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ENAMINES. VII(1). THE REACTION OF ENAMINES WITH SCHIFF BASES. A POSSIBLE CYCLOADDITION PATHWAY.

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The reaction of cyclohexanone enamines with benzylidenaniline in acetic acid gave unexpected N-phenyldecahydroacridine derivatives. The formation of these compounds can be rationalized assuming the [2+2]cycloaddition between enamines and the Schiff base to form an azetidine at the initial stage.

In the previous communication(1), we reported that the reaction of 1-morpholino-1-cyclohexene(Ia) with benzylidenaniline(II) gave the Stork(i.e., Michael-type addition) product when methanol was used as the solvent. We report here an alternative product by the same reaction when acetic acid was used as the solvent, and propose a possible cycloaddition pathway for the product.

The reaction of 1-morpholino-4-R-cyclohexene(Ia,b) or 1-pyrrolidino-1-cyclohexene(Ic) with II in acetic acid gave decahydroacridine derivatives(IIIa,b) in 45-54% yields together with acetanilide. The assignment of the structure of III was mainly based on NMR spectra; the signal for two t-butyl groups in IIIb(R=t-Bu) appears at 9.10τ as a sharp singlet, suggesting their equivalence. The multiplet(22H) at ca. 3τ may be assigned to four phenyl groups and two strongly deshielded olefinic protons. Peaks at 7.2, 7.7, and 8.2τ are due to $-(CH_2)_3-$ protons in IIIa. The benzylic proton appears as a singlet at 6.25τ for IIIa and 6.33τ for IIIb. The conjugated diene structure was established by UV absorption spectra. III decolorized bromine solution, but could not be catalytically hydrogenated under usual conditions, indicating that the double bonds are sterically crowded and well-conjugated.

The data for the structural proof are summarized below.

IIIa: Mp 184-186°C.

Found: C, 90.93; H, 6.53; N, 2.51%.

Calcd for $C_{39}H_{35}N$: C, 90.48; H, 6.82; N, 2.71%.

IR(nujol): ν_{C-N} 1248cm^{-1}.

UV(methanol): λ_{max} 282mμ(ε 37,000).

NMR($CDCl_3$): 8~7τ(m, 12H, C-1,2,3,6,7,8 protons), 6.25τ(s, 1H, C-9 proton), ca. 3τ(m, 22H, two phenyl and two benzylidene protons).

Mass: 517(M^+), 440($M-C_6H_5$)$^+$, 374.5(metastable ion peak).

IIIb: Mp 211-213°C.

Found: C, 89.21; H, 8.68; N, 2.11%.

Calcd for $C_{47}H_{51}N$: C, 89.62; H, 8.61; N, 2.22%.

IR(nujol): ν_{C-N} 1250cm^{-1}.

UV(methanol): λ_{max} 283mμ.

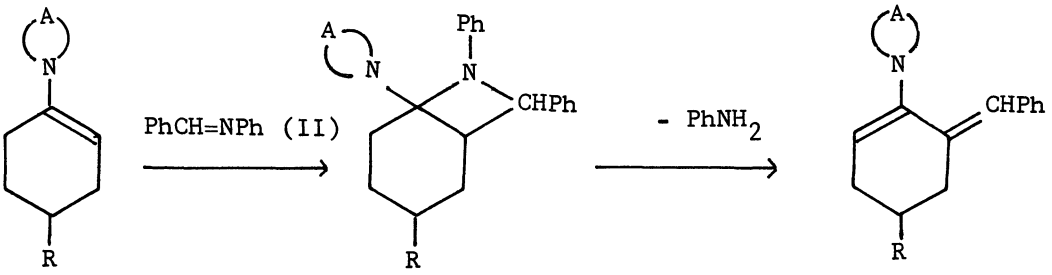
NMR($CDCl_3$): 9.10τ(s, 18H, two t-butyl groups), 8~7τ(m, 10H, C-1,2,3,6,7, 8 protons), 6.33τ(s, 1H, C-9 proton), ca. 3τ(m, 22H, two phenyl and two benzylidene protons).

Mass: 629(M^+), 552($M-C_6H_5$)$^+$, 485.5(metastable ion peak).

The most interesting feature of this reaction is that the aniline moiety came into the structure of the products(IIIa,b), which should involve exchange of morpholino or pyrrolidino group with anilino group. We tentatively assume that the key reaction is the cycloaddition of the C=N double bond of II to the C=C double bond of the enamine to form the azetidine ring. A possible pathway is summarized as shown in the next page.

This mechanism will lead to the formation of the necessary intermediate azetine or cyclohexylidenaniline(VIII). The N-phenyldecahydroacridine ring can then be formed by the reaction between VIII and VI followed by deamination.

