

FORMATION OF 3,10b-DIHYDROPYRROLO[2,1-a]ISOQUINOLINES AS A KEY COMPOUND
FOR 1,3-DIPOLAR CYCLOADDITION OF SOME ISOQUINOLINIUM YLIDES

Yoshiro Kobayashi, Teruo Kutsuma, and Yasuo Sekine
Tokyo College of Pharmacy, Shinjuku-ku, Tokyo 160, Japan

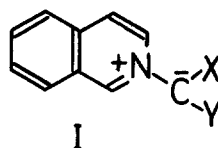
(Received in Japan 16 June 1972; received in UK for publication 7 July 1972)

Aromatic amine N-ylides undergo 1,3-dipolar cycloaddition reaction with various acetylenic compounds and produce indolizines¹⁾ and conjugated dihydroindolizines²⁾, but isolation of any unconjugated dihydroindolizines, considered to be the key compounds for their formation, has not been reported as yet. Basketter³⁾ reported the generation of 2,3-dihydropyrrolo[2,1-a]isoquinolines (V) and pyrrolo[2,1-a]isoquinolines (VI) through a possible intermediate (III) on the reaction of isoquinolinium ylides (I) with acetylenic ester, and they assumed that V could be a precursor of VI since the former isolated was eventually converted to the latter. This proposal does not agree with our present observations and some new facts we found are described below.

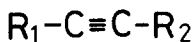
On the reactions of various isoquinolinium ylides (Ia-c) with acetylenic esters (II: $R_1 = R_2 = \text{CO}_2\text{CH}_3$ and $R_1 = \text{CO}_2\text{CH}_3$, $R_2 = \text{H}$), we succeeded in obtaining the key compounds, 3,10b-dihydropyrrolo[2,1-a]isoquinolines (IIIa-c) which are considered to be the intermediates in this reaction. The structures of IIIa-c were determined from their elemental analyses and spectral data. In UV spectra, IIIa showed an absorption [$\lambda_{\text{max}}^{\text{EtOH}}$ 311 nm (ϵ : 9.50×10^3)], IIIb [$\lambda_{\text{max}}^{\text{EtOH}}$ 300 nm (ϵ : 9.10×10^3)], and IIIc [$\lambda_{\text{max}}^{\text{CH}_3\text{CN}}$ 316 nm (ϵ : 7.86×10^3)]. The NMR spectra of IIIa-c exhibited a singlet signal of H^{10b} at ca. δ 5.85 ppm.

When dry HCl gas is passed through a benzene solution of IIIa and IIIb, and the solution is neutralized with K_2CO_3 , the compounds (V, $X = Y = \text{CO}_2\text{CH}_3$, $R_1 = R_2 = \text{CO}_2\text{CH}_3$, and $X = \text{CO}_2\text{CH}_3$, $Y = \text{CN}$, $R_1 = R_2 = \text{CO}_2\text{CH}_3$) are respectively obtained. IIIb undergoes decomposition at 120° and gives pyrroloisoquinoline

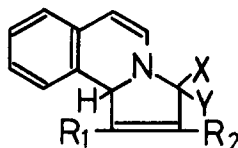
- (Ia) X=Y=CO₂CH₃ (Ii) X=Y=CN
 (Ib) X=CO₂CH₃, Y=CN (Ij) X=CO₂CH₃, Y=CN
 (Ic) X=Y=CO₂CH₃ (Ik) X=H, Y=CO₂CH₃
 (Id) X=Y=CN (Il) X=H, Y=CN
 (Ie) X=H, Y=CO₂CH₃ (Im) X=H, Y=COC₆H₅
 (If) X=H, Y=CN (In) X=H, Y=CO₂CH₃
 (Ig) X=H, Y=COC₆H₅ (Io) X=H, Y=CN
 (Ih) X=Y=CO₂CH₃



+



II



III

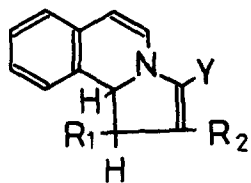
- (IIIa) X=Y=CO₂CH₃, R₁=R₂=CO₂CH₃
 (IIIb) X=CO₂CH₃, Y=CN, R₁=R₂=CO₂CH₃
 (IIIc) X=Y=CO₂CH₃, R₁=CO₂CH₃, R₂=H

iso

iso

internal

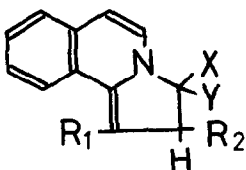
merization



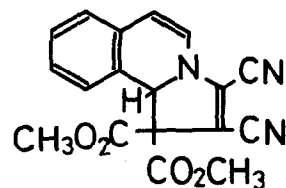
IV

(IVe) $Y=CO_2CH_3$, $R_1=R_2=CO_2CH_3$ (IVf) $Y=CN$, $R_1=R_2=CO_2CH_3$ (IVg) $Y=COC_6H_5$, $R_1=R_2=CO_2CH_3$ (IVl) $Y=CN$, $R_1=R_2=CN$

