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LETTERS TO THE EDITOR

2,3,6-TRIPHENYLPYRIDINE. A NOVEL BY-PRODUCT IN THE SYNTHESIS OF 2,3-DIPHENYL-1-VINYLPYRROLE FROM BENZYL PHENYL KETOXIME AND ACETYLENE IN THE SYSTEM KOH–DMSO

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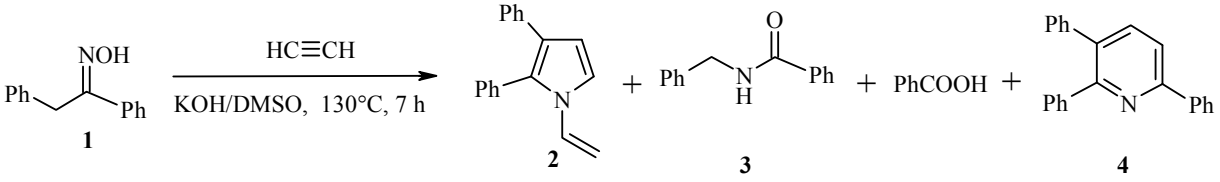
A one pot synthesis of pyrroles and N-vinylpyrroles from ketones and acetylenes (*via* the ketoximes) in a KOH–DMSO superbase system (the Trofimov reaction [1-3]) is used ever more widely thanks to its simplicity and the availability of the starting materials. Depending on the conditions and the structures of the starting compounds, in certain cases there are formed other reaction products along with the pyrroles. These are sometimes formed in acceptable preparative yields (e.g. pyridylpyrroles [4] and carbolines [5]) but most often as minor admixtures [6-10]. The separation and identification of these side products helps a better understanding of the mechanism of the main reaction and, for each individual case, a more targeted optimization of its conditions.

In the preparation of 2,3-diphenyl-1-vinylpyrrole (**2**) from benzyl phenyl ketoxime (**1**) and acetylene in the system KOH–DMSO at atmospheric pressure we have identified the target product **2** (yield 17%) along with N-benzylbenzamide (**3**) (yield 12%), benzoic acid (55%), and 2,3,6-triphenylpyridine (**4**) as a minor component (1.5%).



1 **2** **3** **4**

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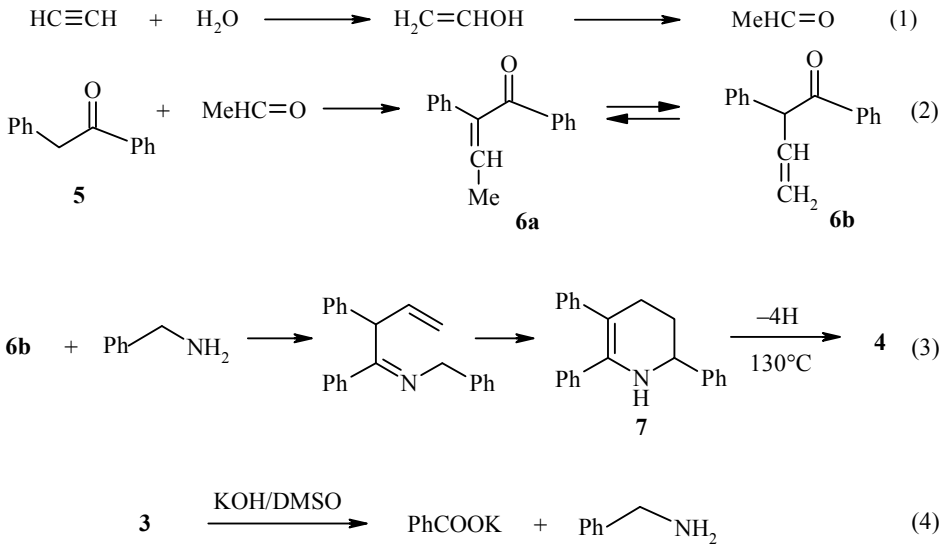
The most unexpected by-product of the reaction in this case is the pyridine **4**. Its formation can be explained by the following reactions:



Benzyl phenyl ketone (**5**, the usual product of partial deoximation of oximes in the conditions for synthesis of pyrroles [11]) condenses with acetaldehyde (hydration of acetylene in superbase media [12], equation 1) to form an equilibrium mixture of the olefinic ketones **6a,b** (equation 2). The **6b** form reacts with benzylamine to give 2,3,6-triphenyltetrahydropyridine **7**. The latter aromatizes (oxidative dehydrogenation in the presence of DMSO at high temperature) to give the pyridine **4** (equation 3).

Benzylamine is the expected product of alkaline hydrolysis of N-benzylbenzamide (**3**) which is confirmed by the presence of benzoic acid in the reaction mixture (equation 4). This scheme is proved by the separation of pyridine **4** from the reaction products of ketone **5** with acetylene and benzylamine (130ºC, 7 h).

