HETEROCYCLES, Vol. 4, No. 3, 1976

PHOTOCHEMISTRY OF ISONICOTINOHYDRAZIDE AND ITS ANALOGS IN ALCOHOL[†]

Ichiya Ninomiya[*] and Okiko Yamamoto

Kobe Women's College of Pharmacy

Motoyamakita, Higashinada, Kobe, Japan

Irradiation of isonicotinohydrazide (Iγ) and its analogs (Iα and Iβ) in alcohols, i.e., methanol, ethanol, isopropyl alcohol, and benzyl alcohol afforded two types of photoproducts, that is, the alkylidenehydrazides (II, IV, VI) and the 2'-(2-hydroxyethyl)hydrazides (III, V, VII), except the cases of the hydrazides having ortho-amino and methoxyl groups which yielded the N-N bond fission products.

During the work on photochemistry of medicinals having a functional group[1,2], we found that isonicotinohydrazide (INAH) (Iγ) underwent facile and interesting reaction when irradiated in an alcohol. This paper deals with study on the general aspect of photochemical behaviour of the acid hydrazide in alcohol.

A 0.02 M methanolic solution of INAH (Iγ) was irradiated with

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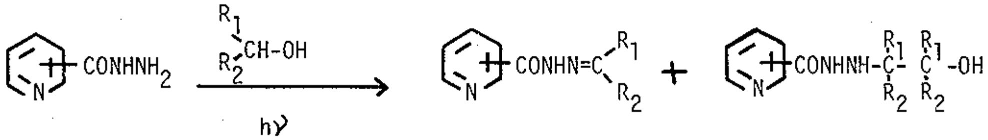
[†] Dedicated to Professor Tsunematsu Takemoto on the occasion of his retirement.

a 120 watt low pressure mercury lamp at room temperature until the t.l.c. showed no remaining starting compound (Iγ). The product was isolated in 38 % yield by chromatography and identified as the 2'-(2-hydroxyethyl)-INAH (VIIa). When the irradiation was carried out in ethanol, the products were the ethylidenehydrazide (VIb) and the 2'-(2-hydroxyethyl)hydrazide (VIIb), while only the former type of products (VIc and d) were obtained when irradiated in isopropyl alcohol or benzyl alcohol.

These photochemical transformations were also observed on the other analogs of INAH such as nicotinohydrazide (Iβ) and picolinohydrazide (Iα), as summarised in Table I.



Iα　II　III
β　IV　V
γ　VI　VII

Table I

	Alcohol		Photoproducts (Yield; %)					
			α -Series		β -Series		γ -Series	
	R_1	R_2	II	III	IV	V	VI	VII
a	H	H	—	35	—	30	—	38
b	Me	H	54	trace	trace	36	60	17
c	Me	Me	54	—	46	—	58	—
d	Ph	H	20	—	8	—	9	—

Then, irradiation of the alkylidenehydrazide (IV) in alcohol was carried out to see if the 2'-(2-hydroxyethyl)hydrazide (VIII) was formed by the reaction of (IV) with alcohol, since this type of photoaddition of alcohol to the imine has been little known.[3,4] As seen from the results shown in Table II, the alkylidenehydrazide (IV) would be the first product, which then undergo facile photoaddition of alcohol to give the corresponding 2'-(2-hydroxyethyl) derivative (VIII).

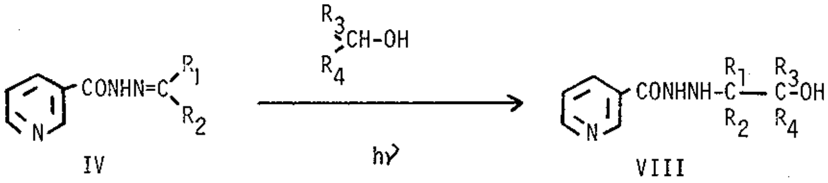


Table II

	Products (VIII) (Yield; %)		
	Starting Materials (IV)		
Alcohol	PyCONHN=CH-Me	PyCONHN=C—Me_2	PyCONHN=CH-Ph
MeOH	10	11	—
EtOH	25	19	21
i-PrOH	22	16	42

Neither the N-N bond fission product[5] nor the alkylation product on the pyridine ring[1,7,8] was obtained, thus showing much higher reactivity of the hydrazide group than the ring.

