Chemistry of Heterocyclic Compounds, Vol. 46, No. 1, 2010

FIRST EXAMPLE OF THE SYNTHESIS OF N-VINYLPYRROLE FROM METHOXY-ALLENE AND METHOXYETHYL ISOTHIO-CYANATE: UNPRECEDENTED ELIMINATION OF METHANOL FROM A β-SUBSTITUTED METHYL ETHYL ETHER

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Using as example 3-methoxy-1-(2-methoxyethyl)-2-methylsulfanylpyrrole, obtained in one preparative stage from α-lithiated methoxyallene and 2-methoxyethyl isothiocyanate, a facile cleavage of a C–O bond in the N-(2-methoxyethyl) substituent by the t-BuOK–DMSO system has been discovered, opening access to a new class of N-vinylpyrroles (through β-elimination of methanol).

Keywords: N-vinylpyrrole, methoxyallene, N-(2-methoxyethyl)pyrrole, 2-methoxyethyl isothiocyanate, *t*-BuOK–DMSO system, synthesis, β-elimination.

N-Vinylpyrroles, together with other N-vinylazoles [1-6], are of interest as monomers, valuable synthetic intermediates, and building-blocks for the design of various polymeric materials and new azole-containing structures, including the more complex [6-14]. Traditionally they are obtained by the addition of NH-pyrroles to alkynes in the presence of various catalytic systems [14-18], more rarely by the indirect vinylation with dihaloalkanes (through substitution–elimination) [14, 15, 18, 19], by vinylic substitution with vinyl halides [14, 20], and with vinyl triflates [14, 21], or isomerization of N-allyl derivatives into N-propen-1-yls [12]. But not one known method permits the preparation of N-vinylpyrroles with such important, and with even rarer heteratom substituents as for example alkoxy- and alkylsulfanyl groups. It has been demonstrated that the introduction into the pyrrole nucleus of heteroatomic substituents may cardinally change the physical, chemical, and biological properties of materials based on them [22-26]. The alkylsulfanyl-substituted pyrroles are particularly attractive for constructing optoelectronic materials [26]. However the known range of such compounds is extremely sparse. Until recently there were no general and effective methods for obtaining hetero-substituted pyrroles.

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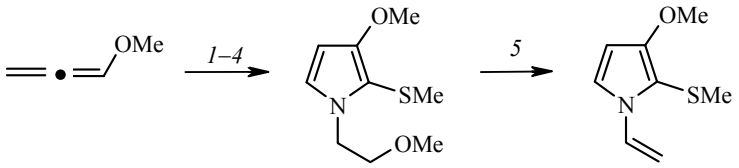
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 72-76, January, 2010. Original article submitted November 27, 2009.

We have proposed a conceptually new methodology for a highly selective one-reactor assembly of the functionalized pyrrole nucleus, including heteroatom substituents, from isothiocyanates, allenes or alkynes, and alkyl halides [6, 14, 27, 28].

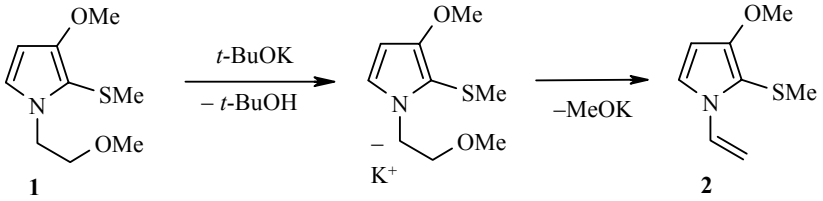
While developing these investigations, we discovered, using the example of the previously unknown 3-methoxy-1-(2-methoxyethyl)-2-methylsulfanylpyrrole (**1**) (synthesized in good yield in one preparative step according to Scheme 1), that in the system *t*-BuOK–DMSO it was readily converted into the also previously unknown 3-methoxy-2-methylsulfanyl-1-vinylpyrrole (**2**).



1, 65% **2**, 63%

1: BuLi/THF/C_6H_{14}; *2*: $MeOCH_2CH_2N{=}C{=}S$; *3*: MeI; *4*: CuI;
5: *t*-BuOK/DMSO, 40 min at ~110°C and 10 min at ~130°C

The process proceeds preferably through the β-elimination of methanol (by analogy with the cleavage of the C–O bond in diethyl ether under the action of ethylsodium published even at the start of the past century [29]).