merization



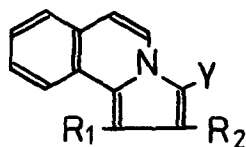
V



VIIh

(Va) $X=Y=CO_2CH_3$, $R_1=R_2=CO_2CH_3$ (Vb) $X=CO_2CH_3$, $Y=CN$, $R_1=R_2=CO_2CH_3$ (Vd) $X=Y=CN$, $R_1=R_2=CO_2CH_3$ (Vh) $X=Y=CO_2CH_3$, $R_1=R_2=CN$ (Vj) $X=H$, $Y=CN$, $R_1=R_2=CN$ $(X=CO_2CH_3, Y=CN, R_1=R_2=CN)$

cis-elimination



VI

(VIa) $Y=CO_2CH_3$, $R_1=R_2=CO_2CH_3$ (VIc) $Y=CO_2CH_3$, $R_1=CO_2CH_3$, $R_2=H$ (VI d) $Y=CN$, $R_1=R_2=CO_2CH_3$ (VIe) $Y=CO_2CH_3$, $R_1=R_2=CO_2CH_3$ (VIf) $Y=CN$, $R_1=R_2=CO_2CH_3$ (VIg) $Y=COC_6H_5$, $R_1=R_2=CO_2CH_3$ (VIh) $Y=CO_2CH_3$, $R_1=R_2=CN$ (VII) $Y=CN$, $R_1=R_2=CN$ (VIj) $Y=CO_2CH_3$, $R_1=R_2=CN$ $Y=CN$, $R_1=R_2=CN$ (VIk) $Y=CO_2CH_3$, $R_1=R_2=CN$ (VII) $Y=CN$, $R_1=R_2=CN$ (VI m) $Y=COC_6H_5$, $R_1=R_2=CN$ (VI n) $Y=CO_2CH_3$, $R_1=CO_2CH_3$, $R_2=H$ (VI o) $Y=CN$, $R_1=CO_2CH_3$, $R_2=H$

(VI_d), 2,3-dihydropyrroloisoquinoline (V_b), and methyl formate. III_c is easily converted to VI_c in the presence of Al₂O₃ or SiO₂. On the other hand, derivation of V_{d,h,j} so obtained to VI_{d,h,j} requires severer conditions than in the above case. These facts revealed that VI is formed directly from III by internal cis-elimination rather than via V, and that V is an independent product formed by isomerization of III. In some reactions of I with acetylenic compounds, III seemed to undergo isomerization in a different way from that to V, giving 1,10b-dihydropyrrolo[2,1-a]isoquinoline (IV). The structures of IV_{e-g} were determined from their elemental analyses and spectral data. In UV spectra, $\lambda_{\max}^{\text{EtOH}}$ nm ($\epsilon \times 10^4$): IV_e showed absorptions at 392 (1.50), 315 (0.47), 253 (1.08); IV_f at 407 (0.70), 320 (0.33), 309 (0.46), 276 (0.66), 272 (0.71); IV_g at 363 (1.87), 296 (0.79), 256 (2.70). In NMR spectra, IV_{e-g} exhibited a doublet signal of H^{10b} ($J_{1,10b} = 13.4$ Hz) at ca. δ 4.53 ppm and a doublet signal of H^{10b} at ca. δ 5.37 ppm. In the reaction of I_h with dicyanoacetylene, a rearrangement-addition product (VII_h) was formed besides V_h and VI_h. The structure of VII_h was determined from its elemental analyses and from its UV absorption [$\lambda_{\max}^{\text{CH}_3\text{CN}}$ 416 nm (1.02)], a signal for H^{10b} in its NMR spectrum (CDCl₃) at δ 7.25 ppm, IR absorption (KBr) at 2213 ($\nu_{\text{C}\equiv\text{N}}$) and 1745 ($\nu_{\text{C}=\text{O}}$) cm⁻¹, and mass spectral peak at 335 (M⁺). In the reaction of I_j and dicyanoacetylene, V_j (X = CO₂CH₃) was not obtained besides VI_j, and a compound V_j (X = H) formed by elimination of methyl formate was produced. The structure of V_j was determined from the fact that its mass spectrum showed M⁺ 244, and because V_j changed into VI_j (Y = CN, R₁ = R₂ = CN) and a dicyano compound on SiO₂. Reactivity of these products will be reported elsewhere.

References

- 1) Y.Kobayashi, T.Kutsuma, and K.Morinaga, Chem. Pharm. Bull., 19, 2106 (1971); T. Sasaki, K.Kanamatsu, Y.Yutimoto, and S.Ochiai, J. Org. Chem., 36, 813 (1971); T.Sasaki, K.Kanamatsu, and Y.Yutimoto, J. Chem. Soc. (C), 481 (1970); C.A.Henrick, E.Ritchie, and W.C.Taylor, Aust. J. Chem., 20, 2467 (1967).
- 2) D.G.Farnum, R.J.Alaimo, and J.M.Dunston, J. Org. Chem., 32, 1130 (1967); I. Zugrănescu, E.Rucinschi, and G.Surpateanu, Tetrahedron Letters, 941 (1970).
- 3) N.Basketter and A.O.Plunkett, Chem. Commun., 1578 (1971).