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## SHORT COMMUNICATIONS

# An Elegant Synthesis of 1-(2-Vinyloxyethyl)- and 1-(2-Hydroxyethyl)pyrrole-3-carbaldehydes*

**N. A. Nedolya[1], L. Brandsma[2], and N. I. Shlyakhtina[1]**

[1] *Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences, ul. Favorskogo 1, Irkutsk, 664033 Russia*
*e-mail: nina@irioch.irk.ru*

[2] *Utrecht University, Utrecht, The Netherlands*

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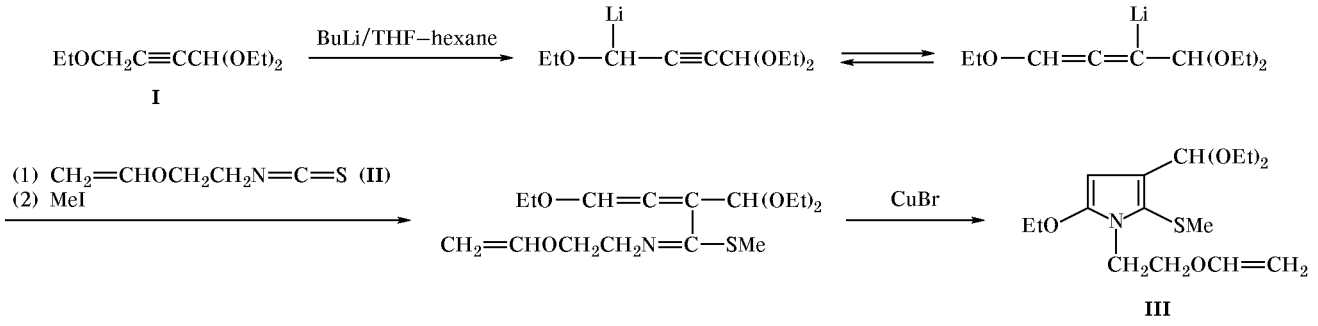
We previously discovered a radically new approach to synchronous construction and functionalization of pyrrole ring, which utilizes isothiocyanates and metal derivatives of 1,2-dienes or alkynes as key building blocks [1–3]. The use in this reaction of functionalized alkynes and isothiocyanates, e.g., 1,1,4-triethoxy-2-butyne (**I**) and 2-vinyloxyethyl isothiocyanate (**II**), ensures direct synthesis of difficultly accessible 1-(2-vinyloxyethyl)- and 1-(2-hydroxyethyl)pyrroles **III**–**V** which are characterized by a rare combination of highly reactive and biogenic functional groups (such as acetal, aldehyde, hydroxy, and vinyl groups) and heteroelement-containing substituents (OR, SR) (Scheme 1). We were the first to effect regioselective protolytic cleavage of the acetal moiety in compound **III** which contains a hydrolytically unstable vinyloxy group. The reaction was carried out in the presence of an acid (aqueous dioxane, hydrochloric acid, 5°C, 1 min), and it led to formation of compound **IV** as the first representative of 1-(2-vinyloxyethyl)pyrrole-3-carbaldehydes. Treatment of pyrrole **III** with hydrochloric acid in aqueous dioxane at 30–35°C (0.5 h) resulted in removal of the acetal protection and hydrolytic cleavage of the vinyloxy group to afford pyrrole **V** (Scheme 2). It should be emphasized that no pyrrole ring opening occurred under these conditions.

**3-Diethoxymethyl-5-ethoxy-2-methylthio-1-(2-vinyloxyethyl)pyrrole (III).** A solution of 22.4 mmol of BuLi in 14 ml of hexane and 30 ml of THF was cooled to –100°C, and 3.72 g (20.1 mmol) of alkyne **I** was added. The mixture was stirred for 15 min at –70°C and cooled to –100°C, and a solution of 2.58 g (20 mmol) of isothiocyanate **II** in 10 ml of THF was quickly added. The mixture was stirred for 15 min at –60°C, 5 g (34.7 mmol) of methyl iodide was added, and then (at 6°C) 0.2 g of finely powdered CuBr was added. The mixture spontaneously warmed up to 20°C (in 10 min), a solution of 0.4 g of NaCN in 30 ml of

