ISSN 1070-4280, Russian Journal of Organic Chemistry, 2015, Vol. 51, No. 9, pp. 1346–1348. © Pleiades Publishing, Ltd., 2015.
Original Russian Text © D.A. Shabalin, E.Yu. Schmidt, M.Yu. Dvorko, N.I. Protsuk, I.A. Ushakov, B.A. Trofimov, 2015, published in Zhurnal Organicheskoi Khimii, 2015, Vol. 51, No. 9, pp. 1372–1374.

SHORT COMMUNICATIONS

Formation of 2-Ethynyl-3,4-dihydro-2*H*-pyrroles in the Synthesis of 3*H*-Pyrroles from Ketoximes and Acetylene in the System KOH–DMSO–Hexane

D. A. Shabalin, E. Yu. Schmidt, M. Yu. Dvorko, N. I. Protsuk, I. A. Ushakov, and B. A. Trofimov

Favorskii Irkutsk Institute of Chemistry, Siberian Branch, Russian Academy of Sciences,
ul. Favorskogo 1, Irkutsk, 664033 Russia
e-mail: boris_trofimov@irioch.irk.ru

Received April 22, 2015

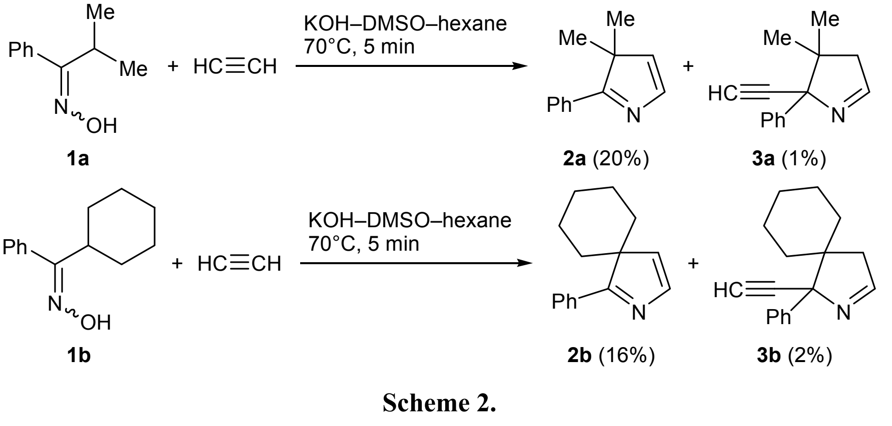
DOI: 10.1134/S1070428015090237

3*H*-Pyrroles constitute a difficultly accessible and therefore poorly studied group of nonaromatic pyrroles. On the other hand, they exhibit potentially rich chemistry due to intrinsic tendency to undergo various rearrangements and addition and cycloaddition reactions [1]. Despite obvious interest attracted by 3*H*-pyrroles and their undoubted promises for organic synthesis as reactive intermediates with unique reactivity, no somewhat general method for their synthesis has been developed so far.

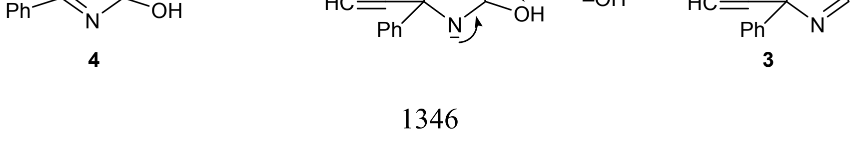
While continuing to develop general methodology for the synthesis of 3*H*-pyrroles by reaction of acetylene with ketone oximes containing only one C–H bond in the α-position with respect to the oxime group [2, 3], we studied the reactions of 2-methyl-1-phenylpropane-1-one oxime (**1a**) and cyclohexyl(phenyl)methanone oxime (**1b**) with acetylene under pressure in the two-phase superbasic system KOH–DMSO–hexane. Unexpectedly, apart from 3*H*-pyrroles **2a** and **2b**, we isolated from the reaction mixtures small amounts of 2-ethynyl-3,4-dihydro-2*H*-pyrroles **3a** and **3b** (Scheme 1).

Presumably, compounds **3** are formed as a result of addition of acetylide ion to the C=N bond (aza-

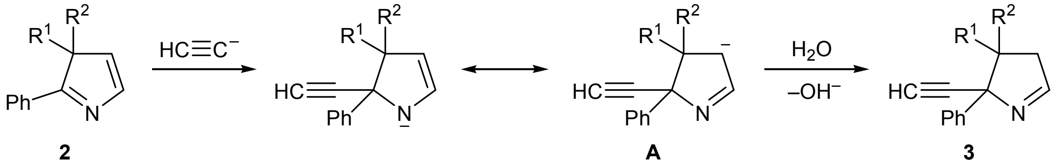
Scheme 1.



