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Rearrangements of sulfoxides and sulfones in the total synthesis of natural compounds †

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Abstract. Data on applications of the most important rearrangements of sulfoxides and sulfones to stereoselective total syntheses of natural compounds are systematised. The bibliography includes 175 references.

I. Introduction

Rearrangements of sulfoxides and sulfones along with other reactions of these compounds (see the review [1]) are widely used in stereospecific total syntheses of natural compounds. The mechanisms of the rearrangements of sulfoxides and sulfones were detailed in the reviews.[2, 3] In the present review, syntheses of natural compounds involving these rearrangements as the key stages are surveyed.

In spite of the fact that the Mislow – Evans rearrangement of sulfoxides can be applied only to the construction of allylic alcohol fragments, whereas the Ramberg – Bäcklund rearrangement can be used only for the formation of C = C bonds, both these reactions are often utilised in the syntheses of complex natural compounds. An important point is that the sulfur-containing group is removed in both processes.

The Pummerer reaction is used much more extensively. This rearrangement was discovered in 1910 [4] and did not come to the attention of chemists for 50 years. Once Horner [5, 6] had demonstrated that this reaction has a general character, the Pummerer rearrangement gained wide acceptance. It should be noted that Pummerer appraised the essence of this reaction quite adequately and related it to the lability of the α-hydrogen atom and generation of the sulfenium cation.[4]

Later on, the assumptions made by Pummerer were supported by the fundamental studies of Oae *et al.*[7, 8] devoted to the mechanism of this process.

Different aspects of the synthetic applications of the Pummerer reaction were considered in many reviews, for example, in the reviews [9 – 13] published in the last decade. However, the data on the use of this reaction as well as of other rearrangements for the preparation of natural compounds have not been systematised. The only exception is the review [14] in which consideration was given to the use of additive Pummerer conversions of enantiomerically pure vinyl sulfoxides in asymmetric syntheses of natural compounds.

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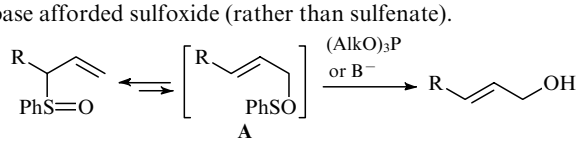
II. Syntheses involving rearrangements of sulfoxides into sulfenates and sulfenates into sulfoxides

The mechanisms of the rearrangements of sulfoxides into sulfenates and sulfenates into sulfoxides and the effects of the structures of the initial compounds and the reaction medium were detailed in a review.[2] Thermal rearrangements of benzyl sulfenates into sulfoxides, which proceed in nonpolar solvents by an ion-pair mechanism, did not find wide use in synthesis. On the contrary, rearrangements of β,γ-unsaturated aliphatic sulfoxides have assumed great importance. This is particularly true for the reversible allyl sulfoxide – allyl sulfenate Mislow – Evans rearrangement and, to a lesser extent, holds for the propargyl sulfenate – allenyl sulfoxide Braverman rearrangement.

1. Syntheses based on the reversible rearrangement of allyl sulfoxides into allyl sulfenates (the Mislow – Evans rearrangement)

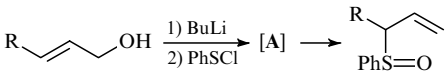
a. General observations

The thermal reversible rearrangement of allyl sulfoxides into allyl sulfenates proceeds as a intramolecular process through a five-membered transition state and is accompanied by migration of the double bond. This rearrangement is presently among the best-studied [2,3]-sigmatropic processes. The structure of allyl sulfoxide is thermodynamically more favourable than that of sulfenate due to which the equilibrium in the liquid phase under normal conditions is virtually completely shifted toward sulfoxide. The occurrence of this equilibrium was assumed [15] based on the fact that racemisation of optically active allyl sulfoxides proceeds much more rapidly than racemisation of saturated sulfoxides. This assumption was additionally supported by the fact that the reaction of allylic alcohol with sulfenyl chloride in the presence of a base afforded sulfoxide (rather than sulfenate).



A

† Dedicated to Academician O M Nefedov with appreciation and on the occasion of his seventieth birthday.

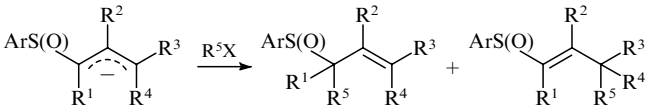


Both reactions proceeded through allyl sulfenate **A**, which is readily isomerised. The mechanism of the intramolecular completely concerted process was proved by kinetic data and by the results of experiments using labelled compounds.[15]

The Mislow–Evans rearrangement is used as a general procedure for the preparation of allylic alcohols.[16] Trimethyl phosphite was proposed as the thiophilic reagent of choice.[16] This reagent moves sulfenate off the equilibrium, which is virtually completely shifted toward allylic alcohol. In some cases, such bases as amines, thiolates or Na_2S are used as thiophiles.

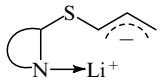
This procedure was later modified[17] so that it involved the one-pot synthesis of allylic alcohol by oxidation of allyl sulfide with 30% H_2O_2 in the presence of a catalytic amount of SeO_2 followed by treatment with 0.1 equiv. of TsOH (alcohols were obtained in ~70% yields).

For this procedure to be successfully employed in the synthesis of complex compounds, it was necessary to find appropriate conditions for α-alkylation of the simplest allyl sulfoxides. Evans and Andrews[16] revealed that selective α-alkylation ($\alpha/\gamma \ll 10$) took place only in the case of allyl sulfoxides that contain the double bond in the ring or bear two terminal alkyl substituents; otherwise noticeable amounts (up to 50%) of γ-alkylated products formed due to which the yield of the target allylic alcohol decreased substantially.



R^1, R^2, R^3, R^4 = H, Alk; R^5 = Alk.

To eliminate this problem, it was suggested[16] that alkylation of allyl sulfides bearing heterocyclic (for example, 2-pyridyl or 2-imidazolyl) substituents at the sulfur atom should be followed by oxidation of the resulting compounds to sulfoxides. These sulfides underwent predominantly α-alkylation due to the chelating effect of the heteroatom.



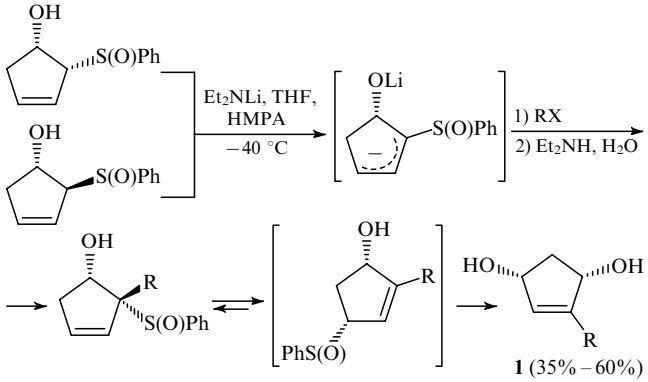
Evans and Andrews[16] also established that deprotonation with alkyllithium in the case of alkylation of allyl sulfoxides with weak electrophiles, such as long-chain halides, must be performed in aprotic solvents at below-zero temperatures.

The advantage of the allyl sulfoxide–allyl sulfenate rearrangement is the stereoselective formation of the (*E*)-C=C bond because the *trans* conformation (according to the nomenclature proposed by Mislow[15]) in the transition state is more favourable. Recently, *ab initio* calculations for 2-methyl-3-phenylsulfinylbut-1-ene confirmed that the formation of the (*E*)-C=C bond is energetically more favourable.[18] However, the difference between the energies of the *trans* and *cis* transition states is small. Hence, isomerisation of sulfoxides can afford up to 10% of the (*Z*)-isomer depending on the character of the substituents. If the double bond is involved in the corresponding ring, the product with the (*Z*) configuration can be obtained in quantitative yield. Recently, it has been demonstrated that distant functional groups exert efficient (*E*)-stereocontrol. Thus the presence of branched groups in the β position[19] or the hydroxy group in the γ position[20] of allyl sulfoxide is favourable for (*E*)-stereoselectivity (80%–99%).

Mislow was the first to note[15] that isomerisation of sulfoxides containing a chiral centre at the C(1) atom is accompanied by migration of this centre to the C(3) atom. The characteristic features of this asymmetric synthesis, which was called self-immolative, and the effects of the bulkiness and the character of the substituents were thoroughly investigated by Hoffmann.[21]

b. Syntheses of natural compounds involving the Mislow–Evans rearrangement

The [2,3]-sigmatropic Mislow–Evans rearrangement was first applied to the syntheses of prostaglandins.[22–27]

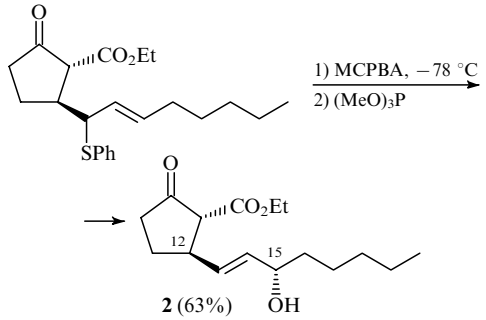


HMPA is hexamethylphosphoramide;

RX = $C_6H_{13}I$, BnBr, $\overline{OCH_2CH_2OCH}(CH_2)_6I$,

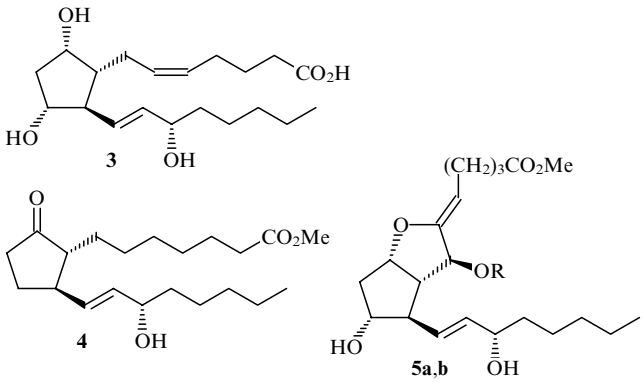
$Bu^tCO_2(CH_2)_2C{\equiv}CCH_2Br$, $Bu^tCO_2(CH_2)_6I$, $PhCH{=}CHCH_2Br$.

This procedure was used for the preparation of *cis*-cyclopentene glycols **1**, which are convenient starting compounds for preparing prostaglandins,[22] and the stereocontrolled construction of the chiral centre at the C(15) atom in compound **2** was carried out. The latter compound was utilised in the synthesis of prostaglandin PgA_2.[23]



MCPBA is *m*-chloroperbenzoic acid.

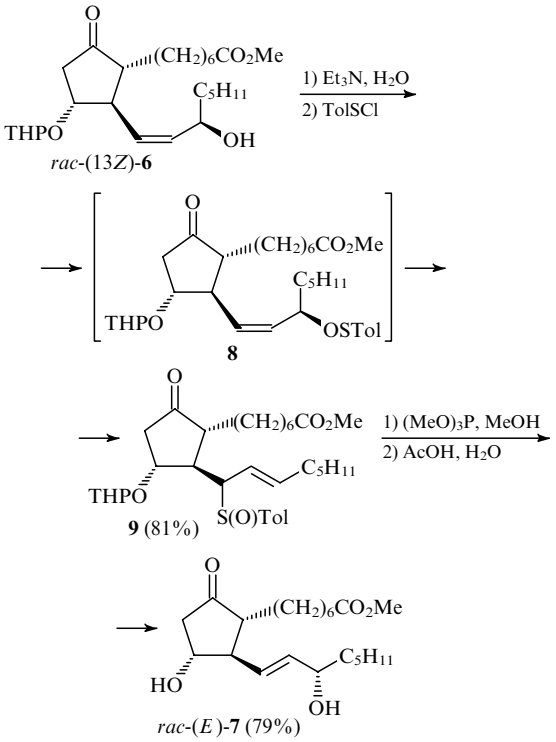
This methodology was also employed for the preparation of racemic products: prostaglandin $F_{2\alpha}$ (**3**),[24] methyl ester of 11-deoxyprostaglandin E_1 (**4**)[25] and stable analogues of prostaglandin PgI_2, *viz*., 7-hydroxy- and 7-acetoxy-PgI_2 (**5a**,**b**).[26]



R = H (**a**), Ac (**b**).

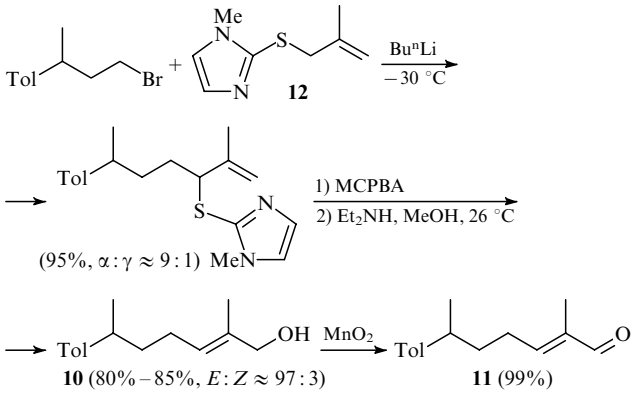
Of special interest is the study, which demonstrated high stereo- and enantioselectivity of the sigmatropic process.[27] The methyl ester of *rac*-PgE_1 (**7**), which is completely identical to the natural specimen, was prepared in high yield by a two-step

procedure starting from the readily accessible *rac*-(13*Z*)-prostaglandin (**6**) through unstable sulfenate **8** and sulfoxide **9**. In this study, both directions of the Mislow – Evans rearrangement were utilised.

