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Preliminary communication

AN EFFICIENT ONE-POT SYNTHESIS OF 2,5-DISUBSTITUTED THIOPHENES FROM 1-PROPYNYLAMINES OR ALLENIC AMINES AND THIOCARBONYL COMPOUNDS

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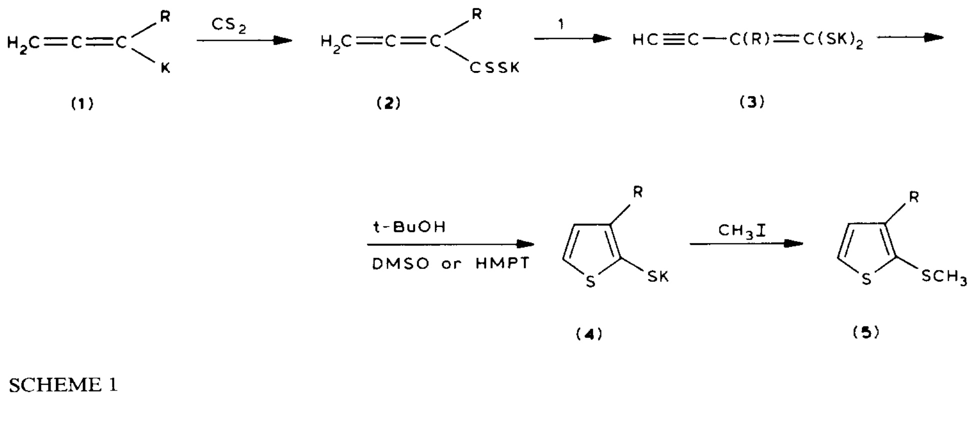
Summary

Metallation of the ynamine $CH_3C{\equiv}CNEt_2$ or the allenic amines $H_2C{=}C{=}CHNR_2$ ($R = CH_3$ or C_2H_5) with Schlosser's reagent BuLi · t-BuOK, followed by reaction with a thiocarbonyl compound $XCSSCH_3$ ($X = Me_2N$, Et_2N, CH_3S, t-Bu, O-t-Bu, Ph or 2-thienyl) and then addition of water, gives 2,5-disubstituted thiophenes (with Me_2N or Et_2N and X as substituents) in good yields.

A few years ago [1], we described the reaction of potassiated 2-alkynes and heterosubstituted allenes $(H_2\bar{C}{-}\bar{C}{=}\bar{C}{-}R)^- K^+$ (**1**) (R = primary alkyl, phenyl, OCH_3, SCH_3, CH_2NR_2 or NR_2) with carbon disulfide. In all cases the initially formed carbodithioate (**2**) underwent a very fast subsequent deprotonation at the terminal carbon atom with formation of the geminal dithiolate **3**. Upon addition of t-butyl alcohol (as proton donor) and a polar solvent (hexamethylphosphoric triamide or dimethylsulfoxide) cyclisation to the potassium salt of a 2-mercapto-3-substituted thiophene (**4**) occurred. After adding methyl iodide, this could be isolated as the methyl sulfide **5** (Scheme 1).



SCHEME 1

The reaction of the metallated acetylenes or allenes examined with other thiocarbonyl compounds (t-BuCSSCH$_3$, PhCSSCH$_3$, 2-thienyl-CSSCH$_3$, R'$_2$NCSSCH$_3$, CH$_3$SCSSCH$_3$ and t-BuOCSSCH$_3$) in general, proceeds analogously, except for the potassiated allenes H$_2$C=C=C(K)NR$_2$.

In this communication we consider the reaction of the metallated aminoallenes **2** with the thiocarbonyl compounds mentioned. Our results show that the regiochemistry with respect to the metallated aminoallenes is completely different from that observed in the reactions involving the other metallated acetylenes or allenes mentioned above.