Later (in 40-50 years) a whole series of publications has appeared on the cleavage of ethers under the action of alkylsodium and alkyllithium [30, 31]. In one of them it was demonstrated experimentally (using compounds labeled with deuterium) that the formation of alkene was linked with β-elimination of alkanol or phenol [31]. The cleavage of vinylic ethers of glycols and glycerol under the action of the KOH–DMSO system (110-150°C, 5 h) also proceeds analogously [32, 33]. Under these conditions, in the example of ethyleneglycol divinyl ether, divinyl ether is formed (15% yield) [33]. However not in any known case were alkyl 2-(pyrrol-1-yl)ethyl ethers investigated, the system *t*-BuOK–DMSO was not used, and no N-vinylpyrroles were obtained.

The discovered simple cleavage of the C–O bond in N-(2-methoxyethyl)pyrroles by the *t*-BuOK–DMSO system, in combination with the approach developed by us towards one-reactor assemblies of the pyrrole nucleus from isothiocyanates and allenes or acetylenic carbanions, may become the main new general strategy for the synthesis of N-vinylpyrroles.

EXPERIMENTAL

The IR spectra were recorded on a Bruker Vertex 70 spectrophotometer. The ^1H and ^{13}C NMR spectra and experiments on heteronuclear correlations were carried out on Bruker DPX-400 and AV-400 (400 and 100 MHz respectively) instruments in $CDCl_3$, internal standard was HMDS. Mass spectra were obtained on a Shimadzu GCMS-QP5050A chromato–mass spectrometer. GLC analysis was carried out on an Agilent 6890N chromatograph.

THF was purified with dispersed KOH (~50 g/liter), by boiling and distilling over Na in the presence of benzophenone in an atmosphere of argon. Dimethyl sulfoxide was made absolute by distillation with *t*-BuOK. Methoxyallene was obtained by the procedure of [34], the previously unknown 2-methoxyethyl isothiocyanate from 2-methoxyethylamine, carbon disulfide, and acetyl chloride by the procedure of [27]. Butyllithium (~2.5 M solution in hexane) and other reagents and solvents used in the work were commercial preparations. Liquid nitrogen was used for cooling.

3-Methoxy-1-(2-methoxyethyl)-2-methylsulfanylpyrrole (1). A mixture of methoxyallene (6 g, 85.7 mmol) and THF (4 ml) was added to a solution of BuLi (67.5 mmol) in hexane (27 ml) and THF (70 ml) with vigorous stirring in an atmosphere of argon at -100°C. The mixture was stirred for 5 min maintaining the temperature of the reaction mixture in the range -60 to -50°C, then cooled to -90°C, and a mixture of methoxyethyl isothiocyanate (5.86 g, 50 mmol) and THF (5 ml) was added. An increase in temperature to -50°C was observed (with cooling). The mixture was stirred at ~ -60°C for 5 min, cooled to -80°C, and MeI (15.9 g, 112 mmol) was added. The cooling bath was taken away, the temperature allowed to increase to -10°C, and CuI (2 g, 10.5 mmol) was added. After increasing the temperature to 18°C, the reaction mixture was heated rapidly to 50°C, and stirred for 30 min at 45-50°C. Then a saturated solution of NH_4Cl (80 ml) and NaCN (~1.5 g) were added, the mixture stirred vigorously, and the organic layer separated. The products from the aqueous fraction were extracted with diethyl ether (3×30 ml), the combined organic fraction was washed with water (2×50 ml), and dried over $MgSO_4$. The solution was passed through a layer (2 cm) of neutral Al_2O_3, then concentrated at reduced pressure at ~50°C (initially on the rotary evaporator then on an oil pump at 1 mm Hg). The residue was a dark-brown mobile liquid (8.81 g), from which two fractions were isolated by redistillation in vacuum. Fraction I (1.5 g), bp 102-117°C (<1 mm Hg) contained pyrrole **1** (79%, by GLC). Fraction II (5.55 g), bp 117-124°C (<1 mm Hg), n_D^{20} 1.5156, light-yellow liquid contained pyrrole **1** (96%, by GLC). Yield of pyrrole **1** was 6.51 g (65%). IR spectrum, ν, cm^{-1}: 3127 w, 3110 w, 2984, 2922 s, 2892 s, 2827, 1638, 1548 s, 1462, 1400, 1355, 1330 s, 1268 w, 1238 w, 1220 w, 1185, 1122 s, 1092 s, 1038 w, 1010, 987, 965, 833, 714, 664 w, 654 w, 616, 474 w. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.67 (1H, d, $^3J_{5,4}$ = 3.2, H-5); 5.86 (1H, d, $^3J_{4,5}$ = 3.2, H-4); 4.12 (2H, t, ^3J = 5.5, NCH_2); 3.79 (3H, s, 3-CH_3O); 3.56 (2H, t, ^3J = 5.5, OCH_2); 3.30 (3H, s, $C\underline{H}_3OCH_2$); 2.16 (3H, s, SCH_3). ^{13}C NMR spectrum, δ, ppm: 151.32 (C-3); 120.86 (C-5); 105.38 (C-2); 94.58 (C-4); 72.29 (OCH_2); 58.68 ($\underline{C}H_3OCH_2$); 57.89 (3-CH_3O); 46.30 (NCH_2); 20.48 (SCH_3). Heteronuclear two-dimensional correlation spectroscopy (HSQC) was used to assign the signals of carbon atoms of NCH_2, OCH_2, 3-CH_3O, and $\underline{C}H_3OCH_2$ in the ^{13}C NMR spectrum. Found, %: C 53.55; H 7.40; S 15.80. $C_9H_{15}NO_2S$. Calculated, %: C 53.70; H 7.51; S 15.93.

