

Photochemistry of 3,5-Dicarboalkoxyppyridines. Reduction and Rearrangement¹

T. J. van Bergen and Richard M. Kellogg*

Contribution from the Department of Organic Chemistry, The University, Zernikelaan, Groningen, The Netherlands. Received March 28, 1972

Abstract: The photochemistry of some 3,5-dicarboalkoxyppyridines has been investigated. For 3,5-dicarbomethoxyppyridine, photoreduction occurs in methanol by overall addition of solvent leading to 1,2- and 1,4-dihydropyridines bearing hydroxymethyl groups in the 2 and 4 positions, respectively. In ethanol chiefly a 1,2-dihydropyridine is found but in isopropyl alcohol, rather than solvent addition, coupling of two pyridyl radicals occurs. Related reduction processes are found with 3,5-dicarboethoxy-2,6-dimethylpyridine and with 3,5-dicarboethoxy-2,6-dimethyl-4-phenylpyridine. However, with 3,5-dicarbomethoxy-2,4,6-trimethylpyridine, the ring-contraction product, 2,4,5-trimethyl-3-carbomethoxyproline, is formed along with 3,5-dicarbomethoxy-2,4,6-trimethyl-1,4-dihydropyridine. A mechanism for this reaction is suggested on the basis of labeling experiments. For more hindered 3,5-dicarboethoxy-2,6-dimethyl-4-isopropylpyridine in cyclohexane, no photoreduction is observed but smooth conversion to 5,6-dimethyl-3,4-dicarboethoxy-2-isopropylpyridine, 2,4-dicarboethoxy-3,6-dimethyl-5-isopropylpyridine, and 2,5-dicarboethoxy-4,6-dimethyl-3-isopropylpyridine occurs. In methanol only the first product accumulates. A mechanism involving Dewar and prismane intermediates is proposed for these transformations. The spectral characteristics of the pyridines have been investigated. Weak fluorescence and fairly strong phosphorescence spectra are obtained. An $n-\pi^*$ absorption at about 295 $m\mu$ was found for 3,5-dicarbomethoxyppyridine. The fluorescence emission was assigned to a $\pi-\pi^*$ state, 0-0 line, ca. 320 $m\mu$, and the phosphorescence to a $\pi-\pi^*$ state, 0-0 line, ca. 390 $m\mu$. Alcohols as well as other substrates were found to quench the fluorescence from 3,5-dicarboethoxy-2,6-dimethylpyridine. The value of $k_q\tau$, where k_q is the quenching rate constant and τ the lifetime of the excited species, was 0.049 l. mol⁻¹. The value of $k_q\tau$ calculated from chemical quenching (plot of $1/\Phi$ against $1/[\text{MeOH}]$ where Φ is the quantum yield for pyridine disappearance) is 0.043 ± 0.07 . Fluorescence quenching and chemical quenching are therefore concluded to be kinetically coupled processes. A singlet excited state is clearly implicated in photoreduction and the various possibilities for the configuration of this state are discussed. The suggestion is made that hydrogen abstraction and photoisomerization may be related through the same distorted singlet state. The reactions of some *N*-methyl salts of the above pyridines were examined. Solvent addition proceeds sluggishly, if at all; the most important photochemical process is photoenolization wherein an excited carbonyl group abstracts a hydrogen from an adjacent alkyl group. This reaction was revealed by deuterium exchange experiments. Similar photoenolization does not occur with the free bases.

Our interest in the area of aza aromatic photochemistry concentrates on three overriding questions. (a) Can effective conversion of light quanta into chemically (and biochemically) useful products be achieved by making use of the known proclivity of aza aromatics to engage in reactions wherein a nitrogen center, activated in some poorly understood fashion, abstracts a hydrogen atom, leading to ultimate reduction of the aromatic systems?² (b) In what fashion do the photochemical reactions reflect the superposition of $n-\pi^*$ and $\pi-\pi^*$ states and can separate roles be assigned to these states or must one speak of a single entity?^{3,4} (c) Have the characteristic photochemical reactions of

aza aromatics been uncovered or are there still undiscovered reaction modes?

The above questions have been examined using 3,5-dicarboalkoxyppyridines chosen because of the utility of these compounds as models for nicotinamide bases.⁵ Moreover, since photoreduction was anticipated as a major reaction (although it had not been defined as such when this program was initiated), the reduction products, derivatives of 1,2- and 1,4-dihydropyridines, were expected to be sufficiently stable to allow isolation and study. This expectation was borne out in fact.⁶ The limitations and scope of this reaction have been defined. In addition, an alternative reaction path, photoisomerization, has been revealed.

Results

A. Reduction Reactions. Pyridines 2b-f were obtained by a Hantzsch synthesis as shown in eq 1; 2a

(d) R. M. Hochstrasser and C. Marzocco, *ibid.*, **46**, 4155 (1967); (e) R. M. Hochstrasser and C. Marzocco, *ibid.*, **49**, 971 (1968).

(4) See for recent work and an accumulation of references: (a) D. G. Whitten and M. T. McCall, *J. Amer. Chem. Soc.*, **91**, 5097 (1969); (b) J. W. Happ, M. T. McCall, and D. G. Whitten, *ibid.*, **93**, 5496 (1971); (c) Y. I. Lee, D. G. Whitten, and L. Pederson, *ibid.*, **93**, 6330 (1971).

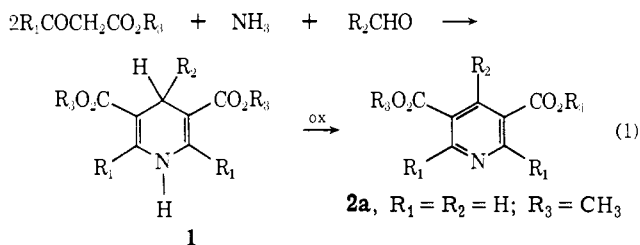
(5) (a) H. R. Mahler and E. H. Cordes, "Biological Chemistry," Harper and Row and J. Weatherhill, Inc., London, 1966; (b) T. C. Bruce and S. Benkovic, "Bioorganic Mechanisms," Vol. 2, W. A. Benjamin, New York, N. Y., 1966; (c) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969; (d) J. L. Kurz, R. Hutton, and F. H. Westheimer, *J. Amer. Chem. Soc.*, **83**, 584 (1961); (e) U. K. Pandit and F. R. Mas Casbré, *Chem. Commun.*, 552 (1971).

(6) Preliminary communication: R. M. Kellogg, T. J. van Bergen, and H. Wynberg, *Tetrahedron Lett.*, 1987 (1969).

(1) Abstracted in part from the Ph.D. Thesis of T. J. van Bergen submitted in Mar 1972.

(2) A partial list of references is given for hydrogen abstraction processes culminating in solvent addition to a variety of aza aromatics: (a) H. Linschitz and J. S. Connolly, *J. Amer. Chem. Soc.*, **90**, 2979 (1968); (b) J. S. Connolly and H. Linschitz, *Photochem. Photobiol.*, **7**, 791 (1968); (c) N. C. Yang, L. S. Gorelic, and B. Kim, *ibid.*, **13**, 275 (1971); (d) M. Ochiai, E. Mizuta, J. Asahi, and K. Morita, *Tetrahedron*, **24**, 5861 (1968); (e) H. Steinmaus, I. Rosenthal, and D. Elad, *J. Amer. Chem. Soc.*, **91**, 4921 (1968); (f) M. Natsume and M. Wada, *Tetrahedron Lett.*, 4503 (1971); (g) R. A. F. Deeleman, H. C. van der Plas, A. Koudijs, and P. S. Darwinkel-Risseuw, *ibid.*, 4159 (1971); (h) L. R. Hamilton and P. J. Kropp, *ibid.*, 1625 (1971); (i) E. C. Taylor, Y. Maki, and B. E. Evans, *J. Amer. Chem. Soc.*, **91**, 5181 (1969); (j) D. Elad, I. Rosenthal, and H. Steinmaus, *Chem. Commun.*, 305 (1969); (k) D. Elad and I. Rosenthal, *ibid.*, 905 (1969); (l) F. R. Stermitz, R. P. Seiber, and D. E. Nicodem, *J. Org. Chem.*, **33**, 1136 (1968); (m) V. I. Stenberg and E. F. Travecedo, *ibid.*, **35**, 4131 (1970); (n) H. Steinmaus, I. Rosenthal, and D. Elad, *ibid.*, **36**, 3594 (1971); (o) see further in text for related references.

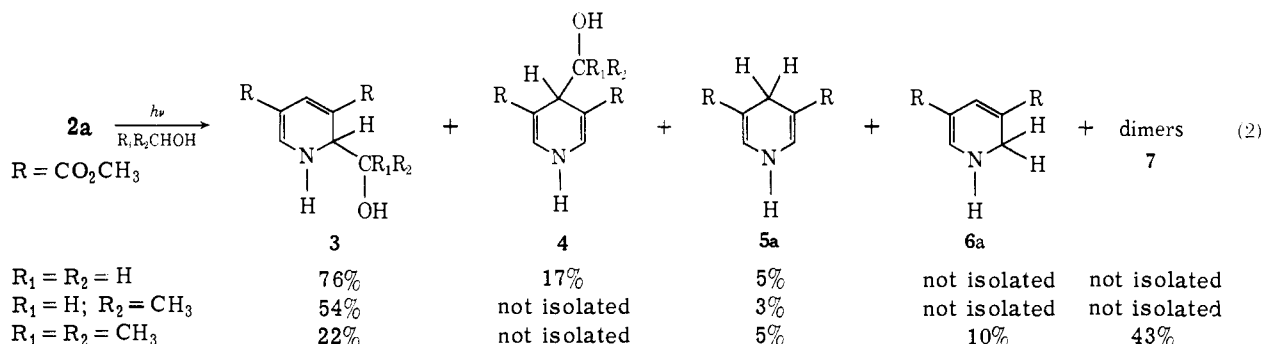
(3) For leading references see: (a) M. A. El-Sayed and M. Kasha, *Spectrochim. Acta*, **15**, 758 (1960); (b) M. A. El-Sayed, *J. Chem. Phys.*, **38**, 2834 (1963); (c) E. C. Lim and J. M. H. Yu, *ibid.*, **45**, 4742 (1966);



	R_1	R_2	R_3
b	CH_3	H	C_2H_5
c	CH_3	CH_3	CH_3
d	CH_3	CH_3	C_2H_5
e	CH_3	C_6H_5	C_2H_5
f	CH_3	$CH(CH_3)_2$	C_2H_5

was obtained by esterification of the commercially available diacid. The 1,4-dihydropyridines **1b-f** served as reference materials in identification of products (see below).

The products derived from 3,5-dicarbomethoxy-pyridine (**2a**) on irradiation at 2537 Å in methanol, ethanol, and isopropyl alcohol are shown in eq 2. All



products were isolated by preparative thick layer chromatography (tlc) on silica gel. Yields are based on consumed starting material; deviations from quantitative recovery are attributable chiefly to difficulties in chromatographic separation. The solvent addition products, **3a** and **4a**, obtained on irradiation in methanol, were identified on the basis of the following considerations: (a) both have molecular ion peaks at m/e 227 corresponding to the addition of methanol to **2a**; (b) **3a** has strong ultraviolet (uv) absorptions at 282 and 394 $m\mu$ indicative of a 1,2-dihydropyridine, whereas **4a** has absorptions at 222, 242 (sh), and 363 $m\mu$ characteristic of a 1,4-dihydropyridine⁷⁻⁹ (the absence of the 280- $m\mu$ band in 1,4 derivatives allows quantitative determination of 1,2 to 1,4 ratios; see below); (c) the nmr spectrum of **3a** indicated the absence of molecular symmetry and, besides the expected ester, vinyl, OH, and NH resonances, showed the diastereomeric protons of the methylene group derived from methanol as an AB system ($J_{gem} = 10.5$ Hz); the nmr spectrum of **4a** in contrast indicated the equivalence of the vinyl hydrogens and of the methoxy methyls. These combined spectral data identify the products; complete spectral data are given in Table I along with data for the other

(7) (a) J. Paleček, L. Pňáčková, and J. Kuthan, *Collect. Czech. Chem. Commun.*, **34**, 427 (1969); U. Eisner, *Chem. Commun.*, 1348 (1969).

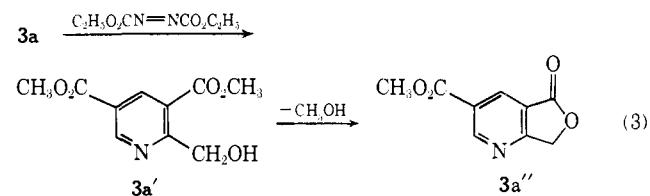
(8) W. Traber and P. Karrer, *Helv. Chim. Acta*, **41**, 2066 (1958).

(9) P. J. Brignell, U. Eisner, and P. G. Farrell, *J. Chem. Soc. B*, 1083 (1966).

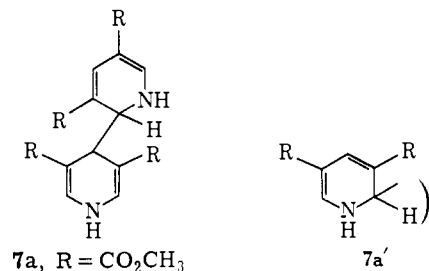
reduction products from **2b** to **2f**. Product **3a** was oxidized to the lactone (**3a''**) on treatment with diethylazo dicarboxylate (eq 3).¹⁰ A minor product (**5a**) from **2a** in methanol was readily identified as 1,4-dihydro-3,5-dicarbomethoxypyridine (**5a**).^{7,9}

Solvent addition also occurs in ethanol giving chiefly the 1,2-dihydropyridines (**3b',b**), which were the only products that could be isolated in respectable yield. Separation into the respective diastereomeric forms **3b** (mp 168.5–176°) and **3b'** (mp 165–168°) was accomplished by tlc.

A distinct change in product distribution takes place when the reaction is carried out in isopropyl alcohol. Modest yields of 1,2-dihydropyridine (**3c**) derived from solvent addition and the 1,2' and 1,4 reduction products of **2a** were obtained. However, the major products were two dimers, **7a** and **7a'**, that crystallized separately from ethanol in two fractions, mp 222.5–223.5 and 219.5–224°, respectively. The mass spectra had molecular ion peaks at m/e 392 indicative of dimeric structures, but the uv and nmr spectra of the two isomers differed. Compound **7a** has uv absorption at 290 (ϵ 19,100) and 392 $m\mu$ (ϵ 6700), which is nearly identical with the spectrum of 1,2-dihydropyridine **3a**. This indicates that



coupling has occurred giving at least one ring containing a 1,2-dihydropyridine unit. The nmr spectrum of this isomer (Table I) shows the protons α to nitrogen as an AB system ($J = 3.0$ Hz) at δ 4.15 and 4.69; moreover, two nonequivalent pairs of vinyl hydrogens are seen. We think that the 2,4'-coupled structure **7a** fits best the spectral data that are now in hand. A 2,2'-coupled structure (meso or *d,l*) is tentatively assigned to **7a'**. This dimer has a symmetry plane as



(10) Y. Yoneda, K. Suzuki, and Y. Nitta, *J. Amer. Chem. Soc.*, **88**, 2328 (1966).

Table I. Spectral and Physical Data for Reduction Products from 2a to 2f

Compd	Mp, °C	Uv (96% —C ₂ H ₅ OH)—		—Ir, cm ⁻¹ (KBr)—			Nmr, δ units	Anal. [Calcd (found)]		
		λ, mμ	Log ε	N-H	OH	C=O		C	H	N
3a	139–142 ^a	218	4.11	3230	3060	1660	3.38 (d, <i>J</i> = 11 Hz, 1, CH ₂ O), 3.68 (d, <i>J</i> = 11 Hz, 1, CH ₂ O), 3.70 (s, 3, OCH ₃), 3.74 (s, 3, OCH ₃), 4.64 (m, 1, CHN), 7.63 (d, <i>J</i> = 1.5 Hz, 1, vinyl H), 7.70 (d, <i>J</i> = 1.5 Hz, 1, vinyl H) ^b	52.86 (52.76)	5.77 (5.97)	6.17 (6.10)
		282	4.26		3350	1690				
		383	3.76							
3b	168.5–170 ^a	282	4.27	3250	3060	1680	0.90 (d, <i>J</i> = 7.0 Hz, 3, CHCH ₃), 3.60 (s, 3, OCH ₃), 3.65 (s, 3, OCH ₃), 4.18 (t, <i>J</i> = 5.0 Hz, 1, CHN), 3.60 (m, 1, CHOH), 7.49 (d, <i>J</i> = 1.5 Hz, 1, vinyl H), 7.65 (d of d, 1, <i>J</i> = 1.5, 6.0 Hz, 1, vinyl H), 8.50 (br s, 1, NH), 4.75 (d, <i>J</i> = 5.0 Hz, 1, OH) ^c	54.77 (54.44)	6.27 (6.25)	5.80 (5.67)
		378	3.77		3420	1700				
3b'	165–168 ^a	282	4.29	3290	3400	1665	1.00 (d, <i>J</i> = 7.0 Hz, 3, CHCH ₃), 3.58 (s, 3, OCH ₃), 3.65 (s, 3, OCH ₃), 4.58 (t, <i>J</i> = 3.0 Hz, 1, CHN), 3.60 (m, 1, CHOH), 7.46 (d, <i>J</i> = 1.5 Hz, 1, vinyl H), 7.68 (d of d, <i>J</i> = 1.5, 6.0 Hz, 1, vinyl H), 8.26 (br s, 1, NH), 4.79 (d, <i>J</i> = 4.5 Hz, 1, OH) ^c	54.77 (54.55)	6.27 (6.28)	5.80 (5.81)
		390	3.72			1695				
3c	158.5–160 ^a	282	4.27	3250	3060	1675	1.06 (s, 6, (CH ₃) ₂ C), 3.68 (s, 3, OCH ₃), 3.73 (s, 3, OCH ₃), 4.52 (s, 1, CHN), 7.68 (d, <i>J</i> = 1.5 Hz, 1, vinyl H), 7.75 (d, <i>J</i> = 1.5 Hz, 1, vinyl H)	56.45 (56.49)	6.71 (6.80)	5.49 (5.53)
		380	3.73		3440	1700				
4a	165–167 ^a	222	4.07	3305	3100	1660	3.20 (d of d, <i>J</i> = 6.0, 4.0 Hz, 2, CH ₂ OH), 3.62 (s, 6, OCH ₃), 3.65 (t, <i>J</i> = 6.0 Hz, 1, CHCH ₃), 4.25 (t, <i>J</i> = 4.0 Hz, 1, OH), 7.25 (s, 2, vinyl H), 8.34 (br s, 1, NH) ^c	52.86 (52.66)	5.77 (5.70)	6.17 (6.24)
		242 (sh)	3.71		3440	1690				
		363	3.90							
6a	127.5–128 ^{a,d}	283	4.24	3290		1660	3.58 (s, 3, OCH ₃), 3.63 (s, 3, OCH ₃), 4.20 (s, 2, CH ₂), 7.30 (d, <i>J</i> = 1.5 Hz, 1, vinyl H), 7.58 (d, <i>J</i> = 1.5 Hz, 1, vinyl H) ^c	54.82 (54.93)	5.63 (5.62)	7.10 (7.13)
		394	3.71			1705				
7a	222.5–223.5 ^c	290	4.28	3380		1660	3.78 (s, 3, OCH ₃), 3.80 (s, 3, OCH ₃), 3.85 (s, 6, OCH ₃), 4.15 (d, <i>J</i> = 3.0 Hz, 1, CHN), 4.69 (d, <i>J</i> = 3.0 Hz, 1, CHN), 7.42 (s, 1, vinyl H), 7.64 (s, 1, vinyl H), 7.57 (d, <i>J</i> = 1.5 Hz, 1, vinyl H), 7.74 (d, <i>J</i> = 1.5 Hz, 1, vinyl H) ^e	55.10 (54.53)	5.14 (5.23)	7.15 (6.99)
		392	3.82			1710				
7a'	219.5–224 ^b	290	3.90	3380		1685	3.58 (s, 6, OCH ₃), 3.96 (s, 1, CHN), 7.08 (s, 1, vinyl H), 7.18 (s, 1, vinyl H), 8.83 (s, 1, NH) ^c	55.10 (55.14)	5.14 (5.20)	7.15 (7.20)
365	3.89									
8a	192–198 ^f	212	4.07	3220	3040	1670	1.24 (s, 3, (CH ₃) ₂ COH), 1.29 (s, 3, (CH ₃) ₂ COH), 2.05 (d of d, <i>J</i> _{gem} = 14.0, <i>J</i> _{vic} = 8.0 Hz, 1, CH ₂ COH), 1.30 (d of d, <i>J</i> _{gem} = 14.0, <i>J</i> _{vic} = 2.5 Hz, 1, CH ₂ COH) ^b	Mass spec parent peak <i>m/e</i> 269		
		283	4.17		3420	1695				
		395	3.70							
8b	123–138	220	<i>g</i>	3280		1660	1.00–2.00 (m, 11, C ₆ H ₁₁), 3.78 (s, 6, OCH ₃), 4.80 (d, <i>J</i> = 6.0 Hz, 1, CHN), 8.04 (d, <i>J</i> = 1.5 Hz, 1, vinyl H), 9.41 (d, <i>J</i> = 1.5 Hz, 1, vinyl H) ^b	Mass spec parent peak <i>m/e</i> 279		
		280				1690				
		380								
9a	121.5–123.5 ^a	212	4.10	3400	3110	1660	1.25 (t, <i>J</i> = 7.0 Hz, 6, OCH ₂ CH ₃), 4.14 (q, <i>J</i> = 7.0 Hz, 4, OCH ₂ CH ₃), 1.42 (s, 3, CH ₃), 2.32 (s, 3, CH ₃), 3.40 (d, <i>J</i> = 10.5 Hz, 1, CH ₂ OH), 4.00 (d, <i>J</i> = 10.5 Hz, 1, CH ₂ OH), 7.80 (s, 1, vinyl H) ^b	59.34 (59.15)	7.47 (7.44)	4.94 (4.74)
		282	4.31		3450	1690				
		380	3.83		3520					
10a	135–136 ⁱ	233	4.24	3340	3500	1690	1.32 (t, <i>J</i> = 7.0 Hz, 6, OCH ₂ CH ₃), 4.20 (q, <i>J</i> = 7.0 Hz, 4, OCH ₂ CH ₃), 2.30 (s, 6, CH ₃), 3.40 (d, <i>J</i> = 6.0 Hz, 2, CH ₂ OH), 4.00 (t, <i>J</i> = 6.0 Hz, 1, CHCH ₃) ^b	59.34 (59.40)	7.47 (7.50)	4.94 (4.91)
		355	3.87							
14	61–63 ^{i,k}	274	4.12	3280	3080	1660	0.64 (t, <i>J</i> = 7.0 Hz, 3, OCH ₂ CH ₃), 0.75 (t, <i>J</i> = 7.0 Hz, 3, OCH ₂ CH ₃), 3.80 (q, <i>J</i> = 7.0 Hz, 2, OCH ₂ CH ₃), 3.87 (q, <i>J</i> = 7.0 Hz, 2, OCH ₂ CH ₃), 1.80 (s, 3, CH ₃), 2.63 (s, 3, CH ₃), 4.07 (d, <i>J</i> = 11.0 Hz, 1, CH ₂ OH), 4.57 (d, <i>J</i> = 11.0 Hz, 1, CH ₂ OH), 7.35 (s, 5, C ₆ H ₅), 3.57 (s, 3, CH ₂ OH) ^{b,k}	64.43 (63.88)	7.47 (7.38)	3.58 (3.64)
		358	3.61		3400	1695				
30	184–186 ^j	215	4.16	3260	3340	1680	1.28 (t, <i>J</i> = 7.0 Hz, 3, OCH ₂ CH ₃), 1.42 (s, 3, CH ₃), 2.33 (s, 3, CH ₃), 1.67 (s, 6, C(CH ₃) ₂), 3.36 (d, <i>J</i> = 11.0 Hz, 1, CH ₂ OH), 3.84 (d, <i>J</i> = 11.0 Hz, 1, CH ₂ OH), 4.15 (q, <i>J</i> = 7.0 Hz, 2, OCH ₂ CH ₃) ^b	Mass spec parent peak <i>m/e</i> 295		
		279	4.26			1700				
		374	3.79							

