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Generation of Magnesium Alkylidene Carbenoids from 1-Halovinyl Sulfoxides with Grignard Reagent-Their Property and Some Synthetic Uses

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Abstract: The first example of magnesium alkylidene carbenoids is described. 1-Halovinyl sulfoxides 3 (X=F, Cl, Br) were synthesized from ketones and aryl halomethyl sulfoxides in three steps in moderate to good overall yields. Ligand exchange reaction of the sulfoxides of 3 with ethylmagnesium halide in THF at low temperature afforded a magnesium alkylidene carbenoid, which reacted with several electrophiles to give new alkylidene compounds.

Carbenes and carbenoids have been recognized as highly reactive carbon species and are frequently used as useful intermediates in organic synthesis.¹ Alkylidene carbenoids are the carbenoids of olefinic carbon and are also known as very interesting reactive intermediates.² Generation of alkylidene carbenoids is mainly carried out by elimination of hydrogen or halogen from 1-halo- or 1,1-dihaloolefines with strong bases such as alkyllithium, alkylzincate, or potassium *tert*-butoxide.^{2,3}

Recently, we have focused our attention on the chemistry of the ligand exchange reaction of sulfoxides and its application to development of new synthetic methods.⁴ In continuation of our studies, we found that the 1-halovinyl sulfoxides **3** (X=F, Cl, Br) reacted with ethylmagnesium halide at low temperature to give a high yield of magnesium alkylidene carbenoid **4**. In this paper we report a synthesis of **3** and generation of the magnesium alkylidene carbenoid **4**; its property and some synthetic applications are also described (Scheme 1).



In order to make the 1-halovinyl sulfoxides 3 having fluorine, chlorine, and bromine as the halogen, we first established a general synthetic method of 3 from aryl halomethyl sulfoxides 2.5^{-5} Chloromethyl *p*-tolyl sulfoxide 2a was treated with LDA at -78 °C followed by cyclopentadecanone to give a chloroalcohol 7a in 97% yield. The hydroxyl group was mesylated in an attempt to eliminate it,^{5a} but this reaction totally failed. Fortunately, this hydroxyl group was acetylated with acetic anhydride in pyridine in the presence of DMAP⁶ to afford the acetate 7b in 94% yield. Elimination of the acetate was carried out with excess NaH and DBU in anhydrous THF at room temperature for 6 h to give the desired 1-chlorovinyl sulfoxide, 8 was treated with *n*-BuLi and *t*-BuLi in THF at -80 °C;^{5a} however, these reactions gave only a complex mixture. Next, 8 was treated with EtMgBr at -80 °C. This reaction gave a very clean product in over 90% yield. Surprisingly, this product was an inseparable mixture of vinylbromide 10b and vinylchloride 10a (10b:10a=2:1). Finally, treatment of 8 with 1.5 equivalents of EtMgCl at - 78 °C for 5 min gave pure chloride 10a in 98% yield and a quantitative yield of ethyl *p*-tolyl sulfoxide.



It appeared obvious that the intermediate of this reaction was the very uncommon magnesium alkylidene carbenoid 9.7 This presumption was ascertained as follows. The reaction was quenched with CD₃OD to afford deutrated vinylchloride 11. Quenching of this reaction with aldehyde gave the adduct 12 in moderate to good yield; however, the carbenoid 9 did not react ketones, for example acetone. Further, stability of 9 was investigated as follows. After treatment of 8 with EtMgCl, the reaction mixture was left to stand at -80 °C for 30 min, then quenched with CD₃OD to give 11 without lowering the yield or deutrium incorporation. From this

		EtMgX			x	E ⁺ R X
F	R S(O)Ar			R	MgX –	
	3		L	4		5 or 6
Entry	3		ΡΜαΥ	Temp (°C)	Flectronhile	5 or 6
	R	x				Yield/% ^{a)}
1	CH ₃ (CH ₂) ₄	CI	EtMgCl	-78	H ₂ O	78 (E=H)
2				-78	CD ₃ OD	80 (E=D)
3				-78	PhCHO	50 (E=CH(OH)Ph)
4				-78 to -35	CH ₃ CH ₂ CHO	54 (E=CH(OH)Et)
5	Ph	CI	EtMgCl	-78	H ₂ O	96 (E=H)
6				-78	CD ₃ OD	99 (E=D)
7				-78 to -50	PhCHO	59 (69) ^{b)} (E=CH(OH)Ph)
8				-78 to -50	CH ₃ CH ₂ CHO	44 (E=CH(OH)Et)
9				0 (30 min)	H ₂ O	c)
10	-(CH ₂) ₁₄ -	F	EtMgCl	-100	H ₂ O	d)
11			t-BuMgCl	-78 to r.t.	H ₂ O	e)
12	Ph	F	EtMgCl	-100	H ₂ O	91 (E=H)
13				-100	CD ₃ OD	88 (E=D)
14	-(CH ₂) ₁₄ -	Br	EtMgBr	-100	H ₂ O	86 (E=H)
15				-100	CD ₃ OD	84 (E=D)
16				-78	CD ₃ OD	82 (E=D)
17				-78 (30 min)	CD ₃ OD	85 (E=D)
18				-90	PhCHO	68 (E=CH(OH)Ph)

 Table 1. Generation of Magnesium Alkylidene Carbenoid 4 from 3 and Its Reaction with Electrophiles

a) Unless otherwise noted the reaction was carried out at the temperature with the corresponding Grignard reagent for 5 min, then the electrophiles were added. Isolated yield after silica gel column chromatography. b) Conversion yield. c) A mixture of diphenylacetylene and 1,1-diphenyl-1-butene was obtained in good yield. d) See text. e) At low temperature this 1-fluorovinyl sulfoxide did not react with *t*-BuMgBr. At 0 °C to room temperature this compound slowly decomposed to give a complex mixture.

result it can be inferred that the carbenoid 9 is stable at -80 °C over 30 min. This reaction was applied to 6undecanone and benzophenone and the results are summarized in Table 1 (entries 1-9).

This procedure was extended to fluoro- and bromo compounds. 1-Halovinyl sulfoxide 3 (X=F, Br) were synthesized from fluoromethyl phenyl sulfoxide (2; Ar=Ph, X=F)⁸ and bromomethyl phenyl sulfoxide (2; Ar=Ph. X=Br)⁹ essentially in the same way as described for 8. The ligand exchange of the 1-fluorovinyl sulfoxide derived from benzophenone with EtMgCl was carried out in THF at -100 °C and the desired vinyl fluoride was obtained in high yield (entries 12 and 13). Interestingly, the vinylfluoride derived from cyclopentadecanone gave a product having an ethyl group from the Grignard reagent (entry 10). Finally corresponding reactions of the bromide (entries 14-18) were investigated and the preliminary results are summarized in Table 1. From the results in Table 1, we feel that the carbenoids (Cl, Br) have similar property; however, 1-fluorovinyl sulfoxide has a somewhat different property compared with the Cl and Br compounds.

We propose that this procedure offers a good new method for chloromethylenation and bromomethylenation¹⁰ of ketones (entries 1, 5, and 14). In some cases fluoromethylenation is also possible (entry 12).

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