CHEMISTRY LETTERS, pp. 853-854, 1975. Published by the Chemical Society of Japan

A NEW METHOD FOR THE SYNTHESIS OF 3-ALKYLFURAN AND 2,4-DIALKYLFURAN

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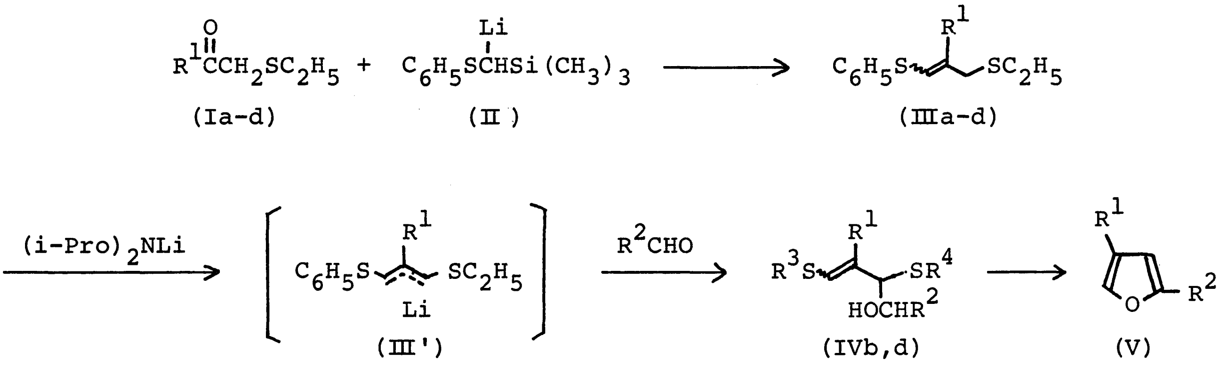
A convenient method for the preparations of 3-alkylfuran and 2,4-dialkylfuran has been established via three step-procedures starting from α-(alkylthio)carbonyl compounds.

We wish to report a convenient method for the preparations of 3-alkylfuran and 2,4-dialkylfuran via three step-procedures starting from α-(alkylthio)carbonyl compounds. The whole reaction schemes are depicted as follows.



$R^3=C_6H_5$ $R^4=C_2H_5$ and $R^3=C_2H_5$ $R^4=C_6H_5$

Concerning the first step, Carey and Court recently reported that the lithium salt of phenyl trimethylsilylmethyl sulfide(II) reacted with carbonyl compounds to afford the corresponding phenyl vinyl sulfides.1) We examined the similar reaction of (II) with α-(alkylthio)carbonyl compounds and it was found that under modified reaction conditions the desired condensation products(III) were obtained in fairly good yields. For example, to a THF solution of the lithium salt(II), prepared by treating phenyl trimethylsilylmethyl sulfide with n-butyllithium in THF at 0°C for 4 hr, by the addition of an n-hexane solution of 2-ethylthiocyclohexanone at -78°C and by the subsequent stirring for 20 hr gradually rising to room temperature, 1-phenylthiomethylene-2-ethylthiocyclohexane(IIIa) was obtained in 65% yield. Similarly, by the reaction of ethylthioacetone(Ib), phenylthioacetone(Ic) and 1-ethylthio-4-phenylbutan-2-one(Id) with the lithium salt(II), the corresponding phenyl vinyl sulfides(IIIb), (IIIc) and (IIId) were obtained in 60, 15 and 67% yields respectively. Lithiation of (III) was easily performed by adding to a THF solution of lithium diisopropylamide and the subsequent treatment of this lithium salt(III') with aldehydes afforded the corresponding alcohols(IVb) and (IVd) in high yields as summarized in Table 1.2)

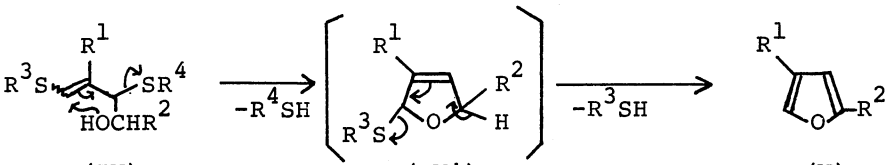
Table 1. Yields of Alcohols (IV)

(III)	R^2CHO	Reaction Conditions	(IV)	Yield (%)
(IIIb)	C_6H_5CHO	-78°C, 15 min.$^{a)}$, -78°C, 15 min.$^{b)}$	(IVb-1)	quant.
(IIIb)	$C_6H_5CH_2CH_2CHO$	-78°C, 25 min.$^{a)}$, -78°C, 45 min.$^{b)}$	(IVb-2)	89
(IIId)	HCHO	0°C, 45 min.$^{a)}$, -78°C, 15 min.$^{b)}$	(IVd)	84

a) Lithiation conditions. b) Addition reaction conditions.

c) Formaldehyde was generated by thermal decomposition of paraformaldehyde.[3)]

The final step, the desired 2,4-dialkylfuran or 3-alkylfuran was obtained by treating the alcohol(IV) with $CuCl_2$ or $HgCl_2$ in the presence of collidine as a hydrogen chloride catcher (Table 2). For example, 2-phenethyl-4-methylfuran was obtained in 52% yield by the reaction of (IVb-2) with 2 equimolar amounts of $CuCl_2$ in the presence of 4 equimolar amounts of collidine in boiling THF for 3 hr.

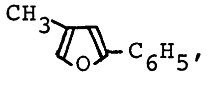


(IV) (IV') (V)

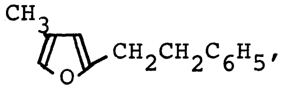
Table 2. Synthesis of 2,4-dialkylfuran and 3-alkylfuran

(IV)	Additive	Solvent	Time (hr)	(V)	Yield (%)
(IVb-1)	$HgCl_2$	CH_3CN	3	(Vb-1)	28
(IVb-2)	$CuCl_2$	THF	4	(Vb-2)	52
(IVb-2)	$HgCl_2$	CH_3CN	4	(Vb-2)	49
(IVd)	$HgCl_2$	CH_3CN	3	(Vd)	62

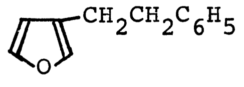
(Vb-1)=



(Vb-2)=



(Vd)=



We are currently investigating the application of the present method to the synthesis of natural occurring 3-substituted furans.

Acknowledgement: We thank Professor T. Mukaiyama of Tokyo University for helpful discussions.

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(Received May 12, 1975)