max} 307; 365, 900 nm)[6]]. If the solutions were too concentrated ($>10^{-3}$ M) or allowed to stand too long, additional absorption bands (not correlated with one another) developed at 408, 430, and 550 nm.

The "**2·**" solution exhibited radical properties but with a lower rate of reaction than **4·** with oxygen and the titrant 1,1′-dimethyl-4,4′-bipyridylium dichloride (paraquat or PQ^{2+}). Formation of the paraquat cation radical ($PQ^{+}\cdot$) (ϵ_{max} 13 000 at 605 nm[10]) is used to quantitate the spectroscopic maxima for "**2·**" in CH_3CN at 245 (ϵ_{max} 5000) and 332 nm (ϵ_{max} 1000). The major species present in the solution of "**2·**" is actually the dimer, **2-2**, of **2·**, and absorption coefficients twice those of the equivalent

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(1) (a) Tel-Aviv University; (b) Tohoku Univeristy; (c) State University of New York, Stony Brook.

(2) (a) Kosower, E. M.; Poziomek, E. J. *J. Am. Chem. Soc.* **1964**, *86*, 5515. (b) The subject of Pyridinyl radicals is reviewed by Kosower, E. M. In "Free Radicals in Biology"; Pryor, W. A., Ed.; Academic Press: New York, 1976; Vol. 2, Chapter 1.

(3) Kosower, E. M. *Prog. Phys. Org. Chem.* **1965**, *3*, 81–164.

(4) Land, E. J.; Swallow, A. J. *Biochim. Biophys. Acta* **1968**, *162*, 327. Corrections to the rates of disappearance have been noted in ref 5.

(5) Kosower, E. M.; Teuerstein, A.; Burrows, H. D.; Swallow, A. J. *J. Am. Chem. Soc.* **1978**, *100*, 5185–5190.

(6) Kosower, E. M; Land, E. J.; Swallow, A. J. *J. Am. Chem. Soc.* **1972**, **94**, 986–987.

(7) Watanabe, H.; Ikegami, Y.; Seto, S., *Chem. Lett.* **1972**, 1107–1110.

(8) Hermolin, J.; Levin, M.; Kosower, E. M. following article in this issue.

(9) Kosower, E. M.; Waits, H. P. *Org. Prep. Proced. Int.* **1971**, *3*, 261–267.

(10) The absorption coefficient reported by Kosower and Cotter (ref 11) and based on two methods is apparently too low. Independent measurements of the absorption coefficent in Sendai and Tel-Aviv by reaction of PQ^{2+} with sodium amalgam, by reaction with sodium dithionite and by titration with a known amount of **4·** radical yield an absorption coefficient of 13 000 ± 600 at 605 nm for $PQ^{+}\cdot$.

(11) Kosower, E. M.; Cotter, J. L. *J. Am. Chem. Soc.* **1964**, *86*, 5524–5527.

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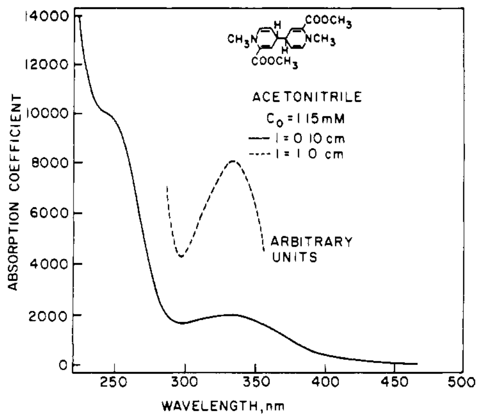

Figure 1. A spectrum of the dimer of 1-methyl-2-(carbomethoxy)pyridinyl (**2-2**) in acetonitrile. $C_0 = 1.15 \times 10^{-3}$ M, $l = 0.10$ cm. A partial spectrum (for $l = 1$ cm) shows the absorption maximum.

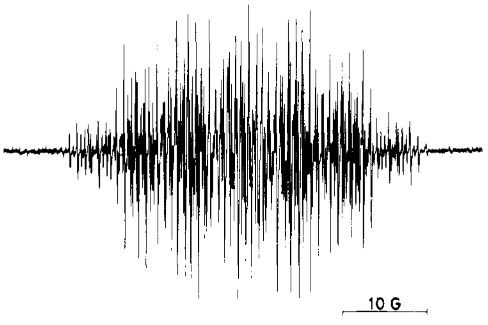

Figure 2. An EPR spectrum of 1-methyl-2-(carbomethoxy)pyridinyl (**2·**) in a CH_3CN solution of the dimer (**2-2**) (8.5×10^{-3} M) in CH_3CN (T = 19 °C).

pyridinyl radical are given for the spectrum (Figure 1).

The properties cited do not vary with the alkyl group (1-methyl, 1-ethyl, 1-isopropyl; the synthesis of the 1-*tert*-butyl-2-(carbomethoxy)pyridinium ion by the Verhoeven procedure[12,13] was not successful). A convenient electrochemical cell for the reduction of electroactive ions to air-sensitive species has been constructed (see Experimental Section) and was used to prepare the dimer **2-2** from $\mathbf{2}^+$ in CH_3CN-$LiClO_4$ (0.2 M). The spectroscopic absorption coefficients based on complete reduction of known amounts of $\mathbf{2}^+$ are similar to those based on PQ^{2+}.

