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Synthesis of Derivatives of 2-Imino-5,6-dihydro-2*H*-thiopyran from 1-Heteroalkyl-1,3-butadienes and Isothiocyanates

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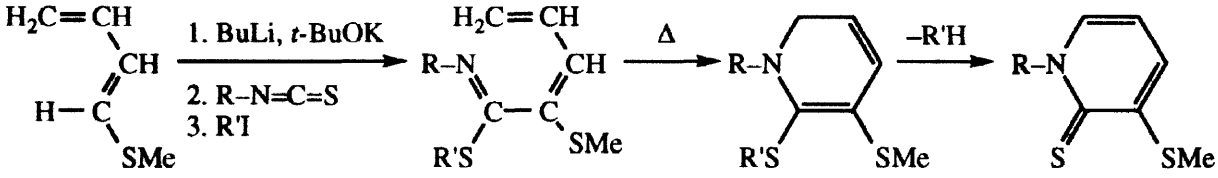
Abstract: A number of derivatives of 2-imino-5,6-dihydro-2*H*-thiopyran have been obtained in fair to good yields by treating the adducts from the α-metallated dienes H_2C=CH–CH=C(M)X (X = OCH_3 or SCH_3) and isothiocyanates with a calculated amount of dilute acid.

Recently,[1] we communicated the synthesis of 1,2-dihydropyridine derivatives and 2*H*-pyridinethiones. The precursors were obtained by reaction of α-metallated *E*-1-methylthio-1,3-butadiene (**1**, X = SCH_3) with alkyl isothiocyanates and subsequent *S*-alkylation of the adducts (see Scheme 1):



Scheme 1

In the present letter we report some results obtained by hydrolyzing the adducts (**2**, X = OCH_3, SCH_3) of metallated 1-methoxy-1,3-butadiene or its sulfur analogue with the stochiometrical amount of dilute acid. The sequence of reactions starting with **1** and isothiocyanates as shown in Scheme 2 led to the heterocyclic

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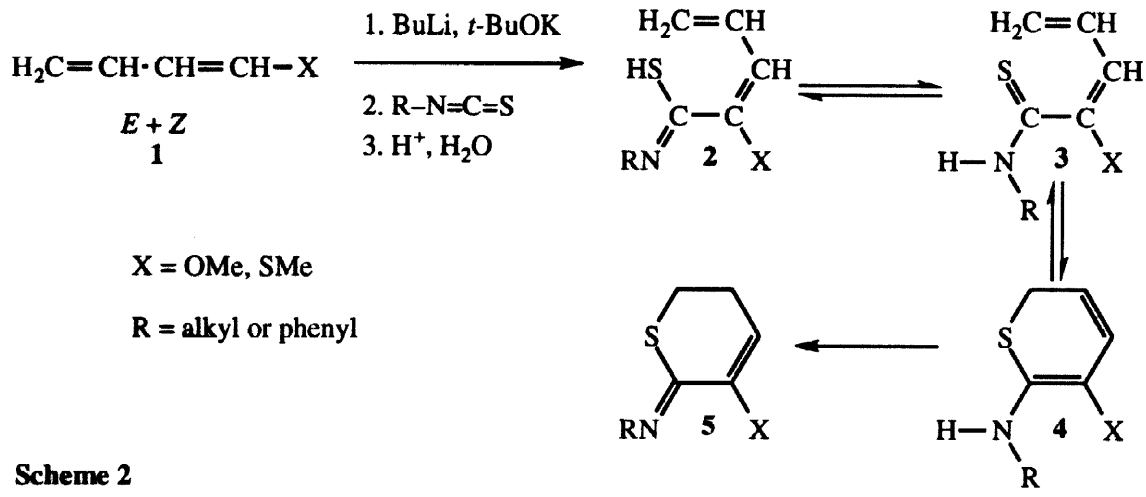
systems **5**. We presume that initially an equilibrium mixture of **2** and **3** is formed, in which the latter undergoes electrocyclization to the 2*H*-thiopyran **4**, which tautomerizes to imino-thiopyran **5**.



Scheme 2

To a solution of 0.10 mol of *n*-BuLi in ~65 ml of hexane was added with cooling below –85 °C (internal) a solution of 0.10 mol of *t*-BuOK in 150 ml of THF. Subsequently 0.10 mol of 0.12 mol of the *E/Z* mixture of the hetero-substituted butadiene **1** (X = OCH_3, ratio ~ 60 : 40; X = SCH_3, ratio ~ 90 : 10)[2,3] was introduced within a few seconds with vigorous stirring, while maintaining the temperature below –80 °C. After an additional 5 min (in the case of X = SCH_3 a very thick white suspension had formed) a mixture of 0.10 mol of phenyl isothiocyanate and 30 ml of THF was introduced very quickly. After about 15 min (without external cooling, in the case X = SCH_3, the solid had dissolved completely), a cold (0 °C) solution of 0.21 mol of hydrochloric acid in 100 ml of water was added with vigorous stirring and cooling, so that the internal temperature was kept below 5 °C. The organic layer and two ethereal extracts were dried over K_2CO_3 and then concentrated under reduced pressure. After standing for ~1 h at room temperature much solid product had formed. The solids were isolated by repeated washing the mixture with pentane followed by crystallization from diethyl ether. The ^1H and ^{13}C NMR-spectra were in agreement with the assumed structures **5**, X = OCH_3 or SCH_3, R = Ph. Microanalyses gave satisfactory results. Yields were about 80% for X = OCH_3 and 85% for X = SCH_3.

