

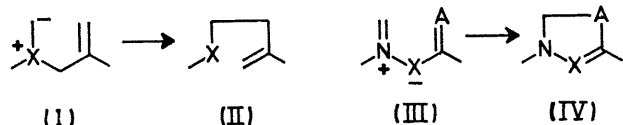
Novel Synthesis of Pyrazolo[1,5-*a*]pyridines via Ylide Intermediates

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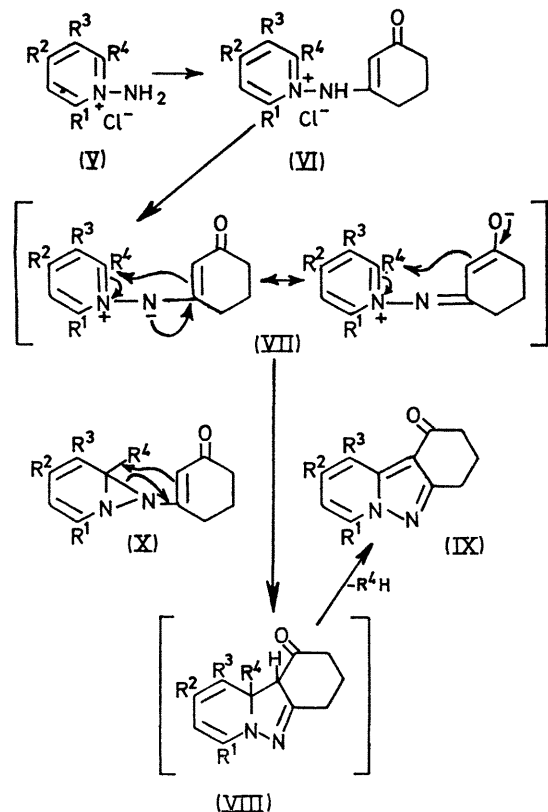
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Summary The thermal reaction of the pyridinium ylides (VII) results in cyclization followed by dehydrogenation to pyrazolo[1,5-*a*]pyridines (IX).

THE thermal rearrangements (type I → II) of sulphur, nitrogen, and phosphorus ylides have been recognized as a very general reaction type.¹ We report here an electrocyclic reaction of the pyridinium *N*-ylides (VIIa—e) which appears to be one example of another generalized reaction of azomethine ylides (type III → IV). This reaction is a convenient method for preparing pyrazolo[1,5-*a*]pyridine derivatives.



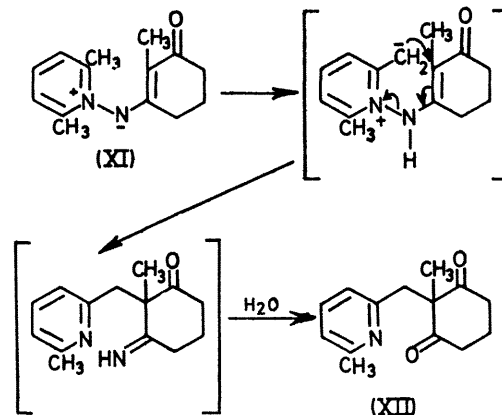
(X = S, N, P)



SCHEME 1.

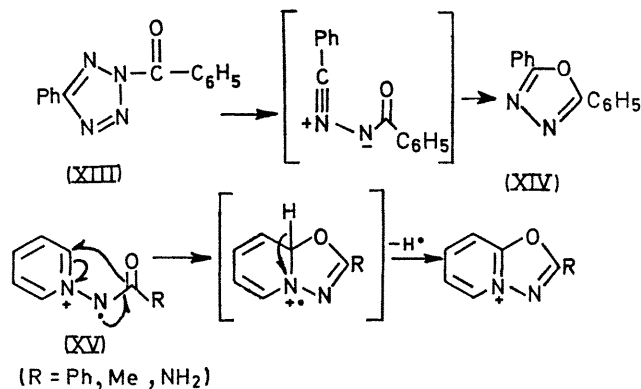
Ylide	Product	Overall yield (%)	M.p.
(VII)a; R ¹ , R ² , R ³ , R ⁴ =H	(IXa)	14	113–114°
b; R ² , R ³ , R ⁴ =H; R ¹ =Me	(IXb)	5	100–101°
c; R ¹ , R ³ , R ⁴ =H; R ² =Me	(IXc)	56	107–108°
d; R ¹ , R ² , R ⁴ =H; R ³ =Me	(IXd)	18	95–96°
e; R ² , R ³ =H; R ¹ , R ⁴ =Me	(IXb)	28	100–101°