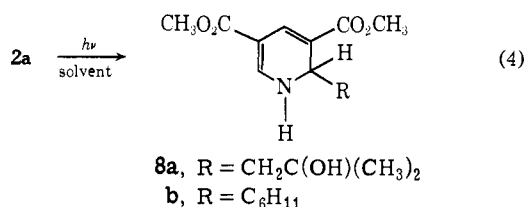
^a Recrystallized from C₂H₅OH. ^b In CD₃OD. ^c In DMSO-*d*₆. ^d A mp of 135–136° is reported in ref 7a. ^e In DMSO-*d*₆ + D₂O. ^f Recrystallized from CCl₄. ^g Approximately equivalent to 8a but not measured quantitatively. ^h In pyridine-*d*₅ + D₂O. ⁱ Recrystallized from C₆H₆. ^j Recrystallized from CH₃OH. ^k This material crystallizes with one molecule of methanol.

indicated by the nmr spectrum (Table I) with one type of methine proton and two types of vinyl hydrogens, which could conceivably indicate a symmetrical dimer cou-

pled at the 4,4' positions. However, the uv spectrum shows a characteristic 1,2-dihydropyridine band at 290 mμ plus a band at 365 mμ with a 1:1 ratio of extinction

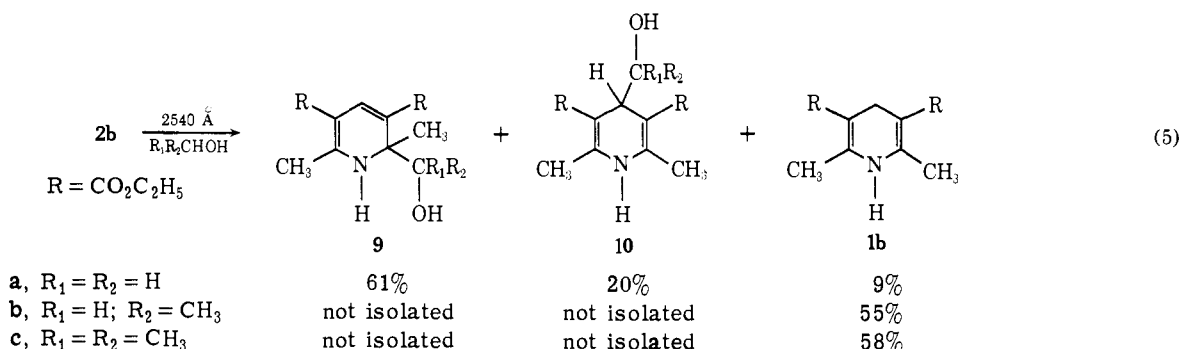
coefficients. These uv absorptions are most consistent with a 2,4'-coupled pyridine dimer but the nmr spectrum is clearly incompatible with this structure. Therefore, the most reasonable possibility is that given.

Solvent addition to **2a** also took place in solvents not having a hydrogen atom activated by hydroxyl. Irradiation in *tert*-butyl alcohol gave the 1,2-dihydropyridine **8a** in 51% yield and irradiation in cyclohexane gave a product in 45% yield with spectral characteristics consistent with **8b** (eq 4). Irradiation of **2a** in a 1:1 mix-



ture of water and *tert*-butyl alcohol gave only **8a** in 43% yield. Analytically pure samples could not be obtained from either **8a** or **8b** but in addition to the expected uv spectra (Table I) the mass spectra showed the correct parent molecular ion peaks at *m/e* 269 and 279, respectively. The geminal dimethyl groups of **8a** are diastereotopic and appear separately at δ 1.24 and 1.29.

Similar reduction processes were found with **2b** in which methyl groups are brought into the 2,6 positions. The results of irradiations in a variety of alcohols are given in eq 5 and spectral and analytical data are com-

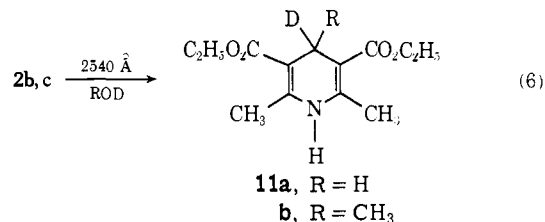


pared in Table I. In this case only the relatively small molecule methanol gives large amounts of solvent addition products whereas overall addition of hydrogen in a 1,4 manner is the predominant reaction with the larger alcohols, ethanol and isopropyl alcohol. With the latter alcohols the characteristic fluorescence of the 1,4 and 1,2 solvent addition products could be observed on the tlc plates but the amounts were insufficient to allow isolation.

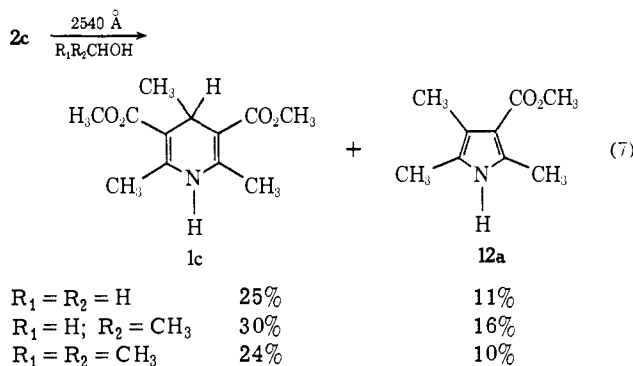
In contrast to the 2,6-unsubstituted compound **2a**, irradiation of **2b** in *tert*-butyl alcohol, cyclohexane, or a 1:1 mixture of *tert*-butyl alcohol-water led to quantitative recovery of starting material.

Irradiation of **2b** in ethanol-*O-d* led to 1,4-dihydropyridine **11a** with one deuterium atom (within nmr experimental error) at the 4 position (eq 6). Exactly the same degree of deuterium incorporation was found for **2c** in methanol-*O-d* solution. The yield of **11a** in ethanol-*O-d* (22%) was consistently lower than in ethanol-*O-h* (55% of **1b**) suggesting a significant isotope effect.

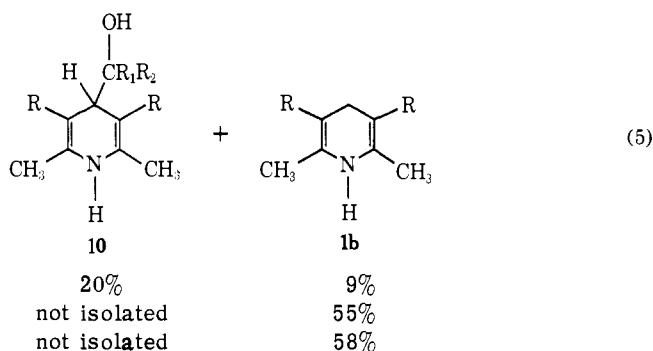
A startling change in behavior was observed with 3,5-dicarboethoxy-2,4,6-trimethylpyridine (**2c**) on irra-



diation in various alcoholic solvents. In methanol, ethanol, and isopropyl alcohol the major product was 1,4-dihydro-3,5-dicarboethoxy-2,4,6-trimethylpyridine (**1c**); in addition 3-carboethoxy-2,4,5-trimethylpyrrole (**12a**) was isolated in moderate yield (eq 7).



The structure of **12a** was established from (a) a molecular ion peak at *m/e* 167 in the mass spectrum con-



cordant with the molecular formula C₉H₁₃NO₂, (b) only one methoxy group in the nmr spectrum, and (c) infrared (ir) absorptions at 3310 and 1670 cm⁻¹ corresponding to N-H and C=O functionalities, respectively. The spectra of **12a**, mp 120.5–123.5° (lit.¹¹ 124.5–126°), were identical with those of a sample prepared by classical methods.¹² The pyridine diethyl ester **2d** reacted equally well giving, in ethanol, **1d** and **12b** in 23 and 16% yields, respectively.

Analysis by glc and uv established that **1c** and **12a** appeared simultaneously during the reaction. Independent irradiation of 1,4-dihydropyridine **1c** failed to give any **12a**; hence, **1c** can be excluded as a precursor of **12a**. Reexamination of the reaction of **2b** (missing the methyl group in the 4 position) by glc demonstrated that no detectable amount of the possible product, 3-carboethoxy-2,5-dimethylpyrrole (**13a**), prepared independently,¹³ was formed.

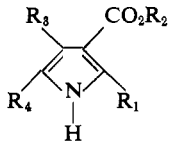
An effort was made to determine whether the ring contraction to pyrrole proceeds by expulsion of one

(11) G. Korschuin, *Ber.*, **38**, 1128 (1905).

(12) L. Knorr and K. Hess, *ibid.*, **44**, 2762 (1911).

(13) A. Hantzsch, *Ber.*, **23**, 1474 (1890).

Table II. Anisotropic Nmr Shifts in Carboalkoxypyrroles



Compd no.	R ₁	R ₂	R ₃	R ₄	$\Delta = \delta^a(\text{CCl}_4) - \delta(\text{C}_6\text{D}_6)$					
					R ₁ (CCl ₄)	Δ	R ₃ (CCl ₄)	Δ	R ₄ (CCl ₄)	Δ
12a	CH ₃	CH ₃	CH ₃	CH ₃	2.39	-0.04	2.06	-0.30	2.06	+0.14
12b	CH ₃	C ₂ H ₅	CH ₃	CH ₃	2.38	-0.07	2.07	-0.31	2.07	+0.14
13a	CH ₃	C ₂ H ₅	H	CH ₃	2.40	-0.07			2.15	+0.17
13b	CH ₃	C ₂ H ₅	C ₆ H ₅	CH ₃	2.38	-0.07			1.97	+0.06
13c	CH ₃	C ₂ H ₅	H	H	2.48	-0.19				

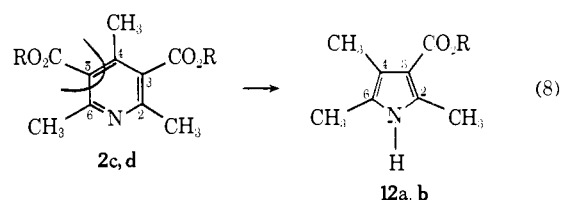
^a All signals are singlets given in δ units. Identical concentrations ($10^{-1} M$) were used.

carboalkoxy group without rearrangement of the remaining carbon framework. A partial answer to this question was obtained by deuterium labeling experiments. Deuterium exchange in $\text{CH}_3\text{OD}-\text{CH}_3\text{ONa}$ was observed to occur with **2c** faster at the 4 than at the 2,6 positions. By careful control of the conditions a sample of **2c** containing 1.38 ± 0.07 deuterons (assayed by nmr) in the 4-methyl group and negligible deuterium ($<5\%$) in the 2,6-methyl groups was obtained. To trace the methyl group in pyrrole **12a**, the resonances of the methyl groups must be assigned. In Table II anisotropic solvent shifts for pyrroles **12a,b** and **13a-c** are given. A portion of the pyrrole skeleton can be viewed as an α,β -unsaturated carbonyl system for which anisotropic solvent shifts have been well investigated.¹⁴ Obviously, an nmr signal at *ca.* δ 2.40 is characteristic for a methyl group in the 2 position of a 3-carboalkoxy-pyrrole; this is shifted downfield in benzene. Introduction of an additional methyl group at the 5 position gives rise to an absorption at δ 2.15 in CCl_4 (see **13a**); this group obviously shifts *upfield* in benzene. On the other hand, in a compound with methyl groups in the 4 and 5 positions, *i.e.*, **12b**, a single peak is seen at δ 2.07 in CCl_4 ; however, in benzene separate resonances are seen with one being shifted appreciably upfield and the other strongly downfield. It is logical that the former arises from the 5-methyl group and the latter from the 4-methyl group. The methyl ester **12a** behaves similarly. These shielding and deshielding effects are in accord with theory.¹⁴

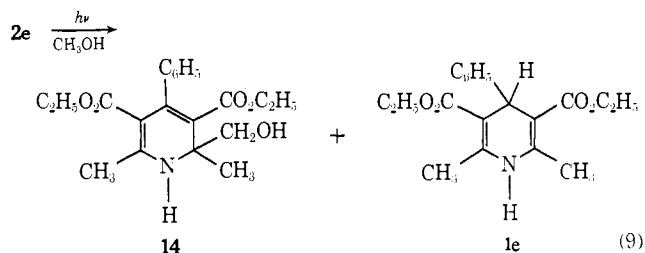
Photochemical reaction was effected with labeled **2c**. The pyrrole was isolated and its nmr spectrum was taken in both benzene and CCl_4 . From careful integration of the nmr resonances it was found that the combined signal for the 4- and 5-methyl groups in CCl_4 was 75% of that expected for six hydrogens whereas the combined signals in benzene for the 2- and 4-methyl groups (integrated together because of extensive deuterium broadening of the 4-methyl resonance) corresponded to 72% of six hydrogens. Therefore, the 4-methyl group of pyrrole **12a** in this experiment must contain 1.59 ± 0.09 atoms of deuterium. Obviously, the 4-methyl group of pyrrole **12a** is derived from the 4-methyl group of starting material **2c**. Further labeling

(14) Review: L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectra in Organic Chemistry," 2nd ed, Pergamon Press, Elmsford, N. Y., 1969, pp 104-113.

material are useless owing to the symmetry of the system. However, in any case, by far the most economical interpretation of the labeling experiment is that by some process (see Discussion) one carboalkoxy group of the pyridine with the ring-carbon atom is expelled without further rearrangement of the pyridine skeleton (eq 8).



Working on the theory that increased substitution and hindrance about the ring might enhance the amount of ring contraction, the photochemistry of 3,5-dicarboethoxy-2,6-dimethyl-4-phenylpyridine (**2e**) was investigated.¹⁵ However, in methanol only a 1,2-solvent addition product (**14**) and the 1,4-reduction product (**1e**) were observed (eq 9) in yields of 64 and 5%, re-



spectively. The 1,4-addition product, 3,5-dicarboethoxy-2,6-dimethyl-4-hydroxymethyl-4-phenyl-1,4-dihydropyridine (**15**), could not be isolated. No trace of 3-carboethoxy-2,5-dimethyl-4-phenylpyrrole (**13b**)¹⁶ could be detected by glc or tlc.

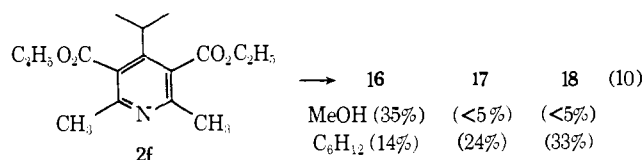
B. Rearrangement Reactions. Still pursuing the overcrowding hypothesis, the photochemical reaction of 3,5-dicarboethoxy-2,6-dimethyl-4-isopropylpyridine (**2f**) was examined.¹⁷ However, monitoring of the reaction indicated that neither photoreduction nor ring contraction to a pyrrole occurred in degassed methanol solution. Likewise, in degassed cyclohexane solution

(15) A. P. Phillips and P. L. Graham, *J. Amer. Chem. Soc.*, **74**, 1552 (1952).

(16) E. Benary, *Chem. Ber.*, **44**, 493 (1911).

(17) The synthesis of 3,5-dicarboethoxy-2,6-dimethyl-4-*tert*-butylpyridine was attempted under Hantzsch conditions. However, even at high temperatures and pressure no condensation of acetoacetic ester, ammonia, and pivaldehyde could be observed. This synthesis was not pursued further.

no longer wavelength ultraviolet bands were seen. However, by glpc and tlc it was established that a new product had nevertheless been formed in methanolic solution and that *three* new products had been formed in cyclohexane solution. The distributions of these products are given in eq 10. Separation of **16–18** was



accomplished by painstaking thick layer chromatography. The molecular weights (mass spectral) were identical with that of **2f**; moreover the ir and uv spectra of **16–18** closely resembled those of **2f** establishing positional isomer relationship. There are 15 possible positional isomers of **2f**. Since **16–18** all showed non-equivalent carboalkoxy groups in the nmr, the one symmetrical isomer, 2,6-dicarboethoxy-4-isopropyl-3,5-dimethylpyridine, is eliminated leaving 14 viable possibilities. Initial probing into the relative position of the carboalkoxy groups was done by investigating the reactions with hydrazine hydrate. Ortho esters are expected to give condensation products that have characteristic uv absorption above 300 m μ .^{18a,b} Reaction of **16** with hydrazine led to unmistakable appearance of long wavelength absorption in the uv. Work-up gave a triazanaphthalene (**19**), mp 279–285°, in 15% yield. On the other hand neither **17** nor **18** showed development of long wavelength absorption in the uv on treatment with hydrazine hydrate. A slight shift owing to hydrazide formation was observed; normal work-up procedures that afforded **19** failed to give any derivative from **17** or **18**. Attempts to effect ring closure of the dihydrazides with 4 *N* HCl were also fruitless. A mixture of **17** with a small amount of **16** gave isolable amounts of **19** contaminated with *no* other triazanaphthalene. On this basis **17** and **18** were concluded not to have ortho-disposed ester functionalities.

