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Preliminary communication

SYNTHESIS OF 2,3-DISUBSTITUTED THIOPHENS VIA METALATED ACETYLENES AND ALLENES

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Summary

2,3-Disubstituted thiophen derivatives have been obtained in reasonable yields by treating 2-alkyne- and allene derivatives with butyllithium and potassium t-butoxide in tetrahydrofuran, adding carbon disulfide to the organometallic intermediate and then successively adding t-butyl alcohol, hexamethylphosphoric triamide and methyl iodide.

Although 3-metalated allenic hydrocarbons II (R = alkyl or aryl) have been known for several years [1] these organometallics have been less used in synthesis than 1-metalated allenes [2—5] RCH=C=CHM and metalated heterosubstituted allenes (II, R = O-alkyl, S-alkyl) [6,7]. In this communication we report a useful application of the 3-metalated allenic compounds II. Treatment of the 2-alkyne derivatives I with a 1/1 mixture of butyllithium (BuLi) and potassium t-butoxide (t-BuOK) in THF and hexane at −70 to −80°C for about 30 min resulted in complete metalation. The formation of the intermediate II was demonstrated by addition of bromohexane, which gave an 80/20 mixture of the corresponding allene and acetylene derivatives (for R = CH_3) in a good yield.

A synthetically more interesting result was obtained from the reaction with carbon disulfide. This compound reacted vigorously with the solutions of II, giving dark brown solutions. Subsequent addition of t-butyl alcohol (t-BuOH) and methyl iodide did not yield any dithioester $RC(CSSCH_3)=C=CH_2$ or $RC{\equiv}CCH_2C(=S)SCH_3$, but 2,3-disubstituted thiophens were isolated in reasonable (ca. 50%) yields. We assume that the primary reaction product with CS_2 is immediately metalated further, either by the t-butoxide present in solution, or by III, affording IV: this conversion is to some extent analogous with the formation of geminal dithiolates $XYC=C(S^-)_2$ from "active" methylene

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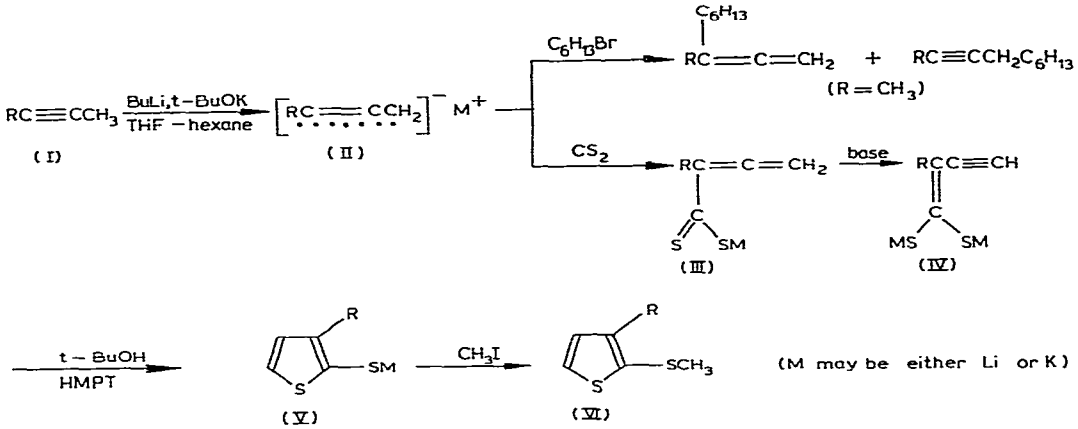
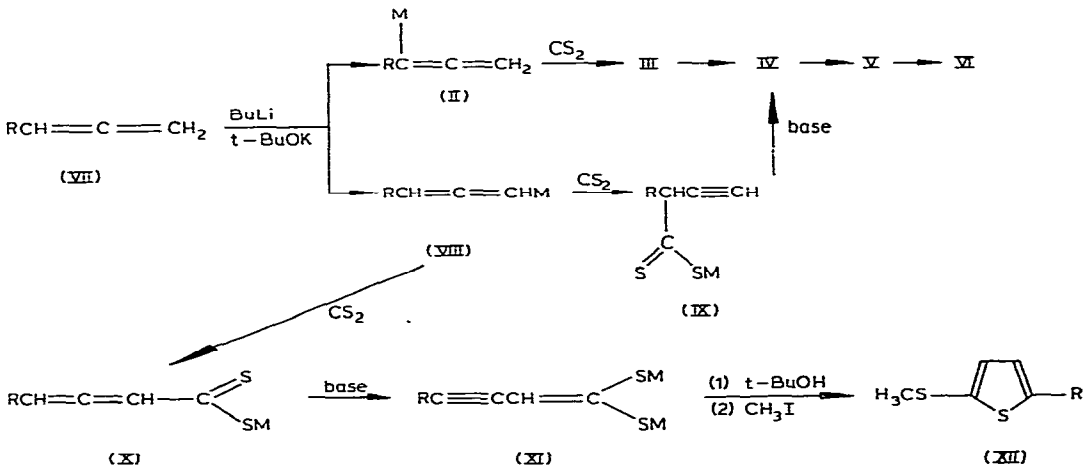


