Mendeleev Commun., 2001, 11(2), 74–75

Unexpected formation of 1-vinyl-2-[2′-(6′-methylpyridyl)]pyrrole from dimethylglyoxime and acetylene in the Trofimov reaction

Alexander M. Vasil'tsov, Alexey B. Zaitsev, Elena Yu. Schmidt,* Al'bina I. Mikhaleva and Andrey V. Afonin

A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, 664033 Irkutsk, Russian Federation. Fax: +7 3952 39 6046; e-mail: lschmidt@irioch.irk.ru

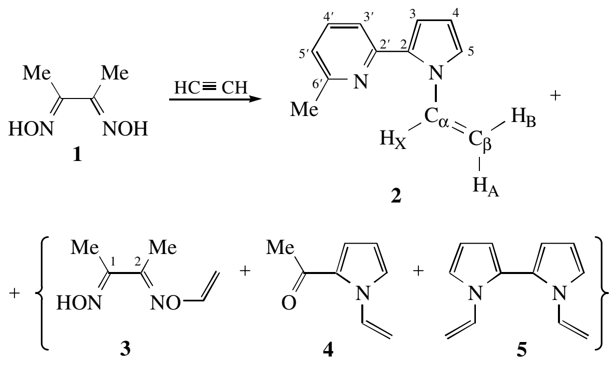
10.1070/MC2001v011n02ABEH001405

Dimethylglyoxime reacts with acetylene under pressure in the KOH–DMSO system to give 1-vinyl-2-[2′-(6′-methylpyridyl)]-pyrrole along with the expected products of the Trofimov reaction (*O*-vinyloxime, pyrrole and dipyrrole).

Ketoximes react with acetylene in the KOH–DMSO system to afford 1-*H*- and 1-vinylpyrroles (Trofimov reaction[1–5]), in some cases, intermediate *O*-vinylketoximes[6–8] and 3*H*-pyrroles[9–11] being isolated. However, the dioximes of α-diketones have never been studied in this reaction, although this might open a new straightforward entry to the dipyrrole chemistry.

Here, we briefly report on the Trofimov reaction extended to dimethylglyoxime **1**, the simplest α-diketoxime.

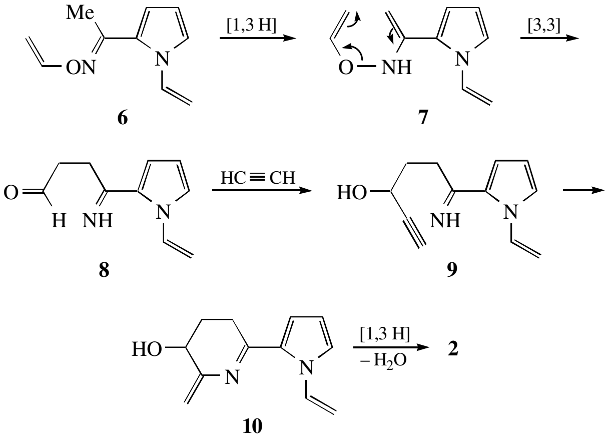
In the reaction mixture obtained under normal conditions (KOH–DMSO, 100–140 °C, acetylene pressure), unexpected 1-vinyl-2-[2′-(6′-methylpyridyl)]pyrrole **2** was identified among the anticipated products such as *O*-vinyldimethylglyoxime **3**, 2-acetyl-1-vinylpyrrole **4** and 1,1′-divinyl-2,2′-dipyrrole **5** (Scheme 1).†



Scheme 1

The pyridylpyrrole **2** content of the product mixture depends on the reaction conditions, reaching 36% in best cases (^{1}H NMR data). Compound **2** can be easily isolated by column chromatography (Al_2O_3).

The position of the methyl group in **2** follows from the signal shape of pyridine ring protons (two doublets and a triplet) corresponding to the only possible structural unit X–CH=CH–CH=Y having no protons at X and Y atoms. The chemical shifts of all relevant protons are consistent with those of 1-vinyl-2-(2′-pyridyl)pyrrole.[12]



Scheme 2

† ^{1}H (250.1 MHz) and ^{13}C NMR (62.9 MHz) spectra were measured in $CDCl_3$, HMDS was used as a standard compound. The assignments of ^{1}H and ^{13}C NMR spectra were performed by COSY, NOESY, HMQC[15] and HMBC[16] experiments.

