Chemistry of Heterocyclic Compounds, Vol. 39, No. 11, 2003

LETTERS TO THE EDITOR

SYNTHESIS OF 3-PHOSPHORYLATED INDOLES FROM α-CHLORO ALDEHYDES

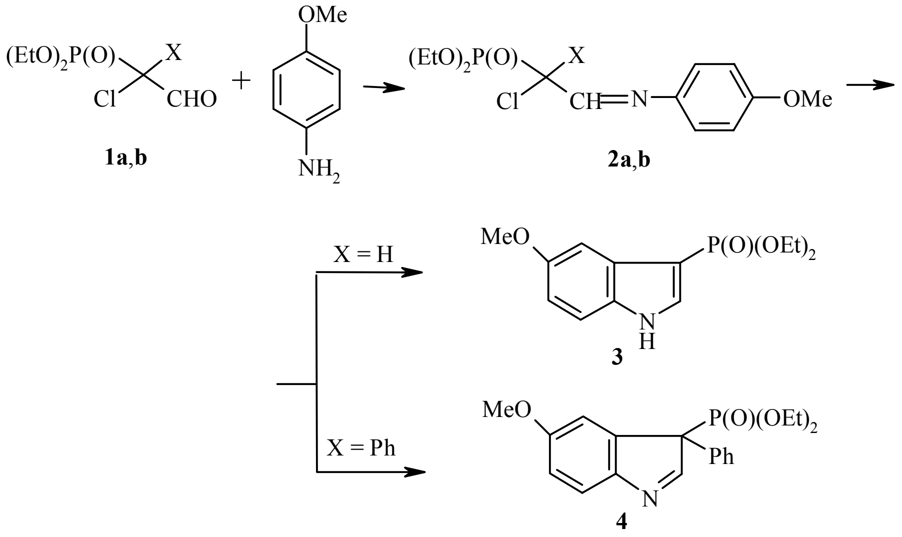
Kh. A. Asadov, P. A. Gurevich, E. A. Egorova, R. N. Burangulova, and F. N. Guseinov

Keywords: azomethine, *p*-anisidine, α-haloacetaldehyde, indolenine, 3-phosphorylated indoles.

Methods for obtaining various derivatives of indole with phosphorus-containing substituents have been generalized in the review [1]. 2- and 3-substituted indoles can be synthesized by condensation of α-halo ketones with aromatic amines, followed by cyclization when treated with acids (the Bischler–Möhlau reaction) [2].

It was reported earlier that phosphorylated α-haloacetaldehydes are convenient synthons for obtaining various heterocyclic compounds [3-5].

We have shown that reacting phosphorylated α-chloro aldehydes **1a,b** with *p*-anisidine under Bischler–Möhlau reaction conditions makes it possible to obtain 3-phosphorylated indoles **3** or indolenines **4**, depending on the nature of the substituent on the α-carbon atom.



1, **2** **a** X = H, **b** X = Ph

In the first reaction step, azomethines **2a,b** are formed, which (without separation as the individual compounds) undergo ring closure to form the corresponding heterocycles **3** and **4** when heated in boiling toluene with addition of catalytic amounts of aluminum chloride.

Kazan State Engineering University, Kazan 420015, Russia; e-mail: Petr_Gurevich@mail.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1727-1728, November, 2003. Original article submitted May 29, 2003.

0009-3122/03/3911-1521$25.00©2003 Plenum Publishing Corporation

In the case of aldehyde **1a**, azomethine **2a** formed is readily converted to indole **3**. The presence of a more sterically hindered substituent on the α-carbon atom in azomethine **2b** makes necessary harsher reaction conditions for its cyclization to indolenine **4** (conducting the reaction at 144°C for 12 h in boiling xylene).

The structure of the synthesized compounds was confirmed by the data of elemental analysis, IR, ^{1}H NMR, and ^{31}P NMR spectroscopy.

O,O-Diethoxy(5-methoxyindol-3-yl)phosphonate (3). Mixture of aldehyde **1a** (4.29 g, 20 mmol) and *p*-anisidine (2.46 g, 20 mmol) was boiled for 6 h in acetonitrile (30 ml). The solvent was evaporated down, and toluene (20 ml) and a catalytic amount of $AlCl_3$ were added to the oil formed; then this mixture was boiled for 4 h. Toluene was removed under vacuum, and the residue was washed with water and extracted with chloroform. After removal of chloroform, compound **3** was obtained as an oil. Yield 3.7 g (65%). IR spectrum, ν, cm^{-1}: 1285 (P=O), 3200 (NH). ^{31}P NMR spectrum, δ, ppm: 18.47. ^{1}H NMR spectrum (100 MHz, $(CD_3)_2CO$, HMDS), δ, ppm (*J*, Hz): 1.00 (6H, t, 2 CH_3); 2.6 (3H, s, OCH_3); 4.00 (4H, m, 2 OCH_2); 7.1 (1H, d, 6-H); 7.3 (1H, s, 4-H); 7.5 (1H, d, 7-H); 7.8 (1H, d, $^3J_{PH}$ = 12.5, =CH); 11.0 (1H, br. s, NH). Found, %: N 4.82; P 10.87. $C_{13}H_{18}NO_4P$. Calculated, %: N 4.95; P 10.85.

O,O-Diethoxy-3-phenyl(5-methyoxyindolenin-3-yl)phosphonate (4) was obtained similarly from aldehyde **1b** (5.81 g, 20 mmol) and *p*-anisidine (2.46 g, 20 mmol) by boiling azomethine **2b** in *p*-xylene in the presence of catalytic amounts of aluminum chloride for 12 h. Yield 4.66 g (65%); mp 133°C (supercooling from alcoholic solution in water (pH ~ 5)). IR spectrum, ν, cm^{-1}: 1280 (P=O), 1630 (C=N). ^{31}P NMR spectrum, δ, ppm: 21.63. ^{1}H NMR spectrum (10 MHz, $(CD_3)_2CO$, HMDS), δ, ppm (*J*, Hz): 1.10 (6H, br. t, 2CH_3); 2.45 (3H, s, OCH_3); 4.00 (4H, m, 2OCH_2); 7.1-7.6 (8H, m, Ph, 4-, 6-, 7-H); 7.9 (1H, d, $^3J_{PH}$ = 12.5, =CH). Found, %: N 3.77; P 8.56. $C_{19}H_{22}NO_4P$. Calculated, %: N 3.90; P 8.64.

REFERENCES

1. P. A. Gurevich and V. A. Yaroshevskaya, *Khim. Geterotsikl. Soedin.*, 1587 (2000).
2. K. V. Vatsuro, G. L. Mishchenko, *Name Reactions in Organic Chemistry* [in Russian], Khimiya, Moscow (1976), p. 58.
3. F. I. Guseinov, Kh. A. Asadov, and R. N. Burangulova, *First All-Russian Conference on Heterocyclic Chemistry in Memory of A. N. Kost* [in Russian], Suzdal' (2000), p. 449.
4. F. I. Guseinov, Kh. A. Asadov, R. N. Burangulova, and V. V. Burangulova, *Khim. Geterotsikl. Khim.*, 1139 (2001).
5. F. I. Guseinov, Kh. A. Asadov, R. N. Burangulova, and V. V. Burangulova, *Khim. Geterotsikl. Khim.*, 1140 (2001).