

SHORT
COMMUNICATIONS

Controlled Cyclization of *N*-Aryl-5,5-dimethyl-1-(methylsulfanyl)hexa-2,3-dien-1-imines: Highly Selective Synthesis of Pyrroles and Quinolines

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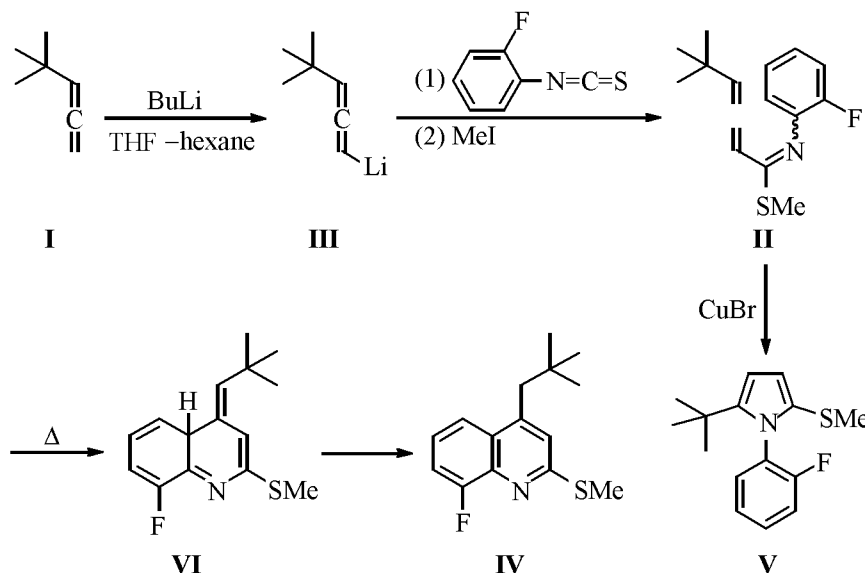
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We showed recently [1, 2] that *N*-phenyl-5,5-dimethyl-1-(methylsulfanyl)hexa-2,3-dien-1-imine prepared by reaction of γ -lithiated 4,4-dimethyl-1,2-pentadiene (**I**) with phenyl isothiocyanate cleanly cyclized at heating into 2-(methylsulfanyl)-4-neopentylquinoline (yield >80%).

We found that *N*-aryl-5,5-dimethyl-1-(methylsulfanyl)hexa-2,3-dien-1-imines (**II**) that fast and quantitatively formed in reaction between 1-lithio-4,4-dimethylpenta-1,2-diene (**III**) and aryl isothiocyanates, e.g., with 2-fluorophenyl isothiocyanate, can readily

transform in high yield and with great selectivity not only into unavailable 2-(methylsulfanyl)-4-neopentylquinolines (**IV**), but also into no less exotic 1-aryl-5-*tert*-butyl-2-(methylsulfanyl)pyrroles (**V**).

A short (2-3 min) heating of compound **II** initiates exothermal electrocyclization reaction accompanied with aromatization of intermediate **VI**. As a result quinoline **IV** is furnished in ~90% preparative yield. In contrast, mild warming of compound **II** in the presence of CuBr (50–60°C, 4–5 h) affords exclusively pyrrole **V** in ~88% yield.



The reaction is general (confirmed by numerous examples) and can be regarded as a new, simple and highly selective preparation method for 4-neopentylquinolines and 1-aryl-5-*tert*-butylpyrroles from the same precursors.

The lithiation of 4,4-dimethyl-1,2-pentadiene (**I**) was carried out by treating with butyllithium in THF-hexane mixture by a known method [1]. The isothiocyanate addition to a solution of intermediate **III** cooled to -100°C followed by adduct alkylation with

methyl iodide afforded compound **II** in a quantitative yield. The structure of the latter compound was confirmed by ^1H NMR spectrum.

