Tetrahedron Letters No. 46, pp 3997 - 4000, 1974. Pergamon Press. Printed in Great Britain.

A NEW TYPE GRIGNARD REAGENT DERIVED FROM ETHYL α-PHENYLSULFINYLACETATE AND ETHYLMAGNESIUM HALIDES

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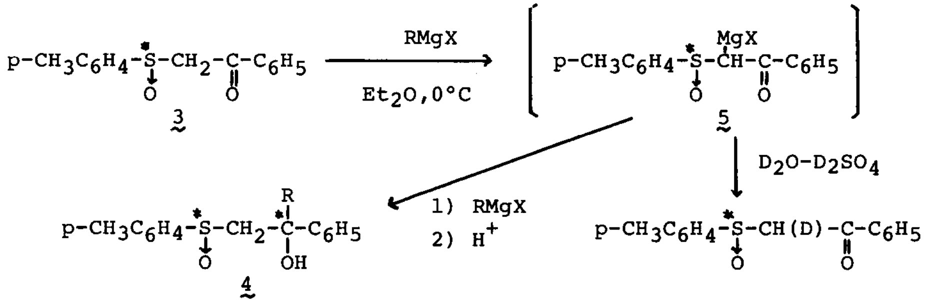
(Received in Japan 28 August 1974; received in UK for publication 8 October 1974)

We wish to report that a new type Grignard reagent (2) derived from ethyl α-phenylsulfinylacetate (1)[1] and 1 equiv of ethylmagnesium bromide or iodide in ethyl ether readily reacts at the α-carbon atom with common electrophiles such as aldehydes and ketones affording the corresponding addition compounds.

The direct addition of the α-sulfinylcarbanions adjacent to the carbonyl group towards the electrophiles has not been entirely successful, since the carbanions are stabilized through an acetyl anion in which charge is highly delocalized onto the oxygen atom of the carbonyl group.

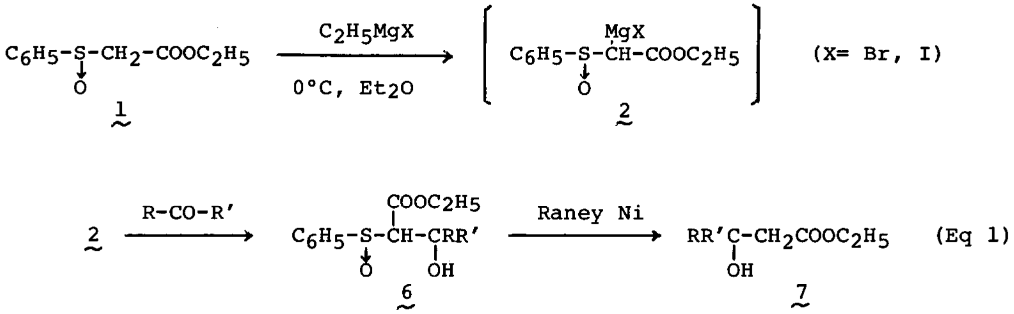
Recently, we have found that the treatment of (+)-(R)-α(p-tolylsulfinyl) acetophenone (3) with 1 equiv of an alkyl Grignard reagent in ethyl ether produces an intermediate (5),[2] and subsequent addition of another 1 equiv of the Grignard reagent yields a mixture of diastereomeric alcohols (4), almost quantitatively.[3] The specific reactivity of the carbonyl group towards the Grignard reagent seemed to be ascribable to the absence of the distribution of charge in the intermediate (5)(Scheme 1). This finding have prompted us to use

(Scheme 1)



the Grignard reagent in ethyl ether, in order to derive the new type Grignard reagent (2).

Treatment of 1 with 1 equiv of ethylmagnesium bromide or iodide in ethyl ether at 0°C quantitatively afforded the Grignard reagent (2) as a milky precipitate. When 2 was treated with carbonyl compounds, a facile reaction occured, and the corresponding addition product (6) was obtained in good yields (Eq 1).(5)



$$\underset{\mathbf{1}}{C_6H_5-\underset{\downarrow O}{S}-CH_2-COOC_2H_5} \xrightarrow[0°C,\ Et_2O]{C_2H_5MgX} \underset{\mathbf{2}}{\left[C_6H_5-\underset{\downarrow O}{S}-\overset{MgX}{CH}-COOC_2H_5 \right]} \quad (X= Br,\ I)$$

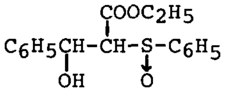
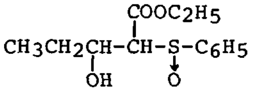
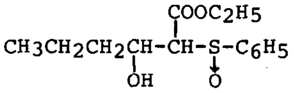
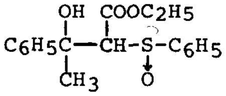
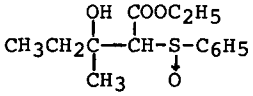
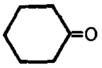
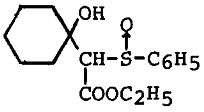
$$\mathbf{2} \xrightarrow{R-CO-R'} \underset{\mathbf{6}}{C_6H_5-\underset{\downarrow O}{S}-\overset{COOC_2H_5}{CH}-\underset{OH}{C}RR'} \xrightarrow{Raney\ Ni} \underset{\mathbf{7}}{RR'\underset{OH}{C}-CH_2COOC_2H_5} \quad (Eq\ 1)$$