IR spectra were taken on a Bruker ISF-25 spectrometer for KBr tablets. ^{1}H, ^{13}C, and ^{15}N NMR spectra were recorded on a Bruker DPX-400 spectrometer (400, 100 and 40 MHz respectively) using $CDCl_3$ with HMDS as internal standard at 0.05 ppm. Electron impact mass spectra (70 eV) were obtained on a Shimadzu GCMS-QP5050A instrument.

2,3,6-Triphenylpyridine (4). A. A mixture of benzyl phenyl ketoxime (**1**) (5.50 g, 26 mmol), KOH (1.46 g, 26 mmol) in DMSO (20 ml) was heated (130ºC, 7 h) while acetylene was passed at 40-45 ml/min. The reaction mixture was cooled, diluted with water (60 ml), and extracted with diethyl ether (5×30 ml). The ether extracts were washed with water and dried using potassium carbonate. After removal of the ether the residue was fractionated on an alumina column (eluent hexane and then hexane–diethyl ether (5:1)) to give 1.08 g (17%) 2,3-diphenyl-1-vinylpyrrole (**2**), mp 109-110ºC (mp 109-110ºC [13])), N-benzylbenzamide (**3**) 0.65 g, (12%), mp 105-106ºC (mp 104-106ºC (Aldrich, 2007-2008, p. 291)), and 2,3,6-triphenylpyridine (**4**) 0.12 g, (1.5%). The aqueous layer was acidified with dilute HCl (1:3) to pH ~ 2-3 and extracted with ether (3×30 ml). The ether extracts were washed with water and dried over Na_2SO_4. Removal of ether gave 1.74 g, (55%) benzoic acid as small crystals; mp 120-121ºC (water) (mp 121-125ºC (Aldrich 2009-1010, p. 237)). The spectroscopic characteristics were identical to known data [14].

Compound (4), white crystals; mp 98-100ºC (hexane). IR spectrum, ν, cm^{-1}: 3055, 3028, 1955, 1894, 1810, 1572, 1521, 1429, 1396, 1369, 835, 762, 745, 694, 629, 581. ^{1}H NMR spectrum, δ, ppm: 8.15 (2H, m, *o*-H, 6-Ph); 7.77 (2H, s, H-4,5), 7.48 (4H, m, *o*-H, 2-Ph; *m*-H, 6-Ph); 7.41 (1H, m, *p*-H, 6-Ph); 7.30 (2H, m, *o*-H, 3-Ph); 7.28 (2H, m, *m*-H, 3-Ph); 7.25 (1H, m, *p*-H, 3-Ph); 7.24 (2H, m, *m*-H, 2-Ph); 7.20 (1H, m, *p*-H,

2-Ph). ^{13}C NMR spectrum, δ, ppm: 156.7 (C-2); 155.8 (C-6); 140.5 (*i*-C, 3-Ph); 140.1 (*i*-C, 2-Ph); 139.4 (C-4); 139.2 (*i*-C, 6-Ph); 134.5 (C-3), 130.3 (*o*-C, 3-Ph); 129.7 (*o*-C, 2-Ph); 129.0 (*p*-C, 2-Ph; *p*-C, 6-Ph); 128.8 (*m*-C, 6-Ph); 128.4 (*m*-C, 2-Ph); 127.9 (*m*-C, *p*-C, 3-Ph); 127.1 (*o*-C, 6-Ph); 118.6 (C-5). ^{15}N NMR spectrum, δ, ppm: -70.9. Mass spectrum, *m/z*: 307 $[M]^+$. Found, %: C 89.79; H 5.65; N 4.48. $C_{23}H_{17}N$. Calculated, %: C 89.87; H 5.57; N 4.56. M 307.

B. A mixture of benzylamine (1.39 g, 13 mmol), benzyl phenyl ketone (**5**) (2.55 g, 13 mmol), and KOH (0.73 g, 13 mmol) in DMSO (10 ml) was heated (130ºC, 7 h) with passage of acetylene at a rate of 35-40 ml/min. The reaction mixture was cooled, diluted with water (30 ml), and extracted with ether (5×30 ml). The ether extracts were washed with water and dried over potassium carbonate. After evaporation of ether the residue was fractionated on an alumina column (eluent hexane, then hexane–diethyl ether (5:1)) to give the starting ketone **5** (0.53 g, 79% conversion) and 0.16 g, (4%) 2,3,6-triphenylpyridine (**4**). The aqueous later was acidified with dilute HCl (1:3) to pH ~ 2-3 and extracted with diethyl ether (5×30 ml). The ether extracts were washed with water and dried over Na_2SO_4. Evaporation of ether gave 0.98 g, (62%) benzoic acid.

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