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METHOXY(PHENYLTHIO)METHANE AS AN AMBI-EQUIVALENT OF A METHOXY- OR PHENYLTHIOMETHYLENE 1,1-DIPOLE

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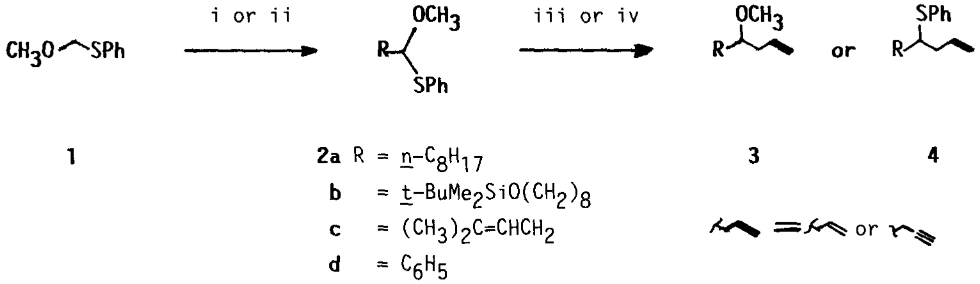
Abstract: Methoxy(phenylthio)methane undergoes electrophilic alkylation followed by nucleophilic allylation or propargylation which is dramatically changed depending on the Lewis acid employed providing a methoxy- or phenylthiomethylene 1,1-dipole synthon.

Methoxy(phenylthio)methane (**1**) is a unique one-carbon homologation reagent whose central carbon involves two functional groups different in chemical reactivities.[1,2) The phenylthio group can be removed easily under acidic or oxidative conditions due to the unsymmetrical disubstitution.[3) In our continuing studies on synthetic applications of **1**, we have found highly selective cleavage of either a phenylthio or methoxy group in the C-C bond formation: the reaction of the alkylation products **2** with allyl(or allenyl)tin compounds **5** was found to proceed smoothly in the presence of a Lewis acid.[4) This procedure compensates the synthetic defect of **1** which fails to undergo dialkylation through a usual basic metallation technique.



1

2a R = n-C_8H_{17}
b = t-$BuMe_2SiO(CH_2)_8$
c = $(CH_3)_2C=CHCH_2$
d = C_6H_5

3 **4**

(i) BuLi (1.3 equiv), RX (1.3 equiv), HMPA (2 equiv), THF, -78 - -15 °C, 3 h.
(ii) BuLi (1.1 equiv), CuI (0.5 equiv), PhI (0.5 equiv), THF, -78 °C, 3 h.
(iii) **5** (2 equiv), BF_3 OEt_2 (1.3 equiv), CH_2Cl_2, -20 °C, 2 h.
(iv) **5** (2 equiv), $TiCl_4$ (1.3 equiv), CH_2Cl_2, -78 °C, 1 h.

Of greater importance is that the reaction course is dramatically dependent on the Lewis acid with extremely high selectivity. Employment of $BF_3 \cdot OEt_2$ leads to homoallyl ethers **3** whearas homoallyl sulfides **4** are produced by use of $TiCl_4$.[5) The allenyltin compound **5c** afforded the same results. Consequently, **1** serves either as a methoxy-[1) or phenylthiocarbene equivalent and we can switch the functionality flexibly upon a slight change of the reaction conditions.

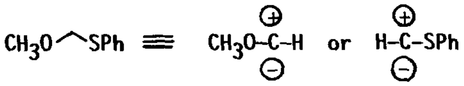
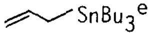
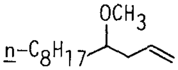
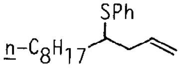
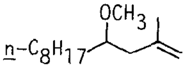
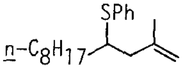
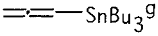
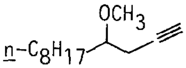
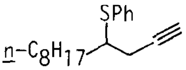
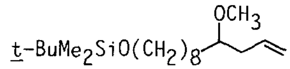
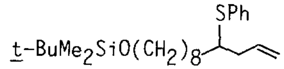
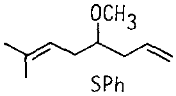
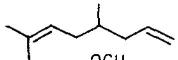
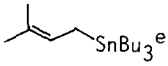
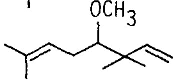
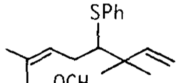
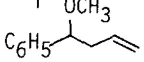
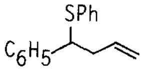
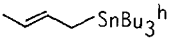
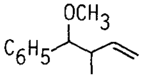
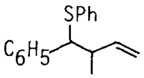


Table I. Reaction of **2** with various organotin nucleophiles[a]

entry	**2**	organotin compd	Lewis acid[b]	product[c]	yield (%)[d]	**3**/**4**[d]
1	**2a**	 [e] (**5a**)	A		72(95)[f]	100:0
2	**2a**	**5a**	B		79	6:94
3	**2a**	 [e] (**5b**)	A		100	100:0
4	**2a**	**5b**	B		93	0:100
5	**2a**	 [g] (**5c**)	A		66	98:2
6	**2a**	**5c**	B		83	3:97
7	**2b**	**5a**	A		74	97:3
8	**2b**	**5a**	B		100	1:99
9	**2c**	**5a**	A		74	99:1
10	**2c**	**5a**	B		62	6:94
11	**2c**	 [e] (**5d**)	A		76	97:3
12	**2c**	**5d**	B		70	7:93
13	**2d**	**5a**	A		69	95:5
14	**2d**	**5a**	B		54	2:98
15	**2d**	 [h] (**5e**)	A		88[i]	99:1
16	**2d**	**5e**	B		64[j]	1:99

