Pergamon

Tetrahedron Letters, Vol. 35, No. 13, pp. 2009-2012, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0239-T

A Novel Synthesis of Homologated Allylic Alcohols Using Dimethylsulphonium Methylide

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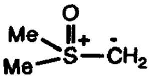
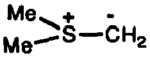
Abstract: *The reaction of excess dimethylsulphonium methylide with various aliphatic and aromatic ketones leads exclusively to homologated allylic alcohols in good yields.*

The use of dimethyloxosulphonium methylide **1** and dimethylsulphonium methylide **2** to generate epoxides from carbonyl compounds is well known[1]. Arsonium semi-stabilized and non-stabilized ylides **3** (depending on the nature of R) have also been shown to react with aldehydes and ketones to afford epoxides in high yields[2,3].



1



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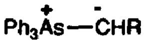
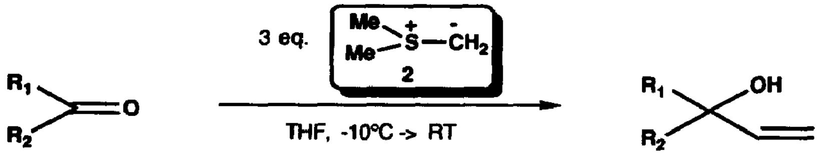


$Ph_3\overset{+}{As}-\overset{-}{C}HR$

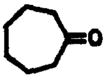
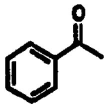
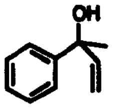
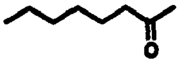
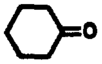
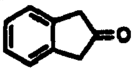
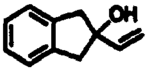
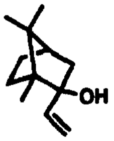
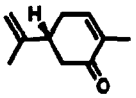
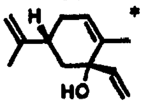
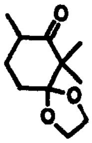
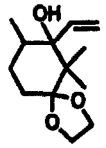
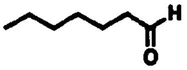
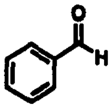
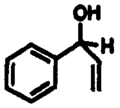
3

In conjunction with ongoing studies in our laboratories on carbanions stabilized by sulphur and arsenic containing functions, we discovered that reaction of an excess of the ylide **2** with various ketones resulted in a convenient synthesis of homologated allylic alcohols in moderate to good yields (Scheme 1).



Scheme 1

The generality of the new reaction of dimethylsulphonium methylide **2** with carbonyl compounds is summarised in Table 1. Surprisingly, low yields of secondary allylic alcohols were obtained from the corresponding aldehydes (entries j, k). It is worthy of note that when ketones reacted with excess amounts of arsonium ylide **3** (R = H), the only isolated products were the corresponding epoxides.

Entry	Substrate	Product	Isolated % Yield*
a			91
b			70
c			62
d			65
e			60
f			83
g			60
h		 **	73
i			70
j			10
k			10