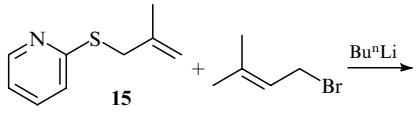


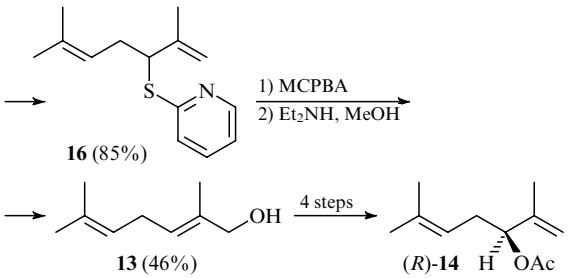
Tol = 4-MeC$_6$H$_4$, THP = .

Linear terpenoids and related compounds were synthesised using the above-mentioned alkylation at the stage of allyl sulfide. (*E*)-Nuciferol (**10**) and the terpenoid (*E*)-nuceferal (**11**) were prepared starting from methallyl imidazol-2-yl sulfide (**12**).[16]

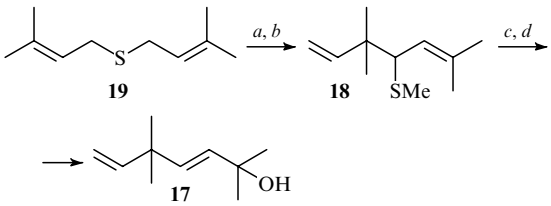


Alcohol (**13**), which is the key compound in the synthesis of the mealybug pheromone, *viz*., (*R*)-2,6-dimethylhepta-1,5-dien-3-ol acetate (**14**), was prepared in four steps starting from methallyl 2-pyridyl sulfide (**15**).[28] After oxidation of intermediate **16** and rearrangement, the alcohol **13** was isolated by chromatography. The pheromone (*R*)-**14** and its (*S*)-enantiomer were prepared in four steps involving asymmetric Sharpless epoxidation. This synthesis allowed the establishment of the absolute configuration of the natural pheromone.



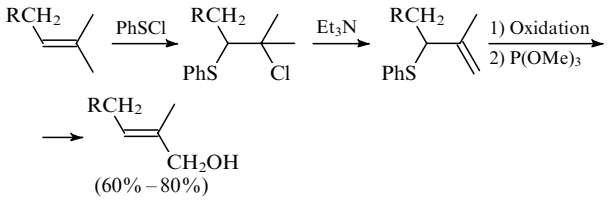


The ingenious short synthesis of yomogi alcohol **17** was carried out starting from sulfide **18**, which was prepared by alkylation of tetramethyldiallyl sulfide **19** with methyl iodide.[16]



(*a*) Bu^{n}Li, TMEDA (1,1,4,4-tetramethylethylenediamine); (*b*) MeI; (*c*) NaIO$_4$; (*d*) Et$_2$NH, MeOH, 25 °C, 24 h.

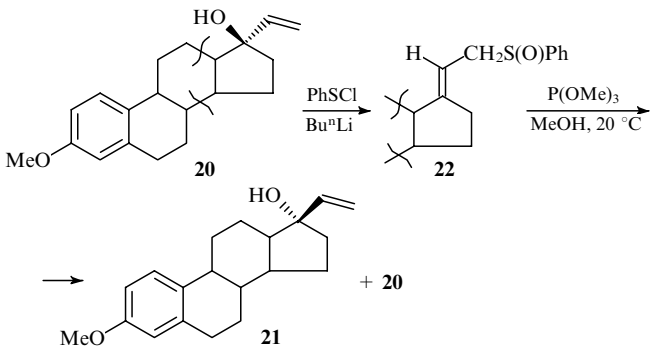
The sulfoxide – sulfenate rearrangement was also used for the functionalisation of the isopropylidene group of farnesol, related isoprenoids [29, 30] and compounds of the terpene – quinone series.[31]



Hence, the sulfoxide-sulfenate rearrangement can be performed as a one-pot procedure after oxidation of allyl sulfide to sulfoxide.

If quinones of the terpene series are used as the starting compounds, the functionalisation products containing ω-hydroxyprenyl or -geranyl chains can serve as convenient building blocks in syntheses of biologically important compounds, such as ubiquinone or vitamins K.[31]

The sulfoxide – sulfenate rearrangement made it possible to perform one-pot epimerisation of 17β-hydroxy-17α-vinylsteroids of type **20** to produce the previously unavailable epimers **21** with the 17α-hydroxy-17β-vinyl group through sulfoxide **22** (the total yield was 88%, the isomer ratio **21** : **20** = 86 : 14).[32]

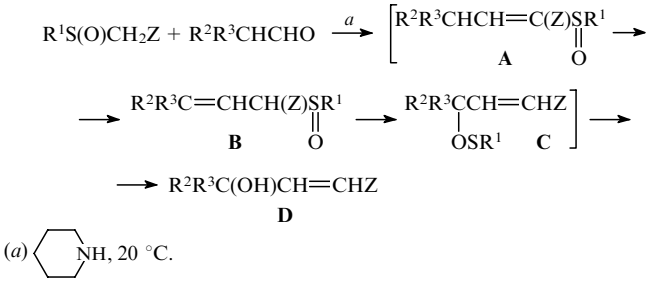


The reaction has a general character and can be applied to steroids containing the *A* rings with different structures.[32]

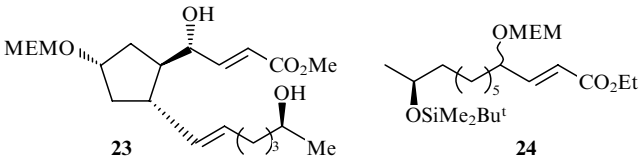
Tandem processes involving other procedures for the preparation of allyl sulfoxides were also described; among them the so-

called SPAC reaction (Sulfoxide Piperidine and Carbonyl)[33] is noteworthy.

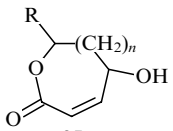
This reaction proceeds under very mild conditions and is typical of sulfoxides containing an electron-withdrawing group in the α position. It is believed that the reactions of the latter compounds with carbonyl groups in the presence of bases proceed according to a cascade mechanism, which involves the Knoevenagel reaction yielding substituted vinyl sulfoxide **A**, its isomerisation to allyl sulfoxide **B** and the subsequent Mislow–Evans rearrangement into sulfenate **C**. In the presence of a base, the latter compound gives the reaction product **D**.



The SPAC reaction and its use in syntheses of natural compounds were considered in detail in a review.[1] This procedure was followed in the preparation of compound **23**, which is a key intermediate in the synthesis of brefeldin A,[34,35] protected seco acid **24**, which is a precursor of (*R*,*R*)-pyrenophorin,[36] and macrocyclic lactones of type **25**.[37]



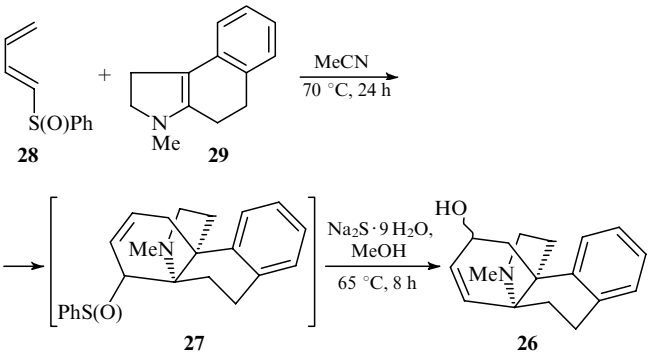
MEM = $MeO(CH_2)_2OCH_2$.



25 (R = H, Me; *n* = 7, 9).

Diene condensations of sulfinyl-substituted 1,3-dienes afford adducts containing the allylsulfinyl fragment due to which they can be used in tandem with the subsequent sulfoxide–sulfenate rearrangement of the adduct (see the review[38]).

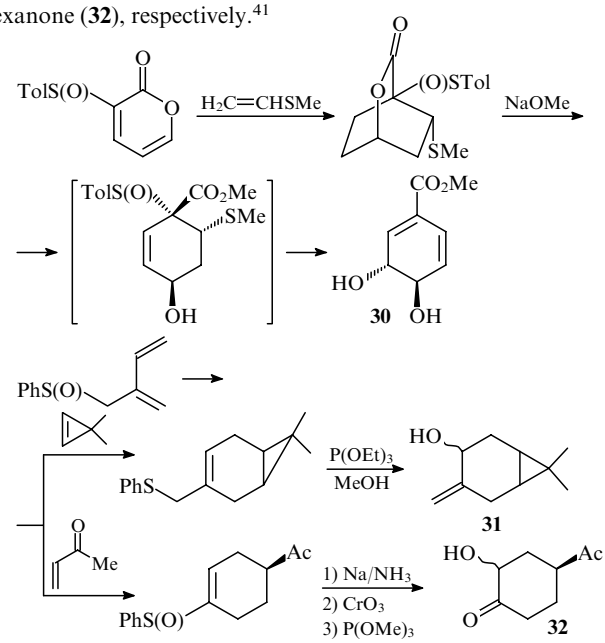
The first example of such a tandem process involving the Diels–Alder reaction and the sulfoxide–sulfenate rearrangement has been described in the early study of Evans *et al.*[39] The authors prepared compound **26** with the skeleton of the alkaloid hasubanan by the transformation (without isolation) of adduct **27**, which was synthesised by the stereoselective reaction of 1-phenylsulfinylbuta-1,3-diene (**28**) with tetrahdydrobenzoindole (**29**).



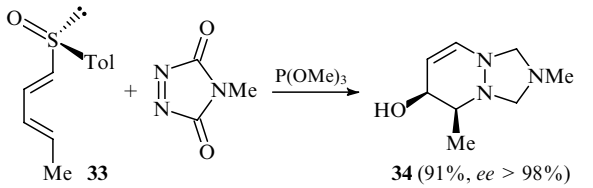
This combination of the reactions offers promise for the synthesis of biologically important substituted cyclohexenols, which cannot be prepared by other procedures.[39] However, this approach has received little use in the synthesis of natural compounds.

There are several examples of the reactions, which do not belong to tandem processes because they involve rearrangements proceeding with the participation of adducts isolated in the pure form.

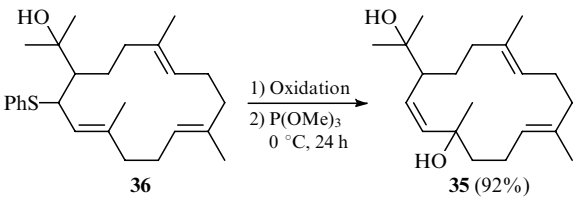
Thus compound **30**, which is a key intermediate in the total synthesis of chorismic acid, was prepared by the rearrangement of the adduct of 2-(tolylsulfinyl)pyrone with ethyl vinyl sulfide.[40] The rearrangements of the adducts of 2-phenylsulfinylbuta-1,3-diene with 3,3-dimethylcyclopropene or methyl vinyl ketone afforded carenols **31** (a mixture of the α- and β-isomers in a ratio of 7.5 : 1) and a mixture of isomers of 4-acetyl-2-hydroxycyclohexanone (**32**), respectively.[41]



The asymmetric tandem process consisting of the Diels–Alder reaction and the sulfoxide–sulfenate rearrangement can be performed with the use of enantiomerically pure 1-arylsulfinylbuta-1,3-dienes containing an electron-withdrawing substituent at position 4. Thus one-pot thermal reactions of such dienes with an excess of *N*-methylmaleimide gave rise to enantiomerically pure cyclohexene-containing compounds in high yields.[38] This methodology has not been extended to the synthesis of natural compounds. However, the recent study carried out by Carreño *et al.*[42] was devoted to the condensation of [S_R]-1-(1*E*,3*E*)-1-(tolylsulfinyl)penta-1,3-diene (**33**) with 4-methyldihydro-1,2,4-triazole-3,5-dione in the presence of trimethyl phosphite. This reaction proceeded in quantitative yield to form enantiomerically pure compound **34** serving as a key intermediate in the synthesis of optically active β-hydroxy-γ-amino acids.