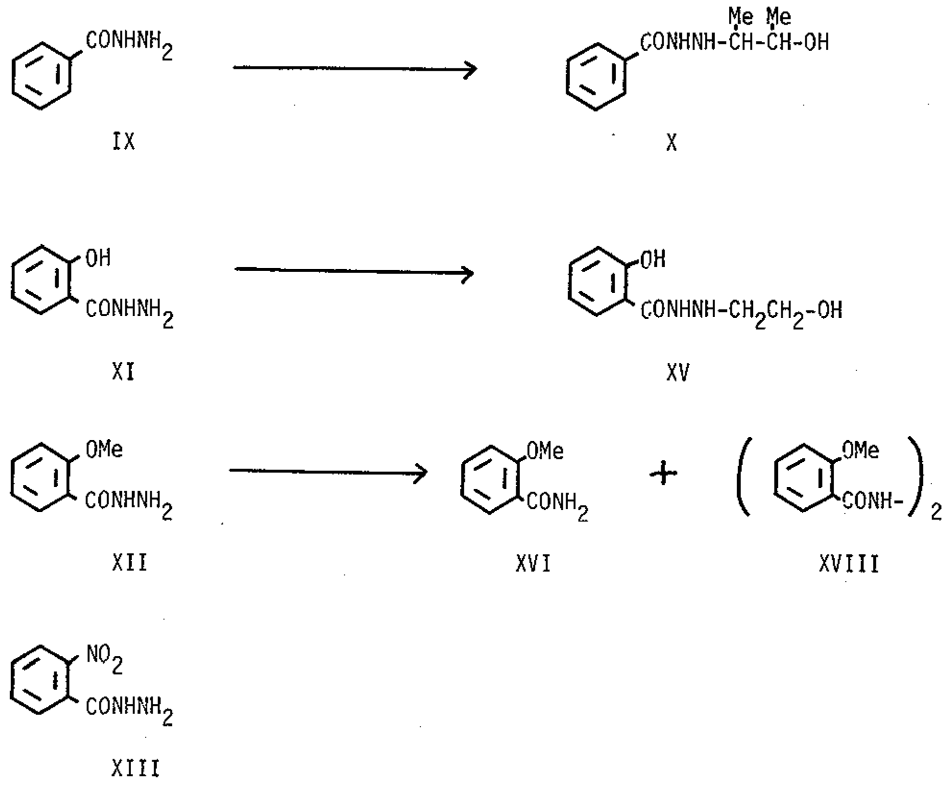
Since alcohol is known to be susceptible to photooxidation[9] upon irradiation to give the corresponding aldehyde or ketone, the formation of these two types of photoproducts was explained as follows; for example, in case of ethanol, acetaldehyde would be formed upon irradiation which readily condenses with an hydrazide to give the corresponding alkylidenehydrazide which would undergo facile photoaddition of alcohol to give the 2'-(2-hydroxyethyl)hydrazide as the final product.

In order to generalise this type of photochemistry, irradiation of benzohydrazide and acetohydrazide was carried out. Although acetohydrazide gave none of the expected product, benzohydrazide (IX), when irradiated in ethanol, afforded the 2'-(2-hydroxyethyl)-hydrazide (X) in 40 % yield, thus showing that this type of photoreaction is of general and applicable nature.

Next, in view of the interesting participation of the ortho-substituents in photochemistry[10,11] we investigated the reactions of some ortho-substituted benzohydrazides.