General procedure. A mixture of 4.0 g (34.5 mmol) of dimethylglyoxime **1** and 1.9 g (27.4 mmol) of KOH·0.5H_2O in 100 ml of DMSO was saturated with acetylene (14 atm), heated at 110 °C for 1 h and cooled to room temperature. The mixture was diluted with 100 ml of water and extracted with diethyl ether (4×30 ml). The extract was washed with water (4×5 ml) and dried over K_2CO_3. After the removal of the extractant, a product mixture (1.6 g) was obtained. According to the ^{1}H NMR spectrum, the mixture contains 36% of 1-vinyl-2-[2′-(6′-methylpyridyl)]pyrrole **2**, 18% of 2-acetyl-1-vinylpyrrole **4** and 15% of 1,1′-divinyl-2,2′-dipyrrole **5**. The products were isolated by column chromatography (Al_2O_3, light petroleum, bp 30–70 °C).

1-Vinyl-2-[2′-(6′-methylpyridyl)]pyrrole **2**: n_D^{20} 1.6084. ^{1}H NMR, δ: 7.84 (dd, 1H, H_X), 7.55 (t, 1H, H-4′), 7.30 (d, 1H, H-3′, $^3J_{H\text{-}3'\text{–}H\text{-}4'}$ 7.8 Hz), 7.19 (dd, 1H, H-5), 6.98 (d, 1H, H-5′, $^3J_{H\text{-}4'\text{–}H\text{-}5'}$ 7.8 Hz), 6.55 (dd, 1H, H-3, $^4J_{H\text{-}3\text{–}H\text{-}5}$ 1.5 Hz), 6.26 (t, 1H, H-4, $^3J_{H\text{-}3\text{–}H\text{-}4} = {}^3J_{H\text{-}4\text{–}H\text{-}5}$ = 3.0 Hz), 5.15 (dd, 1H, H_B, $^3J_{H_B\text{–}H_X}$ 15.5 Hz), 4.71 (dd, 1H, H_A, $^2J_{H_A\text{–}H_B}$ 0.9 Hz, $^3J_{H_A\text{–}H_X}$ 8.8 Hz), 2.58 (s, 3H, Me). ^{13}C NMR, δ: 157.59 (C-6′), 151.30 (C-2′), 136.78 (C-4′), 133.54 (C_α), 132.37 (C-2), 120.40 (C-5′), 119.99 (C-5), 119.65 (C-3′), 112.15 (C-3), 110.00 (C-4), 98.61 (C_β), 24.59 (Me). IR (neat, ν/cm^{-1}): 3107–2822[a–c], 1639[c], 1588[a], 1576[a], 1543[b], 1476[b], 1459[b], 1420[c], 1389[b], 1374[c], 1326 (C–N), 1287[a], 1261, 1243, 1229[a], 1159[a], 1091[b], 1071[b], 1036[b], 995[a], 968[c], 865[c], 806[a], 786[a], 720[b], 653[b], 593[c] (*a* – pyridine, *b* – pyrrole and *c* – vinyl moieties).[1,15] MS, *m*/*z* (%): 183 (16%, $[M - H]^+$), 182 (100%, $[M - 2H]^+$), 168 (38%, $[M - H - Me]^+$), 157 (14%, $[M - H - HC{\equiv}CH]^+$), 130 (27%, $[M - H - H_2C{=}CH{-}C{\equiv}N]^+$), 91 (13%, [2-methylpyridine – 2H]$^+$).

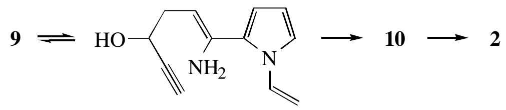
O-*Vinyl dimethylglyoxime* **3**. [KOH–DMSO, 100 °C, 5 min, neutralization of the reaction mixture with CO_2 before the extraction, 10% yield (10% conversion of dioxime **1**)], white needle-shaped crystals (from hexane), mp 63 °C. ^{1}H NMR, δ: 7.71 (s, 1H, OH), 6.95 (dd, 1H, H_X), 4.66 (dd, 1H, H_B, $^3J_{H_B\text{–}H_X}$ 14.3 Hz), 4.18 (dd, 1H, H_A, $^2J_{H_A\text{–}H_B}$ 1.8 Hz, $^3J_{H_A\text{–}H_X}$ 6.7 Hz), 2.04 (s, 6H, 1-Me, 2-Me). ^{13}C NMR, δ: 155.82 (C-2), 155.15 (C-1), 152.55 (C_α), 88.96 (C_β), 10.58 (2-Me), 9.45 (1-Me). IR (KBr, ν/cm^{-1}): 3600–3200 (OH), 3078, 2959, 2936, 2874, 1720, 1701, 1685, 1642, 1601, 1561, 1540, 1508, 1459, 1367, 1341, 1282, 1182, 1129, 1073, 993, 942, 892, 842, 795, 748, 687, 570. MS, *m*/*z* (%): 142 (1%, M^+), 58 (100%), 41 (46%).

