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THE ROLE OF SULFUR FUNCTIONALITIES IN ACTIVATING AND DIRECTING OLEFINS IN CYCLOADDITION REACTIONS

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1. INTRODUCTION

This article reviews (4+2)- and (2+2)-cycloaddition reactions of olefins activated by sulfur atoms at different oxidation states. The reason for the use of sulfur functionalities lies in the fact that the reactivity may be modulated towards the specific substrate by changing the oxidation state of the sulfur atom. For example, while a vinyl sulfide is an electron rich dienophile reacting best with electron poor dienes (inverse-electron-demand cycloadditions), sulfoxides and sulfones impart electrophilicity which causes the olefin to react best with standard or electron rich dienes.

If the dienophile is activated by an optically active sulfoxide group, then the cycloaddition may occur with high diastereoselectivity. The steric and electronic differences of the four substituents at the sulfur atom (usually oxygen, lone pair electrons, alkyl and aryl groups) and the fact that the sulfoxide function may be directly bonded to the reactive prochiral site, make this class of chiral functions very attractive and efficient in asymmetric synthesis.

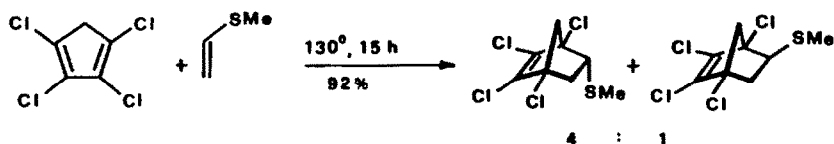
Furthermore, sulfur functionalities are amenable to a variety of synthetically useful transformations, most of which are mild and highly selective. During the discussion, emphasis will be given to the synthetic utilization and to the products which were made available through these reactions.

The present review deals mostly with carbocycles because heterocycles derived from hetero Diels-Alder reactions activated by sulfur containing dienes or dienophiles have already been reviewed.¹ It should also be noted that the effect of a sulfur atom bonded to the dienic counterpart has been reviewed.² We have not included those reactions in which sulfur substituted unsaturated compounds have been used as dipolarophiles.³ These works and the present one are complementary, and

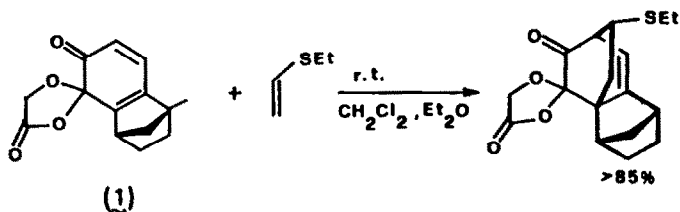
combined, they provide a comprehensive overview on the effect of sulfur functionalities upon cycloaddition reactions.

2. VINYL SULFIDES

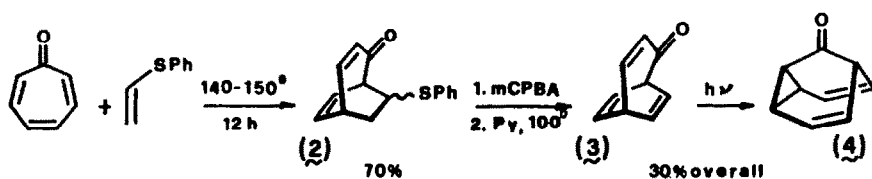
As already mentioned, vinyl sulfides are electron rich dienophiles and, as such, they react best with electron poor dienes, i.e. in inverse-electron-demand type processes. As an example, methyl vinyl sulfide reacts with tetrachlorocyclopentadiene under reasonably mild reaction conditions.⁴



The reaction of vinyl sulfides toward the masked *o*-quinone, **1**, has been used for the construction of the substituted denudatine system.⁵ Once the sulfur functionality has served to activate the dienophile then it can be removed by Raney nickel in methanol. In this context, vinyl sulfides may be regarded as reactive equivalents of ethylene, in inverse-electron-demand type cycloadditions.

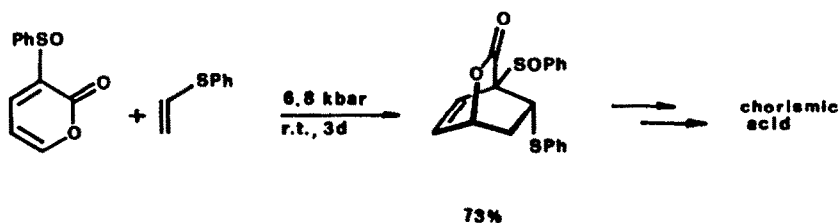


While reductive desulfurization leads to saturated hydrocarbons, oxidation of the adduct to the sulfoxide followed by sulfenic acid elimination afford alkenes so that vinyl sulfides can be regarded also as acetylene equivalents.⁶ As an example, the reaction with tropone gives the bicyclo-[3.2.2]nonanone derivative **2**⁷ and, with the mentioned reaction sequence, the triene **3** which photochemically can be converted into barbaralone (**4**).

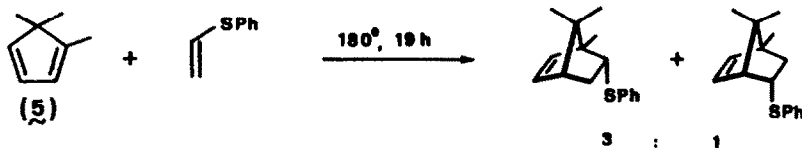
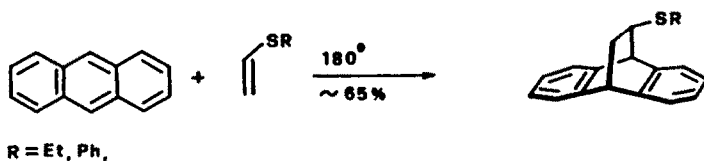
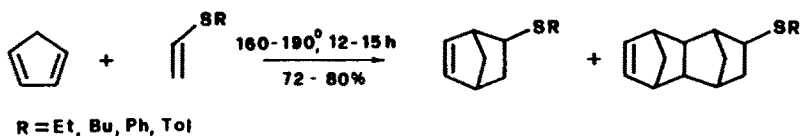


In a previous report, the same cycloadduct to tropone (**2**) was manipulated into more complex structures yielding the bicyclo[5.4.0]undecane ring system which is present in several natural products.⁸

The cycloaddition can be conveniently activated by high pressures as exemplified in the highly diastereoselective reaction of phenyl vinyl sulfide with pyrone sulfoxide which affords an intermediate for a total synthesis of chorismic acid.⁹

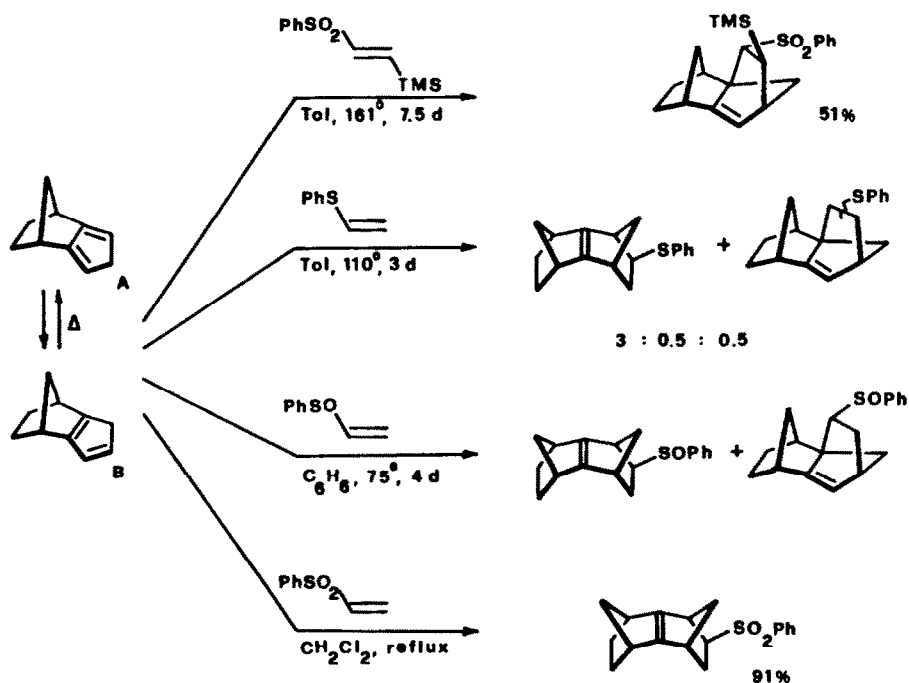


As a result of the frontier orbital coefficients, vinyl sulfides react poorly with standard dienes. Nevertheless, a few cases of the direct cycloaddition to cyclopentadiene,^{10,11} to anthracene,¹¹ and to the trimethyl substituted cyclopentadiene **5** are reported.¹² It is reasonable to assume that other



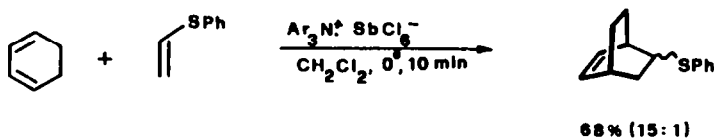
less reactive dienes do not react. The reaction conditions which are employed demonstrate the sluggishness of the reaction. Phenyl vinyl sulfone is reported to react under comparable conditions (180°C , 16 h) but, on the basis of recent knowledge (see below), such a temperature and time are probably unnecessary.

A rank of reactivity which compares vinyl sulfides with their oxidized homologues has been established by the analysis of the product distribution obtained in the addition to isodicyclopentadiene.¹³ It was demonstrated that, while reactive dienophiles add exclusively to the symmetric isomer A to afford linear cycloadducts, less reactive dienophiles add to the more reactive isomer B



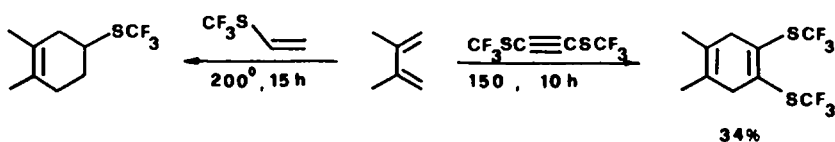
leading to angular adducts. As expected, vinyl sulfones are the most reactive, but somewhat unexpected is the fact that the introduction of a trimethylsilyl group renders the dienophile rather unreactive, even less than the sulfide.

Phenyl vinyl sulfide cycloaddition to electron rich substrates is susceptible to catalysis by triarylaminium salts.¹⁴ Under comparable conditions, without a catalyst the reaction does not occur.

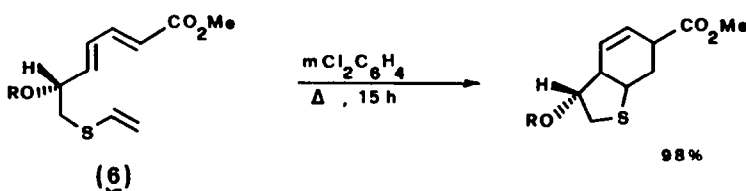


With other dienes, a competition between the (4+2)- and the (2+2)-cycloaddition has been observed.¹⁵ These reactions are radical-cations Diels–Alder cycloadditions which is a class of cycloadditions recently receiving a good deal of attention in view of its higher stereoselection and its synthetic potential.

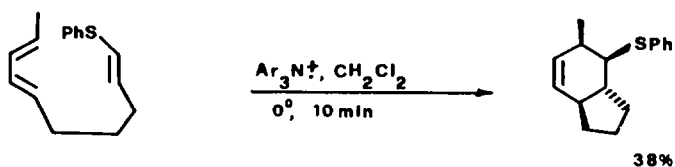
Cycloaddition to electron rich dienes may also be performed with sulfides substituted with electron withdrawing groups. For example trifluoromethyl vinyl sulfide and bis(trifluoromethylthio)acetylene have been shown to react with open chain dienes.¹⁶



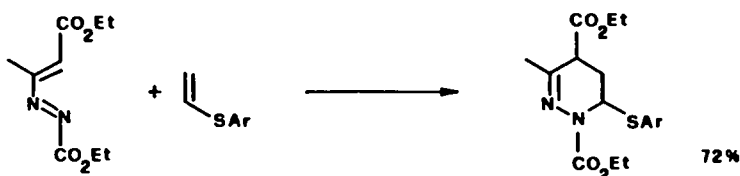
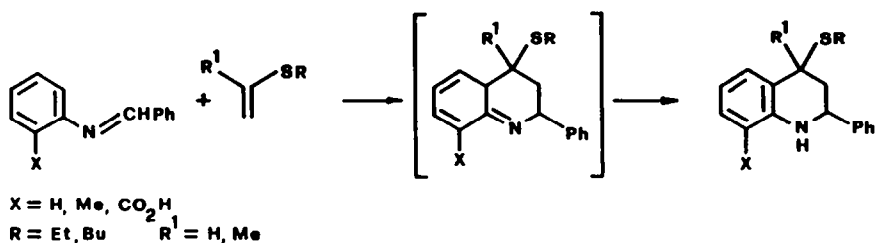
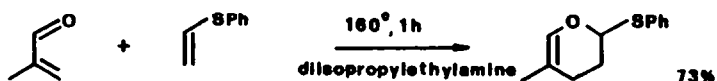
The intramolecular Diels–Alder cycloaddition of vinyl sulfides has been reported in a few cases. For example, the triene **6** cyclizes to form two major and two minor diastereoisomers.¹⁷



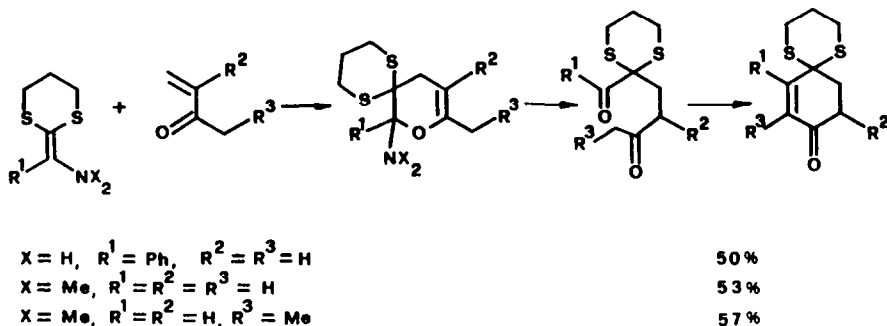
Stereoselection is strongly enhanced in the cation radical intramolecular Diels–Alder reaction. The cyclization shown gave a single diastereoisomer.¹⁸



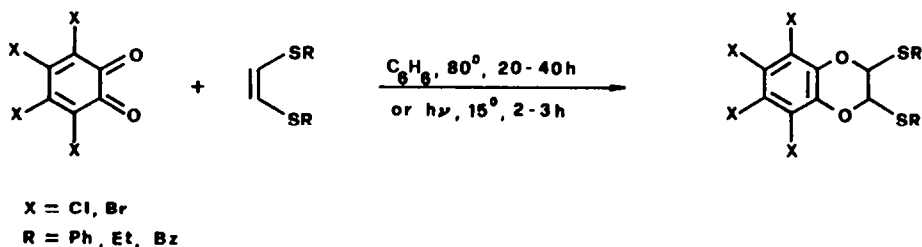
The cycloaddition of phenyl vinyl sulfides is also feasible with heterodienes.¹ The products may be functionalized pyrans,^{19,20} tetrahydroquinolines¹¹ or pyridazines.²¹ Hetero Diels–Alder cycloadditions appear to occur in high yield and with good regioselection.¹ Aminoketenes dithioace-



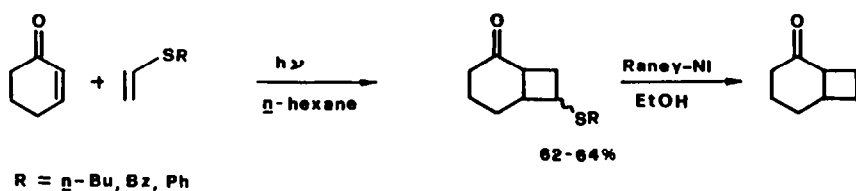
tals react with enones to give δ -diketones which undergo Robinson annelation to provide mono-acetals of cyclohex-2-ene-1,4-diones.²² The reaction of *o*-quinones with dithiosubstituted olefins



gives benzodioxanes.²³ Both (*Z*) and (*E*) isomers can be reacted.

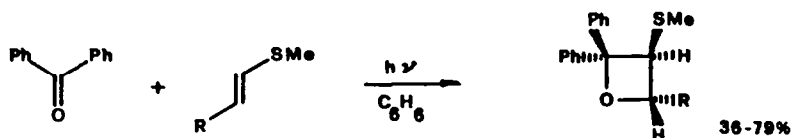


Photochemical cycloadditions of vinyl sulfides occur readily and in rather good yields with unsaturated ketones. Indeed these reagents are useful as synthetic alternatives to ethylene in (2+2)-cycloaddition reactions *via* reduction of the adduct.²⁴ Although not practically demonstrated, it can



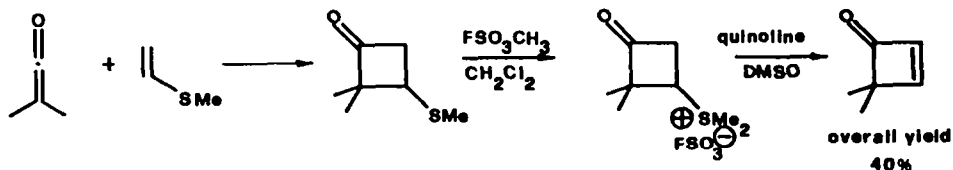
be envisaged that the same reaction sequence may be an alternative route to the use of acetylene in photochemical cycloaddition reactions, *via* oxidation and elimination of the sulfoxide.