Nmr spectroscopy and deuterium exchange experiments allowed further structural probing. In particular the chemical shifts of alkyl groups on the pyridine ring are quite distinctive.¹⁹ Attachment in the 2 or 6 positions leads to a significant downfield shift relative to 3,4,5 positions as is illustrated in the first three entries in Table III. One notes that 2- or 6-methyl groups normally are found at *ca.* δ 2.50 and groups in the 3,4,5 positions at *ca.* δ 2.20. The nmr data can be usefully supplemented by making use of the known acidic properties of methyl groups in the 2,4,6 positions.^{20a,b} Thus, these types of methyl groups are revealed by deuterium incorporation in CD₃OD–

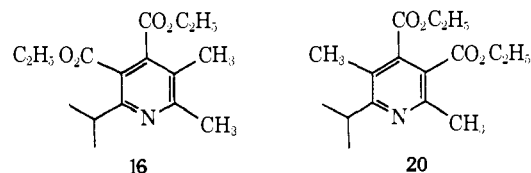
(18) (a) H. L. Yale, K. Losee, J. Martius, M. Hulsing, F. M. Perry and J. Bernstein, *J. Amer. Chem. Soc.*, **75**, 1933 (1953); (b) R. G. Jones, *ibid.*, **78**, 159 (1956).

(19) (a) H. J. Bernstein and W. G. Schneider, *J. Chem. Phys.*, **24**, 469 (1956); (b) J. N. Murrell and V. M. S. Gil, *Trans. Faraday Soc.*, **61**, 402 (1965).

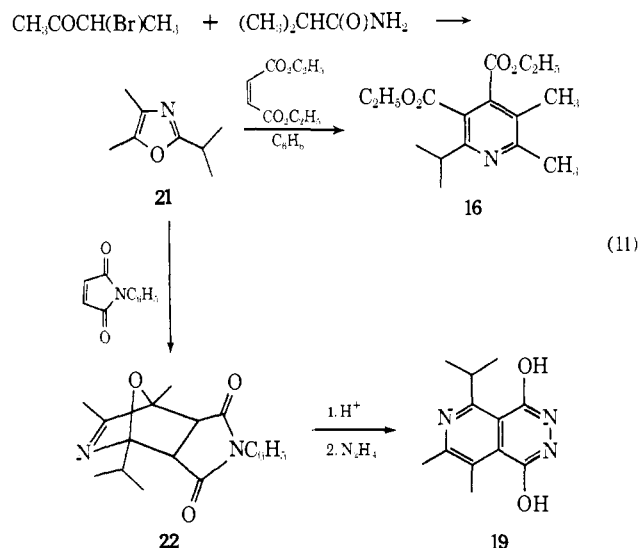
(20) (a) L. A. Paquette, "Principles of Modern Heterocyclic Chemistry," W. A. Benjamin, New York, N. Y., 1968; (b) for recent references, see: J. A. Zoltewicz and P. E. Kandetzi, *J. Amer. Chem. Soc.*, **93**, 6562 (1971); (c) in these highly substituted systems the isopropyl group cannot achieve readily the planar configuration necessary for maximum stabilization of the anion formed by removal of the tertiary proton. Hence deuterium exchange of this proton is unlikely under conditions where the methyl groups may exchange. No detectable exchange of a tertiary proton was ever observed.

CD₃ONa mixtures.^{20c} Pertinent data are also collected in Table III.

The nmr spectrum (CCl₄) of ortho ester **16** showed a heptet for the tertiary proton of the isopropyl group shifted 0.36 ppm *downfield* relative to **2f** strongly suggesting it to be in the 2 or 6 position. The methyl singlets appear at δ 2.23 and 2.53. The latter is characteristic for a 2- or 6-methyl group (Table III). At 86° in CD₃OD–CD₃ONa the methyl group at δ 2.53 exchanges with deuterium much more rapidly than the group at δ 2.23. (Both ethoxy groups exchanged completely with deuteriomethanol within 10 min at room temperature likely owing to an intramolecular catalysis effect.) This establishes the substitution pattern at the 2 and 6 positions and, since **16** is an ortho ester, the two structural possibilities are **16** and **20**. On the basis



of mechanistic considerations structure **16** was guessed to be correct and confirmation was sought through unambiguous synthesis. The successful synthesis of **16** (eq 11) was modeled on an approach to pyridox-



ine.^{21, 22a–c} The previously unknown oxazole **21**^{23, 24} with maleic acid diethyl ester in refluxing benzene gave a 12% yield of **16**, identical in all respects with the photoisomer. Because of the low yield, **21** was also converted to 3,4-dimethyl-5,8-dihydroxy-1-isopropyl-2,6,7-triazanaphthalene (**19**) by reaction with *N*-phenylmaleimide (73%) followed by hydrolysis and treatment with hydrazine (64%). The sample of **19**, mp 285–287°, was identical in all respects with that isolated from photoproduct **16**.

The structure of **17** was elucidated from the following

(21) (a) G. Ya. Kondrat'eva, *Chem. Abstr.*, **52**, 6345a (1958); (b) G. Ya. Kondrat'eva and C.-H. Huang, *ibid.*, **54**, 12131d (1960); (c) G. Ya. Kondrat'eva, *ibid.*, **53**, 21940d (1959).

(22) (a) E. E. Harris, *J. Org. Chem.*, **27**, 2705 (1962); (b) T. Naito and T. Yoshima, *Chem. Phar. Bull.*, **14**, 918 (1966); (c) R. A. Firestone, E. F. Harris, and W. Reuter, *Tetrahedron*, **23**, 943 (1967).

(23) A. Faworsky and B. Issatschenko, *J. Prakt. Chem.*, [2] **88**, 655 (1913).

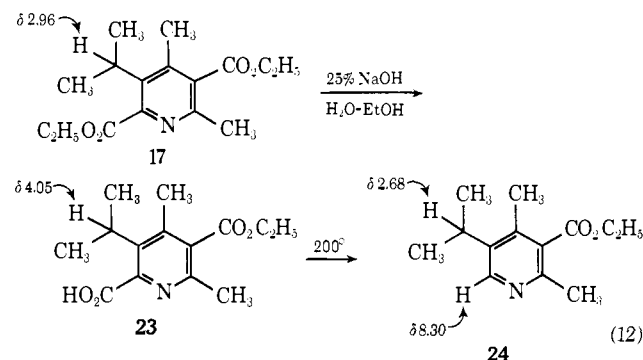
(24) G. Theilig, *Chem. Ber.*, **86**, 96 (1953).

Table III. Chemical Shift and Deuterium Exchange Data for Isomers 16-18 and Reference Compounds

Compd	Alkyl (chemical shift in δ units)	k , l. ($\text{mol}^{-1} \text{sec}^{-1}$) ^a	Hydrogen content ^b	Rel reactivity ^c
2f	2,6-CH ₃ (2.40, s) ^d (2.48) ^e	5.10×10^{-3}	0.71	
2d	4-CH(CH ₃) ₂ (2.90, h) ^{e, f}	15.3×10^{-3}	0.84	$k_{2.6}/k_4 = 1.14$
2,5-Dicarboethoxy- 3,6-dimethylpyridine 16	2,6-CH ₃ (2.48, s) ^d (2.50, s) ^e		0.64 ^g	
	4-CH ₃ (2.23, s) ^d (2.27, s) ^e	j	j	j
	6-CH ₃ (2.80, s) ⁱ			
17	3-CH ₃ (2.59, s) ⁱ			
	CH ₃ (2.53, s) ^d (2.55, s) ^e	3.22×10^{-3}	0.39	$k_{2.53}/k_{2.25} = 15$
	CH(CH ₃) ₂ (3.26, h) ^d			
18	CH ₃ (2.23, s) ^d (2.25, s) ^e		2.61	
	CH ₃ (2.48, s) ^d (2.52, s) ^e		2.22	
	CH(CH ₃) ₂ (2.96, h) ^d	2.30×10^{-3}		$k_{2.24}/k_{2.32} = 1.53$
18	CH ₃ (2.16, s) ^d (2.24, s) ^e		1.89	
	CH ₃ (2.32, s) ^d (2.28, s) ^e		2.94	
	CH(CH ₃) ₂ (2.90, h) ^d	3.62×10^{-3}		$k_{2.22}/k_{2.28} = 28$
	CH ₃ (2.22, s) ^d (2.22, s) ^e		0.51	

^a Pseudo-first-order rate constant for deuterium incorporation in molecule using $7 \times 10^{-2} M$ solutions in CD₃OD with 0.5 M CD₃ONa. ^b Steady-state values obtained at ca. 68 hr. ^c Log ([protons]_a^{t=0}/[protons]_a^{t=1})/log ([protons]_b^{t=0}/[protons]_b^{t=1}). ^d In CCl₄. ^e In CD₃OD. ^f Heptet. ^g Total of both methyl groups. ^h At lower temperature the 4-methyl group is more reactive. ⁱ In CDCl₃. ^j Sample not available; see ref 26.

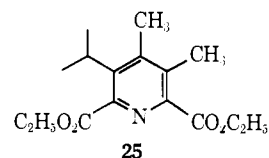
considerations. (a) The two methyl groups appeared at δ 2.16 and 2.48 in the nmr (CCl₄), which strongly suggests that the latter group is in a 2 or 6 position. The tertiary proton of the isopropyl group appears at δ 2.96, very close to its position in starting material. (b) In sharp contrast to ortho ester 16, at room temperature in CD₃OD-CD₃ONa solution one ester group exchanged with solvent within 10 min but the second group was not detectably exchanged after 24 hr at 86°. Under the latter conditions both methyl groups became deuterated at nearly the same rate (Table III). (Note the sluggish reactivity of the 5-methyl group of 16, run for comparison purposes.) The deuterium exchange data and nmr spectra require a 2,4 arrangement of the methyl groups and a structure with isopropyl not adjacent to nitrogen. The great difference in transesterification rates can only mean that one group is not sterically blocked; *i.e.*, one carboalkoxy group is α to nitrogen. Only structure 17 is compatible with these facts. Chemical confirmation of this assignment was based on the predicted ease of selective hydrolysis (eq 12). Test reactions with starting material 2f indicated



that no detectable base-catalyzed hydrolysis could be accomplished even under forcing conditions (several hours reflux in 25% KOH solution containing ethanol). On the other hand, 17 was readily hydrolyzed (eq 12) to monocarboxylic acid 23 in essentially quantitative yield. In 23 the tertiary proton of the isopropyl group was shifted 1.09 ppm downfield whereas the methyl groups were scarcely affected. Location of the acid function at the 2 position was substantiated by ex-

pected²⁵ decarboxylation (100% yield) to 24 wherein the tertiary proton of the isopropyl group was shifted 1.37 ppm upfield compared to 23.²⁶

The structure of 18 was unraveled using essentially the same argumentation as for 17. The nmr spectrum (CCl₄) showed the two methyl groups at δ 2.32 and 2.22 and the isopropyl tertiary hydrogen at δ 2.90. Although the nmr data are completely consistent with 25, this structure clearly is incorrect since one ester

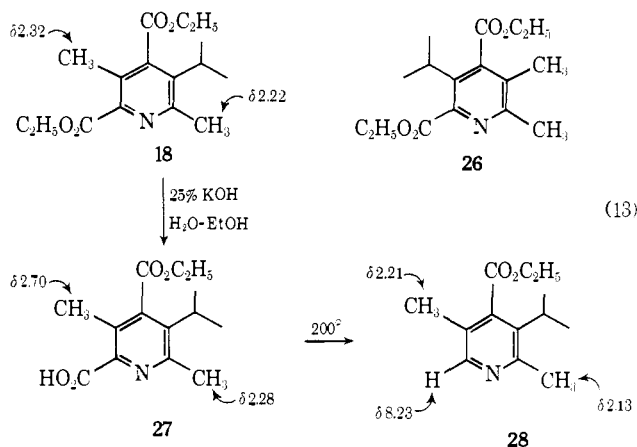


group rapidly transesterified in CD₃OD-CD₃ONa at room temperature, whereas the other was nonreactive at 86° for 24 hr. (Steric hindrance of substitution at the adjacent ester group by the isopropyl group of 25 is not a valid argument since this self-same structural factor gives no problems in 17.) As seen from Table III, one methyl group exchanges protons for deuterons. Since 18 is not an ortho ester and since one carboalkoxy group is sterically hindered whereas the other is in the 2 position, structures 18 and 26 may be considered (eq 13). In 18 there is reason to expect an anomalous upfield shift of the 6-methyl group owing to the proximity of the bulky isopropyl substituent.²⁷ Unambiguous rejection of 26 is, however, not possible purely on the basis of this argument. Selective hydrolysis of 18 occurred in 74% yield giving monocarboxylic acid 27 in which one methyl group was shifted 0.38 ppm downfield. Pyrolysis of 27 at 200° gave 28 in quantitative yield. In 28 the methyl group was shifted

(25) E. P. Oliveto, "Pyridine and Its Derivatives," Part III, E. Klingsberg, Ed., Interscience, New York, N. Y., 1962, p 206.

(26) We are deeply indebted to Professor J. F. Biellmann, University of Strasbourg, France, for supplying us with spectra of 2,5-dicarbo-methoxy-3,6-dimethylpyridine for comparison purposes. The nmr shifts of the methyl protons are given in Table III; good agreement with the shift of the 6-methyl group of 17 is noted.

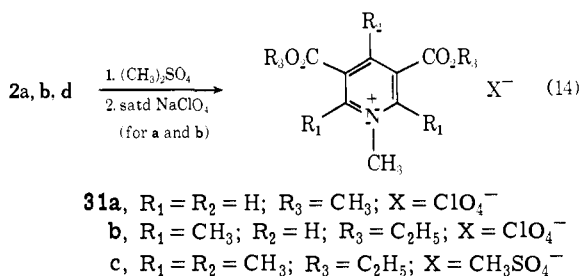
(27) (a) For olefins, see: J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. II, Pergamon Press, Elmsford, N. Y., 1966, p 723. (b) For ortho-substituted furans and thiophenes, see: U. E. Wiersum, Ph.D. Thesis, Groningen, 1968.



0.49 ppm upfield relative to **27**; furthermore, a nuclear Overhauser effect (NOE) between a methyl group at δ 2.21 and the aromatic hydrogen was established (10% enhancement) indicating beyond doubt the incorrectness of **26** and correctness of **18**. Rather surprisingly the aromatic hydrogen was coupled to *both* methyl groups, $J < 1.0$ Hz. No attempt was made to develop independent syntheses of **17** or **18**.

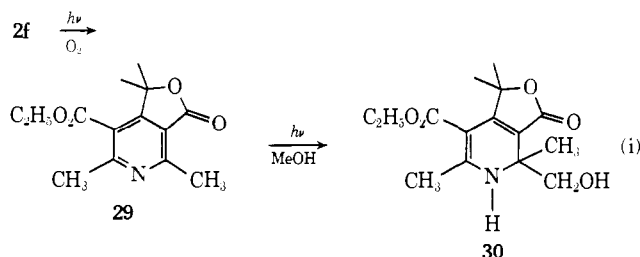
In cyclohexane solution **16**, **17**, and **18** appear concurrently as established by glpc. Independent irradiation of the three photoproducts led chiefly to decomposition with no clearly discernible formation of either starting material **2f** or other photoisomers. Extensive investigations of **2f** at low temperature in alcohol solution gave no indication of the presence of stable valence bond isomers (see Experimental Section).^{28, 29}

C. Reactions of Pyridinium Salts. The reactions of several pyridinium salts were investigated in order to assess partially the effect of the nonbonding electrons on pyridine photochemistry. The *N*-methyl perchlorates (**31a,b**) and *N*-methyl sulfate (**31c**), chosen for their good solubility in methanol, were synthesized as shown in eq 14.^{30, 31}



(28) This problem is still under active investigation: H. Stinissen, unpublished results.

(29) In solutions that are not rigorously degassed, **2f** produces a lactone **29** (eq i). In methanol solution **29** undergoes photoaddition

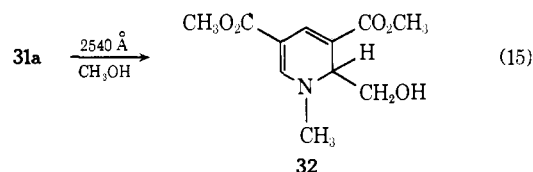


leading to **30**. This problem is not encountered in the absence of oxygen.

(30) P. R. Brook and P. Karrer, *Justus Liebigs Ann. Chem.*, **605**, 1 (1957).

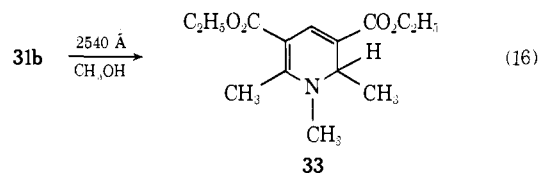
(31) O. Mumm and G. Hingst, *Ber.*, **56**, 2301 (1923).

On irradiation for 24 hr of **31a** in methanol a bright yellow color developed, which arises from **32** obtained by extraction with benzene of the water-soluble products of the reaction mixture (eq 15). Product **32**, ob-



tained in 18% yield calculated on the actual amount of starting material, had uv maxima at 233 (log ϵ 4.14), 286 (4.31), and 390 m μ (3.84) indicating a 1,2-dihydropyridine structure. The nmr spectrum (C_5D_5N) displayed, besides the expected ester and vinylic absorptions, a singlet at δ 3.33 assigned to the *N*-methyl group, a triplet at 6.70 for the hydroxyl proton, and a broad multiplet at 3.90 for the diastereomeric methylene protons. Small amounts of other reduced products were present but these could not be separated by tlc. Starting material **31a** was the only water-soluble product and this was recovered in 50% yield.

Under the same conditions **31b** led to an 11% yield of 1,2-dihydropyridine **33** (eq 16). Starting material

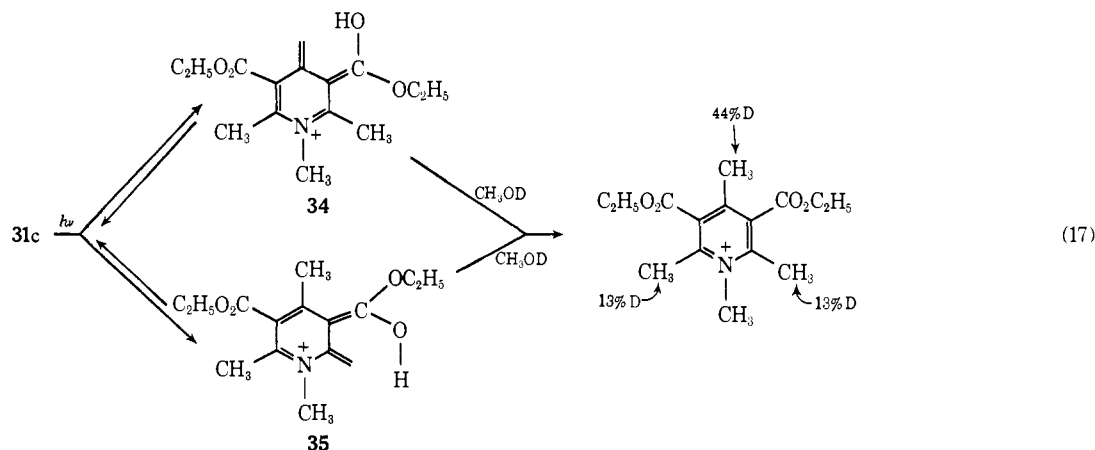


was recovered in 52% yield. An independent synthesis of **33** was accomplished by reduction of **31b** with sodium borohydride.⁸

Even after 45 hr irradiation in methanolic solution no products could be detected from **31c** either by tlc or uv. The starting material was recovered in 77% yield. This virtual nonreactivity of **31c** as well as the sluggish reaction of **31b** led to the suspicion that energy might be dissipated through photoenolization reactions involving an ester function and an adjacent alkyl group. Such a process is depicted in eq 17 for **31c**. The photoenols **34** and **35** can be formed and their presence can be inferred by carrying out the irradiation of **31c** in methanol-*O-d*.^{32a-d} Irradiation of **31c** for 18 hr in methanol-*O-d* led to incorporation of 1.32 deuterium atoms in the 4-methyl group and 0.39 deuterium atom in each of the 2,6-methyl groups. No significant exchange occurred at the *N*-methyl group. On extended standing in the dark no exchange took place; in addition, irradiation of 1,2,4,6-tetramethylpyridinium perchlorate,³³ in which the ester groups are absent, led to no detectable deuterium incorporation. Although the presence of photoenols **34** and **35** is strongly implicated by these observations, attempts at trapping these intermediates with dimethyl acetylenedicarboxylate led to inconclusive results. Irradiation of **31b** under similar conditions led to incorporation of 0.72 deuterium atom in each of the 2,6-methyl groups.

