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RECENT DEVELOPMENTS IN SULFONE CHEMISTRY

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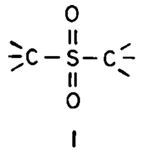
I. INTRODUCTION

The decade from 1966 to 1976 has witnessed an impressive number of original publications devoted to the understanding and applications of organosulfur chemistry. Many highly imaginative syntheses have frequently made use of the unusual and diverse properties of sulfur. Only recently have theoretical organic chemists applied their methods to a more detailed and quantitative understanding of the bonding involvement of sulfur in its various oxidation states. It would be no exaggeration to say that even despite the vast and constantly expanding numbers of publications dealing with sulfides, sulfoxides, sulfones, and various derivatives, much of the chemistry in this area remains unpredictable compared with that of first row analogs. Correspondingly the chemistry of organoselenium and organotellurium compounds is even less predictable.

Turning to the current state of understanding of sulfone chemistry, it is instructive to recall that although the sulfone functional group has been a standard part of organic chemistry for more than a century, it is only within the last few decades that a more diverse range of chemistry has been discovered. It is the intention of this article to describe some of the more important reactions that involve or owe their origin to the sulfone functional group. The sulfone group, in this review is defined as **1**; the adjacent carbon atoms may be attached to any functional groups. The emphasis will be to accentuate the synthetic uses of the sulfone group rather than its physical organic chemistry, although germane to this selection will be a brief outline of the more theoretical aspects, which are of course fundamental to any proper appreciation of sulfone chemistry. Finally, it is hoped that whilst the sulfone functional group is associated with a high degree of thermodynamic stability, thus suggesting a lack of ready manipulation, this review will encourage synthetic organic chemists to include sulfone chemistry in their repetoir of synthetic ideas.



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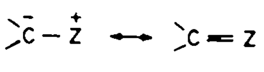

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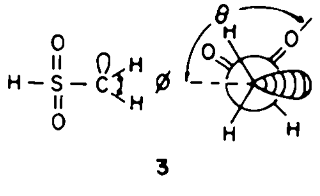

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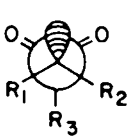
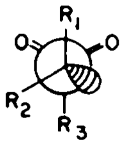
II. THEORETICAL ASPECTS OF THE SULFONYL GROUP AND THE α-SULFONYL CARBANION

A problem that has caused much discussion amongst both theoretical and synthetic organic chemists is the degree of d_π-p_π overlap that can occur, and consequently stabilize, ylides of the general type **2**; where Z is usually a second row element (S, P, etc.) in various states of oxidation. In particular for our purposes the question is addressed to the α-sulfonylcarbanion **2**, Z = SO_2R, which can formally be considered as an ylide, but whose chemistry more typically resembles that of an anion.[1] An intriguing and unexpected property of the α-sulfonyl carbanion **2** Z = SO_2R, is that it can be generated in an asymmetric form and retain its asymmetry under a variety of conditions.[2] Two explanations have been suggested to rationalize this behavior. The α-sulfonylcarbanion may be pyramidal with a high barrier to inversion, or it may be planar with a high barrier to rotation. Elegant experimental evidence has shown that proton transfer to the α-sulfonylcarbanion takes place specifically *syn*- to the two oxygen atoms.[3] More recently MO calculations on the somewhat simplified system $^{-}CH_2SO_2H$ have provided an energy surface as a function of θ and φ **3**. Of the various possibilities **4a–e** it was found that the pyramidal carbanion with the lone-pair bisecting the O–S–O angle, **4a**, has the lowest energy. Furthermore the d-orbitals do not contribute to the stabilization of the carbanion, and only inductive effects need be engendered.[4] The latter conclusion was also reached for calculations concerning the electron deficiency of α,β-unsaturated sulfones.[5] The planar carbanion **4d** was calculated to be some 2.5 kcal mole^{-1} less stable than **4a**, which in turn is some 4.1 kcal mole^{-1} more stable than **4b**. Experimentally it may be that the energy differences between **4a–c** are less than calculated; a value of 1.1 kcal mole^{-1} was arrived at by considering the rate of exchange of diastereotopic protons α- to a sulfonyl group.[6] The α-sulfonyl carbanion can in constrained situations, such as thietan derivatives, be forced to take on a planar conformation.[7]

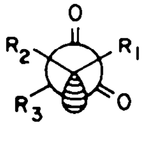
In conclusion it appears that at the present state of theory one need not evoke the 3d-orbitals to explain the asymmetry and stability of the α-sulfonylcarbanion. The asymmetric structure appears to be a consequence of the stereochemical requirements of the two adjacent electron pairs, or an electron pair and adjacent dipole. This is not the end of the story since **3** represents the simplest model of the α-sulfonylcarbanion and the conclusions can only be extended to other systems with extreme caution. Consequently whilst progress has been made in defining the structure of the asymmetric α-sulfonylcarbanion it would be rash to say the problem is now solved.



4a



4b



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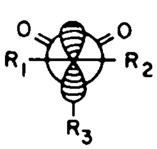
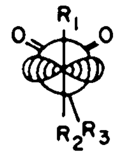


4d



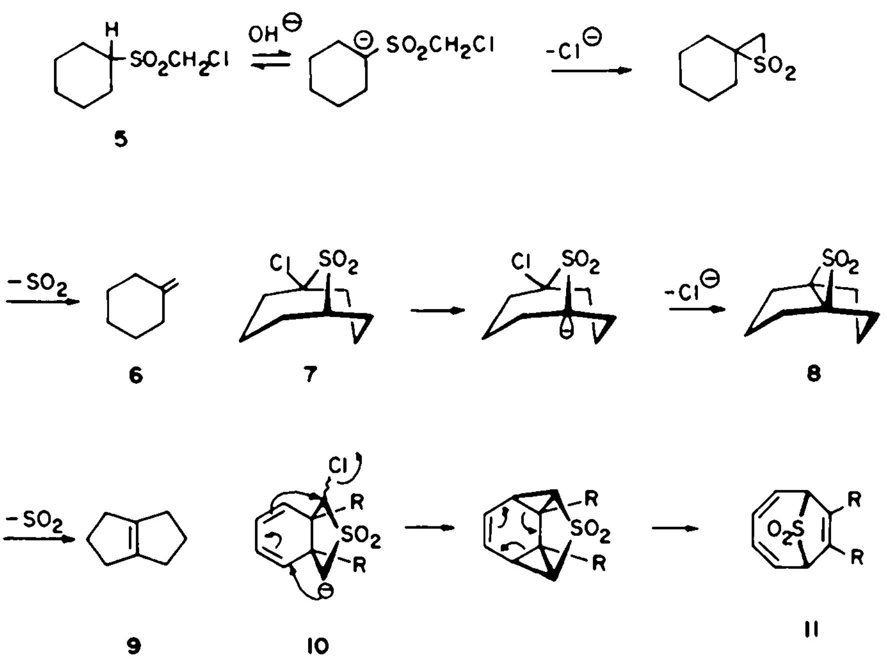
4e

III. THE RAMBERG–BÄCKLUND REACTION

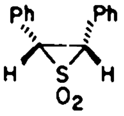
Perhaps the most well known and extensively studied reaction involving the sulfone functional group is the Ramberg–Bäcklund reaction. First discovered in 1940[8] it has been intensively researched by a number of workers.[9,10] A monograph on the Ramberg–Bäcklund reaction and all its ramifications is soon to be available,[11] and as a consequence this section will only discuss those aspects that convey its general synthetic utility. A brief outline of the current status of the mechanism is included.

The most useful feature of the Ramberg–Bäcklund reaction is its intrinsic mechanistic ability to regiospecifically convert an α-halosulfone into an alkene, where the position of the newly formed double-bond is in no doubt. This is illustrated by the conversion of **5** into **6** upon reaction with aqueous sodium hydroxide. The main features of the mechanism are also summarized in this conversion. The bicyclic sulfone **7** is able to support through the pyramidal non-conjugative nature of the α-sulfonylcarbanion, a bridge-head carbanion which undergoes 1,3-elimination to the episulfone **8**, subsequently extruding sulfur dioxide forming **9**. Extremely strained propellanes are available via this type of rearrangement.[12] A fascinating so-called *bis*-homoconjugative version of the Ramberg–Bäcklund reaction converts the α-chlorosulfone **10** into the cyclooctatriene derivative **11**.[13] Analogously a vinylogous equivalent of the Ramberg–Bäcklund reaction converts *cis*- or *trans*-3-bromo-2-pentenylbenzylsulfones into 1-phenyl-2-methyl-1,3-pentadiene.[14]

Whilst the postulated episulfone intermediates in the Ramberg–Bäcklund reaction have not been isolated from a Ramberg–Bäcklund reaction, they have been prepared by other methods.[15] Their decomposition to alkenes is base catalyzed which accounts for the inability to isolate them from a Ramberg–Bäcklund reaction. It has been observed that *cis*- and *trans*-2,3-diphenylthiirane-1,1-dioxide, **12** and **13** respectively, undergo stereospecific decomposition to the corresponding stilbenes. The Woodward–Hoffmann rules exclude a concerted thermal decomposition of thiirane-1,1-dioxides to alkenes, and consequently a dipolar mechanism has been suggested[16] (Scheme 1). There seems to be no reason why thiirane-1,1-dioxides cannot rearrange either concertedly or via a short lived dipolar intermediate to a β-sultine **14**. A β-sultine would be expected to readily extrude sulfur dioxide to give an alkene.[17] The rearrangement of a thiirane-1,1-dioxide to a β-sultine has analogy in the chemistry of thiet-1,1-dioxides which readily rearrange to γ-sultines.[17] The reaction of a diene with sulfur dioxide initially produces a sultine which rearranges to a sulfone. Attempted synthesis of the sultine resulted in the spontaneous loss of sulfur dioxide to give a diene, whereas the isomeric sulfone is quite stable under these conditions;[18] although a Woodward–Hoffmann treatment of the chelotropic extrusion of sulfur dioxide predicts a disrotatory thermal fragmentation.[19] These concepts are presented in Scheme 1. A recent observation that demonstrates that the mechanism of the Ramberg–Bäcklund reaction is by no means solved, is the suggestion that the rearrangement of **15** into **16** involves free-radicals.[20]



5 **6** **7** **8** **9** **10** **11**



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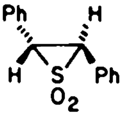

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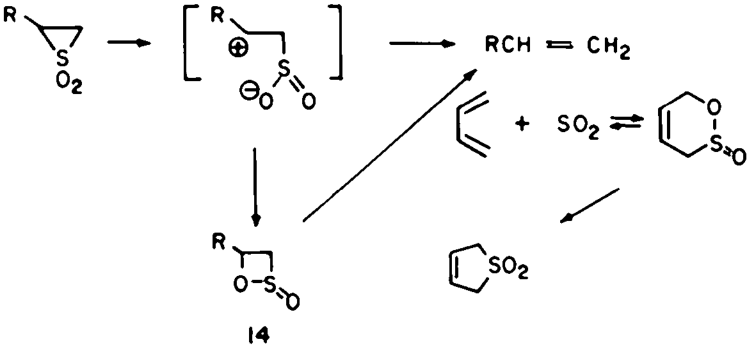

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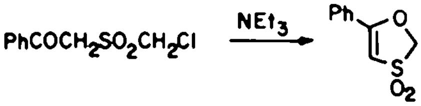
Scheme 1.

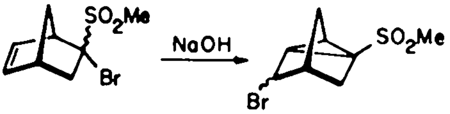
A useful development of the Ramberg–Bäcklund reaction that avoids having to prepare the α-halosulfone in a separate step is to treat a sulfone (having α- and α'-hydrogens) with potassium hydroxide in carbon tetrachloride.[21] The convenience of this procedure is somewhat offset by side-reactions due to polychlorination. Dicyclohexylsulfone gives dicyclohexylidene in 32% yield; benzhydrylsulfones react cleanly to give 1,1-diarylalkenes;[22] di-*sec*-alkylsulfones are converted into 1,1-dichlorocyclopropanes (dichlorocarbene adducts of the initial product), and di-n-alkylsulfones are transformed into *cis*-1,2-dialkylethenesulfonic acids.[23] To explain the formation of sulfonic acids the thiirene-1,1-dioxide intermediate **17** has been proposed.[24] Thiirene-1,1-dioxides are prepared by reacting α,α'-dibromosulfones with triethylamine.[25] Whilst they are more stable than thiirane-1,1-dioxides, thiirene-1,1-dioxides are converted into unsaturated sulfonic acids when exposed to aqueous potassium hydroxide.[24] Attempts to utilize the potassium hydroxide-carbon tetrachloride procedure for the conversion of the cyclic sulfone **18** into the ring contracted alkenes gave the desired product **19** and the vinyl chloride **20** in a ratio of 2:3.[26] Variations on the Ramberg–Bäcklund procedure have been briefly examined. α-Benzoyl-α'-halosulfones **21** do not extrude sulfur dioxide when treated with base, but *via* an enolate give the rare heterocyclic system **22**.[25]



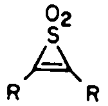
21 22

Whilst α-halosulfones readily undergo displacement of halogen in intramolecular reactions, they are notoriously unreactive in intermolecular displacement processes. The powerful inductive electron withdrawal of the sulfone group renders them a source of positive halogen. Consequently treatment of α-halosulfones or α,α'-dihalosulfones with phosphine reagents results in reduction. The stereochemistry of this process has been studied and it has been deduced that the 1,3-elimination of bromine from **23** proceeds with inversion at C-1 and C-3.[27] Whereas reduction of *erythro*-α-bromo-α-methylbenzyl-α'-methylbenzylsulfone gives *meso*-*bis*-α-methylbenzylsulfone; proceeding with retention.[28] The process of reduction of α-halosulfones by phosphines is given in Scheme 2.[29] This process does have some synthetic applications for when 1,3-tetrabromosulfones are treated with phosphines, the initial thiirene-1,1-dioxides **17** are converted, at 100°, into acetylenes.[30]

A notable synthetic use of the Ramberg–Bäcklund reaction in the natural products area has recently been made. The *bis*-allylsulfone **24** on treatment with KOH–



15 16



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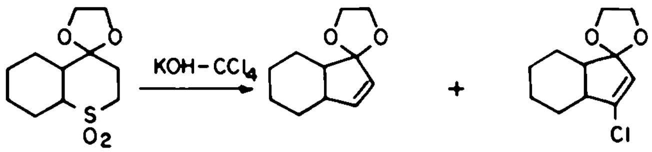
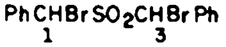
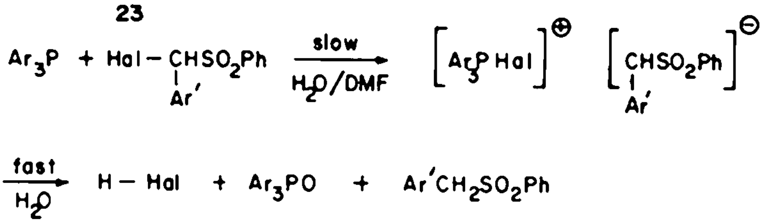


18 19 20

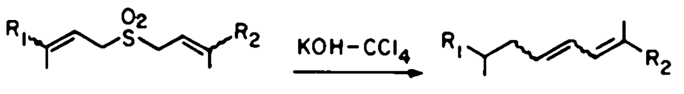


$\underset{1}{\mathrm{PhCHBr}}SO_2\underset{3}{\mathrm{CHBrPh}}$

23



Scheme 2.



24

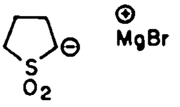
CCl_4 gave a reasonable yield of the triene. This process has been applied to the synthesis of β-carotene and vitamin A,[31a] and α,β-unsaturated acids.[31b]

IV. ANIONS AND DIANIONS

The formation and reactions of α-sulfonylcarbanions has been the subject of recent reviews.[32] This section is intended to illustrate the main methods used to prepare α-sulfonylcarbanions and α,α-sulfonyldicarbanions and some of their chemistry. The use of α-sulfonylcarbanions in more extended synthesis or as a synthon unit is described later.

The *mono*-α-sulfonylcarbanion of sulfolane may be prepared using ethylmagnesium bromide as the base. Condensation of this anion **25** with benzaldehyde gave a separable mixture of *threo*- and *erythreo*- adducts **26**. Sodium borohydride reduction of the β-ketosulfone **27** gave 95% *threo*- and 5% *erythreo*- adducts **26**. When attempts were made to convert the *threo*- adduct **26** into the corresponding chloride using thionylchloride, the reaction proceeded with epimerization, whereas the *erythro*- adduct was converted into the chloride with retention of configuration.[33] Benzylphenylsulfone is converted into the derived α-sulfonylcarbanion using n-butyllithium. Reaction of this anion with benzaldehyde gave a 77:23 mixture of *threo*- and *erythreo*- adducts.[34] When α-sulfonylcarbanions are added to α,β-unsaturated carbonyl systems the usual result is 1,2-addition.[35] A few 1,4-adducts are known but they are extremely rare (p. 20). No cuprates of the α-sulfonylcarbanion have been reported. Simple 1,2-adducts of the α-sulfonylcarbanion with α,β-unsaturated aldehydes, such as **28** can be dehydrated to dienes **29**. Such dienes should be useful in Diels–Alder-type reactions where inverse electron demand might be a valuable expedient to overcome the unreactivity of electron-rich dienophiles.

