

Preparation of ω -Tetrahydropyran-2-ylsulfanylalkylmagnesium Chlorides: Useful Reagents for the Synthesis of 1-(ω -Mercaptoalkyl)-1,2- dihydrobuckminsterfullerenes (C_{60})

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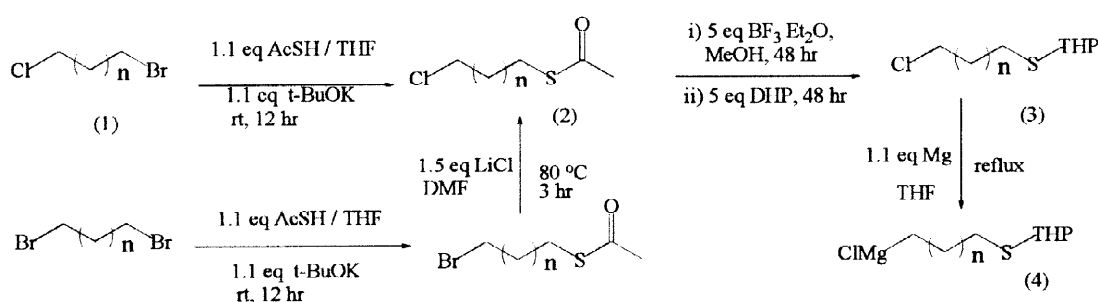
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Abstract: ω -Tetrahydropyran-2-ylsulfanylalkylmagnesium chlorides are prepared as Grignard reagents containing protected mercaptoalkyl chains, which are useful for the direct introduction of ω -mercaptoalkyl chains to electrophiles. In order to prove the usefulness of these reagents, they were reacted with buckminsterfullerene (C_{60}) to give 1-(ω -mercaptoalkyl)-1,2-dihydrobuckminsterfullerenes after the deprotection of THP group with TFA. © 1998 Elsevier Science Ltd. All rights reserved.

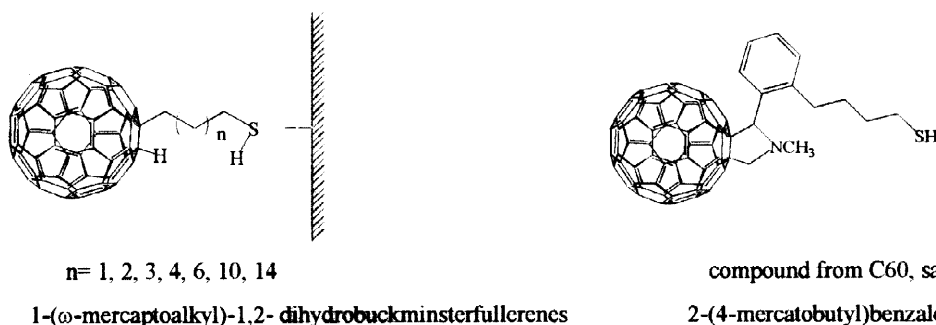
The synthesis and the use of Grignard reagents containing protected thiol, which are regarded as useful reagents in the direct introduction of mercaptoalkyl chains to electrophiles, are not reported yet in the literature, perhaps because of the difficulties in the preparation and their instability.¹ In the case of Grignard reagents prepared from β -haloacetals, the magnesium ion is strongly coordinated to the oxygen atoms, which leads to spontaneous exothermic decomposition during preparation at temperature above 20 °C, due to the Lewis acid character of magnesium.² Thiophenyl sulfides with sp^2 carbon atom in the β - position on the other side is reported to form organomagnesium thiolate, which means the cleavage of sulfide bonds.³ Grignard reagents containing alkylthiomethyl groups, such as benzylthiomethylmagnesium chloride were prepared at –10 °C.^{4,5} Here, we first report the preparation of protected thioalkyl Grignard reagents directly from Mg and tetrahydropyran-2-ylsulfanylalkyl chlorides (Scheme I).

Scheme I



Nucleophilicity of sulfide, leaving tendency of halides, stability of the protecting group to Lewis acids should be considered in this synthesis. The choice of chlorine as halogen and THP as protecting group was crucial for the formation of Grignard reagents. All the efforts to seek for other protecting groups or other halogens resulted in poor results. Especially, we were unable to get any Grignard reagent formation with Mg and tetrahydropyran-2-ylsulfanylalkyl bromides by all means. Among the source of Mg and activation methods in the literature, Mg turnings activated with 1,2-dibromoethane gave best results. Tetrahydropyran-2-ylsulfanylalkyl chlorides were prepared from ω -chloroalkyl thioacetates in two steps without the separation of ω -chloroalkanethiol to have good yields.

In order to test the usefulness of these Grignard reagents, we decided to synthesize 1-(ω -mercaptoalkyl)-1,2-dihydrobuckminsterfullerenes, which seem to be difficult to be prepared unless using our reagents. Since buckminsterfullerene (C_{60}) was synthesized by Krätschmer and Huffman,⁶ numerous derivatives of C_{60} have been prepared. It is well known that C_{60} reacts with nucleophiles such as amines,^{7,8} cyanides,⁹ ketene silyl acetals¹⁰ to give addition products. C_{60} can be alkylated with radicals, electrochemical reduction followed by alkyl halides, carbenes,^{11,12} organometallics such as Grignard reagents,^{13,14} organolithium¹⁵ and organozinc compounds.¹⁶ Especially, the reaction of C_{60} with Grignard reagents was reported to give 1-alkyl-1,2-dihydroalkylbuckminsterfullerene.¹⁴