The cycloaddition reaction to the C=N bond has recently been reviewed by Anselme(2). Most of the known reactions are [3 + 2] or [4 + 2], i.e., 1,3-dipolar or Diels-Alder additions. [2 + 2] cycloadducts are formed between Schiff bases and heterocumulenes with an electron-deficient double bond(3). An olefin with an electron-rich double bond reacts in a different manner. An enol ether, for instance, attacks II to give mainly noncyclic product together with a small amount

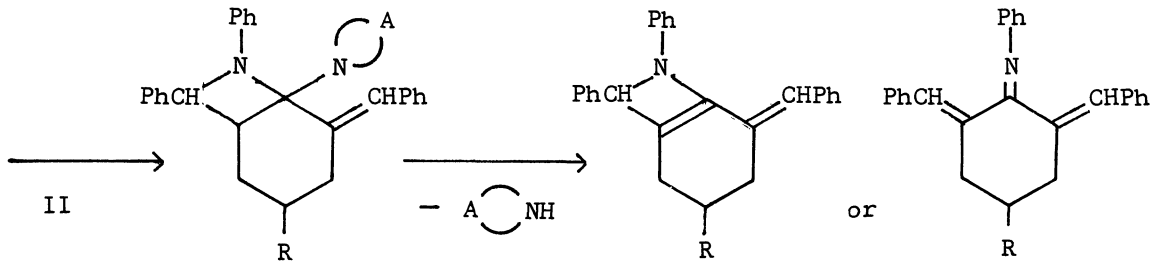


I a) A = $CH_2CH_2OCH_2CH_2$
R = H

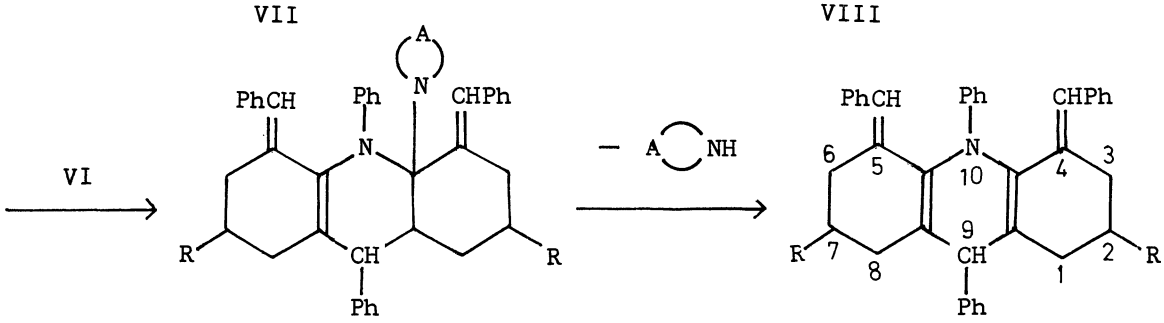
b) A = $CH_2CH_2OCH_2CH_2$
R = t-Bu

c) A = $CH_2CH_2CH_2CH_2$
R = H

V VI



VII VIII



III a) R = H
b) R = t-Bu

of quinoline derivative when the reaction was carried out in acetic acid-sodium acetate(4). When the reaction was carried out in tetrahydrofuran under the presence of catalytic amount of $HCo(CO)_4$ or $Co(CO)_8$, a quinoline was the main product(5).

Interestingly, the products resulting from the addition of ynamines to

imines explainable in terms of an initial cycloadduct, an azetine(6), and the addition of ketene diaminal to N-arylsulfonylbenzamidine gave the azetine(7). Although we failed to isolate any azetidine(V or VII) or azetine(VIII) intermediate, the proposed reaction path seems reasonable in the light of these examples. The reaction would then be the first example of [2 + 2] cycloaddition between a simple C=N and C=C bonds.

Finally a brief comment should be made as for the reason why the course of the reaction is so different in methanol(1) and in acetic acid. A possible explanation is the perturbation of the electron-distribution in II caused by the protonation at the nitrogen atom in the latter solvent. This might make the nitrogen atom more electron-deficient, hence, more favorable for the simultaneous attack of the nitrogen atom on C-1 of I and of the carbon atom of II on C-2 of I to yield the cycloadduct rather than Michael-type addition compounds. Further study is under progress.

REFERENCES

1) Part VI. S. Tomoda, Y. Takeuchi, and Y. Nomura, Tetrahedron Lett., 3549 (1969).

2) J.-P. Anselme, in "Chemistry of the Carbon-Nitrogen Double Bond", ed. by S. Patai, Interscience, New York, 1970, p.299.

3) a) R. Pfleger and A. Jäger, Chem. Ber., 90, 2460(1957).
b) S. A. Procter, P. D. English, and G. A. Taylor, Chem. Commun., 936(1969).
c) I. Ugi, Angew. Chem., 74, 9(1962); W. J. Hale and N. A. Lange, J. Amer. Chem. Soc., 41, 379(1919).

4) L. S. Povarov and B. M. Mikhailov, Izv. Acad. Nauk , SSSR, Ser., Khim., 1910 (1964); Chem. Abstr., 62, 2730g(1965).

5) Z. E. Samoilova, Yu.V. Zeifman, and R. G. Kostyanovskii, Izv. Acad. Nauk , SSSR, Ser., Khim., 2621(1968); Chem. Abstr., 70, 68298d(1969).

6) R. Fuks, R. Buijle, and H. G. Viehe, Angew. Chem.,78, 594(1966).

7) F. Effenberger and R. Maier, ibid., 78, 389(1966).

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