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REACTION OF 6-METHYLBENZ[d]-1,3-OXAZEPINE-2-CARBONITRILE WITH AMINES*

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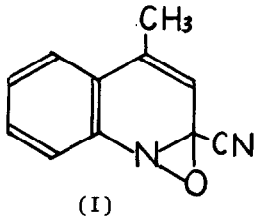
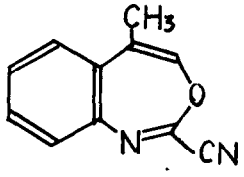
We reported the photochemical isomerization[2] of 2-cyanoquinoline 1-oxides to the corresponding photo-products, whose structure was presumed to have the oxaziridine structure (I) at the early stage of their syntheses. However, the subsequent experiments have demonstrated that these photo-products have a benz[d]-1,3-oxazepine structure[3] (II) and indicated that I-type structure should be given to the transient intermediates in these photochemical isomerizations.[1-4]

Both in connection with the novel photochemical reaction of 2-cyanoquinoline 1-oxides with amines as described in the precedent communication[1] as well as in continuation of the chemical reaction of these seven-membered oxazepine derivatives,[5] we have examined the action of amines on 6-methylbenz[d]-1,3-oxazepine-2-carbonitrile (II) and found a new synthetic route to 3-aminolepidines having $-NR_1R_2$ group in the 2-position of quinoline ring (III).

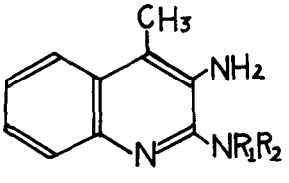


(I)

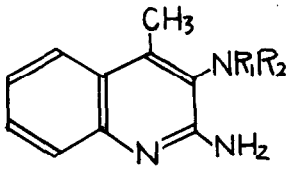
	R_1	R_2		R_1	R_2
a :	H	H	d :	H	CH_2CH_3
b :	H	CH_3	e :	CH_2CH_3	CH_2CH_3
c :	CH_3	CH_3			



(II)



(III)



(III')

* This paper is No. XII in the series entitled "Studies on the N-Oxides of π-Deficient N-Heteroaromatics." For preceding Part XI, cf. Ref. (1).

Thus, by the addition of an aqueous amine solution (R_1R_2NH) to the ether solution of this compound (II) at room temperature with stirring, corresponding 2,3-diaminolepidines (III) were formed in an yield ranging from 30 to 90%. The periodical injection of the ether layer to gas chromatograph revealed that the rate of the reaction is dependent on the kind of amines used and the decreasing order of reactivity to II was found to be secondary amine > primary amine > ammonia. Therefore, while both secondary and primary amines reacted with II in a few minutes, the formation of IIIa took several hrs. The results so far obtained are summarized in Table 1.

TABLE 1.[a,b,c]

Amount of II (g)	Aq. amine (ml)		Product m.p.	yield(g)	Derivative
1.0	28% NH_3	20	IIIa 207-210°(benzene)	0.4	picrate,256-260°
1.0	40% $MeNH_2$	20	IIIb 194-195°(ether)	0.7	
1.0	40% Me_2NH	20	IIIc 82-83° (hexane)	0.7	picrate,176-178°
1.0	40% $EtNH_2$	20	IIId 169-170°(hex.-ether)	0.4	
1.0	40% Et_2NH	20	IIIe oil	0.8	acetate, 97-98°

a. 50 ml. of ether was used as a solvent in each experiment.
b. The reaction was continued for 12 hrs. throughout.
c. Compound in parentheses indicates solvent used for recrystallization.

The U. V. spectra of these diaminolepidines (III) are essentially similar to that of 2-methylamino-3-aminoquinoline (IV), m.p. 140-141°, synthesized by the catalytic reduction of 3-nitro-2-methylaminoquinoline, m.p. 157-158°, resulting from the reaction of methylamine with 3-nitro-2-chloroquinoline[6] (Table 2).

TABLE 2.
Ultraviolet Absorption Spectra in 95% EtOH

Compound	λ_{max} (mμ)	log ε
IV	241, 337, 351	4.58, 4.01, 3.98
IIIa	239.5, 336, 346	4.69, 4.09, 4.09
IIIb	244, 337, 350	4.69, 4.09, 4.09
IIIc	221.5, 253, 348	4.60, 4.57, 4.07
IIId	244.5, 337, 350	4.71, 4.10, 4.09

Though the structure of IIIa was easily confirmed by its conversion to 10-methyl-1,4,9-triazaanthracene (V), m.p. 136°(decomp.), U.V. λ_{max}^{EtOH} mμ (logε): 225.5 (4.61), 258 (4.67), 358 (4.13), by the action of glyoxal, the structural elucidation of IIIb to IIIe was not so straightforward, because the similarity of their U.V. spectra with that of IV does not distinguish between two possible structures, III and III'. The NMR spectrum of IIIb was then measured to obtain a definite choice between these two structures (III and III') (Table 3).