Compound **5** (X = OCH_3, R = Ph) has m.p. 63-64 °C. ^1H NMR-spectrum (90 MHz, CCl_4): δ = 2.63 (m, 2 H, CH_2), 2.83 (m, 2 H, CH_2), 3.70 (s, 3 H, OMe), 5.55 (t, 1 H, CH=), 6.83-7.40 (m, 5 H, Ph) ppm.

Compound **5** (X = SCH_3, R = Ph) has m.p. 93-96 °C. ^1H NMR-spectrum (300 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, SMe), 2.68 (q, 2 H, CH_2), 2.92 (t, 2 H, CH_2), 6.16 (t, 1 H, CH=), 6.90 (d, 2 H, Ph), 7.10 (t, 1 H, Ph), 7.33 (t, 2 H, Ph) ppm.

^{13}C NMR-spectrum (75 MHz, $CDCl_3$): δ = 14.96 (SMe), 26.56 (CH_2), 26.77 (CH_2), 119.86, 124.33,

128.83, 136.04, 160.00 ppm.

The formation of these compounds may be visualized as a tautomerization of the initially formed protonation product **2**, followed by cyclization to **4** (compare ref. 4) and final tautomerization of the latter.

The presence of **3**, X = SCH_3, R = *i*-C_3H_7 in a product mixture, obtained by a similar procedure using *i*-propyl isothiocyanate was indicated by the NMR-spectrum (90 MHz, CCl_4), which showed the following signals: 1.35 (d, 6 H), 2.15 (s, SCH_3), 4.70 (m, NCH), 5.60-6.00 (m, H_2C=), 6.96-7.15 (m, CH=), 8.00 (d, CH=), 8.80 (s, NH) ppm. In the case of X = SCH_3, R = CH_3, the thioamide **3** was present in traces only.

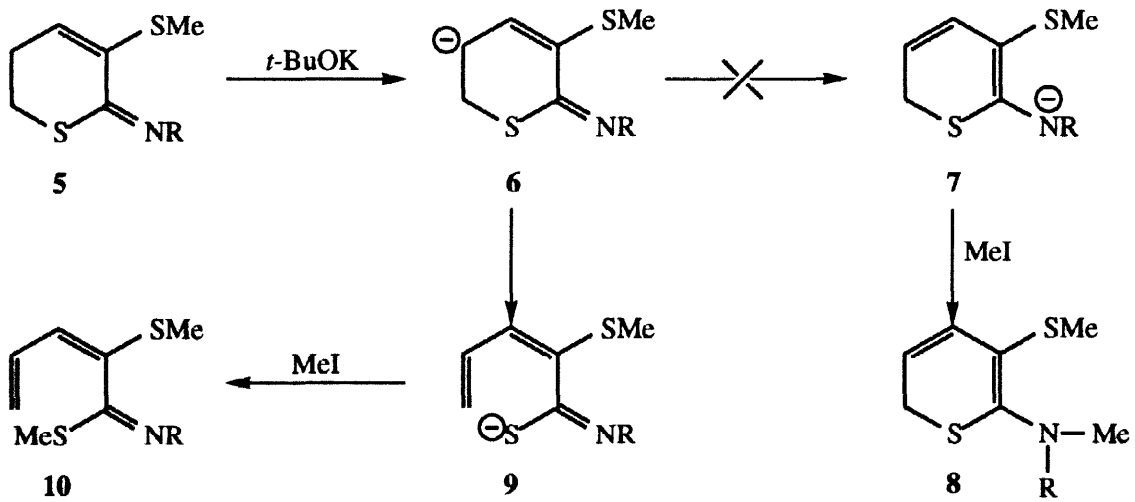
Compounds **5**, having X = SCH_3 and R = CH_3 or *i*-C_3H_7 were isolated in a reasonably pure state (satisfactory microanalytical results) by high-vacuum distillation.

Compound **5** (R = CH_3, X = SCH_3), b.p. ~100 °C/0.5 mm Hg, n^{20}_D 1.636, was obtained in 64% yield. ^{1}H NMR-spectrum (300 MHz, $CDCl_3$): δ = 2.05 (s, SCH_3), 2.47 (q, CH_2), 2.80 (t, CH_2), 3.10 (s, NCH_3), 5.80 (t, CH=) ppm.

Compound **5** (R = *i*-C_3H_7, X = SCH_3), b.p. ~140 °C/1 mm Hg, n^{20}_D 1.5880, was obtained in 45% yield. ^{1}H NMR-spectrum (90 MHz, CCl_4): δ = 1.20 (d, 2 CH_3), 2.15 (s, SCH_3), 2.55 (m, CH_2), 2.93 (m, CH_2), 3.80 (m, NCH), 5.97 (t, CH=) ppm.

Dondoni[5] and Barluenga[6] et al. obtained compounds analogous to **5** by reaction of thioketones or aryl isothiocyanates, respectively, with the systems C=C–C=C=N– and C=C–C(N<)=C–.

In an attempt to convert **5** R = CH_3, X = SCH_3) into the 2-*N*,*N*-disubstituted thiopyran **8** (see Scheme 3) we treated **5** with potassium *tert*-butoxide in THF and subsequently added excess of methyl iodide.



Scheme 3

However, instead of **8** (R = CH_3) the azatriene **10** (R = CH_3) was obtained in a high yield, which led us to assume that **5** had undergone ring opening, possibly through intermediate **6**, with formation of the thioimidate **9** (R = CH_3). The alkylation product **10** (R = CH_3) was indentical with a sample prepared by α-metallation of

H_2C=CH–CH=CHSCH$_3$ and successive addition of CH_3N=C=S and CH_3I (compare ref. 1). An experiment with **5**, R = *i*-C_3H_7 similarly led to **10**, R = *i*-C_3H_7.

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