An extensive study of the anion chemistry of dimethylsulfone has been made by Russell and coworkers.[36] Dimethylsulfone condenses with aromatic aldehydes using DMSO–$KOBu^t$–$HOBu^t$ as the base system to give α,β-unsaturated sulfones, albeit in low yield (20%). This is because the initial adducts (α,β-unsaturated sulfones) condense with the aromatic aldehyde to give complex, but characterizable products. An improved procedure generates the anion of dimethylsulfone using lithium amide in liquid ammonia.[37] Diesters condense with the anion of dimethylsulfone to give potentially useful products (Scheme 3).[38] The anion of dimethylsulfone condenses with isocyanates and isothiocyanates to give the adducts **30** and **31** respectively.[39] The arylog of these condensations is known; *p*-tolylphenylsulfonylcarbanion condenses with aromatic aldehydes to yield stilbenes **32** in moderate yields. This condensation is improved considerably if Schiff bases are used as the electrophile.[40] The anion **33** is prepared using sodamide in liquid ammonia as the base system. It undergoes normal alkylation and acylation reactions, but on warming in tetrahydrofuran it rearranges (Truce–Smiles rearrangement) to the sulfinic acid **34**.[41] The initial adduct between the α-sulfonylcarbanion and an aldehyde or ketone is a β-hydroxysulfone. In a separate synthetic operation these adducts are dehydrated to α,β-unsaturated sulfones. A recent procedure describes a phase-transfer condensation of α-sulfonylcarbanions with aldehydes using aqueous sodium hydroxide-dichloromethane in the presence of a catalytic amount of triethylbenzylammonium chloride (TEBA).[42] This procedure leads directly to α,β-unsaturated sulfones in one-step. Other methods are available for accomplishing



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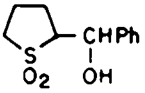

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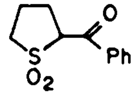

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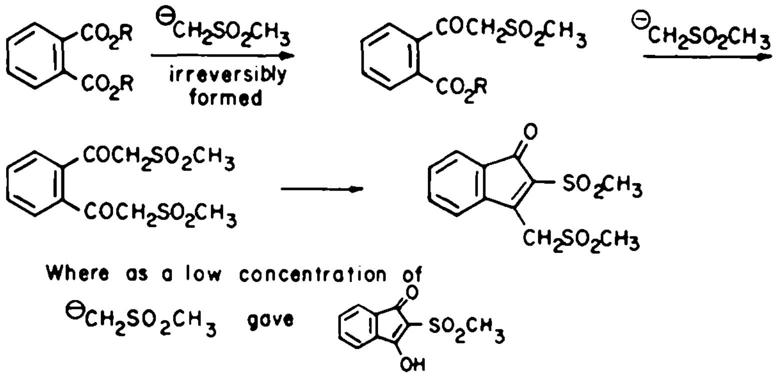
$$\underset{\mathbf{28}}{RSO_2CH_2CH(OH)CH=CHR'} \xrightarrow{H_3PO_4} \underset{\mathbf{29}}{RSO_2CH=CH-CH=CH_2}$$



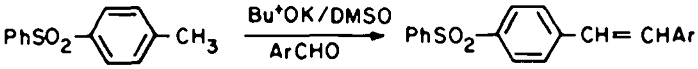
Scheme 3.

$(RNHCO)_2CHSO_2CH_3$

30

$RNHCSCH_2SO_2CH_3$

31



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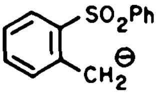

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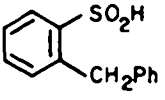

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this transformation, and will be described later, but the above procedure appears to be the most convenient.

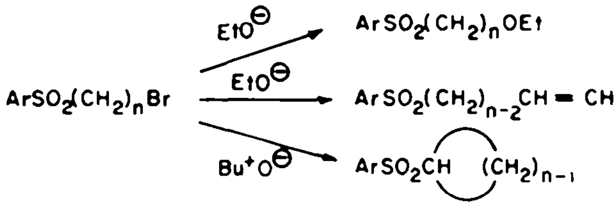
Intramolecular alkylations using α-sulfonylcarbanions have been thoroughly studied, and the three anticipated products **35**, **36**, and **37** are formed in varying proportions depending upon the base, and of course n.[43] 3-Chloropropylsulfones are cyclized by a non-concerted process via an α-sulfonylcarbanion intermediate to cyclopropylsulfones **38**.[44] A study of preferential ring size formation has been made which indicates that, if possible, a 5-membered ring is preferred.[45] An interesting example of cyclopropane formation results from treatment of ferrocenylmethylsulfone-1,1-dianion with 1,2-dichloroethane to give the compound **39**.[46] Recently intramolecular alkylations of the α-sulfonylcarbanion have led to useful syntheses of bicyclobutanes and cyclobutanes[47] (Scheme 4).

When sulfolane is treated with n-butyllithium the 1,3-dianion **40** is formed. Evidence for the existence of the 1,3-dianion is provided by quenching with methyliodide to give 2,5-dimethylsulfolane.[48] Dimethylsulfone also forms a 1,3-dianion.[48] Attempts to prepare 1,2-, 1,3- and 1,4-dianions flanked by two sulfonyl groups was inconclusive.[49] 1,3-Dianions can be oxidized with cupric chloride to give episulfones, that in keeping with Ramberg-Bäcklund chemistry give alkenes.[50]

It is possible to prepare 1,1-dianions of sulfones using n-butyllithium in tetrahydrofuran as the base system. The adduct between a 1,1-dianion and an aldehyde is not an α,β-unsaturated sulfone, presumably because lithium oxide is not a particularly good leaving group. Whereas treatment of a 1,1-dianion with magnesium iodide, followed by an aldehyde gave a good yield of α,β-unsaturated sulfone[51] (Scheme 5). The mixture of E- and Z-isomers **41** can be desulfonated using mercury-aluminum amalgam to the corresponding E- and Z-alkenes. The reduction is stereoselective, Z-1,2-diphenylvinylphenylsulfone and Z-2-*p*-chlorophenyl-1-phenylvinylsulfone gave exclusively the corresponding E-isomers.[52]

When the terpene derivative **42** was treated with n-butyllithium at −78° the 1,1-dianion **43** was formed (D_2O quench). If the dianion **43** is warmed above −70° then ElcB-elimination takes place to give the dianion **44**. Quenching of **44** with methyliodide gave only **45**. The diastereomers **46** and **47** undergo ElcB-elimination (n-BuLi at −78°) to give a single alkene, namely **45**. Interestingly, the reverse process of cyclization of **45** using t-BuOK-t-BuOH gave a 1:1 mixture of **46** and **47**. These results would appear to imply that the forward ElcB-elimination proceeds via α-carbanion inversion rather than *syn*- and *anti*-elimination.[53]

As is evident from the first section of this review the α-sulfonylcarbanion is quite at home in rigid pyramidal situations. A series of 1,3-dianions of the type **48** have been prepared (with differing numbers, and positions of double bonds). Qualitatively, from extended Huckel calculations, the color of these dianions is not associated



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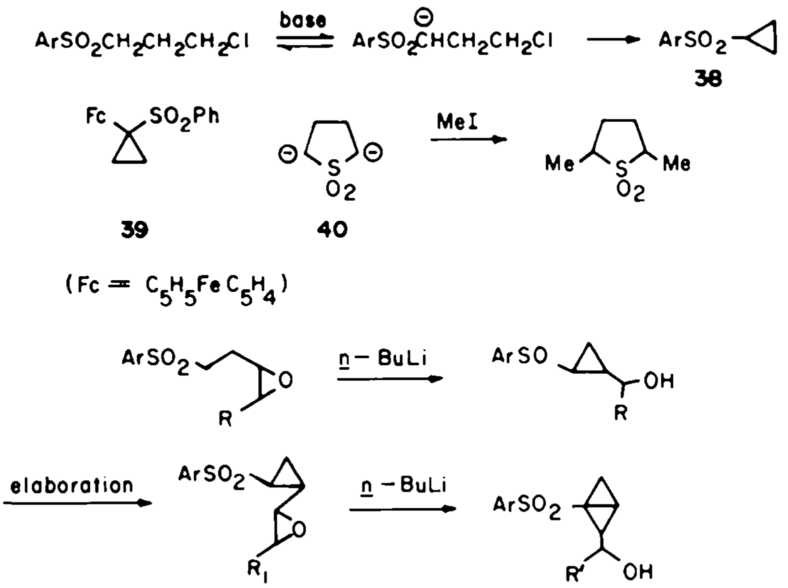
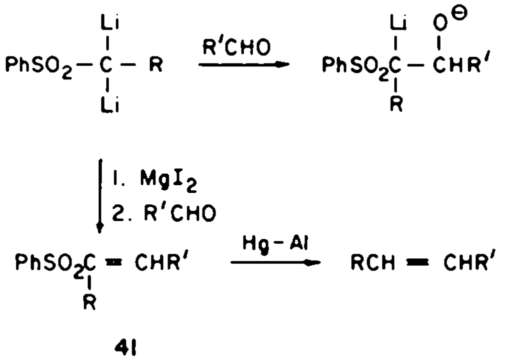


Scheme 4.

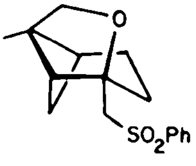


Scheme 5.

with delocalization into the sulfone group. The sulfone group merely renders the bridge head hydrogens acidic.[14]

It has been clearly shown that cyclic α-lithiosulfones, in situations where configurational differences are possible, show a high preference for equatorial positions.[15] This is most dramatically illustrated in the example **49**→**50**.

The most notable feature of the chemistry outlined in this section is the strong bases needed to prepare the α-sulfonylcarbanion. This is rather surprising since the data on pKa values indicate the range 23–27. Once the α-sulfonyl carbanion is formed it qualitatively appears to be somewhat unreactive. The unreactivity of the α-sulfonylcarbanion is most probably a direct reflection of its steric hindrance. Indeed, the α-carbanion is directly



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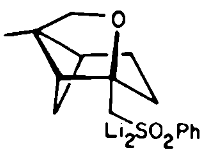

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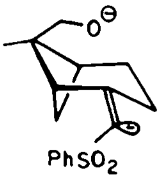

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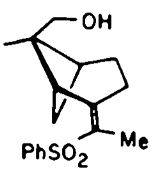

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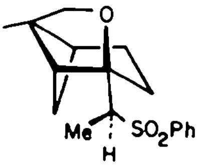

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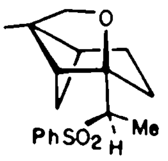

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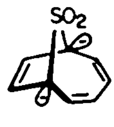

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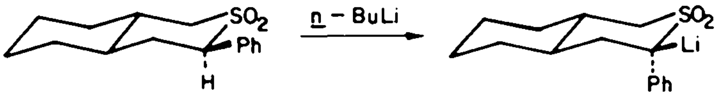


49 **50**

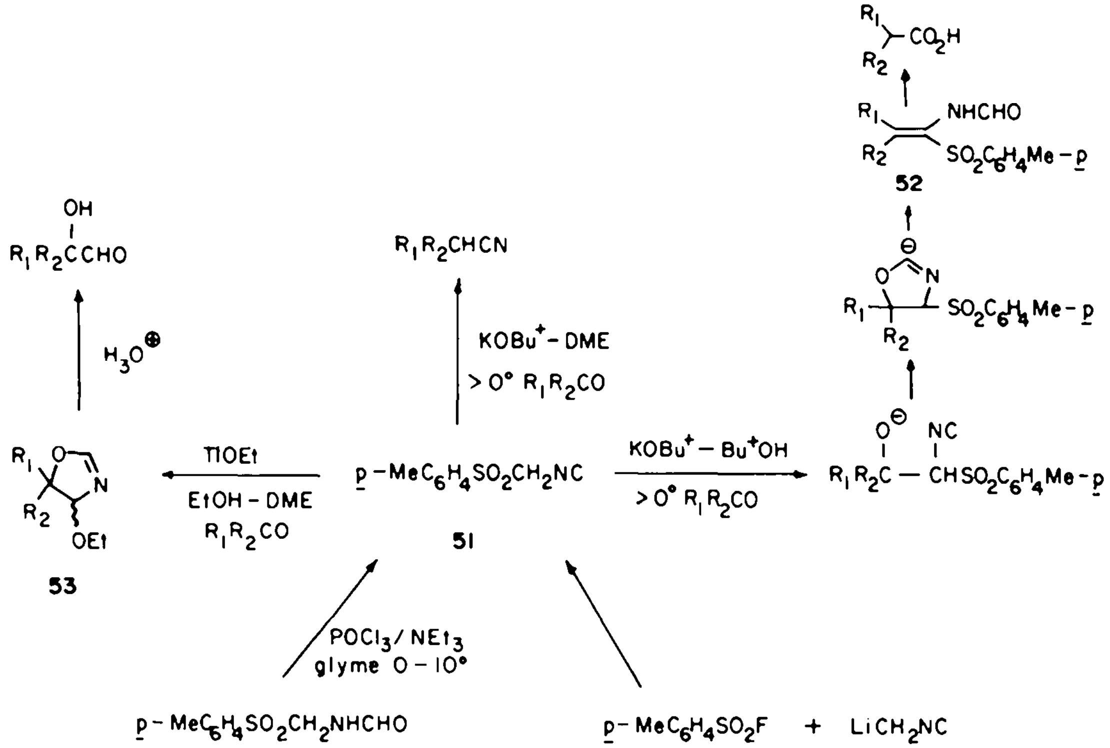
attached to the -SO_2-R group which is at least comparable to a neopentyl situation. Despite these drawbacks it will be seen that the α-sulfonylcarbanion is gradually gaining considerable synthetic importance.

V. REAGENTS THAT UTILIZE THE SULFONE GROUP: SYNTHON UNITS

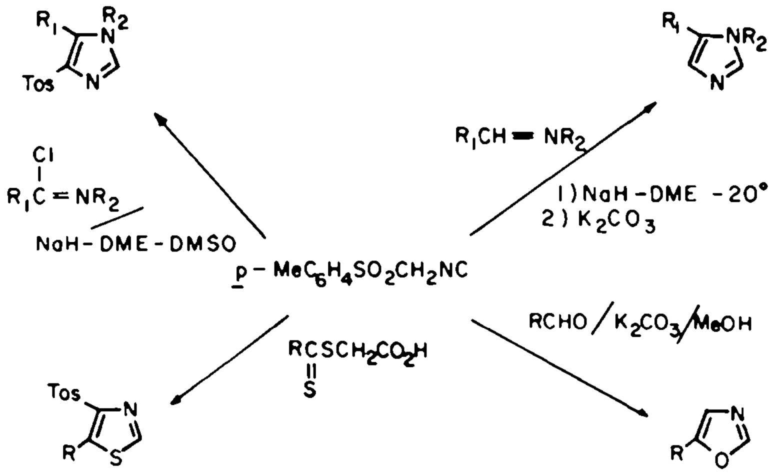
This section concerns itself with reagents that rely upon or make use of the sulfone group. In general the final products no longer have the sulfone group present; it is removed by hydrolysis, reduction or elimination.

An interesting and versatile unit introduced to the organic chemist a few years ago is the reagent *p*-toluenesulfonylmethyl isocyanide; more commonly referred to as TOSMIC **51**.[56] Its preparation is straightforward (Scheme 61) and it is now commercially available. Since the methylene group of TOSMIC is doubly activated the α-sulfonylcarbanion is accessible with comparatively mild bases (NaH or tBuOK) if contrasted to n-BuLi.

Reaction of TOSMIC anion with carbonyl compounds below 0° gave, after acidic work-up, the homologous carboxylic acid. The reaction proceeds via the formamide derivative **52**.[57] No more than minor modification of conditions (Scheme 6) provides a useful synthesis of the homologous nitrile from carbonyl compounds.[58] The methylene carbon of TOSMIC becomes the cyano carbon.[59] α-Hydroxyaldehydes may be synthesized from ketones using TOSMIC, if the base system is changed to thallium ethoxide-EtOH-DME.[60] This unusual reaction proceeds via the intermediate heterocycle **53**. A number of 5-membered ring heterocy-



Scheme 6.