(32) (a) N. C. Yang and C. Rivas, *J. Amer. Chem. Soc.*, **83**, 2213 (1961); (b) N. C. Yang and M. J. Jorgenson, *Tetrahedron Lett.*, 1203 (1964); (c) G. Wettermark, *Photochem. Photobiol.*, **4**, 621 (1965); (d) N. J. Turro, "Molecular Photochemistry," W. A. Benjamin, New York, N. Y., 1967, p 147.

(33) E. M. Kosower and P. E. Klineduist, *J. Amer. Chem. Soc.*, **78**, 3493 (1956).



These results contrast starkly with the behavior of the free bases **2a,b,d**, which during irradiation in alcohol solution incorporate *no* detectable amounts of deuterium into the alkyl groups.

D. Spectroscopic and Kinetic Investigations of Photoreduction. A variety of spectroscopic and kinetic investigations were carried out in order to determine the multiplicity and configuration of the reactive state in the photoreduction reactions. This particular reaction, because it is most common to pyridines, was deemed of sufficient interest to warrant mechanistic investigation. In addition, a variety of experimental factors made this aspect of pyridine photochemistry especially amenable to study. The photoreduction of 2,6-dimethyl-3,5-dicarboethoxypyridine (**2b**) in methanolic solution was chosen for detailed examination. In all cases the cosolvent was *tert*-butyl alcohol in which **2b** was photochemically stable. For spectroscopic investigations the series **2a,b,d,f** was used.

The uv spectra of **2a** in *n*-hexane and methanol are shown in Figure 1a; the spectrum of 1,3-dicarbomethoxybenzene in the same solvents is also given for reference purposes in Figure 1b. The spectra of **2b** and also more alkylated derivatives (not shown) are slightly bathochromically shifted obscuring the detail in the long wavelength region although similar solvent induced differences in spectra were apparent. The decrease in absorbance of **2a** in methanolic solution in the 290-m μ area strongly implicates the presence of the pyridine $n-\pi^*$ transition; similar differences between the *n*-hexane and methanol spectra of 1,3-dicarbomethoxybenzene (Figure 1b) are not found, indicating that an ester $n-\pi^*$ absorption is not involved.³⁴⁻³⁶ The 0-0 line for the pyridine $n-\pi^*$ band is estimated to lie at 310 m μ (92.5 kcal/mol).³⁷ This agrees well with values for 3- and 4-cyanopyridines, for which $n-\pi^*$ singlet maxima are observed at 270 and 290 m μ ,³⁸ respectively.

A weak, broad fluorescence was observed from the

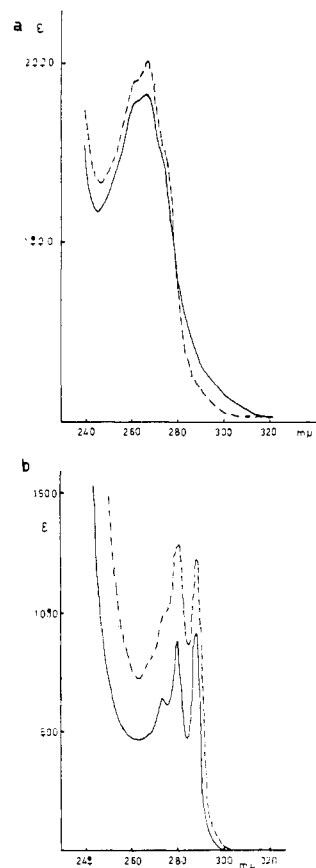


Figure 1. (a) The uv spectra of **2a** in *n*-hexane (—) and in methanol (---). (b) The uv spectra of 1,3-dicarbomethoxybenzene in *n*-hexane (—) and in methanol (---).

pyridines **2** in *tert*-butyl alcohol at room temperature. This is illustrated for **2b** in Figure 2; the emission maximum lies at 408 m μ , whereas for **2a** lacking alkyl substituents the maximum lies at 397 m μ , for trialkylated **2d** the maximum is found at 410 m μ , and for **2f** the maximum is at 392 m μ . For **2b** the 0-0 line is estimated to lie at about 320 m μ (89 kcal/mol). This effect of alkylation parallels closely that found in the absorption spectra. Because of the lack of any apparent mirror image symmetry between absorption and emission spectra of **2b**, a variety of criteria were invoked to ensure that an adventitious impurity was not responsible for the observed emission. The criteria included: (a) unchanged fluorescence intensity on

(34) Attempts to locate the $n-\pi^*$ bands by running spectra in 2 *N* HCl or in *n*-hexane containing acid³⁵ failed owing to a twofold increase in intensity of the $\pi-\pi^*$ transition with accompanying broadening of the absorption band.

(35) G. Coppens, C. Gillets, J. Nasielski, and E. van der Donck, *Spectrochim. Acta*, **18**, 1441 (1962).

(36) The ester $n-\pi^*$ absorption is expected at shorter wavelengths: J. G. Calvert and J. N. Pitts, "Photochemistry," Wiley, New York, N. Y., 1967, pp 427, 434.

(37) Method of H. P. Stephenson, *J. Chem. Phys.*, **23**, 1077 (1954).

(38) (a) S. F. Mason, *J. Chem. Soc.*, 1247 (1959); (b) P. J. Hoover and M. Kasha, *J. Amer. Chem. Soc.*, **91**, 6508 (1969).

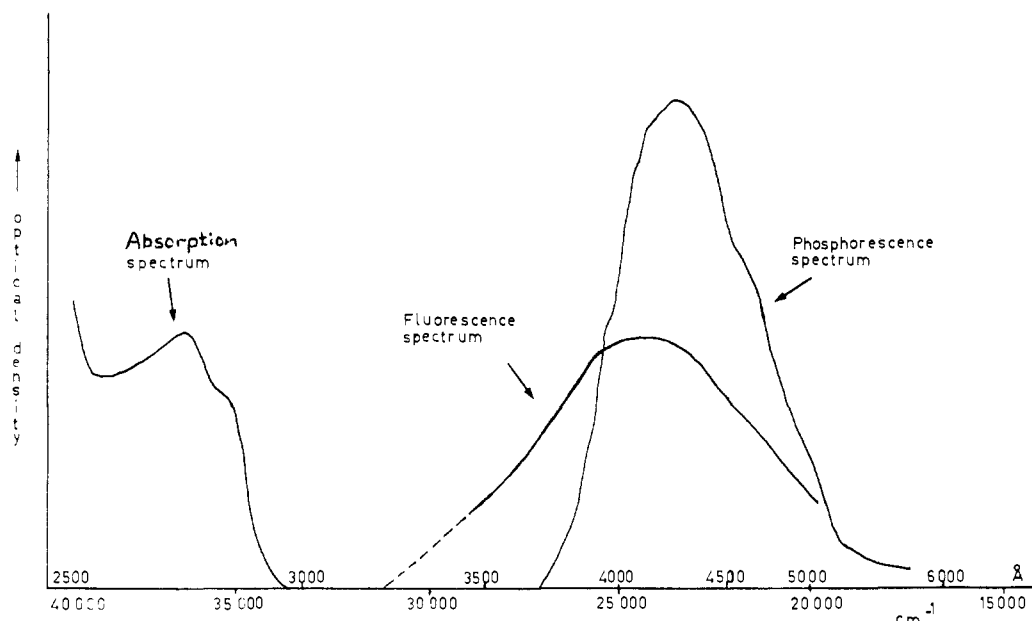


Figure 2. Absorption spectrum (methanol), fluorescence spectrum (methanol) at room temperature, and phosphorescence spectra (EPA glass) at -170° for **2b**.

repeated recrystallization of **2b**; (b) similar but not identical spectra for **2a** and **2b,d,f** obtained by two completely independent synthetic routes; (c) on standing for several hours in the cavity of the spectrophotofluorimeter while being exposed to the powerful light source, the emission at $414\text{ m}\mu$ of a methanolic solution of **2b** decreased while a strong new band at $480\text{ m}\mu$ appeared, which is that of photoproduct **9a** (1,2-dihydropyridines have extremely intense fluorescence spectra) (this obviously represents photoreaction proceeding at the expense of fluorescence from **2b**); (d) under phosphorescence conditions at room temperature, no emission was observed eliminating the possibility that the emission might be arising from long-lived phosphorescence. The fluorescence of these pyridine esters resembles that reported for 1,3-dicarbomethoxybenzene;³⁹ weak fluorescence at about $400\text{ m}\mu$ is also reported for esters of phthalic and benzoic acids.^{40,41}

Solvent induced shifts of the fluorescence maximum of **2b** are collected in Table IV; similar effects were

Table IV. Solvent Induced Shifts of Fluorescence Maximum^a of **2b**

Solvent	Maximum		$\Delta\nu, \text{cm}^{-1}$
	$\text{m}\mu$	cm^{-1}	
Cyclohexane	391	25,600	<i>b</i>
Diethyl ether	395	25,400	-200
<i>tert</i> -Butyl alcohol	408	24,500	-1100
Acetonitrile	410	24,400	-1200
Methanol	414	24,200	-1400
Water	430	23,500	-2100

^a Excitation at $270\text{ m}\mu$. ^b Chosen as standard.

(39) Y. Shigemitsu, Y. Katsuhara, and Y. Odaira, *Tetrahedron Lett.*, 2887 (1971). However, Paterno-Büchi reactions with the carbonyl group are described.

(40) J. B. Dubinskii, *Bull. Acad. Sci. USSR, Phys. Ser.*, 23, 111 (1959).

(41) With our apparatus we could not detect fluorescence from 1,3-dicarbomethoxybenzene but this is most likely due to the limited sensitivity of our instrument rather than any error in the work reported.³⁹

found for the other pyridines. The pronounced bathochromic shift in polar media is diagnostic for a $\pi-\pi^*$ configuration for the emitting species, whereas a hypsochromic shift (as in absorption spectra) is expected for an $n-\pi^*$ species.⁴² This is not an ironclad rule, however, since the $n-\pi^*$ singlets of diazines are reported to show either hypso- or bathochromic shifts.⁴³ However, $n-\pi^*$ emission is usually nonexistent or extremely weak from aza aromatics whereas Φ_f is roughly 10^{-3} for **2b**. Considerable support for the $\pi-\pi^*$ assignment is obtained from the fluorescence spectra of 1,3-dicarbomethoxybenzene where bathochromic shifts are also observed leading to a $\pi-\pi^*$ assignment to the emitting singlet.³⁹ (The $n-\pi^*$ states of aryl carbonyl systems normally do not fluoresce.⁴⁴)

Strong phosphorescence emissions were observed from **2b**, 3,5-dicarboethoxy-1,2,4,6-tetramethylpyridinium methylsulfate (**31c**), and 1,3-dicarbomethoxybenzene in EPA glass at liquid nitrogen temperature. (Although the pyridinium salts phosphoresce, no fluorescence was ever detected.) Their spectra are all similar, having slight vibronic bands with a regular 600-cm^{-1} spacing, and they differ only in band position. Relevant data are compiled in Table V and the spectrum of **2b** is

Table V. Phosphorescence^a Data for Pyridines, Pyridinium Salts, and the Benzene Analog

Compd	0-0	Max,	$t_{1/2}$,	E_T , kcal/mol
	band,			
2b	390	415	1.1	73.4 ± 1.0
31c	380	412	0.6	75.3 ± 2.0
1,3-Dicarbomethoxybenzene	374	395	1.6	76.5 ± 0.5

^a Excitation at $270\text{ m}\mu$.

(42) V. G. Krishna and L. Goodman, *J. Chem. Phys.*, 33, 381 (1960).

(43) H. Baba, L. Goodman, and P. C. Valenti, *J. Amer. Chem. Soc.*, 88, 5410 (1966).

(44) J. A. Bartrop and J. D. Coyle, *J. Chem. Soc. B*, 251 (1971).

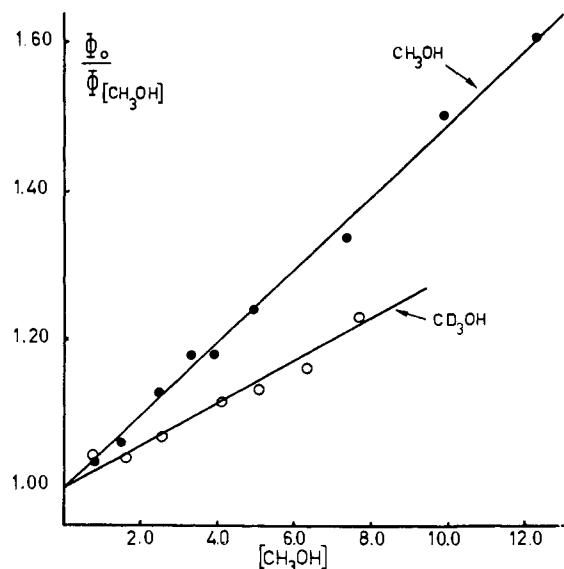


Figure 3. Fluorescence quenching data for **2b** using methanol and trideuteriomethanol as quencher. The pyridine concentration is 10^{-4} M. Excitation wavelength is 270 m μ . The solvent is *tert*-butyl alcohol.

given in Figure 2. The similarities of the spectra given in Table V indicate a $\pi-\pi^*$ configuration for the emitting triplet in all cases. The lack of carbonyl vibronic spacings (*ca.* 1700 cm^{-1}) argues against a localized carbonyl $n-\pi^*$ configuration. Phosphorescence spectra have been reported from several alkyl benzoates,⁴⁴ and $\pi-\pi^*$ configurations with energies of about 75 kcal/mol were also assigned to the emitting triplets.

Attempts to sensitize the photoreduction of **2b** were unsuccessful with a variety of sensitizers. For example, **2b** did not act as a quencher of benzophenone photoreduction in alcohol⁴⁵ indicating that triplet energy transfer did not take place. This is not particularly surprising with aromatic carbonyl compounds as sensitizers since the triplet of **2b** was estimated to lie at 73 kcal/mol, just above the maximal triplet energies of these sensitizers. Attempts to quench a triplet of **2b** using piperylene were frustrated by strong *singlet* quenching as evidenced by diminishment of the fluorescence from **2b**. Below 0.1 M piperylene concentration the photoreduction was not significantly inhibited suggesting that all quenching is attributable to the singlet. Similar phenomena are encountered with acridine where triplet quenching experiments are similarly frustrated.⁴⁶

The fluorescence from **2b** was quenched not only by piperylene but also by various alcohols, amines, sulfides, thiols, etc. In all cases Stern-Volmer plots of Φ_0/Φ_f against the quencher concentration were linear. Quenching of the fluorescence of **2b** by CH_3OH and CD_3OH is shown in Figure 3. The quenching of fluorescence by substrates such as alcohol, wherein photoreduction also takes place, suggested that the fluorescence quenching and photoreduction might be manifestations of one and the same process. In Table VI values are compiled of the slopes of the Stern-Volmer plots. The measurements were carried out in *tert*-butyl alcohol solution, which was shown not to react with **2b** even on extended irradiation. In no case did the

(45) W. M. Moore, G. S. Hammond, and R. P. Foss, *J. Amer. Chem. Soc.*, **83**, 2789 (1961).

(46) D. G. Whitten and Y. J. Lee, *ibid.*, **93**, 961 (1971).

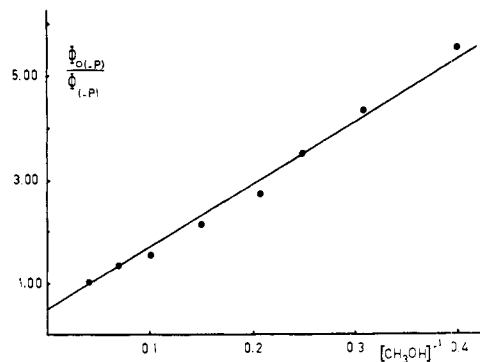


Figure 4. Inverse relative quantum yields for consumption of **2b** (10^{-4} M) plotted against $[\text{MeOH}]^{-1}$. The absolute quantum yield for pyridine consumption is 0.069 (determined at 10^{-2} M).

Table VI. Fluorescence Quenching Data for Pyridines **2b** and **2f**

Quencher	$k_q\tau$, l. mol ⁻¹ a,b	Ionization potential of quencher, eV ^c	Bond dissociation energy, kcal mol ⁻¹ d
CH_3OH	0.049 (0) ^{e,f}	10.84	94
CD_3OH	0.027	10.84 (?)	
$\text{C}_2\text{H}_5\text{OH}$	0.072	10.49	(92)
$(\text{CH}_3)_2\text{CHOH}$	0.060	10.15	91
$\text{CH}_2=\text{CHCH}_2\text{OH}$	0.185	9.67 ± 0.05	(84)
$\text{C}_6\text{H}_5\text{CH}_2\text{OH}$	6.85	9.14	(80)
$\text{CH}_3\text{OCH}(\text{OCH}_3)_2$	0.026		(92)
$\text{CH}_3\text{CH}=\text{CHC}_2\text{H}_5$ (trans)	0.133	9.10	86 ± 1
$\text{CH}_3\text{C}_6\text{H}_5$	0.950	8.82	84
$\text{CH}_3\text{CH}=\text{CHCH}=\text{CH}_2$ (trans)	1.87 (1.10) ^e	8.68	80 ± 1
$(\text{C}_2\text{H}_5)_2\text{NH}$	0.684	8.01	
CH_3SCH_3	2.35		
$\text{C}_3\text{H}_7\text{SH}$	3.20	9.20	83-88
H_2O	0 ^f	12.6	119
<i>n</i> - C_8H_{14}	0 ^f	10.18	98
C_6H_{12}	0 ^f	9.8	95

^a Measured slopes of Stern-Volmer plots. Linear correlations were obtained in all cases. ^b Excitation at 270 m μ except for toluene and benzyl alcohol where 285 m μ was used. ^c "Handbook of Chemistry and Physics," 51st ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1970. ^d Taken or estimated (with considerable error) from: S. W. Benson, *J. Chem. Educ.*, **42**, 502 (1965); K. W. Egger and S. W. Benson, *J. Amer. Chem. Soc.*, **88**, 241 (1966); F. R. Cruickshank and S. W. Benson, *ibid.*, **91**, 1289 (1969); D. M. Golden and S. W. Benson, *Chem. Rev.*, **69**, 125 (1969); J. A. Kerr, *ibid.*, **66**, 465 (1966). ^e For 3,5-dicarboethoxy-2,6-dimethyl-4-isopropylpyridine (**2f**). ^f No quenching detectable.

form of the uv absorption change in the presence of quencher. At the pyridine concentration (10^{-4} M) used for the fluorescence studies, a plot of the inverse ratio of pyridine disappearance against the reciprocal of the methanol concentration was linear (Figure 4). Reactions were run to low conversion to ensure that the product dihydropyridines did not seriously compete with pyridine for the incident light. A modest correction for this effect was made in a straightforward fashion. As a further check, the 1,2- to 1,4-dihydropyridine ratio was shown not to vary significantly (1,2:1,4 = 4.0) over the methanol concentration range used and by uv spectroscopy consumed pyridine was shown to be accounted for quantitatively as dihydropyridines. Owing to the difficulties in obtaining accurate absolute

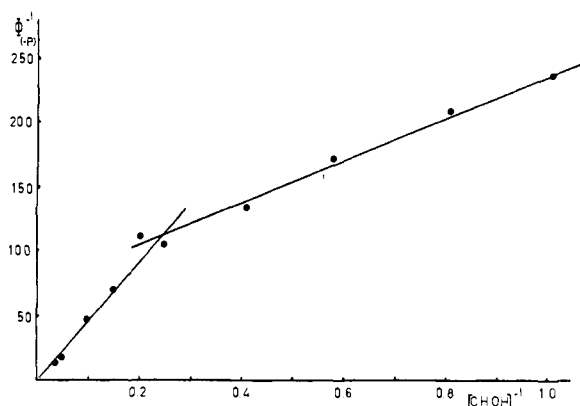


Figure 5. Inverse quantum yields for photoreduction of **2b** (10^{-2} M) against $1/[\text{MeOH}]$. The quantum yield in pure methanol is taken as $\Phi_{(-p)} = 0.069$.

values for the quantum yields at lower concentrations, quantum yields for **2b** (and **2a,c**) were determined at 10^{-2} M concentration; the results are given in Table VII. At 10^{-2} M the correlation of $1/\Phi_{-p}$ with $1/[\text{MeOH}]$ was not linear (Figure 5). However, in contrast to the results at 10^{-4} M, the amounts of dihydropyridine formed decreased with decreasing methanol concentration falling to zero at ca. 2.5 M methanol, which is the point where the rate of pyridine consumption increases in Figure 5. In a preparative run in *tert*-butyl alcohol with 1.5 M methanol, no dihydropyridines were isolated but a heavy viscous material remained with virtually normal pyridine uv absorption. We believe this to be the result of the attack of pyridyl radicals on ground-state pyridine (eq 18a,b). Reaction 18b is suppressed at lower concentrations of pyridine and higher concentrations of methanol.

