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A NEW ROUTE TO 3,4-DIHYDRO-2-PYRIDONES FROM A DIOXOPYRROLINE DERIVATIVE[1]

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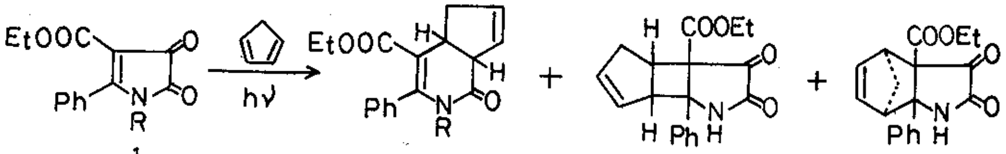
In photocycloaddition of 2-phenyl-3-ethoxycarbonyl-Δ^2-pyrroline-4,5-dione to olefins, the formation of dihydropyridones were observed although the yields were variable depending on the structure of olefins.

In the preceding paper[2] we described that photocycloaddition of cyclopentadiene to 2-phenyl-3-ethoxycarbonyl-Δ^2-pyrroline-4,5-dione (1a) yielded the dihydropyridone (2), together with the cyclobutane (3) and the bicycloheptane derivative (4).



1 a: R=H, b: R=Me 2 3 4

The formation of 2 prompted us to check the generality of this reaction. We show here that in photocycloaddition of 1 to olefins dihydropyridones are usually formed though the yields are variable depending on the structures of olefins.

Irradiation of cyclopentene with 1a in dimethoxyethane with high pressure Hg lamp (100 W, quarz) for 2 hr at 0°C afforded a dihydropyridone (5a), m.p. 143-144°. Cycloolefins, such as 1-trimethylsilyloxycyclopent-1-ene, indene, and cyclohexadiene similarly gave the dihydropyridones (6, 9a and 10), in the yields respectively as shown in Table I. They were easily characterized

Table I. *Photocycloaddition of Dioxopyrrolines with Olefins*

Dioxo-pyrroline	Olefin	Reaction Condition Temp.(°C)	Time(hr)	Dihydropyridone	m.p.	Yield(%)
1a	cyclopentadiene	-30°	1.5	2a	119-120°	30a)
"	cyclopentene	0°	2	5a	143-144°	10b)
"	1-trimethylsilyl-oxycyclopentene	0°	2	6	125-126°	9c)
"	indene	0°	3	9a	194-195°	40b)
"	cyclohexadiene	0°	1.5	10	144-146°	1.5d)
"	styrene	0°	2	13a	134-136°	6e)
"	ethyl vinyl ether	0°	2	14	112-113°	4e)
1b	cyclopentadiene	-30°	1	2b	89-91°	11a,b)

a) ref. 2

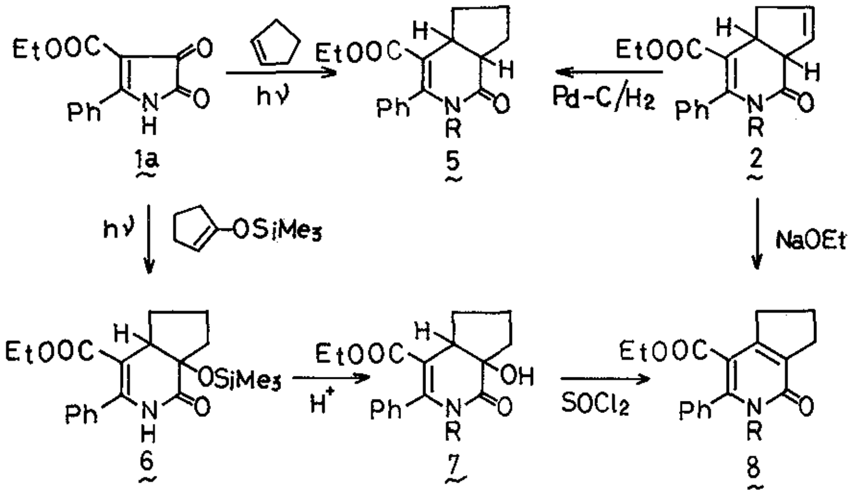
b) The only isolable crystalline product.

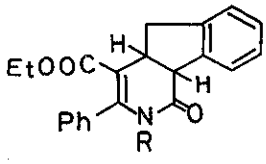
c) Isolated as a major product with several crystalline minor products.

d) Isolated as a minor product with two other products (30%).

e) Isolated as a minor product with formation of cyclobutane derivative (ref. 5).