Electron Paramagnetic Resonance Spectra. Solutions of the dimer **2-2** (10^{-3}–10^{-2} M in CH_3CN or 2-MTHF) exhibit very well resolved EPR spectra (Figure 2), demonstrating the presence of the **2·** radical. The hyperfine structure indicates that the exchange process is "slow" and that the radical concentration is quite low. The splitting constants obtained through simulation of the spectrum are as follows: [splitting constant in gauss (position, number, and nature of the coupled atom) (19 °C)] 6.58 (1, 1 N), 1.40 (3 or 5, 1 H), 6.28 (4, 1 H), 0.94 (5 or 3, 1 H), 2.54 (6, 1 H), 5.64 (NCH_3, 3 H), 0.94 (OCH_3, 3 H). Slightly different constants are obtained for the spectrum in MTHF: (order as above, 20 °C) 6.55, 1.54, 6.30, 1.11, 2.36, 5.67, 0.90.

The temperature dependence of the line width was measured over the range from −40 to 60 °C. Using the relationship between the line width Γ and the mean lifetime of the radical in the slow interconversion limit[14] (eq 2), where Γ_0 is the line width in gauss

$$\Gamma = \Gamma_0 + 1/2\tau\gamma_e \qquad (2)$$

in the absence of interconversion, 2τ is the mean lifetime of the radical, γ_e is the magnetogyric ratio for electron, we obtain the rate constant, k, for spin interchange ($=1/\tau$). A plot of log k vs. $1/T$ led to a line with log $k = 11.06 - 1677T^{-1}$ (Figure 3) and an activation energy of 7.7 ± 0.4 kcal/mol. A similar analysis of line width data for MTHF solutions led to an activation energy of 9.4 ± 0.3 kcal/mol. The temperature dependence of approximate line intensities was parallel to the line width variations. The second-order rate constant for spin exchange, obtained from the $1/\tau$ value and the radical concentration given by the equilibrium constant for association (4×10^5 M^{-1}, see below), is ca. 3×10^9 M^{-1} s^{-1}.

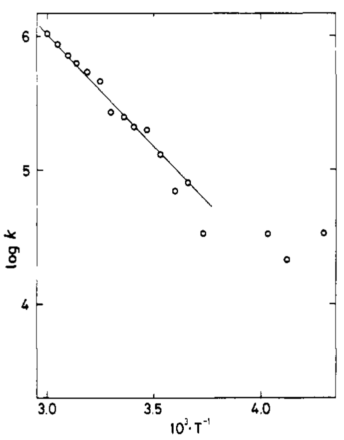

Figure 3. A plot of log k (for spin exchange between two **2·** radicals) vs. the reciprocal of the temperature. Line width data were obtained from EPR spectra of dimer (**2·**) ($C = 2.11 \times 10^{-3}$ M) and k was estimated as described in the text. The least-squares line for data above 283 K corresponds to a ΔH for dimer dissociation of 7.7 ± 0.4 kcal/mol.

The rate constant must represent a diffusion-controlled reaction, and the activation energy largely reflects dissociation of dimer (some additional details are given in the Experimental Section).

Significant Salt Effects on Titration of Dimer. The low solubility of $PQ^{2+}2Cl^-$ in CH_3CN and the low equilibrium concentration of **2·** lead to a slow reaction of the dimer **2-2** with PQ^{2+} dichloride (12 h vs. 5–10 min for reaction with **4·**) (eq 3). The salt, $\mathbf{4}^+ClO_4^-$

$$\mathbf{2\text{-}2} \rightarrow \mathbf{2}\cdot \xrightarrow{PQ^{2+}} \mathbf{2}^+ \qquad (3)$$

(ca. 10^{-3} M), with a favorable reduction potential[15] and greater solubility, accelerated the reaction very much. Excess $\mathbf{4}^+ClO_4^-$ reacts rapidly with **2-2** to produce the **4·** radical (UV-vis, EPR spectra).[16] Using the known absorption coefficients of **4·**,[17] we find those for **2-2** in agreement with the ones obtained by using PQ^{2+}. Addition of $LiClO_4$ (10^{-3}–10^{-1} M) or tetra-*n*-butylammonium perchlorate (0.1 M) also accelerated the rate of reaction of the dimer with PQ^{2+}.

Dimerization Constant for 2·. Addition of $\mathbf{2}^+ClO_4^-$ to **4·** diminished the absorption due to **4·**; addition of $\mathbf{4}^+ClO_4^-$ to the solution restored the original spectrum of **4·**. The dimerization constant for **2·** may be determined from the concentrations of **4·** and $\mathbf{2}^+$ and the standard reduction potentials [E_0^{4+}, −1.081 V and E_0^{2+}, −1.166 V in CH_3CN-$LiClO_4$ (0.25 M); E_0^{4+}, −1.095 V and

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[12] de Gee, A. J.; Sep, W. J.; Verhoeven, J. W.; de Boer, Th. J. *J. Chem. Soc. Perkin Trans. 1*, **1974**, 676.

[13] Kosower, E. M.; Waits, H. P.; Teuerstein, A.; Butler, L. C. *J. Org. Chem.* **1978**, *43*, 800.

[14] Wertz, J. E.; Bolton, J. R. "Electron Spin Resonance"; McGraw-Hill: New York, 1972; pp 198–204.

[15] The ready formation of the dimer **2-2** from the monomer **2·** after one-electron reduction makes the usual polarographic reduction techniques inaccurate. A combination of pulse polarography and reverse pulse polarography, using the reference electrode, Ag^+/0.01 M Ag^+ in 0.25 M $LiClO_4$-CH_3CN, led to the values $E_{4^+} = -1.081$ V and $E_{2^+} = -1.166$ V. The values with respect to the SCE reference are about $E_{4^+} = -0.88$ V and $E_{2^+} = -0.97$ V. Kashti-Kaplan, S.; Hermolin, J.; Kirowa-Eisner, E. *J. Electrochem. Soc.* **1981**, *128*, 802–810.

[16] Kubota, S.; Ikegami, Y. *J. Phys. Chem.* **1978**, *82*, 2739.