2-Acetyl-1-vinylpyrrole **4**: ^{1}H NMR, δ: 7.99 (dd, 1H, H_X), 7.27 (dd, 1H, H-5), 7.01 (dd, 1H, H-3, $^4J_{H\text{-}3\text{–}H\text{-}5}$ 1.0 Hz), 6.24 (t, 1H, H-4, $^3J_{H\text{-}3\text{-}H\text{-}4} = {}^3J_{H\text{-}4\text{–}H\text{-}5}$ 3.3 Hz), 5.19 (dd, 1H, H_B, $^3J_{H_B\text{–}H_X}$ 15.8 Hz), 4.86 (dd, 1H, H_A, $^2J_{H_A\text{–}H_B}$ 1.2 Hz, $^3J_{H_A\text{–}H_X}$ 8.8 Hz), 2.48 (s, 3H, Me). ^{13}C NMR, δ: 188.92 (C=O), 133.71 (C_α), 130.30 (C-2), 125.12 (C-5), 121.25 (C-3), 109.97 (C-4), 101.76 (C_β), 27.53 (Me). IR (neat, ν/cm^{-1}): 3114–2875[a–c], 1655[a], 1637[c], 1591[a], 1576[a], 1550[b], 1529, 1474[b], 1458[b], 1426[c], 1368[c], 1328 (C-N), 1284[a], 1244, 1203, 1161[a], 1083[b], 1036[b], 966[c], 941, 878[c], 787[a], 742[b], 631[b], 594[c] (*a* – acetyl, *b* – pyrrole and *c* – vinyl moieties).[1]

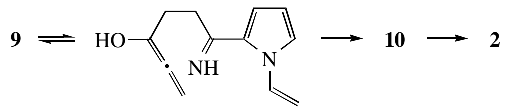
1,1′-Divinyl-2,2′-dipyrrole **5**: ^{1}H NMR, δ: 7.19 (dd, 1H, H-5), 6.68 (dd, 1H, H_X), 6.29 (t, 1H, H-4, $^3J_{H\text{-}3\text{–}H\text{-}4} = {}^3J_{H\text{-}4\text{–}H\text{-}5}$ = 3.0 Hz), 6.22 (dd, 1H, H-3, $^4J_{H\text{-}3\text{–}H\text{-}5}$ 1.5 Hz), 5.04 (dd, 1H, H_B, $^3J_{H_B\text{–}H_X}$ 15.8 Hz), 4.59 (dd, 1H, H_A, $^2J_{H_A\text{–}H_B}$ 1.2 Hz, $^3J_{H_A\text{-}H_X}$ 9.1 Hz). ^{13}C NMR, δ: 131.27 (C_α), 123.70 (C-2), 117.72 (C-5), 113.29 (C-3), 110.03 (C-4), 97.86 (C_β). IR (neat, ν/cm^{-1}): 3109–2852[a,b], 1643[b], 1598, 1551[b], 1482[a], 1459[a], 1428[b], 1377[b], 1351, 1310, 1261, 1236, 1155, 1084[a], 1067[a], 1036[a], 964[b], 861[b], 798, 717[b], 659[a], 591[b] (*a* – pyrrole and *b* – vinyl moieties).[1] MS, *m*/*z* (%): 183 (100%, $[M - H]^+$), 157 (8%, $[M - H - HC{\equiv}CH]^+$), 130 (8%, $[M - H - H_2C{=}CH{-}C{\equiv}N]^+$).

The formation of **2** may be rationalised as follows (Scheme 2): *O*-vinylketoxime **6**, a normal product of the Trofimov reaction with **1**, undergoes the [1,3] prototropic shift under the action of the superbase KOH–DMSO to form vinylhydroxylamine **7**, further rearranging in a [3,3] sigmatropic manner to give iminoaldehyde **8**. The latter is intercepted by acetylene to form acetylenic alcohol **9** (Favorsky reaction), which undergoes cyclization to hydroxymethylenetetrahydropyridine **10** and final aromatization to **2**.

Obviously, acetylenic alcohol **9** can be closed to form the pyridine moiety in a number of ways including preliminary prototropic rearrangements to aminovinyl **11** or allenyl **12** derivatives, and not only after but also before the formation of the 1-vinylpyrrole counterpart (Scheme 3).



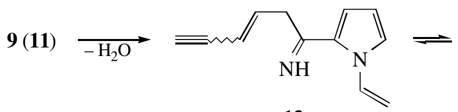
11



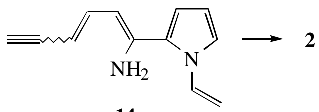
12

Scheme 3

The transformation of alcohols **9** or **11** to pyridylpyrrole **2** can also occur *via* preliminary dehydration to vinylacetylenic derivatives **13**, **14** (Scheme 4).



