Substitution of *S*-Methyl Groups by Grignard Reagents

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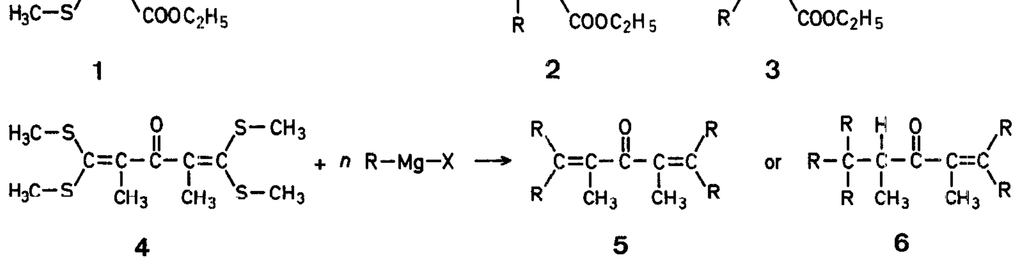
Reactions of doubly activated methylene groups with carbon disulphide and alkyl halides in the presence of a strong base (e.g. sodium hydride) have been known for a long time[1, 2]. More recently both Corey[3] and one of us[4] have described a similar reaction with ketones, so that their α-dithiomethylene derivatives or $\alpha\alpha'$-bis-dithiomethylene derivatives are now easily available.

Following the report of Corey concerning the reaction of α-dithiomethylene ketones with dimethylcopperlithium, we have reacted a variety of similar compounds with Grignard reagents (in the presence of small amounts of copper(I) bromide) and we found that a substitution of both α-dithiomethyl groups by two Grignard residues can be achieved. When the R moiety of Grignard reagent is not bulky, e.g. methyl, ethyl, a 1,4-addition follows the substitution.

We want to report the reaction of two typical systems: α-dithiomethylene derivatives of diethyl malonate (**1**), and the bis-α,α'-dithiomethylene derivatives of diethyl ketone (**4**). Both products were prepared according to our previous work[4].



In the above scheme n represents the appropriate stoichiometric amount of the Grignard reagent. In fact a large excess of the Grignard reagents was always used (100%), but **2** was obtained only when R = CH_3, C_2H_5, or C_6H_5, whereas **3** was obtained with larger groups. Compound **6** was isolated only when R = CH_3. Furthermore, a double 1,4-addition could not be observed with reagent **4**. This fact suggests a possible mechanism based on alternative additions of the Grignard anions followed by eliminations of the Grignard reagent H_3CSMgX. The last step is a 1,4-addition of the RMgX and the obtaining of the insoluble magnesium enol ether does not allow a second 1,4-addition.

Diethyl *t*-Butylmalonate (2; R = CH_3):

To a freshly prepared solution of methylmagnesium iodide (0.1 mol) in dry ether (120 ml) was added copper(I) bromide (50 mg) and the mixture was stirred for 15 min. Diethyl α-dithiomethylmethylene malonate (**1**; 5.28 g, 0.02 mol) in ether (60 ml) was dropped during 1 h into the Grignard solution with cooling in ice water. The mixture was stirred at room temperature for 1 h and then refluxed for 30 min. The mixture was cautiously decomposed with 10% hydrochloric acid (methanethiol evolved) and filtered to remove copper salts. The ether phase was washed with a 15% sodium hydrogen carbonate solution, dried, and evaporated. Distillation of the residue through a Vigreux column gave the pure colourless product; yield: 78%; b.p. 70°/1 torr.

$C_{11}H_{20}O_4$	calc.	C 61.0	H 9.2
(216.0)	found	61.1	9.3

2,6-Dibenzyl-3,5-dimethyl-1,7-diphenyl-2,5-heptadiene-4-one (5; R = $CH_2C_6H_5$):

To a freshly prepared solution of benzylmagnesium chloride (0.16 mol) in dry ether (200 ml + 50 mg copper(I) bromide), was added **4** (5.88 g, 0.02 mol) in ether (200 ml) slowly as above. The mixture was then refluxed for 2 h, decomposed, and worked-up as above. The product was recrystallised from petroleum ether (b.p. 40–60°)/benzene; yield: 35%; m.p. 117°.

$C_{35}H_{34}O$	calc.	C 89.3	H 7.3
(470.0)	found	89.0	7.1

^{1}H-N.M.R.: (see Table 2). Two different peaks for the methylene protons were observed: one for the *cis* at $\delta = 3.34$ ppm and the other for the *trans* at $\delta = 3.51$ ppm.