[17] The values reported in ref 2 have been modified somewhat by more extensive measurements, which will be described in another aricle, ref 18. The absorption coefficient at 395 nm utilized in the present work (which gives results for **2-2·** in agreement with the independently determined coefficients, using PQ^{2+}) is λ_{max} (ϵ_{max}), 395 nm (7500–8100).

[18] Hermolin, J.; Levin, M.; Kosower, E. M., article part 12, following in this issue.

[19] For details concerning the experimental appartus, cf. Huppert, D.; Dodiuk, H.; Kanety, H.; Kosower, E. M., Chem. *Phys. Lett.* **1979**, *65*, 164.

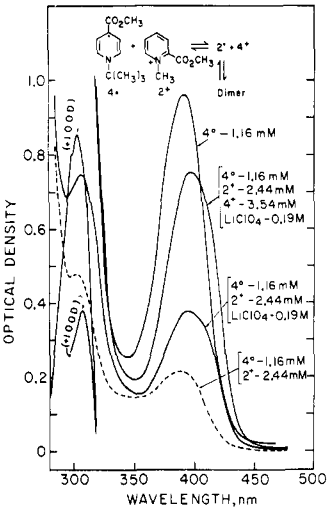

Figure 4. Spectra for determination of the dimerization constant of 1-methyl-2-(carbomethoxy)pyridinyl radical (**2·**) in acetonitrile, based on the equilibrium between the 2-pyridinyl radical dimer (**2-2**), the 1-alkyl-2-(carbomethoxy)pyridinium ion ($\mathbf{2}^+$), the 1-alkyl-4-(carbomethoxy)pyridinium ion ($\mathbf{4}^+$), and 1-alkyl-4-(carbomethoxy)pyridinyl radical (**4·**). The initial spectrum is labeled **4·**, for freshly distilled 1-*tert*-butyl-4-(carbomethoxy)pyridinyl radical, C_0 = 1.16 mM, in CH_3CN (11 mL). The second spectrum (the lowest curve near 400 nm) is obtained after addition of 1-methyl-2-(carbomethoxy)pyridinium perchlorate (6.75 mg, C_0 = 2.44 mM), the next higher curve is obtained after the addition of lithium perchlorate (223 mg, C_0 = 0.19 M), and the final curve (the second highest curve near 400 nm) is obtained after addition of 1-methyl-4-(carbomethoxy)pyridinium perchlorate (9.80 mg, C_0 = 3.54 mM). The sequence of events may be described as follows. Addition of $\mathbf{2}^+ClO_4^-$ to **4·** produces a mixture of **4·** (the only species absorbing near 400 nm), $\mathbf{2}^+$, **2·**, **2-2**, and $\mathbf{4}^+$. The loss of **4·** absorption is a quantitative measure of the amount of $\mathbf{2}^+$ consumed and $\mathbf{4}^+$ formed. $LiClO_4$ complexes with **4·** and thus shifts the position of the equilibrium between **2-2** and **2·** by decreasing the reduction potential of $\mathbf{4}^+$. $LiClO_4$ complexes with **2·** but has only a small effect on the position of the monomer–dimer equilibrium. [$LiClO_4$ changes the splitting constants, but not the signal intensity, in the EPR spectrum of **2·** (Ikegami, Y.; Sawayanagi, M., unpublished results) and shifts the position of the weak visible absorption of 1-methyl-2-acetylpyridinyl radical (see caption for Figure 6).] Addition of $\mathbf{4}^+ClO_4^-$ (the nature of the 1-alkyl group has no influence on these equilibria) leads to further oxidation of **2·**, reflected in the increase of the concentration of **4·**. The dimerization constant may then be calculated from the concentrations of the different species and the reduction potentials, using the equation given in the text.

E_0^{2+}, −1.166 V in CH_3CN-*n*-Bu_4NClO_4 (0.25 M)]. An expression relating the association constant, K_a, and the reduction potentials is derived as shown in eq 4–6, in which C_0 = initial concentration,

$$2(\mathbf{2}\cdot) = \mathbf{2\text{-}2} \qquad K_a = [\mathbf{2\text{-}2}]/[\mathbf{2}\cdot]^2 \tag{4}$$

$$E^{Py^+} = E_0^{Py^+} - RT/F \ln\,[Py\cdot]/[Py^+] \tag{5}$$

$$E_0^{4+} - E_0^{2+} = RT/F \ln\,([\mathbf{2}^+][\mathbf{4}\cdot]/[\mathbf{4}^+]) \times [4K_a/(-1 + [1 + 8K_a(C_0 - [\mathbf{4}\cdot])]^{1/2})] \tag{6}$$

[**4·**] = total radical concentration, and K_a = dimerization constant in M^{-1}. Other concentrations were known from absorption spectra or weights of added salt. Total radical concentrations were verified at the end of the experiment by titration with PQ^{2+}. A typical experiment (which gave a K_a value of 4 ± 1 × 10^5) is illustrated in Figure 4. Lithium perchlorate (0.19 M) does not markedly affect the association constant but shifts the absorption maximum for **4·** from 391 to 397 nm. An electrochemical method based on reverse pulse polarography[15] gave values similar to but somewhat lower than that noted above, the constants being 7 × 10^4 M^{-1} in CH_3CN-*n*-Bu_4NClO_4 (0.025–0.25 M), CH_3CN-$LiClO_4$ (0.025–0.25 M), and CH_3OH-$LiClO_4$ (0.25 M). Rate constants (1–4 × 10^4 M^{-1} s^{-1}) for association were also obtained from the electrochemical measurements.

Photodissociation of Dimer 2-2. Several types of experiments show that the dimer may be photodissociated to the monomer.