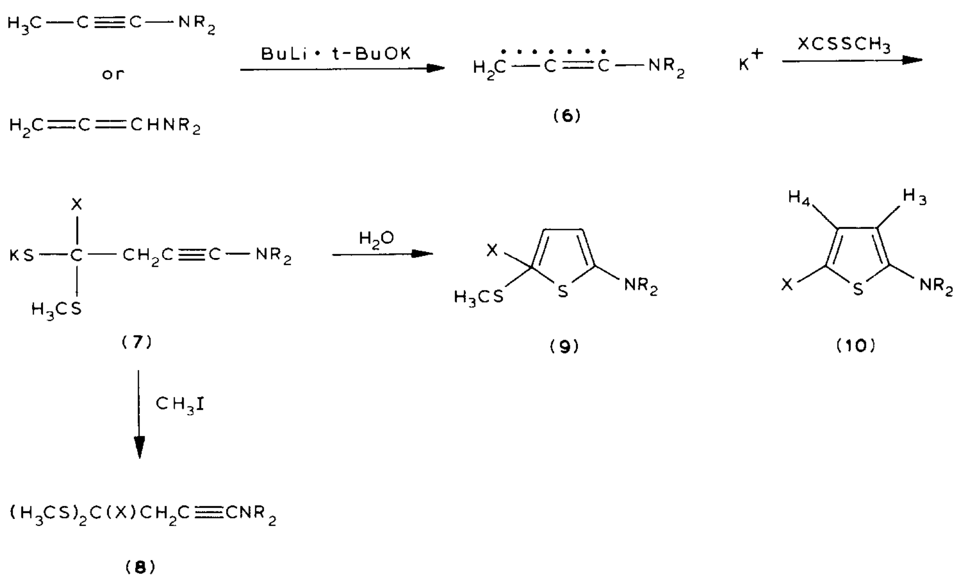
A 80/20 mixture (0.10 mol) of CH$_3$C≡CNEt$_2$ and H$_2$C=C=CHNEt$_2$ (prepared as described in ref. 2) or H$_2$C=C=CHNMe$_2$ (see also ref. 2) was added at −80°C to a solution of t-BuOK (0.10 mol) and BuLi (0.10 mol) in THF (80 ml) and hexane (70 ml) (compare refs. 3 and 4). After 5 min the thiocarbonyl compound (0.09 mol) was added (over 5 min), the temperature being allowed to rise to about −40°C. After 15 min, 20 ml of water was added and the mixture was vigorously stirred for 15 min at room temperature. More water was then added and the product was extracted with diethyl ether. After dyring of the extract over potassium carbonate, the solvent was removed under vacuum. Subsequent distillation of the remaining brown liquid afforded the 2,5-disubstituted thiophenes in good yields. The purity of the products was generally satisfactory, as indicated by ^{1}H NMR spectroscopy and mass spectroscopy. Analytically pure products were obtained by treating the distillates with aqueous 2*N* hydrochloric acid, extracting the aqueous layer with pentane (in order to remove other products without dialkylamino groups), and subsequently adding a dilute aqueous solution of potassium hydroxide. Comparison of the NMR spectra with those of the 2,3-disubstituted isomers showed that only the 2,5-disubstituted thiophenes **10** were present.

TABLE 1

PHYSICAL DATA OF THE 2,5-DISUBSTITUTED THIOPHENES OBTAINED

Thiophene derivative **10**		Yield (%)	b.p. (°C/mmHg)	n_D^{20}	^{1}H NMR chem. shifts [a]			
X	R				X	R	H(3)	H(4)
t-Bu	CH$_3$	85	55/0.1	1.5219	1.33(s)	2.80(s)	5.60(d)	6.33(d)
Ph	CH$_3$	72	92/0.5	–	7.2 (m)	2.73(s)	5.69(d)	6.90(d)
CH$_3$S	CH$_3$	72	48/0.1	1.5982	2.23(s)	2.76(s)	5.43(d)	6.54(d)
t-Bu	C$_2$H$_5$	90	62/0.1	1.5172	1.35(s)	1.16(t) 3.17(q)	5.67(d)	6.31(d)
Ph	C$_2$H$_5$	76	94/0.9	1.6372	7.1 (m)	1.07(t) 3.10(q)	5.57(d)	6.72(d)
CH$_3$S	C$_2$H$_5$	85	60/0.15	1.5782	2.20(s)	1.10(t) 3.17(q)	5.47(d)	6.55(d)
Et$_2$N	C$_2$H$_5$	70	78/0.1	1.5203	1.05(t) 2.96(q)	1.05(t) 2.96(q)	5.76(s)	
2-thienyl	C$_2$H$_5$	51	85/0.1	1.6245	6.67(m)	1.10(t) 3.10(q)	5.53(d)	6.53(d)
t-BuO	C$_2$H$_5$	65	78/0.1	1.5120	1.28(s)	1.05(t) 3.00(q)	5.55(d)	5.81(d)

[a] ~20% solutions in CCl$_4$ with tetramethylsilane, $\delta = 0$ ppm, as internal standard; for all compounds ^3J(CH(3)–H(4)) ≈ 4 Hz.



SCHEME 2. R = CH_3 or C_2H_5, X = Et_2N, CH_3S, O-t-Bu, t-Bu, Ph, or 2-thienyl.

Our results can be explained in terms of Scheme 2.

The intermediate **7** was trapped by adding methyl iodide to give **8** (X = t-Bu, R = C_2H_5) in an excellent yield. In order to investigate the possibility of an initial thiophilic attack with formation of $H_2C{=}C{=}C(NEt_2)S{-}\bar{C}(t\text{-}Bu)SCH_3$ and subsequent 2,3-sigmatropic rearrangements, t-BuCSSCH$_3$ was added at $-100\,^\circ C$ to a solution of $H_2C{=}C{=}C(K)NEt_2$, followed after a few seconds by methyl iodide. However, only **8** (X = t-Bu, R = C_2H_5) was isolated.

Our one-pot synthesis provides an attractive method for preparing 2,5-disubstituted thiophenes (Table 1), which until now have not been readily accessible. The starting compounds $CH_3C{\equiv}CNEt_2$ and $H_2C{=}C{=}CHNMe_2$ are readily available. The aminothiophenes are of interest in connection with cycloaddition reactions (compare ref. 5).

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