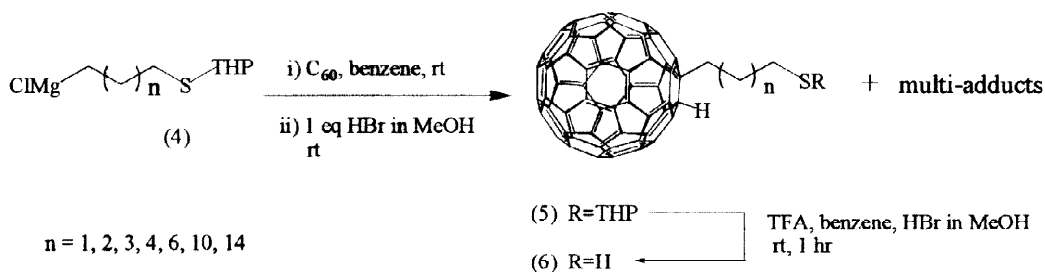


In the literature, a synthesis of C_{60} with substituted thioalkyl group was reported from the reaction of C_{60} with sarcosine and 2-(4-mercatobutyl)benzaldehyde in the study of AFM image of the compound on gold surface.¹⁷ However, to our point of view, we may expect better results with our compounds because our compounds have straight alkyl chains compared to that compound which has intrinsic bent structure and benzene moiety. Recently, the properties of self-assembled monolayers (SAMs) of alkanethiols has been studied widely especially on silver and gold surfaces.¹⁸ Because 1-(ω -mercaptoalkyl)-1,2-dihydrobuckminsterfullerenes have straight thioalkyl chains, they are expected to have well organized monolayer.

Here, we report the synthesis of the thiol derivatives of C_{60} from the reaction of C_{60} with newly synthesized ω -tetrahydropyran-2-ylsulfanylalkylmagnesium chlorides followed by deprotection of the THP protecting group.¹⁹ (Scheme II) The maximum formation ratio of 1-(ω -tetrahydropyran-2-ylsulfanylalkyl)-1,2-dihydrobuckminsterfullerene to C_{60} was checked using HPLC. The reaction mixture was quenched with HBr in MeOH followed by evaporation of solvent, purification on a silica gel column (toluene). Deprotection of THP group was carried out using excess TFA and HBr in the mixture of benzene and MeOH (50:1). 1-(ω -Mercaptoalkyl)-1,2-dihydrobuckminsterfullerenes should be protected from contacting oxygen in order to avoid

the formation of disulfides. The final products were purified on silica gel column briefly using CS₂ as eluent.

Scheme II



The structures of the final compounds were confirmed using ¹H NMR, ¹³C NMR, and FAB Mass spectrum. In the ¹H NMR spectrum, all the expected peaks such as fullereryl hydrogen (δ 6.33) and -SH (δ 1.06, J=7.7 Hz) were observed. In the ¹³C NMR spectrum of 1-thioalkyl-1,2-dihydrobuckminsterfullerenes, 30 carbon peaks are expected in the aromatic region due to the symmetry. Twenty-nine carbon peaks were observed with one peak overlapping in our compounds.

The yields for the formation of protected 1-mercaptoalkyl-1,2-dihydrobuckminsterfullerenes (5) are not optimized and depend on the reaction conditions such as equivalence of Grignard reagents, addition rate and reaction time. (Table 1) When the addition rate or reaction time is increased, the yields of di- and multi-adducts were increased as expected. The structures of di-adducts were not proved at this time.

Table 1. Yields of 1-(ω -Tetrahydropyran-2-ylsulfanylalkyl)-1,2-dihydrobuckminsterfullerene (5) and 1-(ω -mercaptoalkyl)-1,2-dihydrobuckminsterfullerene (6)

	alkyl chain (n)	equiv. of RMgX (eq)	Recovered C ₆₀ (%)	yields of (5) based on consumed C ₆₀ (%)	yields of pure (6) from (5) (%)
a	3	8.9	13	63	86
b	4	5.0	25	12	73
c	5	6.6	18	23	62
d	6	4.1	13	37	65
e	8	2.8	20	25	66
f	12	2.5	25	23	56
g	16	10.5	28	17	84

At present, we are investigating the electrochemistry of these compounds and trying to get STM image. Also, in order to prove the usefulness of these Grignard reagents, we tried the reactions of these reagents with electrophiles such as aldehydes and substituted amides. The results of this work will be reported separately.

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19. FAB mass spectrum for (6a); (matrix; 3-nitrobenzyl alcohol) [M⁺] 796;
 Data for (6f): ¹H-NMR (CS₂; benzene-d₆ = 10 : 1), δ 1.06 (1H, t, J=7.7 Hz, -CH₂SH), 1.11 – 1.61 (24H, m), 1.70 – 1.85 (2H, m, -SCH₂CH₂-), 2.31 - 2.38 (2H, q), 2.40 – 2.50 (2H, m), 3.27 – 3.34 (2H, m, fullerene-CH₂), 6.33 (1H, s, fullereryl-H); ¹³C-NMR (CS₂; benzene-d₆ = 10 : 1), δ 156.40, 154.09, 147.91, 147.78, 147.53, 146.91, 146.86, 146.81, 146.72, 146.68, 146.30, 146.00, 145.96, 145.89, 145.87, 145.18, 145.11, 143.77, 143.10, 142.68, 142.55, 142.51, 142.47, 142.18, 142.15, 140.78, 140.76, 137.04, 136.33, 65.43 (fullereryl quart-C), 60.39 (fullereryl HC), 48.09, 39.89, 35.02, 31.34, 30.83, 30.78, 30.76, 30.73, 30.70, 30.65, 30.58, 30.28, 30.13, 29.52, 29.38, 27.84, 25.79; UV-VIS (heptane) λ_{max} = 211, 257, 323, 431, 659 nm