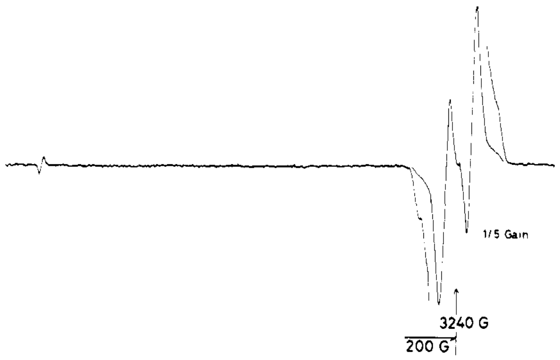

Figure 5. Triplet spectrum of the radical pair generated by photodissociation of 1-methyl-2-(carbomethoxy)pyridinyl dimer (**2-2**) in 2-methyltetrahydrofuran with light of wavelengths longer than 290 nm at 77 K. Dimer concentration = 1.74 × 10^{-2} M. Analysis of the spectrum shown indicates that $2D$ = 313 G, D = 0.0146 cm^{-1}, E = 0, and r = ~5.5 Å.

Laser pulse photolysis of **2-2** in CH_3CN (with a 2-ns pulse at 337 nm from a N_2 laser) increases **2·** light absorption. The rate at which the increased absorption disappears, i.e., the rate of radical recombination, is ca. 10^6 M^{-1} s^{-1}, after extrapolation to low laser pulse intensities. The photodissociation reaction under these conditions is remarkably reversible, since more than 1 einstein of photons per mole of **2-2** could be introduced into the solution over several hours without any change in its spectrum or response to additional pulses of light. We have shown elsewhere[20] that the photodissociation spectrum can be obtained by using reverse pulse polarography as a monitoring technique and that such a spectrum corresponds to the absorption spectrum of the dimer **2-2**.

Monomer could be detected during irradiation (330–400 nm) of **2-2** in MTHF by the rise in the intensity of the EPR spectrum. At 0 °C, the EPR spectrum changed little; at −30 and −50 °C, a substantial rise from an initially low EPR signal intensity was found. At −70 and −90 °C, somewhat smaller changes were seen. The rate of change in signal intensity was high for both light on and light off, except at −70 °C for which the return to equilibrium after the light was turned off was slower (almost 30 min). Photodissociation to the monomer **2·** could also be detected by EPR for a solution of dimer in CH_3CN at 0 °C.

Irradiation (λ >400 nm) of a MTHF glass containing **2-2** at 77 K gave the **2·** radical [λ_{max} 300 and 348 nm, the latter maximum displaced by undissociated dimer (**2-2**)]. A strong triplet signal was also noted in the EPR spectrum (Figure 5) from which a D value of 0.0155 cm^{-1} (average spin separation 5.5 Å) was obtained. Longer irradiation or irradiation with wavelengths between 330 and 400 nm led to some change in the shape of the triplet spectrum.

1-Methyl-2-acetylpyridinyl Radical. Reduction of $(COCH_3)\mathbf{2}^+I^-$ with sodium amalgam in acetonitrile leads, after distillation, to a green film of $(COCH_3)\mathbf{2}\cdot$. The radical in CH_3CN solution is similar in stability to **4·**, with UV–vis maxima at 321 (7300), 370 (2700) (sh), 395 (3000), 790 (500), and 890 nm (500). Electrochemically generated $(CH_3CO)\mathbf{2}\cdot$ in CH_3CN-$LiClO_4$ (0.21 M) has maxima at 324 (8800), 395 (3000), 740 (600), and 830 nm (600) (Figure 6). The shoulder at 370 nm due to dimer is not observed in the latter solution.

An EPR spectrum of the 1-methyl-2-acetylpyridinyl radical in CH_3CN at 20 °C is shown in Figure 7; the EPR signal intensity is very strong in comparison to that of the ester. The splitting constants derives from the spectrum are (format: see EPR data for **2·**) [CH_3CN, 20 °C] 5.47 (1, 1 N), 0.87 (3 or 5, 1 H), 5.28 (4, 1 H), 0.53 (5 or 3, 1 H), 2.88 (6, 1 H), 5.09 (NCH_3, 3H), 3.07 (CH_3CO, 3 H); [MTHF, 10 °C] 5.77 (1, 1 N), 1.09 (3 or 5, 1 H), 5.46 (4, 1 H), 0.69 (5 or 3, 1 H), 2.67 (6, 1 H), 5.36 (NCH_3, 3 H), 2.65 (CH_3CO, 3 H).

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[20] Hermolin, J.; Kirowa-Eisner, E.; Kosower, E. M. *J. Am. Chem. Soc.* **1981**, *103*, 1591.

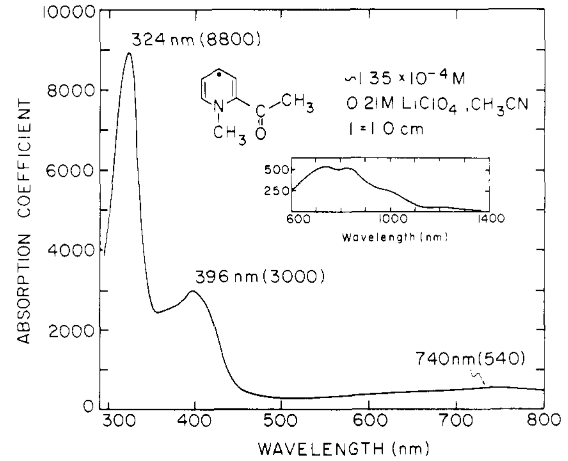


Figure 6. A UV-vis spectrum of 1-methyl-2-acetylpyridinyl radical [(CH$_3$CO)**2**·], generated by electrochemical reduction in CH$_3$CN–LiClO$_4$ (0.3 M). The visible absorption bands (at 740 and 840 nm) are shifted from those of freshly distilled (790 and 890 nm), which change as expected after the addition of LiClO$_4$.