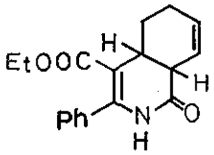
by their UV and IR spectra which were very similar with those of the dihydropyridone (2)[2]. The dihydropyridones (5a, 7a and 9a) were methylated on treatment with dimethyl sulfate in CH$_3$CN to the corresponding N-methyl derivatives: (5b) m.p. 95-97°, (7b)[3] m.p. 80-83°, (9b) m.p. 117-118°.





9

a : R = H
b : R = Me



10

Structural elucidations of these compounds were made as follows. Hydrogenation of 2a over 5% Pd-C in ethanol gave the dihydro-derivative identical with 5a. Hydrolysis of 6 with dilute hydrochloric acid followed by treatment of the resulting hydroxy-compound (7a), m.p. 187-189°, with thionyl chloride in pyridine afforded the pyridone (8a), m.p. 182-184°. The α-pyridone charactor of 8a was demonstrated by its characteristic UV spectrum [λ_{max} 273 (ε=9,900) and 304 nm (ε=7,800)] and by the increase of acidity (pKa 9.18)[4] compared with that of 2a (pKa ~ 14). In agreement with this evidence, 8a was smoothly methylated with diazomethane to the N-methyl derivative (8b), m.p. 117-119°, λ_{max} 273 (ε=10,400) and 305 nm (ε=7,200). The same pyridones 8a and 8b were obtained from 2a and 2b respectively, on treatment with sodium ethoxide.

Table II. *IR and UV Spectra of the dihydropyridones*

dihydropyridones (R=H)	ν_{max} cm^{-1} (Nujol)	λ_{max} (ε) in EtOH	in EtOH-KOH
2a	1695, 1670, 1640	285(9,000)	328(9,060)
5a	1670, 1630	286(11,000)	323(10,000)
6	1695, 1675, 1645	285(10,300)	325(9,650)
7a	1695, 1670, 1640	282(9,900)	321(8,800)
9a	1700, 1680, 1640	287(9,400)	330(9,100)
10	1700, 1680, 1645	287(10,000)	330(8,300)
13a	1695, 1670, 1640	285(9,300)	325(9,700)
14	1700, 1620	284(10,400)	325(10,600)
dihydropyridones (R=Me)			
2b	1670, 1630	286(11,000)	unchanged
5b	1690, 1630	286(11,000)	"
7b	1700, 1670	284(9,400)	"
9b	1690, 1680, 1630	287(9,500)	"
13b	1710, 1680, 1620	286(10,500)	"

To the minor products in photocycloaddition of 1a to acyclic olefins, styrene and ethyl vinyl ether, dihydroazatropolone structures (11) and (12) have been tentatively suggested[5]. It was now revealed that their UV and IR spectra were characteristic of the dihydropyridones. Actually they had the compositions less than those for dihydroazatropolones by CO unit, and now are proved to be 13a and 14, respectively. 13a gave the N-methyl derivative (13b), m.p. 95-97°. Dehydrogenation of 13a and 14 with DDQ in refluxing benzene afforded the pyridones (15a) and (16): 15a, m.p. 219-221° (80% yield)[λ_{max} 280 (ε=9,000) and 328 nm (13,200)] and 16, m.p. 194-196° (∿30% yield)[λ_{max} 290 nm (16,000)], respectively. 15a was methylated with diazomethane to the mixture of N-methyl-(15b), m.p. 122-123° [IR: 1690 and 1647 cm^{-1} ; λ_{max} 284(14,000) and 324 nm (18,000)] and the O-methyl-derivative (17), m.p. 113-114° [IR: 1720 cm^{-1} ; λ_{max} 297 nm (ε=17,800)] in the ratio of 3:1.

