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PHOTOCYCLIZATION OF SUCCINIMIDE DERIVATIVES WITH AMIDO GROUP IN SIDE CHAINS. SYNTHESIS OF TRICYCLIC PYRROLO[1,2-a]PYRAZINE RING SYSTEMS.[1]

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Abstract ------ Succinimide derivatives (2) with amido group in their side chains were irradiated in acetonitrile to give bi- and tricyclic pyrrolo[1,2-a]pyrazines (3).

The photoreactions of cyclic imides have been extensively studied giving rise to a variety of new heterocycles.[2] As to synthesizing various multicyclic fused heterocycles with two nitrogen atoms, we have already reported the photolysis of N-substituted phthalimides such as N-(ω-methylanilino[3] and ω-amino[4])alkylphthalimides. Furthermore, efficiencies of these reactions were highly improved by incorporating an acyl group on the nitrogen atom in their N-alkyl side chains (1).[1b] As an extension of the application of these reactions to the alicyclic imide system, we now wish to report an easy synthesis of bi- and tricyclic aliphatic systems containing two nitrogen atoms.

Substrates 2 and 4 were prepared from succinimidoacetyl chloride and the corresponding amines, and succinimide and the corresponding ω-amidoalkyl acetate, respectively. Their photolysis was performed with a 60 or 120 W low-pressure mercury lamp in acetonitrile (10-24 mM) in an atmosphere of nitrogen and the products were purified by silica gel column chromatography. The results are summarized in Table 1.

The photolysis of 2 which lacks γ- and δ-hydrogens relative to the imide carbonyl[2] gave bi- and tricyclic pyrazine derivatives 3 in moderate yields. In all cases a new carbon-carbon bond was formed between the imide carbonyl and the carbon adjacent to nitrogen in the side chain by initial ε-hydrogen abstraction. These structures were assigned on the basis of the elemental analysis and spectral data. In the IR spectra of 3a-e the bands in the regions 3200-3500 and 1625-1700 cm^{-1} indicated the presence of the cyclol and lactam moieties, respectively. In the ^{1}H-NMR spectra of 3b-d, the methylene signal on the pyrazine ring showed two doublets at 3.46-3.72 and 3.97-4.95 ppm, which exhibit the large coupling constant (J=18-19 Hz) due to the geminal methylene protons. In the ^{13}C-NMR spectra of 3b-d, doublets in the off-resonance decoupled spectra appeared at 62.8-65.8 ppm, suggesting the presence of a tertiary carbon due to a new carbon-carbon bond formation. In the case of 2b-d two diastereoisomers (3-i and 3-ii) were isolated, though their stereochemistry is still unknown.

Upon the irradiation of 4a which also lacks γ-hydrogen, dipyrrolo[1,2-c : 2',1'-e]-imidazoline 5 was obtained in a moderate yield, a product of δ-hydrogen abstraction.[2] In the IR spectrum of 5 the bands at 3280, 1690, and 1660 cm^{-1} indicated the presence of the cyclol and lactam moieties, respectively. The photolysis of 4b-e having γ-hydrogens relative to the imide carbonyl gave mainly keto lactam 6 by a ring expansion reaction.[5]

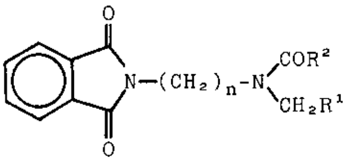
Interestingly, such γ-hydrogen abstraction was not observed with the phthalimide derivatives (1).[1b] In contrast with the photoreactions of the aromatic imides (phthalimides) 1 which are believed to proceed mainly by an electron transfer mechanism,[1b-4] it is worth noting that the reactions of their aliphatic counterparts (succinimides) 4 are initiated predominantly by typical γ-hydrogen abstraction, being parallel to the behavior of the common carbonyl.[6] Although further work is required for the determination of stereochemistry of the photoproducts, this method provides a simple route to the tricyclic nitrogen heterocycles, which will serve as a convenient source of synthetic intermediates for such alicyclic amine systems.

Table 1 Photoproducts from 2 and 4.

Substrate	mp °C	Time(h)	Product	mp °C	Yield(%)
2a	95.5 - 98	1.5	3a	110.5-112	60
2b	141 - 142	1.5	3b-i	135 - 138	11
			3b-ii	81 (dec.)	43
2c*	120 - 122.5	5	3c-i	143 (dec.)	13
			3c-ii	102.5-104.5	9
2d*	88.5 - 91	2	3d-i	160 - 163	29
			3d-ii	142 - 144	21
2e*	185.5-186.5	4	3e	200 (dec.)	26
4a**	138.5-140	1.5	5	131 - 133	51
4b	100 - 101.5	1.5	6b	154 - 156	41
4c	87 - 87.5	1.5	6c	115.5-117.5	31
			succinimide		16
4d*	oil	3.5	6d	115.5-117	23
			succinimide		18
4e	$bp_{0.6}$ 165	2	6e	78 - 81	25

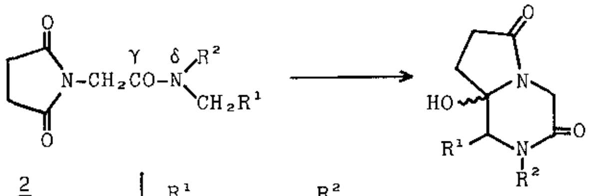
* A 120 W low-pressure mercury lamp was used.

** in methanol



1

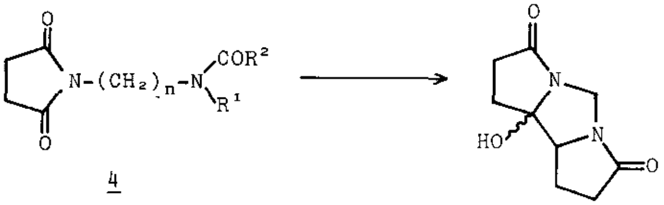
R^1=H, R^2=Me *or ring*



2

3

	R^1	R^2
a	H	CH_3
b	$-(CH_2)_3-$	
c	$-(CH_2)_4-$	
d	$-(CH_2)_5-$	
e	$-CH_2OCH_2CH_2-$	



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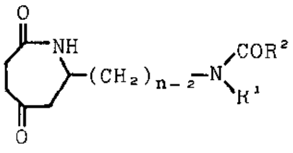

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	n	R^1	R^2
a	1	$-(CH_2)_3-$	
b	2	$-(CH_2)_3-$	
c	2	CH_3	CH_3
d	3	CH_3	CH_3
e	3	CH_3	OC_2H_5

5

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