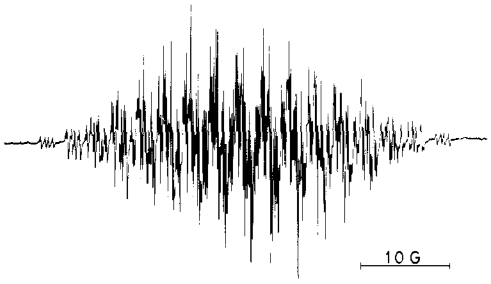


Figure 7. An EPR spectrum of 1-methyl-2-acetylpyridinyl radical ($C_0 < 1 \times 10^{-4}$ M) in CH$_3$CN.

In constrast to **2**·, (CH$_3$CO)**2**· exhibits a comparatively strong EPR signal in MTHF glass at 77 K. Irradiation (380–450 nm) adds a triplet signal to the EPR spectrum. The characteristics of the triplet spectrum are similar to those shown for the 2-(carbomethoxy)pyridinyl radical triplet spectrum in Figure 5, but the lines are broader.

Application of reverse pulse polarographic techniques[15] suggested that $\sim$5% of the (CH$_3$CO)$_2$· is present in dimer in 10^{-3} M LiClO$_4$–CH$_3$CN solutions. The reduction potential of COCH$_3$)**2**$^+$ is similar to that of **4**$^+$, with $E_0 = -1.030$ V.

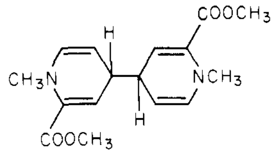
Discussion

Pyridinyl radicals vary in stability, which can be taken to mean the ease with which the radicals may be prepared and observed. 1-Alkyl-4-(carbomethoxy)pyridinyls and 1-alkyl-2-acetylpyridinyls can be readily prepared, distilled, and manipulated even in moderately concentrated solutions. Radicals such as 1-alkyl-2-(carbomethoxy)pyridinyls can be prepared and distilled but are mainly found as the dimer in moderately concentrated solutions. 1-Alkyl-3-(carbomethoxy)- or 1-alkyl-3-carbamidopyridinyl radicals can be observed only after generation by "fast" techniques (e.g., pulse radiolysis) and are isolated only in the form of the dimer.

For the study of the readily dissociable dimeric pyridinyls, we have examined the chemical behavior of dimers (a modern version of the first experiments of Gomberg on the monomer–dimer system of triphenylmethyl,[21] for which the dimer has a bond energy comparable to that of the pyridinyl radical–pyridinyl radical dimer, **2-2**[22]), the electrochemical formation of dimer, and the completely reversible laser pulse dissociation of dimers to monomers. We hope to determine in the future the rate constants for the reaction of pyridinyl radicals with organic halogen compounds and study solvent effects on the EPR spectra of pyridinyl radicals.[2,13,16,23,24] Two important points concern the structure of the radical dimer and the nature of the electronic transition responsible for the longest wavelength absorption of the dimers (332 nm for **2-2**). The latter is discussed in connection with the thin film studies of pyridinyls.[8]

Nature of 1-Alkyl-2-(carbomethoxy)pyridinyl Radicals). 1-Alkyl-2-(carbomethoxy)pyridinyl radicals are found mainly in the form of dimers. However, due to the reasonably rapid dissociation of the dimers to the monomeric pyridinyl radicals (~ 1 s^{-1} at room temperature), the dimers behave chemically and to some extent, physically, as free radicals. Thus, solutions of the dimer **2-2** exhibit EPR spectra, react with one-electron transfer agents such as paraquat and 1-alkyl-4-(carbomethoxy)pyridinium ions and are sensitive to oxygen. In addition, the dimer **2-2** can be distilled at temperatures so low that only the monomer could be volatile. The condensate at low temperature is a π-mer(π complex) of the free radical,[28] but π-mer absorption was never observed for the **2**· radical in solution. The free radical itself can be studied more directly by various techniques, including thin film spectroscopy.[8]

Structure of 2-2. Three possible dimers (6,6′, 4,6′, and 4,4′) may be formed from 1-methyl-2-(carbomethoxy)pyridinyl (**2**·). The 4,4′ dimer (**2-2**) is considered the most likely on the following grounds.



2-2

First, the size of the 1-alkyl group has no effect on the association constants, the absorption maxima, and the rates of reaction with oxygen and paraquat, implicating the 4 position (a site far removed from the 1-alkyl group) as the location of the dimer bond. Second, the 4 position is the least hindered to the approach of another radical. Third, the spin density at the 4 position (coupling constant 6.54) is much higher than that at the 6 position (coupling constant 2.54), enhancing the chance for coupling between the 4 positions. Fourth, the UV spectrum of **2-2** most resembles that of a 1,4-dihydropyridine.[25] Fifth, good NMR evidence supports a 4,4′ structure for the dimer of 1-alkyl-3-carbamidopyridinyls.[26,27] The 4,4′ structure for the dimer of the 1-methyl-2-acetylpyridinyl radical, (CH$_3$CO)**2**-(CH$_3$CO)**2**, is assigned on the basis of similar arguments.

Triplet Spectrum. Triplet EPR absorption, including the transition at $\Delta M = 2$, is observed for **2-2** after irradiation. The D value (0.0155 cm^{-1}) corresponds to an average spin separation of 5.5 Å implying that the pyridinyl radicals are not apposed to one another in the triplet. The acetylpyridinyl radical dimer, (CH$_3$CO)**2**-(CH$_3$CO)**2**, is also photolyzed in a MTHF matrix to a triplet. The triplet spectrum resembles that for irradiated **2-2**, with broader lines that suggest more motion in the acetyl radical in comparison to the carbomethoxy radical. Since acetophenone is less viscous and less dense than methyl benzoate, the difference between the two triplets is explicable on the basis of "local viscosity" being different for the two triplet pairs.