Treatment of *N*-amino-4-methylpyridinium chloride^{2,3} (Vc) with an excess of 1-oxocyclohexen-2-yl chloride at room temperature gave quantitatively *N*-(1-oxocyclohexen-2-yl)amino-4-methylpyridinium chloride (VIc) as a hygroscopic crystalline solid. The pyridinium salt (VIc) was transformed with Amberlite IRA-410 ion-exchange resin in ethanol to hygroscopic orange needles of the ylide (VIIc) [ν_{\max} (KBr) 1505 cm⁻¹; τ (in CDCl₃) 1.74 (2H, d, *J* 7 Hz), 2.37 (2H, d, *J* 7 Hz), 5.91 (1H, s), 7.40 (3H, s), and 7.40–8.30 (6H, m)]. When the ylide (VIIc) was heated under reflux for 1 h in toluene, 2-methyl-10-oxo-7,8,9,10-tetrahydropyrido[1,2-*b*]indazole (IXc) was obtained in 56% overall yield from (Vc). The structure is evident from its elemental analysis and spectral properties⁴ [M^+ 200; λ_{\max} (EtOH) nm (log ϵ) 222sh (4.42), 228 (4.58), 252 (3.79), 260 (3.84), 305sh (4.05), 317 (4.16), and 328sh (4.06); ν_{\max} (CHCl₃) 1660, and 1630 cm⁻¹; τ (in CCl₄) 1.75 (1H, d, *J* 7 Hz), 2.10 (1H, m), 3.30 (1H, dd, *J* 2 and 7 Hz), 6.90–8.00 (6H, m), and 7.52 (3H, s)].



SCHEME 2.

Similar conversion of the ylides (VIIa,b,d) into the corresponding cyclized products (IXa,b,d) was accomplished in yields listed in the Table. In the case of (VIId) only the product of ring closure involving the more hindered side was obtained.⁵



SCHEME 3.

This thermal transformation could well be represented as a sigmatropic reaction (VII \rightarrow VIII), although an alternative pathway (VII \rightarrow X \rightarrow VIII) involving the intermediate (X) cannot be excluded.

Attempts to obtain the possible intermediate (VIII) were unsuccessful. Thus, when the ylide (VIIe) was subjected to cyclization in refluxing toluene for 7 h, (IXb) was isolated in 28% yield. On the other hand, the ylide (XI) prepared from (Ve)³ and 2-methyl-1-oxocyclohexen-2-yl chloride gave a Sommelet-type rearrangement product (XII), m.p. 141—142°, under the same conditions. The structure was established by its elemental analysis and spectral data [M^+ 231; λ_{\max} (EtOH) nm (log ϵ) 260.5sh (3.17), 267 (3.19), and

273sh (3.17); ν_{\max} (CHCl₃) 1720 and 1680 cm⁻¹; τ (in CDCl₃) 2.66 (1H, t, J 6 Hz), 3.14 (1H, d, J 6 Hz), 3.23 (1H, d, J 6 Hz), 6.46 (2H, s), 7.15—7.40 (4H, m), 7.63 (3H, s), 8.66 (3H, s), 7.8—8.1 (1H, bm), and 8.4 (1H, m)].

Other known 1,5-cyclization reactions of the ylides [type III(X=N, A=O) \rightarrow IV] include the thermal transformation⁷ of 2-benzoyl-5-phenyltetrazole (XIII) into 1,3,4-oxadiazole (XIV), and cyclization of the radical cations (XV), generated mass spectrometrically,⁸ which lose one hydrogen atom.

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¹ J. E. Baldwin and M. C. H. Armstrong, *Chem. Comm.*, 1970, 631, and the references cited therein.

² Y. Tamura and N. Tsujimoto, *Chem. and Ind.*, 1970, 926.

³ R. Gösl and A. M. Meuwesen, *Org. Synth.*, 1963, 43, 1.

⁴ C. f. K. T. Potts, U. P. Singh, and J. Bhattacharyya, *J. Org. Chem.*, 1968, 33, 3766.

⁵ T. Sasaki, K. Kanematsu, A. Kakehi, I. Ichikawa, and K. Hayakawa, *J. Org. Chem.*, 1970, 35, 426.

⁶ W. Schneider, *Ber.*, 1928, 61, 2445; 1941, 74, 1252.

⁷ R. Huisgen, J. Sauer, H. J. Sturm, and J. H. Markgraf, *Chem. Ber.*, 1960, 93, 2106.

⁸ M. Ikeda, N. Tsujimoto, and Y. Tamura, *Org. Mass Spectrometry*, in the press.