**Scheme 1.**




**I** **III**

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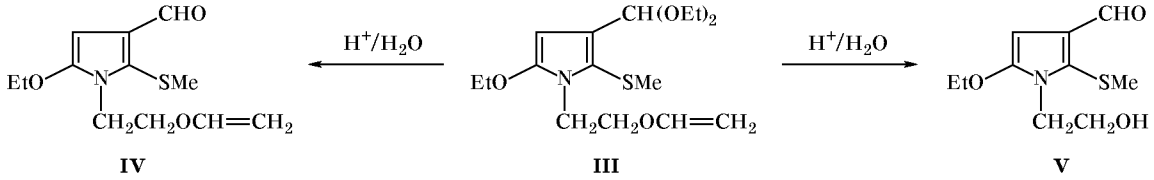
**Scheme 2.**




**IV** **III** **V**

water was added, the mixture was stirred for 10 min, and ~60 ml of a saturated solution of ammonium chloride was added. The organic phase was separated, and the aqueous phase was treated with diethyl ether (3 × 50 ml). The extracts were combined with the organic phase, dried over $MgSO_4$, passed through a column charged with neutral aluminum oxide, and evaporated on a rotary evaporator. The residue was distilled under reduced pressure. Yield 2.83 g (43%), bp 155–157°C (1 mm), $n_D^{20}$ = 1.5040. IR spectrum (film), ν, $cm^{-1}$: 620 sh, 680 br, 740, 810, 860 sh, 900, 960, 990, 1000, 1030 br, 1100 br, 1170, 1200, 1220 br, 1290, 1310, 1360, 1390, 1410, 1430, 1460, 1465, 1500, 1560, 1610, 1630, 2880, 2910, 2980. $^1H$ NMR spectrum, δ, ppm: 6.37 d.d (1H, OCH=, $J_{trans}$ = 14.3, $J_{cis}$ = 6.8 Hz), 5.61 s (1H, OCHO), 5.42 s (1H, 4-H), 4.17 t (2H, $NCH_2$, $J$ = 6.6 Hz), 4.16 d.d (1H, $CH_2$=, $^3J_{trans}$ = 14.3 Hz, $^2J$ = 2.2 Hz), 4.04 q (2H, $OCH_2$, $J$ = 7.0 Hz), 3.96 d.d (1H, $CH_2$=, $^3J_{cis}$ = 6.8 Hz, $^2J$ = 2.2 Hz), 3.84 t (2H, $OCH_2$, $J$ = 6.6 Hz), 3.64 m and 3.53 m [4H, $CH(OCH_2)_2$], 2.16 s (3H, SMe), 1.38 t (3H, Me, $J$ = 7.0 Hz), 1.20 t [6H, $CH(OCH_2Me)_2$, $J$ = 7.1 Hz]. $^{13}C$ NMR spectrum, $\delta_C$, ppm: 151.47 (OCH=), 148.59 (NCO), 127.21 (NCS), 112.41 ($C^3$), 98.44 (OCHO), 86.98 ($CH_2$=), 83.84 ($C^4$), 66.43 ($OCH_2$), 66.00 ($OCH_2$), 61.52 ($2OCH_2$), 40.73 ($NCH_2$), 21.97 (SMe), 15.46 (2Me), 14.97 (Me). Found, %: C 58.35; H 8.22; N 4.14; S 9.47. $C_{16}H_{27}NO_4S$. Calculated, %: C 58.33; H 8.26; N 4.25; S 9.73.

