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PHOTOCHEMICAL ADDITION OF ALCOHOLS, ESTERS, ETHERS, AND AMIDES TO THE AROMATIC N-HETEROCYCLES

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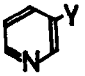
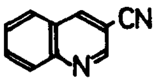
It has been shown recently that pyridine itself reacted with an alcohol photochemically only in an acidic medium to give alkylpyridines,1) whereas the carbinol function was introduced into 3,5-dialkoxycarbonylpyridines when these were irradiated in methanolic solution.2) We have found that only one of the electron-withdrawing groups such as cyano or alkoxycarbonyl function at the β-position of pyridine like Ia or Ib is sufficient to make the compound sensitive to the photochemical addition of methanol. Furthermore, we wish to report that other aromatic N-heterocycles, such as quinolines and isoquinolines having the equivalent type of structure (II, III), are susceptible to the same addition reaction of alcohols, esters, ethers, and amides. Hanovia 450-W high-pressure mercury arc lamp without a filter was used as the UV source throughout this study.

Photochemical Addition of Alcohols

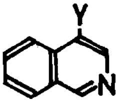
Irradiation of a methanol solution (0.2 mM) of nicotinonitrile (Ia) for 30 min resulted in the formation of a mixture of the corresponding dihydro derivatives possessing the carbinol function at 4 or 6 position in 48% yield (IVa:Va=1:1.6 3)), accompanied by the recovery of 11.5% of Ia. Va,4) mp 114-117°, was isolated from the mixture and its structure was confirmed by its conversion to the known nicotinate5) (VIb) by way of VIa. In the case of ethyl nicotinate (Ib), the carbinol function was introduced exclusively at 6-position, and the photo-product (Vb) was so unstable to furnish a mixture with VIb during work-up that it was characterized as VIb after dehydrogenation in 41% yield from Ib, besides 14% recovery of the starting material.



	Y
Ia	CN
Ib	COOEt

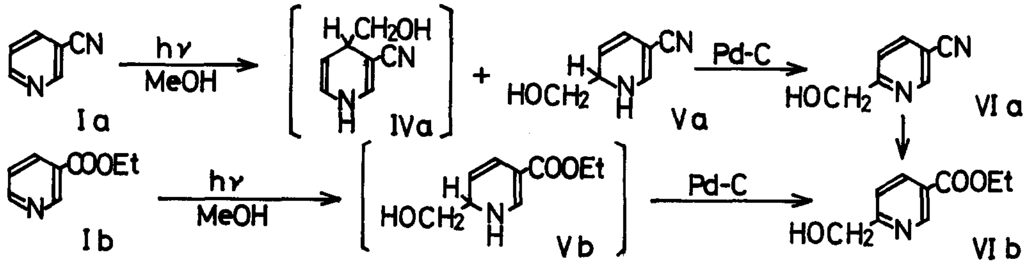


II

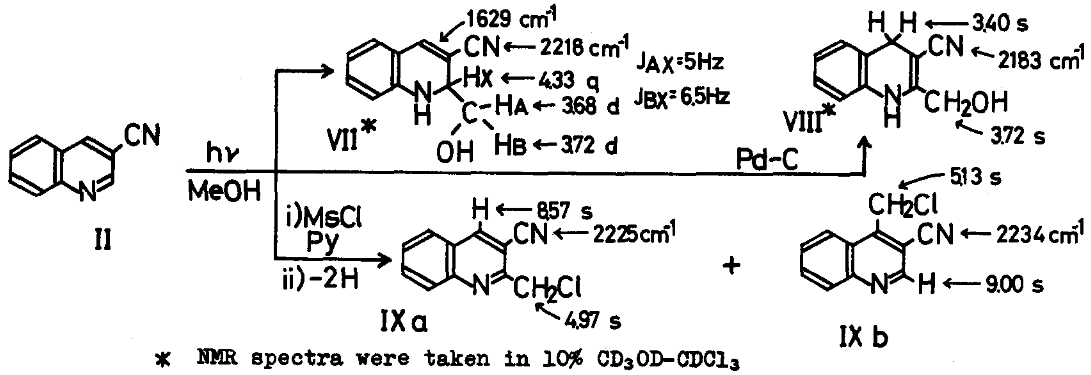


	Y
IIIa	CN
IIIb	COOMe

The photochemical reaction of methanol with 3-cyanoquinoline (II) was complex



at the dihydro stage, because the addition took place both at 2 and 4 positions and, moreover, the double bond between C-3 and -4 seemed to move partially to C-2. Thus, a product⁶⁾ (VII), mp 140-142°(decomp.), was isolated only in 16% yield, when the mixture of photo-products was directly separated by repeated preparative thin-layer chromatography, while another product (VIII), mp 148-149° (10% yield),

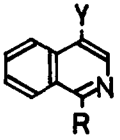


* NMR spectra were taken in 10% CD_3OD-$CDCl_3$

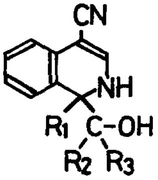
Table 1. Photochemical Addition of Alcohols to Isoquinoline Derivatives

