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A novel synthetic method for alkylidenecyclopropanes based on the reaction of magnesium cyclopropylidenes with lithium α-sulfonyl carbanions

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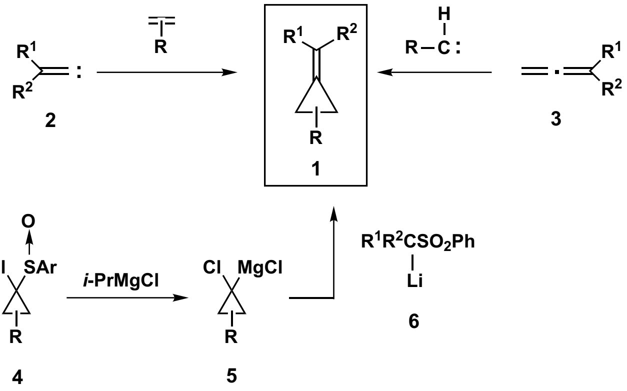
Abstract—Treatment of 1-chlorocyclopropyl phenyl sulfoxides with isopropylmagnesium chloride at low temperature gave magnesium cyclopropylidenes. The reaction of the generated carbenoids with lithium α-sulfonyl carbanions was found to afford alkylidenecyclopropanes in moderate to good yields. This reaction offers a novel, unprecedented, and versatile method for a synthesis of several alkylidenecyclopropanes from olefins in relatively short steps.

Alkylidenecyclopropanes **1**, including methylenecyclopropanes (**1**; R^1, $R^2 = H$), are structurally highly strained; however, usually they are present as stable compounds at room temperature. On account of the strain of the alkylidenecyclopropanes, they show high reactivity with the proper choice of reaction conditions and are widely used in organic synthesis.[1] A variety of methods for the synthesis of the alkylidenecyclopropanes **1** have been reported.[2] Representative examples are the reaction of alkylidene carbenes **2** with olefins[2,3] and the reaction of carbenes with allenes[2] **3** (Scheme 1).

We recently reported a new method for the generation of magnesium cyclopropylidenes **5**[4] from 1-chlorocyclopropyl phenyl sulfoxide **4** and a Grignard reagent via the sulfoxide–metal exchange reaction.[5] The magnesium cyclopropylidenes **5** were found to be stable at below −60 °C and a new method for the synthesis of allenes was realized.[4] In continuation of our interest in the development of new synthetic methods by utilizing the generated magnesium cyclopropylidenes **5** in organic synthesis, we investigated the reaction of **5** with several nucleophiles and found that the reaction of **5** with lithium α-sulfonyl carbanions **6** gave alkylidenecyclopropanes **1** in moderate to good yields.



Scheme 1.

Our investigation is described by using 1-chlorocyclopropyl phenyl sulfoxide **8** as a representative example shown in Scheme 2. Commercially available cyclopropyl phenyl sulfide **7** was first oxidized with 3-chloroperoxybenzoic acid (MCPBA) and the resultant sulfoxide was chlorinated with *N*-chlorosuccinimide (NCS) in CCl_4 to afford 1-chlorocyclopropyl phenyl sulfoxide **8** in 93% overall yield.[4,6] The sulfoxide **8** is a quite stable compound.

The sulfoxide **8** was treated with 2.5 equiv of *i*-PrMgCl at −78 °C. The sulfoxide–magnesium exchange reaction of **8** was found to take place quite rapidly at −78 °C

Keywords: Alkylidenecyclopropane; Magnesium cyclopropylidene; Magnesium carbenoid; Sulfoxide; Sulfoxide–magnesium exchange.