**5-Ethoxy-2-methylthio-1-(2-vinyloxyethyl)pyrrole-3-carbaldehyde (IV).** Pyrrole **III**, 0.8 g (2.43 mmol), was added to a mixture of 12 ml of dioxane, 4 ml of water, and 0.4 ml of 30% hydrochloric acid, cooled to 5°C. The solution was shaken over a period of 1 min and extracted with diethyl ether and hexane, and the extract was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was recrystallized from hexane. Yield 0.56 g (91%), mp 72–74°C. IR spectrum (KBr), ν, $cm^{-1}$: 550, 620, 660, 730, 770, 830, 910, 950, 1010, 1030, 1060, 1100, 1190, 1220, 1320, 1350, 1380, 1400, 1450, 1490, 1570, 1620, 1650, 2780, 2880, 2920, 2980. $^1H$ NMR spectrum, δ, ppm: 10.00 (CH=O), 6.36 d.d (1H, OCH=, $J_{trans}$ = 14.3, $J_{cis}$ = 6.8 Hz), 5.71 s (1H, 4-H), 4.29 t (2H, $NCH_2$, $J$ = 6.0 Hz), 4.18 d.d (1H, $CH_2$=, $^3J_{trans}$ = 14.3, $^2J$ = 2.2 Hz), 4.08 q (2H, $OCH_2$, $J$ = 7.0 Hz), 4.01 d.d (1H, $CH_2$=, $^3J_{cis}$ = 6.8, $^2J$ = 2.2 Hz), 3.92 t (2H, $OCH_2$, $J$ = 6.0 Hz), 2.33 s (3H, SMe), 1.41 t (3H, Me, $J$ = 7.0 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 186.00 (C=O), 151.11 (OCH), 149.71 (NCO), 127.42 (NCS), 127.03 ($C^3$), 87.22 ($CH_2$=), 83.03 ($C^4$), 66.40 ($OCH_2$), 65.75 ($OCH_2$), 41.23 ($NCH_2$), 22.52 (SMe), 14.60 (Me). Found, %: C 56.30; H 6.86; N 5.43; S 12.86. $C_{12}H_{17}NO_3S$. Calculated, %: C 56.45; H 6.71; N 5.49; S 12.56.

**5-Ethoxy-1-(2-hydroxyethyl)-2-methylthiopyrrole-3-carbaldehyde (V).** Dioxane, 7 ml, water, 2 ml, and 30% hydrochloric acid, 0.25 ml, were added to 0.5 g (1.5 mmol) of pyrrole **III**. The mixture was stirred for 30 min at 30–35°C and extracted with diethyl ether and hexane, and the extract was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was reprecipitated from acetone into hexane. Yield 0.315 g (92%), mp 82–84°C. IR spectrum (KBr), ν, $cm^{-1}$: 500, 550, 620, 650, 670, 690, 730, 830, 860, 900, 960, 980, 1010, 1030, 1060, 1080, 1100, 1140, 1170, 1200, 1240, 1310, 1330, 1350, 1370, 1390, 1410, 1440, 1460, 1490, 1560, 1640, 2880, 2920, 2940, 2980, 3450. $^1H$ NMR spectrum, δ, ppm: 9.94 (CH=O), 5.69 s (1H, 4-H), 4.18 t (2H, $NCH_2$, $J$ = 5.6 Hz), 4.08 q (2H, $OCH_2$, $J$ = 7.0 Hz), 3.87 t (2H, $OCH_2$, $J$ = 5.6 Hz), 2.33 s (3H, SMe), 1.41 t (3H, Me, $J$ = 7.0 Hz), 2.59 br.s (1H, OH). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 186.23 (C=O), 149.22 (NCO), 127.53 (NCS), 127.28 ($C^3$), 83.13 ($C^4$), 66.59 ($OCH_2$), 61.54 ($OCH_2$), 44.74 ($NCH_2$), 22.61 (SMe), 14.72 (Me). Found, %: C 50.67; H 6.92; N 5.23; S 13.90. $C_{10}H_{15}NO_3S$. Calculated, %: C 52.38; H 6.59; N 6.11; S 13.98.

The IR spectra were recorded on a Specord 75IR spectrophotometer from samples prepared as thin films or KBr pellets. The $^1H$ and $^{13}C$ NMR spectra of compounds as ~5–10% solutions in carbon tetrachloride–chloroform-*d* were obtained on a Bruker DPX-400 instrument operating at 400 MHz for $^1H$ and 100 MHz for $^{13}C$; hexamethyldisiloxane was used as

internal reference. 1,1,4-Triethoxy-2-butyne (**I**) [4] and 2-vinyloxyethyl isothiocyanate (**II**) [1] were synthesized by known procedures.

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