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PHOTOCHEMICAL RING CONTRACTION, REDUCTION, AND SOLVENT ADDITION IN PYRIDINES

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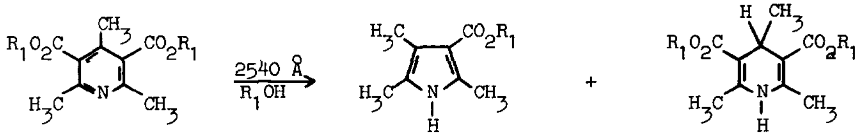
We have found that 3,5-dicarboalkoxy substituted pyridines undergo a confounding variety of photochemical reactions.

In ethanol solution 3,5-dicarboethoxy-2,4,6-trimethylpyridine (1a),[1] when irradiated with 2540 Å light (20 hr, 10^{-2} M, Rayonet photochemical reactor), yields the known 3-carboethoxy-2,4,5-trimethylpyrrole[2] (2a) and 3,5-dicarboethoxy-2,4,6-trimethyl-1,4-dihydropyridine[1] (3a) (eq. 1). The yields are based on consumed starting material (tlc separation). The balance of the product was uncharacterizable. Analyses by glpc and uv established that 2a and 3a appear simultaneously during the reaction. The methyl ester 1b reacts equally well.

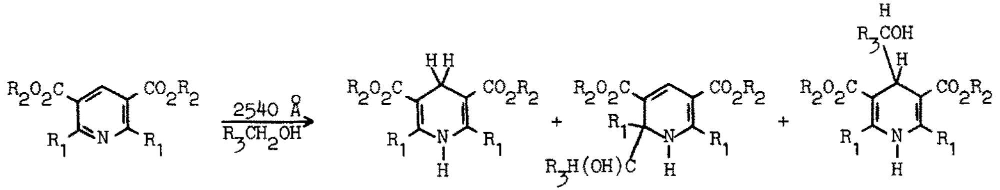


(1)

1	2	3
(a) $R_1 = C_2H_5$	(a) (16%)	(a) (30%)
(b) $R_1 = CH_3$	(b) (11%)	(b) (25%)

The only isolable product from irradiation of 3,5-dicarboethoxy-2,6-dimethylpyridine (4a)[3] in ethanol is 3,5-dicarboethoxy-2,6-dimethyl-1,4-dihydropyridine (5a) (eq. 2).[3] No pyrrole could be detected. Change of solvent to methanol, however, led to only a 9% yield of 5a while 61% and 19% yields, respectively, of the previously unknown isomeric dihydropyridines, 6b and 7b, were obtained.

Product 6b, mp 121.5-123.5°, is identified as 3,5-dicarboethoxy-2-hydroxymethyl-2,6-dimethyl-1,2-dihydropyridine from its uv spectrum [uv max (96% EtOH) 2120 Å (ε 12,700), 2820 Å (ε 20,300), and 3800 Å (ε 6,700)] characteristic of 1,2-dihydropyridines.[4] The nmr spectrum (C_6D_6)



4 5 6 7 (2)

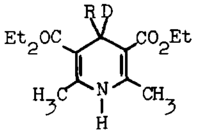
(a) R_1=CH_3, R_2=C_2H_5	R_3=CH_3 (a) 55% R_3=H (a) 9%	(a) not found (b) 61%	(a) not found (b) 19%
(b) R_1=H, R_2=CH_3	R_3=CH_3 (b) 3% R_3=H (b) 5%	(c) 59% (d) 76%	(c) not found (d) 19%

shows nonequivalent ethyl groups [triplets (J = 7.0 Hz) at δ 1.00 and δ 1.06 and quartets (J = 7.0 Hz) at δ 4.00 and δ 4.02], a singlet for the vinylic proton at δ 8.28, singlets for the methyl groups at δ 1.40 and δ 2.12, a poorly resolved singlet for the hydroxymethyl protons at δ 3.85 [in CD_3OD these diastereomeric protons separate cleanly to give an AB quartet (J = 10.5 Hz)], and broad singlets for the amino and hydroxyl protons at δ 3.0 and δ 5.3. The latter two absorptions disappear in CD_3OD. The ir spectrum of a dilute solution of 6b in CH_2Cl_2 shows bands at 3610 cm^{-1} (O-H) and 3405 cm^{-1} (N-H). The mass spectrum shows a parent peak at m/e 283 ($C_{14}H_{21}O_5N$) and the base peak at m/e 252 (-CH_2OH).

Product 7b, mp 135-136°, is identified readily as 3,5-dicarboethoxy-4-hydroxymethyl-2,6-dimethyl-1,4-dihydropyridine on the basis of its uv spectrum [uv max (96% EtOH) 2330 Å (ε 17,300) and 3550 Å (ε 7,400)] characteristic of 1,4-dihydropyridines.[4,5] The mass spectrum showed the parent peak at m/e 283 and the base peak at m/e 252 (-CH_2OH). The nmr spectra in CD_3OD, C_3D_6O, and C_2D_6SO were all fully consistent with the proposed symmetric structure.[6]

Addition of a solvent molecule to the pyridine skeleton was found to be the favored reaction with 4b; the previously unreported products 6c,d and 7d were identified from nmr, ir, uv, and mass spectral data. The diastereomeric forms of 6c, mp 160-166° and mp 152-158°, were separated.

Pyrrole formation has been observed occasionally in reductions of pyridines[7] and has been reported also in the thermolysis (240°) of 3,5-dicarboethoxy-4-carboxy-2,6-dimethyl-1,4-dihydropyridine.[8] To the best of our knowledge, however, no analogy exists in the photochemistry of pyridine systems for either ring contraction or the addition of the elements of hydrogen. The 1,4-dihydropyridines 3a-b are quite stable to 2540 Å irradiation and do not act as pyrrole precursors. When 1a and 4a were irradiated in CH_3OD and C_2H_5OD, respectively, the reduction products 8a,b had >90% deuterium at the 4-position as determined by nmr. On the basis of this evidence, it is tempting to speculate that, after removal of a carbon-bound hydrogen by the nitrogen atom, the



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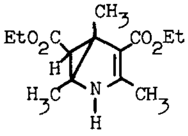
(a) R=CH$_3$
(b) R=H



9

resulting α-hydroxyalkyl radical transfers oxygen-bound hydrogen (deuterium) to the 4-position giving 1,4-dihydropyridine or, alternatively, to the 3-position (with concomitant bond-switching) to give intermediate 9 which subsequently decomposes to pyrrole. (Little, if any, reaction occurs in t-butanol or toluene). Intermediates analogous to 9 have been suggested in the ring expansions of pyrroles to pyridines occurring upon addition of carbenes.[9]

The alcohol addition products can be accomodated by coupling between pyridyl and α-hydroxyalkyl radicals. Addition reactions find precedent in previous observations of incorporation of solvent fragments and/or dimerization of pyridine-like systems.[10,11] The effect of substituents in the pyridine nucleus as well as in the alcohol indicates an unusually delicate energetic balance between the various pyridine-alcohol reaction modes.

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5. Product 3a, for example, has [uv max (96% EtOH) 2340 Å (ε 19,800) and 3500 Å (ε 7,900)].
6. Correct analyses were obtained for all new compounds.

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