

SYNTHESIS OF ROSETHIOPHENE, A NEW FLAVOUR COMPOUND

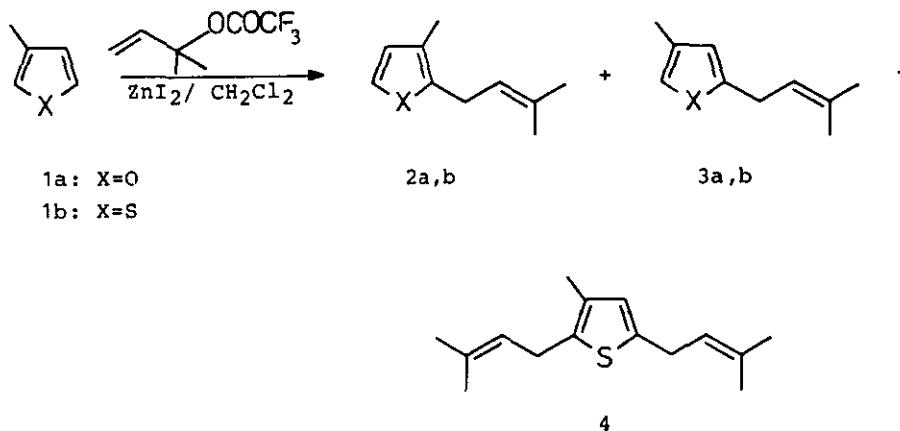
Zeinhom Mostafa Ismail and H. Martin R. Hoffmann*

Department of Organic Chemistry University of Hannover

Schneiderberg 1B, D-3000 Hannover, FRG

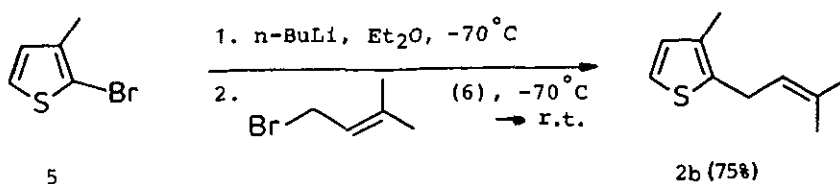
Abstract - Rosethiophene[3-methyl-2-(3-methyl-2-butenyl)thiophene] (2b) has been prepared by two routes and converted into the homogeraniol precursor (8).

The presence of sulfur in a molecule or the replacement of oxygen by sulfur is often assumed to have unpleasant olfactory consequences. We have recently synthesized rosefuran (2a) and some analogues via regiocontrolled prenylation of 3-methylfuran (1a)¹. We have now explored the prenylation of 3-methylthiophene (1b) and obtained the previously unknown rosethiophene (2b) and its isomer (3b) in a regiocontrolled reaction (2b:3b = 88:12), traces of the diprenylated product (4) were also formed.



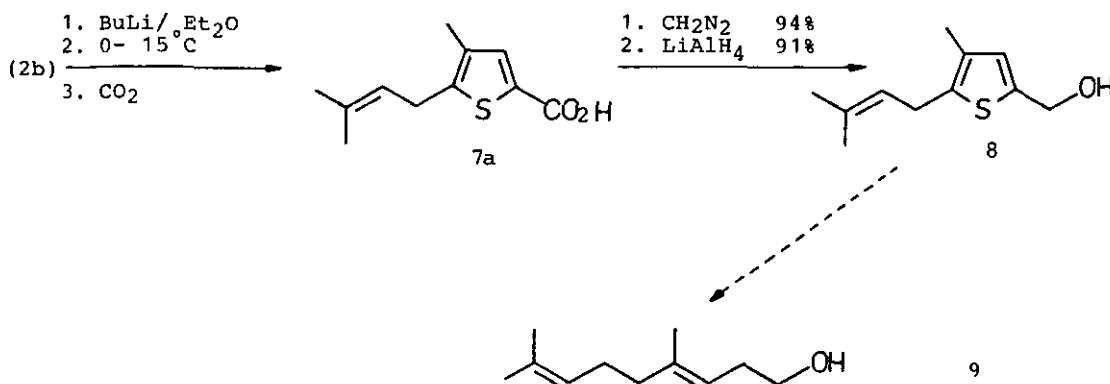
As the total yield of prenylation of (1b) was not promising (ca. 20%), we have prepared (2b) by another route.

2-Bromo-3-methylthiophene (5)² was metallated with *n*-butyllithium at low temperature, and the resulting carbanion was quenched with 1-bromo-3-methyl-2-butene (6), giving rosethiophene (2b) in good yield.



Rosethiophene (2b), which has not yet been found in nature³, appears to have little interest as a perfumery compound, but it is an interesting flavour compound (citrus, grapefruit, lime). It is noteworthy that another sulfur compound, i.e. 1-p-menthene-8-thiol, is a most powerful flavour compound which occurs naturally in grapefruit⁴.

(2b) was used as a starting material for the synthesis of (8). Metallation succeeded above 0°C and was regioselective, giving only the sulfur stabilized anion, which was carboxylated to give (7a) and then reduced to the alcohol (8), which is a potential precursor of homogaranol (9)^{3a,5}.



A solution of 12.3 g (69.6 mM) of (5) in abs. ether (50 ml) was introduced under argon into a 250 ml threenecked flask equipped with a thermometer, dropping funnel and magnetic stirrer. The solution was cooled to -70°C and n-BuLi (48 ml, 72 mM) in hexane was added dropwise at such a rate that the temperature did not exceed -68°C. After complete addition the temperature was kept at -70°C for 30 min and then a solution of (6) (10.3 g, 69.1 mM) in abs. ether (30 ml) was added dropwise within 20 min. The reaction mixture was left at -70°C for 2 h and allowed to reach 25°C overnight. After cautious addition of water, the organic layer was separated and the aqueous layer was re-extracted with ether. The combined organic phase was washed with aq. NaHCO₃, water and dried (Na₂SO₄). After evaporation of the solvent the residue was distilled giving (2b) (8.62 g, 51.9 mM) as a colorless oil of bp 70°C/2.5 torr. IR (neat) 2980 m, 2920 m, 2860 m, 1960 w, 1450 m, 1380 m, cm⁻¹. 90 MHz ¹H NMR (CDCl₃) δ 1.72 (br. s, 6 H, 2 Me), 2.15 (s, 3 H, Me), 3.38 (d, J = 7 Hz, 2 H), 5.16 - 5.44 (t of quin, J = 7 Hz, J = 1.5 Hz, olef. H), 6.75 - 6.96 (dd, AB system, J = 5 Hz, 2 H, arom). ¹³C NMR (CDCl₃) δ 137.8 s, 132.5 s, 131.9 s, 129.9 d, 122.7 d, 121.0 d, 26.8 d, 25.5 q, 17.6 q, 13.4 q.

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