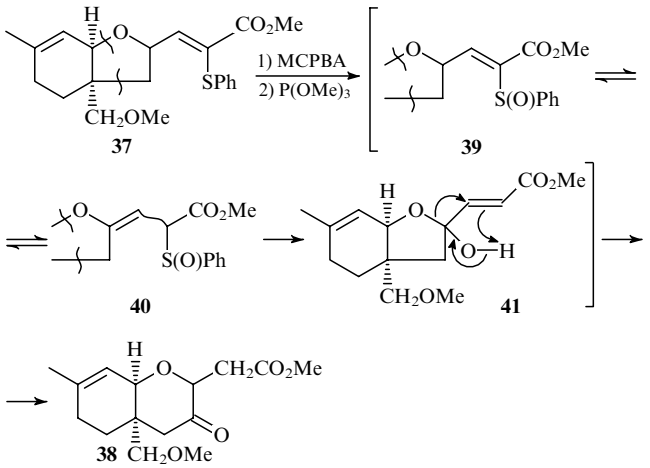


There are also other examples of the use of alcohols, which were prepared by the Mislow–Evans reaction, as key compounds in syntheses of natural products. Thus diol **35** was generated by the rearrangement of an epimeric mixture of sulfoxides, which was obtained by oxidation of sulfide **36**, and served as a key intermediate in the synthesis of cembranoids.[43]



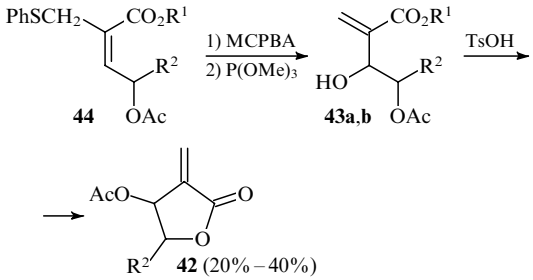
36 **35** (92%)

Bicyclic vinyl sulfide **37** was used for the preparation of derivative **38**,[44] which is a key compound in the facile synthesis of the sesquiterpenoid fragment of the active antitumour agent verrucarin. The scheme involves oxidation of the sulfide **37** to vinyl sulfoxide **39** followed by a cascade process consisting in the isomerisation of allyl sulfoxide **40** and the rearrangement of the latter into allylic alcohol **41**, which is spontaneously isomerised with the ring expansion to give the final product.



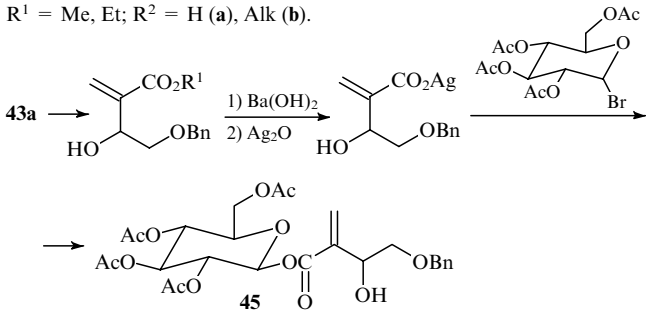
37 **39** **40** **41** **38**

The general procedure for the preparation of β-hydroxy- and β-acetoxy-γ-lactones **42**, which are precursors of compounds possessing allergic action, is based on cyclisation of susbtituted allylic alcohols of type **43**.[45] The latter were prepared by oxidation and the rearrangement of allyl sulfides **4**. This procedure was used in the first synthesis of tuliposide B, which is an agent of allergic dermatitis caused by prolonged contact with tulip bulbs. The precursor of tuliposide B **45** was synthesised starting from allylic alcohol **43a** and acetobromoglucose.



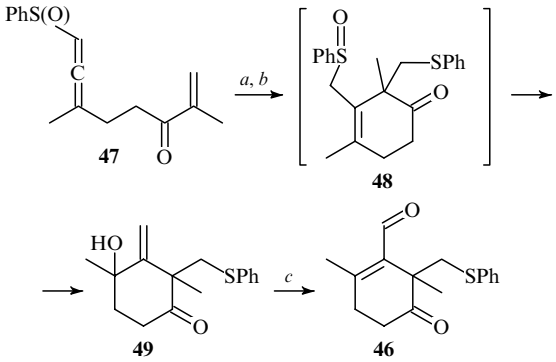
44 **43a**,**b** **42** (20%–40%)

R^1 = Me, Et; R^2 = H (**a**), Alk (**b**).



45

Compound **46**, which is a key intermediate in the route to the synthesis of an active antitumour drug taxol, was prepared starting from allenyl sulfoxide **47**. Its treatment with lithium phenoxide led to the cascade reaction accompanied by cyclisation and the rearrangement of intermediate **48** containing the allyl sulfoxide unit. Oxidation of the resulting tertiary allylic alcohol **49** afforded the target compound **46**.[46] It should be noted that the intermediate **48** was isolated in the reaction of the sulfoxide **47** with less basic nucleophile $PhMe_2Al$.



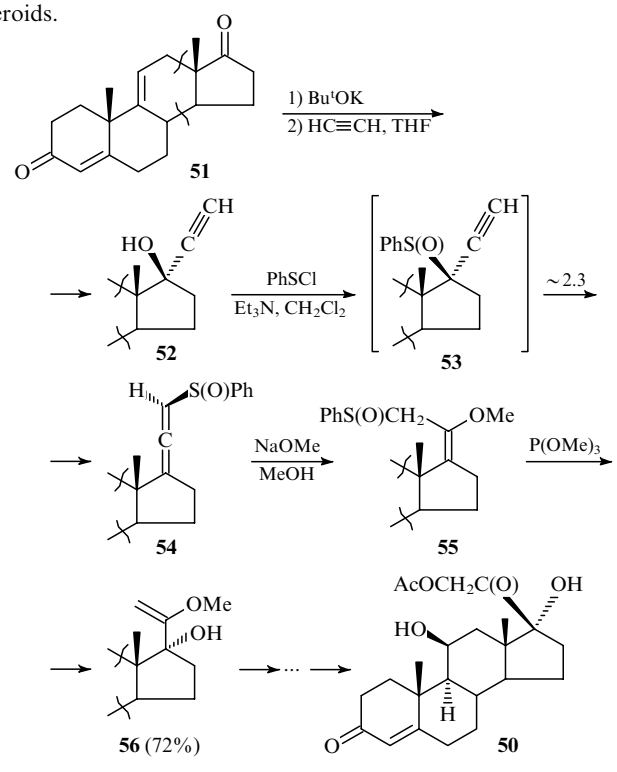
47 **48** **49** **46**

(*a*) LiSPh, THF, 0 °C; (*b*) H_2O; (*c*) Me_2N–pyridinium$\cdot CrO_3\cdot HCl$, $ClCH_2CH_2Cl$, 100 °C

2. Syntheses involving the sigmatropic rearrangement of propargyl sulfenates into allenyl sulfoxides

The rearrangement of propargyl sulfenates into allenyl sulfoxides discovered by Braverman (see Ref. 2) has received little use in syntheses of natural compounds as compared to the Mislow–Evans rearrangement. The former rearrangement is a reversible [2,3]-sigmatropic reaction proceeding under mild conditions. This rearrangement is utilised in syntheses of natural products only as a convenient procedure for the preparation of allenyl sulfoxides starting from available propargylic alcohols. Allenyl sulfoxides can, in turn, be converted into substituted allyl sufoxides by the addition of a nucleophile at the activated C=C bond of allenyl sulfoxide.

A procedure was developed[47] for the preparation of the antiinflammatory agent hydrocortisone acetate (**50**) bearing the $COCH_2OH$ group at position 17β, which is typical of corticosteroids.

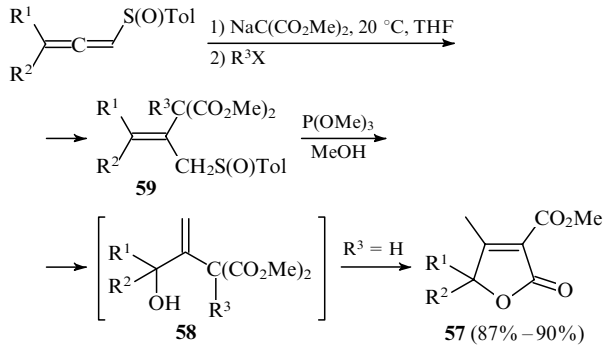


51 **52** **53** **54** **55** **56** (72%) **50**

Readily accessible androst-4,9(11)-diene-3,17-dione (**51**) was used as the starting compound. The reaction of alcohol **52**, which was prepared by the selective addition of acetylene to the carbonyl group at position 17 of compound **51**, with $PhSCl-NEt_3$ afforded sulfenate **53**. The latter is stable only below −40 °C and underwent the [2,3]-rearrangement to give allene sulfoxide **54** as a mixture of isomers. The addition of the methoxy group at the double bond of the sulfoxide **54** gave rise to an epimeric mixture of allyl sulfoxides **55**, which were isomerised into allylic alcohol **56** through the Mislow–Evans rearrangement. This process provides the basis for a general method for the conversion of ketosteroids to corticosteroids. The stereochemistry of all stages of this process was investigated.[47]

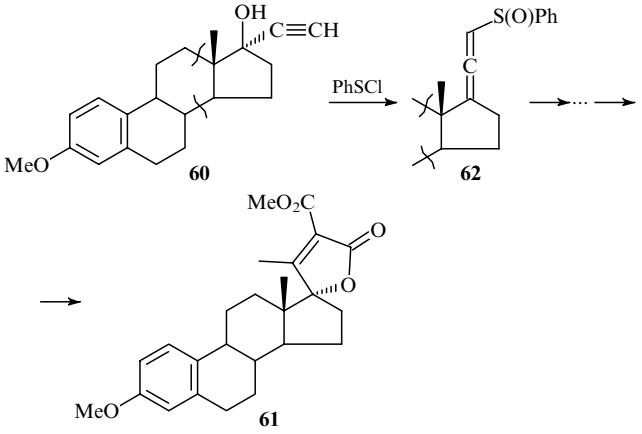
The addition of the alkyne fragment to the carbonyl group followed by desulfinylation of allenyl sulfoxides under the action of MeLi was used for the preparation of steroids containing allene substituents.[48, 49]

In the study,[50] allenyl sulfoxides were utilised as the starting compounds in the development of a general method for the preparation of 2,5-dihydrofuranones **57** by cyclisation of substituted allylic alcohols **58**, which are products of the [2,3]-rearrangement of allyl sulfoxides **59**. The compounds **59** were prepared by the addition of a sodium derivative of dimethyl malonate to allenyl sulfoxides.

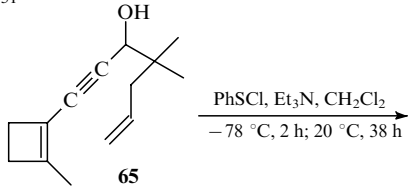


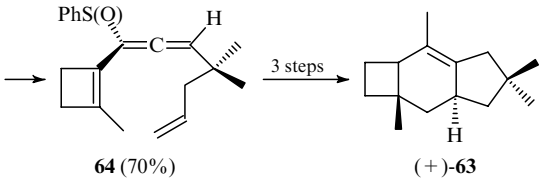
R^1 = H, Me; R^2 = Me; $R^1-R^2 = (CH_2)_5$.

This procedure was also employed for the conversion of mestranol **60** to spiro lactone **61** *via* allenyl sulfoxide **62**.[50]



In the synthesis of sesquiterpenoid sterpurene [(+)-**63**], the key tetraene sulfoxide **64** was derived from propargylic alcohol **65**.[51]

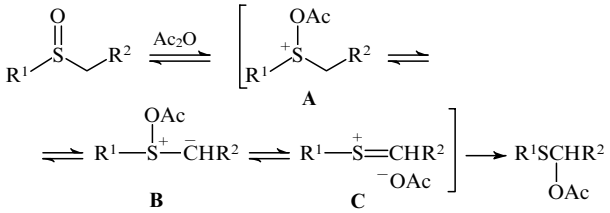




Other examples of the synthetic applications of vinylallenyl-containing sulfoxides prepared in a similar way were presented in a review,[52] which covered the use of vinylallenes in the synthesis of metabolites of vitamin D_3.

III. Syntheses based on the Pummerer reaction

The Pummerer reaction consists in the transformation of sulfoxides bearing at least one α-hydrogen atom under the action of electrophilic reagents. The reactions of saturated sulfoxides resulted in reduction of the sulfinyl group to the sulfide group and oxidation of an α-hydrogen atom. It is believed [7, 8, 11, 53] that the reaction proceeds through successive equilibrium stages of the formation of the acyloxy sulfonium ion **A**, ylide **B** and the sulfenium cation **C**. The reactions ended in the attack of an internal or external nucleophile on the cation **C**.



All three main experimental versions of this reaction are employed in syntheses of natural compounds.

The first version is the classical Pummerer reaction in which sulfoxides containing no unsaturated groups in the α,β positions react with acids or their derivatives (most often with anhydrides and sometimes in the presence of bases). As shown in the above scheme, these reactions afford α-acyloxy sulfides as the primary reaction products.

The second version involves the so-called sila-Pummerer reactions. In this case, the substrate or the electrophilic reagent possesses labile Si–X bonds due to which the reactions often proceed under milder conditions (generally at below-zero temperatures). Trimethylchlorosilane [54] or other silicon-containing electrophiles are used as silylating agents.

