Photochemical Cycloadditions to 5,6-Dihydro-4-pyridones**

Philippe Guerry and Reinhard Neier*

Abstract: 5,6-Dihydro-4-pyridones (**3a–3c**) undergo photochemical [2 + 2]-cycloaddition with olefins activated by an electron withdrawing group. Alkyl substituted double bonds could only be brought to react in the intramolecular cases **3d** and **3e**.

The [2 + 2]-cycloaddition has become a popular photochemical reaction for application in synthetic projects[1]. In contrast to the cyclopentenones and cyclohexenones the corresponding aza-substituted systems have been very scarcely investigated[2]. Most of the reports dealing with vinylogous amides have concentrated on the photochemistry of uracil, thymine[3], and derivatives of these bases[4]. There have been only a few reports dealing with the photochemistry of vinylogous amides as such[5].

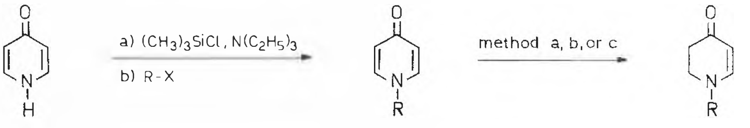
In general the influence of substituents on photochemical reactions is much less predictable than for thermally induced cycloadditions[6]. The lower homologues of the 5,6-dihydro-4-pyridones the 4-pyrrolin-3-ones have been studied[2]. No [2 + 2]-cycloaddition could be observed. In the presence of aliphatic ketones a photochemical aldol addition, probably induced by an electron transfer, occurred. The goal of our study was therefore to determine if 4-pyridones and the corresponding 5,6-dihydro-4-pyridones can be used for photochemical cycloaddition reactions. In agreement with earlier reports[7] neither 4-pyridone (**1**) nor the 1-alkyl-4-pyridones **2a–2c** could be brought to react with a number of different olefins under a variety of reaction conditions. Even for the intramolecular cases **2d**, **2e** no transformation could be observed.

In order to check whether the 5,6-dihydro-4-pyridones could be used more successfully for photochemical cycloaddition reactions, we needed a series of differently substituted *N*-alkyl-5,6-dihydro-4-pyridones **3a–3e**. The starting materials for these experiments were easily obtained from 4-pyridone (**1**) via the sequence: silylation, *N*-alkylation, and reduction[8,9] (Scheme 1). Three different reagents were used for the reduction of the aromatic precursors: a) Birch reduction[7,8], b) RED-Al[8], or c) triethoxy lithium aluminium hydride (TELAH)[9]. The reduction with TELAH had only been described on a small scale. The formation of the reagent was very slow when large quantities were used. Long reaction times (12 hours instead of 1 hour) or very efficient mixing (ultrasonic irradiation) was necessary to obtain a reagent, which could be used reproducibly for the reduction of the *N*-alkyl-4-pyridones.

On irradiation the cycloaddition of the *N*-alkyl-5,6-dihydro-4-pyridones with *Z*-substituted olefins[6] occurred readily to provide the bicyclic products **4**–**6** as mixtures of diastereomers in good yield (Scheme 2). In the case of a monosubstituted olefin like acrylonitrile mixtures of diastereomers and regioisomers were obtained. The separation of these mixtures was difficult. In some cases, e.g. **5**, one of the isomers was unstable during chromatography against retro-cycloaddition. Even if after irradiation the raw material contained no starting material (checked by ^{1}H-NMR and TLC) up to 30% dihydropyridone **3c** and dimethyl fumarate could be isolated after chromatography on silica gel *at room temperature*. The only isolation procedure which allowed to separate the mixtures without losing most of the material was flash chromatography[10] *at low temperature* (−20 °C).