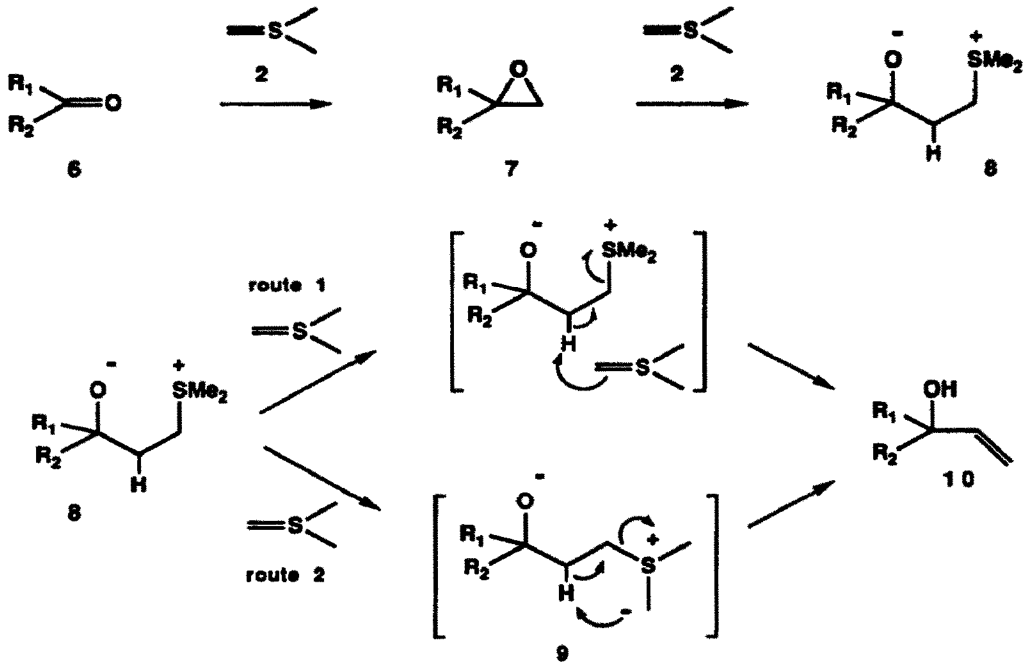
* unoptimized yield
** 10/1 isomer ratio

table 1

Reaction of ylide **2**, with ketones is clearly different from that with dimethyloxosulphonium methylide **1**, which has been reported to yield oxetanes [4,5].

In our hands the carbonyl compounds (entries a-i, table 1) gave the corresponding allylic alcohols as the sole product and in all cases no oxetanes were ever isolated from the final reaction mixtures when using an excess of the ylide **2**. This new application of dimethylsulphonium methylide offers the advantage over vinyllithium and vinylmagnesium halides to afford better yields in the case of hindered or enolizable ketones. For example the intermediate described in table 1 (entry i), which is after dehydration an important intermediate in the synthesis of the A ring of taxol[6], could be obtained in 70% yield.

Our results suggest that the allylic alcohol **10** obtained from carbonyl compound **6** results from a double methylene transfer by two molecules of ylide **2**, *via* the initially formed epoxide **7** and intermediate **8**, as shown in Scheme 2. The two routes described can be envisioned to account for the formation of **10**; whether the betaine intermediate undergoes a β-elimination (route 1)[7] or is deprotonated to the species **9** which then undergoes an α',β-elimination (route 2) remains to be clarified[8].



Scheme 2

A general method for this reaction is as follows :

Trimethylsulphonium iodide (8.5 mmol) was suspended in dry THF (20 cm^3) and cooled to -10 °C. *n*-BuLi (1.6 M in hexane, 8.2 mmol) was added dropwise and the reaction allowed to warm slowly to 0 °C. The solution was cooled to -10°C and the carbonyl compound (2.12 mmol) in dry THF (2 cm^3) was added dropwise, producing a milky suspension. The reaction was allowed to warm to 0 °C over about 30 minutes and then to room temperature and stirred for 2 hours. Water was added at 0 °C and the organic layer separated ; the aqueous layer was extracted with ether and the combined organic layers dried over magnesium sulphate. All compounds were purified by dry-flash chromatography to yield colourless oils, see Table 1 for yields.

Acknowledgments:

J.J. H. thanks the CNRS and L. A. thanks the MRE for financial support. J.R. F. and D.S. S. thank NIH GM 31278 and the Robert A. Welch Foundation. We are grateful to Mr Valleix from the CEA for the mass spectroscopy analysis and to Marie-Lyne Alcaraz for her invaluable collaboration.

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(*Received in France* 25 *October* 1993; *accepted* 29 *January* 1994)