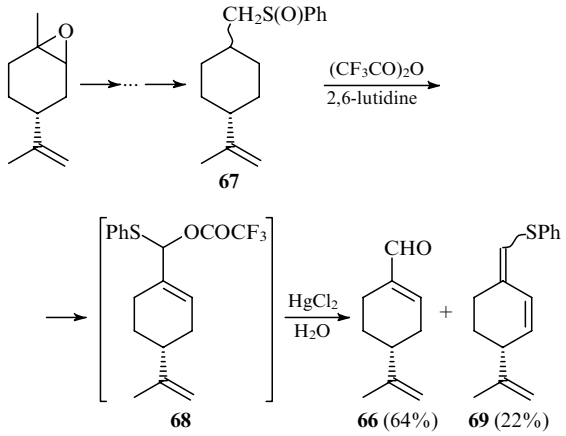
The third version of the Pummerer reaction consists in additive processes involving vinyl sulfoxides as substrates, which undergo Pummerer-like rearrangements under the action of various inorganic or organic electrophilic reagents.[55] The version proposed by Marino and Neisser [56] is of particular interest. In the latter case, dichloroketene generated *in situ* served as the electrophilic reagent.

Examples of the use of the Pummerer reaction in syntheses of biologically active compounds are systematised below according to the nature of the nucleophilic reagent involved in the reaction with the sulfenium cation.

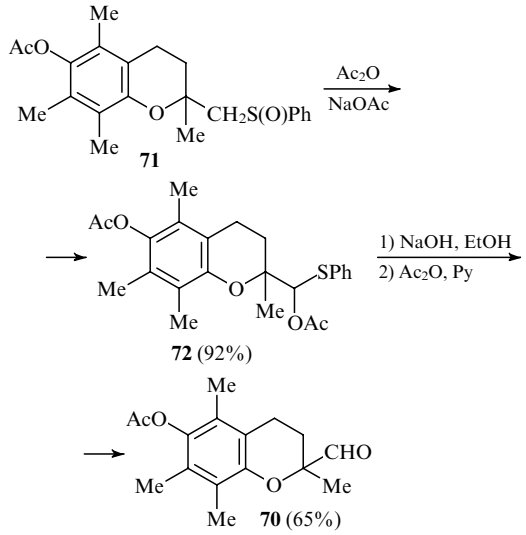
1. Syntheses based on hydrolytic cleavage of α-acyloxy sulfides

Hydrolysis of α-acyloxy sulfides generated in the course of the classical Pummerer reaction provides a convenient way of transforming sulfoxides into carbonyl compounds. These reactions are generally performed under the action of alkalis with the addition of salts, such as $HgCl_2$ or $CaCl_2$, which promote elimination of the RS group. This section is concerned with examples of the applications of this procedure to the construction of carbonyl groups in natural compounds or key intermediates for their syntheses.

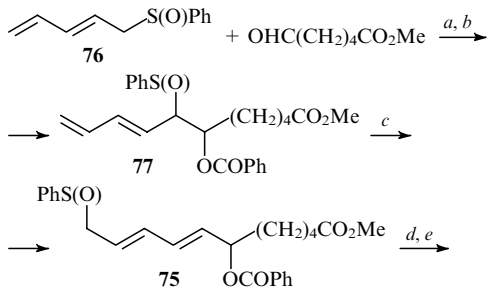
(*R*)-(+)-Perillaldehyde (**66**) was prepared [57] starting from an enantiomeric mixture of optically active sulfoxides **67** [which were synthesised in two steps from (+)-limonene epoxide] by hydrolysis of the Pummerer-reaction product **68** without its isolation. Side chain deacylation of the intermediate **68** afforded vinyl sulfide **69**.

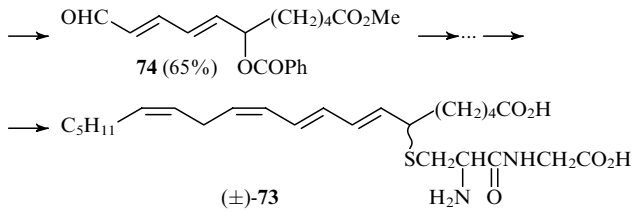


6-Acetoxy-2,5,7,8-tetramethylchroman-2-carbaldehyde (**70**), which is a key starting compound in the total synthesis of α-tocopherol, was derived [58] from sulfoxide **71** by hydrolysis of α-acyloxy sulfide **72** isolated in the individual form.



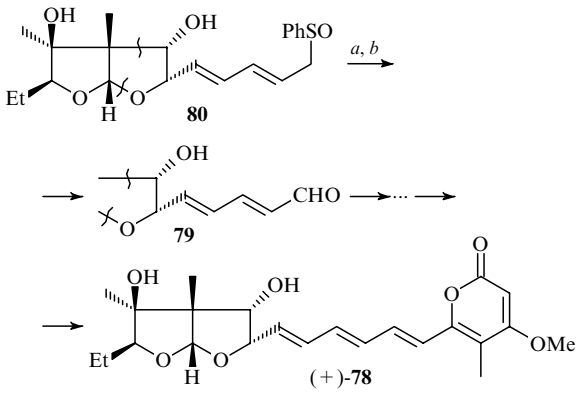
Racemic 5-desoxyleukotriene D [(±)-**73**] was synthesised with the use of aldehyde **74**, which was prepared from sulfoxide **75** without isolation of intermediate acyloxy sulfide. The scheme of the synthesis of the aldehyde **74** involves the reaction of 1-phenylsulfinylpenta-2,4-diene **76** with methyl 5-formylvalerate in the presence of butyllithium followed by migration of the sulfinyl group in benzoyl derivative **77**, which proceeds very readily through a two-step [2,3]-rearrangement.[59]





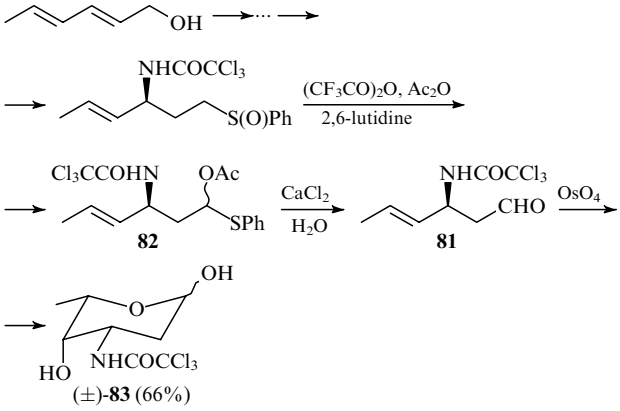
(*a*) Bu^{n}Li; (*b*) PhCOCl, −40 °C; (*c*) 25 °C, 3 h, (*d*) Ac_2O, 2,6-lutidine, $(CF_3CO)_2O$, NaOH; (*e*) $CaCO_3$, $HgCl_2$, MeCN – H_2O.

In the key stage of the total synthesis of asteltoxin [(±-**78**)], aldehyde **79** was generated from sulfoxide **80** also without isolation of intermediate acyloxy sulfoxide.[60]

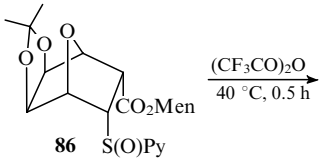


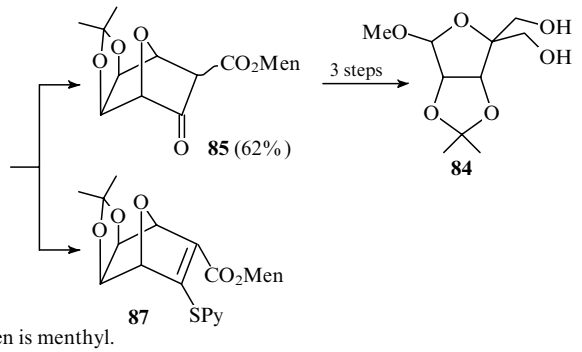
(*a*) $(CF_3CO)_2O$, Ac_2O, 2,6-lutidine; (*b*) $CaCl_2$, $HgCl_2$, MeCN – H_2O.

3-Trichloroacetylaminohex-4-enal (**81**) was synthesised starting from sorbinic alcohol. [61] In this case, acyloxy sulfide **82** was isolated as an intermediate. Hydroxylation of the aldehyde **81** with OsO_4 afforded the *N*-trichloroacetyl derivative of racemic daunosamine (**83**), which is a carbohydrate fragment of the antitumour antibiotic daunorubicin used in clinical practice. Variations of this procedure made it possible to synthesise the related carbohydrates, *viz*., racemic vancosamine and ristosamine.[61]



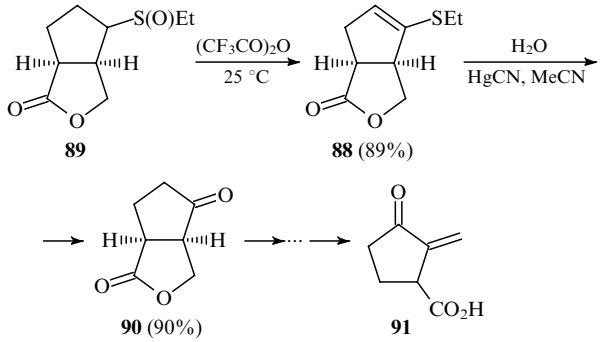
Branched sugar **84** was synthesised [62] in three steps from keto ester **85**. The latter was obtained as the major product of the Pummerer reaction of sulfinyl-substituted ester **86**, which was prepared by diene condensation of menthyl (*S*)-(2-pyridylsulfinyl)acrylate with furan.[63] The Pummerer reaction involving the sulfoxide **86** afforded vinyl sulfide **87** as a by-product. Acid hydrolysis of the latter gave rise to the keto ester **85** in low yield (< 25%).[62]



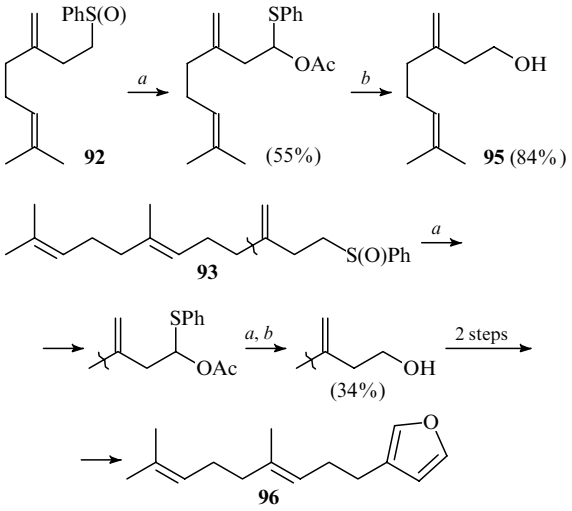


Men is menthyl.

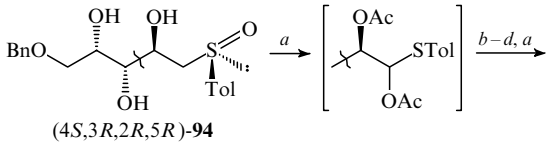
However, some of these reactions proceed readily; examples of such reactions were described in the literature. Thus vinyl sulfide **88**, which was prepared by the Pummerer reaction starting from sulfoxide **89**, was utilised in the synthesis of ketolactone **90**. The latter is the direct precursor in the synthesis of the antitumour agent sarcomycin (**91**).[64]

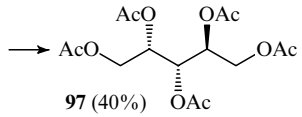


Below is given a scheme illustrating additional potentialities arising from a combination of the classical Pummerer reaction and the subsequent transformation of its products without their isolation. A combination of hydrolysis of acetoxy sulfide and reduction of the intermediate carbonyl compound starting from sulfoxides **92**–**94** made it possible to prepare labile compounds, such as γ-geraniol (**95**),[65] dendrolasin (**96**)[66] and enantiomerically pure penta-*O*-acetyl-L-arabinitol (**97**).[67]



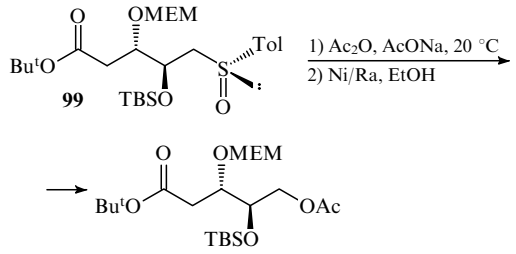
(*a*) Ac_2O, $(CF_3CO)_2O$ (cat); (*b*) $NaBH_4$, EtOH, H_2O.





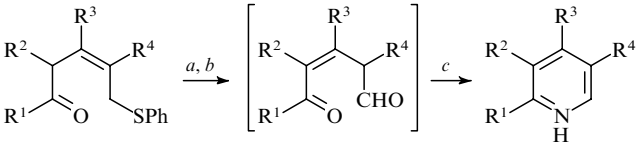
(*a*) Ac_2O, AcONa; (*b*) Bu^i_2AlH; (*c*) Ac_2O; (*d*) Pd/C, C_6H_{10}.