Methyl vinyl sulfides trap excited benzophenone in a stereoselective and regiospecific fashion, yielding oxetanes.²⁵

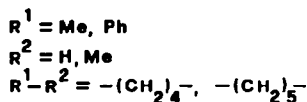
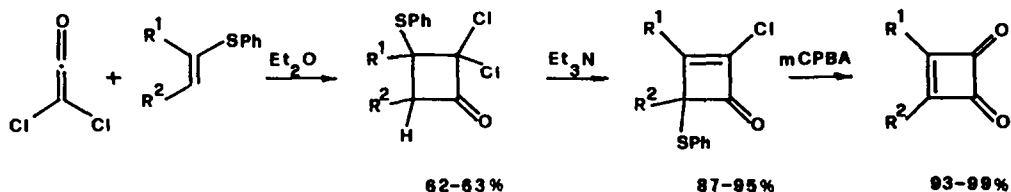


Cyclobutanes *via* (2+2)-cycloaddition of vinyl sulfides are also formed thermally when a zwitterionic intermediate is possible. This is the case of the addition to tetracyanoethylene extensively studied by Huisgen²⁶ and others.²⁷

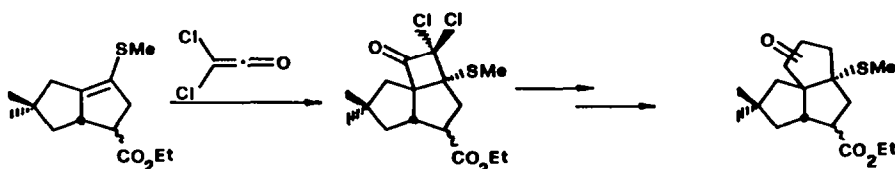
Ketenes give with vinyl sulfides functionalized cyclobutanones which can be elaborated into interesting molecules such as cyclobutenones.²⁸ Dichloroketenes react with a variety of phenyl-



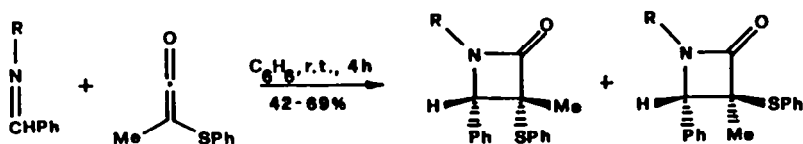
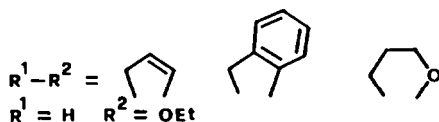
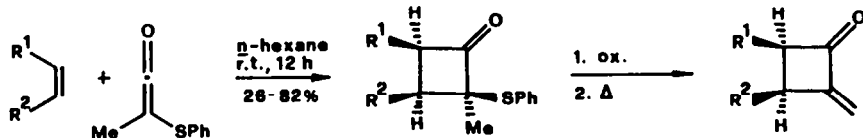
thioenoethers giving products which were transformed into cyclobutenediones.²⁹ These unsaturated



diketones are otherwise difficult to prepare. In a more recent example dichloroketene was added to a trisubstituted vinyl sulfide³⁰ and the adduct was transformed into a tricyclopentane system.

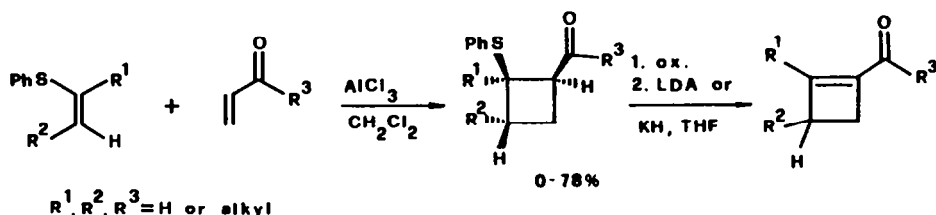


Methyl(phenylthio)ketene is a reactive and versatile reagent which affords functionalized cyclobutanones with a variety of substrates, including olefins, dienes, and imines.³¹ A few examples are



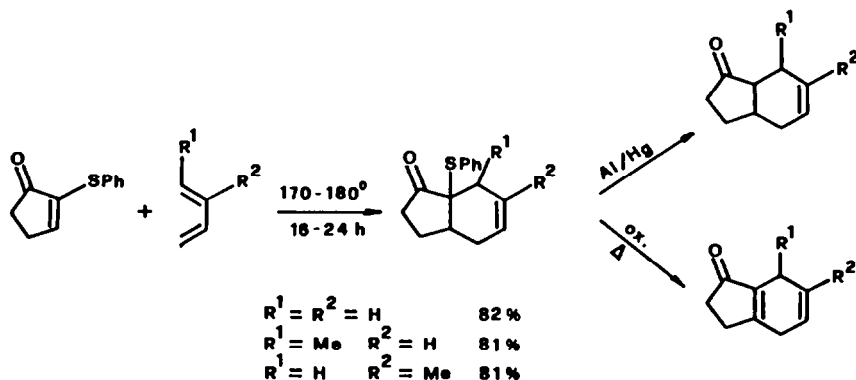
R = Et, *t*-Bu, Ph

illustrated. Thiosubstituted cyclobutanes can be prepared by the reaction of alkenyl sulfides with α,β -unsaturated ketones in the presence of aluminum trichloride. Oxidation and base treatment afford cyclobutenyl ketones in good yields.³²



A vinyl sulfide which is geminally substituted with an electron withdrawing group is more reactive towards electron rich dienes. The reactivity is enhanced not only with respect to the vinyl thioether but also with respect to the electron deficient olefin. In other words a thioether does not diminish the reactivity of a standard electron poor olefin but, in contrast with what one might think, it enhances it synergistically. This type of dienophile has been defined as *capto-dative* because the two groups have opposite polarity.

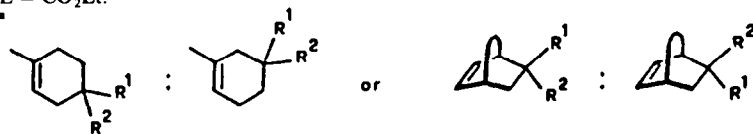
One of the first reported examples is shown below. It allowed the improvement of the yields of the cycloaddition of cyclic ketones with open chain dienes and contributed to the synthetic versatility of the adducts.³³ The reaction is further accelerated by Lewis acids (for example AlCl₃). Under such



conditions the cycloaddition of 2-phenylthio-2-pentenone with isoprene occurs even at 18°C in dichloromethane giving the (4+2) adduct in 93% yield after 15 h. Furthermore the regioselectivity

Table 1. Reaction conditions and yields in the cycloaddition of sulfur containing capto-dative dienophiles $R_1R_2C=CH_2$

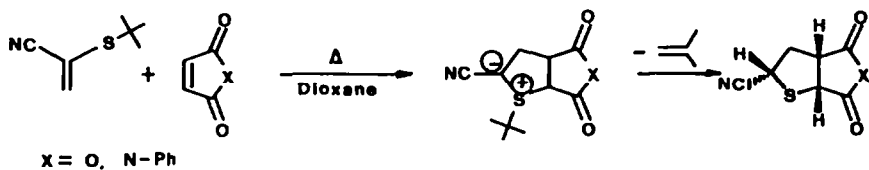
Diene	R_1	R_2	Solvent	Catalyst	Temp. (°C)/time (h)	Yields (%) (ratio) ^a	Ref.
Isoprene	SMe	CN	Neat	—	140/4	62(96:4)	35
Isoprene	SMe	CN	Neat	—	60/24	64(64:36)	36
Isoprene	SMe	CN	Toluene	—	120/4	79(66:34)	36
Isoprene	SMe	CN	Benzene	$AlCl_3$	20/6	81(97:3)	35
Isoprene	SMe	E	Benzene	$AlCl_3$	20/4	84(97:3)	35
Cyclopentadiene	SMe	CN	Neat	—	140/6	57(50:50)	35
Cyclopentadiene	SMe	CN	Neat	—	20/12	85(5:95)	36
Cyclopentadiene	SMe	CN	Neat	—	20/12	85(5:95)	37
Cyclopentadiene	SMe	CN	Toluene	—	140/4	53(34:66)	36
Cyclopentadiene	SMe	CN	Benzene	$AlCl_3$	20/0.25	60(0:100)	35
Cyclopentadiene	SMe	CN	Benzene	$CuBF_4$	20/6	88(0:100)	35
Cyclopentadiene	SMe	E	Benzene	$AlCl_3$	20/4	77(0:100)	35
Cyclopentadiene	SMe	E	Ether	—	rt/14d-3w	35-45 ^b	38
Cyclopentadiene	SiPr	CN	c	—	100/ ^c	100(23:77)	39
Cyclopentadiene	SiPr	CN	Neat	—	20/12	85(25:75)	36
Cyclopentadiene	SBu	CN	Neat	—	20/12	95(40:60)	36
Cyclopentadiene	SPh	CN	Neat	—	20/12	93(23:77)	36
Cyclopentadiene	SBz	CN	Neat	—	20/12	96(22:78)	36
Cyclohexadiene	SMe	CN	Neat	—	160/4	50(23:77)	35
Cyclohexadiene	SMe	CN	Neat	—	80/10	53(34:66)	36
Cyclohexadiene	SMe	CN	Benzene	$AlCl_3$	20/6	72(17:83)	35
Cyclohexadiene	SMe	E	Benzene	$AlCl_3$	20/4	81(0:100)	35
Cyclohexadiene	SMe	E	Phenylthiazine	—	reflux/30	10 ^b	38

E = CO_2Et .^b Ratio not reported.^c Not reported.

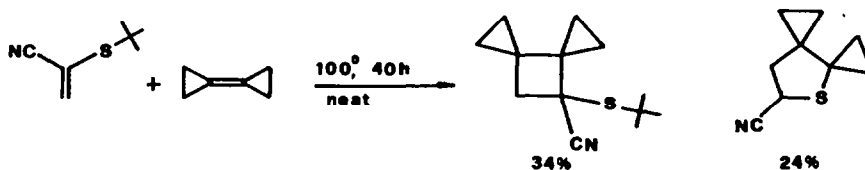
is improved. The cycloaddition of 2-cyclopentenone required longer reaction time (48 h) and occurred in lower yield (21%).

Many other examples of the cycloaddition of sulfur containing capto-dative dienophiles have been reported. Most of them are collected in Table 1. It is worth mentioning that capto-dative sulfur-containing dienophiles are readily accessible by a variety of methods.^{40,41} Among the transformations to which the products can be subjected is included a mild and simple conversion to ketones, thus including capto-dative olefins among the ketene equivalents in (4+2)-cycloaddition reactions (see below).^{35,36}

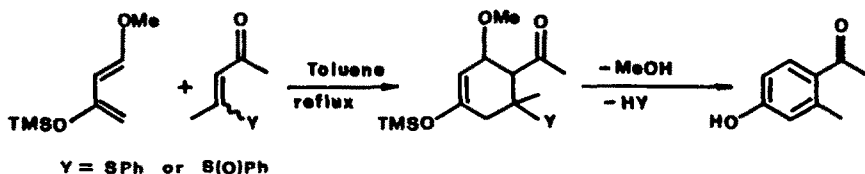
Cyclic thioenolethers undergo (3+2)-cycloaddition to electron poor dienophiles to form unstable five-membered cyclic sulfonium ylids.⁴² In the case of *t*-butylsubstituted thioethers, the ylid loses isobutene and gives stable products.⁴³



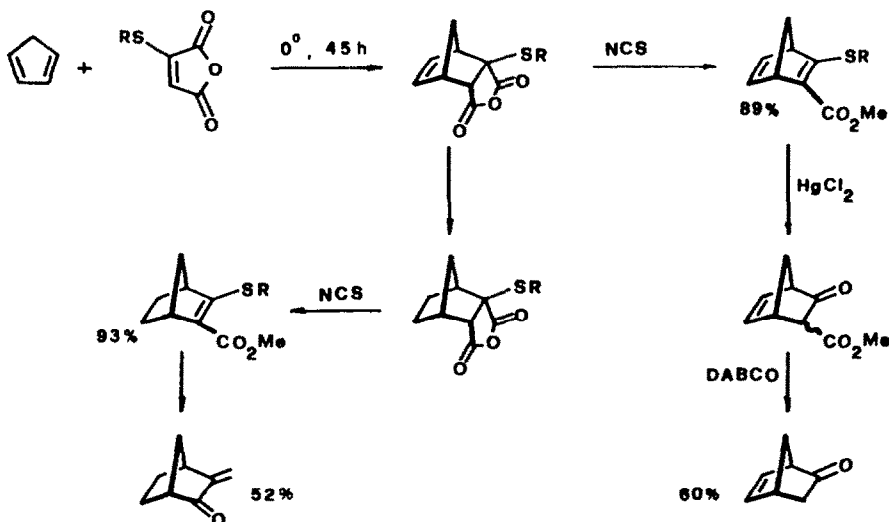
Analogous reactivity has been experienced in the cycloaddition to methylenecyclopropanes.⁴⁴



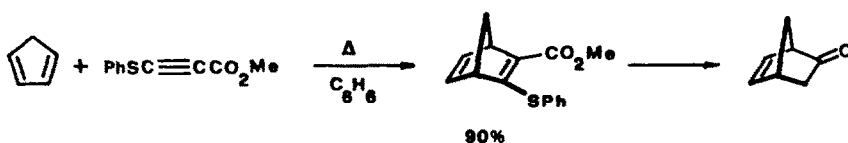
When the thio-substituent and an extra electron withdrawing group are in vicinal positions, then the dienophile is no more capto-dative. The reported examples can be attributed to activation by the electron withdrawing group with no appreciable synergetic effect of the sulfur. There have been reported cycloadditions to cyclopentadiene of vinyl sulfides activated by carboxy⁴⁵ or nitro groups.⁴⁶ In the case shown below, the regioselectivity is dictated by the carbonyl function.⁴⁷



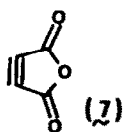
A large variety of cycloadducts (and synthetic transformations thereof) has been accomplished with thiosubstituted maleic anhydrides.⁴⁸ The sequence shown may allow the mimicry of the



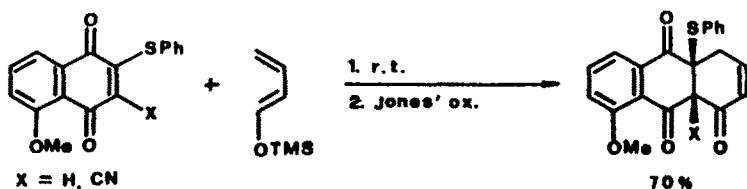
reactivity of a carbene in a (4+2)-cycloaddition meanwhile carbenes themselves give cyclobutanones in a (2+2)-type process.⁴⁹ Cycloaddition of alkylthiopropiolates⁵⁰⁻⁵² has been proposed as a more direct alternative.⁵³



Thiosubstituted maleic anhydrides may be considered as equivalents of the acetylene anhydride 7.⁵⁴



Quinone derivatives with a phenylthio substituent are reactive dienophiles: they have been used in a formal total synthesis of aklavinone.⁵⁵ This strategy allows the synthesis of blocked anthraquinone tautomers.

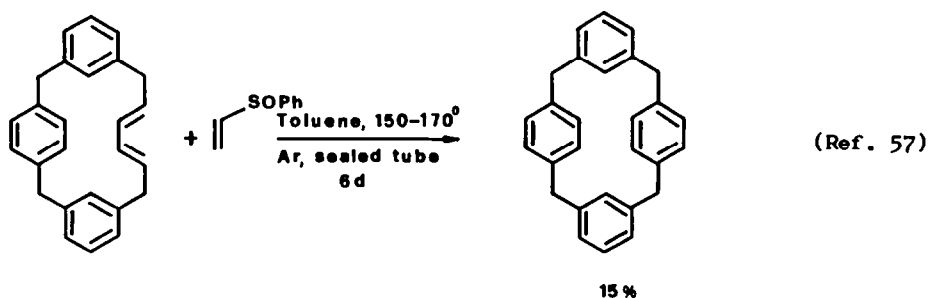
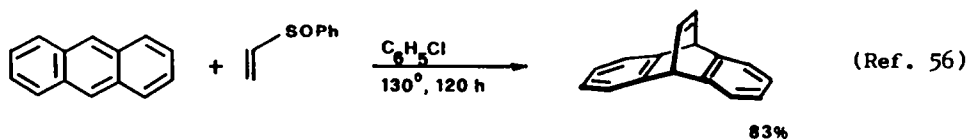


3. VINYL SULFOXIDES

3.1. *Racemic vinyl sulfoxides*

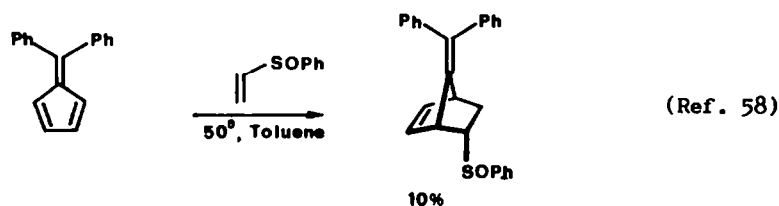
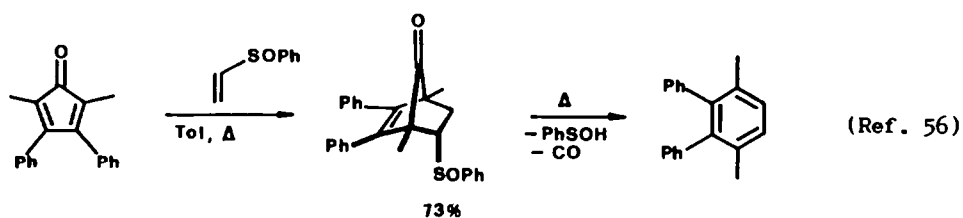
The most important feature of vinyl sulfoxides is that they can be prepared in optically active form. However, there are cases in which the sulfoxide function has been used only as an activating functionality.