Table VII. Quantum Yields for Pyridine Consumption

Compd	Quantum yield (Φ_{-p}) for pyridine ^a disappearance in pure methanol
2a	0.149
2b	0.069
2c	0.030

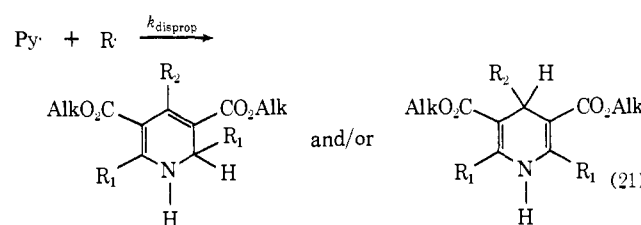
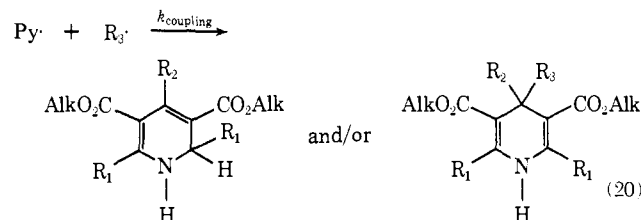
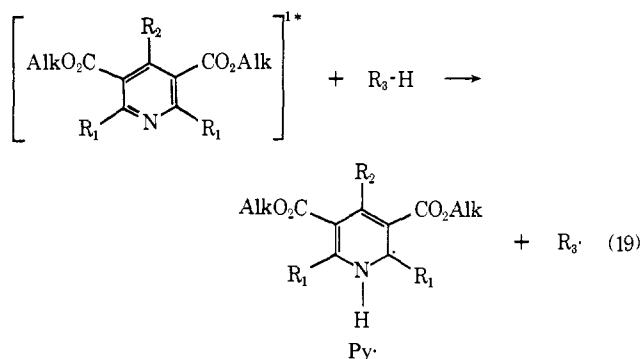
^a At 254 m μ 10^{-2} M pyridine solutions. Nearly quantitative conversion to products was indicated by uv spectroscopy.

Py* + CH₃OH \longrightarrow PyH \cdot + \cdot CH₂OH (18a)
 PyH \cdot + Py \longrightarrow dimers, etc. (18b)

Discussion

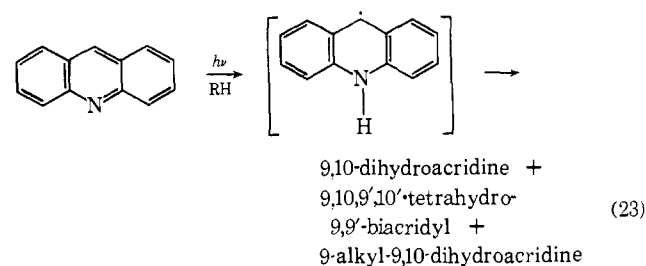
The paramount photochemical reactions of 3,5-dicarboalkoxy pyridines are (a) hydrogen abstraction and (b) photoisomerization. We shall attempt here to define the important intermediates involved in these processes and we shall close with a suggestion for a unified mechanism that interlocks a and b. We turn first to the (nearly) ubiquitous hydrogen abstraction.

The reactions leading to reduced or dimeric products in alcoholic solution are given in eq 19–22. An excited pyridine molecule abstracts a hydrogen atom from solvent giving Py \cdot (eq 19), which may couple with the α -hydroxy radical R₃ \cdot (eq 20), disproportionate (eq 21),



or dimerize (eq 22). Two important assumptions are made in this scheme, namely that the nitrogen atom is the hydrogen atom abstractor and that radical intermediates indeed are formed.

The assumption that the nitrogen atom is the spearhead of reactivity in hydrogen abstraction has impressive literature support, since (a) the acridyl radical has been observed by flash spectroscopy during photoreduction of acridine in hydrocarbon solvents (eq 23),⁴⁷ (b) a corresponding radical from pyridine,



quinoline, and isoquinoline has been observed during their photoreduction in alcohol and ether,⁴⁸ (c) intramolecular hydrogen abstraction from a 2-alkyl group in quinolines can only be explained by a Norrish type II like reaction involving the nitrogen atom as hydrogen abstractor,⁴⁹ and (d) the numerous hydrogen abstraction reactions reported for other aza aromatics.^{2,50}

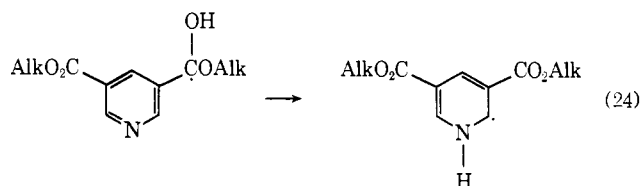
(47) (a) A. Kira, S. Kato, and M. Koizumi, *Bull. Chem. Soc. Jap.*, **39**, 1221 (1966); (b) A. Kira and M. Koizumi, *ibid.*, **40**, 2486 (1967); (c) M. Koizumi, Y. Ikeda, and H. Yamashita, *ibid.*, **41**, 1056 (1968).

(48) (a) G. Allan, A. Castellano, J. P. Cateau, and A. Lablache-Combiere, *Tetrahedron*, **27**, 4687 (1971); (b) S. Caplain, A. Castellano, J. P. Cateau, and A. Lablache-Combiere, *ibid.*, **27**, 3541 (1971).

(49) F. R. Stermitz, C. C. Wei, and C. M. O'Donnell, *J. Amer. Chem. Soc.*, **92**, 2745 (1970).

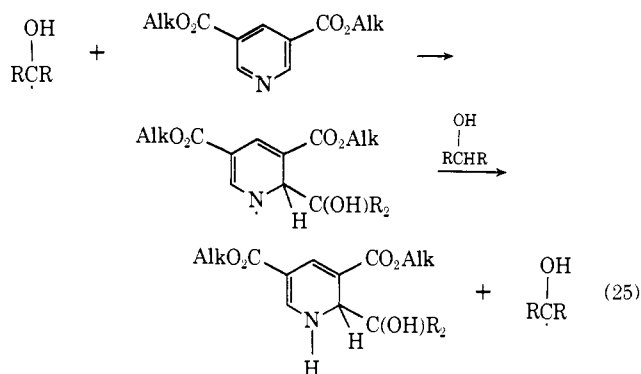
(50) An excellent compilation of references is given in ref 49.

Experimentally, the quantum yield of photoreduction decreases as more substituents are brought about the nitrogen atom (Table VII) and the reactivity decreases in a similar order as shown by the ready photoreduction of 3,5-dicarboethoxypyridine (**2a**) in *tert*-butyl alcohol or cyclohexane whereas 2,6-dimethyl-3,5-dicarboethoxypyridine (**2b**), where the nitrogen atom is more hindered, is photoreduced only in solvents bearing more reactive hydrogen atoms. Experimentally, the incorporation of deuterium from ethanol-*O-d* exclusively in the 4 position of **11a,b** (eq 6) is most easily explained by hydrogen abstraction by the nitrogen atom followed by disproportionation (eq 21). The carbonyl group provides, of course, an alternate site for hydrogen abstraction; however, the necessity of presuming a rapid, specific shift of a hydrogen atom to the nitrogen atom (eq 24), the known sluggish reactivity of aromatic



esters even in intramolecular Norrish type II reactions,⁵¹ as well as the total lack of photoenolization from the reactive and available methyl groups of **2c** (whereas this reaction does occur with the pyridinium salts where intermolecular hydrogen abstraction goes poorly), all attest to the lack of carbonyl group reactivity. Also, the photoreduction of 3-cyanopyridine in alcoholic media proceeds readily.^{2f}

The existence of radical intermediates in the subsequent product forming steps is implied most strongly by the results in eq 2 where a regular transition from coupling ($R_3 = \text{CH}_2\text{OH}$, eq 20) to disproportionation and dimerization ($R_3 = \text{CH}_3\dot{\text{C}}\text{HOH}$ and $(\text{CH}_3)_2\dot{\text{C}}\text{OH}$, eq 21 and 22) is observed. Coupling and disproportionation reactions could occur at least in part within a solvent cage, but with more bulky alcohols sufficient steric problems may be engendered in coupling to allow diffusion out of the cage to compete.⁵² A chain reaction involving attack of an α -hydroxyalkyl radical on the pyridine followed by chain transfer (eq 25) is un-



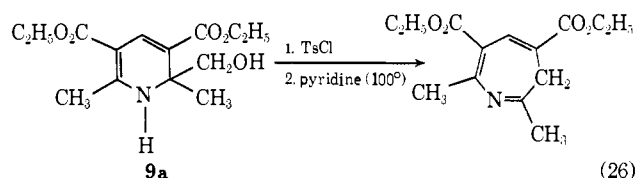
(51) J. C. Pacifici and J. A. Hyatt, *Mol. Photochem.*, **3**, 271, 275 (1971), and references therein.

(52) For example, no clear-cut inhibition of photoreduction could be achieved using alkenes as trapping agents (Results) but this may also be due in part to the low reactivity of alcohol radicals toward addition at room temperature.⁵³

(53) E. S. Huyser, "Free-Radical Chain Reactions," Wiley-Interscience, New York, N. Y., 1970, p 154.

likely.⁵⁴ Note that the α -hydroxyalkyl radical generated during photoreduction by benzophenone in alcohol fails to attack **2b** (see Results).

The factors affecting the coupling:disproportionation ratio are obviously subtle. Happily, a combination of steric and electronic factors leads to a pronounced tendency for coupling to occur with less bulky alcohol radicals yielding chiefly a 1,2-dihydropyridine. This provides a useful entry into unusually stable members of this class of compounds. These may be put to synthetic use; for example, a ring expansion sequence is illustrated in eq 26 wherein the



hydroxymethyl group provides a triggering point for disruption of the residual pyridine skeleton.⁵⁵

The hydroxyalkyl group appears to impart considerable stability to the notoriously reactive 1,2-dihydropyridine system; thus, 3,5-dicarboethoxy-1,2,6-trimethyl-1,2-dihydropyridine, obtained by borohydride reduction of the *N*-methylpyridinium salt, is difficult to handle.⁵⁶ Many other 1,2-dihydropyridines are also quite unstable.⁵⁷

The most significant variation on the coupling-disproportionation-dimerization theme is the ring contraction of **2c** competitive with photoreduction. There is little doubt that this reaction arises from an isomerization of a common pyridyl radical **36** since *no* pyrrole is formed in *tert*-butyl alcohol or cyclohexane, solvents in which no photoreduction takes place either (nor is any trace of photoisomerization noted). Labeling experiments (Results) are most easily interpreted as indicating that a carboalkoxy group is expelled without a change in the relative position of the remaining ring atoms. And, finally, product **1c** does not yield **12a** on irradiation. We believe that the scheme presented in eq 27 adequately explains the results. The ring contraction finds precedent in the catalytic reduction of pyridines⁵⁸; thermal ring contractions of 4-carboxy-1,4-dihydropyridines to pyrroles are also known.⁵⁹ The intermediate homopyrroles have been synthesized and also invoked in other rearrangements.⁶⁰ The reason is not completely obvious why a 4-methyl group promotes ring contraction; one notices that with a 4-phenyl substituent (eq 9) 1,2-dihydropyridines are formed (and with a 4-isopropyl substituent photoreduction does not occur).

(54) E. S. Huyser, personal communication.

(55) T. J. van Bergen and R. M. Kellogg, *J. Org. Chem.*, **36**, 978 (1971).

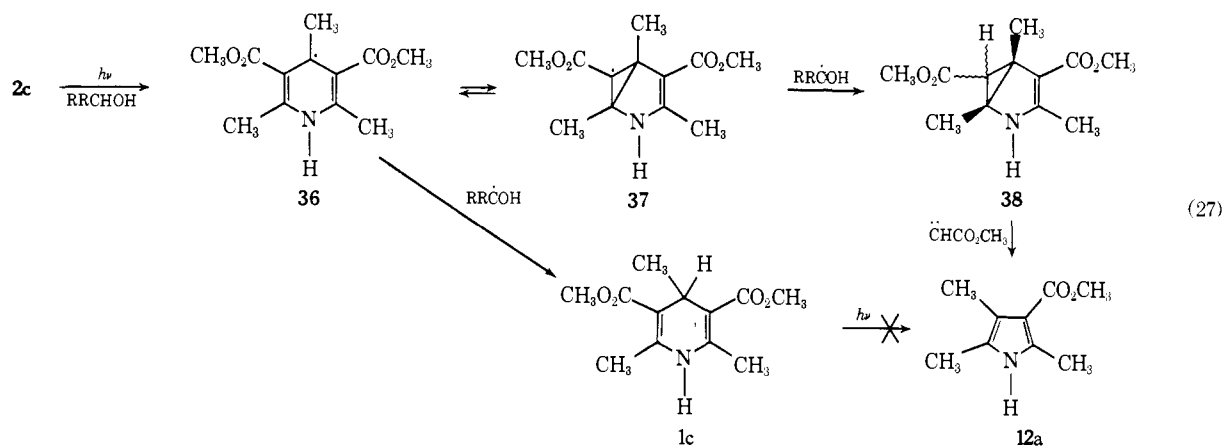
(56) W. Traber and P. Karrer, *Helv. Chim. Acta*, **41**, 2066 (1958).

(57) F. Brody and P. R. Ruby in "Pyridine and Its Derivatives," Part I, E. Klingsberg, Ed., Interscience, New York, N. Y., 1960.

(58) G. M. Badger and J. W. Clark-Lewis in "Molecular Rearrangements," Vol. I, P. de Mayo, Ed., Wiley, New York, N. Y., 1963, pp 618-619.

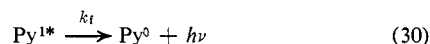
(59) J. F. Biellmann and H. J. Callot, *Chem. Commun.*, 140 (1969); *Tetrahedron*, **26**, 4809 (1970).

(60) (a) Reference 57, p 226; (b) W. E. Parham and H. E. Reiff, *J. Amer. Chem. Soc.*, **77**, 1177 (1955); (c) R. L. Jones and C. W. Ress, *J. Chem. Soc. C*, 2249 (1969); (d) F. W. Fowler, *Chem. Commun.*, 1359 (1969); (e) F. W. Fowler, *Angew. Chem.*, **83**, 147 (1971); (f) A. O. Plunkett, *Chem. Commun.*, 1044 (1969); (g) J. F. Biellmann and M. P. Goeldner, *Tetrahedron*, **27**, 2957 (1971).



Obtainment of information about the excited state responsible for hydrogen abstraction is of fundamental importance. Probably the best literature precedent in aza aromatic chemistry is afforded by acridine, the photochemistry of which is described in eq 23.⁶¹ In this case photoreduction involves a singlet state whose configuration is suggested to be $n-\pi^*$.⁴⁶ This follows from a demonstration that fluorescence, which arises from a $\pi-\pi^*$ state, is only feebly quenched by substrates that cause photoreduction and that there is no kinetic correlation between photoreduction and fluorescence quenching. Since these data exclude the $\pi-\pi^*$ singlet as hydrogen abstractor, the $n-\pi^*$ singlet wins by default.

Hydrogen abstraction in aza aromatics by an $n-\pi^*$ state is especially harmonious with the simple picture developed for carbonyl photochemistry where promotion of a nonbonding electron imparts radical character to the heteroatom.⁶² This analogy has been stressed, particularly by Stermitz.⁶³ However, in imines, related in an obvious fashion to carbonyl compounds, considerable doubt exists whether the $n-\pi^*$ state can participate in hydrogen abstraction reactions.⁶⁴ Failure to implicate any significant triplet contribution to the photoreduction of 2b (Results) as well as the observation of fluorescence quenching by alcohols and other substrates strongly suggests a singlet mechanism. Corroborative support for this idea would be provided by a demonstration that fluorescence quenching and photoreduction are kinetically coupled processes. A kinetic scheme for this possibility is that given in eq 28–33. The excited singlet, whose

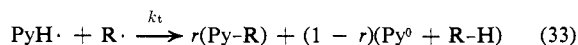
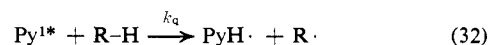
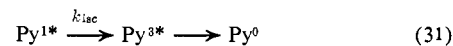


(61) (a) The most recent study is apparently that of ref 46 (see also ref 47). An (incomplete) list of earlier references is: (b) K. Nakamaru, S. Niizuma, and M. Koizumi, *Bull. Chem. Soc. Jap.*, **42**, 255 (1969); (c) A. Kira, Y. Ikeda, and M. Koizumi, *ibid.*, **39**, 1673 (1966); (d) E. Van der Donck and G. Porter, *J. Chem. Phys.*, **46**, 1173 (1967); (e) V. Zanker, E. Erhardt, and J. Thies, *Ind. Chim. Belge*, **32** (III), 24 (1967), and earlier references; (f) H. Goth, P. Cerutti, and H. Schmid, *Helv. Chim. Acta*, **48**, 1395 (1965); (g) for phenazine, see G. A. Davis, J. D. Gresser, and P. A. Carapellucci, *J. Amer. Chem. Soc.*, **93**, 2179 (1971).

(62) For a recent review of carbonyl photochemistry, see P. J. Wagner, *Accounts Chem. Res.*, **4**, 168 (1971).

(63) See, for example (a) F. R. Stermitz, R. P. Seiber, and D. E. Nicodem, *J. Org. Chem.*, **33**, 1136 (1968); (b) F. R. Stermitz, C. C. Wei, and C. M. O'Donnell, *J. Amer. Chem. Soc.*, **92**, 2745 (1970).

(64) (a) A. Padwa, W. Bergmark, and D. Pashayan, *ibid.*, **91**, 2653 (1969); (b) P. J. Collin, J. S. Shannon, H. Silberman, S. Sternhell, and G. Sugowdz, *Tetrahedron*, **24**, 3069 (1968).



configuration for the moment is not specified, is deactivated by fluorescence, k_f , radiationless conversion to the ground state, k_d , intersystem crossing to the triplet, k_{isc} , and chemical quenching, k_q , where a fraction r of the reactions leading to fluorescence quenching also leads to the formation of chemical products. The effect of the quencher, RH, on the relative fluorescence yield is given by the usual Stern–Volmer relationship (eq 34)

$$\frac{\Phi_{f_0}}{\Phi_f} = 1 + \frac{k_q[\text{RH}]}{k_d + k_f + k_{isc}} \quad (34)$$

whereas for photoreduction, eq 35 holds.⁶⁵ Identity of $k_q\tau$ values from eq 34 and 35 where $\tau = (k_d + k_q + k_{isc})^{-1}$, would support this mechanism or any kinetically equivalent mechanism. As seen from Figures 3 and 4

$$\frac{1}{\Phi_{-Py}} = \frac{1}{r} + \frac{(k_d + k_q + k_{isc})}{rk_q[\text{RH}]} \quad (35)$$

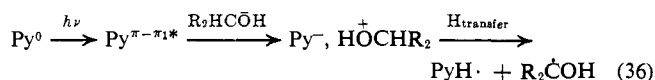
both fluorescence quenching and photoreduction experiments with $10^{-4} M$ solutions of 2b in methanol in roughly the same concentration regions (1–12 M for fluorescence quenching and 2.5–24 M for chemical reduction) give excellent linear correlations. The value of $k_q\tau$ from the slope of the fluorescence quenching plot is $0.049 \text{ l. mol}^{-1}$ and the [intercept/[slope]]⁻¹ ratio from the photoreduction plot is $0.043 \pm 0.07 \text{ l. mol}^{-1}$; the calculated value of r , 0.13 ± 0.01 , is very modest. We believe these $k_q\tau$ values to be alike within experimental error thereby demonstrating that photoreduction and fluorescence quenching in 3,5-dicarboalkoxy-pyridines are kinetically coupled processes.

The situation obtaining here is obviously different from that in acridine.⁴⁶ Although the correlation of fluorescence quenching and photoreduction allows the rejection of a number of mechanistic possibilities, certain ambiguities in interpretation will be unavoidable. We outline, however, what seem to us to be two conceptually different rationalizations of these results based on classical concepts, namely a *single excited state* as opposed to a *two excited state* explanation.

(65) R. S. Cooke and G. S. Hammond, *J. Amer. Chem. Soc.*, **92**, 2739 (1970); this is given in ref 46 for acridine photoreduction.