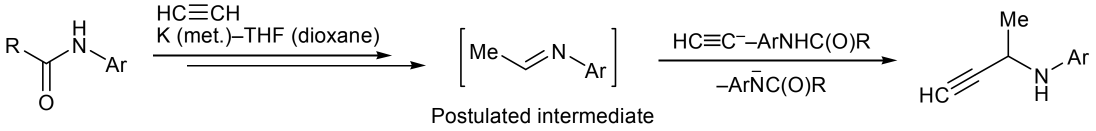
Scheme 2.



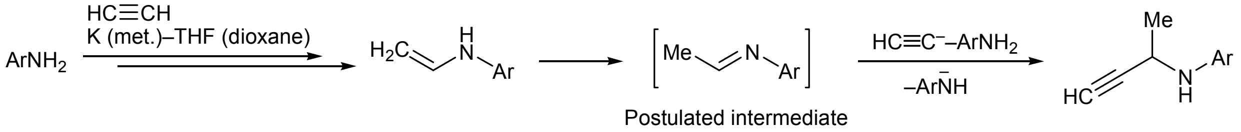
Scheme 3.



Scheme 4.



Scheme 5.



Favorskii ethynylation) of hydroxy derivatives **4** (intermediates isolated in the synthesis of 3*H*-pyrroles [4]) or 3*H*-pyrroles **2**. In the first case, the addition is accompanied by elimination of hydroxide ion (Scheme 2). In the second case, the ethynylation follows the 1,4-addition pattern with subsequent addition of a proton from the medium to carbanion **A** (Scheme 3). Ethynyl derivative **3a** was detected in the reactions of acetylene with both 3*H*-pyrrole **2a** and hydroxydihydropyrrole **4a**, which supports the proposed reaction schemes.

We have found no published examples of direct base-catalyzed ethynylation of C=N bond, though the formation of *N*-(but-3-yn-2-yl)anilines from two molecules of acetylene and *N*-aryl amides (Scheme 4) [5–7] or from aromatic amines and acetylene (Scheme 5) [7, 8] in the presence of metallic potassium has been postulated to involve addition of acetylide ion to the C=N bond of intermediate Schiff base.

The formation of 2-ethynyl-3,4-dihydro-2*H*-pyrroles from ketone oximes and acetylene is of fundamental importance as the first experimental evidence of aza-Favorskii reaction [9]. Furthermore, our results confirm the high reactivity of 3*H*-pyrroles and demonstrate for the first time their susceptibility to nucleophilic attack. In particular, this feature is likely to be responsible for the poor yields of 3*H*-pyrroles.

Reaction of ketone oximes 1a and 1b with acetylene in the system KOH–DMSO–hexane (*general procedure*). A mixture of 12.5 mmol of oxime **1a** or **1b** and 0.81 g (12.5 mmol) of $KOH \cdot 0.5H_2O$ in 50 mL of DMSO was stirred for 1 h on heating at 110–115°C. The resulting homogeneous solution of potassium oximate was transferred into a 250-mL Parr 4576A reactor with an internal stirrer (250 rpm), 40 mL of hexane was added, the mixture was purged with acetylene under pressure to remove air, acetylene was supplied to a pressure of 10 atm (the pressure did not exceed 13 atm during the synthesis), the reactor was heated to 70°C, and heating was immediately turned off (~5 min at 70°C). The reactor was cooled to room temperature and emptied, the upper hexane layer was separated by decanting, and the bottom DMSO layer was poured into ice water (250 mL), neutralized with aqueous ammonium chloride (10 wt %, 15 mL), and extracted with diethyl ether (5 × 50 mL). The extracts were combined with the organic phase, washed with water (3 × 50 mL), and dried over potassium carbonate. The drying agent was filtered off, the solvent was removed, and the residue was subjected to chromatography on a 1.6 × 20-cm column charged with Al_2O_3 using methylene chloride as eluent to isolate 3*H*-pyrrole **2a** (yield 20%) [2, 10] or **2b** (16%) [3]. By repeated chromatography of the enriched fraction (Al_2O_3, 0.8 × 13-cm; hexane–diethyl ether, 1 : 3) we isolated ethynyl derivative **3a** or **3b**.