Phenyl vinyl sulfoxides can effectively function as acetylene equivalents in Diels–Alder reactions⁵⁶ as the primary cycloadducts may spontaneously extrude sulfenic acid. The reaction is possible because the sulfenic acid eliminates better from the saturated adduct than from the olefinic reagent. The following equations show a few examples. Similarly isobenzofuran affords 1,4-diphenyl-

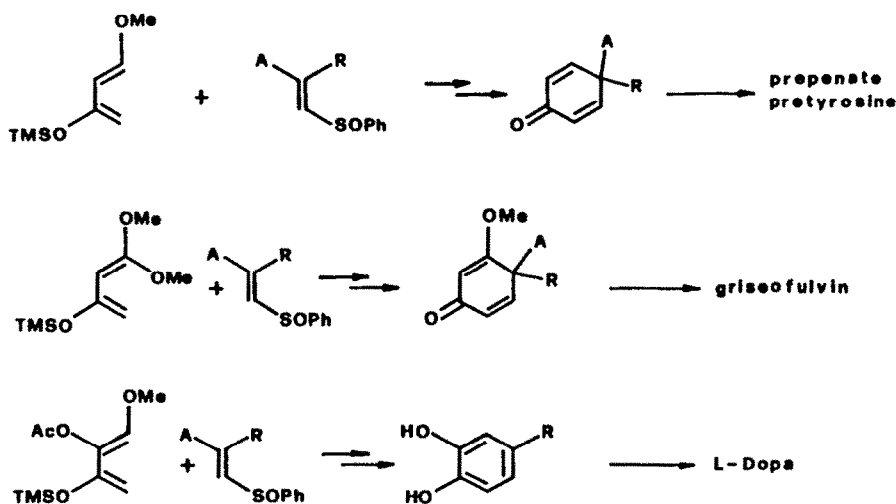


naphthalene (93%), 3,6-diphenyltetrazine yields 1,4-diphenylpyridazine (97%), and tetracyclone gives 1,2,3,4-tetraphenylbenzene (91%) after extrusion of oxygen, nitrogen and carbon monoxide respectively.⁵⁶

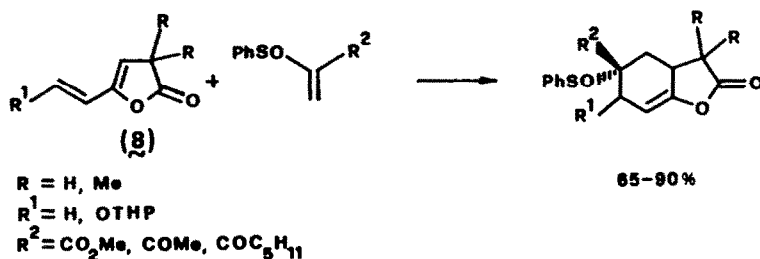
In a few cases the cycloadduct could be isolated and characterized.^{56,58,59} The reactivity of olefins



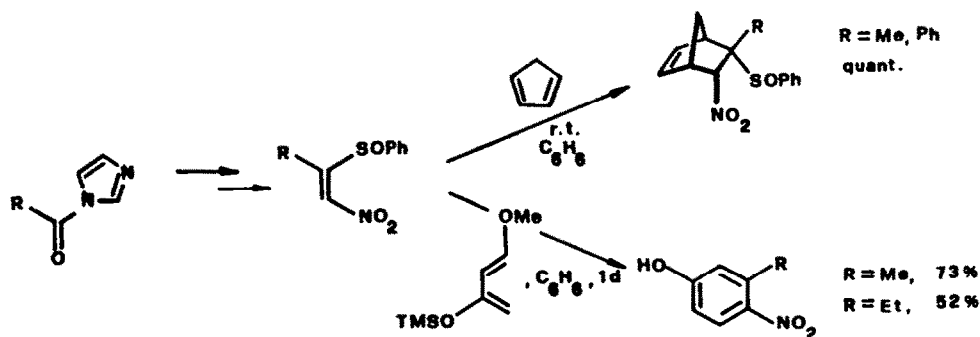
substituted only with a sulfinyl group is poor. It is often necessary to have an extra electron withdrawing group present. Danishefsky and his coworkers have prepared several olefins containing the phenylsulfinyl group and the carbomethoxy group and utilized them for the synthesis of several natural products.⁶⁰



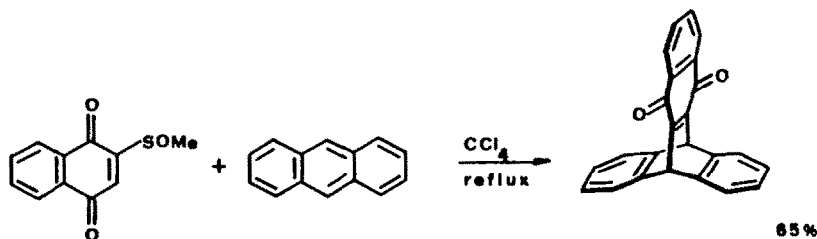
When the extra electron withdrawing group is at the same carbon bearing the sulfoxide, the reactivity is higher and is similar to that observed for the capto-dative vinyl sulfides. In the sulfoxide field no specific studies have been reported, but the capto-dative effect can be identified by the fact that only 1,1-substituted dienophiles reacted with the diene **8**.⁶¹ 2-Sulfinyl substituted acrylates were unreactive.



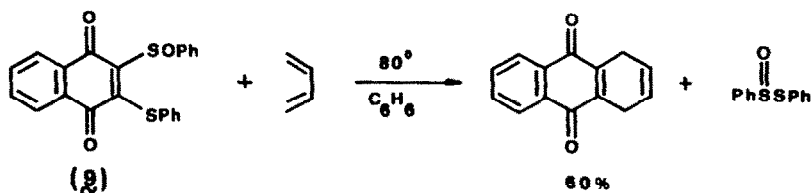
Because of inconvenience in their preparation and their instability, nitroacetylenes are rarely used as dienophiles in Diels-Alder reactions.⁶² However, an alternative is based on the use of phenylsulfinylnitro olefins.⁴⁶ The substituted analogues can be prepared in four steps from acylimidazoles.⁶³



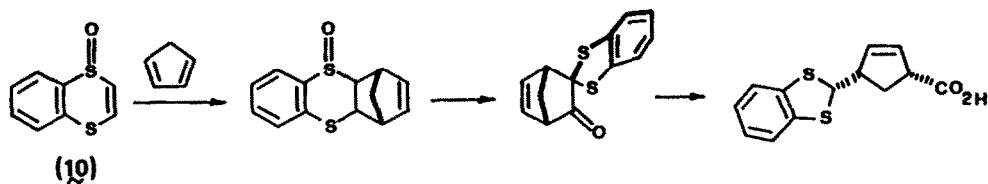
A series of anthraquinone derivatives has been obtained directly by the Diels-Alder cycloaddition of quinone sulfoxides with dienes. The quinone sulfoxide represents a synthetic equivalent of naphthoquinone⁶⁴ because the adducts eliminate sulfenic acid under the reaction conditions.⁶⁵



Alternatively the related naphthoquinone **9** can be used in the same fashion. At variance with the precedent cases the primary adduct does lose a phenylthiosulfinate molecule.⁶⁵ Finally reagent **10**

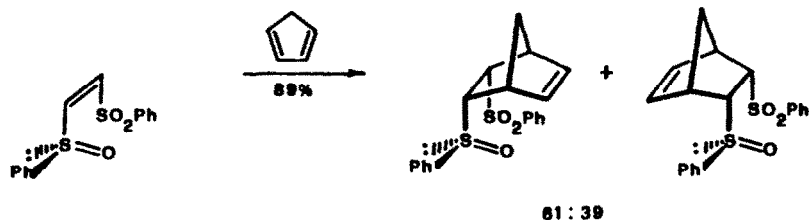


has been reported as a sluggish dienophile, but it is sufficiently reactive to add to cyclopentadiene.⁶⁶ The adducts are of synthetic interest.

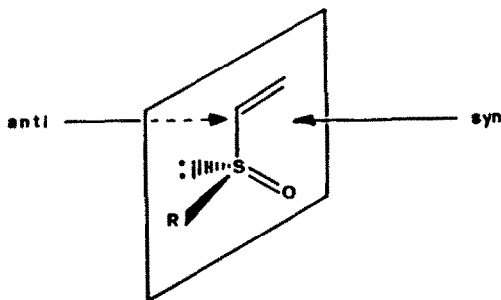


3.2. Stereochemistry of addition

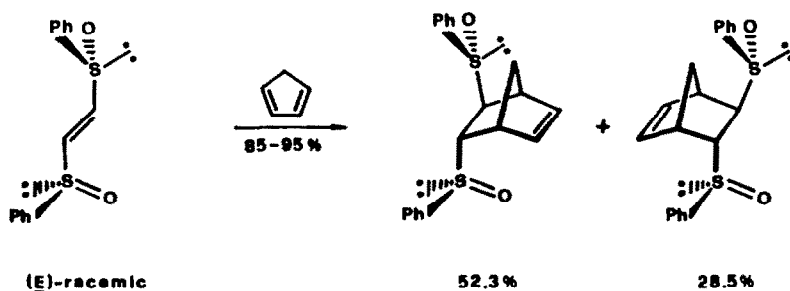
Although the first reports on cycloaddition reactions with chiral vinyl sulfoxides appeared only a few years ago, stereochemical studies on the steric course of the reaction of racemic vinyl sulfoxides have been reported by Montanari *et al.* since the late fifties.⁴⁵ They termed the adducts to cyclopentadiene *syn* or *anti* depending if the S=O bond was below or outside the norbornenyl skeleton when the S—R bond is positioned parallel to the bridgehead proton.* With few exceptions, the preferred way of addition of sulfanyl olefins to cyclopentadiene was shown to be *endo-syn* as in the case of (*Z*)-1-phenylsulfonyl-2-phenylsulfinylethylene.⁶⁷ The following stereochemistry could be demonstrated



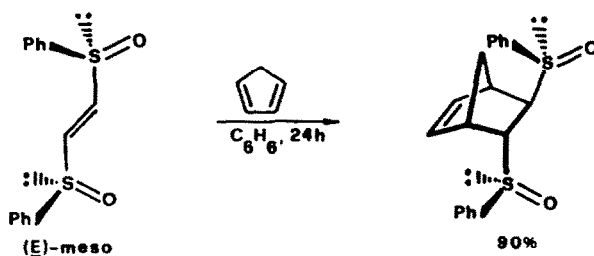
* The stereochemistry of the sulfoxides has been drawn in the same way throughout the text. Namely with the C=C—SR atoms in one plane, with the lone pair on the left and the oxygen on the right side. The adducts have been drawn after consideration of the direction of attack of the diene on the dienophile.



for the bis(phenylsulfinyl)ethylene adducts to cyclopentadiene.⁴⁵ An exception to the *syn* rule was

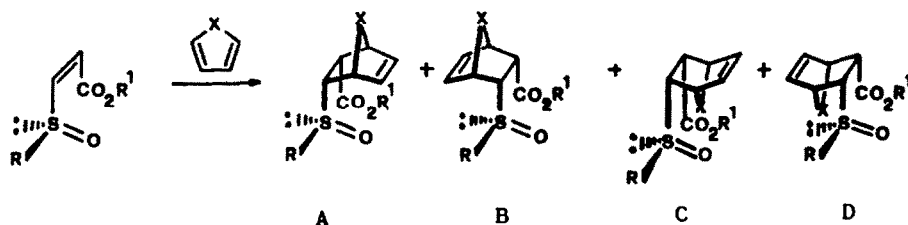


observed with the (*E*)-*meso* isomer. A more complex set of products is produced by the addition



of 3-sulfinylprop-2-enoic acids and their methyl esters to cyclopentadiene. Tables 2 and 3 collect the results obtained for the (*Z*)- and (*E*)-isomers under different conditions and in the presence of Lewis acids. As can be observed, the Lewis acid does not usually promote a synergetic action. On the contrary, in some cases it reverses the ratio in favour of the minor stereoadduct.⁶⁹ In the case in which the sulfinyl group adds in an *exo* fashion, predominance of the *syn* stereoadduct is again usually observed.

Table 2. Reaction conditions and product distribution in the addition of (*Z*)-3-sulfinylprop-2-enoic acids



	X	R	R'	Solvent	Temp. (°C)/time	Catal.	A	B	C	D	Ref.
1	CH ₂	Ph	H	Benzene	80/40 min	—	80 ^a	20 ^a	5	5	68
2	CH ₂	Ph	H	Benzene	80/40 min	—	92 ^{b,c}	8 ^{b,c}	—	—	69
3	CH ₂	Ph	Me	Benzene	80/overnight	—	97 ^c	3 ^c	—	—	69
4	CH ₂	Ph	Me	CH ₂ Cl ₂	rt/28 h	AlCl ₃	79 ^c	21 ^c	—	—	69
5	CH ₂	Ph	Me	Benzene	rt/3 h	SiO ₂	59 ^c	41 ^c	—	—	69
6	CH ₂	Ph	Me	CH ₂ Cl ₂	rt/28 h	SnCl ₄	21 ^c	79 ^c	—	—	69
7	CH ₂	Ph	H	H ₂ O	rt/0.5 h	—	58 ^c	42 ^c	—	—	70
8	O	2-Py	Et	Neat	50/6 d	—	27 ^d	22 ^d	12 ^d	1 ^d	70
9	O	Ar	Et	Neat	50/6 d	—	55 ^d	—	16 ^d	—	70
10	O	Ar'	Et	Neat	rt/7 h	—	58 ^d	5 ^d	7 ^d	1 ^d	70

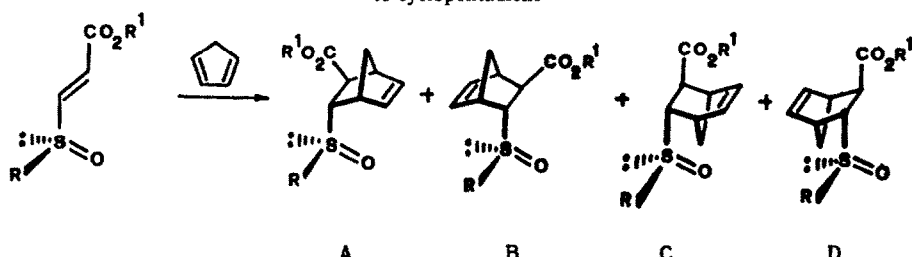
^a Ratio determined after iodolactonization.

^b Ratio determined after methylation with diazomethane.

^c Ratio determined by HPLC.

^d Ratio determined after chemical transformation to 2-carboxy-7-oxabicyclo[2.2.1]heptane.

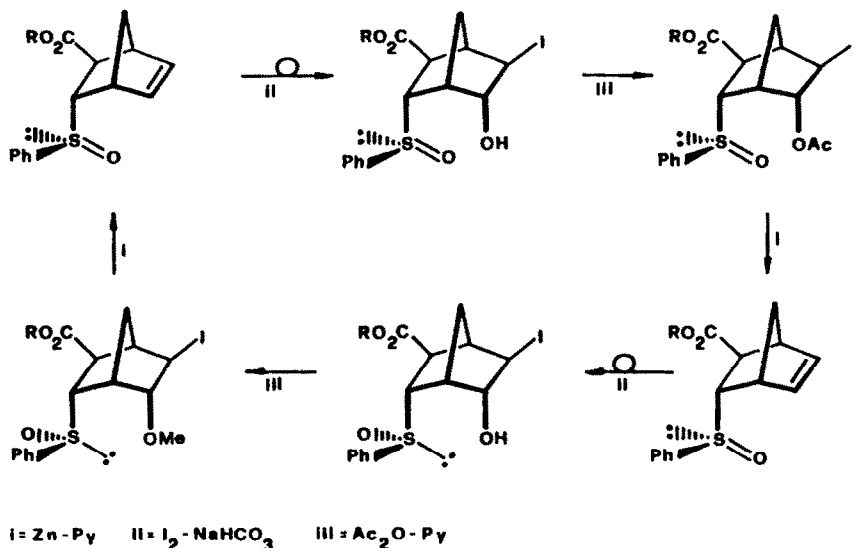
Ar = 3-NO₂-2-Py, Ar' = 3-CF₃-2-Py.

Table 3. Reaction conditions and product distribution in the addition of (*E*)-3-sulfinylprop-2-enoic acids to cyclopentadiene


R	R'	Solvent	Temp. (°C)/time	Catal.	A	B	C	D	Ref.	
1	Ph	H	Benzene	80/2 h	—	39	13	29	19	68 ^a
2	Ph	H	Benzene	80/50 min	—	37	15	36	12	69 ^b
3	Ph	H	H ₂ O	20/0.5 h	—	33	20	38	9	69 ^b
4	Ph	Me	Benzene	80/overnight	—	35	14	39	12	69 ^b
5	Ph	Me	CH ₂ Cl ₂	20/60 h	SnCl ₄	19	19	48	14	69 ^b
6	Ph	Me	CH ₂ Cl ₂	20/4 h	AlCl ₃	35	39	18	8	69 ^b
7	Ph	Me	Benzene	20/4–5 h	SiO ₂	37	20	33	10	69 ^b

^a Ratio determined by iodolactonization.^b Ratio determined after methylation with diazomethane by HPLC.

The stereochemistry at sulfur has been determined in a variety of ways including iodolactonization or iodohydrin formation.⁷¹ These reactions may prove to be useful in the separation of diastereoisomers derived from optically active sulfinyl dienophiles (see next paragraph). In other



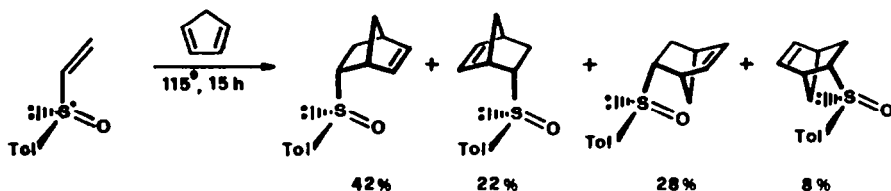
cases, the stereochemistry has been correlated by (i) the reduction by boranes of the sulfoxides to sulfides, (ii) stereochemistry and kinetics of oxidation of sulfoxides to sulfones, (iii) acidities and (iv) infrared and proton magnetic resonance.

It is worth noting that the reaction of sulfinylpropenoic acids is not confined to cyclopentadiene. Recent results have shown that 3-(2-pyridylsulfinyl) acrylates add in high yields to the rather unreactive furan. In the same paper, the enhancement of reactivity and diastereoselectivity with the introduction of electron withdrawing substituents on the pyridyl ring is shown.⁷⁰ The results obtained in this study have been expanded to the optically active molecules by the same authors (see next Section).