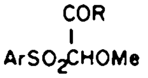
Scheme 7.

clic systems have been synthesized using TOSMIC. These are summarized in Scheme 7.[61]

α-Alkoxysulfones have been studied in detail by Schank, but to-date no reagent-synthon-type chemistry has been reported. Arylsulfinic acids react with α-chloromethylmethylether to give α-methoxymethylenesulfones **54**.[62] This reaction required some clarification since sulfinic esters are also produced in this reaction.[61] Deprotonation of **54** using Bu^{t}OK-THF and condensation with phenolesters gave α-acylated-2-sulfonylethers **55**.[64] The anion derived from **55** may be condensed with formaldehyde to give 1-alkoxyvinylarylsulfones **56**.[61] The unstable anion **57** rearranges with acyl migration and elimination to yield α-acetoxyaldehydes.[66]

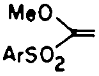
$ArSO_2CH_2OMe$

54



$\underset{ArSO_2CHOMe}{\overset{COR}{|}}$

55



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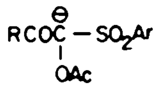


57

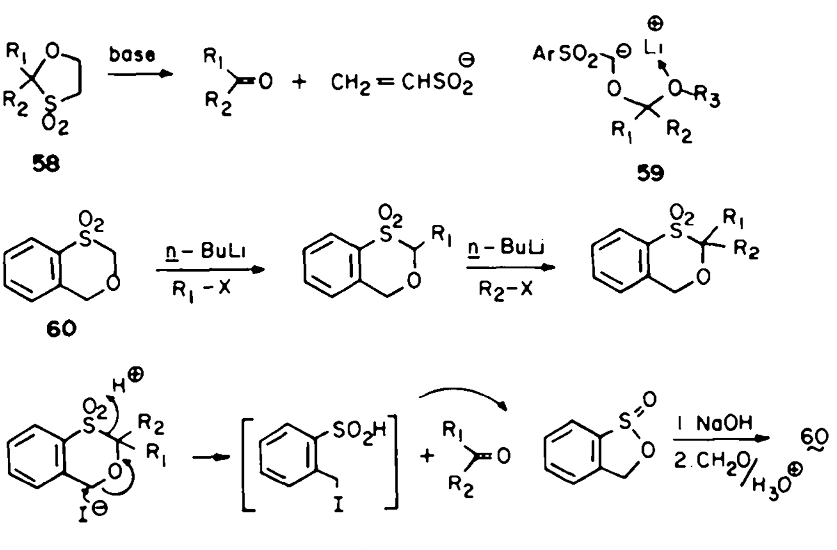
A useful adjunct to the hemithioacetal as a protecting group is the oxidized version, the 1,3-oxathiolane-S-dioxide **58**,[67] although no examples of its use have been reported. Hemithioacetals are readily oxidized by buffered *m*-chloroperbenzoic acid to 1,3-oxathiolane-S-dioxides.[68] Whilst they are extremely stable to acids, treatment with mild bases gives vinylsulfinic acid and the carbonyl component. We have examined α-alkoxysulfonyl carbanions as nucleophilic acylating species. The anion **59** can be deuterated and methylated but other alkyling agents were ineffective. Presumably the anion **59** is extremely hindered and intramolecularly coordinated, and as a consequence is unreactive. To confirm these explanations and develop an α-alkoxysulfone reagent we have prepared the substrate **60**.[68] The unit **60** readily forms a carbanion that can be alkylated with a variety of electrophiles to give in all the cases we have studied so far, crystalline products. Most significantly, the masked carbonyl function is exposed by treatment with a catalytic amount of hydrogen iodide in dichloromethane at room temperature. Furthermore the unit **60** is a recyclable species; the term *heterotropic reagent* is introduced to describe such a reagent.[68] At present this work is in the preliminary stages, but the principles of its operation are established and outlined in Scheme 8.

Julia *et al.* have made extensive use of the sulfone group in synthetic methodology. In the main the sulfone group has been a lever to form carbon-to-carbon bonds. The Scheme 9 summarizes an alkylation, followed by reduction or elimination sequence that leads to the formation of new carbon-to-carbon bonds in a controlled manner.[69] The addition of the palladium-methylene-sulfone adduct **61** to unactivated alkenes is a potentially valuable method of synthesizing allylic sulfones **62**.[70] Allylic sulfonylcarbanions **63** add 1,4- to conjugated esters followed by intramolecular displacement of phenylsulfinate to give cyclopropanes.[71] This is a rare example of the 1,4-addition of an α-sulfonylcarbanion, and more in keeping with the ylide character that can be attributed to the α-sulfonylcarbanion.

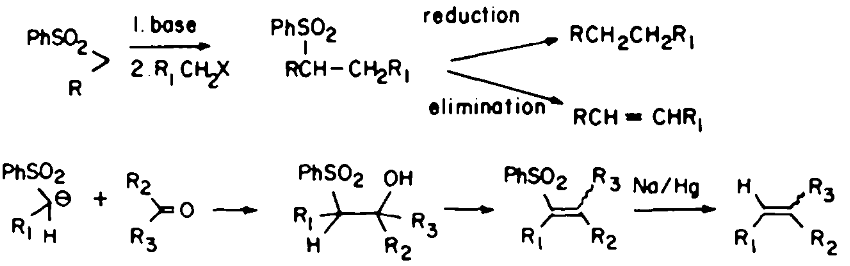
A synthon that has attracted considerable attention is the β-acylequivalent **64**. The unit **65** is easily prepared and serves as a β-acylcarbanion by deprotonation to give the anion **66**.[72] The versatile chemistry of **66** is illustrated by Scheme 10. The high stereoselectivity of the method led to a synthesis of nuciferal **67**. Complimentary to the β-acylequivalent is the β-hydroxycarbanion equivalent.[73]

A particular useful method that converts a carbonyl group into a quaternary carbon atom involves sequentially a Horner-Wittig reaction to give an unsaturated sulfone **68** and 1,4-addition of an organocuprate resulting in **69**. Reduction of **69** to **70** completes the synthetic sequence.[74]

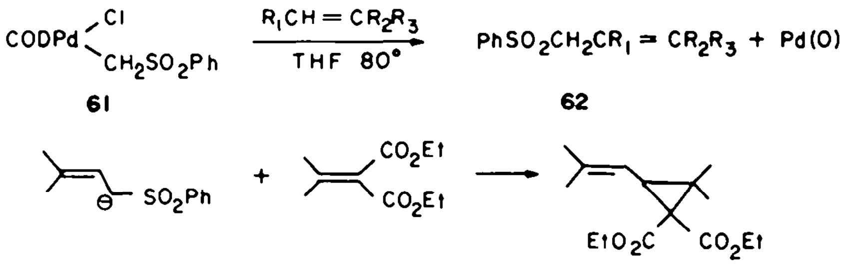
Hendrickson has recently described the synthetic chemistry of the so-called triflones ($R\text{-}SO_2CF_3$).[75] The triflone group allows adjacent carbanion formation even with such mild base systems as potassium carbonate in acetonitrile. Only monoalkylation is observed. To achieve further alkylation then sodium hydride must be used to form the α-sulfonylcarbanion. Quite exceptionally mild conditions allow the elimination of the



Scheme 8.

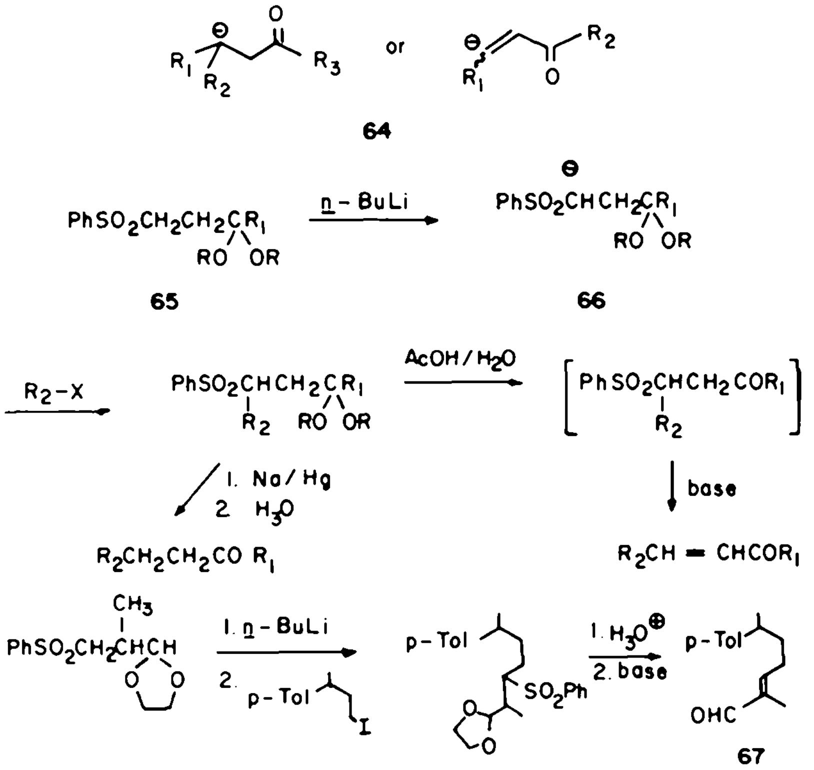


Scheme 9.

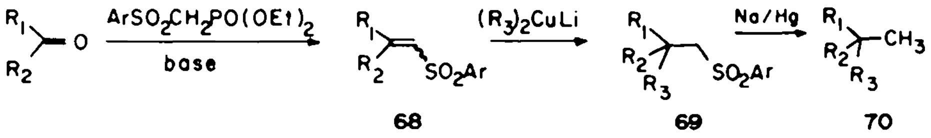


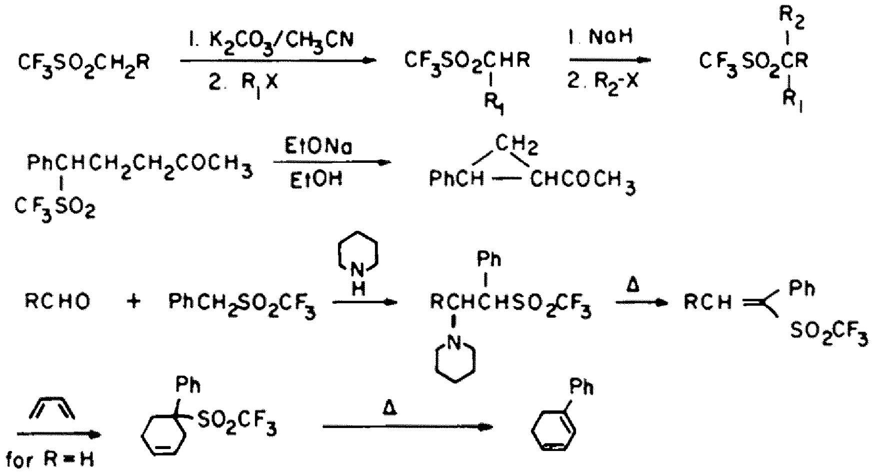
triflone unit or its displacement. Obviously triflone chemistry greatly enhances the scope of the sulfonyl unit in synthesis. These reactions are illustrated in Scheme 11. One limitation associated with triflone chemistry is that triflones themselves are not always readily accessible. This difficulty has been largely irradicated by the useful observation that trifluoromethylsulfinate esters rearrange on mild heating in HMPA to triflones.[76]

It can be seen from this section that strides have been, and are being made, to use the sulfone synthon unit in



Scheme 10.





Scheme 11.

organic synthesis. A significant practical aspect that frequently adds to the desirability of using sulfone synthons is that most intermediates and final products that contain the sulfone group are crystalline and stable (compared to sulfoxides and sulfides). The highly activating nature of the triflones offers much encouragement for further developments.

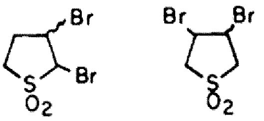
IV. DERIVATIVES OF SULFONES OF SYNTHETIC INTEREST

The objective of this section is to describe some of the chemistry of the sulfone group when it is adjacent to other functional groups. Again the underlying emphasis is on synthetic applications.

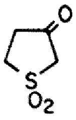
β-Ketosulfones **71** occupy a premier position as derivatives of sulfones, and many methods have been developed for their synthesis, and more especially their alkylation.[77] Alkylation of β-ketosulfones using ion-pair extraction techniques is the most recently developed procedure and offers advantages in its ease of operation and yields.[78] The preparation of the cyclic β-ketosulfone **73** deserves mention. The dibromides **72**, from 2- and 3-sulfolene respectively, on treatment with methanol-sodium hydroxide, followed by acid yield **73**.[79]

$RCOCH_2SO_2R'$

71

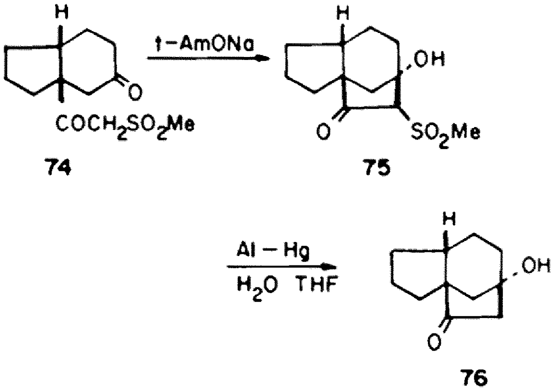


72



73

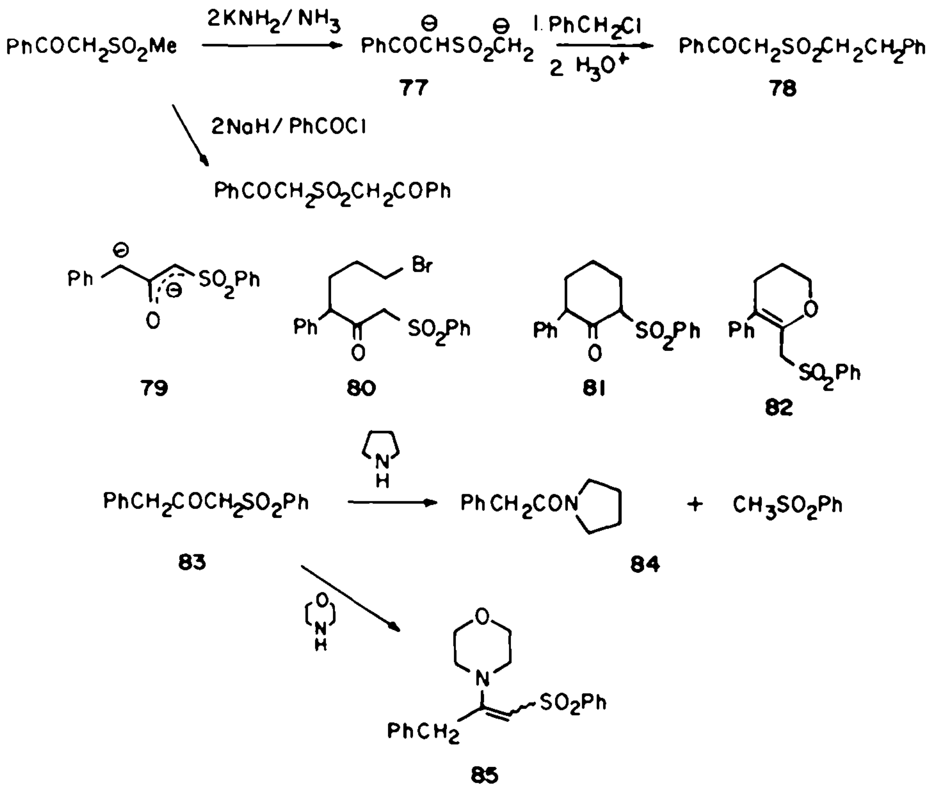
A sequence developed by House has been utilized to assemble a structural feature that is common to a large number of gibberellins. The β-ketosulfone **74** was treated with t-AmONa in benzene to give the intramolecular cyclization product **75**. Reductive cleavage of the sulfone unit using aluminum-mercury amalgam gave **76**.[80] β-Ketosulfones may also be reductively cleaved by electrolytic methods.[81] β-Ketosulfones, like β-diketones, are capable of supporting 1,3-dianions although little use has been made of this capability. The 1,3-dianion **77** is prepared by treating methylphenacylsulfone with potassium amide in liquid ammonia. Benzylation of **77** gave a low yield of the kinetic product **78**.[82] Apparently even sodium hydride can generate a 1,3-dianion.[83] The problem of low yields in the alkylation of 1,3-dianions is overcome by the use of lithium diisopropylamide in THF. The so-formed dianion **79** may be alkylated with 1,3-dibromopropane to give **80** which subsequently cyclized to the C-alkylated product **81** when treated with excess lithium diisopropylamide. When **80** was reacted with sodium hydride only the O-alkylated product **82** was formed.[84] Unexpectedly when **80** was treated with thallium ethoxide, a reagent reputed to give almost exclusive *C*-alkylation with β-diketones,[85] the major product was the O-alkylated isomer **82**.



Attempts to prepare enamines of β-ketosulfones have met with difficulties. When the β-ketosulfone **83** was treated with pyrrolidine a retro-condensation reaction gave **84**.[86] If morpholine is used instead of pyrrolidine the major product is the desired enamine **85** as a mixture of stereoisomers.[87]

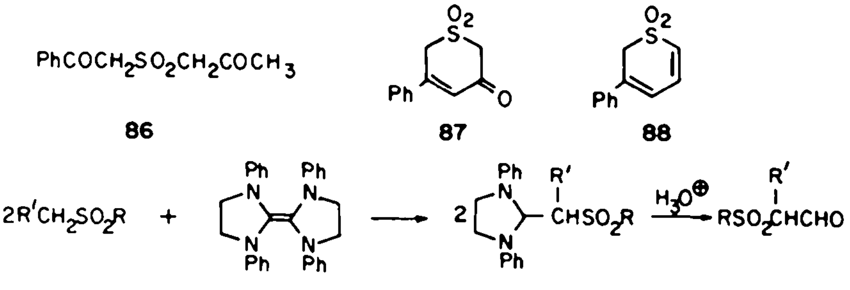
There are a number of studies that describe halogenation and Micheal reactions of β-ketosulfones.[88] The *bis*-β-ketosulfone **86** cyclizes to **87** when treated with sodium acetate-acetic acid; **87** is readily converted into **88** a potentially useful electron deficient diene.[89] β-Formylsulfones are comparatively unknown compounds that can be made as indicated in Scheme 12. They readily trimerize to 1,3,5-trisulfonylbenzenes.[90]

Stable diazo-β-ketosulfones are easily accessible via diazotransfer reactions using tosylazide and a β-ketosulfone.[91] α-Diazosulfones **89** have been prepared by the alkaline decomposition of substituted nitrosourethanes.[92] Irradiation of α-diazosulfones proceeds partly via a low yield Wolff-rearrangement to a sulfene, which is trapped by the protic solvent to give **90**. The

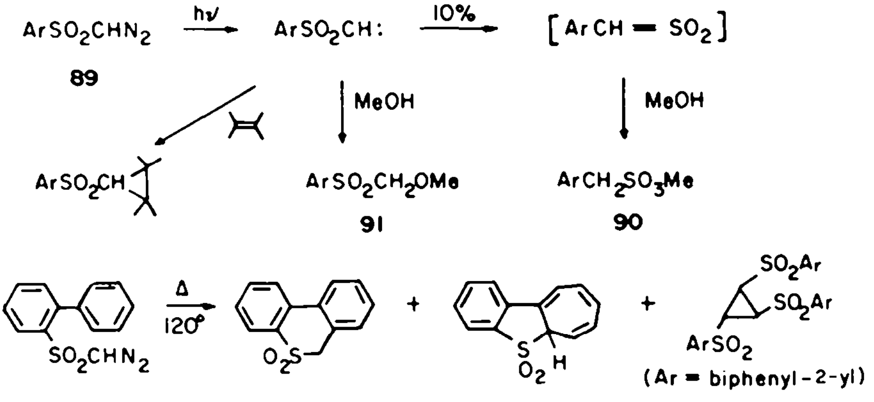


major pathway involves the non-rearranged carbene product **91**.[93] The carbene formed on irradiation of diazosulfones may be trapped with alkenes or intramolecularly with a phenyl group to give the products shown in Scheme 13.[94]

Hydrolysis of α-diazosulfones in aqueous acid proceeds to α-hydroxysulfones which readily decompose to sulfinic acids.[95] In certain cases the decomposition of α-diazosulfones may be conducted using Lewis acids and the product trapped intramolecularly (**92** → **93**).[96] Ox-

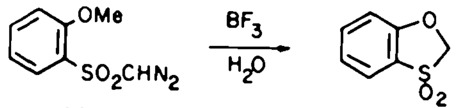


Scheme 12.

