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FIRST EXAMPLE OF SYNTHESIS OF PYRROLE-3-CARBALDEHYDE FROM ISOTHIOCYANATE AND 1,1,4-TRIALKOXY-2-BUTYNE IN ONE PREPARATIVE STEP

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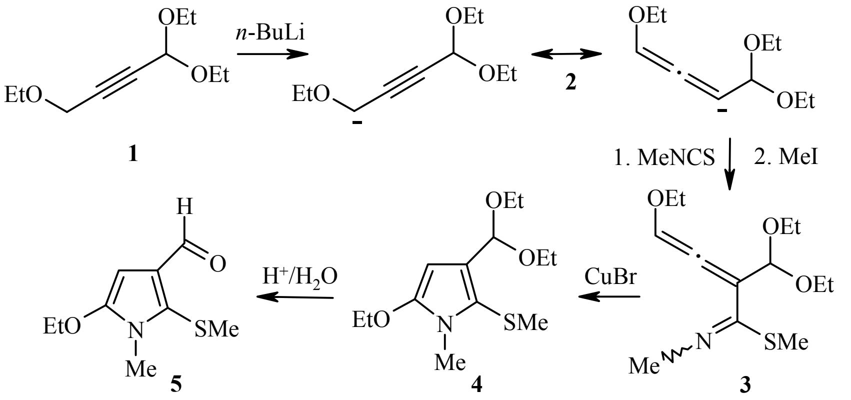
Pyrrole aldehydes, which are not distinguished by either structural diversity or a diversity of approaches and methods for obtaining them [1], are mainly synthesized in a Vilsmeier–Haack reaction [2].

Our discovery of a fundamentally new direct route to difficultly accessible pyrrole-3-carbaldehydes such as 2-(alkylthio)-1-organylpyrrole-3-carbaldehydes of type **5** involves using isothiocyanates and 1,1,4-trialkoxy-2-butynes as the key structural units in simultaneous design and functionalization of the pyrrole ring.

Addition of methylisothiocyanate (in principle, any isothiocyanate) to 1,1,4-triethoxy-2-butyne (**1**) lithiated by butyllithium (intermediate **2**), followed by methylation of the adduct by methyl iodide, leads to azatriene **3**, which in the presence of catalytic amounts of CuBr [3, 4] smoothly undergoes ring closure to acetal **4** (yield, ~96%). The latter is easily hydrolyzed in acid medium to pyrrole aldehyde **5** in > 96% yield.



3-(Diethoxymethyl)- 5-ethoxy-1-methyl-2-(methylthio)pyrrole (4). Butyne **1** (19.2 g, 0.1 mol) was added to a solution (cooled to -100°C) of *n*-BuLi (0.1 mol) in hexane (62 ml) and THF (50 ml) under a nitrogen atmosphere. After 10 min of stirring at -60°C, the reaction mixture was again cooled down to -100°C and a

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solution of methyl isothiocyanate (8 g, 0.1 mol) in THF (20 ml) was rapidly added to it. After the temperature of the reaction mixture was raised to -40°C, MeI (19 g, 0.13 mol) was added to it and then (at 6°C) finely ground CuBr (1 g) was added. After the temperature spontaneously rose to 45°C (over the course of ~10 min) and stirring continued for an additional 10 min, a solution of NaCN (2 g) in water (~50 ml) was added to the reaction mixture; this was stirred for 10 min, and then treated with a saturated NH_4Cl solution (~100 ml). The organic layer was removed, the aqueous layer was extracted with either (3 × ~50 ml). The combined organic fraction was dried over $MgSO_4$, the solution was passed through a column with neutral Al_2O_3, and the solvent was removed under reduced pressure. The residue comtains 26.5 g (95.8%) of pyrrole **4**. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 5.64 (1H, s, CH=); 5.44 (1H, s, CH); 4.02 (2H, q, OCH_2); 3.67 (2H, m, OCH_2); 3.53 (2H, m, OCH_2); 3.43 (3H, s, NMe); 2.12 (3H, s, SMe); 1.36 (3H, t, Me); 1.21 (6H, t, 2Me). ^{13}C NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 148.95 (NCO), 126.40 (NCS), 112.28 (3 × C=), 98.58 (OCHO), 83.16 (CH=), 65.96 (OCH_2), 61.70 ($2OCH_2$), 28.13 (NMe), 21.34 (SMe), 15.37 (2Me), 14.87 (Me).

5-Ethoxypyrrole-1-methyl-2-(methylthio)-3-carbaldehyde (5). Dioxane (40 ml), water (10 ml), and 30% HCl (1.5 ml) were added to pyrrole **4** (3 g, 0.01 mol). After 10 min of stirring at room temperature, the product was extracted with ether and hexane and dried over $MgSO_4$. Then the solvents were removed under reduced pressure. The residue contains 2.1 g (96.3%) of pyrrole **5** as orange-brown crystals; mp 78-80°C (hexane). IR spectrum, ν, cm^{-1}: 1570 (C=C), 1650 shoulder, 1660 (C=O). ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 10.00 (1H, s, CH=O); 5.71 (1H, s, CH=); 4.06 (2H, q, OCH_2); 3.53 (3H, s, NMe); 2.27 (3H, s, SMe); 1.40 (3H, t, Me). ^{13}C NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 186.31 (C=O), 150.26 (NCO), 127.05 (NCS), 126.97 (3 –C=), 82.38 (CH=), 66.46 (OCH_2), 28.61 (NMe), 21.48 (SMe), 14.63 (Me). Found, %: C 54.00; H 6.80; N 7.19; S 15.99. $C_9H_{13}NO_2S$. Calculated, %: C 54.25; H 6.58; N 7.03; S 16.09.

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