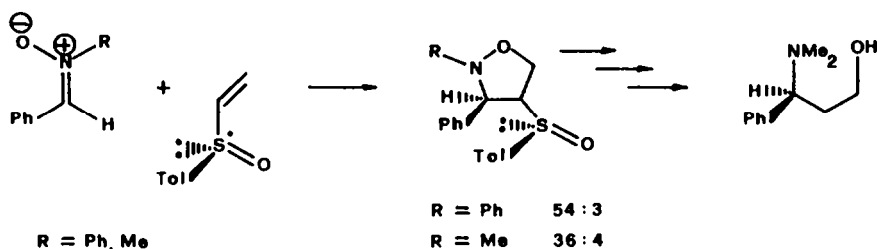
The stereochemistry of addition of sulfinyl dienophiles has recently been examined from a computational point of view by Hehre and Kahn,⁷² but the matter is still controversial.⁷³

3.3. Chiral vinyl sulfoxides

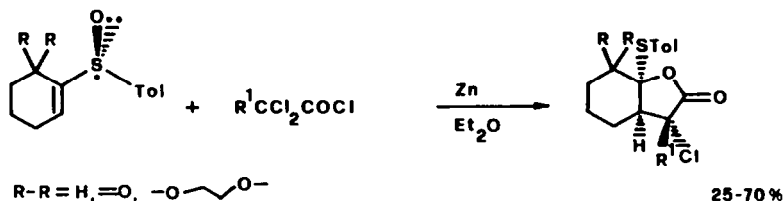
In recent years examples have been reported on Diels–Alder reactions of optically active sulfinyl dienophiles. The first report is by Maignan and Raphael⁵⁹ who utilized (+)-(*R*)-*p*-tolyl vinyl sulfoxide. The stereochemistry of the carbon skeleton was assigned by transformation to



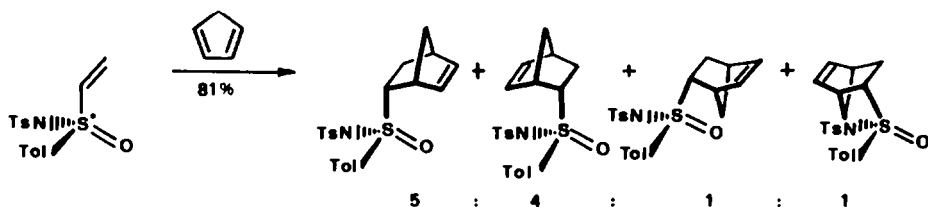
dehydronorcamphor. The stereochemistry at the sulfur atom was not reported but can be suggested to be as shown by analogy to other works and from the fact that the configuration of the carbon skeleton corresponds to the *syn* usual way of addition. Although this was the first asymmetric Diels–Alder addition to be reported with an optically active chiral sulfoxide, other types of asymmetric cycloadditions have been studied. For example, Koizumi showed that the dipolar cycloaddition to nitrones occurs with high asymmetric induction.⁷⁴



Marino studied the reaction of vinyl sulfoxides with ketenes and reported complete asymmetric induction for such a process.⁷⁵ The Diels–Alder reaction of chiral sulfoximines is a process strongly

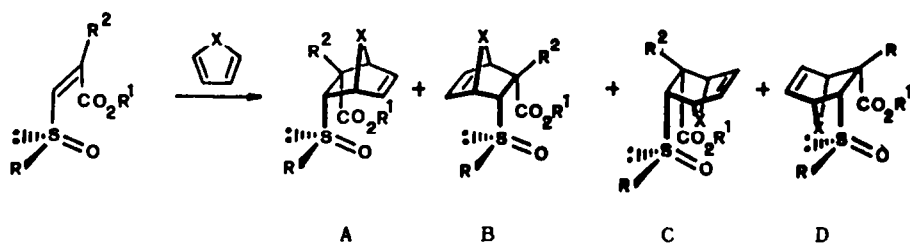


related to the one with vinyl sulfoxides.⁷⁶ It should be noted that the stereochemistry of the adduct to cyclopentadiene still favours the *endo-syn* isomer. The reaction has been reported with other



cyclic and acyclic dienes and with different chiral sulfoximines. These reagents are much more reactive than the sulfoxides and competition experiments have shown them to be even more reactive than vinyl sulfones in Diels–Alder reactions. The products are amenable to a variety of transformations, including reduction to alkanes, elimination to alkenes, or oxidation to ketones.

The poor reactivity toward dienes of simple chiral vinyl sulfoxides has led to the development of other dienophiles in which an additional electron withdrawing group is present. Tables 4 and 5 collect the reported examples for (*Z*)- and (*E*)-sulfinylpropenoic esters. Comparison with the results obtained with racemic substrates (Tables 2 and 3) shows that there are obviously no major

Table 4. Reaction conditions, yields and stereoisomeric distribution in the addition of chiral (*Z*)-sulfinylpropenoic esters

	R	R'	R''	X	Solvent (Catal.)	Temp. (°C)/time (h)	A	B	C	D	Yield (%)	Ref.
1	Tol	Et	Me	CH ₂	Neat	90/5	63 ^a	2	35	—	91 ^b	77
2	Tol	Me	H	CH ₂	Toluene	4/60	93 ^c	—	7	—	100	78
3	Tol	<i>n</i> -Bu	H	CH ₂	Benzene	Reflux/2	77 ^a	3	11	—	91	79
4	^d	Me	H	CH ₂	CDCl ₃	5/24	98 ^c	—	—	—	98	80
5	^d	Me	H	CH ₂	MeOH	5/24	98 ^c	—	—	—	98	80
6	^d	Me	H	CH ₂	Me ₂ CO	5/24	98 ^c	—	—	—	98	80
7	^e	Me	H	CH ₂	CDCl ₃	5/24	95 ^c	—	—	—	95	80
8	^c	Me	H	CH ₂	MeOH	5/24	98 ^c	—	—	—	98	80
9	^f	Me	H	CH ₂	CH ₂ Cl	-78/100	98 ^c	—	—	—	98	81
10	2-Py	Ment	H	O	Neat (EtAlCl ₂)	rt/7d	93	7	96	4	69	82
11	2-Py	Ment	H	CH ₂	Neat (EtAlCl ₂)	-78/3	96	—	—	—	96	83

^a Ratio determined by HPLC.

^b Isolated yields.

^c Ratio determined by NMR.

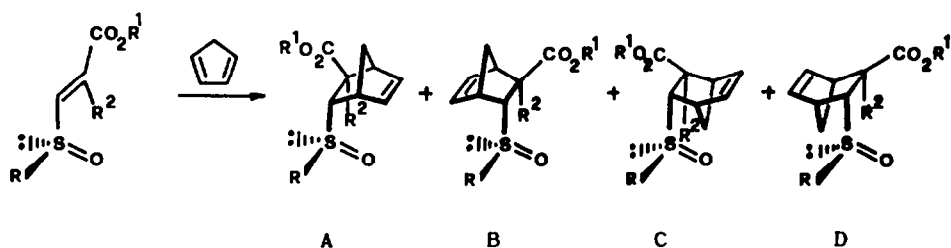
^d Isoborneol.

^e Borneol.

^f 2-Phenyl-2-hydroxyethyl.

differences. Small variations are probably due to different methods of products analysis. In the (*Z*) series it is worth noting the effect of the methyl group (entry 1) which decreases the diastereomeric ratio. Product C has been utilized in the synthesis of (+)-*epi*- β -santalene.⁸⁴

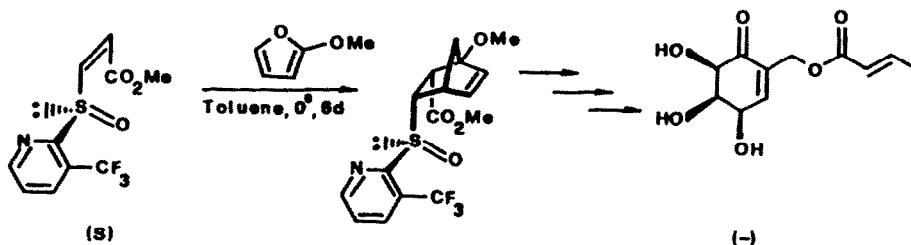
Recent interest has been devoted to the reaction with furan because the derived cycloadducts can be transformed into optically active natural products. With this objective standard chiral sulfinyl

Table 5. Reaction conditions, yields and stereoisomeric distribution in the addition of chiral (*E*)-sulfinylpropenoic esters to cyclopentadiene

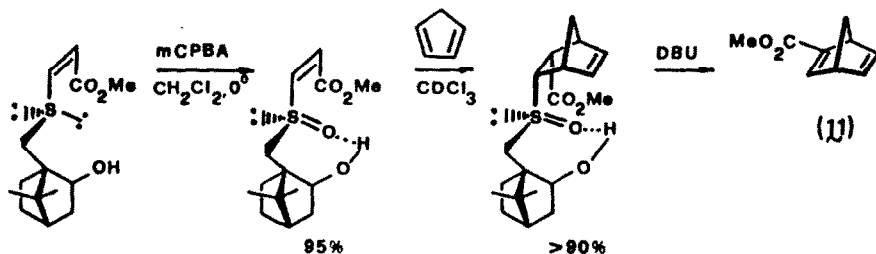
	R	R'	R''	Solv.	Temp. (°C)/time (h)	Catalyst	A	B	C	D	Yield (%)	Ref.
1	Tol	Et	Me	Neat	90/5	—	63	15	22	—	91	77
2	Tol	<i>n</i> -Bu	H	C ₆ H ₆	Reflux/2	—	37	6	42	15	92	79
3	Tol	<i>n</i> -Bu	H	Toluene	0/3.5	BF ₃	56	22	19	3	98	79
4	Tol	<i>n</i> -Bu	H	Neat	0/3.5	SnCl ₄	23	3	55	19	82	79
5	Tol	<i>n</i> -Bu	H	Neat	0/3.5	TiCl ₄	25	21	29	25	63	79
6	^a	Me	H	CHCl ₃	5/24	—	mixture			>90	80	

^a Isoborneol or borneol.

dienophiles are not sufficiently reactive so a more reactive one had to be developed by Koizumi.⁸² In such a dienophile the ester residue is a menthyl group that allowed the resolution of the sulfoxides by fractional crystallization. The Diels–Alder reaction gives, with high diastereoselectivity, the *syn* adduct, as deduced by the configuration of the resulting carbon skeleton. The diastereoselectivity can also be improved by catalysis with diethylaluminium chloride. Notable examples of the application of these reagents are the highly enantioselective total synthesis of glyoxalase I inhibitor,⁸⁵ D-showdomycin, D-2,5-anhydro-allose derivatives,⁸⁶ (–)-aristeromycin and (–)-neplanocin A.⁸³ The first of these examples is illustrated below.



The most detrimental aspect of the utilization of chiral sulfoxides in asymmetric synthesis is the difficulty and the poor yields in their preparation. The preparation of optically active sulfinyl dienophiles usually makes use of routes which start from menthyl sulfinate (that is the Andersen method).⁸⁸ With the intention of providing more direct and stereospecific routes, the synthesis of chiral sulfoxides by self-induced diastereoselective oxidation has been proposed.⁸⁰ The strategy allows the stereoselective synthesis of optically active sulfinyl dienophiles in two steps (Michael addition and oxidation) from cheap and readily available starting materials. The presence of a chiral hydroxy group drives the oxidation of the sulfide predominantly to one epimeric sulfoxide. Once the sulfoxide is formed this helps to give conformational rigidity to the molecule by hydrogen bonding with the sulfoxide oxygen. Indeed such a designed dienophile shows high asymmetric induction both in the oxidation and especially, in the Diels–Alder reaction.⁸⁰



Cycloaddition of the two epimeric sulfoxides occurs diastereoselectively and depends upon the configuration of the sulfur atom. The diastereoselection is primarily due to the sulfoxide and not to the chiral auxiliary (as independently shown in other cases).⁸² Cycloadditions of the corresponding sulfones show little or no diastereoselection.

The adducts can be subjected to base induced elimination to form optically active carbomethoxy-norbornadienes, but the chiral auxiliary is recoverable with difficulty. To solve this drawback, the analogous sulfoxide derived from optically active styrene oxide was developed.⁸¹

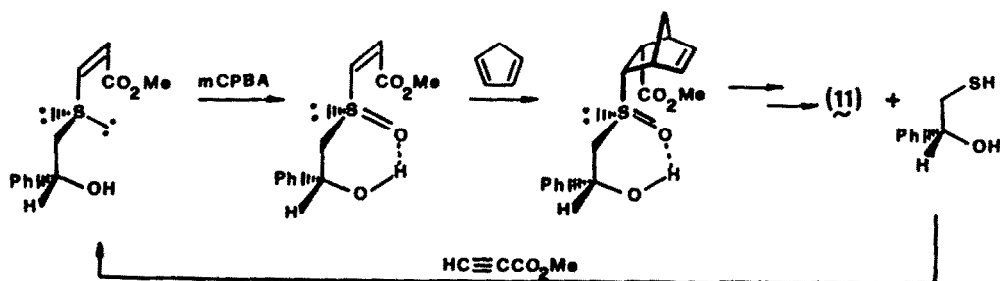
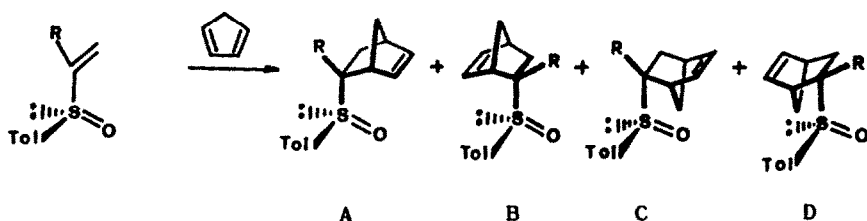
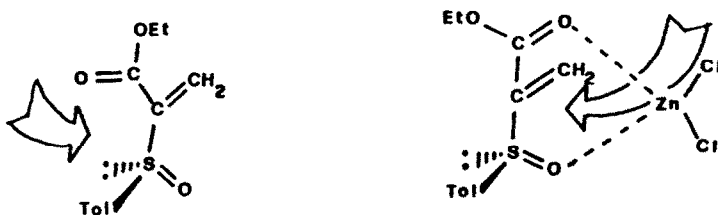


Table 6. Reaction conditions, yields and stereoisomeric distribution in the addition of chiral (*E*)-sulfinylpropenoic esters to cyclopentadiene

	R	Solvent	Temp. (°C)/time (h)	Catalyst	A	B	C	D	Yield (%)	Ref.
1	CO ₂ Me	C ₆ H ₆	rt/6	—	23	2	64	11	100	89
2	CO ₂ Me	CH ₂ Cl ₂	0/3	ZnCl ₂	2	19	2	77	100	89
3	COMe	CH ₂ Cl ₂	20/12	—	<5	<5	38	56	>94	78

Chiral 2-substituted sulfinylpropenoic esters are reported to be more reactive than the 3-substituted isomers;⁸⁹ indeed they added to several dienes and with anthracene afforded a single diastereoadduct. The reaction with cyclopentadiene (Table 6) exhibited peculiar differences in diastereoselection in the presence of Lewis acids. Such differences have been rationalized on the



basis of complex formation shown.⁸⁹ These results seem to be discordant with the stereochemistry of cycloaddition of the isomeric 3-substituted sulfinylpropenoic esters just described.

4. VINYL SULFONES

4.1. Monosubstituted vinyl sulfones

Vinyl sulfones are known to be good dienophiles. Early reports by Alder, dated 1938, describe the addition of vinyl tolyl sulfone and of dehydrothiophene 1,1-dioxide.¹⁰ Several examples have been published later in view of the utility of the adducts. Most of the more common dienes have been collected in Table 7, while a few more complex ones are given below. Phenyl vinyl sulfone may

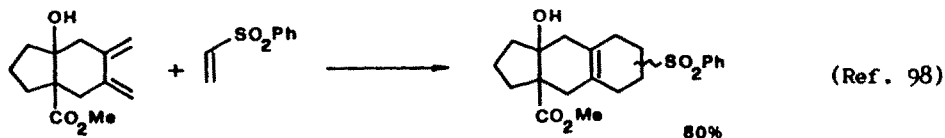
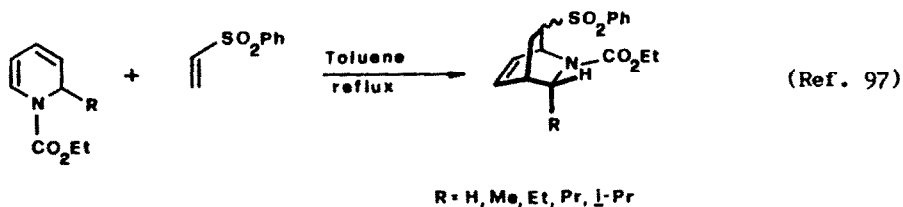
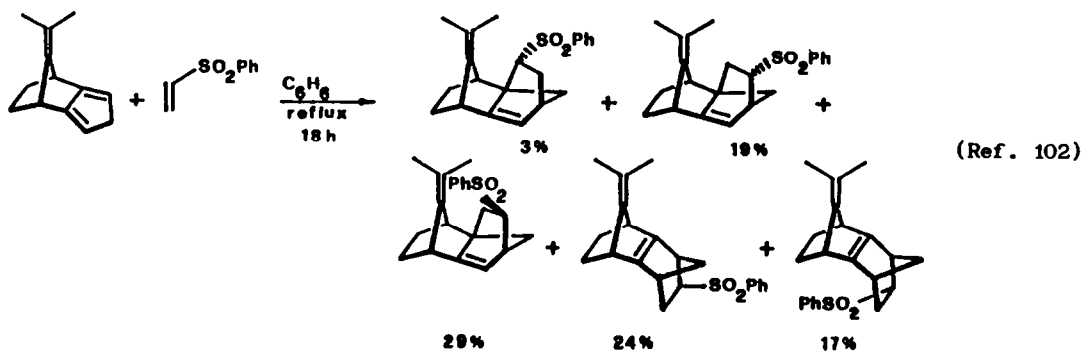
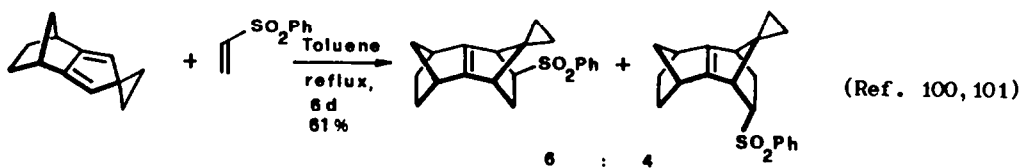
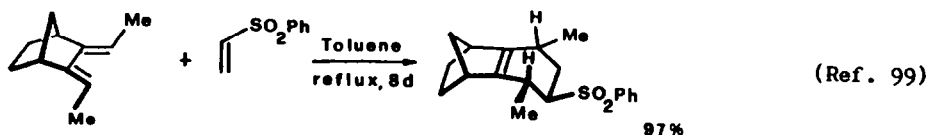
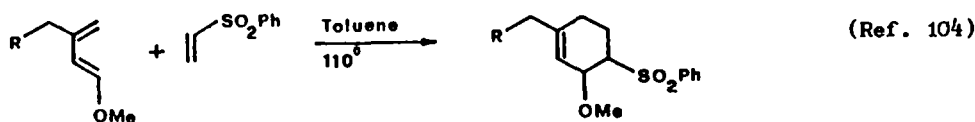
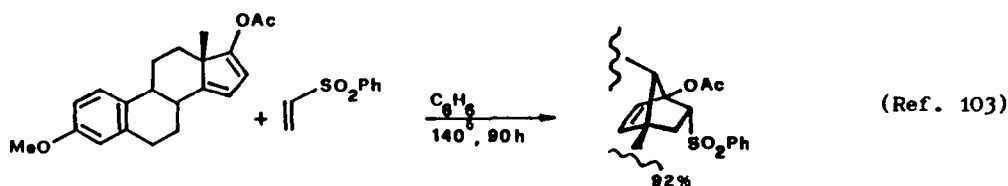