Conclusions

The 1-alkyl-2-(carbomethoxy)- and 2-acetylpyridinyl radicals and their dimers are attractive materials for mechanistic inves-

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(21) Gomberg, M. *J. Am. Chem. Soc.* **1900**, *22*, 757.

(22) Cf. summary in Forrester, A. R.; Hay, J. M.; Thomson, R. H. In "Organic Chemistry of Stable Free Radicals"; Academic Press; London, 1968; Chapter 2.

(23) Kosower, E. M.; Schwager, I. *J. Am. Chem. Soc.* **1964**, *86*, 5528.

(24) Mohammad, M.; Kosower, E. M., *J. Am. Chem. Soc.* **1971**, *93*, 2709, 2713.

(25) Eisner, U.; Kuthan, J., *Chem. Rev.* **1972**, *72*, 1.

(26) Biellmann, J.; Lapinte, C., *Tetrahedron Lett.* **1978**, 683–686.

(27) Moracci, F. M.; Liberatore, F.; Carelli, V.; Arnone, A.; Carelli, I.; Cardinali, M. E. *J. Org. Chem.* **1978**, *43*, 3420–3422; Carelli, V.; Liberatore, F.; Casini, A.; Mondelli, R.; Arnone, A.; Carelli, I.; Rotilio, G.; Mavelli, I., *Bioorg. Chem.* **1980**, *9*, 342–351.

(28) Itoh, M.; Nagakura, S., *J. Am. Chem. Soc.* **1967**, *89*, 3959–3965.

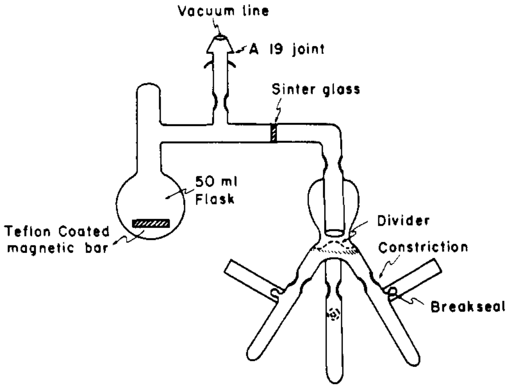

Figure 8. Apparatus for the preparation and distribution of solutions of stable pyridinyl radicals or pyridinyl radical dimers.

tigations of free-radical reactions, especially atom-transfer and one-electron-transfer reactions. The radicals and/or dimers are moderately easy to prepare and handle, the products are characterizable, and the reactions can be followed spectroscopically. Although these points are valid for 1-alkyl-4-(carbomethoxy)-pyridinyl radicals, the free 4 position makes the 2-substitued pyridinyls particularly interesting, with the *caveat* that dimerization could produce some kinetic and spectroscopic complications.

Experimental Section

Vacuum line techniques were standard, with particular precautions for pyridinyl radicals as follows. Carefully degassed solvent were stored over appropriate agents in flasks bearing Rotaflow valves: acetonitrile (Mg turnings and 1,1′-trimethylenebis(4-(carbomethoxy)pyridinium) iodide, effectively removing residual oxygen and other radical reactive impurities without introducing volatile light-absorbing impurites into the system); 2-methyltetrahydrofuran (sodium anthracenide); isopentane (potassium film). Pressure was 10^{-6} torr or less, and the system was normally pumped for up to 12 h to ensure degassed surfaces; flaming of surfaces was carried out where practical.

Instrumentation. UV–vis spectra were recorded on a Cary Model 17 spectrophotometer, EPR spectra were recorded on a Varian Model E-109E spectrometer, and irradiations in the EPR spectrometer cavity were carried out with a Ushio 500-W xenon lamp and Toshiba light filters. Polarographic reduction techniques are outlined elsewhere.[15]

1-Methyl-2-(carbomethoxy)pyridinyl Radical Dimer (2-2). 1-Methyl-2-(carbomethoxy)pyridinium (2^+) iodide (140 mg, 0.5 mmol), 3% sodium amalgam (500 mg, ~0.65 mmol of Na), and a glass- or Teflon-sealed stirred bar (see Figure 8) were sealed into a flask connected to a vacuum line.[29] After ~2 h of pumping, dry, degassed CH_3CN (~10–15 mL) was distilled in, the mixture was stirred for ~0.5 h at about 0 °C, the solvent was replaced by 2-methyltetrahydrofuran (2-MTHF) or isopentane without warming, and the green extract was filtered through a sinter into a manifold and divided into three to six tubes bearing breakseals. The solutions of **2-2** prepared in this way could be stored in the freezer for periods up to 1 year. Extraction with isopentane by using ultrasonic mixing was necessary for the preparation of solutions free of sodium iodide and other salts. The extraction with isopentane was carried out many times, the extract filtered, and part of the solvent distilled back taking care not to distill the extract to dryness.

A tube of **2-2** solution was connected through the breakseal to a distillation apparatus bearing two UV cells (0.1 cm, 1.0 cm), an EPR tube, and, separated by a breakseal, a tube containing 1,1′-dimethyl-4,4′-bipyridylium dichloride (paraquat) as titrant (Figure 9). After pumping, the seal was broken, the 2-MTHF removed, and the residue distilled (50–70 °C) onto the Dewar surface (liquid N_2) as a beautiful blue film of an appearance and color very similar to that formed on distillation of the 1-ethyl-4-(carboxy)pyridinyl radical.[2] Acetonitrile (or any other suitable degassed solvent) was distilled onto the blue film, and the colorless solution of **2-2** produced after warming was sealed off with that poriton of the apparatus bearing the cells and the titrant. [Sealing off was carried out without freezing in order to avoid high local concentrations of pyridinyl radical **2·**. Cooling the constriction with liquid N_2 soaked cotton was necessary.] The solutions of **2-2** prepared in this way generally exhibited optical densities between 0.1 and 1.0 (l = 1.0 cm) at 332 nm (cf. Figure 1 for a typical spectrum). Experiments were carried out with freshly prepared solutions of **2-2**, since slow disproportionation, more serious at higher concentrations, led to visible absorptions at 408, 430, and 550 nm accompanied by loss of paraquat-reactive material. The blue film of 1-methyl-2-(carbomethoxy)pyridinyl radical was often produced by distillation onto a layer of the desired solvent in order to avoid high local concentrations of radical and radical dimer during the warming procedure. The yields of **2-2** usually exceeded 50% (paraquat titration), but no effort was made to maximize this figure in view of the instability of the solutions.