compounds $XYCH_2$, CS_2 and base (compare for instance refs. 8—10. In one case, viz. R = CH_3, IV was methylated prior to addition of t-BuOH, which gave the enyne $(CH_3S)_2C{=}C(CH_3)C{\equiv}CH$ in about 60% yield.

These results are totally different from those obtained from lithiated 2-alkynes (II, M = Li) (prepared by addition at 25°C of 2-alkynes to butyllithium in THF): mainly intractable tars were obtained in the latter case, the thiophen derivative being completely absent.

Allenes $RCH{=}C{=}CH_2$ may be deprotonated either terminally or on carbon atom 3, dependending on the nature of R [2,6,7] and the result of the reactions of the metalated allene with CS_2 in the cases where R represents a heterosubstituent might therefore differ from that for R = alkyl. In practice, however, both the heterosubstituted allenes VII, R = CH_3S or CH_3O and the alkylallene VII, R = C_4H_9 gave 2,3-disubstituted thiophens VI. The similar results can be explained by assuming that the most likely routes for R = CH_3O or CH_3S and for R = alkyl coincide at compound IV.



From t-butylallene (VII, R = Bu^t), however, the 2,5-disubstituted thiophen XII was obtained and VI was completely absent in the crude product. In the case steric hindrance by the t-butyl group causes VIII to react exclusively on the terminal carbon atom with CS_2. The scope of this new thiophen synthesis as well as further applications of metalated 2-alkynes are under investigation.

Experimental

To a cold (—80°C) solution of 0.05 mol of t-BuOK in 60 ml of THF was added 0.05 mol of the acetylene I or the allene VII. A solution of 0.05 mol of n-butyllithium in about 35 ml of hexane was then added dropwise during 10 min, the temperature of the mixture being kept between —70 and —80°C. After 40 min a solution of 0.03 mol of carbon disulfide in 5 ml of THF was added within 1 min. During this addition the temperature was maintained between —60 and —70°C. After stirring for an additional period of 20 min (—70°C) a mixture of 0.07 mol of t-BuOH, and 5 ml of THF was introduced at about —70°C. The cooling bath was removed, 20 ml of HMPT were added and the temperature was allowed to rise to about 0°C. Methyl iodide (0.04 mol) was then added dropwise during 10 min. After this addition, water (200 ml) was added and the organic products were extracted with diethyl ether. The combined extracts were washed with water, dried over potassium carbonate and then concentrated in vacuo. Pentane (100 ml) was added to the remaining oil. After vigorous shaking, the pentane solution was poured off from the tar and again concentrated in vacuo. Distillation of the residue gave the thiophen derivative. The purities (^{1}H NMR and GLC) were at least 95%.

TABLE 1

SYNTHESIS OF THIOPHEN DERIVATIVES VI AND XII FROM 2-ALKENES AND ALLENES

Starting compound	R	b.p. (°C/mmHg)	n_D^{20}	Products VI and XII [b] yield (%) [a]
I	CH_3	86/25	1.5762	52
	C_2H_5	49/0.9	1.5664	50
	$N(C_2H_5)_2$	91/2	1.5587	49
	$CH_2N(C_2H_5)_2$	84/0.2	1.5397	51
	SCH_3	71/1	1.6373	51
	Ph	106/0.3	1.6462	48
VII	SCH_3	95/25	1.6375	49
	OCH_3	48/0.3	1.5788	47
	C_4H_9	92/1.5	1.5456	47
	cyclo-C_6H_{11}	64/0.7	—	49 [c]
	t-Bu	89/1.5	1.5413	42

[a] Yields are based on the starting compounds (0.05 mol). [b] Only VII, R = t-Bu gave compound XII. [c] About 15% 2,5-disubstituted thiophen present

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