The first and simplest variant on the single excited state argument is to presume that a $\pi-\pi^*$ state is responsible for hydrogen abstraction; this follows since both the solvent shift data as well as theoretical considerations⁴² implicate the $\pi-\pi^*$ state as the fluorescing species and, if the fluorescing species is identified, then the kinetic correlation identifies the hydrogen abstractor. However, this conclusion goes particularly strongly against the analogies drawn from carbonyl chemistry, which predict that the $n-\pi^*$ state should be reactive. In addition PPP-SCF calculations with configuration interaction (assuming identity of the geometries of ground and excited states) indicate no change in electronic density at the nitrogen atom on excitation.⁶⁶ In addition, the pyridinium salts derived from **2a-c** certainly show no great avidity for hydrogen abstraction, which may result from the absence of nitrogen $n-\pi^*$ states. The apparent photoenolization, a process not occurring with the free bases, leads to the suspicion that here the sluggish *intramolecular* hydrogen abstraction is caused by the carbonyl groups. However, arguments using pyridinium salts are admittedly complicated by the possible inversion of states on alkylation as well as by the resulting increase in steric hindrance about the nitrogen atom.

The possibility that the $\pi-\pi^*$ state is nevertheless responsible for hydrogen abstraction cannot be discarded *a priori*, however. For example, photoreduction of aromatic ketones having lowest lying $\pi-\pi^*$ states (normally leading to diminished hydrogen abstracting ability) may be accomplished *via* an electron transfer mechanism with substrates such as amines and sulfides which have removable nonbonding electrons.⁶⁵ Since fluorescence quenching of the $\pi-\pi^*$ states of a variety of aromatic compounds also is known to involve electron transfer mechanisms,⁶⁹ one inquires whether a similar effect could be involved with pyridines. The rudiments of this possibility are outlined in eq 36. Examination



of the fluorescence quenching data allows some conclusions about the validity of eq 36. The appreciable isotope effect for fluorescence quenching observed in CD_3OH ($k_q(\text{H})/k_q(\text{D}) = 1.81$) indicates that quenching is not likely diffusion controlled. An accurate estimate of τ for determination of k_q is not possible; in particular, use of the integrated absorption band is difficult because of uncertainty over the true band shape in the absorption spectrum. A lifetime of roughly 10^{-8} sec can be estimated by this method. For pyrazines and pyrimidines singlet lifetime values range from 10^{-8} to 10^{-9} sec,⁷⁰ for acridine $\tau = 4.30 \times 10^{-8}$ sec⁴⁶ and for aminopyridine values

(66) Calculations were carried out using the Coulomb and repulsion integrals given by Zahradnik.⁶⁷ Details of the calculations can be found in the thesis of T. J. v. B. No change in electron density occurs at the nitrogen and C-4 because both the HOMO and LUMO are noded at these positions. The computer program was provided by Professor M. J. Janssen and Dr. E. Bouwhuis of this department.

(67) R. Zahradnik, J. Fabian, A. Mehlhorn, and V. Kvasnicka, *Organosulfur Chem.*, 203 (1967).

(68) (a) S. G. Cohen and N. M. Stein, *J. Amer. Chem. Soc.*, **93**, 6542 (1971), and earlier references; (b) G. A. Davis, P. A. Carapellucci, K. Szoc, and J. D. Gresser, *ibid.*, **91**, 2264 (1969).

(69) For a general review, see D. Rehm and A. Weller, *Israel J. Chem.*, **8**, 259 (1970).

(70) B. J. Cohen and L. Goodman, *J. Chem. Phys.*, **46**, 713 (1967).

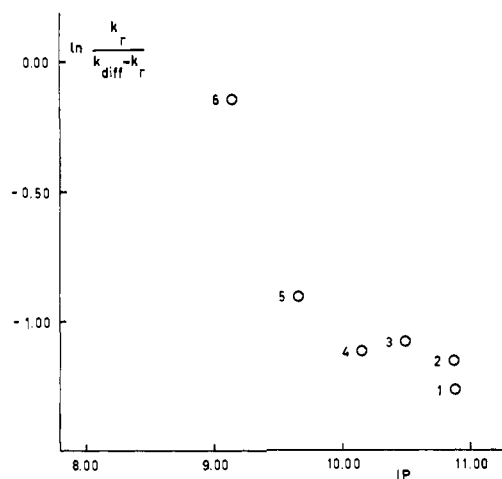
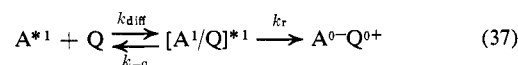


Figure 6. Plot of quenching parameter against ionization potential (IP) in electron volts: 1, CD_3OD ; 2, CH_3OH ; 3, $\text{C}_2\text{H}_5\text{OH}$; 4, $(\text{CH}_3)_2\text{CHOH}$; 5, $\text{CH}_2=\text{CHCH}_2\text{OH}$; 6, $\text{C}_6\text{H}_5\text{CH}_2\text{OH}$.

of 10^{-8} sec are found.⁷¹ By assuming that quenching is diffusion controlled in the best quencher examined, benzyl alcohol, a value of $\tau = 3.2 \times 10^{-9}$ sec is calculated using $k_{diff} = 2.17 \times 10^9 \text{ l. mol}^{-1} \text{ sec}^{-1}$.⁷² It is unlikely that τ is greater than 10^{-8} sec. Now, for both acridine and naphthalene, fluorescence quenching of $\pi-\pi^*$ states can be rationalized by assuming the mechanism given in eq 37 wherein an encounter



complex is formed at a diffusion controlled rate. Assuming that k_r will reflect the free energy of activation for electron transfer, then it is readily demonstrated that eq 38 holds⁷³ where k_q' is the quenching rate

$$\ln k_r/k_{-q} = \ln \left(\frac{k_q'}{k_{diff} - k_q'} \right) \propto \Delta G^\ddagger \propto \text{ionization potential (IP)} \quad (38)$$

constant derived from Stern-Volmer plots. Good correlations of the quantity $\ln(k_q'/k_{diff} - k_q')$ with the ionization potential of amines are found. Establishment of a similar correlation for the quenching of 3,5-dicarboalkoxy pyridine fluorescence by alcohols would provide support for the scheme detailed in eq 36, namely that the charge transfer like state decays into a radical pair. Ionization potentials for alcohols are less abundant than for amines. A plot for a limited sample is shown in Figure 6; k_q values are taken from Table VI using $\tau = 10^{-8} \text{ sec}^{-1}$. There is no obvious correlation. For example, isopropyl alcohol and methanol quench equally well despite an ionization potential difference of 0.69 eV. Hence one strongly suspects that another quenching mechanism is operative here (note the alcohol IP values are about 1 eV higher than for structurally similar amines making an electron transfer mechanism even more dubious).⁷¹

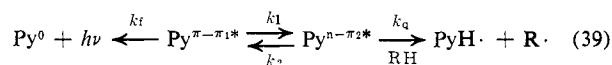
A more successful model involves the $n-\pi^*$ as true

(71) (a) R. G. Bennett, *Rev. Sci. Instrum.*, **31**, 1275 (1960); S. J. Ladner and R. S. Becker, *J. Phys. Chem.*, **67**, 2481 (1963); (b) A. Weisstuck and A. C. Testa, *ibid.*, **72**, 1982 (1968).

(72) International Critical Tables, Vol. VII, McGraw-Hill, New York, N. Y., 1930, p 218.

(73) (a) T. R. Evans, *J. Amer. Chem. Soc.*, **93**, 2082 (1971); (b) T. R. Evans, R. W. Wake, and M. M. Sifain, *Mol. Photochem.*, **3**, 275 (1971).

hydrogen abstracting species, which removes a hydrogen in a radical-like reaction.⁷⁴ (A great deal of misery could obviously be saved by assigning the fluorescence to a $n-\pi^*$ state. However, we are unaware of any argument justifying this assignment.) Since the fluorescence is almost certainly caused by the $\pi-\pi^*$ state, this requires a two excited state mechanism. The kinetic coupling of fluorescence quenching and photo-reduction can be achieved if these two states are in equilibrium (eq 39). It is easily shown that using



eq 39 and a scheme analogous to that in eq 28–33, equivalent values of $k_q\tau$ are obtained from fluorescence and chemical quenching experiments; τ becomes $k_2k_{\pi-\pi^*} + k_1k_{n-\pi^*}$ where $k_{\pi-\pi^*}$ and $k_{n-\pi^*}$ are the summation of the individual deactivation processes for each excited state. Another kinetic possibility is that the $n-\pi^*$ state is selectively populated and that it decays irreversibly ($k_1 = 0$, eq 38) to the $\pi-\pi^*$ state. This seems less likely in view of the fact that absorption is dominated by the $\pi-\pi^*$ band. The kinetic situation suggested to pertain in acridine, that is selective population of the $\pi-\pi^*$ state, which is in partial equilibrium ($k_2 \approx k_q[\text{RH}]$) with the $n-\pi$ state, is not applicable since curvature of fluorescence quenching plots is expected.⁴⁶ Thermal equilibrium of two states is feasible owing to their near superposition (92.5 kcal/mol for the $n-\pi^*$ state in apolar media and higher in alcohols and 89–95 kcal/mol for the $\pi-\pi^*$ state depending on the method of estimation). This type of reasoning has been used in carbonyl photochemistry^{52,75} and extension to our situation seems *a priori* justified. Using the available data, this two excited state model appears to be workable. It is not completely clear what role hydrogen bonding phenomena play in this mechanism; thus the pyridines are nearly completely hydrogen bonded in the ground state but whether this is true in the excited state is not known.⁴² Also, a thermal equilibrium mechanism is realistic only if the energy separation of the states is small, since K_{eq} is related exponentially to the energy separation.

We have thus far ignored the fact that profound spectroscopic effects occur as states of the same multiplicity but differing configuration are brought into energetic proximity.^{36,76} This is a necessary criterion for the thermal equilibration mechanism. There is a progressive breakdown in the validity of the Born–Oppenheimer approximation as the states approach the same energy leading, even at room temperature, to broadening of absorption peaks³⁶ (note the pronounced broadening in the spectrum of **2a**, Figure 1a, compared to 1,3-dicarbomethoxybenzene, Figure 1b) and the destruction of mirror image correlations in emission spectra (observe the absence of mirror image symmetry in the fluorescence spectrum of **2b**, Figure 2). These effects result from coupling of the vibronic levels of the two adjacent states.^{3a,e} Since strong

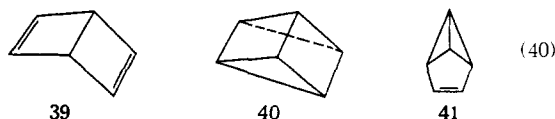
(74) It perhaps is more than simply amusing to note that the $k_q\tau$ values in Table VI can be correlated reasonably well with the *bond dissociation energies* for the weakest C–H bond in the quencher. The greatest problem is obtaining accurate bond dissociation energies (see Table VI).

(75) P. J. Wagner, A. E. Kempainen, and H. N. Schott, *J. Amer. Chem. Soc.*, **92**, 5280 (1970).

(76) F. C. Lim and J. M. H. Yu, *J. Chem. Phys.*, **45**, 4742 (1966).

coupling obviously exists in the pyridines studied here, the possibility, borrowed from carbonyl photochemistry,⁷⁷ must be considered that the $\pi-\pi^*$ state develops sufficient $n-\pi^*$ character to allow it to abstract hydrogen atoms (if indeed two discrete but strongly coupled states are distinguishable from a single mixed state). In effect, one returns to a single excited state mechanism using vibronic coupling arguments to justify enhanced reactivity of a $\pi-\pi^*$ state. This has the obvious advantage of sidestepping a potential difficulty of the two excited state mechanism, namely that the rates of interconversion between the $n-\pi^*$ and $\pi-\pi^*$ states must be high compared to the known high radiationless decay in aza aromatics.⁷⁸ Although vibronic coupling mechanisms seem to be of limited importance in carbonyl chemistry,⁷⁵ they may be more pronounced in aza aromatics.

The preceding mechanistic discussion hinges clearly on classical concepts, namely that the photochemistry of 3,5-dicarboalkoxypyridines may be discussed in terms of discrete $n-\pi^*$ and $\pi-\pi^*$ states. Although two seemingly viable possibilities, thermal equilibration or vibronic coupling of discrete $n-\pi^*$ and $\pi-\pi^*$ states can be developed, we stress that this classical approach anticipates no reactions other than hydrogen abstraction. But photoisomerization takes place. One has two basic choices in handling this observation: (a) consider it as a unique, anomalous (and somewhat embarrassing) deviation from a well-established reactivity pattern prompted most likely by overwhelming steric effects or (b) devise an intrinsic role for photoisomerization within the framework of aza aromatic photochemistry. We shall attempt the latter. In doing so we are fully aware that we may be reducing our classical arguments and perhaps those of other workers to shambles. However, we feel that we may be edging a bit closer to the truth by the very questioning of the validity of these classical concepts. Let us begin by first laying a background for photoisomerization in aromatic systems. Photochemical isomerizations in aromatic systems commonly involve Dewar (39), prismane (40), and benzvalene (41) structures, illustrated for benzene (eq 40). If the latter structure



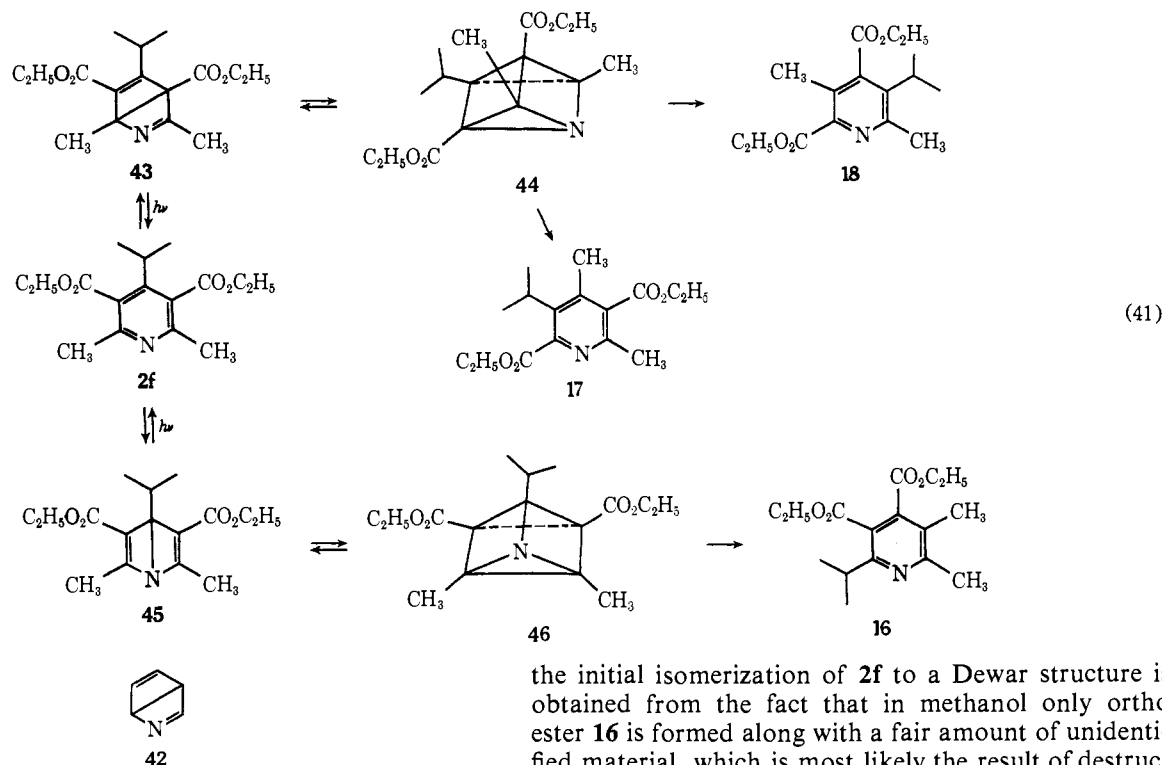
is involved in a photoisomerization, the net consequence will be an interconversion of the position of *two* adjacent atoms, whereas a prismane intermediate, formed, for example, by closure of a Dewar, will on rearomatization cause a sequential change in *two* pairs of adjacent atoms.^{79,80} The 2,5-bonded Dewar isomer **42** has been

(77) N. C. Yang and R. L. Dusenberg, *J. Amer. Chem. Soc.*, **90**, 5898 (1968).

(78) In dipirydylethylenes $k_{\text{daet}} \approx 10^9\text{--}10^{10} \text{ sec}^{-1}$; see: (a) D. G. Whitten and M. T. McCall, *ibid.*, **91**, 5097 (1969); (b) J. W. Happ, M. T. McCall, and D. G. Whitten, *ibid.*, **93**, 5496 (1971); (c) Y. J. Lee, D. G. Whitten, and L. Pederson, *ibid.*, **93**, 6330 (1971); for pyrazine, pyrimidine, and pyridazine $k_{\text{ic}} \approx 10^9\text{--}10^{10}$, $k_{\text{iso}} \rightarrow 10^8\text{--}10^9 \text{ sec}^{-1}$,⁷⁰ and radiationless deactivation is fast with pyridine itself (exact value unknown); (d) J. Lemaine, *J. Phys. Chem.*, **71**, 612 (1967).

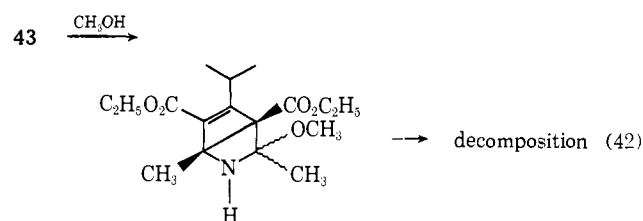
(79) For a recent review of valence bond isomerizations in aromatic systems, see: (a) E. E. van Tamelen, S. P. Pappas, and K. L. Kirk, *J. Amer. Chem. Soc.*, **93**, 6092 (1971); (b) E. E. van Tamelen and T. H. Whitesides, *ibid.*, **93**, 6129 (1971).

(80) For a discussion of labeling consequences, see: H. Wynberg, R. M. Kellogg, H. van Driel, and G. E. Beekhuis, *ibid.*, **89**, 3501 (1967).



demonstrated as a photoproduct of pyridine.⁸¹ A stable 1,4-bonded Dewar form and a prismane have been isolated from irradiation of pentakis(pentafluoroethyl)pyridine.⁸² A prismane may also be involved in the low yield rearrangement of 2-methylpyridine to 4-methylpyridine.⁸³ Examination of the three photoproducts formed from **2f** in cyclohexane shows that they are all the result of sequential interchange of three adjacent ring atoms. Their formation is readily accommodated within the following scheme (eq 41).⁸⁴ The 2,5-bonded Dewar isomer **43**, on closure to prismane **44**, can reopen in three possible ways leading back to **43** (or to **2f** on complete rearomatization) or to two new Dewar structures (not shown), which could be precursors of **17** and **18**. The 1,4 bonded Dewar isomer **45**, because of symmetry in the derived prismane **46**, can lead only to **2f** and ortho ester **16**. In eq 41, both Dewar and prismane structures are suggested as ground-state intermediates; the isolation of Dewar pyridine suggests the former and the observation of rearrangement implicates the latter isomer. However, we cannot rule out direct photochemical isomerization of **2f** to prismanes **44** and **46**, which rearomatize without intervention of a Dewar structure. Indirect evidence for

the initial isomerization of **2f** to a Dewar structure is obtained from the fact that in methanol only ortho ester **16** is formed along with a fair amount of unidentified material, which is most likely the result of destruction by methanol addition to the imino function of **43** (eq 42). This process with pyridine does lead



to identifiable products.^{81,85} Thus far actual valence bond isomers have not been isolated; examination of systems is in progress in which better stabilization of the valence bond isomer is expected.²⁸

Why does **2f** isomerize whereas less highly substituted isomers undergo photoreduction? The 4-isopropyl substituent obviously introduces considerable bulk causing increased shielding of the nitrogen to bimolecular attack; thus virtually no fluorescence quenching by methanol is observed (Table VI). Other processes can now compete with hydrogen abstraction. Now photoisomerization demands that the excited state distorts its geometry thereby somewhat alleviating substituent-substituent interactions. *The converse—that substituent-substituent interactions are necessary for excited state distortion—is not true.* Witness the formation of Dewar pyridine (**42**)⁸¹ and the formation of benzvalene (**41**) from benzene⁸⁶ at longer wavelengths and of Dewar benzene (**39**) at shorter wavelengths.⁸⁷ The true role of substituents, particularly bulky ones, in promoting valence bond isomerizations is most likely to destabilize the normal flat aromatic geometry rela-

(81) K. E. Wilzbach and D. J. Rausch, *J. Amer. Chem. Soc.*, **92**, 2178 (1970).

