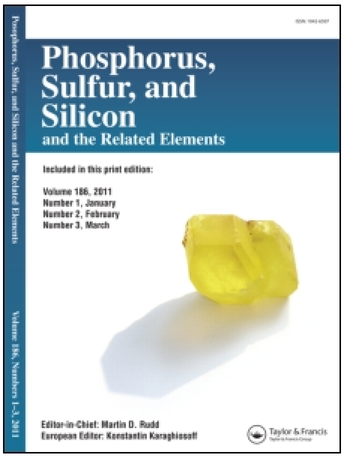

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METALATION REACTIONS. VIII. METALATION OF BENZYL METHYL SULFIDE

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METALATION REACTIONS. VIII. METALATION OF BENZYL METHYL SULFIDE

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The metalation of benzylmethyl sulfide with *n*-butyllithium in hexane and in the presence of TMEDA has been investigated. The results show that metalation occurs only at the benzylic position with no Wittig type rearrangement, cleavage of thioether bond and aliphatic or aromatic substitution. The lithium derivative has been allowed to react with some electrophiles.

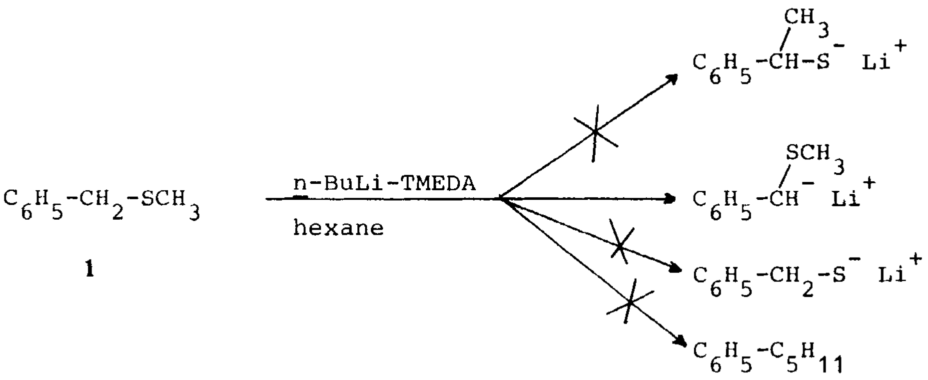
In a previous work[1] it has been shown that reactions of organolithium compounds with benzylalkyl sulfides give metalation of the benzyl moiety mixed with products from Wittig like rearrangement, cleavage of thioether bond and from aliphatic and aromatic substitution.

Because of the competition among such reactions, the corresponding amount of the products obtained by electrophilic attack on the benzylic metalated position decreased.