13



14

Scheme 4

The isolation of 1-vinyl-2-[2′-(6′-methylpyridyl)]pyrrole **2** from the reaction mixture of **1** with acetylene is important for a better understanding of the mechanism of the Trofimov pyrrole synthesis. Although iminoaldehydes like **8** were long ago[1–3] suggested to be formed in the reaction, they, together with vinylhydroxylamines **7**, remain the only two intermediates in the multi-step pyrrole ring-closing scheme,[1–3] which were not isolated. The pyridine-ring closure now observed during the pyrrole synthesis implies the trapping of the iminoaldehyde with acetylene and hence can be considered as an additional experimental support to the proposed mechanism[1–3] of the Trofimov reaction.

On the other hand, this new extension of the Trofimov reaction, in spite of the modest (unoptimised) yield of pyridylpyrrole **2**, may have a preparative value (particularly, when optimized and supported with a modern isolation technique), as a direct one-pot synthesis of alkaloids related to nicotine from readily available starting materials (dimethylglyoxime and acetylene). Few known syntheses of pyridylpyrrole[12–14] are multistep reactions involving the attachment of a second heterocycle.

References

1 B. A. Trofimov and A. I. Mikhaleva, N-*Vinilpirroly* (N-*Vinylpyrroles*), Nauka, Novosibirsk, 1984 (in Russian).

2 B. A. Trofimov, in *Adv. Heterocycl. Chem.*, ed. A. R. Katritzky, Academic Press, San Diego, 1990, vol. 51, p. 177.

3 B. A. Trofimov, in *The Chemistry of Heterocyclic Compounds, Pyrroles*, ed. R. A. Jones, Wiley, New York, 1992, vol. 48, part 2, p. 131.

4 R. J. Tedeschi, in *Encyclopedia of Physical Science and Technology*, Academic Press, New York, 1992, vol. 1, p. 27.

5 G. P. Bean, in *The Chemistry of Heterocyclic Compounds, Pyrroles*, ed. R. A. Jones, Wiley, New York, 1990, vol. 48, part 1, p. 153.

6 B. A. Trofimov, A. I. Mikhaleva, A. N. Vasil'ev and M. V. Sigalov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1979, 695 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1979, **28**, 651).

7 O. A. Tarasova, S. E. Korostova, A. I. Mikhaleva, L. N. Sobenina, R. N. Nesterenko, S. G. Shevchenko and B. A. Trofimov, *Zh. Org. Khim.*, 1994, **30**, 810 (*Russ. J. Org. Chem.*, 1994, **30**, 863).

8 B. A. Trofimov, A. I. Mikhaleva, A. M. Vasil'tsov, E. Yu. Schmidt, O. A. Tarasova, L. V. Morozova, L. N. Sobenina, T. Preiss and J. Henkelmann, *Synthesis*, 2000, 1125.

9 B. A. Trofimov, S. G. Shevchenko, S. E. Korostova, A. I. Mikhaleva and V. V. Shcherbakov, *Khim. Geterotsikl. Soedin.*, 1985, 1573 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1985, **21**, 1299].

10 T. N. Borisova, A. B. Varlamov, N. D. Sergeeva, A. T. Soldatenkov, O. V. Zvolinsky, A. A. Astakhov and N. S. Prostakov, *Khim. Geterotsikl. Soedin.*, 1987, 937 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1987, **23**, 799].

11 S. E. Korostova, S. G. Shevchenko and M. V. Sigalov, *Khim. Geterotsikl. Soedin.*, 1991, 1371 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1991, **27**, 1101].

12 O. V. Petrova, A. I. Mikhaleva, L. N. Sobenina, E. Yu. Schmidt and E. I. Kositsyna, *Mendeleev Commun.*, 1997, 162.

13 R. M. Acheson, M. J. Ferris, S. R. Critcheley and D. J. Wartin, *J. Chem. Soc., Perkin Trans. 2*, 1980, 326.

14 L. Brandsma, S. F. Vasilevsky and H. D. Verkruijsse, *Application of Transition Metal Catalysts in Organic Synthesis*, Springer, Berlin, 1997, p. 264.

15 A. Bax and S. Subramanian, *J. Magn. Reson.*, 1986, **67**, 1986.

16 A. Bax and M. F. Summers, *J. Am. Chem. Soc.*, 1986, **108**, 2093.

17 A. R. Katritzky and A. P. Embler, in *Physical Methods in Heterocyclic Chemistry*, ed. A. R. Katritzky, Academic Press, New York, 1963.

Received: 5th December 2000; Com. 00/1731