3-Methoxy-2-methylsulfanyl-1-vinylpyrrole (2). Pyrrole **1** (1.18 g, 5.9 mmol) was added to a solution of *t*-BuOK (1.2 g, 10.7 mmol) in absolute DMSO (3.7 ml). The mixture was heated for 40 min at 110-112°C and for 10 min at 128-134°C, then cooled to ~20°C, and water (10 ml) added. The reaction products were extracted with diethyl ether (4×30 ml), and the combined organic fraction was washed with water (3×5 ml), and dried over $MgSO_4$. The solvent was removed under reduced pressure at ~50°C (initially on a rotary evaporator, then on an oil pump at 1 mm Hg). The residue (0.76 g, after taking out numerous test samples) was purified from resinous substances by column chromatography (through a 1 cm layer of neutral Al_2O_3, eluent petroleum ether (40-70°C) and petroleum ether–Et_2O, 10:1). A liquid (0.73 g) was obtained containing (according to data of ^{1}H NMR spectra) N-vinylpyrrole **2** (85%) (yield 63%) and the initial N-(2-methoxyethyl)pyrrole **1**. By repeated chromatography on a column of Al_2O_3 N-vinylpyrrole **2** was isolated with a content of main substance of ~99% (GLC data), n_D^{24} 1.5630, light-yellow liquid. IR spectrum, ν, cm^{-1}: 3185 w, 3116 w, 3084 w, 3043 w, 2999, 2953, 2920, 2839, 1669 sh, 1638 s, 1556 s, 1478 w, 1460, 1438, 1397, 1375 s, 1304, 1270, 1242 w, 1180 w, 1151 w, 1094 s, 1030, 1010 w, 967 and 960 d, 864, 715, 693, 663, 610 w, 584 w, 469. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.29 (1H, dd, $^3J_{trans}$ = 15.9, $^3J_{cis}$ = 8.8, $NC\underline{H}=CH_2$); 6.97 (1H, d, $^3J_{5,4}$ = 3.4, H-5); 6.00 (1H, d, $^3J_{4,5}$ = 3.4, H-4); 5.09 (1H, dd, $^3J_{trans}$ = 15.9, $^2J_{gem}$ = 1.0, $NCH=C\underline{H}_2$); 4.67 (1H, dd, $^3J_{cis}$ = 8.8, $^2J_{gem}$ = 1.0, $NCH=C\underline{H}_2$); 3.81 (3H, s, OCH_3); 2.14 (3H, s, SCH_3). ^{13}C NMR spectrum, δ, ppm: 152.10 (C-3); 130.09

(N<u>C</u>H=CH_2); 116.22 (C-5); 106.23 (C-2); 97.81 (C-4); 96.72 (CH_2=); 58.11 (OCH_3); 22.10 (SCH_3). Heteronuclear two-dimensional correlation spectroscopy was used for the assignment of the signals of carbon atoms C-4 and CH_2= in the ^{13}C NMR spectrum. Mass spectrum, *m/z* (I_{rel}, %): 169 (53) $[M]^+$. Found, %: C 56.89; H 6.40; S 18.75. $C_8H_{11}NOS$. Calculated, %: C 56.77; H 6.55; S 18.95.

The work was carried out with the financial support of the Russian Fund for Fundamental Investigations (Project 09-03-00890a) and of the Presidium of the Siberian Branch of the Russian Academy of Sciences (Program of Fundamental Investigations of the Presidium of the Russian Academy of Sciences, Project 18.20).

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