[a] All reactions were carried out on a 1 mmol scale. [b] A:$BF_3 \cdot OEt_2$ B:$TiCl_4$. [c] Major products. [d] Determined by GLC analysis. All products were characterized by IR, NMR, and

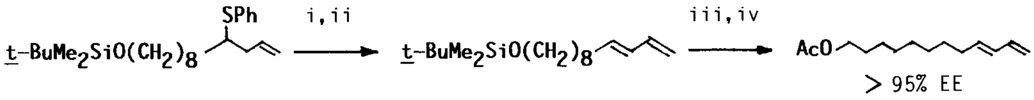
mass spectra, or by comparison with authentic samples. e) The allylstannanes were prepared with the corresponding allyl Grignard reagents. f) Based on the consumed starting materials. g) Y. Ueno and M. Okawara, J. Am. Chem. Soc. **101**, 1893 (1979). h) E. Matarasso-Tchiroukhine and P. Cadiot, J. Organomet. Chem. **121**, 155 (1976). i) Syn/anti = 53:47 on the basis of GLC. j) Syn/anti = 67:33.

Monoalkylation of **1** is readily achieved by treating the BuLi-generated α-metallo species with alkyl halides[1,3a] except iodobenzene. Phenylation was conducted successfully by using the corresponding cuprate. To a dichloromethane solution of **2** (1 equiv) were added allyl- or allenyltin (2 equiv) and a Lewis acid (1.3 equiv) in this order at -78 °C. The mixture was stirred for 2 h at -20 °C in the presence of BF_3·OEt_2 while at -78 °C for 1 h in the $TiCl_4$-promoted reaction. Usual workup and column chromatography provided either **3** or **4**.[6] Table I represents the remarkable bias of the reaction products caused by alternation of the Lewis acid. Ito and coworkers have reported the reaction of monothioacetals with allylsilanes in the presence of various Lewis acids.[7] Homoallyl ethers or sulfides were produced with varying ratios depending on the combinations of monothioacetals and Lewis acids. Actually, we observed that the $TiCl_4$-promoted reaction of **2a** with allyltrimethylsilane in place of organotin compounds led to **3** and **4** in a 28:72 ratio while the BF_3·OEt_2 effected the exclusive formation of **3** but in low yield (39%). Thus, organotin compounds are crucial in attaining the high yields and high selectivities.

The difference in reactivity of the Lewis acid may rationalize the unique switching effect. The high affinity of $TiCl_4$ towards oxygen[8] leaves the phenylthio group intact in the allylation or propargylation.[9] On the other hand, BF_3·OEt_2 can activate both of the functional groups as boranes can form adducts with ethers as well as thioethers. Apparently, the predominant affinity of the tin in the reagents to sulfur as well as the preferred stability of an intermediary α-methoxy carbocation governs the direction of the BF_3·OEt_2-promoted reaction.

Equqivqlents for methoxy- and phenylthiomethylene 1,1-dipoles are difficult to obtain through simple manipulations. Dimethoxymethane fails to serve as the methoxymethylene 1,1-dipole due to the difficulties in electrophilic alkylation of the conjugate base despite the well-known allylation of acetals with various allylic metals.[10] Bis(phenylthio)methane also is hardly converted into the phenylthiomethylene 1,1-dipole: it undergoes facile alkylation via α-metallo species,[11] but nucleophilic allylation of the resulting alkylation products occurs only sluggishly.[12] Obviously, the present results reveal that the reactivity is enhanced by replacing one of the phenylthio groups with a methoxy group to facilitate the formation of homoallyl ethers and sulfides.

The utility of the present procedure is illustrated by the simple synthesis of 1-acetoxy-9,11-dodecadiene, the pheromone of Diparosis Castanea.[13]



(i) mCPBA, CH_2Cl_2, -50 °C, 3 h (100%). (ii) $CaCO_3$, toluene, reflux, 12 h (67%), (iii) Bu_4NF, THF, 15 °C, 3 h (100%). (iv) Ac_2O-Py, 15 °C, 12 h (69%).

In conclusion, **1** has proved to be synthetically useful equivalents of methoxy- and phenylthiomethylene 1,1-dipoles, generation of which can be switched simply by changing the Lewis acid. Coexistence of both methoxy and phenylthio groups is pivotal to the preceding electrophilic alkylation as well as nucleophilic allylation or propargylation. These results open a new entry into not only the carbon homologation method but also the allylation (or propargylation) of acetal derivatives with organometallic compounds which has received extensive attention recently.

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(9) Formation of an allyltitanium species as suggested by Keck et al.[5)] is not plausible in our case since the initial mixing of **5a** and $TiCl_4$ followed by addition of **2d** led to the inconsistent results: **3** (23%), **4** (2%), and the corresponding dithioacetal (35%).

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(11) E. Block, "Reactions of Organosulfur Compounds", Academic Press: New York, 1978.

(12) From the reaction of benzaldehyde bis(phenylthio)acetal with **5a** in the presence of $BF_3 \cdot OEt_2$ (-20 °C, 2 h) or $TiCl_4$ (-78 °C, 1 h), we obtained the homoallyl sulfide in 21 and 5% yields, respectively.

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