Table 7. Dienes, reaction conditions and yields in the Diels-Alder cycloaddition of vinyl sulfones $\text{RSO}_2\text{CH}=\text{CH}_2$

Diene	R	Solvent	Temp. (°C)/time	Yields (%)	Ref.
1,3-Butadiene	Me	Benzene	50/11 d	*	91
1,3-Butadiene	Cl	Neat	rt/2d + 50/20 h	93	91
Isoprene	Me	Benzene	Reflux/10 d	80.5	91
Isoprene	Ph	Benzene	120/28 h	93	92
Isoprene	Cl	Neat	rt/24 h	95	91
2,3-Dimethylbutadiene	Me	Benzene	rt/12 h + 100/4 d	81	91
2,3-Dimethylbutadiene	C_4F_9	*	rt/48 h	100	93
2,3-Dimethylbutadiene	Ph	*	135/32 h	94	92
2,3-Dimethylbutadiene	Tol	Benzene	150/105 h	*	10
2,3-Dimethylbutadiene	Cl	Neat	rt/overnight	82	91
Myrcene	Ph	Benzene	155/22 h	98	92
1-Methoxy-3-trimethylsilyloxy-1,3-butadiene	Ph	Benzene	Reflux/28 h	85	94
Cyclopentadiene	Me	Neat	rt/4d	83	91
Cyclopentadiene	Me	CCl_4	rt/4d	92.4	95
Cyclopentadiene	C_4F_9	*	rt/a	100	93
Cyclopentadiene	Ph	Benzene	25/110 h	100	92
Cyclopentadiene	Cl	Neat	rt/overnight	57	91
1,5,5'-Trimethylcyclopentadiene	Ph	Neat	180/16 h	25	12
1,3-Cyclohexadiene	Ph	Benzene	125/17 h	89	92
1-Methoxy-1,3-cyclohexadiene	Ph	Benzene	135/18 h	68	92
Anthracene	Ph	Benzene	155/100 h	96	92
Anthracene	Ph	$\text{C}_6\text{H}_5\text{Cl}$	130/120 h	83	56
Nopadiene	Ph	Benzene	150/28 h	98	92
Thebaine	Me	Toluene	110/40 h	46	96
Thebaine	C_2H_5	Toluene	110/46 h	59	96

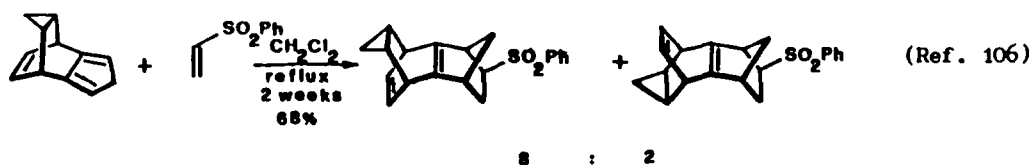
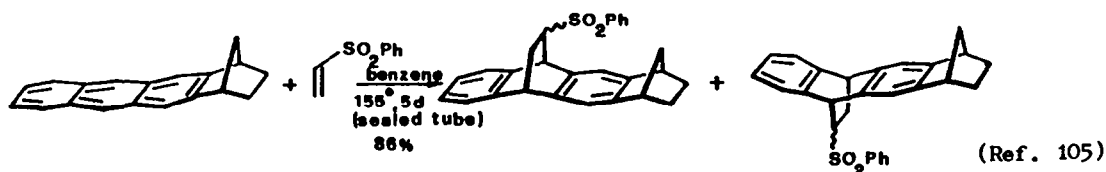
* Not reported.



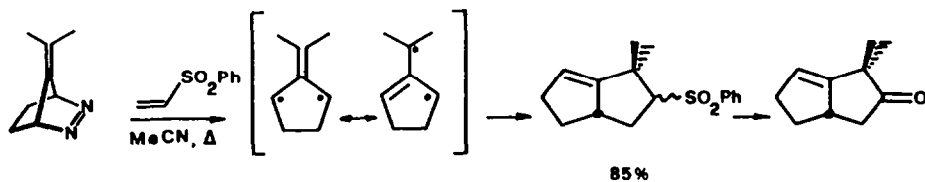


R = $n\text{-C}_5\text{H}_{11}$
 R = SPh
 R = OH

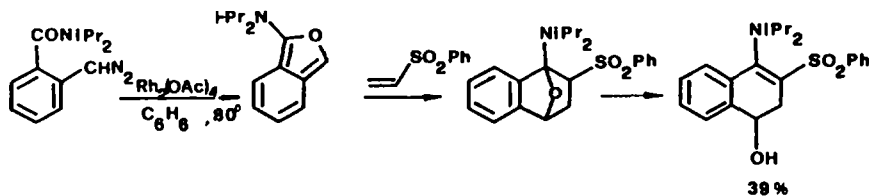
endo/exo	38 : 62	53%
" "	23 : 77	99%
" "	37 : 63	85%



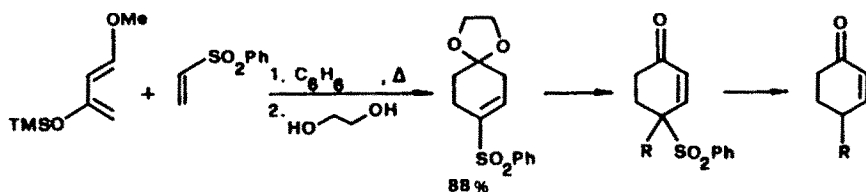
be used as a trapping agent for 1,3-diyls generated by nitrogen extrusion from azoalkanes¹⁰⁷ as shown by Little.¹⁰⁸



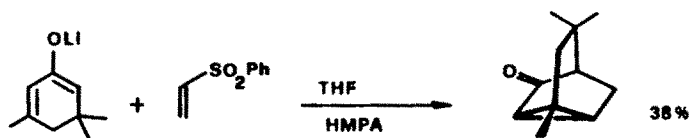
Phenyl vinyl sulfone reacts with 1-(dialkylamino)-isobenzofuran, generated *in situ* from metal catalysed decomposition of *o*-(diazomethyl)benzamide. This gave a product derived from a rearrangement of the primary cycloadduct.¹⁰⁹



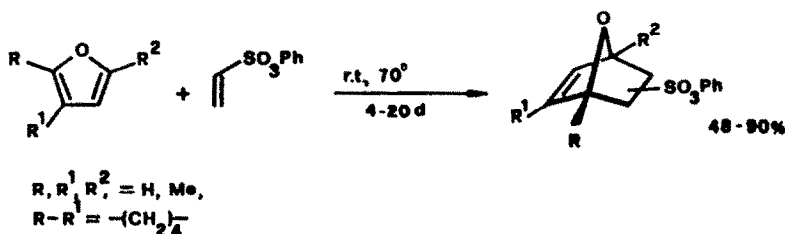
Cycloaddition of phenyl vinyl sulfone to the Danishefsky diene, followed by direct ketalization provides a sulfonyl functionalized adduct in high yield. This has been developed as a 4(2-cyclohexenyl)anion synthon.⁸⁴ Although not a proper Diels–Alder cycloaddition the reaction of phenyl



vinyl sulfone with lithiated isophorone gives, in a single step, the tricyclic ketone shown.¹¹⁰ Unsatu-

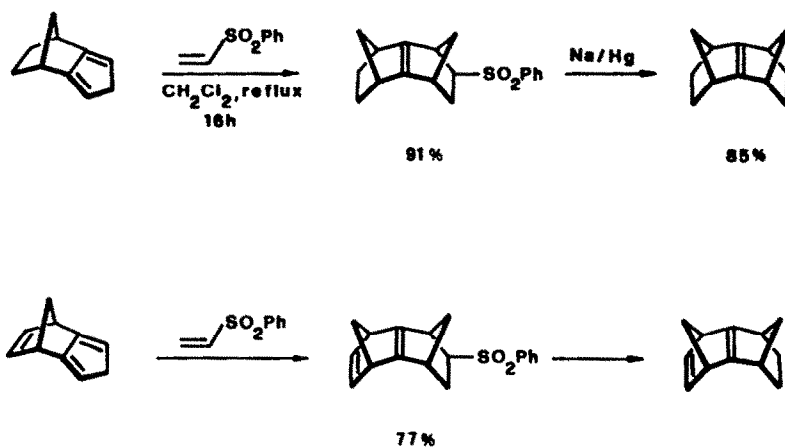


rated sulfonates are also reactive dienophiles.¹¹¹ The parent vinyl phenylsulfonic ester adds to several substituted furans.¹¹² Trifluoromethanesulfonyl groups impart, as expected, greater acti-



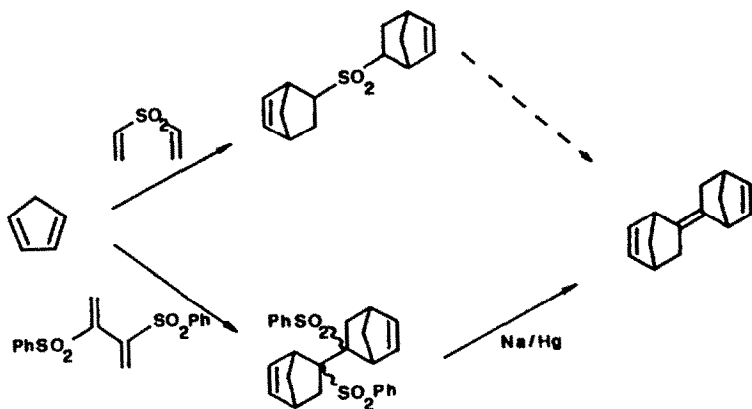
vation. Diels–Alder reactions involving vinyl fluoroalkylsulfones have been reported.^{113–115} Activation is sufficient to promote cycloaddition also of alkyl substituted olefins, a process which is usually difficult to accomplish with other sulfones (*vide infra*). The vinylnonafluorobutylsulfone is probably the most reactive vinyl sulfone as it reacts with 2,3-dimethylbutadiene even at room temperature⁹³ (cf. Table 7).

The reaction of aryl vinyl sulfones is of particular interest because the adducts may be transformed either into the alkane¹¹⁶ or into the ketone.^{108,117} Thus these reagents may serve as reactive equivalents of ethylene and ketenes. Among the several cases in which a vinyl sulfone has been utilized as an ethylene equivalent the first, and up to date the only, preparation of *syn*-sesquinorbornene¹¹⁸ and sesquinorbornadiene¹¹⁹ is of particular importance. The utilization can be



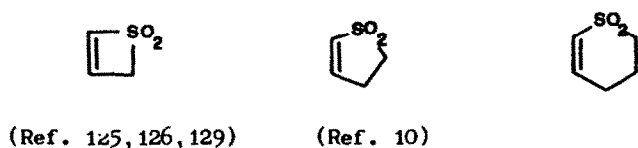
expanded to the equivalency of terminal olefins, since the adducts can be transformed into the corresponding anion which can be alkylated.⁹² However, it is not possible to utilize aryl vinyl sulfones as equivalents of acetylene in cycloaddition reactions, because the base-induced elimination of sulfinic acid to the corresponding olefin occurs with difficulty.¹²⁰

An attractive dienophile is divinylsulfone. This cheap, commercially available reagent can add two moles of diene. Very few cases of cycloaddition have been reported and most of them describe only the 1:1 adduct.¹²¹ The remaining double bond has been reacted with several reagents, but not with other dienes. We thought to utilize divinylsulfone as a conjunctive reagent and then transform the adducts into olefins by a Ramberg-Bäcklund rearrangement.¹²² The reaction with cyclo-

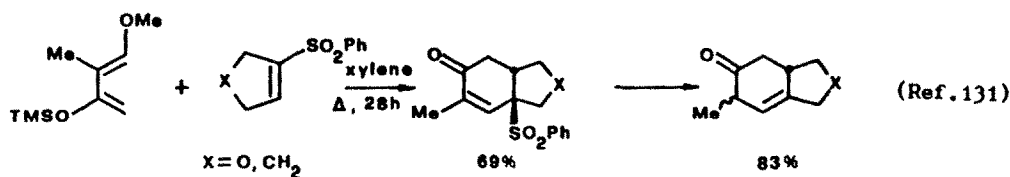
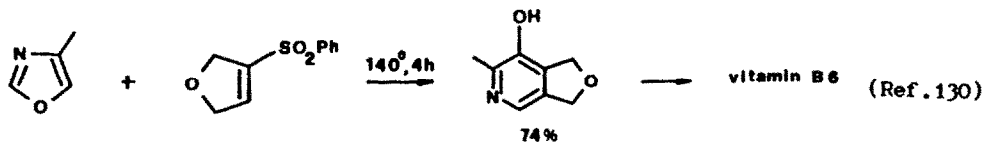


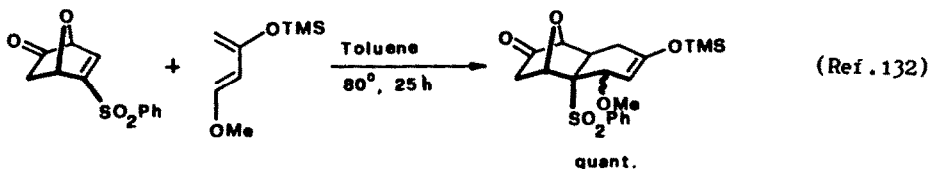
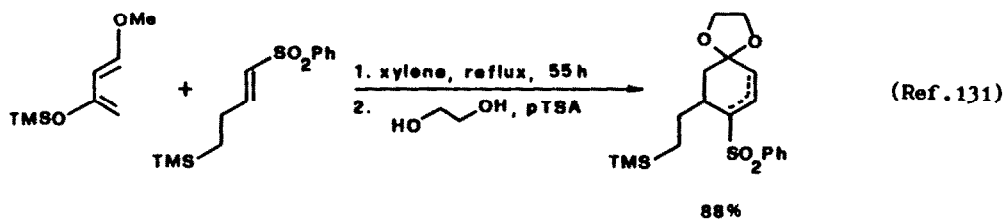
pentadiene afforded a mixture of three isomers which were separated, but that could not yet be transformed into the triene shown. On controlling reagents ratio and conditions, the reaction can be stopped at the 1:1 adduct, allowing the possibility of adding different dienes. In order to obtain the desired olefin, another route based on 2,3-bis(phenylsulfonyl)-1,3-butadiene was examined. This reagent which can be readily obtained from cheap starting materials¹²³ reacts with cyclopentadiene to afford the 1:1 or the 2:1 cycloadduct depending on the reaction conditions and the adducts can be desulfonated to the triene.¹²⁴

Substituted vinyl sulfones are only moderately reactive as dienophiles^{10,125,126} but they enter readily into 1,3-dipolar cycloadditions.^{127,128} The reactivity is probably a function of the ring strain or of the electronic situation imposed by the geometry of the system. No cycloaddition reactions seem to have been reported for the six-membered sulphone. Many other examples of Diels-Alder

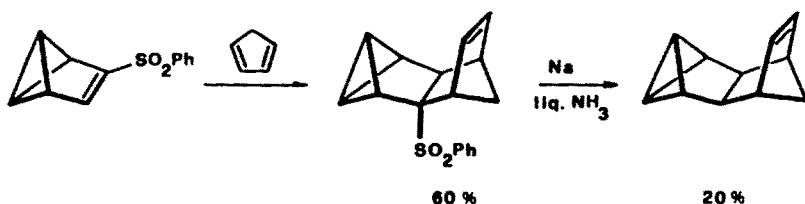


reactions with olefins activated by phenylsulfonyl group have been reported. A few representative cases are shown below. As can be deduced by the examples shown, the cycloaddition occurs readily

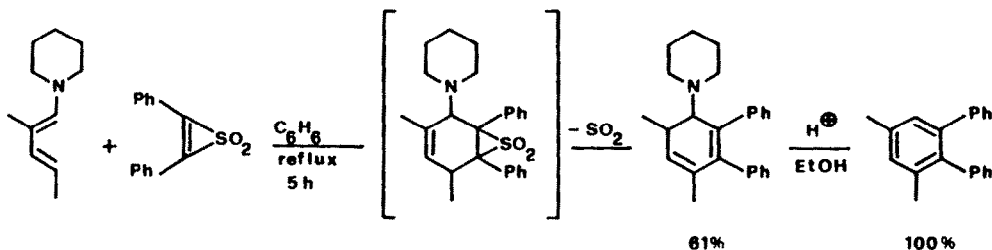




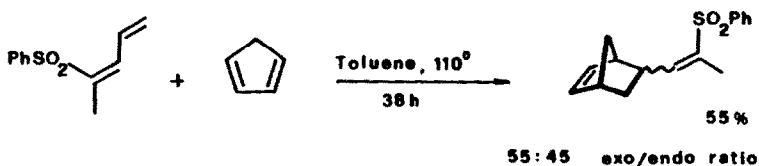
with somewhat activated dienes or with sulfones activated by fluoroalkyls.⁹⁸ In the latter case (*E*)- β -styrylnonaflon only reacted with 2,3-dimethylbutadiene after one week at 100°C in *n*-nonane, whilst cyclopentadiene needed a few days at room temperature. Rare are the examples in which dialkyl substituted unsaturated aryl sulfones have been shown to react with standard dienes. In the example shown below the reaction likely occurs because of the electronic and the geometrical contribution of the benzvalene moiety.¹³³



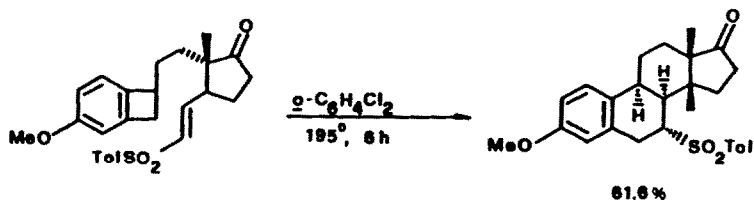
The cycloaddition of thiirene-1,1-dioxide with the nitrogen activated diene evidently occurs because of its strained nature.¹³⁴ A result which demonstrates the limits of reactivity of substituted