2-Ethynyl-3,3-dimethyl-2-phenyl-3,4-dihydro-2*H*-pyrrole (3a). Yield 0.025 g (1%), dark yellow oily material, R_f 0.21. IR spectrum, ν, cm^{-1}: 3301, 2964, 2934, 2105, 1684, 1620, 1448, 1368, 1253, 973, 750, 702. ^1H NMR spectrum, δ, ppm: 0.48 s (3H, Me), 1.43 s (3H, Me), 2.50 d (1H, 4-H, J = 17.0 Hz), 2.58 s (1H, ≡CH), 2.77 d (1H, 4-H, J = 17.0 Hz), 7.29–7.37 m (3H, *m*-H, *p*-H), 7.48–7.50 m (2H, *o*-H), 7.94 s

(1H, 5-H). ^{13}C NMR spectrum, δ_C, ppm: 24.7 (Me), 25.3 (Me), 46.2 (C^3), 52.1 (C^4), 74.7 (C≡**C**H), 80.4 (C^2), 84.2 (**C**≡CH); 127.4, 128.0, 129.4, 139.6 (Ph); 169.9 (C^5). ^{15}N NMR spectrum: δ_N –39.9 ppm. Mass spectrum: *m*/*z* 197 $[M]^+$.

1-Ethynyl-1-phenyl-2-azaspiro[4.5]dec-2-ene (3b). Yield 0.045 g (2%), yellow oily material, R_f 0.18. IR spectrum, ν, cm^{-1}: 3304, 2933, 2855, 2105, 1626, 1600, 1491, 1448, 1299, 983, 751, 701. ^{1}H NMR spectrum, δ, ppm: 0.29–0.37 m, 0.81–1.00 m, 1.10–1.31 m, 1.41–1.47 m, 1.54–1.66 m, 1.75–1.82 m, and 2.11–2.18 m (10H, CH_2); 2.59 s (1H, ≡CH), 2.61 d and 2.76 d (1H each, 4-H, J = 17.4 Hz), 7.29–7.37 m (3H, *m*-H, *p*-H), 7.44–7.46 m (2H, *o*-H), 7.91 s (1H, 5-H). Mass spectrum: *m*/*z* 237 $[M]^+$.

The IR spectra (films) were recorded on a Bruker IFS25 spectrometer. The ^{1}H, ^{13}C, and ^{15}N NMR spectra were measured on Bruker DPX-400 and AV-400 spectrometers [400.1 (^{1}H), 100.6 (^{13}C), and 40.5 MHz (^{15}N)] from solutions in $CDCl_3$ using hexamethyldisiloxane (^{1}H, ^{13}C) or nitromethane (^{15}N) as internal standard. The mass spectra were obtained on an Agilent Technologies 6890N/5975C GC/MS instrument (HP-5MS column, 0.25 mm × 30 m, film thickness 0.25 μm; carrier gas helium; electron impact, 70 eV). The elemental analyses were obtained on a Flash EA 1112 Series analyzer. Analytical TLC was performed using Silufol plates (hexane–Et_2O, 1 : 1).

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 14-03-00426).

REFERENCES

1. Sammes, M.P., *Pyrroles*, Jones, R.A., Ed., Hoboken, NJ: Wiley, 1990, part 1, p. 549.
2. Korostova, S.E., Shevchenko, S.G., and Sigalov, M.V., *Chem. Heterocycl. Compd.*, 1991, vol. 27, p. 1101.
3. Shabalin, D.A., Dvorko, M.Yu., Schmidt, E.Yu., Protsuk, N.I., Ushakov, I.A., Mikhaleva, A.I., and Trofimov, B.A., *Mendeleev Commun.*, 2015, vol. 25, p. 129.
4. Trofimov, B.A., Korostova, S.E., Mikhaleva, A.I., Sobenina, L.N., Shcherbakov, V.V., and Sigalov, M.V., *Chem. Heterocycl. Compd.*, 1983, vol. 19, p. 231.
5. Trofimov, B.A., Vyalykh, E.P., and Malysheva, S.F., *Zh. Org. Khim.*, 1976, vol. 12, p. 2469.
6. Trofimov, B.A., Malysheva, S.F., and Vyalykh, E.P., *Zh. Org. Khim.*, 1981, vol. 17, p. 1583.
7. Trofimov, B.A. and Gusarova, N.K., *Russ. Chem. Rev.*, 2007, vol. 76, p. 507.
8. Trofimov, B.A., Malysheva, S.F., and Vyalykh, E.P., *Zh. Org. Khim.*, 1979, vol. 15, p. 880.
9. Favorskii, A.E., *Zh. Russ. Khim. Ob–va.*, 1906, vol. 37, p. 643.
10. Shabalin, D.A., Glotova, T.E., Schmidt, E.Yu., Ushakov, I.A., Mikhaleva, A.I., and Trofimov, B.A., *Mendeleev Commun.*, 2014, vol. 24, p. 100.