In more recent studies, for example, in the synthesis of 2-deoxy sugars[68] or in the construction of a fragment of the antibiotic nystatin A_1 containing five chiral alcoholic centres, Solladié *et al.*[69] used yet another modification of the acyloxy sulfide group. The Pummerer-reaction product, which was purified only by column chromatography, was immediately subjected to desulfurisation with Raney nickel. This procedure is exemplified by the preparation of derivative **98** of (2-deoxy-D-ribonic acid) starting from sulfoxide **99**.



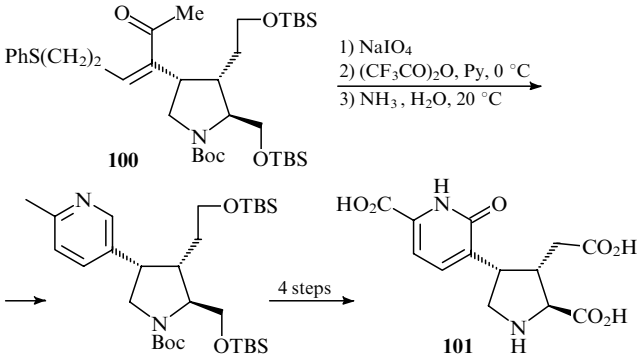
TBS = Bu^tMe_2Si.

The procedure developed for the synthesis of substituted pyridines[70] involves a combination of four reactions, *viz.*, oxidation of sulfide to sulfoxide, the classical Pummerer reaction, hydrolysis of α-acyloxy sulfide and the formation of the pyridine ring by the reaction of ammonia with intermediate 1,5-ketoaldehyde.



(*a*) $NaIO_4$, MeOH, H_2O; (*b*) $(CF_3CO)_2O$, Py; (*c*) NH_3, MeOH, H_2O.

This procedure made it possible[71] to synthesise natural neurotoxin, *viz.*, acromelic acid A (**101**), starting from phenylthio-substituted pyrrolidine **100**. Isomeric acromelic acid B was prepared analogously.[72] More complex synthetic schemes involving the Pummerer reaction as the key stage are considered at the end of the section.



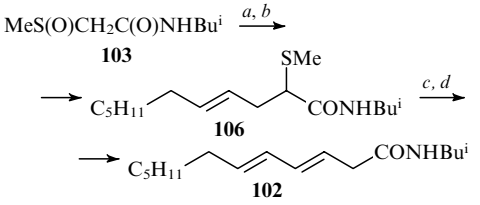
Boc = Bu^tOCO.

2. Syntheses based on intermolecular reactions of sulfenium cations with C = C bonds of alkenes

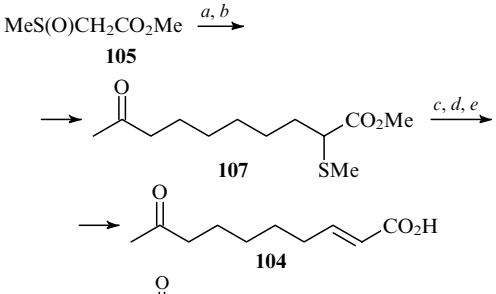
The sulfenium cation is a highly electrophilic reagent, particularly, if the initial sulfoxide bears activating electron-withdrawing

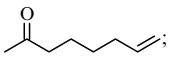
groups (most often carbonyl groups). This cation can react even with the weakly nucleophilic C=C bond. Analogous intermolecular processes were used in syntheses of predominantly linear unsaturated components of pheromones. In most studies, no consideration has been given to intermediates and hence, the mechanism of this reaction is unknown. Ishibashi and coworkers [73–77] proposed the ene-type mechanism involving the sulfenium cation.

The natural insecticide pellitorine (**102**) was prepared [73] by the reaction of oct-1-ene with the product of the Pummerer rearrangement of (methylsulfinyl)acetamide (**103**). (*E*)-9-Oxodec-2-enoic acid (the queen substance) (**104**) was synthesised analogously from methyl methylsulfinylacetate (**105**) and oct-1-en-7-one.[74] Additional C=C bonds were generated by thermolysis of sulfoxides prepared by oxidation of adducts **106** and **107**.

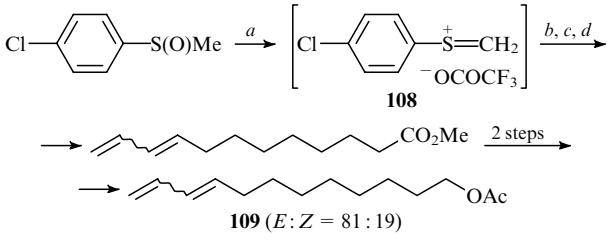


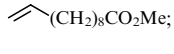
(*a*) $(CF_3CO)_2O$; (*b*) $C_6H_{13}CH=CH_2$; (*c*) $NaIO_4$; (*d*) Δ.

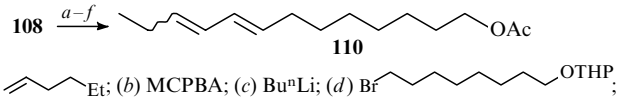


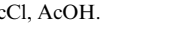
(*a*) $(CF_3CO)_2O$; (*b*) ; (*c*) $NaIO_4$; (*d*) Δ; (*e*) OH^-.

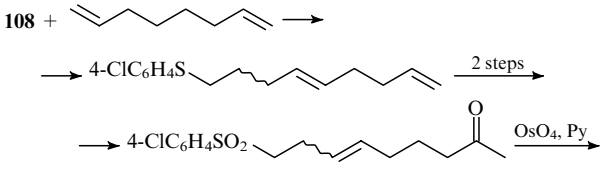
p-Chlorophenylmethyl sulfoxide proved to be a particularly convenient starting compound in such reactions. The Pummerer reaction involving primary product **108** afforded numerous biologically active compounds, for example, the sex pheromone of red cotton moth (**109**) with the ratio of the (*E*)- and (*Z*)-isomers identical to that observed in the natural substance,[75] the pheromone of some tortricids **110** [76] and bicyclic *exo*-brevicomin **111**, which is the aggregation pheromone of fir moth (in a mixture with 11% of the *endo* epimer).[77]

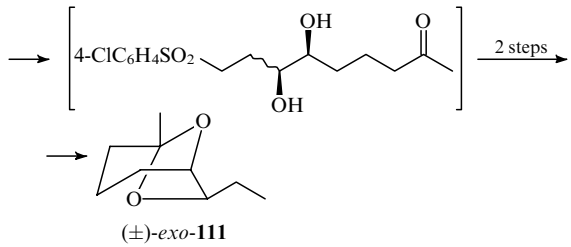


(*a*) $(CF_3CO)_2O$; (*b*) ; (*c*) MCPBA; (*d*) Δ.



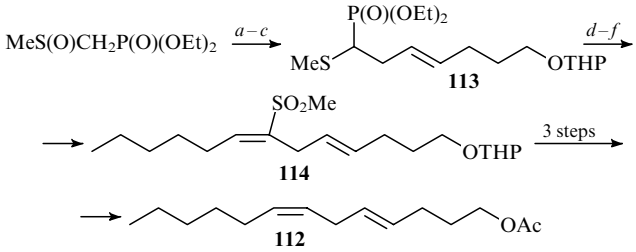
(*a*) ; (*b*) MCPBA; (*c*) Bu^nLi; (*d*) ;
(*e*) EtNHLi; (*f*) AcCl, AcOH.

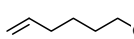
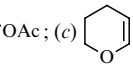
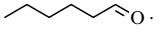




(±)-*exo*-**111**

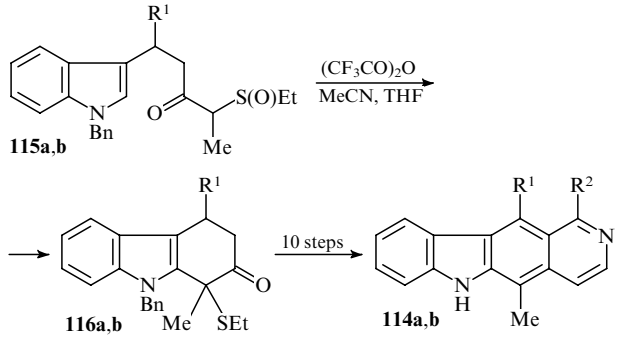
Trideca-(4*E*,7*Z*)-4,7-dien-1-ol acetate (**112**), which is the potato moth pheromone, was synthesised [78] starting from phosphorus-substituted sulfide **113**. The latter was derived from (methylsulfinyl)phosphonate by the Pummerer reaction followed by the reaction with 5-heptyl acetate. The synthesis ended in oxidation of the sulfur atom in the adduct to the sulfonyl group, chain elongation by the Horner–Wadsworth–Emmons reaction with hexanal and a three-step modification of intermediate **114**.



(*a*) $(CF_3CO)_2O$; (*b*) ; (*c*) , H^+; (*d*) MCPBA;
(*e*) Bu^nLi; (*f*) .

3. Cyclisations based on intramolecular reactions of sulfenium cations with C=C bonds

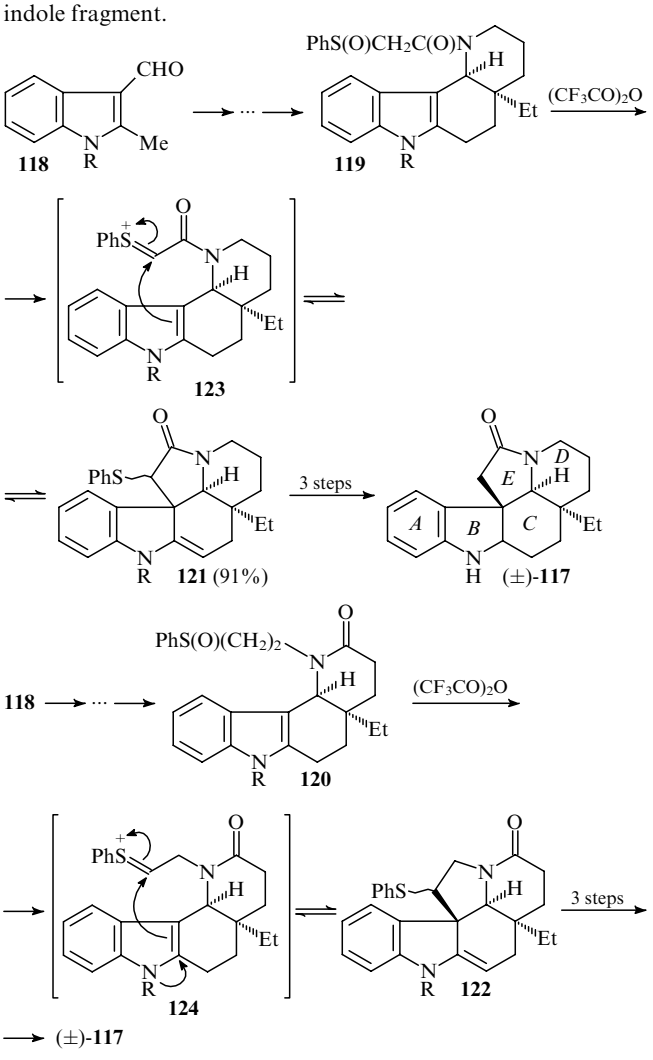
Intramolecular coupling of the Pummerer-reaction products and C=C bonds proved to be much more fruitful. The reaction of the sulfenium cation, which was derived from the sulfinyl fragment of compounds **115a**,**b**, with the C=C bond of the indole fragment was the key step in the synthesis of tetracyclic pyrido[4.3-*b*]carbazole alkaloids olivacine (**114a**) and ellipticine (**114b**). The target alkaloids **114a**,**b** were prepared in rather high yields by ten-step transformations of intermediates **116a**,**b**.[79]



Compound	R^1	R^2	Yield (%)
116a	H		51
116b	Me		55
114a	H	Me	28
114b	Me	H	23

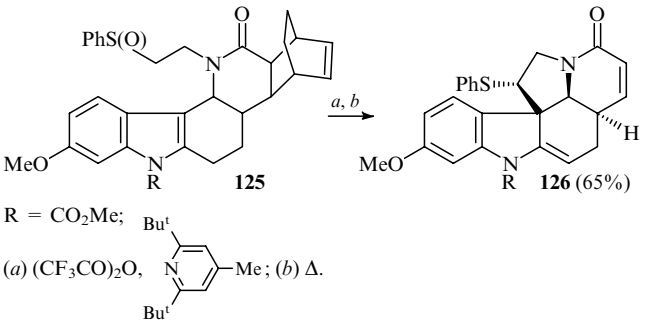
Magnus and coworkers carried out systematic research into the synthesis of polycyclic indole alkaloids (see the review [80]) and devised the [2,3]-quinodimethane strategy for constructing these alkaloids. (±)-Aspidospermidine (**117**), which is the simplest representative of pentacyclic alkaloids from *Aspidosperma sp.* plants, was a convenient compound for the development of the methodology. Gallagher *et al.*[81] synthesised tetracyclic precur-

sors, *viz*., substituted octahydro-7*H*-pyrido[3,2-*c*]carbazole **119** and **120**, starting from nitrogen-protected 3-formyl-2-methylindole (**118**). The compound **119** contains the sulfinyl-substituted exocyclic amide group, whereas the compound **120** bears the endocyclic amide group. Under the conditions of the Pummerer reaction, compounds **119** and **120** very readily undergo cyclisation to compounds **121** and **122** to form the *E* ring (apparently through intermediates **123** and **124**, respectively). After deprotection of the indole nitrogen atom and reductive removal of the carbonyl and sulfide groups, racemic aspidospermidine **117** was obtained through the compounds **119** and **120** in total yields of 6.3% of 11.7%, respectively. Cyclisation proceeded with exceptional stereoselectivity resulting in the natural *cis*-fusion of the rings. Cyclisation proceeded readily due to the close arrangement of the sulfenium cation and the π-electron system of the nucleophilic indole fragment.