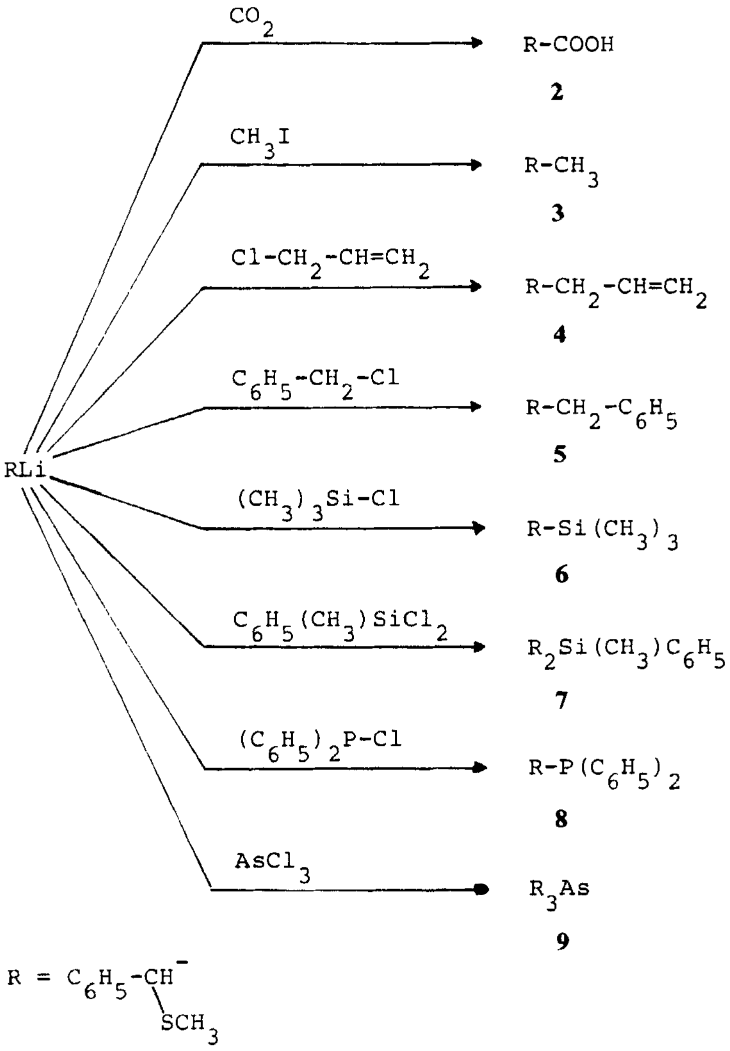
As Wittig like rearrangements are promoted both by strong bases and polar solvents,[2–4] and because the reactions, previously reported,[1] have been carried out in a polar solvent (diethyl ether), we planned to reexamine such reactions by carrying them out in hexane and in the presence of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA). We have used the non polar hexane in order to avoid or to limit rearrangements, whereas TMEDA, converting the *n*-butyllithium from hexamer or tetramer into the more reactive monomer, should enhance its ability to pull out the proton from the reagent. Moreover, we carried out the reactions at low temperature, to limit the formation of side products from cleavage and substitution.

We found that the substrate (**1**) reacted with one equivalent of *n*-butyllithium giving solely and in good yield the benzylic anion, stable in hexane. No appreciable amounts of rearrangement, cleavage and substitution products have been detected (Scheme 1). In fact, [α-(methylthio)]-benzeneacetic acid (**2**) was the only compound obtained (yield: 75%) by treating the lithiated product with carbon dioxide, whereas the reaction in diethyl ether gave lower yields (55%) of the acid (**2**), together with products from rearrangement, cleavage and substitution.[1]

Furthermore, by addition of a set of electrophiles to this carbanion (Scheme 2), a series of derivatives have been obtained, where the benzylic carbon atom becomes chiral when the various functional groups are introduced.



SCHEME 1



SCHEME 2

EXPERIMENTAL

The ^1H NMR spectra were determined in deuteriochloroform on a Varian FT 80 A spectrometer using tetramethylsilane as internal reference in the case of (**2**–**5**, **8**, **9**) and without reference in the case of (**6**) and (**7**). Analyses by GLC were carried out with a Carlo Erba Fractovap 4200 Gas Chromatograph equipped with a flame ionization detector, and a 3% SE 52 on Chromosorb W (80–100 mesh) column, using nitrogen as the carrier gas. Microanalyses were carried out on a Carlo Erba model 1106 Elemental Analyzer. Melting points were determined on a Tottoli apparatus and are uncorrected.

Metalation of [(*Methylthio*)*methyl*]*benzene* (**1**). To a solution of (**1**) (0.036 mol), TMEDA (0.036 mol) and dry hexane (150 ml) at −10°C under nitrogen 1.6 M *n*-butyllithium in hexane (0.036 mol) was added dropwise. When the addition was complete, the mixture was stirred at the same temperature for almost three hours.

[*α*-(*Methylthio*)]*benzeneacetic acid* (**2**). The mixture containing the metalated compound (**1**) was added to crushed carbon dioxide and worked up in the same manner previously described.[1] From the bicarbonate solution the acid (**2**) was obtained in 75% yield. Only starting material was detected by GLC analysis of the non acidic solution.

General Procedure for the Synthesis of Derivatives (**3**–**9**). To a mixture of the appropriate electrophile (0.036 mol in the case of monohalogenated compounds, 0.018 mol in the case of bihalogenated compounds and 0.012 mol in the case of trihalogenated compound) in dry hexane (20 ml) at −10°C under nitrogen the metalated compound (**1**) (0.036 mol) was added dropwise. When the addition was complete, the mixture was stirred at the same temperature for eight hours. The mixture was then hydrolyzed with water, extracted with diethyl ether, the organic layers combined and dried over sodium sulphate. After solvent evaporation, the crude product was chromatographed on a silica gel column using petroleum ether (40–70°C) : diethyl ether = 3 : 1 as eluent.

