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Regioselective Cyclopropanation of 2-Phenylsulfonyl 1,3-Dienes

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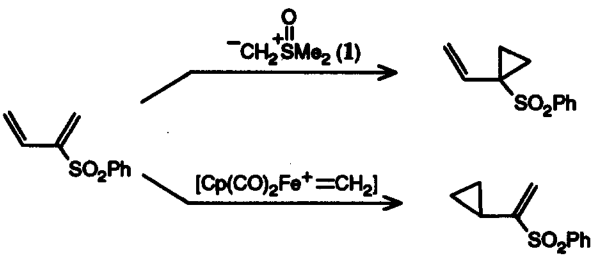
Abstract. Regioselective cyclopropanation of 2-phenylsulfonyl 1,3-dienes at either double bond was achieved by employing two different reagents. Sulfur ylide **1** resulted in a regiospecific cyclopropanation at the electron deficient double bond whereas an iron carbene, thermally generated from **5a**, gave cyclopropanation exclusively at the electron rich double bond.

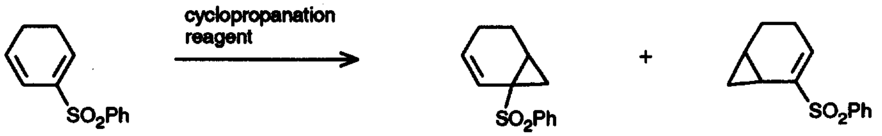
Electron-deficient conjugated dienes have recently attracted considerable interest in organic synthesis.[1-6] We [1,5] and others [2,3] have explored the synthetic utility of 2-phenylsulfonyl 1,3-dienes and demonstrated their use in cycloaddition reactions and as multicoupling reagents. Furthermore, regioselective functionalization of one of the double bonds of these sulfonyl dienes leads to useful synthetic intermediates.[1b,5] Previously we reported selective epoxidation reactions[1b] which allow the preparation of either regioisomer of the monoepoxide. One objective with our studies was to extend these epoxidations to related regioselective cyclopropanation reactions. This would lead to the corresponding vinylcyclopropanes, which are an important class of compounds.[7] In this communication we report that reaction of 2-phenylsulfonyl 1,3-dienes with electrophilic and nucleophilic cyclopropanation reagents lead to highly regioselective cyclopropanation of either double bond (Scheme I).

Scheme I



2-Phenylsulfonyl 1,3-dienes have one electron-deficient and one electron-rich double bond. For the cyclopropanation of the former double bond we chose the sulfur ylid reagent **1**,[8] which is known to cyclopropanate the double bond of α,β-unsaturated ketones and esters. Reaction of 2-(phenylsulfonyl)-

1,3-cyclohexadiene (**2a**) with **1** resulted in a very efficient reaction to give vinylcyclopropane **3a** in essentially quantitative yield (eq. 1, Table 1, entry 1). Several other 2-phenylsulfonyl 1,3-dienes were transformed to the corresponding vinylcyclopropanes by reagent **1** (method A, Table 1). Cyclic sulfonyl dienes gave a high yield of cyclopropane product, whereas the corresponding acyclic dienes gave moderate to good yields.

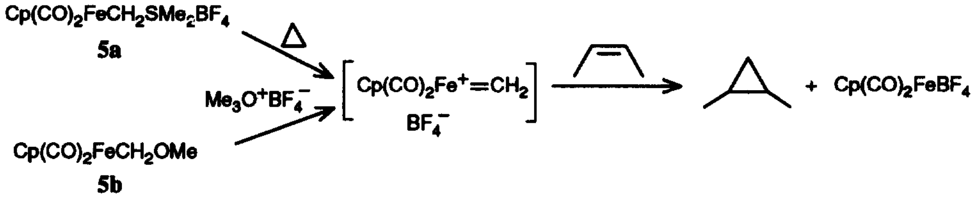


2a **3a** **4a** (1)

	3a		**4a**
$^{-}\mathrm{CH_2}\overset{\overset{\mathrm{O}}{\|}}{\overset{+}{\mathrm{S}}}\mathrm{Me_2}$ (**1**)	100	:	0
CH_2I_2/Zn-Cu	83	:	17
$Cp(CO)_2FeSMe_2BF_4$ (**5a**)	0	:	100

