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# DEVELOPMENT OF A NEW APPROACH TO PYRROLE RING FORMATION: FIRST EXAMPLE OF A 3-(1-ALKYNYL)-2-(ALKYLTHIO)PYRROLES

**N. A. Nedolya[1], L. Brandsma[2], and S. V. Tolmachev[1]**

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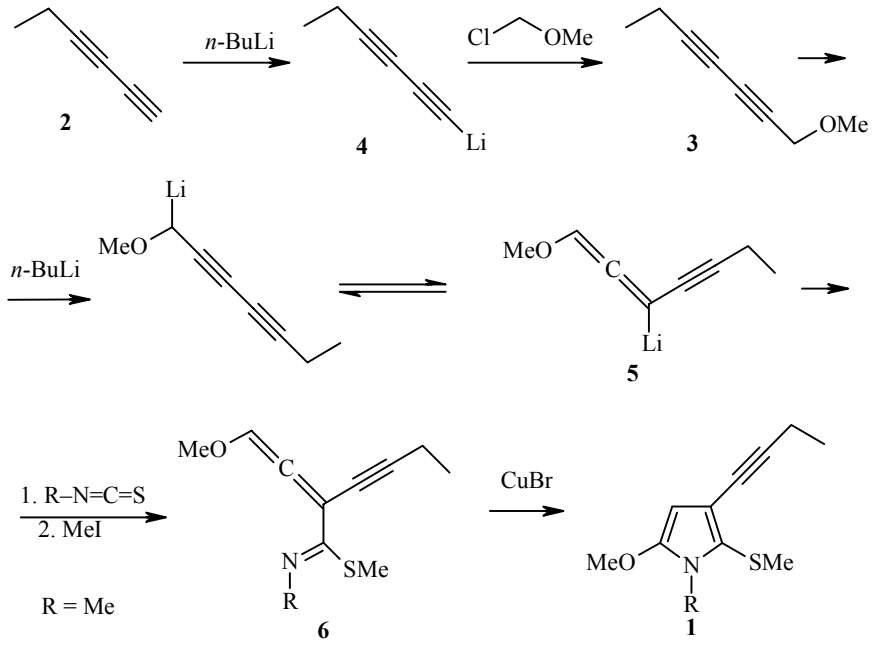
New experimental data have been obtained confirming the broad scope and great synthetic potential of our fundamentally new approach to the synthesis of heterocyclic structures, including pyrroles [1-3], involving the reactions of carbanions generated from alkynes and dienes with heterocumulenes. Lithiated diacetylenes have not yet been tried in this reaction.

The first example of previously unreported 3-(1-alkynyl)pyrroles, namely, 3-(1-butynyl)-5-methoxy-1-methyl-2-(methylthio)pyrrole (**1**) was synthesized from 1,3-hexadiyne (**2**) and methyl isothiocyanate in a single procedure involving six steps in one flask. 1-Methoxy-2,4-heptadiyne (**3**) required for formation of the pyrrole ring is readily obtained from 1-lithium 1,3-hexadiyne (**4**) and chloromethoxymethane. Deprotonation of




[1] A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch, Russian Academy of Sciences, 664033 Irkutsk, Russia; e-mail: nina@irioch.irk.ru. [2] Julianalaan 273, 3722 GN, Bilthoven, The Netherlands; e-mail: l.brandsma@wxs.nl. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 843-845, June, 2002. Original article submitted March 14, 2002.

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heptadiyne **3** by butyllithium, subsequent reaction of intermediate **5** with isothiocyanate (R = Me), and alkylation of the adduct with methyl iodide leads to methyl 2-(1-butynyl)-4-methoxy-N-methyl-2,3-butadienimidothioate (**6**), which cyclizes in the presence of catalytic amounts of CuBr to give pyrrole **1**.

The scope of this approach to the synthesis of 3-(1-alkynyl)pyrroles is probably not limited to the example given and there are no obvious limitations to its extension to other isothiocyanates and diynes. Furthermore, the use of other electrophiles instead of methoxychloromethane in the reaction with intermediate **4** should permit the ready variation of substituents at C(5) of the pyrrole ring.

**3-(1-Butynyl)-5-methoxy-1-methyl-2-methylthiopyrrole (1).** A solution of *n*-BuLi (0.07 mol) in hexane (42 ml) was added to a solution of diyne **2** (5.6 g, 0.07 mol) in THF (50 ml) cooled to -100°C. After rapidly raising the temperature to -70°C, chloromethoxymethane (5.5 g, 0.07 mol) was added to the reaction mixture and warmed to 40°C over 3-5 min. The reaction mixture was recooled to -100°C. A solution of *n*-BuLi (0.07 mol) in hexane (42 ml) was added and stirred for 10 min at from -75 to -75°C. The reaction mixture was cooled to -90°C and a solution of methyl isothiocyanate (4.5 g, 0.06 mol) in THF (10 ml) was added. Cooling was terminated and methyl iodide (12 g, 0.08 mol) was added at -25°C. The mixture was then warmed to 14°C and CuBr (1.2 g) was added. After slowly raising the temperature to 20°C, the reaction mixture was heated for 15 min at 30°C, cooled to room temperature, and treated with a solution of sodium cyanide (2 g) in saturated aq. $NH_4Cl$ (~100 ml). After 10 min stirring, the organic layer was separated. The aqueous layer was treated with three 50-ml ether portions. The combined organic fraction was dried over $MgSO_4$. The solvents were removed at reduced pressure. The residue was distilled in vacuum to give 2.4 g (~19%) pyrrole **1**; bp ~80°C (0.8 mm Hg). $^1H$ NMR spectrum ($CCl_4$, 90 MHz), δ, ppm: 1.22 (3H, t, Me); 2.20 (3H, s, SMe); 2.48 (2H, q, $CH_2$); 3.45 (3H, s, NMe); 3.78 (3H, s, OMe); 5.25 (1H, s, CH=). Found, %: C 63.25; H 7.29; N 6.52; S 15.15. $C_{11}H_{15}NOS$. Calculated, %: C 63.12; H 7.22; N 6.69; S 15.32.

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