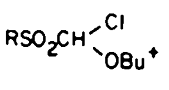


Scheme 13.

idative decomposition of α-diazosulfones with t-butylhypochlorite gives α-chloro-α-t-butoxysulfones **94**.[97] Whilst in general simple α-substituted sulfones do not undergo SN2-type displacements, the product **95**, from treatment of an α-diazosulfone with trifluoromethylsulfonic acid, reacts with nucleophiles under mild conditions to give typical SN2 displacement products.[98]



92 **93**



$$\mathrm{RSO_2CH}{<}^{\mathrm{Cl}}_{\mathrm{OBu^t}}$$

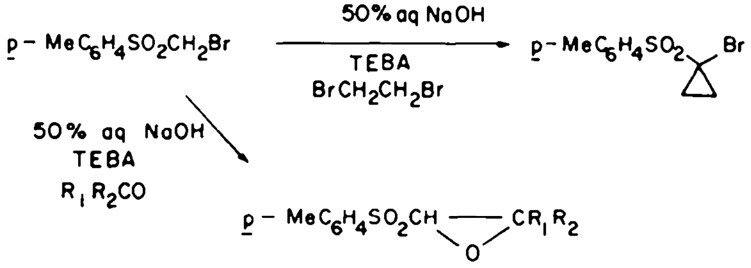
94

$$p\text{-}\mathrm{MeC_6H_4SO_2CH_2OSO_2CF_3} \xrightarrow{:\mathrm{Nuc}} p\text{-}\mathrm{MeC_6H_4SO_2CH_2Nuc}$$

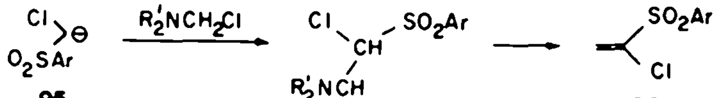
95

α-Halosulfones that are structurally prevented from undergoing the Ramberg–Bäcklund reaction can enter into other interesting modes of chemistry. Both α-chloro- and α-bromomethylarylsulfones are converted into carbanions in the presence of concentrated sodium hydroxide and a quaternary ammonium salt catalyst. These carbanions are readily condensed with carbonyl compounds to give oxiranes, and are easily alkylated (Scheme 14).[99] The α-chloro-α-sulfonylcarbanion **95** condenses with chloromethylamines to yield α-chloro-α,β-unsaturated sulfones **96**.[100] A general route to α,β-epoxysulfones involves the reaction of the carbanion **95** with aldehydes or ketones.[101] The initial adducts **97** may be separated into diastereoisomers and upon treatment with base are converted into the *cis*- and *trans*-epoxides **98** respectively.[101] α,β-Epoxysulfones are unstable compounds and rearrange to β-ketosulfones (**99**→**100**).[102] This rearrangement is catalyzed by Lewis acids.

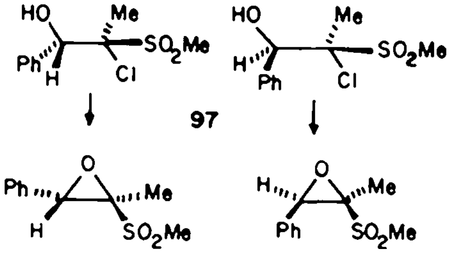
An interesting example of this rearrangement is the



Scheme 14.



95 **96**

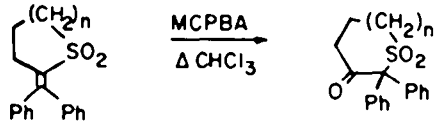


97

98

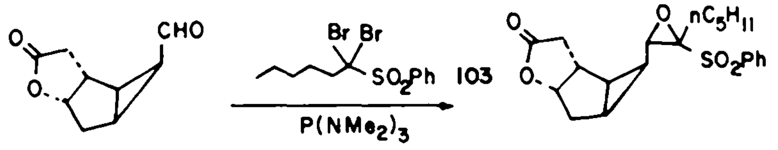
$$\mathrm{PhCH\overset{O}{—}CHSO_2C_6H_4Me}\text{-}p \longrightarrow \mathrm{OHC-\overset{Ph}{C}HSO_2C_6H_4Me}\text{-}p$$

99 **100**

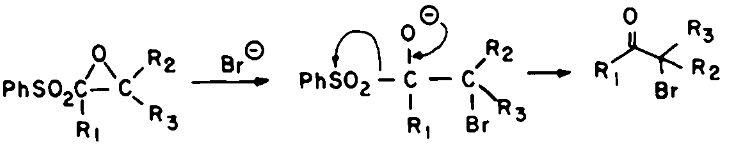


101 **102**

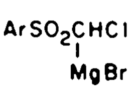
attempted epoxidation of the cyclic sulfone **101** using *m*-chloroperbenzoic acid to give the β-ketosulfone **102**.[101] The α,α-dibromosulfone **103** reacts with the prostaglandin intermediate **104** in the presence of $P(NMe_2)_3$ to give the epoxysulfone **105**.[104] Unfortunately **105** could not be further elaborated in a desired fashion. α,β-Epoxysulfones can act as precursors to α-halocarbonyl compounds by treatment with magnesium bromide (Scheme 15).[105] This reaction renders the α,β-epoxysulfone unit a useful R_1R_2COR precursor that should find further applications in synthesis. The α-chloromagnesium compounds **106** show no tendency towards α-elimination, instead they are stable and give the usual reactions of Grignard compounds.[106] The sulfonamide derivative **107** is apparently capable of forming a 1,1-dianion when treated with n-butyllithium (2 equiv.). The presence of the dianion **108** was evidenced by alkylation with methyliodide to give **109**.[107] The chemistry of the monoanion **110** has been examined. It condenses with ketones to give chlorohydrins that can be converted using *t*-BuOK in THF to α,β-epoxysulfonamides **111**.[108]



104 105

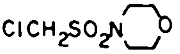


Scheme 15.



$ArSO_2\underset{\displaystyle MgBr}{C}HCl$

106



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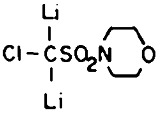
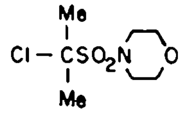


108



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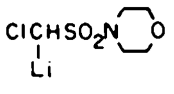

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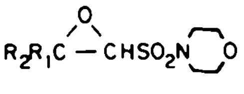


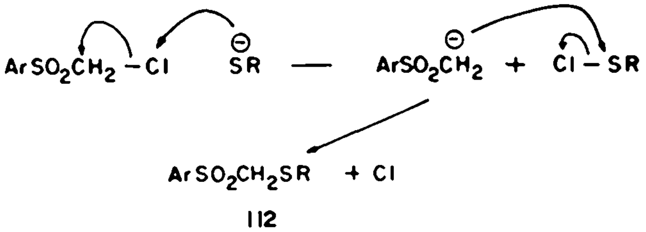
111

A procedure that should find applications in sulfone chemistry involves treating an α-bromosulfone with a trialkylborane in the presence of t-BuOK/t-BuOH to give an alkylsulfone.[109] It is reported that α-chlorosulfones react with sodium thiolates to give α-thioalkylsulfones **112**.[110] This unusual reaction need not be explained as being an exceptional S_N2-type displacement but may proceed as in Scheme 16. The displacement on chlorine, followed by a sulfenylation reaction would appear to be a more reasonable explanation.

At this juncture a mention of α,β-unsaturated sulfones is presented since they may be considered to be derivatives of sulfones of synthetic interest. They are described in more detail later. α,β-Unsaturated sulfones are generally available via the Wittig-Horner reaction, and a number of similar publications have described this procedure.[111]

Sulfonyl stabilized oxosulfonium ylides **113** are best prepared from dimethyloxosulfonium methylide and an arylsulfonyl fluoride. The resulting ylide **113**, is, as expected, exceptionally stable.[112] Sulfonyl stabilized phosphonium ylides **114** provide the only useful route to sulfonylcyanides **115**. Treatment of **114** with nitrosylchloride gives **115**.[113] When sulfonylcyanides **115** are reacted with nucleophiles they act as a source of electrophilic cyanide and yield cyanogen derivatives and sulfinic acids.[114] Whilst ordinary cyanides are somewhat unreactive towards cycloaddition reactions sulfonylcyanides readily add diazomethane or cyclopentadiane derivatives to give adducts (Scheme 17).[115]

An interesting class of substituted sulfones is β-di-



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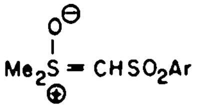
Scheme 16.



$Me_2\overset{\oplus}{S}(O^\ominus)=CHSO_2Ar$

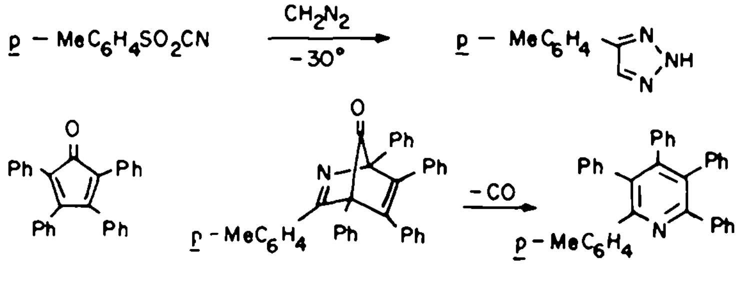
113

$RSO_2\overset{\ominus}{C}H\overset{\oplus}{P}Ph_3$

114

$RSO_2CN \xrightarrow{X^\ominus} X-CN + RSO_2^\ominus$

115



Scheme 17.

sulfones **116**. Condensation of methylene bis-phenylsulfone with aldehydes proceeds in a straightforward manner to give **117**, but formaldehyde condensation with **116** gives **118** and **119**. In the presence of piperidine (Mannich-type conditions) the anticipated adduct **120**,[116] was formed. Abnormal Knoevenagel condensation of **116** can take place (Scheme 18).[117] Alkylation of the salts of **116** with chloromethylmethylether or N-chloromethylphthalimide gave **118** (R = Ph), whereas simple non-formaldehyde equivalents such as bromoacetic acid gave the expected products.[118] Salicylaldehyde condenses with methylene bis-ethylsulfone **116** (R = Et) in the presence of piperidine to give the benzofuran **121**.[119] The anion of methylene bis-alkylsulfones conjugatively adds to vinylsulfonium salts to give cyclopropanes, albeit in moderate yields, as indeed do simple α-sulfonyl carbanions.[120]

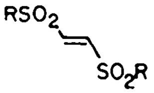
Bis-(perfluoroalkylsulfonyl)methanes readily form salts with Grignard reagents and the resulting anions can be alkylated.[121] Mercuric acetate reacts with **116** to produce insoluble mercuric salts, reflecting the highly acidic nature of the methylene group.[122]

β-Cyano- and β-carbethoxysulfones undergo Knoevenagel condensation to give products of the type **122**. Treatment of **122** with sodium azide in DMF provides a

$(RSO_2)_2CH_2$ **116**

$(RSO_2)_2CH=CHR'$ **117**

$(RSO_2)_2CHCH_2CH(SO_2R)_2$ **118**



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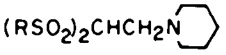

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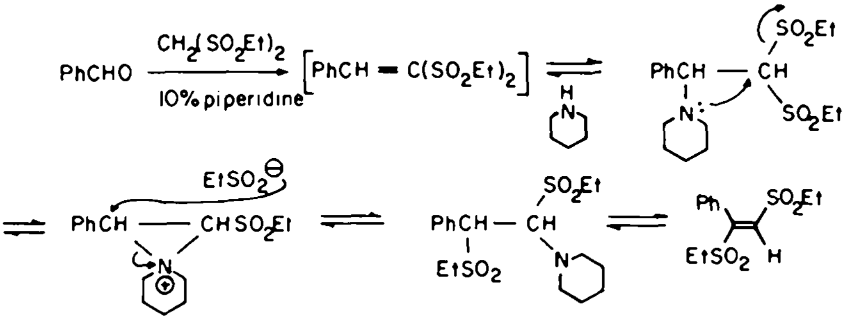
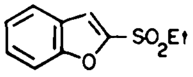


Scheme 18.



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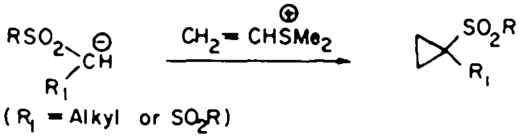
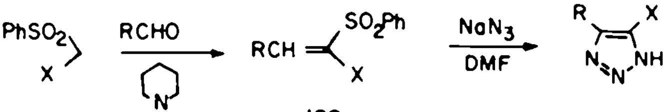


convenient 1,2,3-triazole synthesis.[123] The methylene bis-alkylsulfonyl carbanion reacts with carbon disulfide to give adducts that are alkylated *in situ* to produce dithioketene acetals **123**.[125] A similar reaction takes place with the α-sulfonylcarbanion.[126]



122

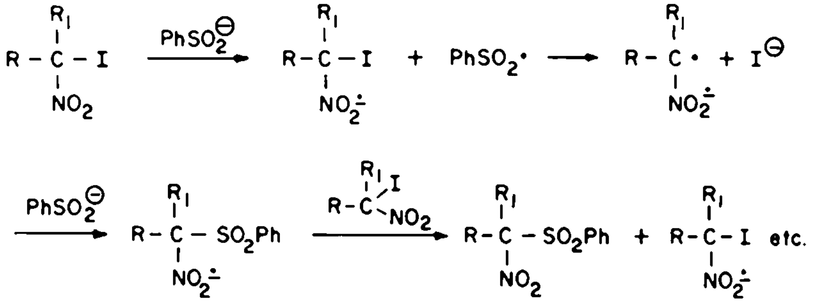
124

(X = CN, CO_2Et, CO_2H) If X = CO_2H then decarboxylation takes place.

$$(MeSO_2)_2CH_2 \xrightarrow[\substack{2.\ CS_2\\ 3.\ MeI}]{1.\ t\text{-}BuOK/DMSO} (MeSO_2)_2C=C(SMe)_2$$

123

α-Nitrosulfones **124** are intriguing compounds in that they have demonstrated a new, and hitherto unsuspected type of displacement process. α-Iodonitro compounds react with sodium sulfinates to give α-nitrosulfones via a radical-chain process and not an S_N2- reaction[127] (Scheme 19). Another route to α-nitrosulfones is to treat α-sulfonylcarbanions with alkylnitrates.[128] The sulfone group is displaced from α-nitrosulfones by nitroparaffin salts and malonate anions via a mechanism that possesses the characteristics of radical anion-free radical process.[129] Nitronic acid esters **125** may be prepared by alkylation of α-nitrosulfones with diazomethane.[130] Pyrolysis of **125** gave the α-oximinosulfone **126**, whereas reaction of **125** with t-butoxyradicals gave the unstable species **127**.[130]



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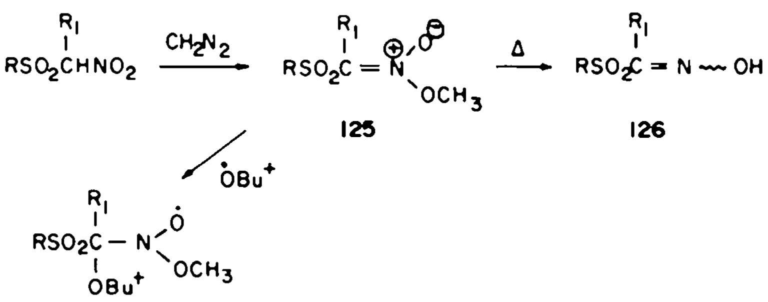
Scheme 19.