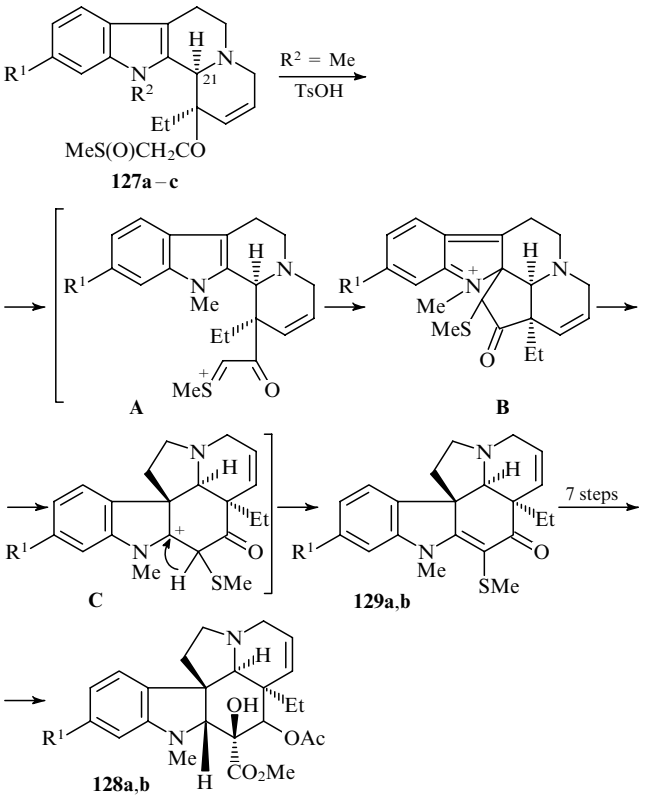
R = $SO_2C_6H_4OMe$-4.

The electronic or steric factors inhibiting the ring formation can (owing to the equilibrium character of this reaction) promote other conversions of a sulfenium-containing intermediate. Thus researchers failed to construct the *E* ring of indole alkaloids of the aspidospermine group under the standard conditions of the Pummerer reaction starting from model compound **125**, which contains the electron-donating methoxy group in the benzene ring typical of alkaloids of the vinblastine and vindoline groups. Cyclisation was successfully performed under the action of trifluoroacetic anhydride in the presence of 2,6-di-*tert*-butyl-4-methylpyridine as a base.[82] After thermolysis, compound **126** was obtained in rather high yield.



R = CO_2Me; (*a*) $(CF_3CO)_2O$, 2,6-di-*tert*-butyl-4-methylpyridine; (*b*) Δ.

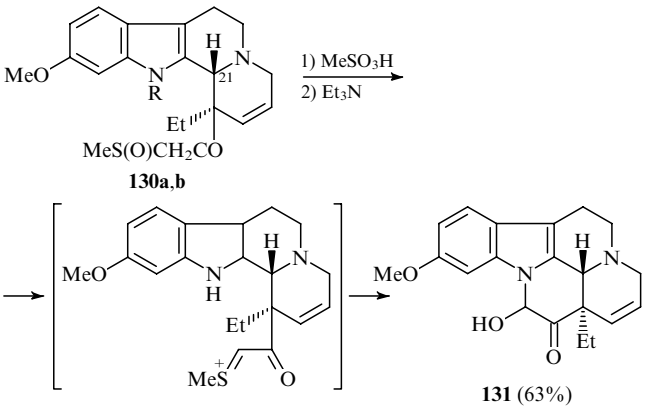
Magnus did not extend this discovery to natural alkaloids of the vinblastine and vindoline series, probably, because Langlois and coworkers [83] have reported an ingenious procedure for their preparation, which was also based on the Pummerer reaction but which utilised β-ketosulfinyl-containing tetrahydroindolo[2,3-*a*]-quinolizidines of type **127** as the starting compounds. Vindoline (**128a**) and vindorosine (**128b**) were prepared from the compounds **127a**,**b** in which the indole nitrogen atom was protected with the methyl group. Under the conditions of the Pummerer reaction, the compounds **128a,b** underwent a retrobiomimetic rearrangement *via* the intermediates **A** → **B** → **C**. The reaction started with the coupling of the sulfenium cation with the indole C=C bond and ended in the construction of the *E* ring in **129a**,**b**, which are key compounds in the synthesis of the target alkaloids. If the indole nitrogen atom is not protected (as in the precursors **127c** or **130a**), the indole C=C bond can couple with the nearby sulfenium cation (*via* the intermediate **D**) under the conditions of the Pummerer



Compound	R^1	R^2	Yield (%)
127a	OMe	Me	–
127b	H	Me	–
127c	H	H	–
128a	OMe		10 (total)
128b	H		–
129a	OMe		73
129b	H		70

reaction giving rise to eburn-type alkaloids, for example, to compound **131**. However, for this reaction pathway to become dominant, the indole C=C bond must be additionally shielded by the β-hydrogen atom at the C(21) atom as in indoloquinolizidine **130a**.[84]

The Pummerer reaction involving the epimeric compound **127c**, which bears an α-hydrogen atom at the C(21) atom, afforded a mixture of aspidospermidine- and eburn-type alkaloids with the former predominating.[85]

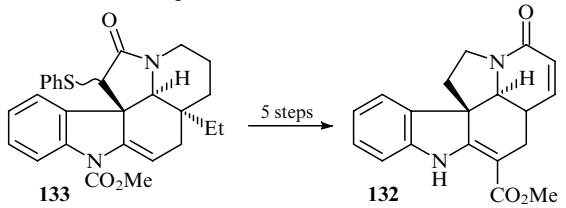


130a,b **131** (63%)

R = H (**a**), Me (**b**).

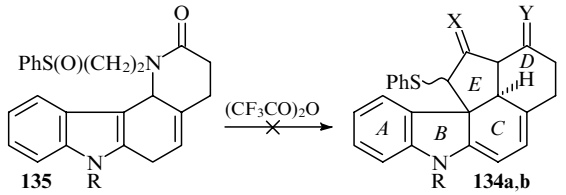
Vindoline **128a** can be prepared with equal ease from the C(21)-epimeric precursors **127a** or **130b**. It was assumed [84] that the compound **130b** was converted into the compound **127a** due to rapid reversible Mannich-type isomerisation. Apparently, this reversible process is also responsible for racemisation, which was observed in attempting to prepare enantiomerically pure alkaloids of this series from optically pure indoloquinolizidines.[84, 86]

Further progress in studies on the synthesis of alkaloids of the aspidospermine group performed by Magnus and coworkers [87] was achieved owing to the employment of additional functionalisation of pentacyclic thio-containing amides. Thus racemic 8-oxotabersonine (**132**) was prepared [87] from pentacyclic compound **133** in five steps.



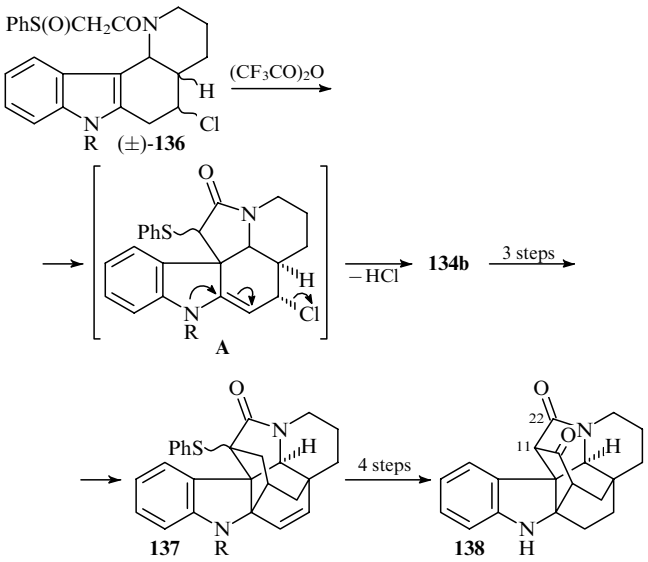
133 **132**

The synthesis of heptacyclic alkaloids of the kopsan series was a more complicated problem. For this purpose, key compound **134a** containing the diene system in the *C* ring was constructed. Under the conditions of the Pummerer reaction, aromatisation of the *C* ring competed with cyclisation due to which the use of the diene precursor **135** did not afford the target compound **134a**. The reaction involving chlorine-containing analogue **136** took the desired path [88] and the intermediate **A** readily underwent dehydrochlorination.



135 **134a,b**

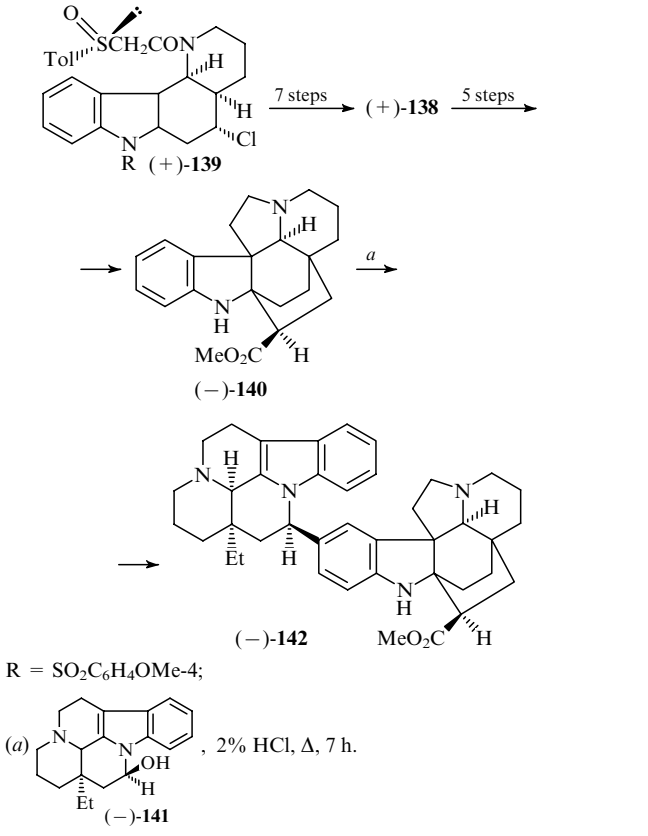
R = $SO_2C_6H_4OMe$-4; X = H, Y = O (**a**); X = O, Y = H (**b**).



R = $SO_2C_6H_4OMe$-4.

The one-pot synthesis of heptacyclic compound **137** containing all major elements of the kopsan system was carried out with the use of the pentacyclic compound **134b**. For this purpose, the starting compound was allylated at the C(11) atom followed by intramolecular diene condensation involving the diene system of the *C* ring. The key alkaloid of this series, *viz*., (±)-10,22-dioxokopsan (**138**), was synthesised from the compound **137** in four steps [the keto group at the C(22) atom was formed by the Pummerer reaction of the intermediate C(22)-sulfoxide]. C(22)-Oxokopsan and epimeric C(22)-kopsanols were readily derived from the compound **138**.

An analogous procedure was also used [89] for the preparation of optically active (+)-dioxokopsan [(+)-**138**] based on enantiomerically pure (taking into account the sulfinyl group) tetracyclic precursor (+)-**139**. In the cited study,[89] the data on the optical



R = $SO_2C_6H_4OMe$-4;

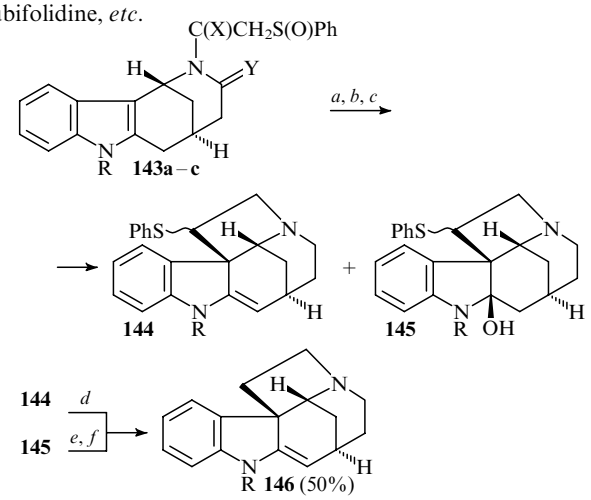
(*a*)

, 2% HCl, Δ, 7 h.

