

Synthesis of 1-nitro-2-phenylindolizine by the ring transformation of oxazolo[3,2-*a*]pyridinium salt in the reaction with nitromethane

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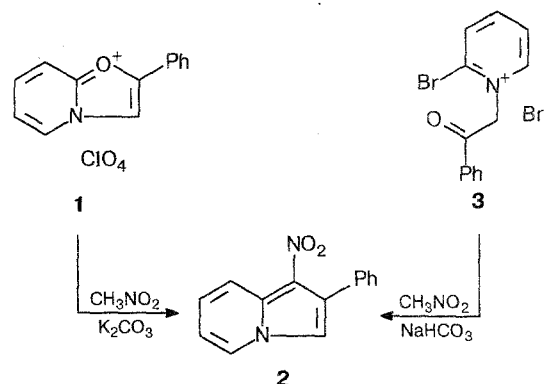
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1-Nitroindolizines are used for preparing potentially biologically active aminoderivatives.^{1,2} There are two synthetic approaches known for obtaining the starting 1-nitroindolizines, *i.e.*, nitration of indolizines in sulfuric acid³ or cyclocondensation of 2-(nitromethyl)pyridine with α -halogenketones². The first route, however, can not use 2-phenylindolizine (and 2-arylindolizines with donor groups) because of the competing nitration in the benzene ring. A weak point of the second route is the explosiveness of 2-(nitromethyl)pyridine.

For the synthesis of 1-nitroindolizines we used the insertion of a carbon atom from nitromethane, which served as a binucleophilic agent that closes a nitropyrrolic fragment, in the reactions with the appropriate bielectrophiles. This synthetic approach is widely used for preparing nitroazines or nitroarenes and rather uncommon for obtaining five-membered nitroheterocycles.^{4,5} Suitable starting compounds for the reaction with nitromethane, which leads to 1-nitroindolizines, can be either derivatives of 1-(β -oxoalkyl)-2-halopyridinium salts, which are widely used as precursors of bridgehead azolopyridines,⁶ or heterocyclic synthons, *e.g.*, the derivatives of oxazolo[3,2-*a*]pyridinium, which are known to give ANRORC-reactions under treatment with some heteroatomic nucleophiles.^{6,7}

We have found that on nitromethane action under mild conditions in the presence of potassium carbonate the cation of 2-phenyloxazolo[3,2-*a*]pyridinium (**1**) undergoes the recyclization of its oxazolic fragment into pyrrolic one to give 1-nitro-2-phenylindolizine (**2**). This product can be prepared also by an unambiguous synthesis during cyclocondensation of nitromethane with the *N*-phenacyl-2-bromopyridinium bromide salt (**3**). Characteristics of the nitroindolizine (**2**) obtained correspond to those known from the literature,² and the ¹H NMR spectrum has the expected downfield shift of the H-8 resonance, which caused by the influence of a 'peri'-positioned magneto-anisotropic nitro group.

The reaction of the perchlorate **1** (0.2 g, 6.8 mmol) with excess nitromethane (5 ml) was carried out in the presence of potassium carbonate (0.14 g, 1 mmol). The reaction mixture was heated at 100°C for 1 h, then silica gel was added (2 g), the mixture was stirred for 30 min, solvent was evaporated, and the dry residue was kept for 12 h. The product was eluted with chloroform to yield 0.12 g (74 %) of 1-nitro-2-phenylindolizine **2**, m.p.



156–157 °C (lit.: m.p. 151–156 °C).² ¹H NMR spectrum (CDCl₃, δ , ppm): 6.94 (t, 1 H, H-6), 7.19 (s, 1 H, H-3), 7.40 (m, 4 H, Ph, H-7), 7.52 (m, 2 H, Ph), 8.06 (d, 1 H, H-8), 8.47 (d, 1 H, H-5), $J_{5,6} = 9.0$ Hz, $J_{6,7} = 6.7$ Hz, $J_{7,8} = 6.3$ Hz.

The reaction of bromide **3** (0.35 g, 1 mmol) with nitromethane (7 ml) was carried out in the presence of sodium bicarbonate (0.2 g, 2.5 mmol). The reaction mixture was heated at 100°C for 4 h, solid residue was filtered off, and the filtrate was evaporated and chromatographed on a column with Al₂O₃ (chloroform) to yield 0.066 g (29%) of nitroindolizine **2**, the characteristics of which (m.p., ¹H NMR and IR spectra) were identical to those of the product prepared in the above experiment.

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