125

126

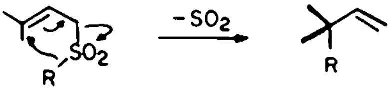
127

VII. α,β-UNSATURATED SULFONES

In a study of the position of equilibrium between α,β- and β,γ-unsaturated sulfones it was established that for **128** ⇄ **129** the β,γ-isomer was at least 99% of the equilibrium mixture. It has been the general observation that the β,γ-unsaturated sulfone is more stable than the α,β-isomer.[131] This is in accordance with some of the ideas in Section II. Interconversion of *cis*- and *trans*-α,β-unsaturated sulfones is not direct but proceeds through the intermediacy of the β,γ-isomer.[132] β,γ-unsaturated sulfones **130** are not thermally stable, at 300–400° they extrude sulfur dioxide.[133] This reaction has recently been used to assemble quaternary carbon atoms.[134] The Sulfo-Cope rearrangement of allylvinylsulfones **131** produces a sulfene intermediate which is captured by nucleophiles.[135] A rapid Cope rearrangement can, in the case of **132**, compete effectively with the more usual fragmentation involving the extrusion of sulfur dioxide.[136]

α,β-Unsaturated sulfones, being electron-deficient alkenes, enter into the Diels–Alder reaction, although very

128 **129**



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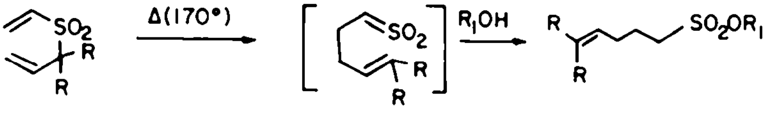

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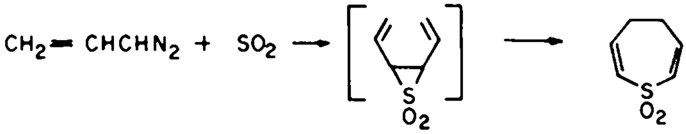
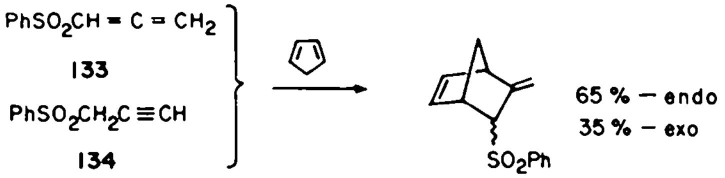


few examples of this use have been reported.[137-139] Allenic and acetylenic sulfones act as dienophiles, indeed **133** and **134** are equivalent species in the Diels–Alder reaction with cyclopentadiene.[138]

Nucleophilic additions to the electron-deficient double-bond constitute the main chemistry of α,β-unsaturated sulfones. Cyclohexanone enamines react with phenylvinylsulfone to give the expected adduct **135**,[139] although it had been suggested that the cyclobutane **136** might be the product.[140] Alkaline epoxidation (H_2O_2/OH^-) of α,β-unsaturated sulfones shows similar features to α,β-unsaturated carbonyl compounds and give epoxysulfones.[141]

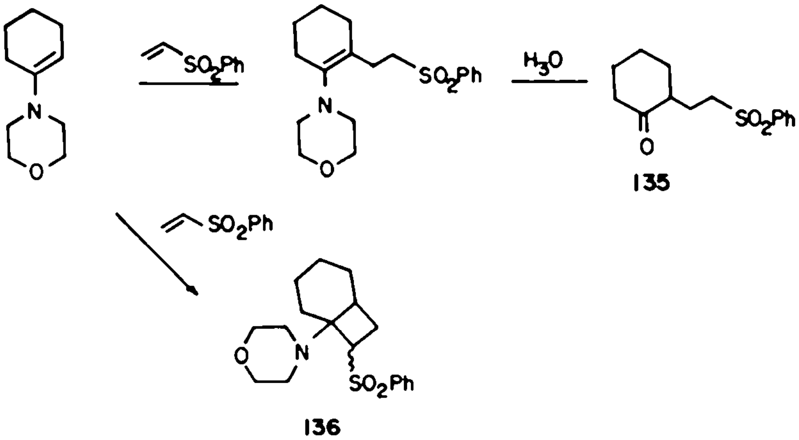
cis-1-Phenyl-2-(*p*-toluenesulfonyl)ethene **137** or its *trans*- isomer, with alkaline hydrogenperoxide in aqueous acetone affords the *trans*-epoxysulfone **138**. Apparently under these conditions the initially formed adduct has sufficient life-time to undergo rotational equilibration yielding the thermodynamically more stable *trans*- epoxide. Whereas reaction of **137** with ClO^- in aqueous dioxane gave only the *cis*-epoxysulfone **139**.



133

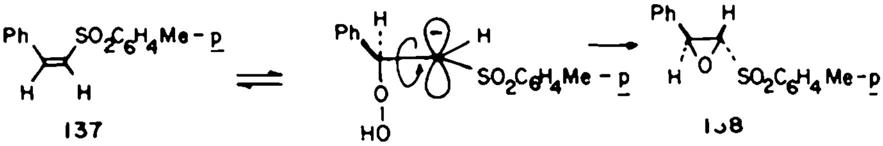
134

65 % — endo
35 % — exo

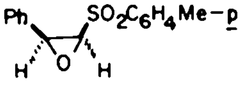


135

136



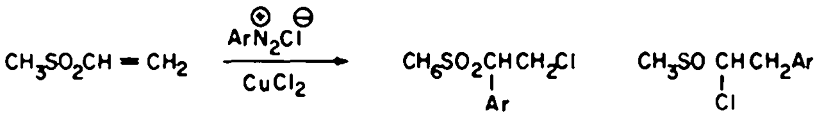
137 **138**



139

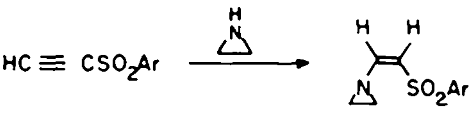
The stereochemistry of the epoxidation of **137** depends upon the nature of the epoxidizing nucleophile. In going from t-BuOO$^-$, HOO$^-$, m-ClC$_6$H$_4$CO$_3^-$ to ClO$^-$ the reaction proceeds from being highly stereoselective to completely stereospecific. These findings are rationalized by the leaving group ability which is expected to increase in the order t-BuO$^-$ < HO$^-$ < m-ClC$_6$H$_4$CO$_2$ < Cl$^-$; clearly as the leaving group ability is enhanced expulsion of the leaving group can compete favorably with bond rotation.[141] α,β-Epoxysulfones are somewhat unstable to the reaction conditions (H$_2$O$_2$/NaOH) and cleave to sulfinic acids and α-hydroxyaldehydes.[141,142]

The Meerwein-Arylation of vinylsulfones has been briefly studied and some controversy existed over whether the newly introduced aryl group was α- or β- to the sulfone group. It was claimed that methylvinylsulfone **140** reacted with an aryldiazonium chloride to give **141**.[143] Whereas Truce *et al.* have good evidence that the opposite orientation, namely **142** is formed.[144]



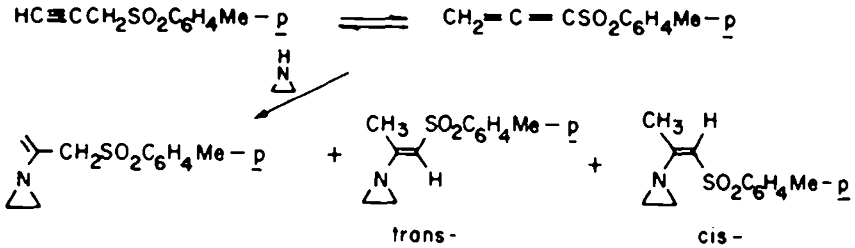
140 **141** **142**

The addition of nucleophiles such as amines, alcohols and sulfides to α,β-unsaturated sulfones has been extensively studied and would constitute a separate review to do full justice to this topic. It is perhaps sufficient to supply key references and briefly outline some of the results. Addition of ethyleneimine to allenic and propargylic sulfones led to the formation of the non-conjugated adduct by 1,2-addition to the allene directly, or through initial isomerization of the propargyl system to the allene (Scheme 20).[145] If the temperature at which these conjugate additions are conducted is lowered then the *cis*-adduct predominates. The *trans*- addition process giving the *cis*- adduct is the kinetically controlled process, whilst *cis*- addition yielding the *trans*- product is thermodynamically more favorable. Addition of ethyleneimine to the acetylenic sulfone **143** gives, almost exclusively, the *cis*- adduct **144** via a *trans*- addition process.[146] If α-sulfonylvinylcarbanions are intermediates in these additions then evidence has been presented that they do not isomerize (*cis* ⇄ *trans*) under the reaction conditions used in the conjugate additions.[147] The sulfonyl acetylenes used in the conjugate addition reactions are conveniently prepared by the free-radical chain addition of sulfonyliodides to acetylenes.[148]

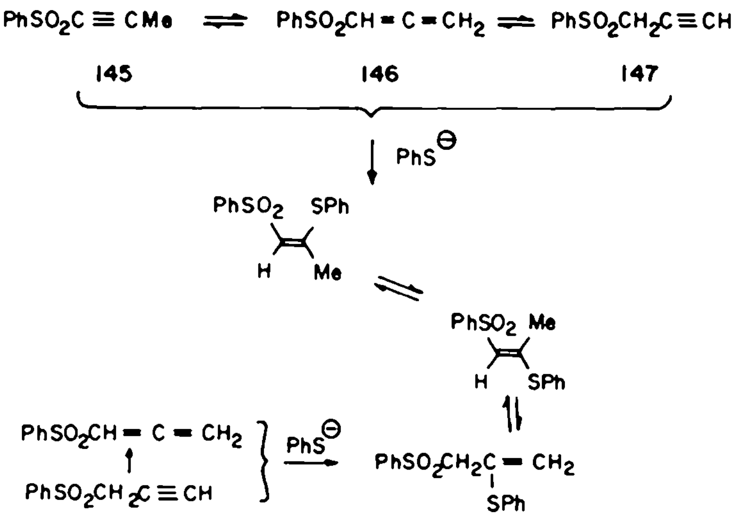


143 **144**

An extensive series of papers describing elimination-



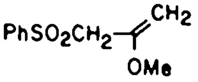
Scheme 20.



Scheme 21.

addition reactions to unsaturated sulfones has been published by Stirling and coworkers; some of the results are given below. Addition of thiolate anions to the sulfones **245**, **146** and **147** results in the *cis*- product **148** (Scheme 21).[149]

In contrast to the above result, when **145**, **146** and **147** were treated with sodium methoxide (0.10N) the adduct **149** was the only product from each sulfone.[150] A recent review covers the latest results,[151] and detailed discussion of the interconversions of **145**, **146** and **147** is available.[152]



149

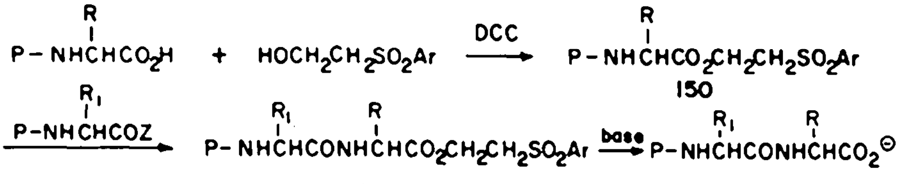
The elimination reactions of β-substituted sulfones has been used as a method for carboxyl group protection.[153] α-Amino acids are condensed with a β-hydroxysulfone using dicyclohexylcarbodiimide as the condensing agent, to give β-sulfonylesters **150**. These esters are subsequently coupled to give a dipeptide **151**, and treatment with base removes the protecting group by β-elimination.[153] Phosphate groups have been protected during nucleotide synthesis using the O-2(arylthio)ethyl group, $ArSCH_2CH_2O$–. It is removed by oxidation to the sulfone, followed by β-elimination with dilute sodium hydroxide.[154] The Wittig reagent **152** was used in the synthesis of pyrenophorin **153**. Eventually the sulfonyl protecting group was removed under mild conditions using 1,5-diazobicyclo[4.3.0]non-5-ene to effect β-elimination. This mild method of removal is an essential feature of this synthesis.[155]

VIII. ELIMINATION, EXTRUSION, AND REARRANGEMENTS OF SULFONES

Most of the chemistry described so far has in some way demonstrated that the sulfone functional group is a particularly stable unit surviving a large number of transformations. It is the intention of this section to describe a few reactions that rely on the disruption of the sulfone group, (*re* references 133 and 134). Whilst the thermal elimination of sulfenic acid from a sulfoxide is a relatively mild and well studied process, the elimination of a sulfinic acid from a sulfone is recognized to be extremely difficult. When the arylsulfone **154** was heated with t-BuOK in pyridine, elimination took place to give alkenes.[156] The *p*-dimethylamino group in **154** has an activating effect since **154** thermally eliminated to pentenes without base being present, whereas simple phenyl- or *p*-tolylsulfones did not. Benzyl-2-phenethylsulfone reacts with ethylmagnesium bromide in dry xylene at reflux to give 1,3-diphenylpropene and stilbene.[157]

An interesting double γ-elimination illustrates that under particularly favorable geometrical circumstances the phenylsulfonyl group can act as a leaving group[158] (**155** → **156**). Aromatic sulfones are reputedly thermally stable compounds, but when *p*-tolylsulfone in benzene was dropped into a heated column (800°) packed with alumina, biphenyl (48%), *p*-bitolyl (22%) and *p*-toluenesulfinic acid (2%) were formed.[159] Pyrolysis of the bis-sulfone **157** at 500° gave the [2.2]-metacyclophane **158**.[160] This procedure has been applied to the synthesis of other metacyclophanes.[161]

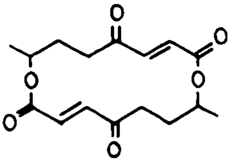
Dihydrothiophene-S-dioxides **159** may be converted into butadienes **160** when they are pyrolyzed or photolyzed. The reaction is 99.9% stereospecific.[162] The dihydrothiophene-S-dioxide **161** readily loses sulfur dioxide when treated with hydrazine to give **162**.[163]



P = protecting group

$Ph_3P{=}CHCO_2CH_2CH_2SO_2C_6H_4Me$-p

152



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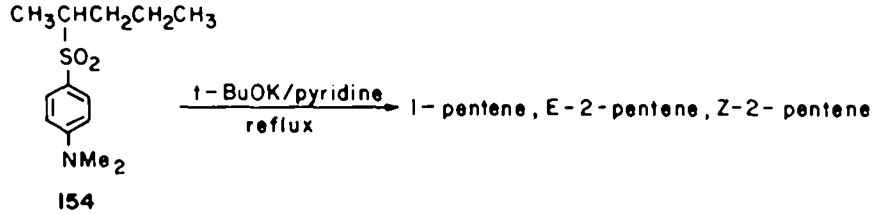

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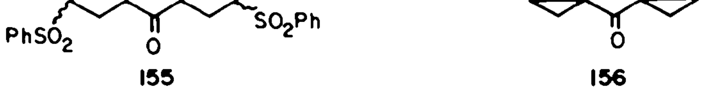
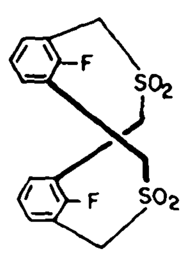


155 **156**



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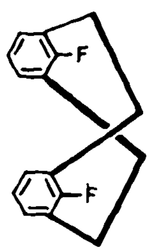

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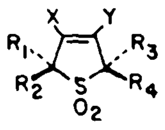

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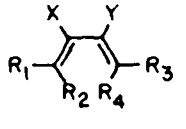

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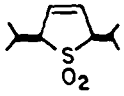


161

162

α-Sulfonylcarbanions can undergo rearrangement processes; the anion **163** α-eliminates to give, via the carbene **164**, triphenylethylene.[164] Treatment of either *cis*- or *trans*-2,4-diphenylthietane-1,1-dioxide **165** with ethylmagnesium bromide gave *trans*-1,2-diphenylcyclopropanesulfinic acid **166**.[165] Naphthothiete sulfone **167** is reduced by lithium aluminum hydride to give the thioaldehyde **168**, which may be hydrolyzed to the aldehyde or further reduced to a thiol.[166] Diallenic sulfones **169** are thermally unstable and rearrange at temperatures as low as 75° to thiophene-1,1-dioxides **170**.[167]

The Truce–Smiles rearrangement has been the subject of several papers;[168] the general mechanism is given in Scheme 22. If mesityl *p*-tolylsulfone is treated with n-butyllithium, followed by rapid work-up, a 4a,9a-dihydrothioxanthene-10,10-dioxide can be isolated.[169] This experiment provides evidence for the addition-elimination pathway.

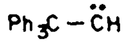
Relatively few papers have concerned themselves with the photochemistry of sulfones, presumably because of the high energy radiation needed to excite the chromophoric unit. Predictably, β-ketosulfones **171** undergo typical photochemical cleavage.[170] Diarylsulfones **172** on irradiation in benzene give biaryls **173**.[171] Irradiation of phenyl 2,3,5,6-tetra-O-acetyl-α-D-glucofuranosyl sulfone **174** in acetone with a 450w medium pressure mercury lamp gave SO_2, biphenyl, the 2,3,5,6-tetra-O-acetyl derivatives of 1,4-anhydro-D-glucitol, α-D-glucofuranosylbiphenyl and its anomer.[172] Scheme 23 outlines this complex reaction.