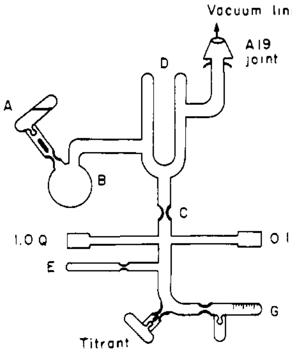

Figure 9. Apparatus for titration of pyridinyl radicals or radical dimers after distillation. A sample tube for ESR is also attached. The radical solution (cf. Figure 8) in the breakseal tube A is transferred to the distilling flask B, the solvent distilled into a receiver on the vacuum line, liquid N_2 poured into the Dewar, and the radical gently warmed [25–50 °C is normally sufficient for **2·** or (CH_3CO)**2·**]. A blue or green solid condensate collects on the Dewar. Pure CH_3CN is distilled from the line onto the Dewar, the liquid N_2 removed, and the solution allowed to flow into the manifold below. The manifold is sealed off at the constriction C. Some solution is poured into the ESR and tube E, which is then sealed off. After volume measurement (graduated tube G), the radical (or radical dimer) solution is mixed with the titrant, and the spectrum of the solution is taken. Two cells l = 1.0 cm and l = 0.1 cm) ensure that the OD will be in an accessible range.

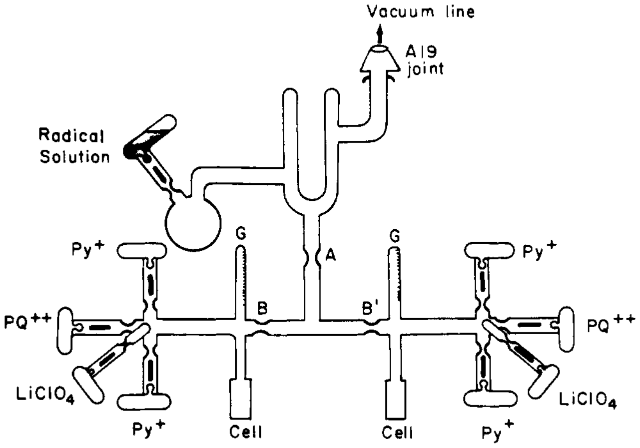

Figure 10. Measurement of association constant: Apparatus for the distillation of 1-methyl-2-(carbomethoxy)pyridinyl (**2·**) and the titration of solutions of the dimer (**2-2**) with $4^+ClO_4^-$, followed by addition of $LiClO_4$ and then $PQ^{2+}2Cl^-$. The same apparatus is used to follow the reaction of $2^+ClO_4^-$ with **4·**. (See the description of the experiment in the caption for Figure 4.) The appartus consists of two independent sides, allowing a test of reproducibility. After introduction of a radical solution and sealing off at A (see caption for Figure 9), the radical solution is poured around both sections of the manifold before sealing off at B or B′. Py^+ may be either 4^+ or 2^+, depending upon the experiment. PQ^{2+} is paraquat dichloride. G is a graduated tube for measurement of the volume of the solution.

Measurements of Association Constants through Titration. The apparatus (Figure 10) is used as follows. The radical solution (**2·** or **4·**) is prepared from material distilled onto the Dewar, using solvent from the line. Constriction A is sealed and the solution (~20 mL) divided about equally between the two sections of the manifold. The solution is poured into all parts of the apparatus to ensure that no adventitious oxidizing agents could disturb the comparability of the measurements done in the two halves of the manifold. The sections are then separated by sealing

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[29] The apparatus used was adapted from that described in ref 9. Changes in the procedure were introduced to take into account the instability of **2·** in comparison with the 1-alkyl-4-(carbomethoxy)pyridinyls, **4·**.

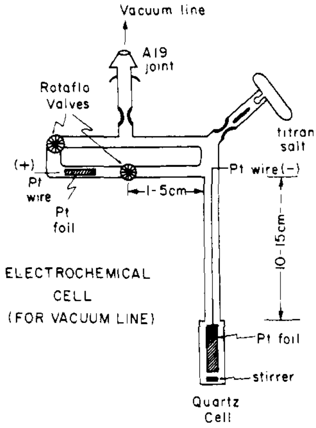

Figure 11. Electrochemical cell for use on a vacuum line. The Pt foil in the quartz cell is closer to the side wall than to the center of the cell, ensuring a clear optical path through the cell. The apparatus is easily inserted into the cell holder in a Cary Model 17 cell compartment, and spectra are measured, using a black cloth to shield the photomultiplier against room light.

off at constriction B. The absorption spectrum of the radical is measured, the appropriate titrant introduced through its breakseal, and reaction followed through the absorption spectrum. Each titration comes to completion within less than 10 min of thorough mixing. A typical sequence of spectra is shown in Figure 4 (details are described in the caption).

