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EXAMPLE OF THE SYNTHESIS OF QUINOLINES BY THE REACTION OF LITHIATED ALLENES WITH PHENYL ISOTHIOCYANATE: 2-METHYLTHIO-4-CYCLOHEXYLQUINOLINE

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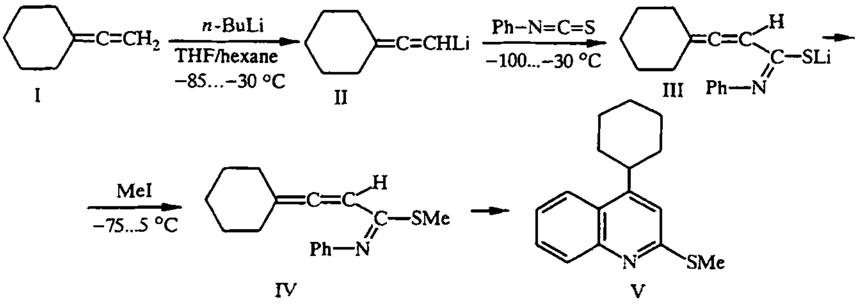
The Skraup and Doebner–Miller methods and also their many variations have found the widest use in the synthesis of quinolines [1]. There are no data in the literature on the use of isothiocyanates and organometallic compounds in the synthesis of quinolines.

We showed for the first time that the reaction of lithiated allenes with phenyl isothiocyanate opens up a fundamentally new path to substituted quinolines [2]. Thus, the previously unknown 2-methylthio-4-cyclohexylquinoline (V) was obtained in a single preparative stage with yields of up to 75% by the addition of lithiovinylidenecyclohexane (II) to phenyl isothiocyanate followed by methylation of the intermediate lithium thiolate (III):



The 1,3,4-azatriene (IV) was isolated with a quantitative yield. The structure of compounds (IV, V) was confirmed by elemental analysis and ^{1}H and ^{13}C NMR spectroscopy.

The ^{1}H and ^{13}C NMR spectra were recorded on Varian EM-390 (90 MHz, 20% solution in carbon tetrachloride, internal standard TMS) and Bruker AC-300 (^{1}H, 300 MHz; ^{13}C, 75 MHz, 20% solution in deuterochloroform, internal standard TMS). Gas-liquid chromatography was carried out on a Varian 3400 gas chromatograph (flame-ionization detector, capillary column, 15,000 × 0.53 mm, coated with 1.5 μ of DB-5, carrier gas, nitrogen).

All the operations were conducted in an atmosphere of nitrogen. The vinylidenecyclohexane (I) was synthesized by the method in [3]. The tetrahydrofuran was shaken with mechanically dispersed potassium hydroxide (50 g/liter) and distilled over lithium aluminum hydride in the presence of benzophenone in an atmosphere of nitrogen. The butyllithium (a 1.6 M solution in hexane) was supplied by Chemetall (Germany).

2-Methylthio-4-cyclohexylquinoline (V). To a solution of 0.05 mole of *n*-butyllithium in 80 ml of dry THF and 35 ml of hexane, cooled to −85°C, we added 0.07 mole of the vinylidenecyclohexane (I). The mixture was stirred at −35 to −30°C for 2 h. It was then recooled to −100°C, and a solution of 0.05 mole of phenyl isothiocyanate in 10 ml of THF was

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added in small portions while the temperature was kept in the range of −100 to −95°C. The cooling was then removed. After the temperature had risen to −30°C (25 min) the reaction mixture, which was a light-cream suspension, was recooled to −75°C, and 0.07 mole of methyl iodide was added. When the temperature had increased to 5°C, the vigorously stirred reaction mixture was treated with 60 ml of cold water. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic fraction was dried with potassium carbonate. After evaporating the solvent on a rotary evaporator we obtained 12.9 g (100%) of the azatriene (IV) (a light-colored mobile liquid, n_D^{20} 1.6085). ^{1}H NMR spectrum (90 MHz, δ, ppm): 5.70 m (1H, CH=); 2.35 s (3H, SMe), 2.20 m, 1.60 m [10H, $(CH_2)_5$]; 7.30-6.65 m (5H, Ph).

After heating the azatriene to 200°C and then distilling we obtained 9.6 g (75%) of the quinoline (V), which crystallized at room temperature; mp 67°C (from ethanol). ^{1}H NMR spectrum (300 MHz, δ, ppm): 7.15 s (1H, $H_{(3)}$); 8.00 t (2H, $H_{(5,8)}$); 7.44 t (1H, $H_{(6)}$); 7.63 t (1H, $H_{(7)}$); 3.24 s (1H, CH); 1.84-2.06 m, 1.47-1.65 [10H, $(CH)_2)_5$]. ^{13}C NMR spectrum (75 MHz, δ, ppm): 159.50 ($C_{(2)}$), 116.79 ($C_{(3)}$), 148.37 ($C_{(4)}$), 124.60 ($C_{(4a)}$), 152.01 ($C_{(8a)}$), 128.78, 124.60, 122.91 ($C_{(5-8)}$), 38.56, 33.23, 26.73, 26.13 (cyclohexyl), 12.62 (SMe).

Found %: C 74.35; H 7.69; N 6.00; S 12.98. $C_{16}H_{19}NS$. Calculated %: C 74.71; H 7.39; N 5.45; S 12.45.

REFERENCES

1. D. Barton and W. D. Ollis (eds.), Comprehensive Organic Chemistry. Vol. 8. Nitrogen-Containing Heterocycles [Russian translation], P. G. Sams (ed.) [translation N. K. Kochetkov (ed.)], Khimiya, Moscow (1985), pp. 196-255.
2. L. Brandsma, N. A. Nedolya, R. J. de Lang, and B. A. Trofimov, Izv. Akad. Nauk. Ser. Khim., No. 12, 3024 (1996).
3. L. Brandsma and H. D. Verkruijsse, Studies in Organic Chemistry. 8. Synthesis of Acetylenes, Allenes, and Cumulenes. A Laboratory Manual, Elsevier, Amsterdam−Oxford−New York (1981), pp. 158-159.