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SYNTHESIS OF 5-ALKOXY-2-ALKYLTHIO-3-PYRROL-2-YLPYRROLES

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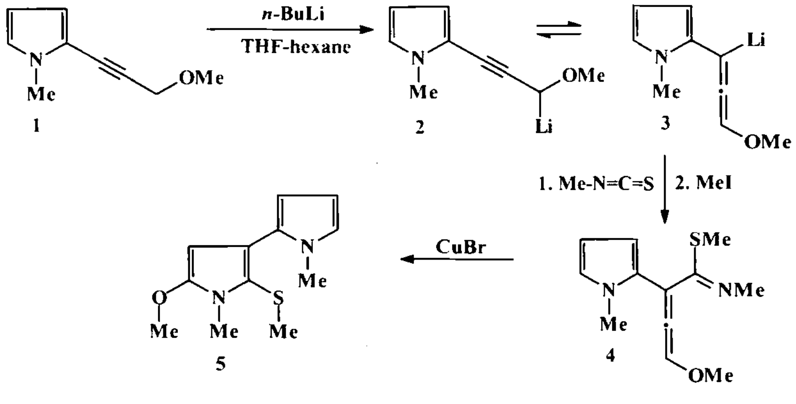
We have discovered a fundamentally new general approach to one-pot assembly of a 1,2,3,5-tetra-substituted pyrrole ring from lithiated 2-alkynyl esters and isothiocyanates [1], providing a simple way to obtain pyrroles with uncommon substituents (alkoxy- and alkylthio groups), such as 3-(pyrrol-2-yl)pyrroles of type **5**. The precursor of pyrrole **5**, azatriene **4**, is obtained by addition of methylisothiocyanate to 2-(3-methoxyprop-1-ynyl)-1-methylpyrrole (**1**) lithiated by butyllithium (intermediates **2**, **3**) followed by methylation of the adduct by methyl iodide. The last step of the reaction is carried out in the presence of catalytic amounts of CuBr [1,2]. The yield of pyrrole **5** is ~70%.

2-(3-Methoxyprop-1-ynyl)-1-methylpyrrole (1). A solution of 2-iodo-1-methylpyrrole (obtained by the method [3]) (27 g, 0.13 mol), $PdCl_2(PPh_3)_2$ (0.5 g), and Ph_3P (0.5 g) in diisopropylamine (20 ml) was heated under a nitrogen atmosphere at 40°C for several minutes. First 3-methoxyprop-1-yne (11 g, 0.16 mol) was added and then CuBr (0.3 g) and LiBr (1.5 g) in THF (7 ml) at 20°C. After ~10 min of stirring, water was added to the reaction mixture. The aqueous layer was extracted with ether. The combined organic fraction, after drying with $MgSO_4$, was passed twice through a column with neutral Al_2O_3; the solvent was removed and the residue was distilled. Obtained 16.5 g (85%) of pyrrole **1**, ~100% purity (GLC); bp ~100°C/0.8 mm Hg. ^1H NMR spectrum (90 MHz, CCl_4), δ, ppm: 6.50 (1H, m, CH=); 6.30 (1H, dd, CH=); 5.95 (1H, dd, CH=); 4.25 (2H, s, OCH_2); 3.60 (3H, s, OMe); 3.35 (3H, s, NMe).



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5-Methoxy-1-methyl-3-(1-methylpyrrol-2-yl)-2-(methylthio)pyrrole (5). A solution of *n*-BuLi (0.037 mol) in hexane (23 ml) was added to a solution of pyrrole **1** (4.5 g, 0.03 mol) in THF (50 ml) and ether (20 ml), cooled down to -100°C, under a nitrogen atmosphere. Then the temperature of the reaction mixture was raised up to -60°C, it was cooled down again to -100°C, and a solution of of methylisothiocyanate (2.2 g, 0.03 mol) in THF (15 ml) was added rapidly. After the temperature of the reaction mixture was raised up to -35°C, MeI (10 g, 0.07 mol) was added, followed by CuBr (0.7 g) (at 15°C). After 30 min of stirring at 45°C, of a saturated NH_4Cl (~200 ml) solution with ~10% NaCN was added to the reaction mixture; this was stirred for 10 min and the layers were separated. The aqueous layer was extracted with ether and pentane. The combined organic fraction was dried with K_2CO_3 and the solution was passed through a column with neutral Al_2O_3; the solvent was removed and the residue was distilled. Obtained 5 g (70%) of pyrrole **5**, 99% purity (GLC); bp 140-145°C/~0.5 mm Hg. ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 6.71 (1H, t, CH=); 6.21 (2H, m, 2 CH=); 5.40 (1H, s, CH=); 3.87 (3H, s, OMe); 3.62 (3H, s, NMe); 3.58 (3H, s, NMe); 2.15 (3H, s, SMe). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ, ppm: 149.24, 128.83, 121.71, 120.01, 113.18, 108.74, 106.98, 86.02, 57.18 (OMe), 34.54 (NMe), 28.52 (NMe), 20.88 (SMe). Found, %: C 60.79; H 6.75; N 11.91; S 13.50. $C_{12}H_{16}N_2OS$. Calculated, %: C 60.98; H 6.82; N 11.85; S 13.57.

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