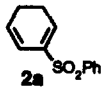
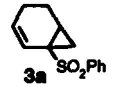
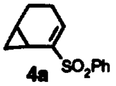
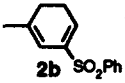
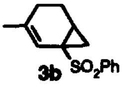
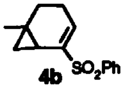
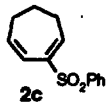
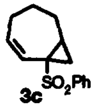
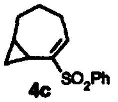
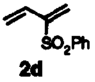
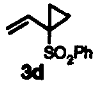
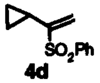
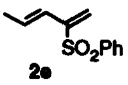
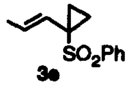
To obtain a cyclopropanation of the electron-rich double bond we initially tried to use Simmon-Smith type cyclopropanation reagents. However these reagents produced a mixture of the two possible vinylcyclopropanes with a predominance for attack at the electron-deficient double bond. For example, reaction of diene **2** with CH_2I_2/Zn-Cu afforded a 83:17 mixture of the vinylcyclopropanes **3a** and **4a**, respectively, in a moderate yield. This shows that the Simmon-Smith carbene is quite nucleophilic in character.

Recently, a new type of electrophilic cyclopropanation reagents, which involve iron-carbene intermediates, have been developed.[9-13] Different reagents **5** (Cp = η^5-cyclopentadienyl) have been used to generate a reactive iron-carbene in situ, which subsequently cyclopropanates the olefin. The reactive iron-carbon complex is positively charged and therefore presumably electrophilic in character.



Reaction of 2-(phenylsulfonyl)-1,3-cyclohexadiene (**2a**) with reagent **5a** in acetonitrile according to the original procedure for cyclopropanation[9] led to a slow reaction. Using this procedure only 25% of cyclopropane product was obtained together with unreacted starting material even after 24 h in refluxing acetonitrile. Interestingly, the reaction was highly regioselective and only *cyclopropanation at the electron-rich double bond was observed* (eq. 1). A change of reaction conditions to refluxing nitromethane[14] led to significant improvement. Thus, reaction of **2a** and **5a** in refluxing nitromethane for 6h resulted in complete transformation of the starting material and cyclopropane **4a** was obtained in 68% yield (Table 1, entry 2). There was no trace of the regioisomeric vinylcyclopropane in the reaction mixture, showing that the carbene reagent is highly electrophilic in its character. Cyclopropanation of some additional 2-phenylsulfonyl

Table 1. Regioselective Cyclopropantion of 2-Phenylsulfonyl 1,3-Dienes

entry	diene	method[a]	reaction time	product	% yield[b]
1	 **2a**	A	15 min	 **3a**	99
2		B	6h	 **4a**	68
3	 **2b**	A	30 min	 **3b**	98
4		B	6h	 **4b**	55
5	 **2c**	A	3h	 **3c**	80
6		B	6h	 **4c**	69
7	 **2d**	A	15 min	 **3d**	52
8		B[c]	6h	 **4d**	40
9	 **2e**	A	3h	 **3e**	71

a. Method A: The diene in THF at 20°C was added to a solution of 1 in DMSO generated from Me_3SOI and NaH. The reaction was stirred at 20°C. Method B: Unless otherwise noted the diene (0.4 mmol) and **5a** (0.9 mmol) was heated (101°C) in nitromethane (0.5 ml). b. Isolated yield. c. The diene was generated in situ from 3-(phenylsulfonyl)sulfolen by SO_2 elimination (ref. 3c).

1,3-dienes with reagent **5a** was accomplished and the results are given in Table 1. Cyclic dienes gave fair to good yields of cyclopropanation product, whereas acyclic dienes afforded moderate yields. The high selectivity of reagent **5a** is noteworthy and should be useful in selective cyclopropanation of double bonds with different electron density.[15]

In this paper we have demonstrated highly selective cyclopropanations of either the 1,2 or the 3,4 double bond in 2-(phenylsulfonyl) 1,3-dienes leading to both regioisomers of synthetically useful vinylcyclopropanes.

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