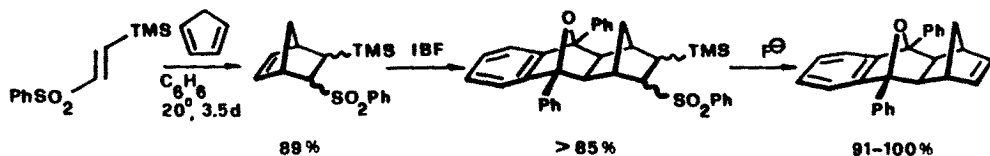
sulfones has recently been reported. Cyclopentadiene reacts with the unactivated part of the diene.¹³⁵



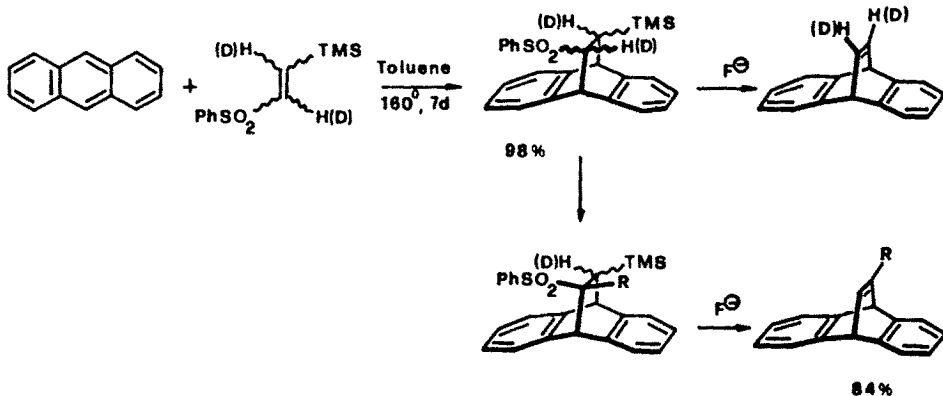
Because of the more favourable entropy, intramolecular processes give better results.¹³⁶ The



elimination of the sulfone function with the formation of a double bond is a very inefficient process unless a relatively acidic proton is present in the vicinal position. In order to obtain a double bond and utilize a sulfone as an acetylene equivalent (*E*)-1-phenylsulfonyl-2-trimethylsilyl ethylene has been synthesized and reacted with several dienes. The elimination to the alkene is smoothly accomplished by fluoride ion.¹³⁷ The utility of this dienophile and its dideuterioderivative is

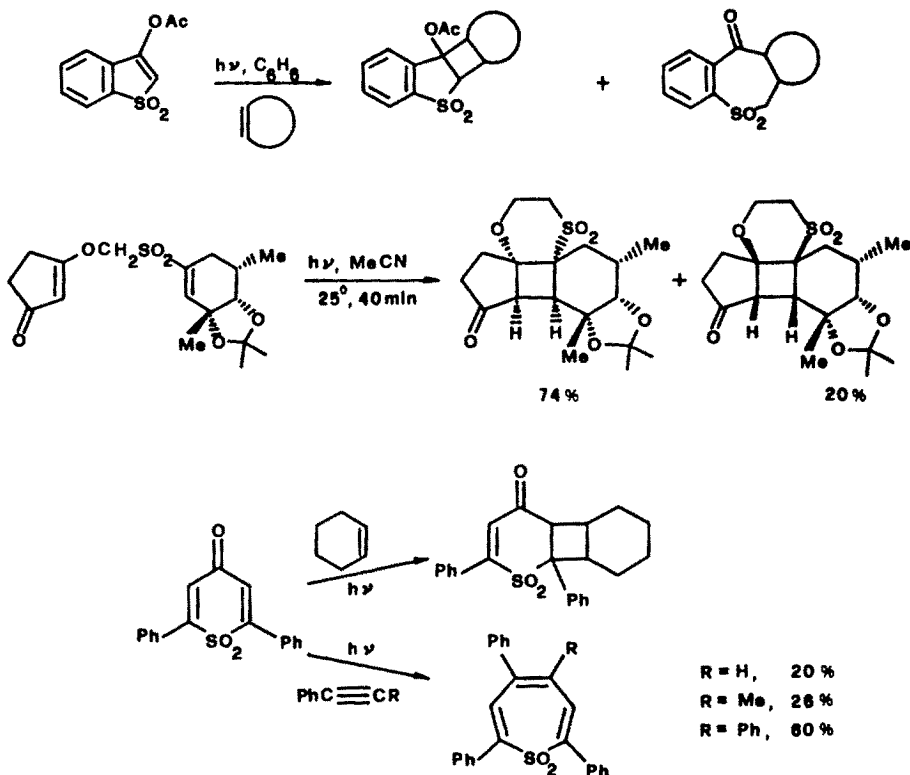


demonstrated by the synthesis of several deuterium-substituted dibenzobarrelenes. In a different

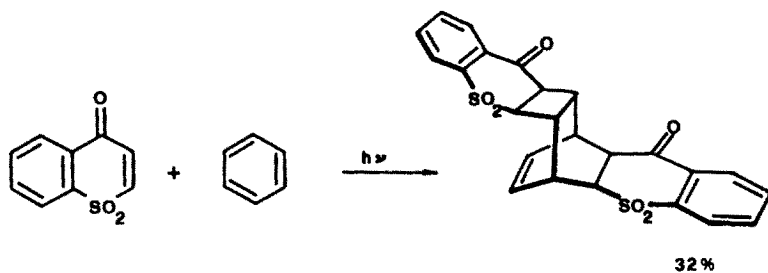


approach, the adducts were alkylated and transformed into the corresponding olefin. This simulates the addition of terminal acetylenes.¹³⁸

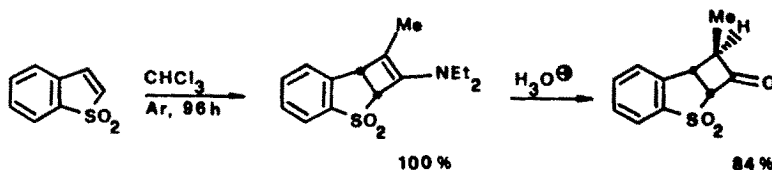
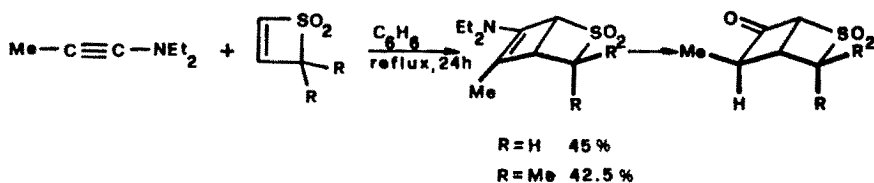
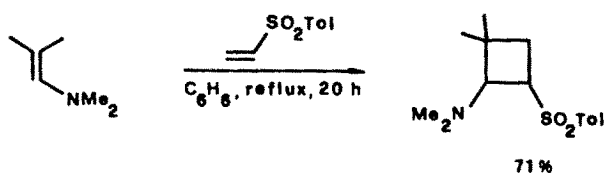
The (2+2)-cycloaddition of unsaturated sulfones to afford cyclobutanes can be achieved both photochemically and thermally. A few examples of photochemical processes are shown.¹³⁹⁻¹⁴¹ Of



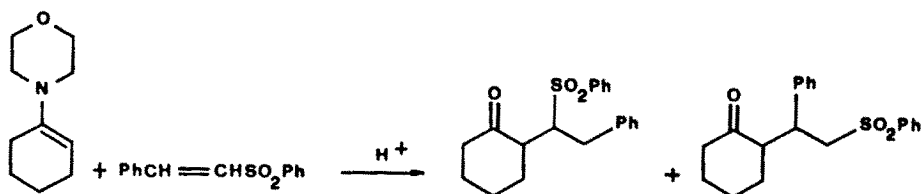
particular interest is the photoaddition of thiochromone 1,1-dioxide with benzene and related aromatic compounds.¹⁴² The reactions of vinyl sulfones with enamines and ynamines afford cyclo-



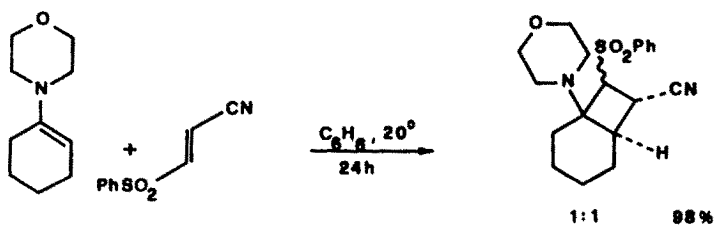
butanes^{129,143,144} and cyclobutenes.¹⁴⁵



The addition of (*E*)- and (*Z*)-phenyl styryl sulfones to enamines derived from cyclohexanone is not regiospecific. This shows that with these substrates, both steric and electrostatic interactions are

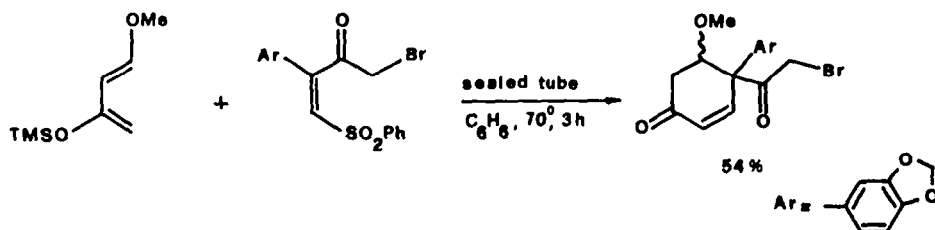


operative.¹⁴⁶ With (*E*)-cyanovinyl phenyl sulfone, the cycloaddition occurs as shown.¹⁴⁷



4.2. Disubstituted vinyl sulfones

The introduction of a second electron withdrawing group enhances the reactivity and the cycloaddition to dienes unreactive with monosubstituted dienophiles, becomes possible. The extra function can be a ketone^{148,149} as in the following example,¹⁵⁰ or a carboxy, ester or nitro group (Table 8) or another sulfonyl group (Tables 9 and 10).



The reaction of diarylsulfonylethylenes is of synthetic utility because the two sulfonyl groups can be reductively removed with sodium amalgam¹⁵⁷ or magnesium in methanol¹⁶² under very mild reaction conditions to the corresponding olefin. The products correspond to the Diels-Alder adducts of acetylene. A few olefins which have been prepared are shown. A valuable example is the



preparation of 7-oxabicyclo[2.2.1]hept-2-ene and of the corresponding diene¹⁶¹ which are otherwise difficult to prepare. Recently the synthesis of the first known member of the 1,7-cyclo-

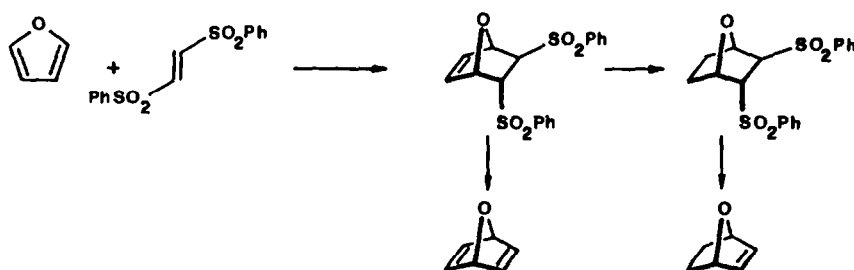


Table 8. Reaction conditions and yields in the Diels-Alder cycloaddition of most common dienes with sulfonyl ethylenes of the type $\text{PhSO}_2\text{CH}=\text{CHX}$

Diene	X	E, Z	Solvent	Temp.(°C)/time	Yields (%)	Ratio ^a	Ref.
Butadiene	CF ₃	E	^b	180/72 h	94	100:0	151
Perylene	NO ₂	E	Toluene	100/4 h	95	50:50	37, 152
1-TMSO-butadiene	NO ₂	E	Toluene	110/1.5 h	76	50:50	152
2,3-Dimethylbutadiene	NO ₂	E	Toluene	110/1.5 h	97	50:50	152
1,3-Pentadiene	NO ₂	E	Toluene	100/4 h	95	50:50	152
Cyclopentadiene	NO ₂	E	CH ₂ Cl ₂	20/30 min	82	75:25	37
Cyclopentadiene	NO ₂	E	CH ₂ Cl ₂	20/30 min	82	50:50	152
Cyclopentadiene	CO ₂ H	Z	Benzene	80/30 min	97.6	91:9	153
Cyclopentadiene	CO ₂ H	E	Benzene	80/2 h	96.4	100:0	153
Cyclopentadiene	CF ₃	E	^b	0/1 h	80	20:80	151
Dehydroisodicyclopentadiene	CO ₂ Me	Z	Neat	55-60/12 h	100	0:100	154
Furane	NO ₂	E	CH ₂ Cl ₂	20/7 h	89	50:50	152
Cyclohexadiene	NO ₂	E	Toluene	110/6 h	94	50:50	152
Cyclohexadiene	CO ₂ H	Z	Benzene	150/2 h	58	100:0	153
Cyclohexadiene	CO ₂ H	E	Benzene	150/2 h	100	100:0	153
<i>o</i> -Quinodimethane	CF ₃	E	^b	70/0.5 h	86	100:0	151
Cycloheptatriene	NO ₂	E	Toluene	110/12 h	93	50:50	152
Anthracene	NO ₂	E	Toluene	110/3 h	90	50:50	152

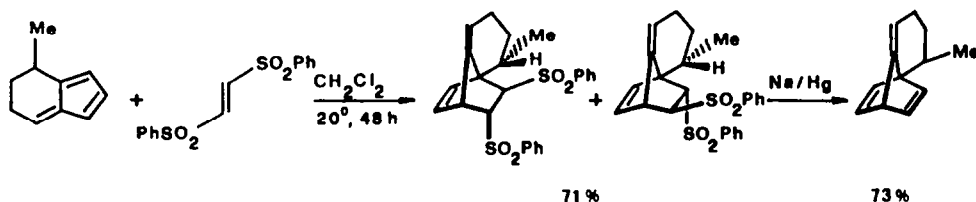
^a *endo*:*exo* ratio respect to the SO₂Ph group.

^b Not reported.

Table 9. Dienes, reaction conditions and yields in the Diels–Alder cycloaddition of (Z) and cyclic bis(sulfonyl)ethylenes $\text{RSO}_2\text{CH}=\text{CHSO}_2\text{R}$

Diene	R	Solvent	Temp. (°C)/time	Yields (%)	Ref.
1,3-Butadiene	Tol	Benzene	100/24 h	95	149
Piperylene	—C ₆ H ₄ —	CH ₂ Cl ₂	50/10 h	96	155
Piperylene	Tol	Benzene	reflux/2 d	96	149
Piperylene	—C ₆ H ₄ —	CH ₂ Cl ₂	50/10 h	98	155
2,3-Dimethylbutadiene	Ph	Benzene	reflux/20 h	60	156
2,3-Dimethylbutadiene	Tol	Benzene	reflux/2 d	96	149
2,3-Dimethylbutadiene	—C ₆ H ₄ —	CH ₂ Cl ₂	rt/25 h	99	155
Cyclopentadiene	Ph	Benzene	rt/40 h	98	156
Cyclopentadiene	Ph	CH ₂ Cl ₂	25/3 h	98	157
Cyclopentadiene	Tol	Benzene	rt/5 min	93	156
Cyclopentadiene	—C ₆ H ₄ —	CH ₂ Cl ₂	rt/1 h	95	155
Cyclopentadiene	—C ₆ H ₄ —	CH ₃ NO ₂	80/2 h	74	66
Cyclohexadiene	Ph	Dioxane	150/5 h	48	153
Cyclohexadiene	Ph	Toluene	111/14 h	91	157
Cyclohexadiene	—C ₆ H ₄ —	CH ₂ Cl ₂	50/10 h	96	155
Cycloheptatriene	Ph	Toluene	111/14 h	92	157
Norbornadiene	Ph	Toluene	111/24 h	92	157
Quadricyclane	Ph	CH ₂ Cl ₂	25/120 h	93	157
2,5-Dimethylfuran	—C ₆ H ₄ —	CH ₂ Cl ₂	rt/20 h	98	155
Diphenylfulvene	—C ₆ H ₄ —	CH ₂ Cl ₂	rt/20 h	99	155
(E)-1,2-Dichlorobenzocyclobutene	—C ₆ H ₄ —	o-C ₆ H ₄ Cl ₂	reflux/6.5 h	83	155
Anthracene	Ph	Neat	160/18 h	46	157
Anthracene	Tol	Neat	155–160/20 h	24 + 28	149
Anthracene	—C ₆ H ₄ —	Toluene	reflux/4 h	83	155
Anthracene	—C ₆ H ₄ —	CH ₃ NO ₂	reflux/6 h	94	66

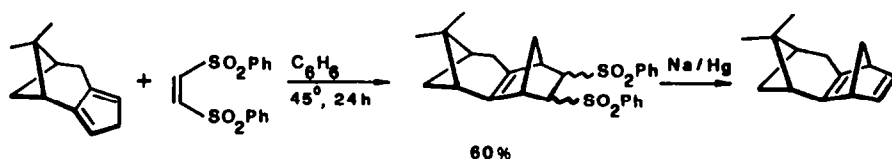
alkenenorbornadiene class of molecules has also been reported.¹⁶⁵ More recently the parent deriva-

Table 10. Dienes, reaction conditions and yields in the Diels–Alder cycloaddition of (E)-bis(sulfonyl)ethylenes $\text{RSO}_2\text{CH}=\text{CHSO}_2\text{R}$