For the cycloaddition of dimethyl maleate with **3a** three different diastereomers could be isolated. A tentative assignment of the relative configuration based on H-H couplings and ^{13}C shifts showed that in two of the products the ester groups were in *trans* positions to each other. This result shows that either during or before the photochemical cycloaddition an isomerization has to take place. Tetracyanoethylene was the only olefin studied, which reacted not in a [2 + 2]-manner but via an addition-elimination process (Scheme 3). The product of the reaction was coloured

Scheme 1



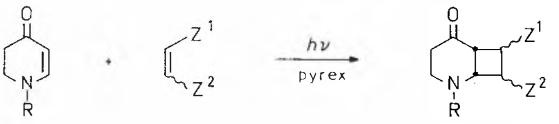
1

2

3

a: R = CH_3
b: R = $CH_2C_6H_5$
c: R = $CH(C_6H_5)_2$
d: R = $(CH_2)_2CH{=}CH_2$
e: R = $(CH_2)_3CH{=}CH_2$

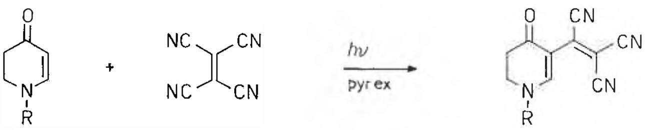
Scheme 2



3

4: R = CH_3 $Z^1, Z^2 = COOCH_3$
5: R = $CH_2C_6H_5$ $Z^1, Z^2 = COOCH_3$
6: R = $CH(C_6H_5)_2$ $Z^1, Z^2 = COOCH_3$

Scheme 3



3 b
3 c

7: R = $CH_2C_6H_5$
8: R = $CH(C_6H_5)_2$

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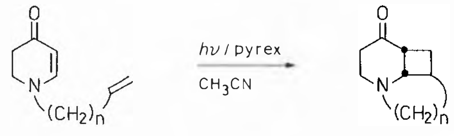
due to the extended chromophore (absorption maximum at λ = 422 nm).

The only cases where the photochemical cycloaddition could be observed with non-activated double bonds, were the intramolecular reactions of **3d** and **3e** (Scheme 4). In both cases good yields of tricyclic products could be isolated.

Scheme 4



3d : n = 2
3e : n = 3

9 : n = 2
10 : n = 3

Experimental:

^{13}C-NMR spectra: Bruker AM 360; if not mentioned $CDCl_3$ was used as solvent and TMS as standard. – MS: VG-7070 E. – The olefins were commercial products. The synthesis of the *N*-alkylated 4-pyridones **2a**–**2e** and of the 5,6-dihydro-4-pyridones has been described[8].

Typical Procedure for the Photochemical Cycloaddition of 5,6-Dihydro-4-pyridones with Olefins (reaction of **3a** with dimethyl maleate): 650 mg (5.8 mmol) **3a** and 1.00 g (6.9 mmol, 1.2 equiv.) of dimethyl maleate in 120 mL nitrogen-degazed acetone were irradiated for 3 h by filtering the light of a 125 W mercury lamp through a pyrex filter. The solvent was evaporated in vacuum. The residue was flash-chromatographed[10] at –20 °C with ethyl acetate (cf. Table 1).

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Table 1. Cycloadducts **4**–**10**.