(82) (a) N. G. Barlow, J. G. Dingwall, and R. N. Hazeldine, *Chem. Commun.*, 1580 (1970); (b) Dewar pyrimidines have also been suggested: K. L. Wierzchowski, D. Shugar, and A. Katritzky, *J. Amer. Chem. Soc.*, **85**, 827 (1963).

(83) (a) C. Captain and A. Lablache-Combiere, *Chem. Commun.*, 1247 (1970); (b) O. S. Pascual and L. O. Tuazen, *Philipp. Nucl. J.*, **1**, 49 (1966); *cf. Chem. Abstr.*, **66**, 115127 (1967).

(84) (a) For his intellectual amusement, the interested reader is invited to convince himself that the products formed from benzvalene and prismane routes are not identical (barring any equilibration of benzvalene and Dewar structures). (b) Although arylthiophenes rearrange smoothly by valence bond tautomerization on irradiation⁸⁰ the corresponding thienylpyridines completely fail to rearrange. Rather, addition of solvent to the pyridine ring occurs by a free-radical pathway. The reasons for this discrepancy are unclear: T. J. van Bergen and R. M. Kellogg, unpublished work.

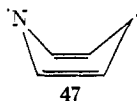
(85) (a) J. Jousset-Dubien and J. Houdard, *Tetrahedron Lett.*, 4389 (1967); (b) J. Jousset-Dubien and J. Houdard, *C. R. Acad. Sci.*, **267**, 866 (1968); (c) J. Jousset-Dubien and J. Houdard, *Bull. Soc. Chim. Fr.*, 2619 (1969).

(86) K. E. Wilzbach, J. S. Ritscher, and L. Kaplan, *J. Amer. Chem. Soc.*, **89**, 1031 (1967).

(87) D. Bryce-Smith, A. Gilbert, and D. A. Robinson, *Angew. Chem.*, **83**, 803 (1971).

tive to the bent geometry of the (ground state) valence tautomer.^{79a,88-90} Given a longer lease on life by this means, the chances increase of the valence bond isomers accumulating and undergoing rearrangement.

The essential point is that not only 2f but other less substituted isomers may be more or less drastically distorted from a planar geometry in the excited state.^{91,92} If the geometry is appreciably different from that of the normal aromatic molecule, then the concept of $n-\pi^*$ and $\pi-\pi^*$ states is of, at best, dubious validity. We note also that in geometry 47 tantamount



to a 1,4-bonded Dewar pyridine in which ring closure is not yet complete, the nitrogen atom has taken on radical character by virtue of its rehybridization to a more nearly sp^3 condition.⁹³ This is, of course, what is needed for hydrogen abstraction by the nitrogen atom. If the excited state is geometrically flexible, as is suggested by both 1,4 and 2,5 bonding in 2f, with a constant flux between different conformations, then one wonders whether photoreduction and photoisomerization are both artifacts of the reactions of this bent state. With the limited evidence in hand, this idea seems conceptually sound.

Full resolution of this problem will require among other things a detailed kinetic investigation of the photoisomerization reactions. We believe, however, that further probing into the "crepuscular"⁹⁴ events leading to product formation will reveal a hitherto little anticipated role of geometrically distorted states. Hence, this suggestion is offered as an impetus to further research.

Experimental Section

Melting points are corrected, whereas boiling points are uncorrected. Gas chromatography was done on F&M Models 700 and M-810 apparatus. Nmr spectra were obtained on a Varian A-60 or on an XL-100 spectrometer. Ultraviolet spectra were measured on a Zeiss PMQ II apparatus. Fluorescence and phosphorescence spectra were measured using an Aminco-Bowman spectrofluorimeter. Solvents and quenchers for spectral measurements were distilled repeatedly until all extraneous emissions and absorptions had disappeared. Emission spectra are corrected.⁹⁵ Preparative photochemistry was carried out in a Rayonet reactor equipped with 254-m μ lamps or in a Hanau TQ-81 apparatus. Quantitative work was done using a standard turntable arrangement using uranyl oxalate actinometry. Low-temperature work was done in a low-temperature ir cell with CaF windows. Temperatures were ca. -20 to -70°. The light source was a Philips SP-500 lamp.

(88) K. E. Wilzbach and L. Kaplan, *J. Amer. Chem. Soc.*, **87**, 4006 (1965).

(89) A. W. Burgstahler and P. L. Chien, *ibid.*, **86**, 2940 (1964).

(90) E. M. Arnett and J. M. Bolinger, *Tetrahedron Lett.*, 3803 (1964).

(91) The excited state of 1,2,5-thiadiazole is nonplanar as derived from spectroscopic data: E. Firkins and A. W. Richardson, *Chem. Commun.*, 1368 (1971).

(92) For speculation about the excited states involved in benzene photochemistry, see: (a) D. Bryce-Smith, *ibid.*, 806 (1969); (b) D. Bryce-Smith and H. C. Longuet-Higgins, *ibid.*, 593 (1966).

(93) Available evidence would suggest that $R_2N\cdot$ radicals are extremely reactive: (a) K. U. Ingold and B. P. Roberts, "Free-Radical Substitution Reactions," Wiley-Interscience, New York, N. Y., 1971; (b) C. J. Albisetti, D. D. Coffman, F. W. Hoover, E. L. Jenner, and W. E. Mochel, *J. Amer. Chem. Soc.*, **81**, 1489 (1959).

(94) Defined in the sense given by M. D. Kamen, "Primary Processes in Photosynthesis," Academic Press, London, 1963, p 37, derived from the French "crepuscule," meaning twilight, with implications of ghostly, evanescent, etc.

(95) W. H. Melhuish, *J. Opt. Soc. Amer.*, **52**, 1256 (1962).

Syntheses of the 3,5-dicarboalkoxy pyridines (2a-f) were carried out as described in the literature. Compound 2a was prepared by esterification of the diacid with diazomethane. The 1,4-dihydropyridines 1b-f obtained as intermediates in the Hantzsch synthesis of 2b-f had physical constants identical with those reported in the literature.⁹⁶⁻⁹⁹

3,5-Dicarbomethoxy-1,4-dihydropyridine (5a) was obtained by reduction of 2a with $NaBH_4$.^{7b}

3-Carboalkoxy pyrroles (12a,b and 13a-c) were prepared by Knorr or Hantzsch pyrrole synthesis.

3,5-Dicarbomethoxy-2,6-dimethyl-4-deuteriomethylpyridine (2g) was formed when 2.00 g (8.4 mmol) of 2c in 10 ml of CH_3OD with sodium methanolate (50 mg, 0.93 mmol) was heated for 2 hr at 70°. The mixture was cooled and a few drops of D_2O were added and the solvent was evaporated. A solution of the residue in dichloromethane was extracted with water and dried over sodium sulfate. Evaporation of the solvent gave 1.83 g (7.7 mmol, 91% yield) of 2g (mp 77.5-79°) with 6 and 46% of deuterium incorporated in the two α - and the one γ -methyl substituents respectively, as confirmed by nmr and mass spectral analysis.

The irradiations of pyridines 2a-f were carried out in a Rayonet photochemical reactor with solutions of 6 mmol (1.25-1.80 g) of the pyridine in 650 ml of solvent in a quartz vessel equipped with a mechanical stirrer; 2537-Å lamps were used. A stream of dry nitrogen was led through the solution prior to irradiation although this seemed not to be essential. The period necessary to convert about 90% of the starting material increased with an increasing number of substituents on the pyridine ring (especially in the α positions) and varied from 16 to 35 hr. During the photolysis the solution became bright yellow.

A general work-up procedure was followed by which the solvent was removed on a rotary evaporator and the residue, dissolved in methanol, was separated by preparative tlc on silica gel PF₂₅₄ (100 × 20 cm plates) with ether or ether-chloroform mixtures as eluents. Often the multiple elution technique was applied (one-three times). The chromatography was carried out in the dark when chloroform was used. The 1,2- and 1,4-dihydropyridines were easily located by virtue of their respective yellow and blue fluorescences. The bands were collected and the compounds removed from the absorbent by shaking it with methanol and filtering and washing it several times on a glass filter. The solvent was evaporated and the residue, dissolved in a small amount of alcohol, was again filtered to remove traces of silica gel. The thus obtained solution gave upon evaporation a product that usually had to be recrystallized only once to obtain an analytically pure sample. Chloroform must be avoided as a solvent for the dihydropyridines since it causes oxidation.

The yields reported in the results were calculated on consumed starting material of which the unreacted part (in all cases about 10%) was recovered. Physical constants, analysis, and spectral data of previously unreported products are given in Table I. The other products were characterized by comparison of their spectra and mixture melting point determination with an authentic sample.

Remarks on Individual Photoreactions. The diastereomeric forms of 3,5-dicarbomethoxy-2(1-hydroxyethyl)-1,2-dihydropyridine (3b and 3b') were separated on the tlc plate by threefold elution. Although the two isomers had almost the same retention time they could be located by a slight difference in their yellow fluorescence colors.

The isomeric dimers 7a and 7a' formed by the irradiation of 2a in isopropyl alcohol were collected in one fraction from the tlc plate. Recrystallization from ethanol gave a first fraction mp 219.5-224° (7a') and a second one mp 222.5-223.5° (7a).

The separation of the isomers 16-18 from the photoreaction mixtures of 2f in methanol and cyclohexane or *n*-hexane was accomplished by preparative tlc on silica gel using ether and/or a benzene-ether (5:1) mixture. The mixture obtained from irradiation of 1.750 g (0.060 mol) of 2f in methanol gave after separation 0.540 g (0.019 mol) of starting material and 0.425 g (0.015 mol, 35%) of 16, mp 92.5-94.5°. Separation of a mixture from a similar irradiation in cyclohexane gave two oily fractions weighing 0.602 and

(96) A. Singer and S. M. McElvain, *Org. Syn.*, **14**, 30 (1934).

(97) L. Gattermann, *Prax. Org. Chem.*, 312 (1962).

(98) (a) L. E. Hinkel, E. E. Ayling, and W. H. Morgen, *J. Chem. Soc.*, 1839 (1931); (b) E. E. Ayling, *ibid.*, 1014 (1938).

(99) (a) CIBA Ltd., *Neth. Appl.*, **6**, 307, 414 (1965); *Chem. Abstr.*, **64**, 714a (1966); (b) A. P. Phillips and P. L. Graham, *J. Amer. Chem. Soc.*, **74**, 1552 (1952); (c) H. Bohlmann and F. Bohlmann, *Chem. Ber.*, **86**, 1419 (1953).

0.726 g. Nmr and glc integration established that 0.457 g of **2f** remained and that **16**, **17**, and **18** were formed in 14, 24, and 33% yields, respectively, calculated on consumed starting material.

The molecular composition of isomer **17**, purified by preparative glc (10% Carbowax column), was determined by its high resolution mass spectrum, which showed a parent peak at m/e 293.1626 \pm 0.0000 (calcd for $C_{16}H_{23}NO_4$, 293.1626).

An analytically pure sample of **18** was obtained by distillation; bp 109–111° (0.05 mm).

Anal. Calcd for $C_{16}H_{23}NO_4$: C, 65.52; H, 7.90; N, 4.77. Found: C, 65.45, 65.56; H, 7.92, 7.96; N, 4.91, 4.72.

The irradiations in deuterated alcohols were carried out under the same conditions as described above with the minor difference that a vessel with a 2-cm diameter was used.

A sample of **2c** (503 mg, 2.12 mmol) was irradiated for 24 hr in 40 ml of CH_3OD . There was obtained 71 mg (0.29 mmol, 14% yield) of **11b**: mp 145–148.5° (mmp with **1c**, 149–154°); ir (KBr) 1675 (C=O), 3340 cm^{-1} (N–H); nmr (CD_3OD) δ 0.89 (s, 3, $CDCH_3$), 2.22 (s, 6, 2 \times CH_3), 3.69 (br s, 6, 2 \times OCH_3). Nmr showed no deuterium incorporation in the recovered starting material (206 mg).

A sample of **2b** (500 mg, 2.00 mmol) was irradiated for 22 hr in 40 ml of C_2H_5OD . There was obtained 108 mg (0.43 mmol, 22% yield) of **11a**: mp 170.5–173.5° (mmp with **1b** (mp 176–179°) was 170–176°); ir (KBr) 1690 (C=O), 3340 (NH), 2130 cm^{-1} (C–D); nmr (acetone- d_6) δ 1.23 (t, $J = 7$ Hz, 6, 2 \times OCH_2CH_3), 2.18 (s, 6, 2 \times CH_3), 3.25 (br s, 1, CHD), 4.13 (q, $J = 7$ Hz, 4, 2 \times OCH_2CH_3). The recovered starting material (25 mg) had not incorporated any deuterium as indicated by its nmr spectrum.

The 1,4-dihydropyridines **1b** and **1c** were refluxed for 1 hr in CH_3OD . The nmr spectrum of the recovered compounds showed no deuterium incorporation in the 4 position.

3,5-Dicarbomethoxy-2,6-dimethyl-4-deuteriomethylpyridine (2g) (1.22 g, 5.15 mmol) gave on irradiation in 550 ml of methanol 110 mg (0.66 mmol, 17% yield) of pyrrole: mp 121.5–123.5°; nmr (CCl_4) δ 2.05 (br s, 4- and 5- CH_3 , 25% D), 2.38 (s, 2- CH_3 , 2% D), 3.63 (3, OCH_3 , 0% D); nmr (C_6D_6) δ 1.77 (s, 5- CH_3 , 4% D), 2.31 (br s, 2- and 4- CH_3 , 28% D), 3.58 (s, OCH_3 , 0% D). These data are consistent with a deuterium content of 52% in the 4-methyl substituent. The number determined from the mass spectrum was 53%. The recovered starting material (275 mg) still contained 5 and 50% deuterium, respectively, in the α - and γ -methyl groups.

The pyrroles **12a,b** (250 mg) were irradiated in 150 ml of ethanol with a high-pressure mercury lamp (Hanau S-81) equipped with a quartz jacket. The reaction was followed by glc and over a 24-hr period only a slow decrease of the starting material was observed. More than 65% of the pyrroles could be recovered.

The 1,4-dihydropyridines **1b–d** (330 mg) were irradiated for 25 hr in 150 ml of ethanol or methanol with a high-pressure mercury lamp (Hanau S-81) equipped with a quartz jacket. No pyrrole formation was observed during the irradiation, which was followed with glc. The starting material was recovered almost quantitatively in the cases of **1c** and **1d**. From the irradiation of **1b** there was isolated 40% of the starting material and 31% of **2b** (preparative tlc). In all three cases a 1,2-DHP could be detected as a minor product on the tlc plate by its yellow fluorescence.¹⁰⁰

Conversion of the photoisomer **16** to **19** was achieved by refluxing overnight 130 mg (0.44 mmol) of the isomer in 2 ml of hydrazine hydrate with enough ethanol to dissolve all the material. The reaction mixture was concentrated and the residue dissolved in hot water and filtered. Acidification with acetic acid gave a colorless precipitate that was collected by filtration and dried at 100°. The isolated compound (15 mg, 0.07 mmol, 15% yield) had mp 279–285°, m/e at 223, and was in all respect identical with **19** synthesized separately (mmp with authentic **19** gave no depression, see below).

4,5-Dimethyl-2-isopropylloxazole (21) was formed when isobutyric amide (14.2 g, 0.16 mol) and 3-bromobutanone²⁴ (9.9 g, 0.07 mol) were heated for 3 hr at 120–140°. The reaction mixture was poured into water and made alkaline with sodium hydroxide. The organic contaminants were extracted with dichloromethane. The basic compounds were separated from the nonbasic materials by extraction with dilute hydrogen chloride. Neutralization and extraction with dichloromethane of this aqueous mixture afforded after drying and distillation 4.02 g (47%) of **21**: bp 163–164°; nmr (CCl_4) δ 1.28 (d, 6, $(CH_3)_2CH$), 1.98 and 2.17 (s, 3, CH_3), and 2.88 (h, 1, $(CH_3)_2CH$).

Anal. Calcd for $C_8H_{13}NO$: C, 69.03; H, 9.42; N, 10.06. Found: C, 69.08, 68.80; H, 9.61, 9.53; N, 10.24, 10.27.

3,4-Dicarboethoxy-5,6-dimethyl-2-isopropylpyridine (16a) was obtained when **21** (2.0 g, 14.4 mmol) and maleic acid diethyl ester (5.0 g, 29.0 mmol) in 10 ml of benzene were refluxed for 3 days. Acid–base separation of the cooled reaction mixture gave a chloroform solution (dried over magnesium sulfate) containing mainly the oxazole **21** and pyridine **16a**. These were separated by glc on a silicon rubber SE-30 column. The oily pyridine **16a** (50 mg; 12%) was collected: nmr (CCl_4) δ 1.23 (d, 6, $(CH_3)_2CH$), 2.23 (s, 3, CH_3), 2.53 (s, 3, CH_3), 3.26 (h, 1, $(CH_3)_2CH$), 1.35 and 4.25 (respectively, t, 6, and q, 4, 2 \times OCH_2CH_3); nmr (C_6D_6) δ 1.44 (d, 6, $(CH_3)_2CH$), 1.96 (s, 3, CH_3), 2.25 (s, 3, CH_3), 3.53 (h, 1, $(CH_3)_2CH$), 1.07 and 4.14 (t, 6, and q, 4, 2 \times OC_2H_5); mass spectrum m/e (parent) 293.

The adduct **22** was prepared by refluxing overnight **21** (1.5 g, 10.8 mmol) and *N*-phenylmaleimide (1.8 g, 10.4 mmol) in 10 ml of benzene. A precipitate was formed. Partial evaporation of the solvent gave upon cooling 2.37 g (73%) of crystalline **22**: mp 165° dec (recrystallized from benzene); ir (KBr) 1700 and 1775 ($C=O$), 1630 cm^{-1} ($C=N$); nmr (pyridine- d_5) δ 1.22 and 1.64 (d, 3, $(CH_3)_2CH$), 1.85 and 2.06 (s, 3, CH_3), 2.63 (h, 1, $(CH_3)_2CH$), 3.20 and 3.47 (d, 1, $CHCH$), 7.40 (m, 5, C_6H_5).

Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 69.23; H, 6.46; N, 8.97. Found: C, 69.05, 69.32; H, 6.36, 6.34; N, 8.92, 9.02.

The triazanaphthalene (**19**) was obtained by refluxing **22** (2.9 g, 9.3 mmol) in 40 ml of dioxane with several drops of concentrated hydrogen chloride for 1 hr. The solvent was removed and the residue dissolved in benzene. This solution was washed with sodium bicarbonate, dried, and evaporated to give 1.5 g (58%) of dehydrated product: mp 118–120° (recrystallized from ethanol); ir (KBr) 1710 and 1765 cm^{-1} ($C=O$); nmr ($CDCl_3$) δ 1.33 (d, 6, $(CH_3)_2CH$), 2.67 (s, 6, two CH_3), 4.05 (h, 1, $(CH_3)_2CH$), 7.44 (s, 5, C_6H_5).

Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.46; H, 6.16; N, 9.52. Found: C, 73.14, 73.11; H, 6.10, 6.16; N, 9.53, 9.60.

Conversion to **19** was accomplished by heating the above product (1.280 g, 4.40 mmol) in 20 ml of hydrazine hydrate and ethylene glycol each for 16 hr at 110°. The hydrazine hydrate was removed under reduced pressure and the residue diluted with 50 ml of benzene. Extraction with dilute sodium hydroxide and acidification of the extracts with acetic acid gave a colorless precipitate, which was collected by filtration and dried at 100°. There was obtained 0.650 g (2.72 mmol, 64% yield) of **19**: mp 285–287° (recrystallized from ethanol); uv_{max} (96% ethanol) 242 $m\mu$ ($\log \epsilon$ 3.66), 277 (3.79), and 325 (3.81); nmr (pyridine- d_5) δ 3.57 (d, 6, $(CH_3)_2CH$), 3.68 and 3.88 (s, 3, CH_3), 5.30 (h, 1, $(CH_3)_2CH$), 7.40 (br s, OH).

Anal. Calcd for $C_{12}H_{13}N_3O_2$: C, 61.80; H, 6.48; N, 18.01. Found: C, 61.97, 61.70; H, 6.38, 6.51; N, 18.19, 18.35.

Quantitative rearomatization of **3b** and **9a** to the pyridines **2a** and **2b** was observed when these dihydropyridines were dissolved in ethanol and the solutions left at room temperature for several days.

