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LETTERS TO THE EDITOR

HETARENES WITH A BRIDGE NITROGEN ATOM. 5.* SYNTHESIS OF THE INDOLIZINE RING BY TRANSFORMATION OF THE OXAZOLO[3,2-*a*]PYRIDINIUM CATION WHEN TREATED WITH ACETYLACETONE

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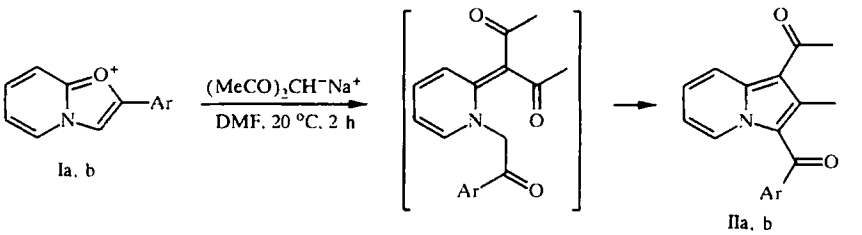
Standard synthesis schemes for the indolizine ring are generally strategies for joining the pyrrole (pyridine) fragment to an existing monocycle [2]. Syntheses of indolizines by transformation of other binuclear heterocycles by means of transformation of other binuclear heterocycles are quite rare, and are represented only by isomerization of pyrrolo[1,2-*a*]pyrazinium salts to 6(8)-aminoindolizines [3] and our own recently observed recyclization of oxazolopyridinium cations I when treated with nitromethane [4]. In the latter reaction, the one-carbon binucleophilic nitromethane fragment formally replaces the oxygen heteroatom in the oxazole fragment of cation I. In the literature, another possibility is described for transformation of an annelated oxazole fragment to pyrrole in the example of recyclization of oxazolo[3,2-*b*]pyridazinium cations to pyrrolo[1,2-*b*]pyridazines when treated with β-dicarbonyl compounds and derivatives of β-ketoacids [5]. In this case, the two-carbon fragment of the CH-acid participates in building up the pyrrole fragment of the bicycle. However, such a strategy has not yet been used in synthesis of indolizines, for which oxazolopyridinium cations I obviously could act as precursors.

We have found that 2-phenyloxazolo[3,2-*a*]pyridinium perchlorate (Ia) in reaction with the sodium salt of acetylacetone undergoes recyclization in 55% yield, with formation of 1-acetyl-2-methyl-3-benzoylindolizine (IIa).



Ia, b IIa, b

The reaction easily occurs over the course of 2 h at 20°C in DMF solution. The reaction mixture (1 mmole perchlorate Ia, 1.2 mmoles sodium salt of acetylacetone in 10 ml DMF) was treated with water and extracted with chloroform; the organic layer was held over silica gel for 12 h and chromatographed on a column (SiO_2, $CHCl_3$). We obtained 1-acetyl-2-methyl-3-benzoylindolizine (IIa) in 55% yield, T_{mp} 100-104°C. Found, %: C 77.12; H 5.69; N 4.53. $C_{18}H_{15}NO_2$. Calculated, %: C 77.96; H 5.45; N 5.05. PMR spectrum (200 MHz, $CDCl_3$): 9.41 (1H, d, J_{56} = 7 Hz, 5-H); 8.45 (1H, d, J_{78} = 9 Hz, 8-H); 7.72-7.50 (5H, m, C_6H_6); 7.39 (1H, dd, J_{67} = 7 Hz, J_{78} = 9 Hz, 7-H); 6.97 (1H, t, J_{56} = J_{67} = 7 Hz, 6-H); 2.60 (3H, s, 1-$COCH_3$); 2.23 ppm (3H, s, 2-CH_3). IR spectrum (Vaseline oil): 1612, 1642, cm^{-1}.

The structure of the indolizine obtained follows unambiguously from its PMR spectrum. The presence of downfield shifts for the signals from both 5-H and 88-H protons is characteristic for 1- and 3-acyl-substituted indolizines [6], due to the

*For Communication 4 see [1].

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familiar *peri* effect in 1- and 3-substituted indolizines [7]; assignment of the other signals both in the aromatic and aliphatic regions is definite. A possible reaction scheme probably includes initial nucleophilic attack by the carbanion with rupture of the CO bond adjacent to the bridge carbon atom. In the monocyclic intermediate formed, the acetyl group acts as the carbonyl component in the reaction of cyclocondensation with the phenacyl residue at the nitrogen atom.

The proposed novel (recyclization) scheme for building the indolizine skeleton thus represents formal formation of $C_{(2)}-C_{(3)}$ and $C_{(9)}-C_{(1)}$ bonds in the pyrrole fragment. When using the more electrophilic 2-(*p*-nitrophenyl)oxazolopyridinium Ib, the reaction yield decreases. Thus 1-acetyl-2-methyl-3-(*p*-nitrobenzoyl)indolizine (IIb) is obtained similarly from perchlorate Ia in 15% yield (T_{mp} 107-109°C; the material is difficult to purify). Mass spectrum: 322 (M+), 307, 292, 279 (M^+ − COMe), 261, 204, 157. PMR spectrum ($CDCl_3$): 9.62 (1H, d, J_{56} = 7 Hz, 5-H); 7.9-8.4 (5H, m, 8-H, C_6H_4); 7.47 (1H, m, 7-H); 7.06 (1H, t, J_{56} = 7 Hz, 6-H); 2.60 (3H, s, 1-$COCH_3$); 2.20 ppm (3H, s, 2-CH_3). IR spectrum (Vaseline oil): 1595, 1615, 615 cm^{-1}.

We have not yet been able to extend the proposed scheme by using other CH acids. In reactions of malonodinitrile and cyanoacetic ester with cations I in DMF, quite unstable products are formed, while replacing the solvent with alcohols leads to domination of side reactions of opening of the pyridine fragment.

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