IX. DESULFONYLATION AND THE REDUCTION OF SULFONES TO SULFIDES

Most uses of the sulfone group in synthesis ultimately involve its reductive removal. A recent improved procedure involves treatment of an arylalkylsulfone with excess 6% Na–Hg amalgam in methanol, in the presence of 4 equiv. of disodium hydrogen phosphate.[173] The α,β-unsaturated sulfonyl group can be converted into an alkene; the sulfonyl group is replaced by an alkyl group when reacted with a trialkylborane.[174] When the sulfonyl group is attached directly to a chiral center **175** desulfonylation with Raney nickel, pretreated with acetone, gave **176**, with predominant retention of configuration, whereas Raney nickel in ethanol gave inversion.[175] A little exploited method of reductive cleavage is electrochemical reduction of arylalkylsulfones to hydrocarbons.[176]

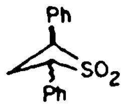
$Ph_3C\overset{\ominus}{C}HSO_2Ph$

163



$Ph_3C-\ddot{C}H$

164



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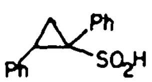

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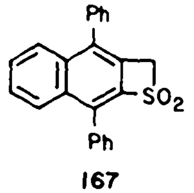

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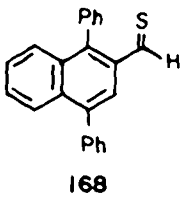

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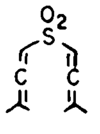

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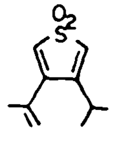

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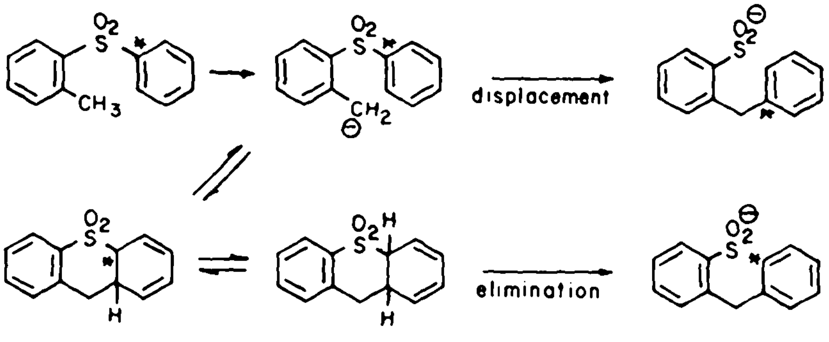
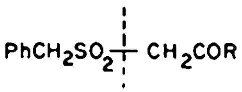
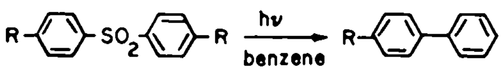


Scheme 22.



$PhCH_2SO_2 \vdots CH_2COR$

171



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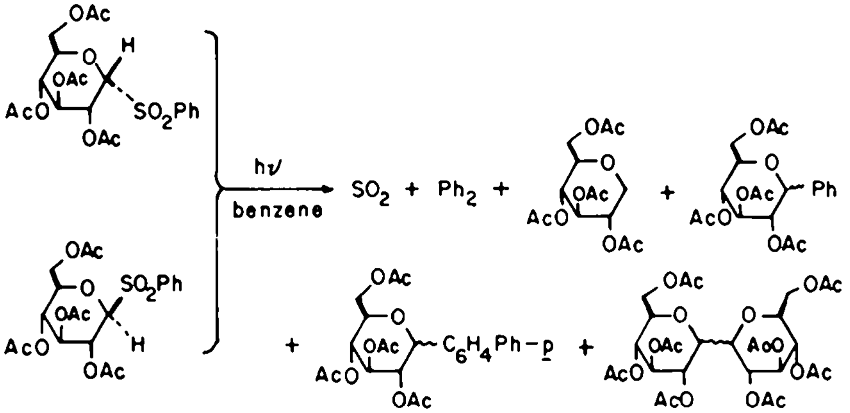

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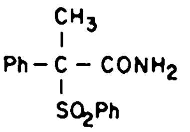
Scheme 23.

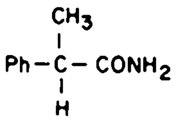
Until recently the reduction of the sulfonyl group to a sulfide has not been a particularly viable procedure. Diisobutylaluminum hydride (Dibal-H) cleanly reduces sulfones to sulfide and solves this outstanding transformation.[177] Lithium aluminum hydride reduces 4- and 5-membered ring sulfones to the corresponding sulfides, but with 6-membered rings the α-monoanion and α,α'-dianion is formed, and little reduction occurs.[178] If the anion of a 5-membered ring sulfone is treated with lithium aluminum hydride a cyclobutene is formed.[179]

Finally before describing the applications of sulfone chemistry in the synthesis of natural products a mention is made concerning the protonation and O-alkylation of sulfones. When dialkylsulfones are dissolved in fluorosulfonic acid antimonypentafluoride-sulfurylchloride-fluoride solution at −80°, protonation occurs on oxygen.[180] Decomposition of phenyldiazomium tetrafluoroborate in sulfolane gave the crystalline aryloxysulfonium salt 176.[181]



$Ph-\underset{SO_2Ph}{\overset{CH_3}{C}}-CONH_2$

174



$Ph-\underset{H}{\overset{CH_3}{C}}-CONH_2$

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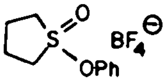

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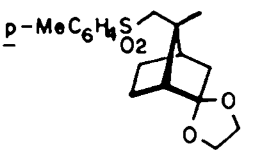

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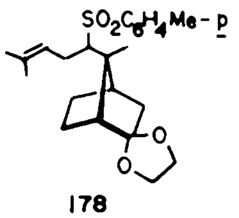

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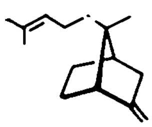

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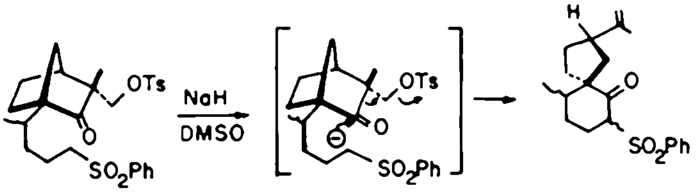

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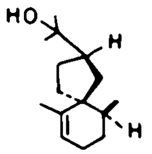

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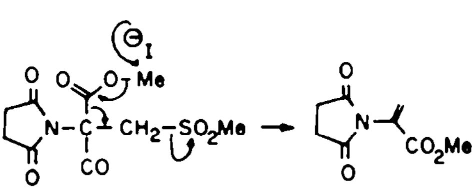

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184

X. THE SULFONYL GROUP IN THE SYNTHESIS OF NATURAL PRODUCTS

As a conclusion to this review a number of examples of how the sulfone group has been used in the synthesis of natural products is presented. A synthesis of sesquifenchene reported by Grieco utilizes a sulfone alkylation followed by desulfonylation procedure. The sulfone **177** was alkylated using n-butyllithium as the base, and 3,3-dimethylallylbromide as the alkylating agent to give **178**. Desulfonylation (Li/H_2NEt −78°) and subsequent transformations gave sesquifenchene **179**.[182] A similar sequence, namely alkylation of a sulfone followed by desulfonylation was used to synthesize (±)-diumycinol, a sesterterpene.[182] The bicyclic sulfone **180**, prepared from (−)-β-pinene was treated with NaH–DMSO to give the spiro-[4.5]decane **181**, which was converted into (+)hinesol **182**.[183] Fragmentation of the sulfone **183** with potassium iodide in DMF at 110° gave dimethylsulfone, carbon dioxide, and (±)-versimide **184**.[184] Both α-santalene and α-santalol have been synthesized by Julia *et al.* utilizing routes that involve sulfone alkylation.[185]

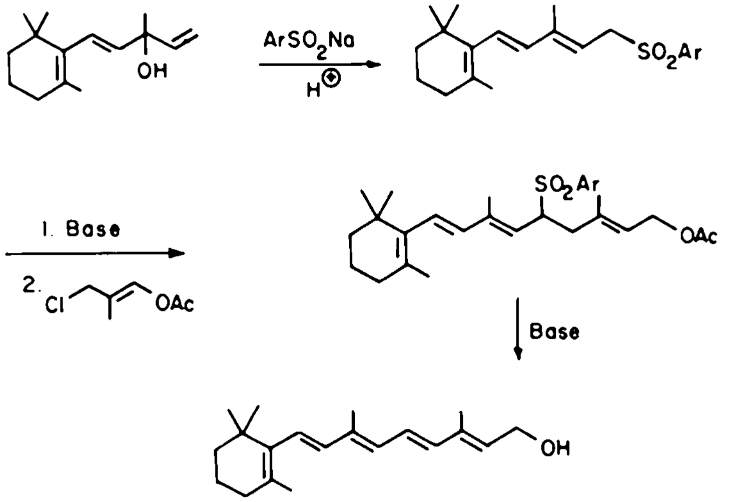
Vitamin A alcohol **185** has been synthesized via the route outlined in Scheme 24; of particular note is the facile elimination of arylsulfinic acid to create the completely conjugated system.[186] The type of chemistry outlined in Scheme 24, first described by Julia, has been the cornerstone of a number of polyene syntheses.[187] Alkylation of conjugated arylsulfonyl carbanions, prepared from the corresponding allylic sulfones and allylic halides bearing terminal carbonyl groups, leads to polyene sulfones which readily eliminate arylsulfinate to give polyenes[188] (Scheme 25). Naturally one can anticipate many strategic combinations of sulfone and allylic halide; two are outlined in Scheme 26.[189,190]

The formation of a cyclopropyl system via the unusual 1,4-addition of an α-sulfonylcarbanion to an α,β-unsaturated ester has been exploited in the synthesis of (±)-presqualene alcohol **186**.[191] Using pure (2E,6E)-sulfone and (6E)-ester, condensation followed by reduction gave (±)-presqualene alcohol **186** (Scheme 27).

Combination of two C_5-units **187** and **188** has shown great flexibility leading to short syntheses of linalool, nerolidol, isophytol and vitamin A.[192] The principle of method is outlined below (Scheme 28). Squalene **189** has been synthesized utilizing a coupling reaction of a sulfone followed by desulfonylation.[193]

The carboxysulfone **190** underwent cyclization when treated with concentrated sulfuric acid to give the lactone **191**.[194] This cyclization procedure was used in the synthesis deoxytrisporone. Cyclization of **192** with concentrated sulfuric acid gave an umpolung of cyclocitral, **193**. Oxidation (SeO_2), and alkylation of **194**, followed by desulfonylation gave deoxytrisporone **195**.[195]

Synthetic proof of the revised structure of de-



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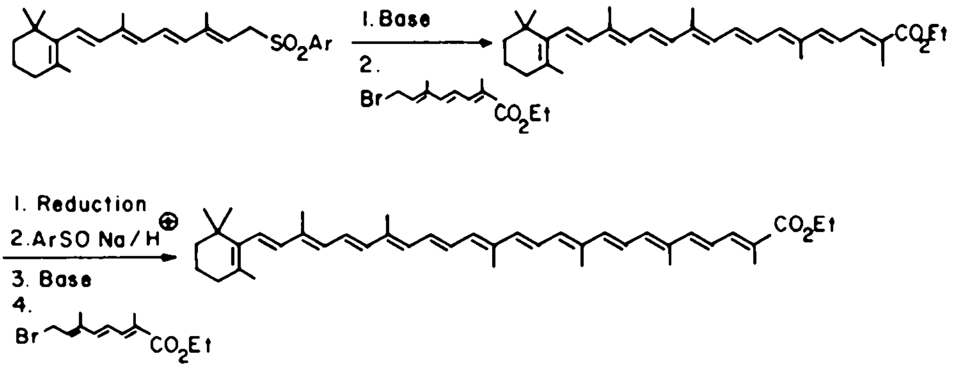
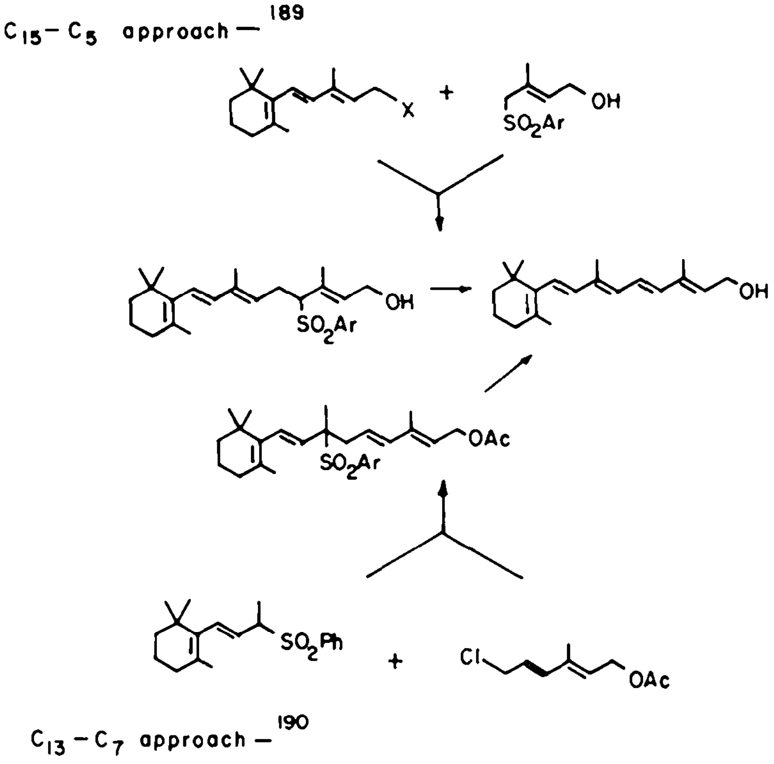
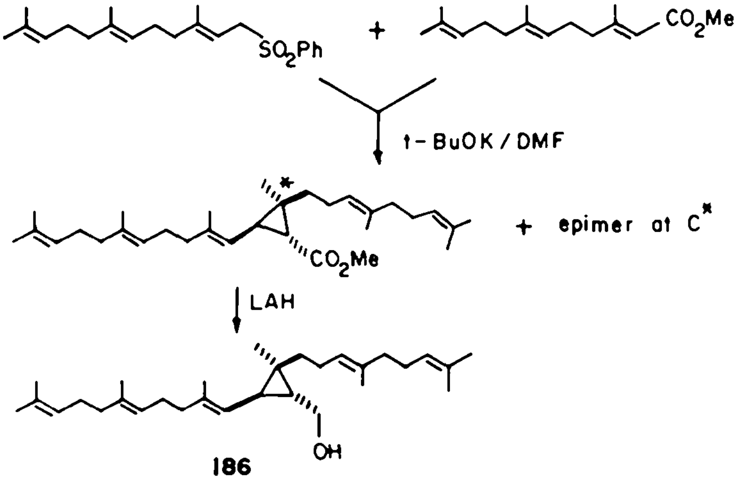
Scheme 24.



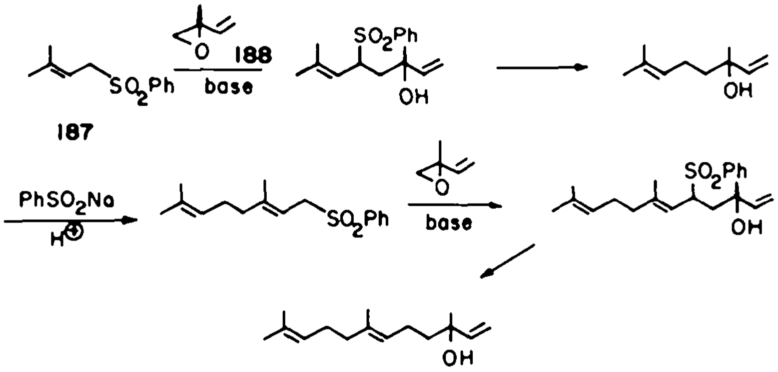
Scheme 25.



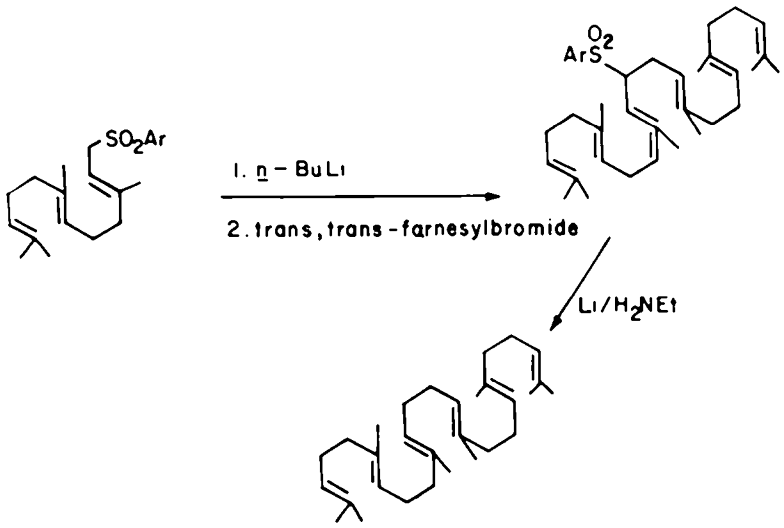
Scheme 26.



Scheme 27.



Scheme 28.