In a typical reaction, a solution of 1 (212.3 mg, 1 mmol) in ethyl ether was treated dropwise with an ethereal solution of ethylmagnesium iodide (1 mmol) at 0°C with vigorous stirring. After the stirring for 3 min, benzaldehyde (106 mg, 1 mmol) was added. The mixture was stirred for 1.5 hr at room temperature, followed by hydrolysis with a saturated solution of ammonium chloride. The ethereal layer was separated and the water layer was extracted with chloroform. Evapolation of the combined extracts under reduced pressure gave a crystalline residure which was recrystallized from carbontetrachloride to give ethyl 2-phenylsulfinyl-3-hydroxy-3-phenylpropionate (6a) (white needles, 84% yield). Similarly, propionaldehyde, butyraldehyde, acetophenone, ethyl methyl ketone and cyclohexanone readily react with 2 to yield the corresponding adducts, 6b∿f. The results are summarized in Table 1.

By the use of Raney nickel,[4)] the adduct (6) could easily be desulfurized to produce the corresponding β-hydroxycarboxylic acid ethyl ester (7).

Further study on the applications of organic syntheses of the Grignard reagent (2) is in progress.

Table 1. Reactions of 2 and carbonyl compounds

Aldehydes or ketones	Products		Yields(%)
C_6H_5CHO	 $C_6H_5\underset{\mid \atop OH}{CH}-\overset{COOC_2H_5 \atop \mid}{CH}-\underset{\downarrow \atop O}{S}-C_6H_5$	(6a)	84
CH_3CH_2CHO	 $CH_3CH_2\underset{\mid \atop OH}{CH}-\overset{COOC_2H_5 \atop \mid}{CH}-\underset{\downarrow \atop O}{S}-C_6H_5$	(6b)	95
$CH_3CH_2CH_2CHO$	 $CH_3CH_2CH_2\underset{\mid \atop OH}{CH}-\overset{COOC_2H_5 \atop \mid}{CH}-\underset{\downarrow \atop O}{S}-C_6H_5$	(6c)	95
$C_6H_5COCH_3$	 $C_6H_5\overset{OH \atop \mid}{\underset{\mid \atop CH_3}{C}}-\overset{COOC_2H_5 \atop \mid}{CH}-\underset{\downarrow \atop O}{S}-C_6H_5$	(6d)	75
$CH_3CH_2COCH_3$	 $CH_3CH_2\overset{OH \atop \mid}{\underset{\mid \atop CH_3}{C}}-\overset{COOC_2H_5 \atop \mid}{CH}-\underset{\downarrow \atop O}{S}-C_6H_5$	(6e)	82
		(6f)	93

(6a); nmr(60 MHz,CDCl3): δ 1.00(3H,t),3.73(1H,s),3.96(2H,q),5.35(1H,q),
Anal: Calcd. C 64.13, H 5.70, Found C 63.89, H 5.90
(6b); nmr: δ 0.94(3H,t),1.08(3H,t),1.65(2H,q),3.50 and 3.60(1H,s),
4.05(2H,q)

(6c); nmr: δ 0.90(3H,m),1.12(3H,t),1.60(4H,m),3.50 and 3.58(1H,s), 4.10(2H,q), Anal: Calcd. C 59.13, H 7.09, Found C 59.03, H 7.03

(6d); nmr: δ 0.85 and 1.15(3H,t),1.73 and 1.90(3H,s),3.83 and 4.16(2H,q), 3.94 and 4.00(1H,s)

(6e); nmr: δ 0.96(3H,t),1.04(3H,t),1.78(2H,q),3.57(1H,s),4.04(2H,q)

(6f); nmr: δ 1.05(3H,t),1.65(10H,m),3.54(1H,s),4.03(2H,q), Anal: Calcd. C 61.91, H 7.14, Found C 61.98, H 7.03

References and Notes

1) Ethyl α-phenylsulfinylacetate (1) could be readily prepared by the condensation of diethyl carbonate with 1 equiv of phenylsulfinylcarbanion ($C_6H_5SOCH_2^-$) in 73% yield. nmr(60 MHz,$CDCl_3$): δ 1.17(3H,t), 3.80(2H,q), 4.10(2H,q), Anal: Calcd. C 56.58, H 5.70, Found C 56.00, H 5.83.

2) When the intermediate (5) was treated with D_2O-D_2SO_4, the methylene hydrogens of recovered 3 were found to be deuterated (degree of deuteration; ca. 50%)(see Scheme 1).

3) N. Kunieda, J. Nokami, and M. Kinoshita, Chem. Lett., 369(1974).

4) G.A. Russell, E.T. Sabourin, and G. Hamprecht, J. Org. Chem., 34, 2339(1969); G. Tsuchihashi, S. Iriuchijima, and M. Ishibashi, Tetrahedron Lett., 4608(1972).

5) The carbanion which was derived from 1 and an ordinary base (such as sodium hydride or n-butyl lithium) in an ordinary solvent (such as tetrahydrofuran, dimethylsulfoxide or dimethylformamide) was unreactive to the ketones and the aldehydes.