New synthesis of quinolines from lithiated allenes and isothiocyanates

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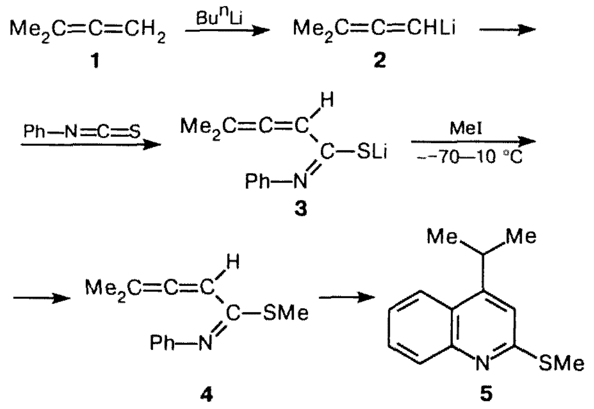
A new route was proposed for the synthesis of quinolines based on the reaction of lithiated allenes with phenyl isothiocyanate.

Key words: phenyl isothiocyanate, allenes, butyllithium, lithiation, alkylation, azatrienes, quinolines.

Data on the synthesis of quinolines by the reaction of organometallic compounds with isothiocyanates is lacking in the literature.[1]

We carried out for the first time the synthesis of quinolines, 4-isopropyl-2-methylthioquinoline (**5**) being an example, (Scheme 1) by adding lithium 3,3-dimethylallenide (**2**) to phenyl isothiocyanate followed by alkylation of thiolate **3** with methyl iodide to yield 1-aza-1,3,4-triene (**4**). Compound **4** was isolated in a quantitative yield. It transformed into quinoline **5** in an exothermal reaction, which started already at ~40 °C. The structure of compound **5** was confirmed by the data from IR and ^{1}H and ^{13}C NMR spectroscopy.

Scheme 1



Experimental

The IR spectra were recorded on a Specord IR-75 spectrophotometer in thin films. The NMR spectra were recorded on Varian EM-390 (90 MHz; ~20% solution in CCl_4; Me_4Si as the internal standard) and Bruker AC-300 (300 and 75 MHz for ^{1}H and ^{13}C NMR spectra, respectively; ~20% solution in $CDCl_3$; Me_4Si as the internal standard) spectrometers. A GLC analysis was carried out on a Varian 3400 gas chromatograph (flame ionization detector; 15 m×0.53 mm capillary column; the thickness of the DB-5 liquid phase was 1.5 μm; nitrogen was the carrier gas).

All operations were carried out in an atmosphere of nitrogen. 1,1-Dimethylallene (**1**) was synthesized according to the procedure reported in Ref. 2. Tetrahydrofuran was purified with mechanically dispersed KOH (~50 g L^{-1}) and by distillation over $LiAlH_4$ in the presence of benzophenone in an atmosphere of nitrogen. Butyllithium (1.6 *M* solution in hexane) was supplied by Chemetall (Germany).

4-Isopropyl-2-methylthioquinoline (5). 1,1-Dimethylallene (**1**) (9.8 g, 0.14 mol) was added to a solution of Bu^nLi (0.11 mol) in dry THF (80 mL) and hexane (70 mL) cooled to −60 °C. The mixture was stirred at −30 °C for 50 min. Then the mixture was cooled to −100 °C, and a solution of phenyl isothiocyanate (13.5 g, 0.10 mol) in THF (~20 mL) was added portionwise (the temperature was maintained at −100 °C). The reaction mixture was kept for 15 min, during which its temperature increased to −70 °C. Then methyl iodide (19 g, 0.13 mol) was added. The mixture was stirred at 10 °C for 10—15 min and then diluted with cold water (~60 mL). The organic layer was separated. The aqueous layer was extracted with pentane and ether. The combined organic layers were dried with potassium carbonate, and the solvent was evaporated. Azatriene (**4**) was obtained in a yield of 21.7 g (100%), n_D^{20} 1.6054. ^{1}H NMR (90 MHz, CCl_4), δ: 6.65—7.30 (m, 5 H, Ph); 5.65 (m, 1 H, CH=); 2.32 (s, 3 H, SMe); 1.76 (s, 6 H, 2 Me).

After heating of compound **4** to ~40 °C, the exothermal heterocyclization started (the temperature increased spontaneously to ~245 °C). Distillation *in vacuo* gave 4-isopropyl-2-methylthioquinoline (**5**) in a yield of 16 g (74%), the purity was 96% (GLC), b.p. 125—145 °C (~0.5 Torr), n_D^{20} 1.6285. Found (%): C, 71.46; H, 6.93; N, 6.48; S, 15.24. $C_{13}H_{15}NS$. Calculated (%): C, 71.89; H, 6.91; N, 6.45; S, 14.75. IR, ν/cm^{-1}: 600 w, 680 w, 750, 830 v.w, 860, 900, 960 w, 1020 w,

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1070, 1100, 1140, 1160, 1290, 1375 w, 1400, 1450 w, 1490 v.w, 1540, 1590, 2860, 2920, 2960, 3050. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.11 (dd, 1 H, 8-H); 7.95 (dd, 1 H, 5-H); 7.65 (td, 1 H, 7-H); 7.44 (td, 1 H, 6-H); 7.24 (s, 1 H, 3-H); 3.58 (m, 1 H, CH); 2.79 (s, 3 H, SMe); 1.36 (d, 6 H, 2 Me). ^{13}C NMR, δ: 159.31 (2-C); 152.70 (8a-C); 148.37 (4-C); 128.57, 124.46, 122.79 (5-C—8-C); 124.40 (4a-C); 116.04 (3-C); 27.82 (CH); 22.31 (Me).

References

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