In this manner, starting from iodomethane, allyl chloride, benzyl chloride, chlorotrimethylsilane, dichloromethylphenylsilane, chlorodiphenylphosphine and arsenic trichloride, respectively, the following compounds were obtained:

[(*1-Methylthio*)*ethyl*]*benzene* (**3**). Yield 88%; n_D^{18} 1.5439 (lit.[6] n_D^{20} 1.5497).

4-(*Methylthio*)*-4-phenyl-1-butene* (**4**). Yield 74%; n_D^{20} 1.5700. ^1H NMR: δ 7.15 (m, 5 H, Ar—H), 5.73 (m, 1 H, CH_2—$C\underline{H}$=CH_2), 4.98 (m, 2 H, CH_2—CH=$C\underline{H}_2$), 3.65 (t, 1 H, $C\underline{H}$—SCH_3), 2.55 (m, 2 H, $C\underline{H}_2$—CH=CH_2) and 1.68 ppm (s, 3 H, SCH_3). Anal. Calcd. for $C_{11}H_{14}S$: C, 74.10; H, 7.91; S, 17.98. Found: C, 74.03; H, 7.84; S, 17.85.

1-(*Methylthio*)*-1,2-diphenylethane* (**5**). Yield 66%; n_D^{20} 1.5982. ^1H NMR: δ 7.05 (m, 10 H, Ar—H), 3.78 (t, 1 H, $C\underline{H}$—SCH_3), 3.00 (d, 2 H, $C\underline{H}_2$—C_6H_5) and 1.68 ppm (s, 3 H, SCH_3). Anal. Calcd. for $C_{15}H_{16}S$: C, 78.89; H, 7.06; S, 14.04. Found: C, 78.78; H, 6.98; S, 13.95.

[*α*-(*Methylthio*)*benzyl*]*trimethylsilane* (**6**). Yield 78%; n_D^{18} 1.5470. ^1H NMR: δ 7.20 (m, 5 H, Ar—H), 3.11 (s, 1 H, $C\underline{H}$—SCH_3), 1.84 (s, 3 H, SCH_3) and 0.00 ppm (s, 9 H, $(CH_3)_3Si$). Anal. Calcd. for $C_{11}H_{18}SSi$: C, 62.80; H, 8.62; S, 15.24. Found: C, 62.71; H, 8.54; S, 15.13.

Bis-[*α*-(*methylthio*)*benzyl*]*methylphenylsilane* (**7**). Yield 63%; n_D^{18} 1.6055. ^1H NMR: δ 7.23 (m, 15 H, Ar—H), 3.15 (s, 2 H, $C\underline{H}$—SCH_3), 1.82 (s, 6 H, SCH_3) and 0.00 ppm (s, 3 H, CH_3Si). Anal. Calcd. for $C_{23}H_{26}S_2Si$: C, 70.00; H, 6.64; S, 16.25. Found: C, 70.15; H, 6.57; S, 16.13.

[*α*-(*Methylthio*)*benzyl*]*diphenylphosphine* (**8**). Yield 45%; m.p. 212–214°C. ^1H NMR: δ 7.50 (m, 15 H, Ar—H), 4.30 (s, 1 H, $C\underline{H}$—SCH_3) and 1.94 ppm (s, 3 H, SCH_3). Anal. Calcd. for $C_{20}H_{19}PS$: C, 74.50; H, 5.94; S, 9.94. Found: C, 74.35; H, 5.83; S, 9.81.

Tris-[*α*-(*methylthio*)*benzyl*]*arsine* (**9**). Yield 43%; m.p. 113–115°C. ^1H NMR: δ 7.24 (m, 15 H, Ar—H), 4.07 (s, 3 H, $C\underline{H}$—SCH_3) and 1.89 ppm (s, 9 H, SCH_3). Anal. Calcd. for $C_{24}H_{27}AsS_3$: C, 59.24; H, 5.59; S, 19.77. Found: C, 59.13; H, 5.47; S, 19.61.

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