

A New Synthesis of Indolizines and Related Nitrogen-bridgehead Compounds

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WE have recently recorded successful indolizine reaction¹ and by a cyclisation of 2-(2-oxoethyl)-syntheses by an extension of the Tschitschibabin pyridines.² Such methods involve closure of the

¹ D. R. Bragg and D. G. Wibberley, *J. Chem. Soc.*, 1963, 3277.

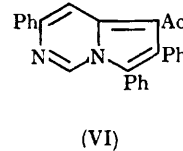
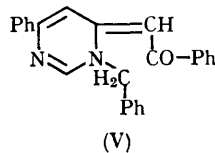
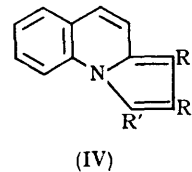
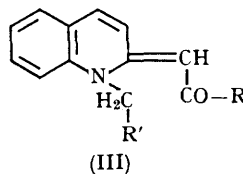
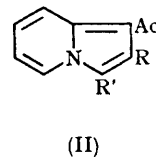
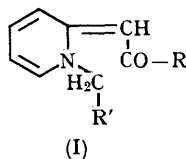
² J. Hurst, T. Melton, and D. G. Wibberley, *J. Chem. Soc.*, 1965, forthcoming.

indolizine ring in its 1-2 and 3-4 positions, respectively. We now report the success of a new route which involves closure at the 2-3 position by an intramolecular aldol-type condensation. Thus 2-benzoylmethylene-1-benzyl-1,2-dihydropyridine (I; $R=R'=Ph$), which was readily prepared in one stage by the dehydrobromination and benzoylation of 1-benzyl-2-methylpyridinium bromide, gave an excellent yield of 1-acetyl-2,3-diphenylindolizine (II; $R=R'=Ph$) on treatment with boiling acetic anhydride. The method was also successful for the preparation of various 2- and 3-substituted alkyl- or aryl-indolizines and for the preparation of 2-acetoxy-1-acetyl-3-phenylindolizine (II; $R=OAc$, $R'=Ph$) from 1-benzyl-2-ethoxycarbonylmethylene-1,2-dihydropyridine (I; $R=OEt$, $R'=Ph$). In certain cases, however, where, either the *N*-methylene group, or the side-chain carbonyl group were not appreciably activated, transacylation occurred with subsequent formation of 2-methylindolizines.

We have previously reported² that we were unable to cyclise 2-ethoxycarbonylmethylene-1,2-dihydro-1-phenacylquinoline (III; $R=OEt$, $R'=Ph-CO$). With acetic anhydride, however, a pyrrolo[1,2-*a*]quinoline (IV; $R=Me$, $R'=PhCO$, $R''=CO_2Et$) was one of two products isolated. In a similar manner 2-benzoylmethylene-1-benzyl-1,2-dihydroquinoline (III; $R=R'=Ph$) yielded 3-acetyl-1,2-diphenylpyrrolo[1,2-*a*]quinoline (IV; $R=R'=Ph$, $R''=Ac$).

Only two pyrrolo[1,2-*c*]pyrimidines have been described.³ By the above method 4-benzoylmethylene-3-benzyl-3,4-dihydro-6-phenylpyrimidine (V) yields the pyrrolopyridine (VI).

Satisfactory analyses have been obtained for all the nitrogen-bridgehead compounds described and their infrared spectra are consistent with the structures postulated. The u.v. spectra of the three systems were all closely similar, showing bands in the regions 225-240, 270-310, and 330-360 $m\mu$, previously quoted by Armarego⁴ for indolizines.



(Received, March 29th, 1965.)

² Ochiai and Yanai, *J. Pharm. Soc. Japan*, 1939, **59**, 18; V. Boekelheide and S. S. Kertelj, *J. Org. Chem.*, 1963, **28**, 3212.

⁴ W. L. F. Armarego, *J. Chem. Soc.*, 1964, 4226.