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PHOTOCYCLIZATION OF N-CHLOROACETYLBENZYLAMINES TO ISOQUINOLINE DERIVATIVES

Masaki Ikeda, Ken-ichi Hirao, Yohmei Okuno and Osamu Yonemitsu
Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo, Japan

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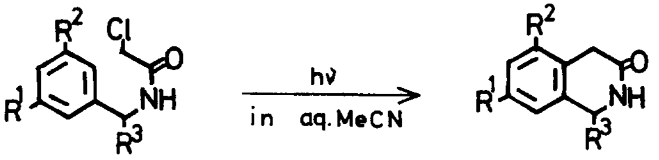
The Pomeranz-Fritsch method[1] is useful for the preparation of 7- and 5,7-substituted isoquinolines which are difficult to be synthesized by other isoquinoline syntheses. However, the reaction usually proceeds only in a strong acid, which sometimes causes side reactions.

Various novel heterocycles have been synthesized photochemically from N-chloroacetylphenethylamines.[2] Among these photoreactions, the most typical one is the formation of 1,2,4,5-tetrahydro-3H-3-benzazepin-2-ones and it is expected to be extended for the synthesis of isoquinoline derivatives.

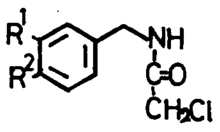
When N-chloroacetylbenzylamines (I) in aqueous ethanol or acetonitrile were irradiated, the corresponding N-acetyl or N-hydroxyacetyl derivatives were isolated without any detectable formation of cyclization products. However, m-hydroxy derivatives (II) gave easily 3-oxo-1,2,-3,4-tetrahydroisoquinolines (III) in fair yields.

A 50% aqueous acetonitrile solution of II (ca. 10 mM) was irradiated with a 100 W high pressure mercury lamp under nitrogen for 1-3 hr. Tetrahydroisoquinolines III, whose structures were easily confirmed by mass and nmr spectra, were isolated by recrystallization and by chromatography, if necessary. The results are shown in Table.



II R^1 = OH
R^2 = OH, H
R^3 = H, Me, CH_2Ar

III



Ia : R^1=OMe, R^2=H
Ib : R^1, R^2= OMe
Ic : R^1, R^2=OCH_2O

Table. Photocyclization of II to III.

II				III			Yield (%)	mp°C
	R^1	R^2	R^3		R^1	R^2		
IIa	OH	H	H	IIIa	OH	H	55	236-238
				IIIa'	H	OH	7	227-228
IIb	OH	OH	H	IIIb	OMe[a]	OMe[a]	45	191-194
IIc	OH	H	Me	IIIc	OH	H	74	228-230
				IIIc'	H	OH	13	218-220
IId	OH	H	$CH_2C_6H_5$	IIId	OH	H	69	200-201
				IIId'	H	OH	16	170-171
IIe	OH	OH	$CH_2C_6H_5$	IIIe	OH	OH	64	220-223
IIf	OH	H	CH_2Ar^1[b]	IIIf	OH	H	49	174-175
IIg	OH	H	CH_2Ar^2[c]	IIIg	OH	H	36	229-231
				IIIg'	H	OH	7	169-171
IIh	OH	OH	CH_2Ar^2[c]	IIIh	OH	OH	59	260-263

a; treated the reaction mixture with diazomethane.
b; Ar^1 = 4-methoxyphenyl. c; Ar^2 = 3,4,5-trimethoxyphenyl.

The common initial step of these photocyclizations has been proposed to be the ejection of an electron from the singlet excited state of the aromatic nucleus.[3] The clear difference in reactivity between I and II can be interpreted by the ease of the electron ejection from phenols and/or the reactivity of the resultant phenoxy radicals. Further synthetic application of this reaction is in progress.

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