2-(Methylsulfanyl)-4-neopentyl-8-fluoroquinoline (IV), **2-(tert-butyl)-5-(methylsulfanyl)-1-(2-fluorophenyl)pyrrole (V)**. To a solution of 56 mmol of BuLi in 35 ml of hexane and 65 ml of THF was added 7.5 g (78 mmol) of allene **I** at 30°C (the temperature rose to 5°C). The solution was stirred for 35 min at -40...-30°C, the reaction mixture was cooled to -100°C, and a solution of 7.7 g (50 mmol) of 2-fluorophenyl isothiocyanate in 10 ml of THF was quickly poured to the reaction mixture (reaction with strong heat evolution: Notwithstanding cooling the temperature rose to -40°C). After 10 min of stirring at -30°C to the reaction mixture was added 16.6 g (115 mmol) of MeI, the mixture was heated to 45°C and then stirred for ~50 min at 35-45°C. The reaction mixture was divided in two equal portions. The first one was treated first with water, and then extracted with ethyl ether (2-50 ml). The combined organic solutions were dried over K_2CO_3 , the solvent was removed on a rotary evaporator. We obtained as a residue 6.63 g (~100%) of nonviscous fluid whose ^1H NMR spectrum corresponded to *N*-(2-fluorophenyl)-5,5-dimethyl-1-methylsulfanylhexa-2,3-dien-1-imine (**II**) (a mixture of *syn*- and *anti*-isomers). ^1H NMR spectrum, δ , ppm: 6.95 m (4H, Ph), 5.83 d (1H, CH=), 5.50 d (1H, CH=), 2.42 s, 2.36 s (3H, SMe), 1.30 s, 1.12 s (9H, *t*-Bu).

To compound **II** 10 ml of toluene was added, the solution was heated for 2-3 min, and on completion of the exothermal electrocyclization reaction the product was distilled in a vacuum. Yield of quinoline **IV** 5.9 g (90%), content of the main substance 96.5% (GLC), bp ~170°C (~1 mm Hg.), n_D^{20} 1.5625. ^1H NMR spectrum, δ , ppm: 7.60 m, 7.22 m (3H, Ph), 6.95 s (1H, 3-CH=), 2.75 s (2H, CH₂), 2.70 s (3H, SMe), 0.95 s (9H, *t*-Bu). Found, %: C 68.51; H 6.99; F 7.01; N 5.44; S 12.05. $\text{C}_{15}\text{H}_{18}\text{FNS}$. Calculated, %: C 68.40; H 6.89; F 7.21; N 5.32; S 12.18.

To another portion of the reaction mixture was added a solution of powdered CuBr (3.86 g) and LiBr

(4.95 g) in 50 ml of THF, and the mixture was heated at stirring to 50-60°C for ~4-5 h. Then to the reaction mixture 10% solution of NaCN in 100 ml of saturated NH_4Cl solution was added, the stirring was continued for 5-10 min, the organic layer was separated, the water layer was extracted with ethyl ether (3-50 ml). The combined organic solutions were dried over CaCO_3 , the solution was passed through a column packed with neutral Al_2O_3 , the solvent was removed on a rotary evaporator. As a residue we observed 6.57 g (~100%) of pyrrole **V**, content of the main substance 96% (GLC). On vacuum distillation 5.8 g (88%) of product was obtained, bp ~130°C (~1 mm Hg), content of the main substance ~100% (GLC). IR spectrum, cm^{-1} : 540, 655, 670, 740, 800, 910, 945, 965, 1000, 1030, 1090, 1200, 1230, 1240, 1300, 1340, 1370, 1440, 1465, 1490, 1570, 2860, 2900, 2950, 3050. ^1H NMR spectrum, δ , ppm: 7.23 m (4H, Ph), 6.26 d (1H, CH=), 5.96 d (1H, CH=), 2.00 s (3H, SMe), 1.12 s (9H, *t*-Bu). Found, %: C 68.55; H 7.03; F 7.13; N 5.22; S 12.07. $\text{C}_{15}\text{H}_{18}\text{FNS}$. Calculated, %: C 68.40; H 6.89; F 7.21; N 5.32; S 12.18.

IR spectra were recorded on spectrophotometer Specord 75IR from thin films. ^1H NMR spectra were registered on spectrometer Varian EM-390 (operating frequency 90 MHz) from ~20% solutions in CCl_4 , internal reference TMS. 4,4-dimethylpenta-1,2-diene (**I**) and 2-fluorophenyl isothiocyanate were prepared by procedures from [3] and [1] respectively.

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REFERENCES

1. Nedolya, N.A., *Novel Chemistry Based on Isothiocyanates and Polar Organometallics*, Utrecht University, 1999, 144 p.
2. Nedolya, N.A., Brandsma, L., de Lang, R.-Zh., and Trofimov, B.A., *Zh. Org. Khim.*, 1997, vol. 33, p. 1437.
3. Brandsma, L. and Verkruijsse, H.D., *Synthesis of Acetylenes, Allenes and Cumulenes*, New York: Elsevier, 1981, p. 157.