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SYNTHESIS OF 1-METHOXY-2-OXOALKYL PHENYL SULFIDES AND THEIR SYNTHETIC APPLICATION TO 3-SUBSTITUTED FURANS

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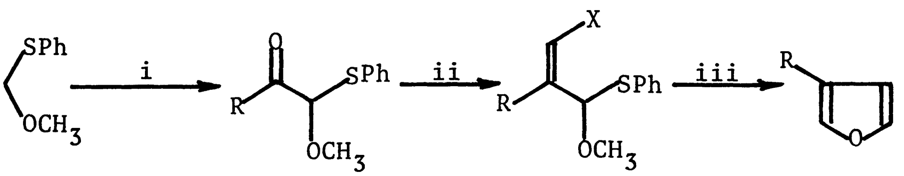
1-Methoxy-2-oxoalkyl phenyl sulfides were newly synthesized from methoxy(phenylthio)methane and various N,N-dimethylalkanamides. Synthetic application of the compounds thus obtained to several 3-substituted furans also is reported.

In the previous paper,1) we reported that methoxy(phenylthio)methane (1) and methoxy(phenylsulfonyl)methane (2) can serve as good one carbon homologation reagents and that the alkylation or hydroxy products obtained by treating the carbanions of 1 and 2 with alkyl halides, aldehydes, and epoxides can be successfully transformed to aldehydes, methylals, carboxylic acids, and enol ethers.

In connection with our study on synthetic utilization of 1 and 2, we have found that employment of N,N-dimethylalkanamides as an electrophile affords 1-methoxy-2-oxoalkyl phenyl sulfides 3 in good yields, which further proved to be novel intermediates for 3-substituted furans often encountered in natural products.2)

3-Substituted furans were prepared according to the following sequence of reactions (Scheme 1). A carbanion of 1 (generated by n-BuLi in THF at -78 °C for 1 h) was treated with N,N-dimethylalkanamides at -78 °C for 1 h and the reaction mixture was shaken with H_2O-benzene. Usual workup gave 3 in good yields. Condensation of 3 with a carbanion of methyl diethylphosphonoacetate (1.5 equiv.) in THF at room temperature for 12 h gave 4a, which then was subjected to reduction with DIBAL in ether at -30 °C for 1.5 h to yield allylic alcohols 4b. Furans 5 were successfully obtained by heating 4b in benzene under reflux for 1 h in the presence of a catalytic amount of p-toluenesulfonic acid. These procedures provide a new synthetic method for 3-substituted furans whose efficient preparation receives considerable recent attention2) and the results are summarized in Table 1.

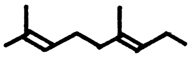
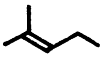
Scheme 1



1 3 4a X=CO_2Me 5
4b X=CH_2OH

i: n-BuLi, $RCONMe_2$, ii: $(EtO)_2P(O)CH_2CO_2Me$, NaH, $^{i}Bu_2AlH$, iii: p-TsOH

Table 1. Preparation of 3-substituted furans 5

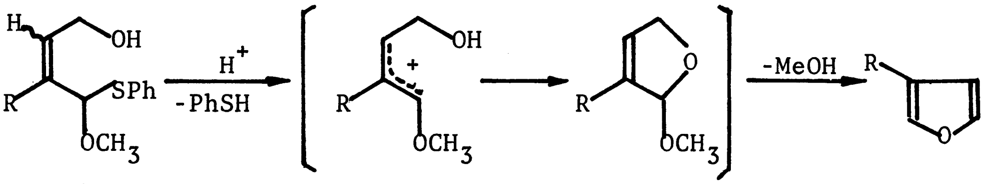
Entry	R	Yield/%			
		3[a]	4a[a,b]	4b[a,b]	5[a]
1	Ph	81	86	68	87
2	$C_{11}H_{23}$	82	75	83	75
3		79	61	73	68
4		76	83	78	60
5	$PhS(CH_2)_3$	78	72	92	86

[a] Isolated yields after column chromatography (silica gel).

[b] Yields of a mixture of (E)- and (Z)-isomers. The isomeric ratio can be determined approximately by ^{1}H NMR spectra (ca. 7/3 - 5/5).

According to the present method, we have achieved a synthesis of furanoterpenoids, dendrolasin[2c] and perillene,[2d] from readily available starting materials, geranyl and prenyl chlorides, respectively (Entries 3 and 4).

In the above reaction, we have obtained allylic alcohols 4b as a mixture of (E)- and (Z)-isomers. It is apparent that on the basis of the yields of 5 the (E)-isomer as well as its (Z)-counterpart was consumed to give furans 5. Accordingly, we can deduce the following reaction mechanism which involves an isomerization step of the (E)-alcohol to the (Z)-form. Facile acid-prompted elimination of phenylthio group is due to the presence of α-methoxyl group as is evident from our previous observation that alkylation products of 1 were easily converted to methylals by a catalytic amount of p-toluenesulfonic acid in methanol.[1]



4b 5

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