Isoquinoline derivative	Alcohol	Product	mp (°C)	Yield (%)	Recovery (%)
IIIa	MeOH	XIa	139-141	69	0
IIIa	EtOH	XIb	solid**	36	0
IIIa	iso-PrOH	XIc	163-165	29	43
Xa	MeOH	XId	151-154	31	11
Xb	MeOH	XIe	176-178	20	39
IIIb	MeOH	Xc	syrup	27	—

** Mixture of two diastereomeric isomers

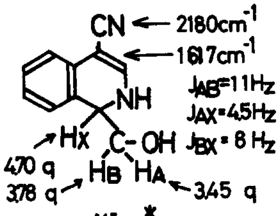


	R	Y
Xa	Me	CN
Xb	$CH_2C_6H_5$	CN
Xc	CH_2OAc	COOMe



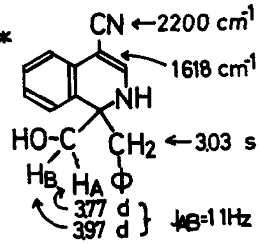
	R_1	R_2	R_3
XIa	H	H	H
XIb	H	H	Me
XIc	H	Me	Me
XId	Me	H	H
XIe	$CH_2C_6H_5$	H	H

was a single isolable compound by the reaction sequence similar to the case of Ib. A better result was obtained by a brief treatment of the photo-reaction mixture with methanesulfonyl chloride in pyridine at room temperature, followed by dehydrogenation with chloranil, and IXa, mp 168-168.5°, and IXb, mp 178-179°, were produced in 13% and 18% yield, respectively.



XI a*

XI e*



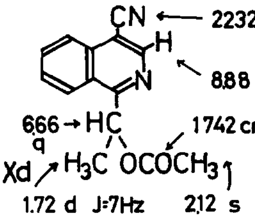
Facile reaction with various kinds of alcohols was achieved in the case of isoquinoline derivatives with an electron-withdrawing group at 4 position (IIIa, IIIb, Xa, and Xb) as summarized in Table 1, since the reaction site was limited to one position and, furthermore, the resulting dihydro derivatives (XIa-XIe) were fairly stable due to the partial structure of the vinylogous cyanamide as well as to the hydrogen bonding, except the compound derived from IIIb, whose structure was verified by its direct conversion to Xc. Physical constants of the typical dihydro products (XIa, XIe) are illustrated above.

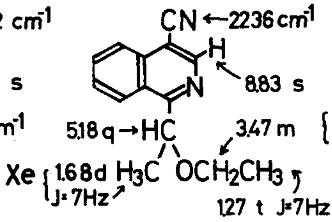
Photochemical Addition of the Ester, Ether, and Amide

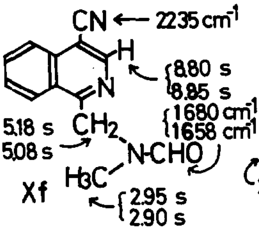
During the course of the experiment to find a suitable solvent for the photochemical reaction of general alcohols other than simple ones, we noted that ethyl acetate, diethyl ether, dimethylformamide, and N-methylpyrrolidone could be added photochemically to IIIa from the carbon atom adjacent to the heteroatom. Irradi-

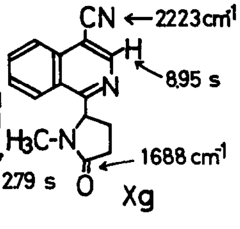
Table 2. Photochemical Addition of the Ester, Ether, and Amide to IIIa

Addition compound	Solvent	Irradiation time (min)	Product	mp (°C)	Yield (%)
EtOAc	—	30	Xd	114.5-115.5	9
EtOEt	—	30	Xe	62-63	48
DMF	—	50	Xf	178-178.5	15
N-Methyl-pyrrolidone	Acetone	80	Xg	207-208	12



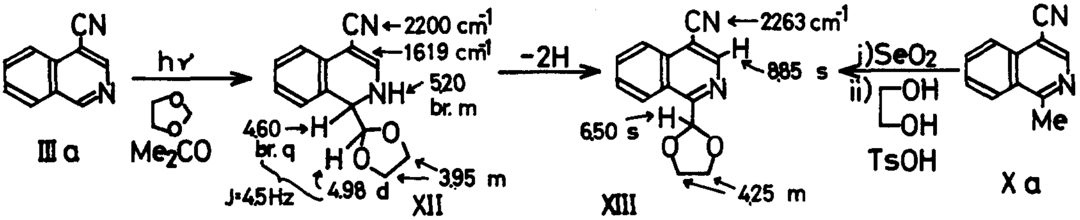






ation was made for the period cited in Table 2 and the resulting adducts of the dihydro form were dehydrogenated with chloranil to be characterized as Xd to Xg, whose structure was easily determined by the assignment of their NMR spectra. This kind of photochemical addition reaction of the ester, ether,[7) and amide seems to be uncommon, contrary to several precedences[8) for the addition of alcohols to the aromatic N-heterocycles, especially having many heteroatoms in rings.

In order to extend this knowledge to the direct functionalization of the group equivalent to an aldehyde, an acetone solution (0.11 mM) of IIIa was irradiated for 45 min in the presence of 1,3-dioxolane (43 molar equivalent with respect to IIIa), and the expected product (XII), mp 152-154°, was obtained in 27% yield. Dehydrogenation of XII produced the isoquinoline derivative (XIII), mp 139-141°, which was identical with the specimen synthesized from Xa by the known method.



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