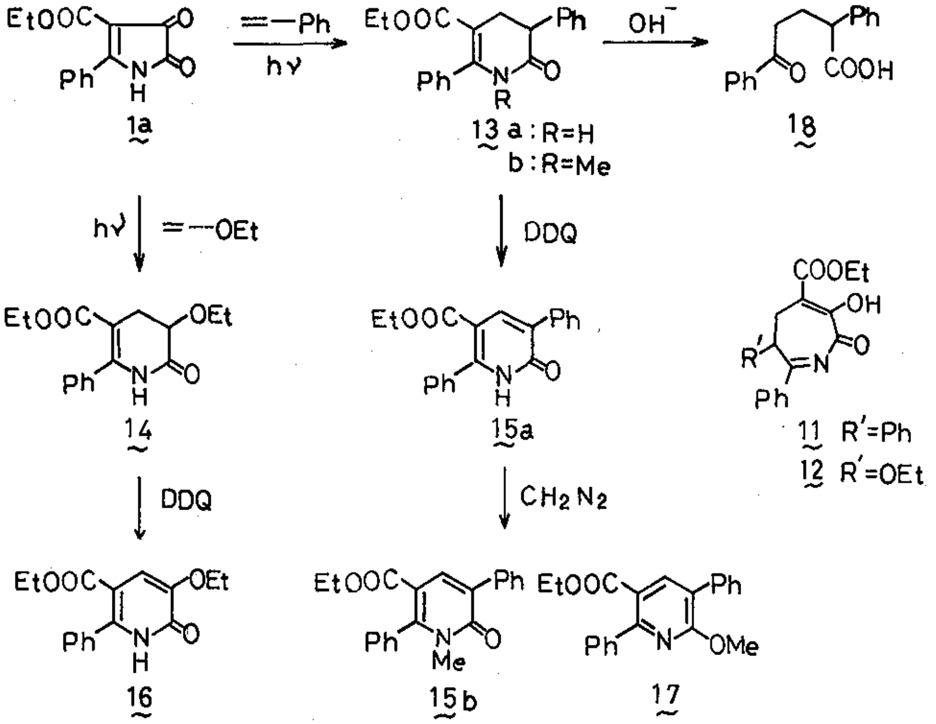
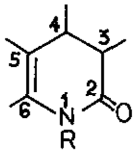
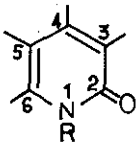
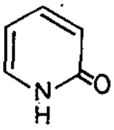


Table III.

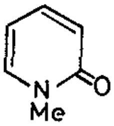
Assignment of ^{13}C-NMR shifts of dihydropyridones and pyridones (δppm in $CDCl_3$ from TMS)







19



20

Dihydropyridone	2	3	4	5	6
2a	166.6	48.0	37.3	107.9	142.9
2b	167.5	36.9	32.3	111.1	146.9
5a	167.2	43.0	40.0	108.6	143.7
6	167.0	80.6	48.2	109.3	142.8
7b	165.5	78.9	32.5	114.4	142.8
9a	167.0	48.4	39.7	107.8	144.2
9b	167.3	48.9	39.0	110.7	147.6
10	166.9	40.1	34.3	109.4	144.8
13a	166.6	45.9	30.0	105.5	145.9
14	166.6	73.2	29.4	104.2	145.3
Pyridones					
8a	166.2	131.5	148.5	109.9	156.2
19[7]	165.3	120.1	134.8	106.7	141.6
15a	166.2	128.4	139.7	109.9	150.7
15b	165.1	129.1	137.4	110.2	150.0
20[8]	161.8	119.1	139.5	104.8	139.5

Hydrolysis of 13a with methanolic sodium hydroxide yielded, accompanied by decarboxylation, a keto-acid (18)[6], m.p. 144-145°, [λ_{max} 240 nm (ε=11,600) and 278 nm (ε=760) for PhCO- ; δ2.88 (2H, t, J=7.2Hz), 2.40 (2H, m), and 3.78 ppm (1H, t, J=7.2 Hz) for $-CH_2-CH_2-CH$], thus establishing the structure.

The CMR spectra (Table III) of dihydropyridones and of pyridones also supported our structural assignments: for example, C-3 of 15 showed no ^{13}C-H coupling but C-4 appeared as a doublet in the off-resonance spectra.

The above results show that the reactions of cycloolefins, particularly cyclopentene derivatives, with the dioxopyrroline (1) yield dihydropyridones as major product (up to 40%), whereas acylic olefins gave dihydropyridones only in a minute amount. This difference should be attributable to stability of the intermediate cyclobutane derivatives[2]. However, there may be still another factor to be clarified, since the reaction of 1a with norbornadiene gave only a cyclobutane derivative, m.p. 205-208°, and reaction of cyclopentene with 1-methyldioxopyrroline derivative (1b) did not give any characterizable product.

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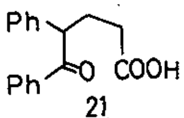
2. see Part VIII

3. Trimethylsilyloxy group had been hydrolysed concomitantly.

4. The pKa was determined by UV absorption in buffered solution.

5. T. Sano and Y. Tsuda, Heterocycles, 4, 1229 (1976).

6. The carboxylic acid (18) has been reported [E. C. Horning and A. F. Finelli, J. Amer. Chem. Soc., 71, 3204 (1949)]. However, our reexamination of his procedure (Friedel-Craft reaciton of α-phenylglutaric anhydride with benzene) revealed that the product was not the acid (18), but was the known isomeric acid (21). [E. Knoevenagel., Chem. Ber., 21, 1351 (1888)]



21

7. L. F. Johnson and W. C. Jankowski, Carbon-13 NMR Spectra. A Collection of Assigned, coded, and Indexed Spectra No. 107, 1972, A Wiley-Interscience Publication. In this reference the chemical shifts of C-3, -4, -5, and -6 were not rigidly established. We now assigned those as illustrated in the Table III.

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