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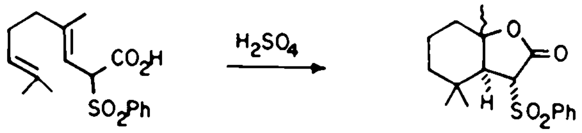
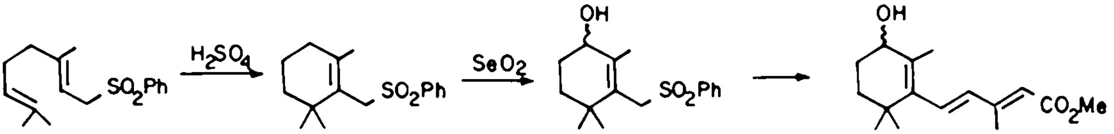


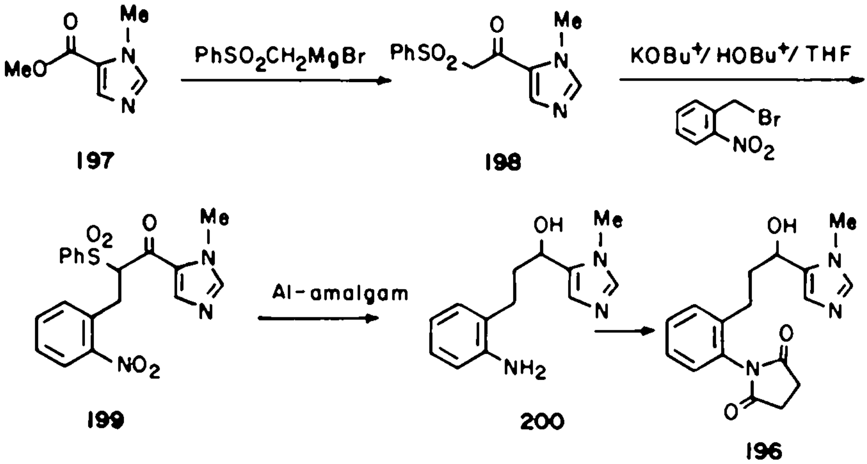
190 **191**

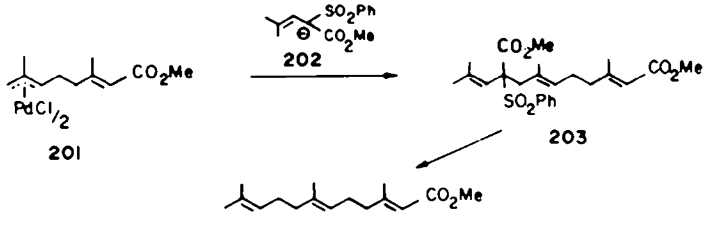


192 **193** **194** **195**

hydroisolongistrobine **196** was provided by total synthesis.[96]

The imidazole **197** was condensed with methylphenyl sulfonylmagnesium bromide to give the β-ketosulfone **198**. Alkylation of **198** using o-nitrobenzylbromide provided **199**, which was desulfonylated to give **200**. Further straightforward transformations of **200** gave dehydroisolongisotrobine **196**.





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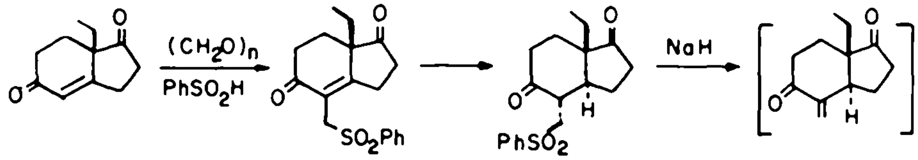


Scheme 29.

Trost has illustrated the value of π-allylpalladium complexes such as **201** in synthesis; for example, treatment of **201** with the α-sulfonylcarbanion **202** gave **203**, which was decarboxymethylated and desulfonylated to give **204**.[197] An interesting, and presumably general transformation illustrated in steroid chemistry, is the use of a sulfone group as a latent enone precursor. This is presented in Scheme 29.[198]

The sulfone functional group, as can be seen from this review, has found its way into a wide range of organic chemistry. It is hoped that the examples given will encourage those who have so far not included sulfone chemistry in their repetoir, to do so. One major practical advantage of incorporating a sulfone group into synthetic chemistry is that intermediates are likely to be crystalline and stable. As a pointer to future developments that could greatly extend the use of sulfone chemistry would be the ability to convert the unit $RCH_2{-}SO_2R_1$ into $RCH(OH)SO_2R_1 \equiv RCHO$. If this is achieved then an equivalency of carbonyl and sulfone chemistry becomes possible via the so-called nucleophilic acylation principle.

REFERENCES

[1] D. J. Cram, *Fundamentals of Carbanion Chemistry*. Academic Press, New York (1965).

[2] D. J. Cram, D. A. Scott and W. D. Nielsen, *J. Am. Chem. Soc.* **83**, 3696 (1961); D. J. Cram, W. D. Nielsen and B. Rickborn, *Ibid.* **82**, 6415 (1960); E. J. Corey and E. T. Kaiser, *Ibid.* **83**, 490 (1961); H. L. Goering, D. L. Townes and B. Dittmer, *J. Org. Chem.* **27**, 736 (1962).

[3] E. J. Corey, H. König and T. H. Lowry, *Tetrahedron Letters* 515 (1962); E. J. Corey and T. H. Lowry, *Ibid.* 793 and 803 (1965).

[4] S. Wolfe, A. Rauk and I. G. Csizmadia, *J. Am. Chem. Soc.* **91**, 1567 (1967); S. Wolfe, A. Rauk, L. M. Tel and I. G. Csizmadia, *J. Chem. Soc.* (B), 136 (1971).

[5] C. Muller and A. Schwerg, *Tetrahedron* 3973 (1973); B. Solouki, H. Bock and R. Appel, *Angew. Chem.* Intern. Edit. **11**, 927 (1972).

[6] R. R. Fraser and F. J. Schuber, *J. Chem. Soc.* Chem. Commun. 1474 (1969).

[7] L. A. Paquette, J. P. Freeman and M. J. Wyvratt, *J. Am. Chem. Soc.* **93**, 3216 (1971).

[8] L. Ramberg and B. Backlund, *Arkiv. Kemi Mineral. Geol.* **13A**, No. 27 (1940); *Chem. Abstr.* **34**, 4725 (1940).

[9] L. A. Paquette, *Mechanisms of Molecular Migrations* (Edited by B. S. Thyagarajan) Vol. I, pp. 121–156. L. A. Paquette, *Accounts Chem. Res.* **1**, 209 (1968).

[10] F. G. Bordwell, *Organosulfur Chemistry* (Edited by M. J. Janssen). Interscience, New York (1967); F. G. Bordwell, *Accounts Chem. Res.* **3**, 281 (1970).

[11] L. A. Paquette, *Base Induced Rearrangement of α-Halosulfones, Organic Reactions*. In press.

[12] L. A. Paquette, *Int. J. Sulfur. Chem.*, C. Vol. **7**, 73 (1972).

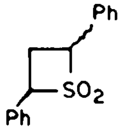
[13] L. A. Paquette, R. E. Wingard, Jr. and R. H. Meisinger, *J. Am. Chem. Soc.* **93**, 1047 (1971).

[14] R. B. Mitra, M. Y. Natekar and S. D. Virkar, *Indian J. Chem.* **13**, 251 (1975).

[15] G. Opitz and H. Fischer, *Angew. Chem.* Internat. Ed. Engl. **4**, 70 (1965); L. A. Carpino and R. H. Rynbrandt, *J. Am. Chem. Soc.* **88**, 5682 (1966).

[16] F. G. Bordwell, E. B. Hoyt, Jr., B. B. Jarvis and J. M. Williams, Jr., *J. Org. Chem.* **33**, 2031 (1968); F. G. Bordwell, J. M. Williams, Jr., E. B. Hoyt, Jr. and B. B. Jarvis, *J. Am. Chem. Soc.* **90**, 429 (1968).

[17] F. Jung, N. K. Sharma and T. Durst, *J. Am. Chem. Soc.* **95**, 3420 (1973). This reference describes an alkene synthesis based on β-sulfines; J. F. King, K. Piers, D. J. H. Smith, C. L. McIntosh and P. de Mayo, *J. Chem. Soc.* Chem. Commun. 31 (1969); N. K. Sharma, F. Reinach-Hirtzbach and T. Durst, *Can. J. Chem.* 3012 (1976). The sulfone



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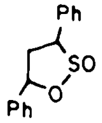

[18] R. F. Heldeweg and H. Hogeveen, *J. Am. Chem. Soc.* **98**, 2241 (1976); F. Jung, M. Molin, R. Van Der Elzen and T. Durst, *Ibid.* **96**, 935 (1974).

[19] S. Ašperger, D. Hegedić, D. Pavlović and S. Borčic, *J. Org. Chem.* **37**, 1745 (1972).

[20] J. C. Philips and M. Oku, *Ibid.* **95**, 6495 (1973); J. C. Philips and M. Oku, *Ibid.* **94**, 1013 (1972).

[21] C. Y. Meyers, A. M. Malte and W. S. Matthews, *Ibid.* **91**, 7510 (1969).

[22] C. Y. Meyers, W. S. Matthews, G. J. McCollum and J. C. Branca, *Tetrahedron Letters* 1105 (1974).

[23] C. Y. Meyers and L. L. Ho, *Ibid.* 4319 (1972); C. Y. Meyers and I. Sataty, *Ibid.* 4323 (1972); C. Y. Meyers, L. L. Ho, G. J. McCollum and J. Branca, *Ibid.* 1843 (1973).

[24] L. A. Paquette and L. S. Wittenbrook, *J. Am. Chem. Soc.* **90**, 6790 (1968); L. A. Paquette and L. S. Wittenbrook, *Ibid.* **89**, 4487 (1967).

[25] L. A. Carpino and L. V. McAdams, *Ibid.* **87**, 5804 (1965); U. Jacobsson, T. Kempe and T. Norin, *J. Org. Chem.* **39**, 2722 (1974).

[26] J. Kattenberg, E. R. de Waard and H. O. Huisman, *Tetrahedron Letters* 1481 (1973).

[27] F. G. Bordwell, B. B. Jarvis and P. W. R. Corfield, *J. Am. Chem. Soc.* **90**, 5298 (1968); F. G. Bordwell and B. B. Jarvis, *Ibid.* **95**, 3585 (1973).

[28] F. G. Bordwell and E. Doomes, *J. Org. Chem.* **39**, 2298 (1974).

[29] B. B. Jarvis and B. A. Marien, *Ibid.* **40**, 2587 (1975).

[30] L. A. Carpino and J. R. Williams, *Ibid.* **39**, 2321 (1974).

[31a] G. Buchi and R. M. Freidinger, *J. Am. Chem. Soc.* **96**, 3332 (1974); [b]P. A. Grieco and D. Boxler, *Synth. Commun.* **5**, 315 (1975)

[32] B. S. Thyagarajan, *Mech. React. Sulfur. Compounds* **4**, 115 (1969); M. Gresser, *Ibid.* **4**, 29 (1969); L. Field, *Synthesis* 101 (1972).

[33] W. E. Truce and T. C. Klinger, *J. Org. Chem.* **35**, 1834 (1970); D. F. Tavares and P. F. Vogt, *Can. J. Chem.* **45**, 1519 (1967); E. M. Kaiser and C. R. Hauser, *Tetrahedron Letters* 3341 (1967).

[34] C. A. Kingsbury, *J. Org. Chem.* **37**, 102 (1972).

[35] J. W. McFarland and D. N. Buchanan, *Ibid.* **30**, 2003 (1965).

[36] G. A. Russell, H-D. Becker and J. Schoeb, *Ibid.* **28**, 3584 (1963).

[37] D. F. Tavares and P. F. Vogt, *Can. J. Chem.* **45**, 1520 (1967).

[38] G. A. Russell, E. T. Sabourin and G. Hamprecht, *J. Org. Chem.* **34**, 2339 (1969).

[39] M. von Strandtmann, S. Klutchko, D. Connor and J. Shavel, *Ibid.* **36**, 1742 (1971).

[40] H-D. Becker, *Ibid.* **29**, 2891 (1964).

[41] G. P. Crowther and C. R. Hauser, *Ibid.* **33**, 2228 (1968).

[42] G. Cardillo, D. Savoia and A. Umani-Ronchi, *Synthesis* 453 (1975).

[43] A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc.* (B), 808 (1967).

[44] R. Bird and C. J. M. Stirling, *Ibid.* 111 (1968); H. E. Zimmerman and B. S. Thyagarajan, *J. Am. Chem. Soc.* **82**, 2505 (1960); W. E. Truce and L. B. Lindy, *J. Org. Chem.* **26**, 1463 (1961).

[45] W. E. Truce, K. R. Hollister, L. B. Lindy and J. E. Parr, *Ibid.* **33**, 43 (1968).

[46] J. B. Evan and G. Marr, *J. Chem. Soc.* Perkin I. 2505 (1972).

[47] Y. Gaoni, *Tetrahedron Letters* 503 (1976); B. Corbel and T. Durst, *J. Org. Chem.* **41**, 3648 (1976).

[48] E. M. Kaiser, R. D. Beard and C. R. Hauser, *J. Organometallic Chem.* **59**, 53 (1973); E. M. Kaiser and C. R. Hauser, *Tetrahedron Letters* 3341 (1967).

[49] L. Field and E. J. Boyd, *J. Org. Chem.* **29**, 3273 (1964).

[50] J. S. Grossert, J. Buter, E. W. H. Asveld and R. M. Kellogg, *Tetrahedron Letters* 2805 (1974).

[51] V. Pascali, N. Tangari and A. Umani-Ronchi, *J. Chem. Soc.* Perkin I. 166 (1973); A. Bongini, D. Savoia and A. Umani-Ronchi, *J. Organometallic Chem.* 112 (1976).

[52] V. Pascali and A. Umani-Ronchi, *J. Chem. Soc.* Chem. Commun. 351 (1973).

[53] N. Bosworth and P. D. Magnus, *Ibid.* Perkin I. 2319 (1973).

[54] L. A. Paquette, R. H. Meisinger and R. Gleiter, *J. Am. Chem. Soc.* **95**, 5414 (1973).

[55] D. I. Davies and P. J. Rowley, *J. Chem. Soc.* 1832 (1968); T. Durst, *Tetrahedron Letters* 4171 (1971).

[56] A. M. van Leusen, G. J. M. Boerma, R. B. Helmholdt, H. Siderius and J. Strating, *Ibid.* 2367 (1972).

[57] U. Schollkopf, R. Schroder and E. Blume, *Liebigs Ann.* Chem. **766**, 130 (1972); U. Schollkopf and R. Schroder, *Angew. Chem.* Int. Ed. 311 (1972).

[58] O. H. Oldenziel and A. M. van Leusen, *Tetrahedron Letters* 1357 (1973); O. H. Oldenziel and A. M. van Leusen, *Synth. Comm.* 281 (1973).

[59] A. M. van Leusen, H. Siderius, B. E. Hoogenboom and D. van Leusen, *Tetrahedron Letters* 5337 (1972).

[60] O. H. Oldenziel and A. M. van Leusen, *Ibid.* 167 (1974).

[61] O. H. Oldenziel and A. M. van Leusen, *Ibid.* 2777 (1972); A. M. van Leusen and O. H. Oldenziel, *Ibid.* 2373 (1972); A. M. van Leusen, B. E. Hoogenboom and H. Siderius, *Ibid.* 2369 (1972).

[62] K. Schank and A. Weber, *Synthesis* 367 (1970); K. Schank, *Liebigs Ann. Chem.* **707**, 75 (1967).

[63] R. J. Mulder, A. M. van Leusen and J. Strating, *Tetrahedron Letters* 3061 (1967).

[64] K. Schank, H. Hasenfratz and A. Weber, *Chem. Ber.* **106**, 1107 (1973).

[65] G. Ferdinand and K. Schank, *Synthesis* **404**, 406 (1976); G. Ferdinand, K. Schank and A. Wever, *Liebigs Ann. Chem.* 1484 (1975).

[66] K. Schank, *Chem. Ber.* **103**, 3087 and 3093 (1970).

[67] K. Schank, R. Wilmes and G. Ferdinand, *Int. J. Sulfur. Chem.* 397 (1973).

[68] Y. Inoue, F. Cooke and P. D. Magnus, Unpublished results from these laboratories.

[69] M. Julia and J-M. Paris, *Tetrahedron Letters* 4833 (1973); M. Julia and D. Arnold, *Bull. Soc. Chim. Fr.* 743 and 746 (1973).

[70] M. Julia and L. Saussme, *Tetrahedron Letters* 3443 (1973).

[71] M. Julia and A. G. Ronault, *Bull. Soc. Chim. Fr.* 1411 (1967).

[72] M. Julia and B. Badet, *Ibid.* 1363 (1975); K. Kondo and D. Tunemoto, *Tetrahedron Letters* 1007 (1975); K. Kondo and D. Tunemoto, *Ibid.* 1397 (1975).

[73] M. Julia, D. Ugven and A. Callipolitis, *Bull. Soc. Chim. Fr.* 519 (1976).

[74] G. H. Posner and D. J. Brunelle, *Tetrahedron Letters* 935 (1973); G. H. Posner and D. J. Brunelle, *J. Org. Chem.* **38**, 2747 (1973).

[75] J. B. Hendrickson, A. Giga and J. Warren, *J. Am. Chem. Soc.* **96**, 2275 (1974).

[76] J. B. Hendrickson and P. L. Skipper, *Tetrahedron* 1627 (1976).

[77] W. E. Truce, W. W. Bannister and R. H. Knospe, *J. Org. Chem.* **27**, 2821 (1962); P. G. Gassman and G. D. J. Richmond, *J. Org. Chem.* **31**, 2355 (1966); G. A. Russell and G. J. J. Mikol, *J. Am. Chem. Soc.* **88**, 5498 (1966).

[78] B. Samuelsson and B. Lamm, *Acta Chem. Scand.* **25**, 1555 (1971).

[79] K. G. Mason, M. A. Smith, E. S. Stern and J. A. Elvidge, *J. Chem. Soc.* (C). 2171 (1967).

[80] H. O. House and J. K. Larson, *J. Org. Chem.* **33**, 61 (1968).

[81] B. Lamm and B. Samuelsson, *Acta Chem. Scand.* **24**, 561 (1970).

[82] N. M. Carroll and W. I. O'Sullivan, *J. Org. Chem.* **30**, 2830 (1965).

[83] M. L. Mills and C. R. Hauser, *Ibid.* **29**, 2329 (1964).

[84] F. Cooke and P. D. Magnus, *J. Chem. Soc.* Chem. Comm. 519 (1976).