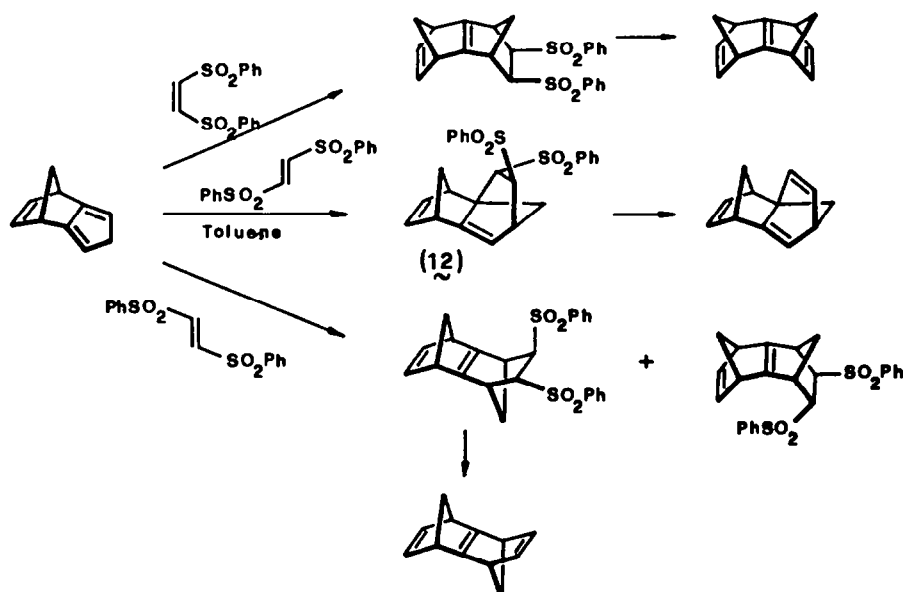
Diene	R	Solvent	Temp. (°C)/time	Yields (%)	Ref.
1,3-Butadiene	Ph	Butylether	122/13 h	93	158
1,3-Butadiene	Tol	Butylether	115/23 h	90.4	158
Isoprene	Tol	Benzene	reflux/48 h	77	158
Isoprene	Ph	Neat	25/4d	91	159
2,3-Dimethylbutadiene	Ph	Benzene	reflux/20 h	69	156
Cyclopentadiene	Ph	Benzene	reflux/17 h	93	158
Cyclopentadiene	Ph	Benzene	rt/40 h	37.4	156
Cyclopentadiene	Ph	CH ₂ Cl ₂	25/1 h	98	157
Cyclopentadiene	Tol	CH ₂ Cl ₂	reflux/1.5 h	89.2	149
2-Acetoxy-cyclopentadiene	Ph	*	reflux/2 h	76	144
2-Trimethylsilyloxycyclopentadiene	Ph	*	40/12 h	90	144
Cyclohexadiene	Ph	Dioxane	150/6 h	97	153
Cyclohexadiene	Ph	Toluene	111/1 h	97	157
2-Acetoxy-cyclohexadiene	Ph	*	reflux/1.5 h	19	160
2-Trimethylsilyloxycyclohexadiene	Ph	Toluene	120/1.5 h	67	160
Cycloheptadiene	Ph	Toluene	111/48 h	77	157
Cycloheptatriene	Ph	Toluene	111/15 h	92	157
Cyclooctatetraene	Ph	o-Cl ₂ C ₆ H ₄	160/12 h	84	157
Furan	Ph	CH ₂ Cl ₂	25/48 h	94	157, 161
Anthracene	Tol	Neat	fusion	82	158
Anthracene	Ph	Neat	170/24 h	89	157

* Diene generated *in situ*.

tive and its quadricyclane valence tautomer have been obtained utilizing the (*Z*) isomer.¹⁶⁶ Similarly the homochiral pinene-fused norbornadiene have been prepared.¹⁶⁷



Finally *syn* and *anti* sesquinorbornadiene and the sesquinorbornatrienes have been prepared *via* this route.¹⁶⁸ As shown in the following equations, while the addition of the *Z* isomer gives the *syn* adduct as expected on the basis of precedent, the stereochemistry of addition of the *E* isomer is opposite. This discovery has allowed the preparation of both *syn*- and *anti*-sesquinorbornadienes and trienes. Furthermore, on heating the reagents in toluene the rearranged adduct **12** could be obtained from which the angular triene was synthesized. The stable derivatives shown below,



experienced a photoinitiated quadricyclane–quadricyclane rearrangement.¹⁵⁴ The same rearrangement does not occur in the parent polycycle as was shown by the related experiment with the deuteriosubstituted analogue, obtained by cycloaddition of (*E*)- $\text{PhSO}_2\text{CD}=\text{CHSO}_2\text{Ph}$.



Beside the formation of the carbon–carbon double bond, the bis-sulfone adducts are amenable to the direct production of the carbon–carbon single bond. This possibility may be useful when single isomeric alkenes are desired as in the following example.¹⁵⁹

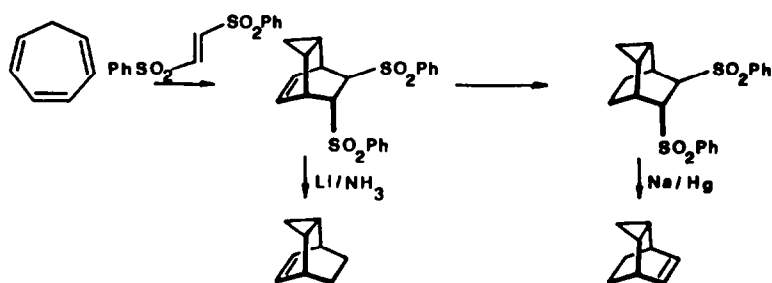
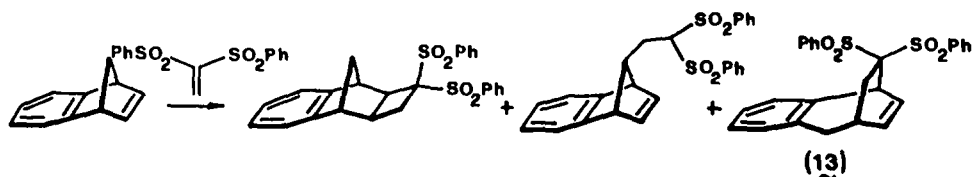


Table 11. Dienes, reaction conditions and yields in the Diels–Alder cycloaddition of 1,1-bis(sulfonyl)ethylenes $(\text{RSO}_2)_2\text{C}=\text{CH}_2$

Diene	R	Solvent	Temp. (°C)/time (h)	Yields (%)	Ref.
1,3-Butadiene	Ph	Benzene	100–110/3.5	75	172
1-Acetoxy-1,3-butadiene	Ph	Benzene	100–110/3.5	57	172
2-Trimethylsilyloxy-1,3-butadiene	Ph	CH_2Cl_2	rt/24	79	172
Cyclopentadiene	Ph	CH_2Cl_2	rt/24	80	172
Cyclopentadiene	Ph	CH_2Cl_2	rt/24	90	173
2-Acetoxy-cyclopentadiene	Ph	Isopropenyl acetate	96/8	80	173
1,3-Cyclohexadiene	Ph	Benzene	100–110/3.5	42	172
1,3-Cyclohexadiene	Ph	Neat	110/2	90	173
Cycloheptatriene	Ph	Neat	110/5	30	173
Norbornadiene	Ph	Neat	110/5	50	173
Quadricyclane	Ph	CH_2Cl_2	20/24	90	173

On these lines, two research groups have recently reported on the higher reactivity of benzo-1,4-dithiadiene disulfone (see Table 9).^{66,155} The utility of this dienophile is somewhat reduced by the more elaborate preparation.

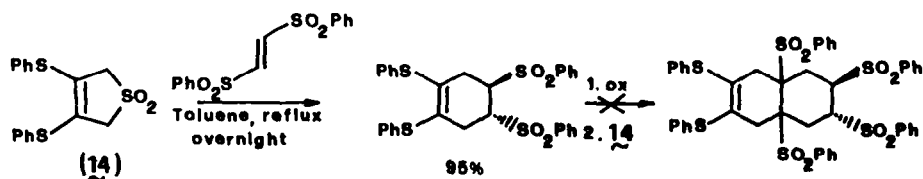
The isomeric 1,1-bis(benzenesulfonyl)ethylene¹⁷¹ is also a good dienophile (Table 11) but it can react also with strained π bonds to give the products derived by an intermediate dipole.¹⁷⁴ For example, the set of adducts shown has been observed in the reaction with benzonorbornadiene. The adduct **13** is formed by a rearrangement of benzonorbornadiene into benzocycloheptatriene under



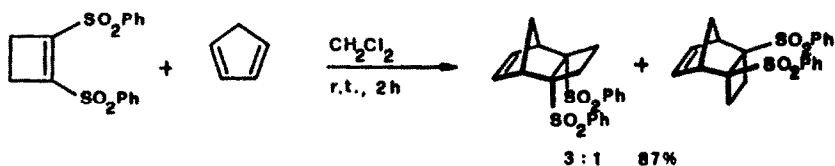
the reaction conditions. The dipolar reactivity may be explained with the strong polarization of the dienophile and the propensity of the bis-sulfonyl substituted carbon atom to host a negative charge. Since the resulting geminal disulfone can be reduced to alkanes, 1,1-bis(phenylsulfonyl) ethylene can be regarded as a synthon of the ethylene 1,2-dipole. Furthermore, because the reduction can be stopped at the monosulfone stage, it is possible to transform the adducts into ketones or alkylate the anion to a variety of homologues.¹⁷⁴

The relative reactivity of the three bis-phenylsulfonyl substituted isomers toward cyclopentadiene appears to be $E > Z > 1,1$ -bis(phenylsulfonyl)ethylene. A reason may be found in the tilting of the π orbitals caused by steric interaction between the sulfonyl groups in the Z and 1,1-isomers.¹⁶⁶ In these dienophiles, the resistance to free rotation of the sulfonyl groups might lead to incorrect orbital alignment and diminished activation.

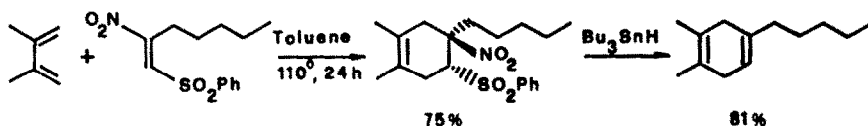
Alkyl and aryl substituted vinyl bis-sulfones show a dramatic drop in reactivity. Even the introduction of a single methyl group is sufficient to suppress the reactivity with, for example, cyclopentadiene. A correlation might be found in the half-wave potentials which show marked differences, but steric factors play a major role. In the example shown below, such low reactivity precluded a reiterative sequence for the synthesis of polycyclic hydrocarbons.¹²³



Steric perturbation between the sulfonyl groups may be minimized in compounds containing small rings. For example, in contrast with larger rings, the cyclobutene derivative was found to react with cyclopentadiene and furan.¹²⁸

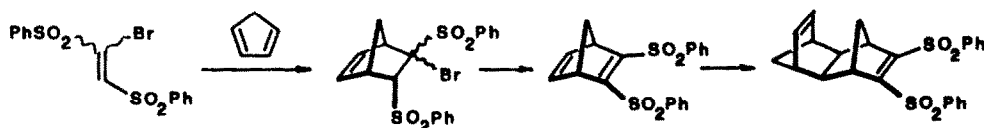


The limitation mentioned seems not to be present in β -nitro sulfones. These reagents react smoothly with most dienes, and even alkyl substituted derivatives add with ease.^{46,152} The scope of



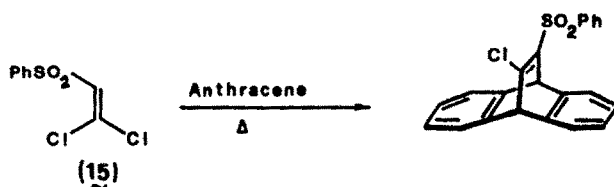
the reaction has not yet been established. Denitrodesulfonation has been accomplished with tin hydride.

The reactivity of bis(benzenesulfonyl)ethylenes containing halogen atoms is of interest when further elaboration of the adducts is required. The reaction of a bromoderivative has been utilized for the synthesis of the bis(benzenesulfonyl)substituted norbornadiene. This product underwent a further reaction with another molecule of cyclopentadiene to give the adduct shown. A related norbornadiene has recently been shown to possess similar reactivity.¹⁷⁶ More recent investigations



in our laboratories have shown that only the adducts of the (*Z*) isomer of the chloro analogs allow base induced elimination. Unfortunately the (*E*) isomer is more reactive.¹⁷⁷ Similar reactivity has been demonstrated with the dichloro diarylsulfonyl ethylenes; only the *E* form reacted with cyclopentadiene or butadiene.¹⁷⁸

It has been shown that the cycloaddition of the sulfone **15** with anthracene proceeds with hydrochloric acid elimination.¹⁷⁹

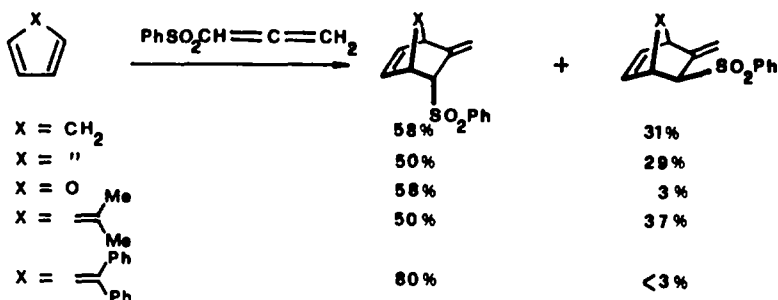


The reaction of 1-bromo 1-methylsulfonyl ethylene with cyclopentadiene, followed by the Ramberg-Bäcklund rearrangement affords methylenenorbornadiene in high yield.¹⁸⁰



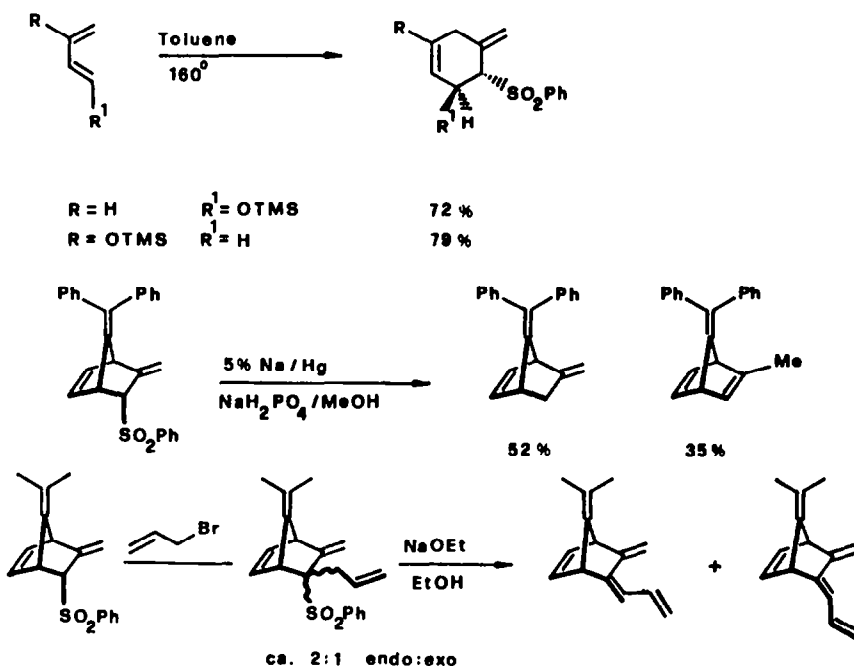
4.3. Allenic sulfones

Though allenic sulfones are moderately reactive in cycloaddition reactions, they give functionalized products of good synthetic potentiality. The parent allene ($\text{PhSO}_2\text{CH}=\text{C}=\text{CH}_2$) is isomeric with the corresponding acetylene ($\text{PhSO}_2\text{C}\equiv\text{CMe}$) with which it interconverts under proper reaction conditions. The first report of the cycloaddition of the parent phenylsulfonyl allene with cyclopentadiene¹⁸¹ has recently been revisited. The scope and utility of the reaction have been determined.¹⁸² Depending on the substrate the reaction may be highly stereo- and regio-selective.

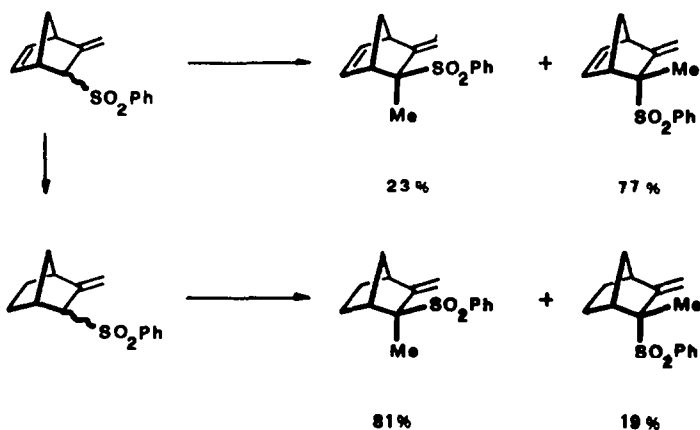


The reactivity with furan is remarkable¹⁸⁴ because this diene is usually poorly reactive in Diels-Alder cycloadditions. The products may well be useful for the synthesis of natural products.

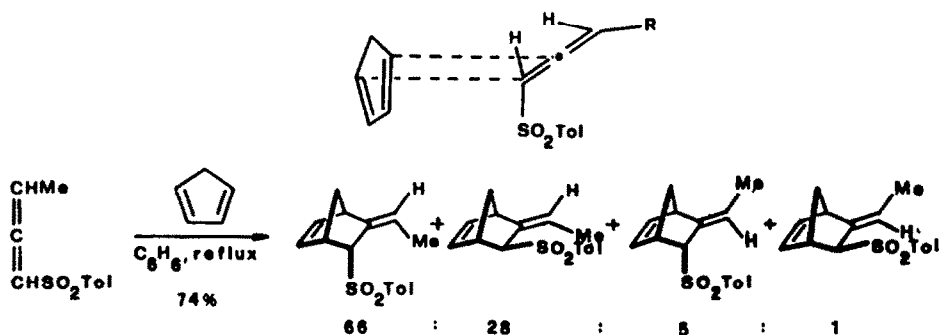
Desulfonylation and/or alkylation followed by desulfonylation provides a convenient entry into exocyclic trienes.¹⁸²



The stereochemistry of alkylation is independent of the stereochemistry of the starting sulfone since either the pure *exo* or pure *endo* isomer gives the same product distribution.¹⁸⁵ Unexpectedly, the saturated system gives predominantly the product derived by an *endo* attack of the alkylating agent.