The lactone **3b''** was obtained when **3b** (310 mg, 1.36 mmol) and diethyl azodicarboxylate (240 mg, 1.38 mmol) in dioxane were stirred for 2 days followed by a few hours reflux. The dihydropyridine uv absorption band at 380 $m\mu$ had disappeared. Evaporation gave a residue that was separated by preparative tlc (silica gel, dichloromethane). There was isolated 135 mg (0.70 mmol, 51%) of **3b''**: mp 166.5–168° (recrystallized from acetone); ir (KBr) 1720 and 1770 cm^{-1} ($C=O$); uv_{max} (96% ethanol) 222 $m\mu$ ($\log \epsilon$ 4.02) and 274 (3.62); nmr (pyridine- d_5) δ 3.89 (s, 3, OCH_3), 5.50 (s, 2, OCH_2), 8.75 and 9.55 (d, 2, aryl H).

Anal. Calcd for $C_9H_7NO_4$: C, 55.94; H, 3.66; N, 7.26. Found: C, 55.90, 56.00; H, 3.69, 3.64; N, 7.61, 7.58.

3,5-Dicarbomethoxy-2-hydroxymethylpyridine (3b') was obtained when **3b** (150 mg, 0.64 mmol) and tetracyanoethylene (75 mg, 0.59 mmol) were refluxed for 4 hr in 4 ml of tetrahydrofuran. The reaction mixture was concentrated and cooled. Colorless crystals of **3b'**, 22 mg (0.09 mmol, 15%), separated from the reaction mixture: mp 84–87°; ir (KBr) 1720 ($C=O$), 3460 cm^{-1} (O–H); uv_{max} (96% ethanol) 229, 269, and 277 $m\mu$; nmr (acetone- d_6) δ 3.95 (s, 6, 2 \times OCH_3), 5.02 (s, 2, CH_2OH), 9.06 and 9.52 (d, 1, aryl H, $J = 20$ Hz).

Diels–Alder reactions of equimolar amounts of **9a** with tetracyanoethylene, maleic anhydride, *N*-phenylmaleimide, and 4-phenyl-1,2,4-triazoline-3,5-dione¹⁰¹ and **9b** with tetracyanoethylene and dicarbomethoxyacetylene were attempted in refluxing tetrahydrofuran. Although in some cases charge transfer complexes seemed to be formed no new adducts were present as was shown by tlc.

Saponification of **17** was carried out with a 40-mg (0.14 mmol) sample purified by preparative glc. The substance was treated for

(100) U. Eisner, J. R. Williams, B. W. Matthews, and H. Ziffer, *Tetrahedron*, **26**, 899 (1970).

(101) B. T. Gillis and J. D. Hagarty, *J. Org. Chem.*, **32**, 330 (1967).

45 min at 100° with 0.6 ml of 25% aqueous NaOH, to which sufficient ethanol was added to obtain a clear solution. The reaction mixture was cooled in ice and neutralized to pH 7 with concentrated H₂SO₄. On ether extraction at this point only 5 mg of not readily identifiable organic material was obtained. Acidification of the water layer to pH 4 and reextraction gave after drying (MgSO₄) 27 mg (0.11 mmol, 80%) of **23**: ir 1735 and 1720 (C=O), 3250 cm⁻¹ (OH); ν_{\max} (ethanol) 278 m μ (log ϵ 3.36); nmr (CCl₄) δ 8.58 (s, 1, OH), 2.21 and 2.54 (s, 3, CH₃), 1.33 and 4.05 (d, 6, and h, 1, CH(CH₃)₂), 1.40 and 4.40 (t, J = 7 Hz, 3, and q, J = 7 Hz, OCH₂CH₃).

Pyrolysis of **23** was done with a 20-mg sample for 200 sec at 200–210° in a metal bath. Quantitative formation of **24** was observed: m/e 221; ir 1720 cm⁻¹ (C=O); ν_{\max} (ethanol) 275 m μ (log ϵ 3.31); nmr (CCl₄) δ 8.50 (s, 1, aryl H), 1.27 and 2.68 (d, J = 7 Hz, 2, and h, 1, CH(CH₃)₂), 2.14 and 2.44 (s, 3, CH₃), 1.37 and 4.36 (t, J = 7 Hz, 3, and q, J = 7 Hz, OCH₂CH₃).

Saponification of **18** was carried out with a 150-mg (0.5 mmol) sample and 3 ml of 25% aqueous NaOH with sufficient ethanol (0.5 ml) to obtain a clear solution. The mixture was refluxed for 45 min after which time it was cooled in ice. On neutralization with concentrated H₂SO₄ to pH 7 followed by an ether extraction, drying the extracts with MgSO₄, and evaporating the solvent gave **27** as a thick syrup: m/e 265; ir 1760 and 1720 (C=O), 3250 cm⁻¹ (OH); ν_{\max} (ethanol) 276 m μ (log ϵ 3.58); nmr (CCl₄) δ 11.83 (s, 1, OH), 2.28 and 2.70 (s, 3, CH₃), 1.26 and 2.98 (d, 6, and h, 1, CH(CH₃)₂), 1.39 and 4.42 (t, 3, and q, 2, OC₂H₅).

Pyrolysis of **27** was carried out with 80 mg (0.30 mmol) as described for **23**. According to nmr a quantitative yield of **28** was obtained: m/e 221; ir 1720 cm⁻¹ (C=O); ν_{\max} (ethanol) λ_{\max} 267 m μ (log ϵ 3.32), 275 (sh) (3.28); nmr (CCl₄) δ 8.23 (s, 1, aryl H), 2.13 and 2.21 (s, 3, CH₃), 1.22 and 2.89 (d, 6, and h, 1, CH(CH₃)₂), 1.36 and 4.35 (t, 3, and q, 2, OC₂H₅).

Deuterium exchange experiments were done with 0.07 mol l⁻¹ solutions of the pyridine in CD₃OD containing 0.50 mol l⁻¹ CD₃ONa in a sealed nmr tube at 72 and 86°. The deuterium content of the methyl groups was determined by nmr integration.

Photoisomer **18** (220 mg, 0.75 mmol), containing about 10% of **16**, was refluxed for 11 hr with 2.5 ml of hydrazine hydrate and ethanol each. A work-up procedure, as described above for isomer **16**, was followed. In this way only a trace (3.0 mg) of **19** but no other dihydroxytriazanaphthalene precipitated. The acidic solution, obtained after filtration, was evaporated and the residue was subsequently refluxed in 5.0 ml of 4 *N* HCl to promote cyclization of any *o*-dihydrazide. In the case of positive reaction a triazanaphthalene should precipitate and a new uv absorption above 300 m μ should appear. However, neither was observed.

Photoisomer **17** (156 mg, 0.53 mmol) was treated with hydrazine hydrate as described above for **18**. The formation of a triazanaphthalene was not observed even after prolonged heating in 4 *N* HCl.

Attempted saponification of **2f** was carried out by boiling a sample in a 25% KOH-water mixture containing sufficient ethanol to bring **2f** into solution. After 12 hr no detectable amount of hydrolysis had occurred.

3,5-Dicarboethoxy-1-methylpyridinium perchlorate (31a) was prepared by heating **2a** (6.0 g, 0.031 mol) and dimethyl sulfate (8.0 g, 0.063 mol) for 2 hr at 70–140°. The viscous reaction mixture was dissolved in 20 ml of water and the quaternized pyridine was precipitated by adding a saturated sodium perchlorate solution. In this manner 5.4 g (0.018 mol, 57%) of **31a** was collected: mp 237–239° (recrystallization from ethanol-water (1:1)); ν_{\max} (CH₃OH) 271 m μ (log ϵ 3.72); nmr (DMSO-*d*₆) δ 4.01 (s, 6, 2 \times OCH₃), 4.50 (s, 3, NCH₃), 9.11 and 9.97 (t, 1, and d, 2, aryl H).

Anal. Calcd for C₁₀H₁₂ClNO₈: C, 38.80; H, 3.90; N, 9.52; Cl, 11.46. Found: C, 38.69, 38.97; H, 4.04, 3.96; N, 4.65, 4.66; Cl, 11.93, 11.78.

3,5-Dicarboethoxy-1,2,6-trimethylpyridinium perchlorate (31b) was prepared by quaternization of **2b** with dimethyl sulfate as described by Karrer.³⁰ A sample of **2b** (6.0 g, 0.024 mol) yielded 7.2 g (0.020 mol, 83%) of **31b**, mp 107.5–108° (lit.³⁰ 107–108°).

3,5-Dicarboethoxy-1,2,4,6-tetramethylpyridinium methylsulfate (31c) was obtained from **2d** and dimethyl sulfate. A sample of **2d** (2.6 g, 9.8 mmol) gave 3.5 g (9.0 mmol, 91%) of **31c**, mp 161–164° (lit.³¹ 172–174°).

1-Methylnicotinamide iodide was prepared from nicotinamide and methyl iodide. The isolated product had mp 205.5–206.5° (lit.¹⁰² 204°).

(102) P. Karrer, G. Schwarzenbach, F. Benz, and U. Solmssen, *Helv. Chim. Acta*, **19**, 811 (1936).

3,5-Dicarboethoxy-1,2,6-trimethyl-1,2-dihydropyridine (33) was obtained from reaction of sodium borohydride (50 mg, 1.32 mmol) with **31b** (500 mg, 1.36 mmol) dissolved in 100 ml of ethanol to which was added a solution of 500 mg of sodium carbonate in 1.5 ml of water.⁹ The yellow reaction mixture was extracted with dichloromethane and the extracts were dried on sodium sulfate. Removal of the solvent gave a residue that was separated by tlc (silica gel and ether) allowing the collection of **33** as a yellow oil (85 mg, 0.32 mmol, 24%): ir (CCl₄) 1680 cm⁻¹ (C=O); ν_{\max} (96% ethanol) 218, 286, and 381 m μ ; nmr (CCl₄) δ 1.09 (d, 3, CH₃), 1.30 (t, 6, 2 \times OCH₂CH₃), 2.49 (s, 3, CH₃), 3.20 (s, 3, NCH₃), 4.33 (q, 1, CH), 4.12 and 4.14 (q, 2, OCH₂CH₃), and 7.48 (s, 1, vinyl H).

The irradiations were carried out as described for the free bases.

3,5-Dicarbomethoxy-1-methylpyridinium perchlorate (31a) (1.9 g, 6.2 mmol) was dissolved in methanol (650 ml) and irradiated for 24 hr. An aqueous solution of the residue, obtained after evaporation of the solvent, was extracted several times with benzene. The extracts gave upon drying and removal of the solvent a yellow solid, which was purified by tlc (silica gel and ether) to give 263 mg (1.1 mmol, 18%) of **32**: mp 148–150° (recrystallized from benzene); ir (KBr) 3410 (OH), 1670 and 1690 cm⁻¹ (C=O); ν_{\max} (96% ethanol) 223 m μ (log ϵ 4.14), 296 (4.31), and 390 (3.84); nmr (pyridine-*d*₅) δ 3.33 (s, 3, NCH₃), 3.67 and 3.73 (s, 3, OCH₃), 3.90 (br m, 2, CH₂O), 4.87 (q, 1, CH), 6.70 (t, 1, OH), 7.86 and 8.03 (s, 1, vinyl H).

Anal. Calcd for C₁₁H₁₅NO₅: C, 54.76; H, 6.27; N, 5.81. Found: C, 54.84, 54.83; H, 6.27, 6.25; N, 5.71, 5.71.

The tlc displayed, besides a spot for **32**, two small spots with fluorescences and *R_f* values expected for 3,5-dicarbomethoxy-1-methyl-1,2- and 1,4-dihydropyridine. The concentrated water layer yielded a viscous residue showing nmr resonances identical with those of the starting material. However, attempted crystallization of this material met with insurmountable difficulties.

3,5-Dicarboethoxy-1,2,6-trimethylpyridinium perchlorate (31b) (0.960 g, 2.72 mmol) dissolved in methanol (650 ml) was irradiated for 20 hr. The solvent was evaporated and the residue was dissolved in water. Extraction with ether and evaporation of the solvent gave a residue that was purified by column chromatography (silica gel and ether) to give 84 mg (0.31 mmol, 11%) of a yellow oil, which was identified spectroscopically as **33**. The starting material was recovered in 52% yield (0.5 g, 1.37 mmol) by evaporating the solvent and recrystallizing the residue from ethanol. This product was identified by nmr spectroscopy.

3,5-Dicarboethoxy-1,2,4,6-tetramethylpyridinium methylsulfate (31c) (491 mg, 1.25 mmol) was irradiated (Hanau S-81 lamp) in 145 ml of ethanol for 45 hr. The solvent was removed and an aqueous solution of the residue was extracted with ether. The residue from these extractions displayed no uv absorption between 300 and 400 m μ and no clearly definable products by means of tlc. The remaining water layer gave upon evaporation 377 mg (0.96 mmol, 77%) of a viscous material that was identified as **31c**. Attempted recrystallization failed.

1-Methylnicotinamide iodide (1.50 g, 0.006 mol) dissolved in 650 ml of ethanol was irradiated for 24 hr. The residue, obtained after evaporating the solvent, exhibited no uv absorptions above 300 m μ and no components capable of moving on a silica gel layer with organic eluents.

Deuterium incorporation in **31c** was observed when it (200 mg, 0.51 mmol) was irradiated for 18 hr in 30 ml of methanol-*O-d*. The same equipment was used as described for the experiments with labeled alcohols. The solvent was removed at room temperature on a rotary evaporator and the residue gave after laborious recrystallization from ethanol 70 mg of a solid, mp 156–160° (mmp with **31c** undepressed) having a deuterium content of 44 and 26% in the γ -methyl and the two α -methyl substituents, respectively, as determined by nmr spectroscopy using the ethoxy and *N*-methyl resonances as internal standards. No deuterium incorporation in **31c** was observed when a sample dissolved in methanol-*O-d* was kept at room temperature for several days or when it was refluxed for 3 hr.

Deuterium incorporation in **31b** was observed when it (190 mg, 0.51 mmol) was irradiated in 39 ml of methanol-*O-d* as described above. The residue obtained after removal of the solvent displayed a decrease in the nmr resonance of the α -methyl groups corresponding to a deuterium content of 58%. The singlet of the 4-aryl hydrogen atom was used as a standard. Again this residue could not be obtained in crystalline form. No deuterium incorporation was observed when **31b** was treated under similar conditions in the dark.

1,2,4,6-Tetramethylpyridinium perchlorate (160 mg) was irradiated for 17 hr in 40 ml of methanol-*O-d*. Removal of the solvent and recrystallization of the residue from methanol gave 155 mg (97%) of the starting material, mp 196–202° (lit.³³ 204.5–205.5°). No detectable deuterium incorporation in the 2-, 4-, and 6-methyl groups was observed as confirmed by the integration value of the nmr spectrum using the β -aryl hydrogens and the *N*-methyl group as internal standards.

Attempted trapping of a photoenol from 31b was carried out by irradiating the salt (2.20 g, 6.0 mmol) in the presence of dimethyl acetylenedicarboxylic acid (0.63 g, 6 mmol) in 300 ml of a 1:1 mixture of *tert*-butyl alcohol and water. (This medium, in which

photoinduced deuterium incorporation in the 2- and 6-methyls also occurred, was chosen especially to prevent photoreduction.) The experiment was followed by uv and glc. Although glc analysis demonstrated that the acetylenic ester was consumed during the irradiation, no changes were observed in the uv absorptions of the solute. The residue, obtained after 24 hr of irradiation and evaporation of the solvent, showed only resonances corresponding to those of the starting material.

Acknowledgment. We express our gratitude to Mr. C. Kruk of the University of Amsterdam for carrying out many of the 100-MHz nmr experiments.

Empirical Rules for Estimating the Reduction Potential of α,β -Unsaturated Carbonyl Compounds¹

Herbert O. House,* Larry E. Huber, and Michael J. Umen

Contribution from the School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332. Received June 1, 1972

Abstract: The polarographic reduction potentials (*vs. sce*) for a series of α,β -unsaturated carbonyl compounds have been measured in the aprotic solvent, dimethylformamide. For a variety of cyclic or acyclic aldehydes, esters, and ketones, a simple set of empirical rules (Table I) serves to predict within ± 0.1 V the reduction potentials for compounds, $R_3R_4C=CR_2COR_1$, as the position and nature of the substituents are varied among the series $R = H, \text{alkyl, alkoxy, or phenyl}$.

A knowledge of the reduction potentials of α,β -unsaturated carbonyl compounds *in aprotic media* can be of considerable value both for assessing the feasibility of performing selective reductions of these conjugated systems with dissolving metals or electrochemically² and for determining whether these unsaturated systems will be suitable substrates for the conjugate addition of lithium dialkylcuprates and possibly other organometallic reagents.³ Although several compilations of polarographic reduction potentials are available,⁴ most of the data pertain to reductions in protic media (typically ethanol or aqueous dioxane) where the reduction potentials of unsaturated carbonyl compounds are substantially less negative than in the aprotic media.^{4c,5} However, the reduction potentials in aprotic media are the appropriate values to employ for reactions involving organometallic reactants, reductions with alkali metals, and many electrochemical reductions.

For this reason, we have measured the polarographic $E_{1/2}$ values (*vs. sce*) for *ca.* 10^{-3} M solutions of a number of representative α,β -unsaturated aldehydes, ketones,

and esters in dimethylformamide (DMF) containing 0.5 M tetraalkylammonium salt (either *n*-Pr₄NClO₄ or *n*-Bu₄NBF₄) as a supporting electrolyte. Although the lifetimes of the anion radicals formed in these reductions may be markedly diminished by the presence of low concentrations (10^{-1} – 10^{-3} M) of proton donors (*t*-BuOH, H₂O) or lithium salts,⁵ the $E_{1/2}$ values of the unsaturated carbonyl compounds studied become only slightly (0.1 V or less) more positive under these circumstances. Thus, no serious error is being introduced in these polarographic reduction potentials even when competing protonation of the anion radicals *in the reaction solution* is preventing their formation under truly reversible conditions.⁶

The polarographic $E_{1/2}$ values obtained for α,β -unsaturated carbonyl compounds in measurements reported here and in an earlier paper⁵ are summarized in Table II. As noted elsewhere,⁷ these reduction potential values provide a measure of the energy difference between an anion radical **2** with an extra electron in the lowest antibonding molecular orbital (*i.e.*, the π^* orbital) and the unsaturated carbonyl system **1**.

(1) This research has been supported by Public Health Service Grant No. 7-RO1-CA-12634 from the National Cancer Institute.

(2) For recent reviews, see (a) M. Smith in "Reduction," R. L. Augustine, Ed., Marcel Dekker, New York, N. Y., 1968, pp 95–170; (b) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, pp 145–227.

(3) H. O. House and M. J. Umen, *J. Amer. Chem. Soc.*, **94**, 5495 (1972).

(4) (a) M. Kotake, Ed., "Constants of Organic Compounds," Asakura Publishing Co., Ltd., Tokyo, 1963, pp 680–693; (b) L. Meites, "Polarographic Techniques," 2nd ed, Wiley-Interscience, New York, N. Y., 1965, pp 671–711; (c) C. K. Mann and K. K. Barnes, "Electrochemical Reactions in Nonaqueous Systems," Marcel Dekker, New York, N. Y., 1970, pp 177–189.

(5) K. W. Bowers, R. W. Giese, J. Grimshaw, H. O. House, N. H. Kolodny, K. Kronberger, and D. K. Roe, *J. Amer. Chem. Soc.*, **92**, 2783 (1970).

(6) This assumption is probably not valid for measurements of the $E_{1/2}$ values for certain unsubstituted vinyl and ethynyl carbonyl compounds such as acrolein ($E_{1/2} = -1.73$, $\alpha n = 0.3$), 1-butyne-3-one ($E_{1/2} = -1.79$, $\alpha n = 0.6$), and methyl vinyl ketone ($E_{1/2} = -1.97$, $\alpha n = 0.5$). In these cases, it seems likely that the anion radical reacts with a second molecule of the highly reactive starting unsaturated carbonyl compound before it has diffused from the electrode surface resulting in an apparent $E_{1/2}$ value which is more positive than the reversible value by 0.1–0.3 V. For recent reviews, see J. D. Anderson, J. P. Petrovich, and M. M. Baizer, *Advan. Org. Chem.*, **6**, 257 (1969); M. M. Baizer and J. P. Petrovich, *Progr. Phys. Org. Chem.*, **7**, 189 (1970). Presumably, a related phenomenon, protonation of the anion radical before it diffuses from the electrode surface, accounts for the significantly less negative $E_{1/2}$ values observed when α,β -unsaturated carbonyl compounds are reduced in media containing high concentrations of proton donors.

(7) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1961, pp 173–185.