[85] E. C. Taylor, G. H. Hawkes and A. McKillop, *J. Am. Chem. Soc.* **90**, 2421 (1968); E. C. Taylor and A. McKillop, *Accounts Chem. Res.* 3, 338 (1970).

[86] J. J. Looker, *J. Org. Chem.* **31**, 2714 (1966).

[87] Unpublished observations from these laboratories.

[88] D. Diller and F. Bergmann, *J. Org. Chem.* **37**, 2147 (1972); T. Komeno, S. Ishihara and H. Itami, *Tetrahedron* 4719 (1972); B. Koutek, L. Pavličkova and M. Souček, *Coll. Czech.* Chem. Comm. **38**, 3872 (1973).

[89] S. Rossi and G. Pagani, *Tetrahedron Letters* 2129 (1966).

[90] H-W. Wanzlick and H. Ahrens, *Chem. Ber.* 1580 (1966).

[91] A. M. van Leusen, P. M. Smid and J. Strating, *Tetrahedron Letters* 337 (1965).

[92] A. M. van Leusen and J. Strating, *Rec. Trav. Chim.* **81**, 966 (1962); A. M. van Leusen and J. Strating, *Ibid.* **84**, 151 (1964); A. M. van Leusen, P. M. Smid and J. Strating, *Tetrahedron Letters* 337 (1965).

[93] R. J. Mulder, A. M. van Leusen and J. Strating, *Ibid.* 3057 (1967).

[94] A. M. van Leusen, R. J. Mulder and J. Strating, *Rec. Trav. Chim.* **86**, 225 (1967); R. A. Abramovitch, V. Alexanian and E. M. Smith, *J. Chem. Soc.* Chem. Comm. 893 (1972).

[95] B. Zwanenburg and J. B. F. N. Engberts, *Rec. Trav. Chim.* **84**, 165 (1964); J. B. F. N. Engberts and B. Zwanenberg, *Tetrahedron Letters* 831 (1967); B. Michel, J. F. McGarrity and H. Dahn, *Chimia.* **27**, 320 (1973).

[96] A. M. van Leusen, P. Richters and J. Strating, *Rec. Trav. Chim.* **85**, 323 (1966).

[97] B. Zwanenburg, W. Middelbos, G. J. K. Hemke and J. Strating, *Ibid.* **90**, 429 (1971).

[98] K. Hovius and J. B. F. N. Engberts, *Tetrahedron Letters* 2477 (1972).

[99] A. Jonńceyk, K. Bańko and M. Makosza, *J. Org. Chem.* **40**, 266 (1975).

[100] H. Bohme and W. Stammberger, *Liebigs Ann. Chem.* **754**, 56 (1971).

[101] F. Bohlmann and G. Haffer, *Chem. Ber.* **102**, 4017 (1969).

[102] D. F. Tavares, R. E. Estep and M. Blezard, *Tetrahedron Letters* 2373 (1970); P. F. Vogt and D. F. Tavares, *Can. J. Chem.* **47**, 2875 (1969).

[103] T. Durst and K.-C. Tin, *Tetrahedron Letters* 2369 (1970).

[104] D. R. White, *Ibid.* 1753 (1976).

[105] F. de Reinach-Hirtzbach and T. Durst, *Ibid.* 3677 (1976).

[106] H. Stetter and K. Steinback, *Liebigs Ann. Chem.* **766**, 89 (1972).

[107] W. E. Truce and L. W. Christiansen, *J. Chem. Soc.* Chem. Comm. 588 (1971).

[108] W. E. Truce and L. W. Christiansen, *Tetrahedron* 181 (1969); W. E. Truce and D. J. Vrencur, *Can. J. Chem.* **47**, 860 (1969); W. E. Truce and L. W. Christiensen, *J. Org. Chem.* **36**, 2538 (1971); W. E. Truce and L. W. Christiansen, *Tetrahedron Letters* 3075 (1969).

[109] W. E. Truce, L. A. Mura, P. J. Smith and F. Young, *J. Org. Chem.* **39**, 1449 (1974).

[110] P. Robson, P. R. H. Speakman and D. G. Stewart, *J. Chem. Soc.* (C), 2180 (1968).

[111] I. C. Popoff, J. L. Dever and G. R. Leader, *J. Org. Chem.* **34**, 1130 (1969); I. Shahak and J. Almog, *Synthesis* 170 (1969) and 145 (1970); G. H. Posner and D. J. Brunelle, *J. Org. Chem.* **37**, 3547 (1972); M. Mikolajczyk, S. Grzejszczak, W. Midura and A. Zatorski, *Synthesis* 278 (1975).

[112] W. E. Truce and G. D. Madding, *Tetrahedron Letters* 3681 (1966).

[113] A. M. van Leusen, B. A. Reith, A. J. W. Iedema and J. Strating, *Rec. Trav. Chim.* **91**, 37 (1972).

[114] A. M. van Leusen and J. C. Jagt, *Tetrahedron Letters* 967 (1970).

[115] A. M. van Leusen and J. C. Jagt, *Ibid.* 971 (1970).

[116] H. Stetter and K. Steinbeck, *Leibigs Ann. Chem.* 1315 (1974).

[117] A. R. Friedman and D. R. Graber, *J. Org. Chem.* **37**, 1902 (1972).

[118] L. A. Carpino, *Ibid.* **38**, 2600 (1973).

[119] M. L. Oftedahl, J. W. Baker and M. W. Dietrich, *Ibid.* **30**, 296 (1965).

[120] G. Becker and J. Gosselck, *Tetrahedron Letters* 4083 (1971).

[121] R. J. Koshar and R. A. Mitsch, *J. Org. Chem.* **38**, 3358 (1973).

[122] V. M. Neplyuev, R-G. Dubenko and P. S. Pel kis, *Zh. Org. Khim.* **6**, 2113 (1970).

[123] H. Dressler and J. E. Graham, *J. Org. Chem.* **32**, 985 (1967); G. Beck and D. Gunther, *Chem. Ber.* **106**, 2766 (1973).

[124] M. Seshapathirao Naidu and E. D. Ehaskar Reddy, *J. Indian. Chem. Soc.* 53 (1975).

[125] W. E. Truce, J. E. Tracy and M. L. Gorbaty, *J. Org. Chem.* **36**, 237 (1971).

[126] D. Ladurée, P. Rioult and J. Vialle, *Bull. Soc. Chim. Fr.* 637 (1973).

[127] N. Kornblum, M. M. Kestner, S. D. Boyd and L. C. Gottram, *J. Am. Chem. Soc.* **95**, 3356 (1973).

[128] W. E. Truce, T. C. Klingler, J. E. Parr, H. Fener and D. K. Wu, *J. Org. Chem.* **34**, 3105 (1969).

[129] N. Kornblum, S. D. Boyd and N. Ono, *J. Am. Chem. Soc.* **96**, 2580 (1974).

[130] J. J. Zeilstra and J. B. F. N. Engberts, *Ibid.* **97**, 7091 (1975).

[131] D. E. O'Connor and W. I. Lyness, *Ibid.* **86**, 3840 (1964); C. D. Broaddus, *Ibid.* **88**, 3864 (1966); C. D. Broaddus, *Ibid.* **90**, 5504 (1968).

[132] I. Sataty and C. Y. Meyers, *Tetrahedron Letters* 4161 (1974).

[133] E. M. LaCombe and B. Stewart, *J. Am. Chem. Soc.* **83**, 3457 (1961).

[134] J. B. Hendrickson and R. Bergeron, *Tetrahedron Letters* 3609 (1973).

[135] J. F. King and D. R. K. Harding, *J. Chem. Soc. Chem. Comm.* 959 (1971); J. F. King and D. R. K. Harding, *J. Am. Chem. Soc.* **98**, 3312 (1976).

[136] L. A. Paquette and S. Maiorana, *Ibid.* 313 (1971).

[137] W. E. Truce, M. G. Rossmann, F. M. Perry, R. M. Burnett and D. J. Abraham, *Tetrahedron* 2899 (1965).

[138] L. Veniard, J. Benaim, G. Pourcelot and M. H. Normant, *C.R. Acad. Sc. Paris* (C), 1092 (1968).

[139] A. Risaliti, S. Fatutta, M. Forchiassin and E. Valentin, *Tetrahedron Letters* 1821 (1966); S. Fatutta and A. Risaliti, *J. Chem. Soc.* Perkin I. 2387 (1975).

[140] J. Elguero, R. Jacquier and G. Tarrago, *Bull. Soc. Chim. Fr.* 1149 (1968).

[141] R. Curci and F. DiFuria, *Tetrahedron Letters* 4085 (1974); G. Berti, *Top. Stereochemistry* 7, 93 (1972); B. Zwanenburg and J. ter Wiel, *Tetrahedron Letters* 935 (1970).

[142] E. N. Prilezhaeva and L. I. Shmonina, *Zh. Org. Khim.* **8**, 548 (1972).

[143] E. Siegel and S. Petersen, *Angew. Chem.* **74**, 873 (1962).

[144] W. E. Truce, J. J. Breiter and J. E. Tracy, *J. Org. Chem.* **29**, 3009 (1964).

[145] S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc.* B, 351 (1967).

[146] W. E. Truce and L. D. Markley, *J. Org. Chem.* **35**, 3275 (1970); W. E. Truce and D. G. Brady, *Ibid.* **31**, 3543 (1966).

[147] H. Hogeveen, G. Maccagnani, F. Montanari and F. Taddei, *Boll. Sci. Fac. Chem. Ind. Bologna* **21**, 259 (1963).

[148] W. E. Truce and G. C. Wolf, *J. Org. Chem.* **36**, 1727 (1971).

[149] C. J. M. Stirling, *J. Chem. Soc.* 5856 (1964); A. T. Kader and C. J. M. Stirling, *Ibid.* 3686 (1962).

[150] C. J. M. Stirling, *Ibid.* 5863 (1964).

[151] C. J. M. Stirling, *Int. J. Sulfur. Chem.* Vol. 6, 41 (1971).

[152] C. J. M. Stirling, *J. Chem. Soc.* 5875 (1964). For the conjugate addition of amines to α,β-unsaturated sulfones. See S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc.* (B), 348 (1967); S. T. McDowell and C. J. M. Stirling, *Ibid.* 343 (1967); S. T. McDowell and C. J. M. Stirling, *Ibid.* 351 (1967).

[153] A. W. Miller and C. J. M. Stirling, *J. Chem. Soc.* (C), 2612 (1969); M. J. S. A. Amaral, G. C. Barnett, H. N. Rudon and J. E. Willett, *Ibid.* 807 (1966); A. T. Kader and C. J. M. Stirling, *J. Chem. Soc.* 258 (1964).

[154] K. L. Agarwal, M. Fridkin, E. Jay and H. G. Khorana, *J. Am. Chem. Soc.* **95**, 2020 (1973).

[155] E. W. Colvin, J. A. Purcell and R. A. Raphael, *J. Chem. Soc.* Chem. Comm. 1031 (1972).

[156] A. K. Colter and R. E. Miller, Jr., *J. Org. Chem.* **36**, 1898 (1971).

[157] R. M. Dodson, P. P. Schlangen and E. L. Mutsch, *J. Chem. Soc.* Chem. Comm. 352 (1965).

[158] W. L. Parker and R. B. Woodward, *J. Org. Chem.* **34**, 3085 (1969).

[159] W. Z. Heldt, *Ibid.* **30**, 3899 (1965).

[160] V. Boekelheide and C. H. Tsai, *Ibid.* **38**, 3931 (1973).

[161] H. J. J-B. Martel and M. Rasmussen, *Tetrahedron Letters* 3843 (1971).

[162] R. M. Kellogg and W. L. Prins, *J. Org. Chem.* **39**, 2366 (1974); K-D. Grundermann and P. Holtmann, *Angew. Chem.* Intern. Ed. **5**, 668 (1966).

[163] C. S. Argyle, K. G. Mason, M. A. Smith and E. S. Stern, *J. Chem. Soc.* (C), 2176 (1967).

[164] H. E. Zimmerman and J. H. Munch, *J. Am. Chem. Soc.* **90**, 187 (1968).

[165] R. M. Dodson, P. D. Hammen, E. H. Jancis and G. Klose, *J. Org. Chem.* **36**, 2698 (1971); R. M. Dodson, E. H. Jancis and G. Klose, *Ibid.* **35**, 2520 (1970); R. M. Dodson, P. D. Hammen and R. A. Davis, *Ibid.* **16**, 2693 (1971).

[166] D. C. Dittmer and N. Takashina, *Tetrahedron Letters* 3809 (1964).

[167] S. Braverman and D. Seger, *J. Am. Chem. Soc.* **96**, 1245 (1974).

[168] W. E. Truce, C. R. Robbins and E. M. Kreider, *Ibid.* **88**, 4027 (1966); W. E. Truce and W. W. Brand, *J. Org. Chem.* **35**, 1828 (1970).

[169] V. N. Drozd and T. Yu. Frid, *Zh. Org. Khim.* **3**, 373 (1967); V. N. Drozd, L. I. Zefirova and U. A. Ustynyuk, *Ibid.* **4**, 1794 (1968); V. N. Drozd, *Dokl. Akad. Nauk SSSR* **169**, 107 (1966).

[170] C. L. McIntosh, P. de Mayo and R. W. Yip, *Tetrahedron Letters* 37 (1967); A. M. van Leusen, P. M. Smid and J. Strating, *Ibid.* 1165 (1967).

[171] A. I. Khodair, T. Nakabayashi and N. Kharasch, *Int. J. Sulfur Chem.* Vol. 8, 37 (1973).

[172] P. M. Collins and B. R. Whitton, *J. Chem. Soc.* Perkin I. 1069 (1975); P. M. Collins and B. R. Whitton, *Carbohydrate Res.* **36**, 293 (1974).

[173] B. M. Trost, H. C. Arndt, P. E. Strege and T. R. Verhoeven, *Tetrahedron Letters* 3477 (1976). Contain leading references to desulfonylation procedures.

[174] N. Miyamoto, D. Fukuoka, K. Utimoto and H. Nozaki, *Bull. Chem. Soc. Japan* **47** (2), 503 (1974).

[175] R. A. Grimm and W. A. Bonner, *J. Org. Chem.* **32**, 3470 (1967).

[176] J. Simonet and G. Simonet, *Bull. Soc. Chim. Fr.* 2754 (1971).

[177] J. N. Gardner, S. Kaiser, A. Krubiner and H. Lucas, *Can. J. Chem.* **51**, 1420 (1973).

[178] T. A. Whitney and D. J. Cram, *J. Org. Chem.* **35**, 3964 (197); W. P. Wever, P. Stromquist and T. I. Ito, *Tetrahedron Letters* 2595 (1974).

[179] L. A. Paquette and J. M. Photis, *J. Am. Chem. Soc.* **96**, 4715 (1974).

[180] G. A. Olah, A. T. Ku and J. A. Olah, *J. Org. Chem.* **35**, 3904 (1970).

[181] G. R. Chalkley, D. J. Snodin, G. Stevens and M. C. Whiting, *J. Chem. Soc.* (C), 1682 (1970).

[182] P. A. Grieco and Y. Masaki, *J. Org. Chem.* **40**, 150 (1975); P. A. Grieco, Y. Masaki and D. Boxler, *Ibid.* **40**, 2261 (1975).

[183] D. Buddhsukh and P. D. Magnus, *J. Chem. Soc.* Chem. Comm. 952 (1975).

[184] P. R. Atkins and I. T. Kay, *Ibid.* 430 (1971).

[185] M. Julia and P. Ward, *Bull. Soc. Chim. Fr.* 3065 (1973); Recent examples of the use of sulfones in synthesis, see—J. Martel, C. Huynh, E. Toromanoff and G. Nominé, *Ibid.* 982 (1969); J. Martel and C. Huyuh, *Ibid.* 985 (1967); M. Julia and A. Guy-Roualt, *Ibid.* 1411 (1967).

[186] M. Julia and D. Arnold, *Ibid.* **746**, 743 (1973).

[187] P. S. Manchand, M. Rosenberger, G. Saucy, P. A. Wehrli, H. Wong, L. Chambers, M. P. Ferro and W. Jackson, *Helv. Chim. Acta.* **59**, 387 (1976).

[188] A. Fischli and H. Mayer, *Ibid.* **58**, 1492 (1975).

[189] G. L. Olson, H-C. Cheung, K. D. Morgan, C. Neukom and G. Saucy, *J. Org. Chem.* **41**, 3287 (1976).

[190] A. Fischli, H. Mayer, W. Simon and H-J. Stoller, *Helv. Chim. Acta.* **59**, 397 (1976).

[191] R. V. M. Campbell, L. Crombie, D. A. R. Findley, R. W. King, G. Pattenden and D. A. Whiting, *J. Chem. Soc.* Perkin I. 897 (1975).

[192] M. Julia and D. Uguen, *Bull. Soc. Chim. Fr.* 513 (1976).

[193] P. A. Grieco and Y. Masaki, *J. Org. Chem.* **39**, 2135 (1974).

[194] S. Torii, K. Uneyama and M. Kuyama, *Tetrahedron Letters* 1513 (1976).

[195] S. Torii, K. Uneyama and M. Isihara, *Chem. Letters* 479 (1975).

[196] M. A. Wuonola and R. B. Woodward, *J. Am. Chem. Soc.* **95**, 284 (1973); R. B. Woodward and M. A. Wuonola, *Tetrahedron* 1085 (1976).

[197] B. M. Trost and L. Weber, *J. Org. Chem.* **40**, 3617 (1975).

[198] G. Sauer, U. Eder, G. Haffer, G. Neef and R. Weichert, *Angew. Chem.* Internat. Ed. **14**, 417 (1975).