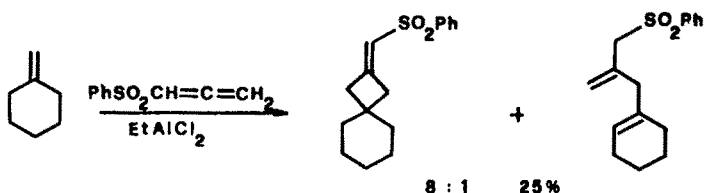


Direct cycloaddition of 3-(tolylsulfonyl)buta-1,2-diene gives the *endo* and *exo* adducts in a 1 : 4 ratio and in 32% yield.¹⁸³

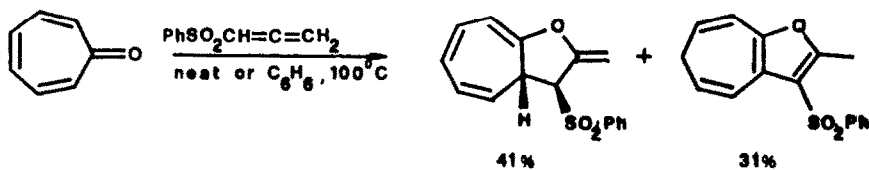


The cycloaddition of the chiral allenic sulfone with cyclopentadiene gives, as main products, the diastereoisomers derived by attack of the diene upon the less hindered face of the dienophile.¹⁸³

Peculiar types of cycloadditions have been observed in the Lewis acid catalysed addition to alkenes.¹⁸⁶ An example is the following in which a (2+2) and a rearranged product have been observed. Generally the (2+2)-cycloadduct predominates. This appears to be one of the very few cycloadditions in which a vinyl sulfone has been efficiently activated by a Lewis acid. The reaction

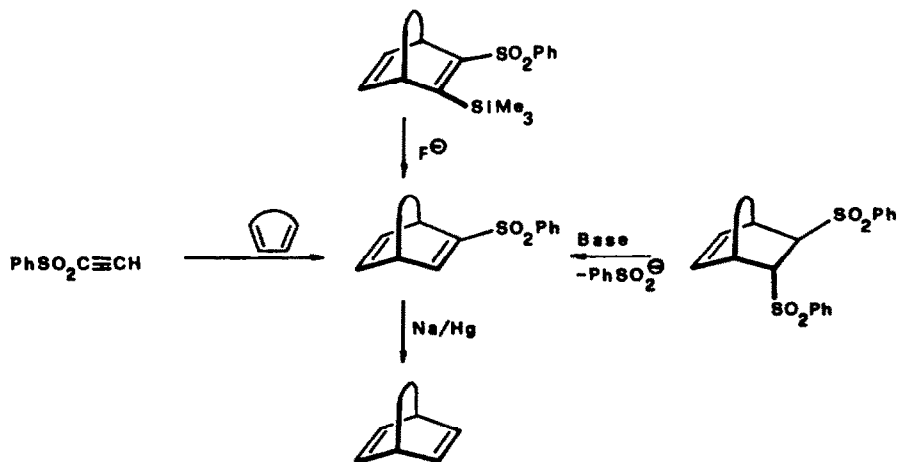


with tropone and derivatives is also of interest as it affords compounds of the (8+2)-cycloaddition type.¹⁸²

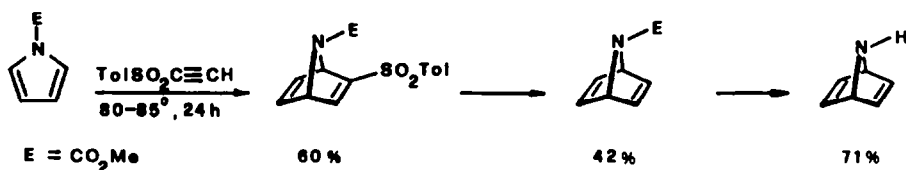


4.4. Acetylenic sulfones

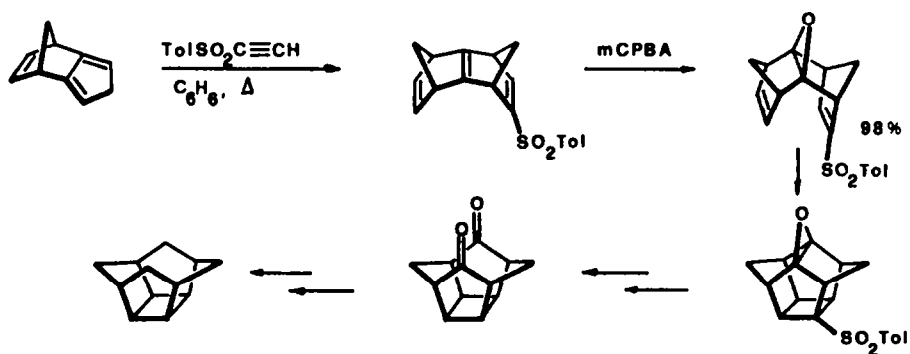
Acetylenic sulfones are good dienophiles and have synthetic utility comparable with the bis(phenylsulfonyl)ethylenes already discussed. Phenylsulfonyl acetylene adducts can also be prepared from the adducts of bis(sulfonyl)ethylenes by treatment with base¹⁶⁰ or from the adducts of 1-phenylsulfonyl 2-trimethylsilylacetylene by reaction with fluoride ions.¹⁷⁶ The synthetic utility of



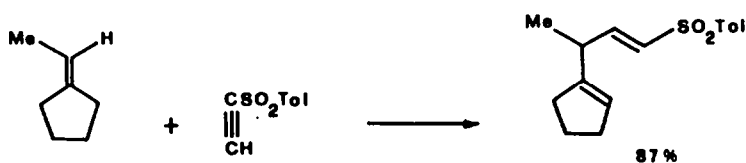
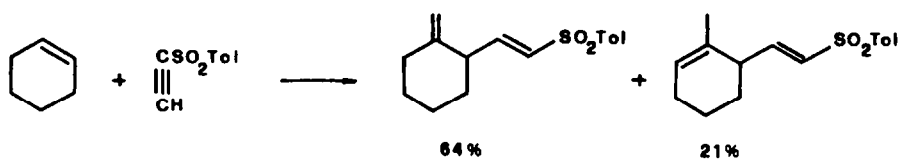
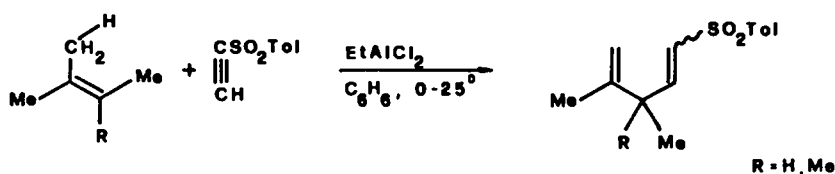
the unsaturated adducts is high because they may be transformed into several other functional groups.¹⁸⁷ Indeed the very first utilization of a sulfur-containing dienophile as a synthetic equivalent of acetylene in cycloaddition reactions made use of tolylsulfonyl acetylene.¹⁸⁸ Subsequently the method could prove its potentiality in the synthesis of new molecules. An example is the first preparation of an azanorbornadiene.¹⁸⁹ Another utilization is the synthesis of 4-peristylane a bowl-



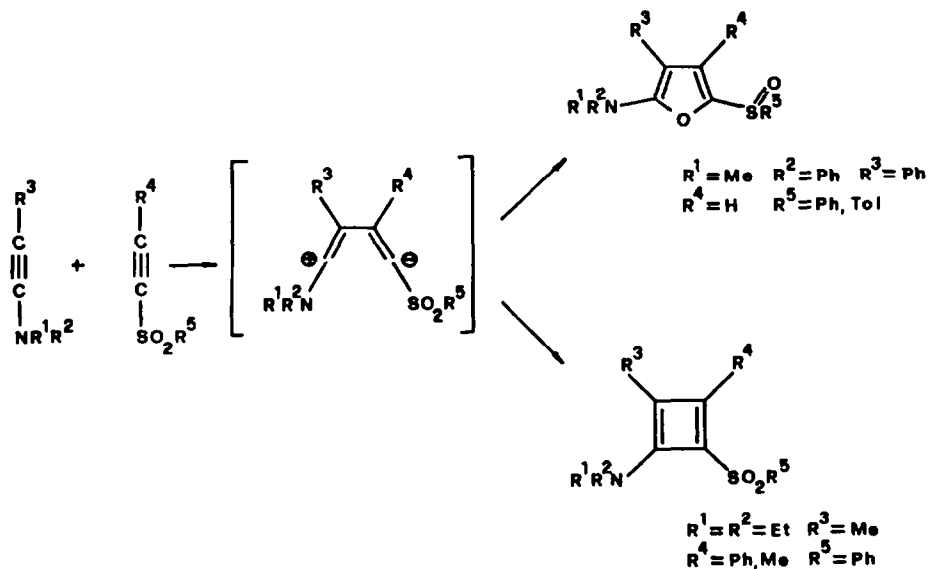
shaped hydrocarbon.¹⁹⁰ Lewis acids, such as EtAlCl_2 catalyse the reaction with a number of



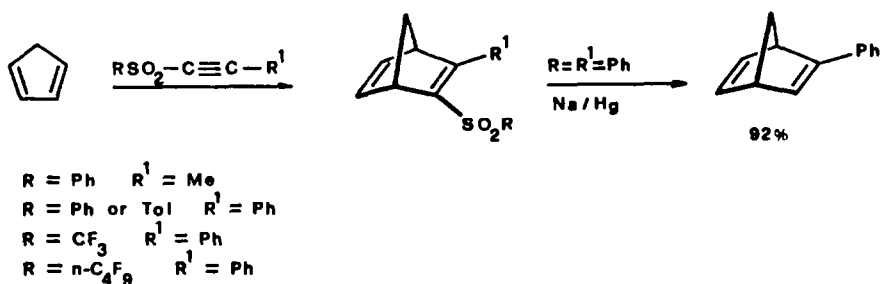
substrates. The products from alkenes containing allylic hydrogens are 1,4-dienes which are formed from an ene-type reaction.¹⁹¹ The high regioselectivity of addition suggests a dipolar intermediate.



While the parent tolylsulfonylacetylene reacts with ynamines giving 2-amino-5-sulfinylfurans,¹⁹² the phenyl and methyl substituted analogues give the (2+2)-cycloadducts.¹⁴⁵ The products arise from the cyclization of a common dipolar intermediate. Alkyl- and aryl-substituted arylsulfonylacetylenes

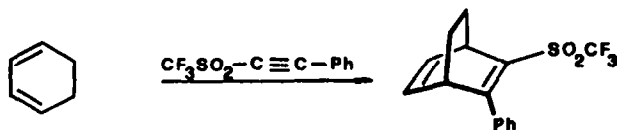
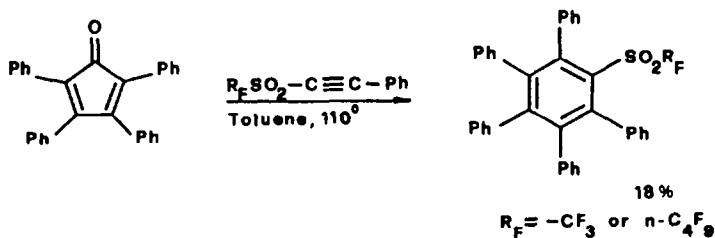


are moderately reactive towards dienes.^{193,194} With the methyl substituted acetylene and the isomeric allene the product derived from the cycloaddition to the acetylenic form is found in the reaction of the allene. Other acetylenes with different sulfonyl groups have been reacted with cyclopentadiene.

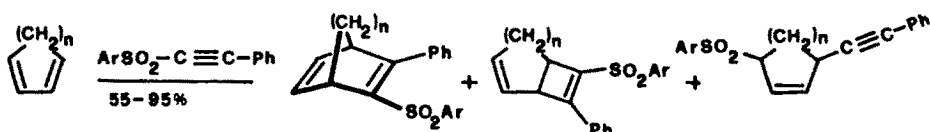


The reductive desulfonylation of the phenyl substituted adduct gives the corresponding phenyl substituted norbornadiene.¹⁹³ In our experience this route provides the best synthesis of this interesting diene. Possibly it can be used for the preparation of other differently substituted norbornadienes which may find application in solar energy storage. The scope of such methods is under investigation in our laboratories.

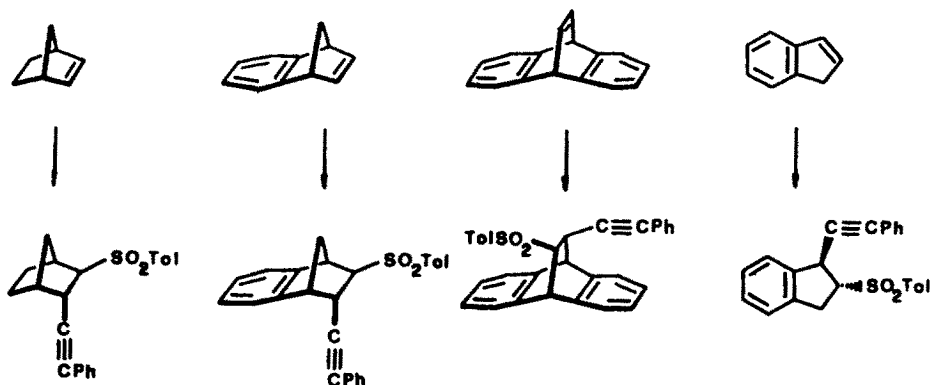
The fluoroalkanesulfonyl derivatives exhibit, as expected, a greater reactivity. Good yields of adducts have been reported with somewhat sluggish dienes.¹⁹⁵⁻¹⁹⁷ Phenylarylsulfonyl acetylenes



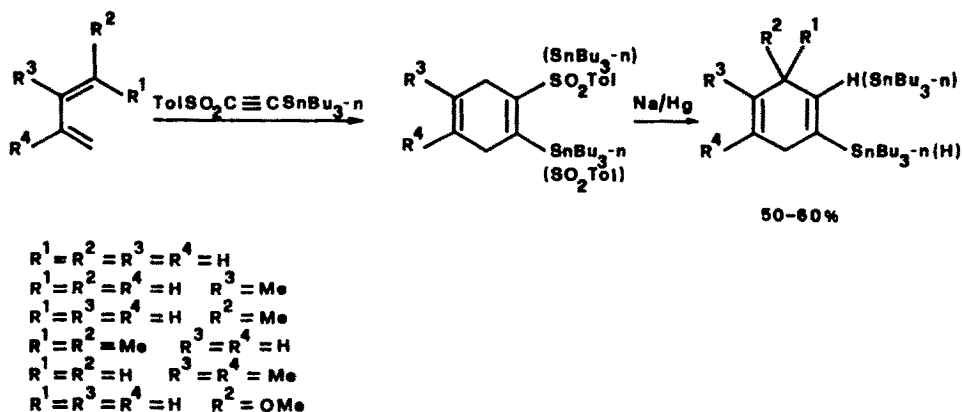
react with higher homologues of cyclopentadiene but in lower yields. Together with the expected adducts, products of a different nature are also formed. For example, while cyclopentadiene affords, as already mentioned, the standard Diels–Alder cycloadduct, cyclohexadiene and cycloheptadiene give mixtures of the (4+2)- and (2+2)-cycloadducts plus products of addition of the two fragments derived from C—S bond cleavage. The latter type of product is the only one observed in the reaction with cyclooctadiene.¹⁹³ A reasonable rationale of this unexpected behavior may be found by analogy



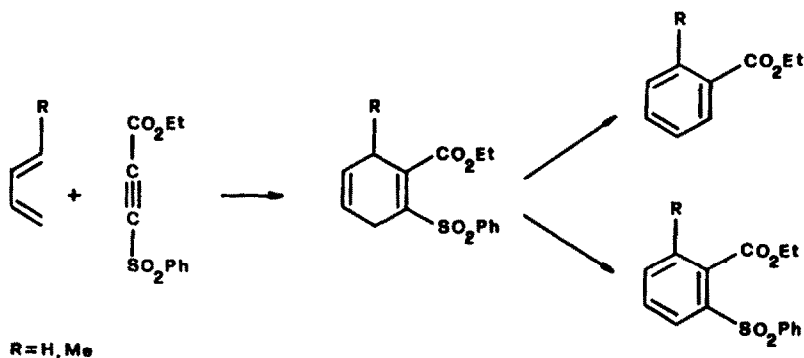
of other reactions of arylsulfonyl acetylenes, where the occurrence of radical processes has been evidenced.¹⁹⁸ This type of reaction is not limited to dienes, but it can be extended to some reactive olefins.¹⁹⁹ The reaction usually exhibits a high degree of regio- and stereo-selection.



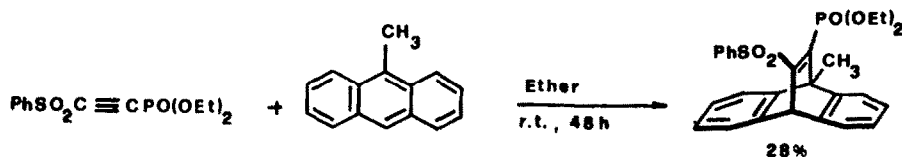
If another functional group is present in the acetylene, then the reaction may gain in synthetic potentiality. Examples are the cycloadditions of silicon^{167,200} and tin substituted sulfonyl-acetylenes.²⁰¹ The following route has served as a way of introducing a tributyltin residue on a six-membered ring.²⁰¹ If the substituent is another electron withdrawing group, for example carboxy,



the reactivity is very high. For example, the synthesis of the aromatic functionalized molecule shown has been accomplished in high yield and with complete regioselection.²⁰² More recently the

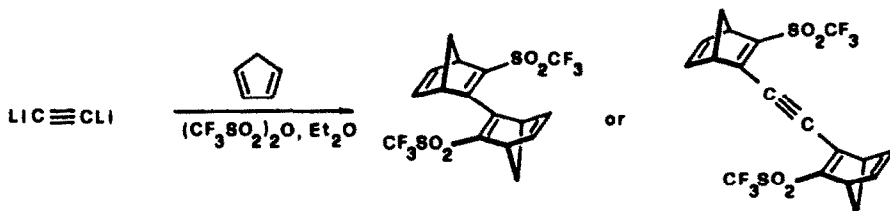


diethylphosphonate substituted acetylenic sulfide, sulfoxide and sulfone have been prepared and shown to be reactive with dienes and dipoles. The reactivity of the sulfone is such to promote cycloaddition to 9-methylantracene at room temperature and to afford the single cycloadduct shown.²⁰³



The corresponding sulfoxide and sulfide required more vigorous conditions. The latter exhibited opposite regiochemistry.

In the context of acetylenes substituted with two electron withdrawing groups it is worth mentioning that the bis(arylsulfonyl)activated acetylenes ($\text{ArSO}_2\text{C}\equiv\text{CSO}_2\text{Ar}$) are still unknown, although surrogates are now available.¹⁷⁷ The only acetylene of this type to have been synthesized is the di-*t*-butyl one ($t\text{-BuSO}_2\text{C}\equiv\text{CSO}_2t\text{-Bu}$)²⁰⁴ but its reactivity towards dienes appears not to have been studied. Efforts to prepare the bistriflyl derivative ($\text{CF}_3\text{SO}_2\text{C}\equiv\text{CSO}_2\text{CF}_3$) failed and attempts to capture it *in situ* with cyclopentadiene led mostly to polymeric materials in addition to the Diels-Alder adducts shown.¹⁹⁶



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