1-Methyl-2-acetylpyridinyl Radical [$(COCH_3)\cdot$]. 1-Methyl-2-acetylpyridinium iodide, mp 160–1 °C, crystallized from CH_3OH–Et_2O, from 2-acetylpyridine and methyl iodide, was converted to the pyridinyl radical as described for **2·**.

Electrochemical Cell for Vacuum Line. A "spectroelectrochemical" cell was constructed for use on the vacuum line (Figure 11) and was used for rapid generation of pyridinyl radicals and dimers (particularly those which were nonvolatile) and for determination of the spectroscopic (and chemical) properties. The catholyte and anolyte compartments were separated either by a sintered glass disk or, still better, by a Rotaflo valve (in which a Teflon plug makes the seal), because (a) compartment separation is controllable and (b) catholyte may be manipulated without contamination from the anolyte. The electrolytes were platimum foils (~6 cm^2) connected by platinum wires and separated by a distance of 10–15 cm, chosen so that current could readily pass under the conditions used. A breakseal tube contains titrant. A glass- or Teflon-coated stirring bar in the quartz optical-reaction cell is necessary. (Poor mixing may result in the formation of dihydropyridines or other reduced compounds.)

The radical concentration by titration was compared to that expected from the pyridinium salt weight (confirmed by absorption spectra) and an accurately measured volume of CH_3CN. The absorption coefficients were obtained from the pyridinyl radical absorption and concentration. The 395-nm maximum for **4·** had a ϵ_{max} value of 8000 M^{-1} cm^{-1}, probably the most accurate determination yet made.

The cell containing the pyridinium salt and lithium perchlorate [e.g., 1-methyl-2-(carbomethoxy)pyridinium perchlorate ($2^+ClO_4^-$) (0.52 mg, 2.1 μmol), lithium perchlorate (300 mg, 2.8 mmol)] was pumped on the vacuum line for ~2 h, and acetonitrile (~13.5 mL) was distilled in. Pyridinium salt concentration was verified by OD at λ_{max} (e.g., 270 nm). Current (~100 μA, Model 245 Data Precision digital multimeter) under Elron Model CHG-1 Galvanostat control, was passed until spectra indicated that the pyridinyl radical formed (dimer **2-2** maximum near 335 nm) had begun to decrease as a result of further reduction. (Electrochemical yield of radical ranges between 60 and 95%.) The Rotaflow valves were then closed to isolate the anolyte from the catholyte, allowing the stable free radicals or radical dimers to survive for a long time in the optical cell. Constant-current technique allows a greatly simplified electrochemical system to be used and faster reduction. Overreduction may be avoided if the reduction is monitored. The technique is successful if the first and second reduction potentials are well separated, as is true for pyridinium ions.

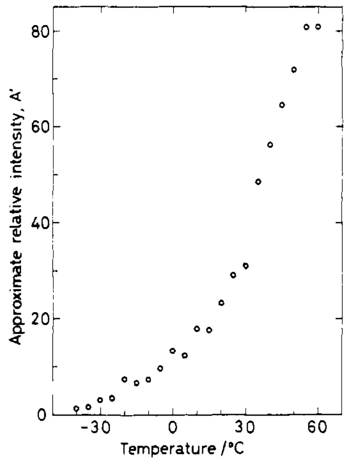

Figure 12. Plot of relative line intensity vs. temperature in the EPR spectrum of 1-methyl-2-carbomethoxy)pyridinyl radical (**2·**) in CH_3CN, C_0 (dimer = 2.11×10^{-3} M. The units of A' are arbitrary.

Absorption Coefficient of $PQ^{+}\cdot$. PQ^{2+}, $2Cl^-$ (2.13 mg, 8.55 μmmol), and 3% sodium amalgam (500 mg, 0.7 mg-atom of Na) were reacted with stirring in CH_3CN (10.95 mL) in the absence of oxygen, with formation of $PQ^{+}\cdot$ followed using a quartz cell (0.202 cm) separated from the reaction flask by two sintered glass filters. Maximum absorption, corresponding to a ϵ_{max} value at 605 nm of 12 900, was attained after 7 h, after which the absorption decreased. Either $\mathbf{4}^+ClO_4^-$ of $LiClO_4$ can be added to decrease the reaction time to as little as 0.5 h.

Electron Paramagnetic Resonance Spectra. EPR spectra were measured at carefully controlled temperatures. The line widths, Γ, were evaluated from the ΔH_{pp} through the relationship

$$\Gamma = 1/2(\Delta H_{pp})3^{1/2}$$

with Γ_0 obtained from the spectra measured at temperatures lower than −10 °C. The value for CH_3CN solution was 76.2 mG, while that found in MTHF was 65.0 mG.

An approximate relative intensity, A', was estimated from the relationship

$$A' = \Gamma^2 \times 2Y'_{max}/2Y'_{max}(ref)$$

in which $2Y'$ = peak-to-peak amplitude of the hyperfine line; $2Y'(ref)$ = peak-to-peak amplitude for the reference signal, that of Mn^{2+} ion. The temperature dependence of A' is shown in Figure 12 for **2·** in CH_3CN. The EPR spectrum (Figure 2) was obtained for 8.5×10^{-3} M **2-2**.

Laser Pulse Experiments. Solutions of **2-2** (c = ~10^{-3} M in CH_3CN, from OD at 332 nm) in 1-cm quartz cells were sealed off and exposed to 2-ns pulses from a N_2 laser. The OD increase between 330 and 400 nm or at 65 nm was measured, using a xenon light source, a monochromator, a photomultiplier, and an oscilloscope.[19] Plots of 1/ΔOD (at 350 nm) vs. time gave failry good straight lines (second-order behavior). The laser intensity was varied, and extrapolation to low intensity was made. The average of six measurements was 10^6 M^{-1}/s^{-1}. The spectrum after flashes totalling more than 1 einstein per mole was unchanged, indicating that the reaction was completely reversible.

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