Mass spectrum: $m/e = 470$ ($M^{\oplus}$, 1%), 379 (18%), 288 (12%), 211 (28%), 91 (100%).

Diisopropylmethylene Malonodianilide:

Sodium hydride (100 mg) was added to a solution of **3** (R = *i*-C_3H_7) (1 g) in aniline (5 ml). The mixture was refluxed for 1 h, cooled, and poured on to an excess of ice-cold 10% hydrochloric acid. The product was collected and recrystallised twice from dilute methanol. The yield is nearly quantitative: m.p. 198°. The compound crystallised with half a molecule of water.

$C_{22}H_{26}N_2O_2 \cdot {}^1/_2H_2O$	calc.	C 73.5	H 7.3	N 8.0
(359.0)	found	73.5	7.4	8.3

I.R. (Nujol): $\nu_{max} = 3280$ (m), 1670 (s), 1600 (s) cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 9.4$ (s, 2H), 7.6–7.0 (m, 10H), 1.9 (q, 2H), 0.9 ppm (d, 12H).

Table 1. Reaction of Grignard Reagents with **1**

R	Product type	Yield (%)[a]	b.p./torr[b] or m.p.	Empical formula[c]	I.R. (nujol) ν cm^{-1} (>C=O)	^{1}H-N.M.R. (CDCl$_3$) δ ppm
CH_3	**2**	78	70°/1	$C_{11}H_{20}O_4$ (216.0)	1730, 1750	0.82 (s, 9H), 1.30 (t, 6H), 3.10 (s, 1H), 3.90 (q, 4H)
C_2H_5	**2**	72	93°/0.3	$C_{14}H_{26}O_4$ (258.0)	1730, 1750	0.90 (t, 9H), 1.32 (t, 6H), 1.40 (q, 6H), 3.12 (s, 1H), 3.90 (q, 4H)
i-C_3H_7	**3**[d]	60	92°/0.2	$C_{14}H_{24}O_4$ (294.0)	1705, 1725	0.95 (d, 12H), 1.30 (t, 6H), 1.90 (q, 2H), 4.25 (q, 4H)
C_6H_5	**2**	60	m.p. 133°	$C_{26}H_{26}O_4$ (402.0)	1728, 1746	1.28 (t, 6H), 3.14 (s, 1H), 3.92 (q, 4H), 7.28 (m, 15H)
$C_6H_5CH_2$	**3**[e]	42	—	$C_{22}H_{24}O_4$ (352.0)	1706, 1727	2.80 (s, 4H), 7.30 (m, 10H), 10.7 (s, 2H)

[a] Yield of analytically pure product.

[b] b.p.'s are corrected.

[c] All compounds gave satisfactory elemental analyses (C ±0.30%, H ±0.30%) and showed correct molecular ion peaks in the mass spectra.

[d] The dianilide is prepared

[e] Isolated as the diacid; N.M.R. data for diacid are given.

Table 2. Reaction of Grignard Reagents with **4**

R	Product type	Yield (%)	b.p./torr or m.p.	Empirical formula[a]	I.R. (nujol) ν cm^{-1} (>C=O)	^{1}H-N.M.R. (CDCl$_3$) δ ppm
CH_3	**6**[b]	60	142°/1	$C_{12}H_{22}O$ (182.0)	1680	0.84 (s, 9H), 1.20 (d, 3H), 1.60 (s, 6H), 1.70 (s, 3H), 2.80 (q, 1H)
C_6H_5	**5**	32	m.p. 228°	$C_{31}H_{26}O$ (414.0)	1620	2.00 (s, 6H), 7.21 (m, 20H)
$C_6H_5CH_2$	**5**	35	m.p. 117°	$C_{35}H_{34}O$ (470.0)	1670	2.05 (s, 6H), 3.34 (s, 4H), 3.51 (s, 4H), 7.15 (m, 20H)
4-H_3C—C_6H_4	**5**	30	m.p. 202°	$C_{35}H_{34}O$ (470.0)	1610	2.14 (s, 6H), 3.32 (s, 12H), 7.18 (m, 16H)

[a] All compounds gave satisfactory elemental analyses (C ±0.30%, H ±0.30%) unless otherwise stated.

[b] Correct elemental analysis not obtained, product apparently contained a small amount of **5** (R = CH_3)

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