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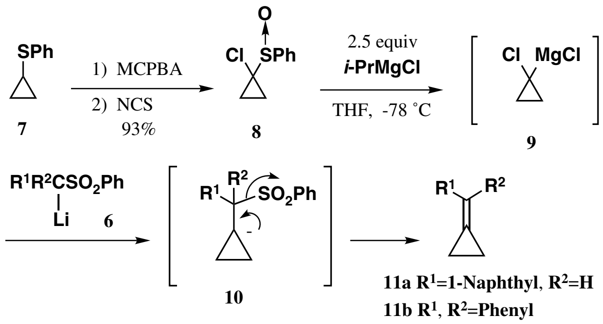
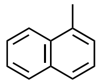
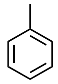
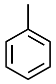
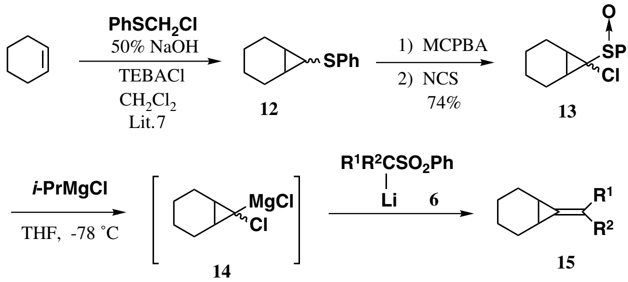
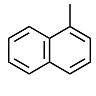


Entry	Sulfone		Conditions	11
	R^1	R^2		Yield / %
1		H	-78 °C, 3 h	39
2			-78 °C~-60 °C, then -60 °C, 3 h	43
3			-78 °C~-50 °C, then -50 °C, 3 h	61
4			-78 °C~-40 °C, then -40 °C, 3 h	50
5			-78 °C, 3 h	3
6			-78 °C~-60 °C, then -60 °C, 3 h	19
7			-78 °C~-50 °C, then -50 °C, 3 h	48
8			-78 °C~-40 °C, then -40 °C, 3 h	25

Scheme 2.



Entry	Sulfone 6		Conditions	15
	R^1	R^2		Yield / %
1		H	-78 °C, 3 h	trace
2			-78 °C~-50 °C, then -50 °C, 3 h	15
3			-78 °C~-30 °C, then -30 °C, 3 h	63
4			-78 °C~ room temp. 4 h	64

Scheme 3.

within 1 min to give the magnesium cyclopropylidene **9**. After 5 min, 3 equiv of lithium carbanion of (1-naphthyl)methyl phenyl sulfone at −78 °C was added to the solution of the carbenoid through a cannular, and the temperature of the reaction mixture was slowly allowed to warm to room temperature. We obtained an oily product, which has $C_{14}H_{12}$ as the molecular formula. From detailed inspection of the spectral data, the product was determined to be the alkylidenecyclopropane **11a** ($R^1 = $ 1-naphthyl, $R^2 = H$). The yield was about 50%.

We investigated the proper conditions of this reaction, and the results are summarized in the table in Scheme 2. Entries 1 and 5 indicate that the reaction of the magnesium carbenoid **9** and lithium α-sulfonyl carbanions **6** took place rather slowly at −78 °C. Entries 2 and 6 indicate that the reaction proceeds better at −60 °C than at −78 °C. Entries 4 and 8 show that the carbenoid **9** is not stable at −40 °C and gave lower yields. So far, the best conditions were found to be those in entries 3 and 7, and we obtained the alkylidenecyclopropanes **11a** and **11b** in 61% and 48% yields, respectively.

In order to know the universality of this reaction with 1-chlorocyclopropyl phenyl sulfoxides, the chloro-sulfoxide **13** was synthesized from cyclohexene through the sulfide **12**[7] (Scheme 3). The chloro-sulfoxide **13** was treated with *i*-PrMgCl followed by the lithium α-carbanion of sulfones **6** under the best conditions described in Scheme 2 (entry 2 in Scheme 3); however, the desired alkylidenecyclopropane **15** was obtained in only 15% yield. The temperature of the reaction mixture was allowed to warm to −30 °C and the temperature was kept for 3 h (entry 3) to give a much better yield. Finally, the conditions described in entry 4 were found to be the most convenient for our purpose and 64% yield of the desired alkylidenecyclopropane was obtained. From these results the best conditions were found to be somewhat characteristic for the generated magnesium cyclopropylidenes.

The examples for the synthesis of alkylidenecyclopropanes **15** from 1-chlorocyclopropyl phenyl sulfoxide **13** are summarized in Table 1. Entries 1 and 2 indicate that the reaction of the carbenoid **14** and lithium α-sulfonyl carbanions **6** proceeds smoothly when the sulfones have an aromatic group on the carbanion carbon. Even diphenyl-substituted alkylidenecyclopropane was obtained in 50% yield (entry 3). In contrast to this, the carbanion having an alkyl group (entry 5) gave markedly decreased yield (32%). The triple bond-conjugated alkylidenecyclopropane could be obtained by this method albeit in low yield (entry 4).