(−)-**141**

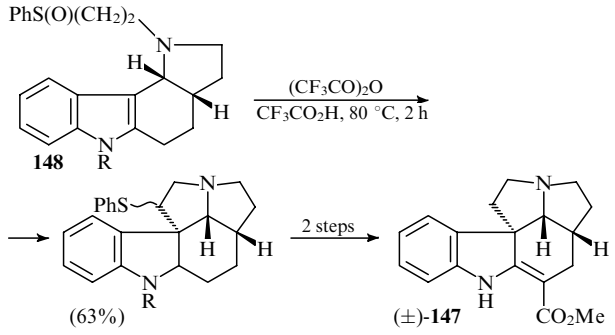
purity and absolute configurations of the products are lacking. However, the conversion into (−)-kopsinine (**140**) followed by its condensation with optically pure (−)-eburnamine [(−)-**141**] afforded bis-indole (−)-norpleiomutine [(−)-**142**] characterised by an optical rotation identical to that of the natural alkaloid.

The application of Magnus's procedure to the construction of the fifth ring of the more strained systems of alkaloids from plants of the *Strychnos* family utilising either precursor **143a**, which contains the exocyclic sulfinylamide group, or precursor **143b**, which is an endocyclic amide, has not met with success.[90] In the study of Bosch and coworkers,[91] steric hindrances to the favourable arrangement of the sulfenium ion relative to the indole C=C bond were overcome with the use of the more flexible sulfinylalkylamine group in tetracyclic precursor **143c**. In the latter case, after the standard treatment with trifluoroacetic anhydride, the process was terminated at the stage of formation of α-acyloxy sulfide, which was converted without isolation into cyclisation product **144** under the action of boron trifluoride etherate. The yield was insufficiently high because the undesirable hydration product **145** was simultaneously obtained. However, the cited study[91] can be considered as a facile synthesis of strychnine alkaloids. Compound **146** was obtained in 50% yield. It is a 20-deethylated analogue of the final intermediate (which was prepared previously[92]) in the synthetic pathway of the most important representatives of strychnine alkaloids, *viz*., tubifoline, tubifolidine, *etc*.



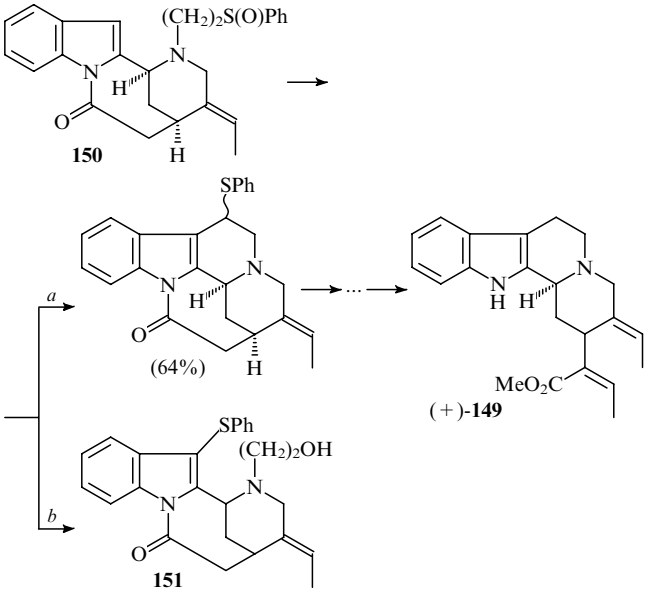
R = CO_2Me; X = O, Y = H_2 (**a**); X = H_2, Y = O (**b**); X = Y = H_2 (**c**); (*a*) X = Y = H_2, $(CF_3CO)_2O$; (*b*) $BF_3 \cdot Et_2O$; (*c*) CH_2Cl_2, Δ, 4 h; (*d*) Ni/Ra; (*e*) TsOH, 20 °C; (*f*) Ni/Ra.

Sulfinylalkylamines were successfully used in syntheses of other groups of alkaloids. (±)-Deethylibophyllidine (**147**) was prepared[93] according to the standard Pummerer reaction from tetracyclic compounds **148** by the construction of the fifth ring.



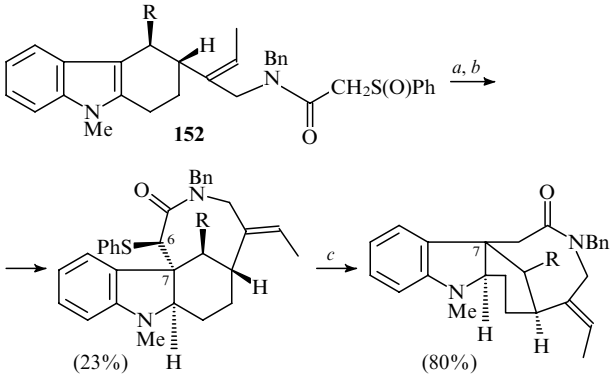
R = CO_2Me.

In the facile synthesis of (±)-geissoschizine (**149**) starting from precursor **150**, the six-membered ring was successfully constructed only under the conditions of the sila-Pummerer reaction.[94] Under the conditions of the classical Pummerer reaction, the unexpected formation of hydroxy sulfide **151** from the compound **150** was observed instead of cyclisation. In a special study,[95] it was demonstrated that such an anomalous Pummerer reaction is typical of C(3)-unsubstituted indole derivatives and is attributable to the prior formation of the seven-membered ring.



(*a*) Me_3SiOCF_3, 20 °C; (*b*) $(CF_3CO)_2O$, CF_3CO_2H.

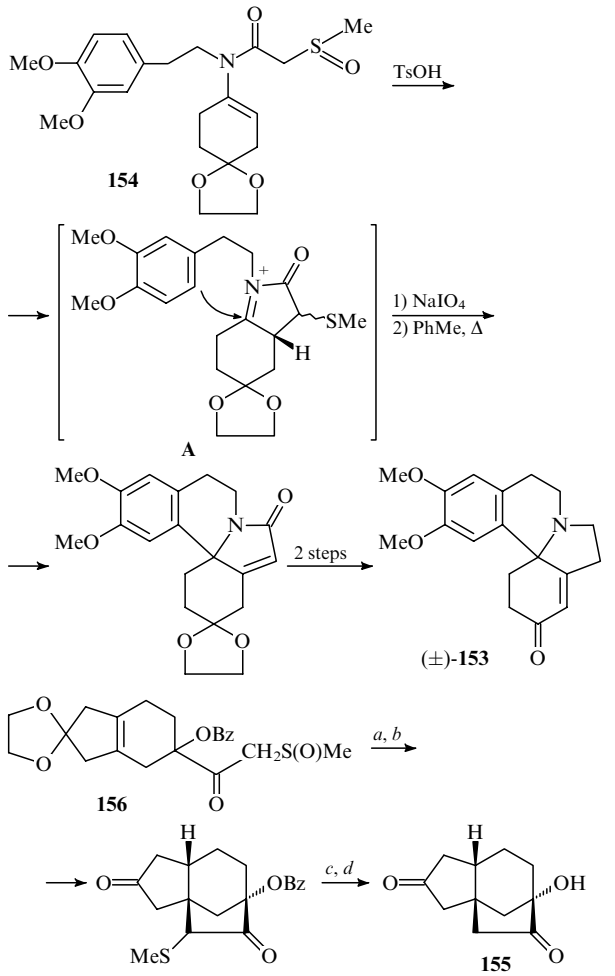
This research group[96] carried out the first synthesis of an alkaloid of the 3,4-secoakuammilan series by cyclisation of sulfoxide **152** under the conditions of the Pummerer reaction. In this synthesis, the strongly strained quaternary centre at the C(7) atom was generated through the formation of the eight-membered lactam ring.



(*a*) $(CF_3CO)_2O$, CH_2Cl_2; (*b*) $NaCNBH_3$; (*c*) Ni/Ra, EtOH.

4. Synthesis of cyclic compounds by intramolecular reactions of sulfenium cations with various nucleophilic traps

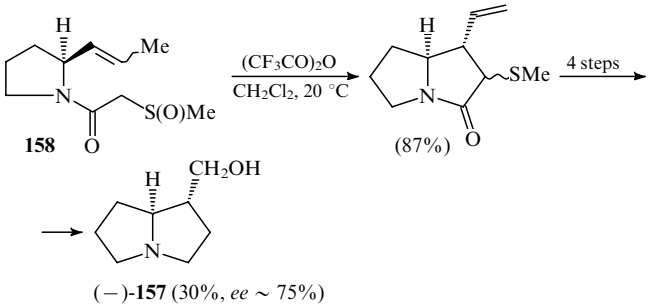
The Pummerer reaction is finding increasing use in the construction of various rings, including those present in natural compounds, primarily, of heterocycles (see the review[12]), and, to a lesser extent, of carbocycles. Natural heterocycles are constructed by intramolecular binding of the sulfenium cation to various nucleophilic traps. The C=C bonds other than those present in indoles can serve as nucleophiles as exemplified by the ingenious synthesis of the alkaloid (±)-3-demethoxyerythratidinone (**153**).[97] The latter was prepared starting from substituted sulfinylacetamide **154**, which was subjected to double cyclisation *via* intermediate **A**.



(*a*) $(CF_3CO)_2O$; (*b*) $SnCl_4$; (*c*) Ni/Ra; (*d*) H_2, Pd/C.

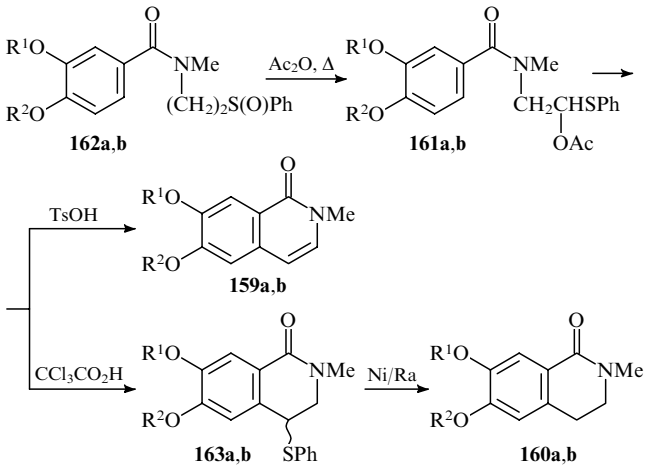
In the synthesis of the key starting compound **155** for the preparation of gibberellic acid, cyclisation also proceeded through the intramolecular coupling of the sulfenium cation with the double bond of compound **156**.[98]

Ishibashi and coworkers used the intramolecular coupling of the sulfenium cation with the C=C bond in the development of a general facile procedure for the synthesis of pyrrolizidine alkaloids [99] and in the construction of the optically active (−)-trachelanthamidine (**157**) from precursor **158**.[100]



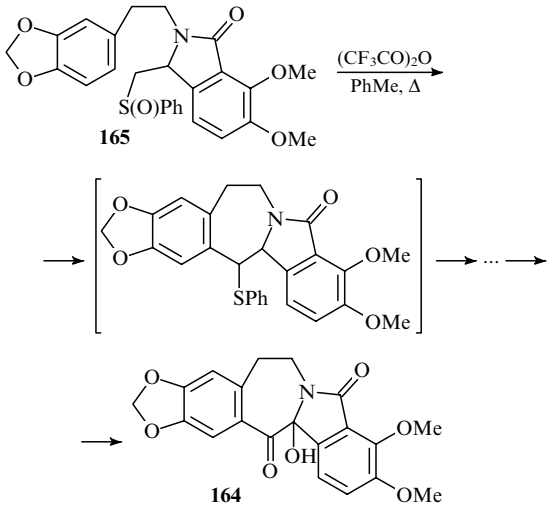
(−)-**157** (30%, *ee* ~ 75%)

Cyclisation can proceed through a Friedel–Crafts-like coupling of the sulfenium cation with the aromatic ring containing activating alkoxy groups. Thus isoquinolone alkaloids, *viz*., dimethoxymethylisocarbostyril (**159a**) and doryanine (**159b**), as well as *N*-methylcorydaldine (**160a**) and oxyhydrastinine (**160b**) were synthesised starting from common precursors **161a**,**b**.[101] The latter were prepared by the reactions of Ac_2O with alkylamides **162a**,**b**. Cyclisation of α-acetoxy sulfides **161a**,**b** under the action of TsOH afforded alkaloids **159a**,**b**, whereas treatment of the compounds **161a**,**b** with CCl_3CO_2H gave rise to intermediates **163a**,**b**, which were subjected to desulfurisation to form the compounds **160a**,**b**.

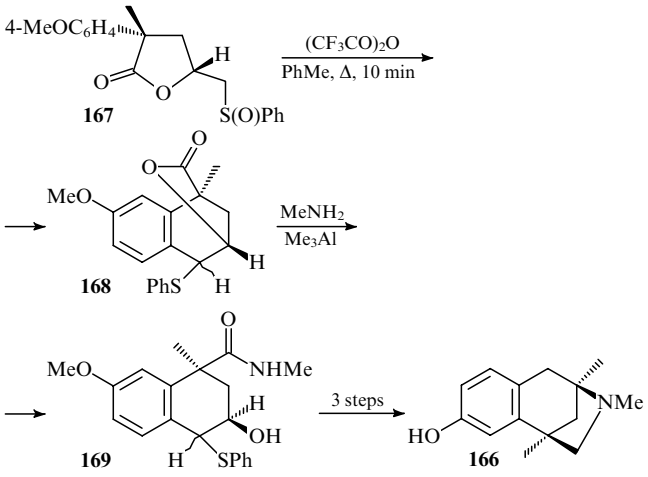


$R^1 = R^2 = Me$ (**a**), $R^1–R^2 = CH_2$ (**b**).