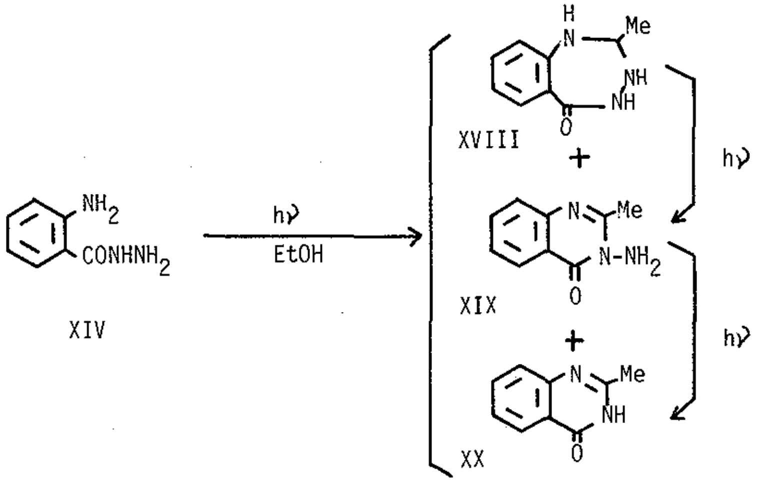
Irradiation of salicylohydrazide (XI) in methanol afforded the corresponding 2'-(2-hydroxyethyl)hydrazide (XV) in 25 % yield, while the o-anisohydrazide (XII) afforded two unprecedented products, the benzamide (XVI) and its dimeric product (XVII), which apparently were formed by radical fission of the N-N bond followed by coupling.

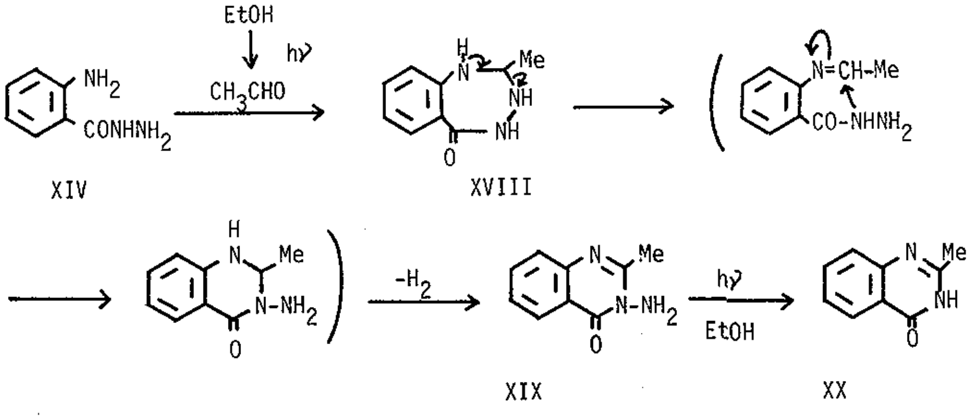
o-Nitrobenzohydrazide (XIII) was expected to have an interesting result from the known o-nitro group participation[10,11] but was found to be too unstable toward the reaction condition, resulting only decomposition of the starting hydrazide.



Finally, we investigated the reaction of anthranilohydrazide (XIV). Irradiation of (XIV) in ethanol afforded a mixture of three photoproducts, the benzotriazepine (XVIII), the aminoquinazolone (XIX), and the quinazolone (XX). The ratios of their formations, which were calculated from their g.l.c., varied by the reaction time. Furthermore, the benzotriazepine (XVIII) was photochemically transformed into the aminoquinazolone (XIX) and the quinazolone (XX), which was also obtained from the former

(XIX) upon irradiation. These facts clearly indicate the reaction course and suggest that acetaldehyde, which would be photochemically formed from ethanol, would condense with anthranilohydrazide (XIV) to afford the benzotriazepine (XVIII)[12], which would then undergo ring opening followed by recyclisation to afford the aminoquinazolone (XIX) and as reported[5], the homolytic cleavage of the N-N bond would then occur to form the quinazolone (XX) as the final product as shown below.





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The structures of the compounds described herein were confirmed either by direct comparisons with the authentic samples prepared or by the n.m.r. spectra.

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Received, 22nd December, 1975