Finally, monosubstituted 1-chlorocyclopropyl phenyl sulfoxide **16** was synthesized from the corresponding olefin. We examined the synthesis of alkylidenecyclopropane **17** and, at the same time, the feasibility of the reaction for generation of allene **18** as a by-product. The allene **18** is expected to generate by the Doering–Moore–Skattebol reaction[4,8] from the intermediate magnesium cyclopropylidene (Table 2).

In any event, **16** was first treated with 2.5 equiv of *i*-PrMgCl at −78 °C and then lithium α-sulfonyl carbanion derived from (1-naphthyl)methyl phenyl sulfone was added to the reaction mixture. The temperature of the reaction mixture was gradually allowed to warm to room temperature (Table 2, entry 1). This reaction gave

Table 1. Synthesis of alkylidenecyclopropanes **15** from 1-chlorocyclopropyl phenyl sulfoxide **13** and lithium α-sulfonyl carbanions

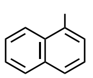
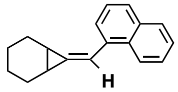
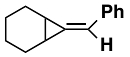
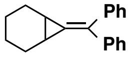
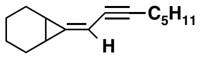
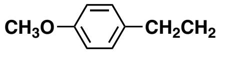
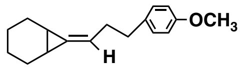
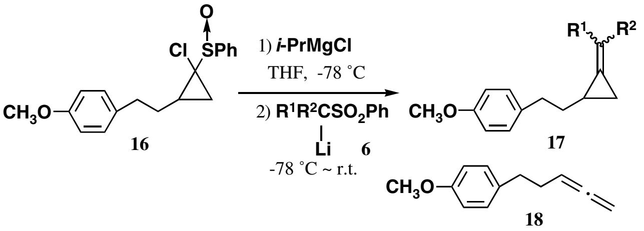
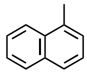
Entry	Sulfone **6**		Alkylidenecyclopropane **15**	Yield (%)
	R^1	R^2		
1		H		64
2	Ph	H		73
3	Ph	Ph		50
4	$—C{\equiv}CC_5H_{11}$	H		25
5		H		32

Table 2. Synthesis of alkylidenecyclopropanes **17** from 2-substituted-1-chlorocyclopropyl phenyl sulfoxide **16** and lithium α-sulfonyl carbanions



Entry	Sulfone		**17**
	R^1	R^2	Yield (%)
1		H	78[a,b]
2		H	91[a,c]
3	CH_3	H	56[a,d]
4			34
5		CH_3	49[a,e]

[a] A mixture of two diastereomers. The structure has not been determined yet.

[b] The ratio 7:1.

[c] The ratio 25:1.

[d] The ratio 2:1.

[e] The ratio 3:1.

a quite good result and the desired alkylidenecyclopropane **17** was obtained as a mixture of two diastereomers.

From a careful inspection of the products of this reaction, we found that the expected allene **18** was present albeit in trace amount. This result implied that the reaction of the α-sulfonyl carbanion reacts faster with the magnesium cyclopropylidenes than the isomerization to allene **18** (Doering–Moore–Skattebol reaction). Other examples are shown in Table 2. As shown in Table 2, the magnesium cyclopropylidene generated from the sulfoxide **16** showed high reactivity with the lithium α-sulfonyl carbanions **6**. The carbanion derived from benzyl phenyl sulfone gave the desired alkylidenecyclopropane in high yield (entry 2). Even the carbanion having an alkyl group (in this case a methyl group) gave the desired product in 56% yield (entry 3). Diphenyl-substituted alkylidenecyclopropane was obtained; however, the yield was somewhat lower compared with the case in Table 1. Even in this case, the allene **18** was observed in trace amount (entry 4). The carbanion having both methyl and phenyl groups also gave the desired product in 49% yield (entry 5).

In conclusion, we have found that the reaction of the magnesium cyclopropylidenes with lithium α-sulfonyl carbanions gave alkylidenecyclopropanes. This is the first example of the synthesis of alkylidenecyclopropanes by the alkenylation of the activated cyclopropane moiety with nucleophiles (carbanions) and offers a novel and relatively short synthesis of alkylidenecyclopropanes from olefins.

Acknowledgements

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