TABLE 3[a]

Compound	aromatic-H	NH-CH_3	NH_2	$NHCH_3$	C_4-CH_3	C_4-H
IIIb	2.4-3.0, m	3.72,q J=4	5.19, s	7.03, d J=4	7.72, s	--
IIIb[b]	2.4-3.0, m	--	--	7.0, s	7.68, s	--
IV	2.4-3.0, m	3.65, q J=4	4.86, s	7.01, d J=4	--	3.07
IV[b]	2.4-3.0, m	--	--	6.98, s	--	3.0

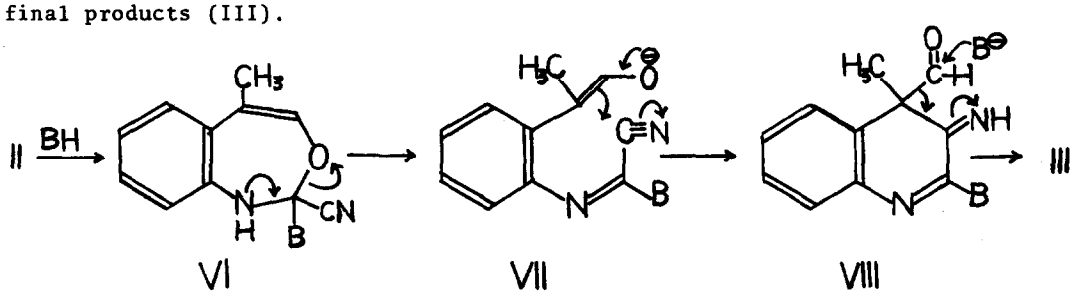
a 60 Mc/s in DMSO-d_6 with TMS as internal reference. Chemical shifts are in τ-units, coupling constants in cps; s = singlet, d = doublet, q = quartet, m = multiplet.

b The spectrum was obtained after addition of D_2O.

The proton signals of IIIb gave two separate signals at 3.72 τ(1H) and 5.19 τ(2H) due to the N-H functions. The appearence of 1H proton quartet at a far lower field than the other signal suggests strongly the correctness of IIIb as its possible structure. To verify this assumption, the spectrum of IV was measured under an identical condition. The spectrum as expected showed two sets of N-H signals at almost identical positions (3.65τ ;1H and 4.86τ ;2H) to those of IIIb. These experiments clearly indicate that a series of products (IIIb to IIId) are 3-aminolepidines having a substituent at their 2-position which originated from the added nucleophiles (amines).

The following mechanistic pathway, II → VI → VII → VIII → III, is tentatively suggested to account for the present reaction. Addition of amines (designated as BH) to II leads first to VI, which by the path indicated gives a ring-opened anion (VII). The recyclization of this species to VIII, followed by the loss of -CHO, as in the case of the well-known β-diketone cleavage, may then form the

final products (III).



It seems worthy to note the following observations, none of which is inconsistent with the above postulation: (i) The yield of III generally increases as the amines become more basic and aniline does not react with II at all. (ii) Tertiary amine (i.e., trimethylamine) does not react with II. (iii) Application of this reaction to benz[d]-1,3-oxazepine-2-carbonitrile[1,3] (the compound having hydrogen instead of CH_3 group in II) results in the formation of a resinous product, resisting to crystallize, and no 2,3-diaminoquinolines (IV, for example) are obtained. This may be due to the blocking of the final step (i.e., VIII →III) caused by the direct aromatization of the intermediates (H instead of CH_3 in formula VIII) to unstable 2,3-diaminoquinolines having an aldehyde group at 4-position. (iv) Use of CH_2Cl_2 instead of ether retards the reaction rate in all cases. Further, by adding 28%-ammonia solution to or by passing gaseous ammonia through the CH_2Cl_2 solution of II, no formation of IIIa is observed within 10 hrs. and the starting material is recovered.

The action of other nucleophiles (OR^-, SR^-, etc.) to II is now under investigation.

Satisfactory elemental analyses have been obtained for all the compounds described and spectroscopical properties were consistent with the postulated structures.

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