Product[a])	Irradiation time [h] (solvent)	Yield [%] (solvent for chromatography)	*m.p.* [°C]	^{13}C-NMR[b]) δ	MS (70 eV) *m/z* (rel. int. %)
4	3 (acetone)	60 (ethyl acetate)			
4a		18	oil	207.3 (s, C(5)); 172.8, 170.4 (2s, 2 $COOCH_3$); 61.3 (d, C(1)); 52.3, 51.9 (2q, 2 H_3CO); 51.4 (t, C(3)); 44.9 (d, C(7) or C(8)); 44.5 (d, C(8) or C(7)); 43.2 (q, CH_3–N); 40.3 (d, C(6)); 39.1 (t, C(4))	255 (2), 111 (100)
4b		27	oil	208.2 (s, C(5)); 172.0, 171.3 (2s, 2 $COOCH_3$); 62.3 (d, C(1)); 52.2, 51.9 (2q, 2 H_3CO); 49.7 (t, C(3)); 45.4 (d, C(7) or C(8)); 42.5 (d, C(8) or C(7)); 41.2 (q, CH_3–N); 40.4 (t, C(4)); 40.1 (d, C(6))	255 (2), 113 (100)
4c		15	oil	270.1 (s, C(5)); 172.7, 171.3 (2s, 2 $COOCH_3$); 60.7 (d, C(1)); 52.2, 52.1 (2s, H_3CO); 47.8 (t, C(3)); 45.9 (d, C(7) or C(8)); 41.1 (q, CH_3–N); 40.9 (t, C(4)); 40.0 (d, C(7) or C(8)); 38.6 (d, C(6))	255 (3), 111 (100)
5[c])	4 (acetonitrile)	66 (ether: hexane: dichloromethane = 5:4:1)	oil		
5a		34	115–117 (dichloromethane/hexane)	207.4 (s, C(5)); 172.7, 170.3 (2s, 2 $COOCH_3$) 137.7 (s, C(1) arom); 128.4, 128.2 (2d, 4C arom); 127.1 (d, C(4)arom); 59.3 (d, C(1)); 58.8 (t, CH_2-Arom); 52.3, 52.0 (2q, 2 H_3CO); 46.8 (t, C(3)); 45.2, 44.9 (2d, C(7) and C(8)); 40.1 (d, C(6)); 39.3 (t, C(4))	331 (3), 113 (100)
6[c])	2 (acetone)	60 (ether: dichloromethane: hexane = 1:1:2)	oil		
6a		20	130–131 (ether/hexane)	207.8 (s, C(5)); 172.0, 171.0 (2s, 2 $COOCH_3$); 142.0, 140.6 (2s, 2 C(1) arom); 128.6, 128.5, 128.3, 127.6, 127.3 (6d, arom C); 70.4 (d, CH $(Arom)_2$); 56.7 (d, C(1)); 52.1, 51.9 (2q, 2 CH_3–O); 46.4 (d, C(7) or C(8)); 43.1 (t, C(3)); 41.2 (t, C(4)); 40.9 (d, C(6)); 38.4 (d, C(8) or C(7))	407 (11), 167 (100)
7[d])	2 (acetonitrile)	75 (ethyl acetate: hexane = 4:1)	175–176 (acetonitrile/chloroform)	185.0 (s, C(4)); 158.7 (d, C(2)); 133.8, 133.4 (2s, C(1) arom and $C(CN)_2$); 128.7, 128.3 (2d, arom C); 128.5 (d, C(4) arom); 114.5, 114.0, 113.6 (3s, 3 CN); 104.4 (s, C(3)); 75.8 (s, C(CN)); 60.8 (t, CH_2–Ph); 46.0 (t, C(6)); 34.3 (t, C(5))	
8[e])	2 (acetonitrile)	80 (ether: hexane: ethanol = 10:9:1)	195–196 (acetone/chloroform)	185.5 (s, C(4)); 157.3 (d, C(2)); 136.6 (s, 2 C(1) arom); 136.0 (s, $C(CN)_2$); 130.0, 129.6 (2d, arom. C); 129.7 (d, 2 C(4) arom); 114.6, 114.5, 113.9 (3s, 3 CN); 105.4 (s, C(3)); 79.9 (s, C(CN)); 74.7 (d, CH–Ph); 48.7 (t, C(6)); 35.6 (t, C(5))	364 (1), 167 (100)
9	1.5 (acetonitrile)	56 (dichloromethane: methanol = 19:1)	oil	216.6 (s, C(2)); 62.2 (d, C(9)); 48.4, 45.9 (2t, C(4) and C(6)); 41.8 (d, C(1)); 36.0 (d, C(8)); 32.3 (t, C(3)); 30.4 (t, C(10)); 26.9 (t, C(7))	151 (13), 82 (100)
10[f])	5 (acetonitrile)	48 (ether: hexane: dichloromethane = 6:3:1)	oil	58.7 (d, C(10)); 50.7, 48.8 (2t, C(4) and C(6)); 43.1 (d, C(1)); 39.1 (t, C(3)); 31.0 (t, C(11)); 22.8, 22.3 (2t, C(7) and C(8))	165 (25), 96 (100)

a) The cristalline products **5a**, **6a**, **7**, and **8** gave satisfactory elemental analysis (C ± 0.10, H ± 0.15, N ± 0.10).
b) The complex ^1H-NMR spectra have been interpreted but for the sake of clarity they have been omitted.
c) The oils **5** and **6** were mixtures of two diastereoisomers. In each case one of the isomers could be crystallized.
d) The ^{13}C-NMR spectrum has been measured in d_6-DMSO.
e) The ^{13}C-NMR spectrum has been measured in d_6-acetone.
f) The signals for C(2) and C(9) could not be unequivocally identified.