Analogous procedures were used for the preparation of the tetrahydroisoquinoline alkaloid hydrohydrastinine from the corresponding aromatic amino sulfoxide [102] and for the facile synthesis of the polycyclic alkaloid chilenine (**164**),[103] the seven-membered ring of the latter being constructed upon cyclisation of precursor **165**.

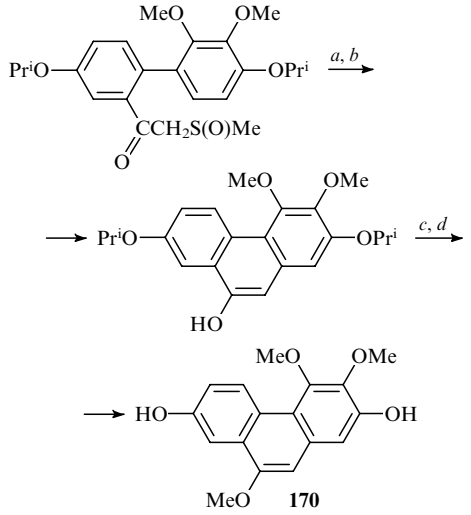


(+)-Aphanorphine (**166**), which exhibited specific optical rotation identical to that of the natural alkaloid, was synthesised [104] from optically active sulfinyl-substituted lactone **167**. The Pummerer reaction was accompanied by cyclisation to yield a



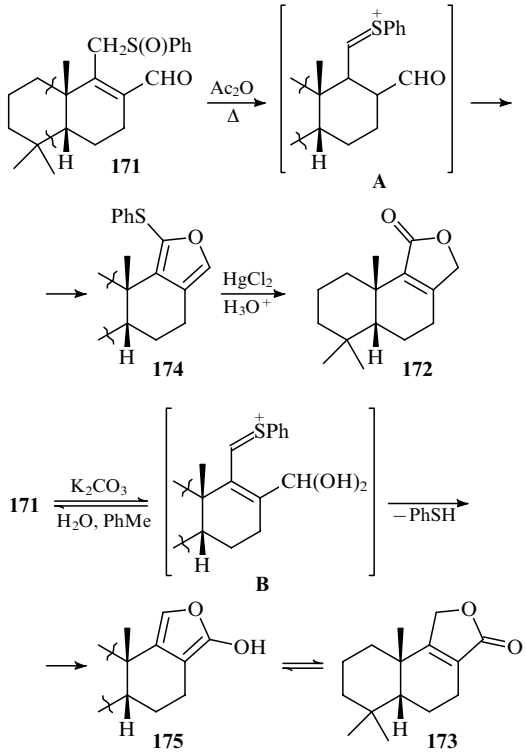
mixture of enantiomeric lactones **168**. The lactone-ring opening was performed under the action of methylamine and the resulting bicyclic intermediate **169** was converted into the target alkaloid **166** in three steps.

The short synthesis of gymnopusin (**170**),[105] which is the first representative of natural phenanthrenes with the oxygen-containing substituent at the C(10) atom, provides yet another example. It should be noted that the results of this synthesis proved the structure of natural gymnopusin.

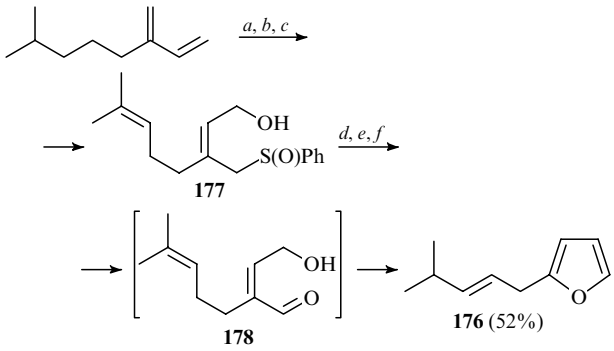


(*a*) $(CF_3CO)_2O$; (*b*) Na/NH_3; (*c*) $(MeO)_2SO_4$, $CaCO_3$; (*d*) BCl_3, CH_2Cl_2.

Oxygen-containing groups can also be involved in intramolecular coupling with the sulfenium cation to form oxacycles. Thus the involvement of the aldehyde group of sulfinyl-substituted α,β-unsaturated aldehyde **171** in cyclisation under the conditions of the Pummerer reaction made it possible to synthesise butenolides isodrimenin (**172**) or confertifolin (**173**) *via* intermediate compounds **174** or **175** containing substituted furan rings.[106, 107] The possible mechanism of this process involves the free (under the action of Ac_2O) or hydrated aldehyde group (upon heating in aqueous dioxane in the presence of K_2CO_3) (transition states **A** and **B**, respectively).

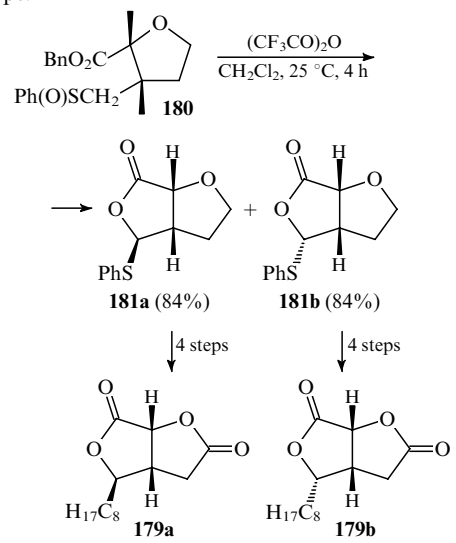


The short one-pot synthesis of furanoterpene perylene (**176**) (a component of insect communication pheromones) was carried out using the sila-Pummerer rearrangement of hydroxy-containing allyl sulfoxide **177**, which was readily derived from the adduct of β-myrcene with benzenesulfinyl chloride.[108] The authors of the cited study believed that the furan ring was generated from intermediate hydroxyaldehyde **178**.

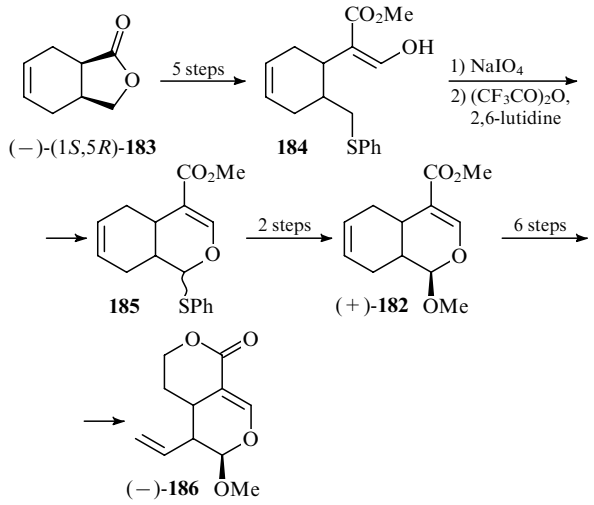


(*a*) PhSOCl, 5 kbar; (*b*) AcOK, AcOH; (*c*) H_2SO_4, MeOH; (*d*) Bu^nLi, −85 °C; (*e*) Me_3SiCl, −85 to 25 °C; (*f*) H_2O, C_5H_{12}.

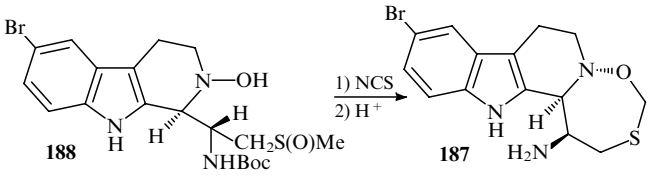
The synthesis of bicyclic lactones **179a**,**b**, which are 3-normethylene analogues of avenaciolide and isoavenaciolide, respectively, provides an example of the involvement of the ester group in cyclisation of the above-mentioned type.[109] The Pummerer reaction of optically active sulfenyl-substituted ester of tetrahydrofuranocarboxylic acid **180** afforded a mixture of diastereomeric bicyclic compounds **181a**,**b** in a ratio of 5 : 1. Both these compounds were converted into the target compounds **179a**,**b** in four steps.



The ring closure can occur with the participation of the OH group. Optically active pyran derivative (+)-**182** serves as the common key intermediate in enantiospecific syntheses of iridoid monoterpenes. This derivative was prepared[110] from bicyclic lactone **183** containing the required chiral centres. The compound **183** was converted into sulfide **184** by reactions in which the latter centres remained intact. Oxidation to sulfoxide and cyclisation, which occurred through the Pummerer reaction involving the enol hydroxy group, gave rise to compound **185** in which the SPh group was replaced by OMe. The methylacetal of iridoid aglycone sweroside **186** was prepared from the compound **182** in six steps.



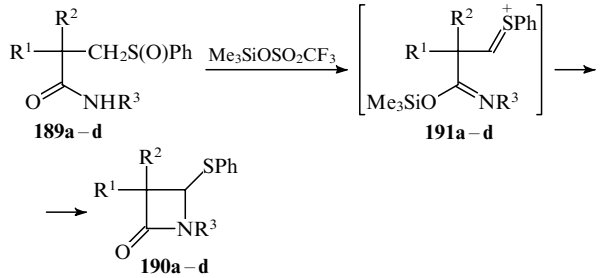
To construct the seven-membered oxathiazepine ring involved in the L-eudistamine molecule (**187**),[111] which shows activity against *Herpes simplex*, the Pummerer reaction was carried out with the use of intermediate **188** in the course of which the sulfenium ion was coupled with the adjacent N—OH group.



NCS is *N*-chlorosuccinimide.

The Pummerer reaction was used in the chemistry of penicilins and related biologically active lactams. This reaction allows one to convert rather inactive sulfoxides of the penam series into penem derivatives exhibiting high biological activities (see, for example, Refs 112 and 113).

The most interesting results were obtained on cyclisation of β-amido sulfoxides in which intramolecular coupling of the sulfenium cations with the nitrogen atom of the imino group occurred to form substituted lactams. Thus Kaneko [114] was the first to perform intramolecular cyclisation in mild conditions of the sila-Pummerer reaction under the action of silyl trifluoromethanesulfonate on β-amidosulfoxides **189a–d** and obtained 4-arylthio-substituted lactams **190a–d**. Kaneko demonstrated that the compound **189c** containing one β-alkyl substituent produced predominantly *cis*-3,4-disubstituted lactam **190c**, whereas enantiomerically pure precursors, *viz*., (*R*)- or (*S*)-**189d**, yielded optically active (*R*)- or (*S*)-lactams **190d** with *ee* ~ 67% (see Ref. 115).‡ These results provided supporting evidence for the assumption as to the correlation between the mechanism of the

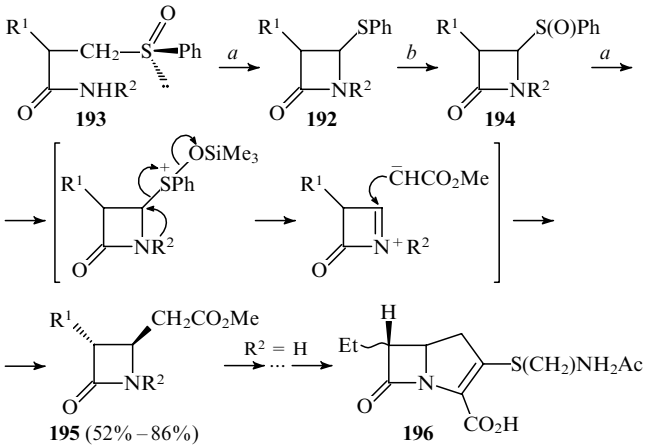


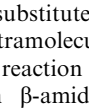
$R^1 = R^2 = Me$, $R^3 = OBn$ (**a**); $R^1 = R^2 = H$, $R^3 = OBn$ (**b**); $R^1 = Me$, $R^2 = R^3 = H$ (**c**); R^1, R^2, $R^3 = H$ (**d**).

‡ Unfortunately, the absolute configurations of the compounds used in the investigation [115] were not established.

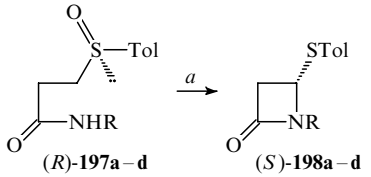
Pummerer reaction (involving sulfenium intermediate **191**) and the first stage of the biosynthesis of lactam antibiotics.

Kita and coworkers made a considerable contribution to the solution of the problems associated with the synthesis of β-lactams. The authors demonstrated that nitrogen heterocycles containing the thio group in the α position can be readily synthesised with the use of versatile silylating agents, *viz*., silyl ketene acetals.[116] This methodology was first examined for the Pummerer cyclisation of ω-amido sulfoxides to obtain intermediates utilised in the synthesis of pyrrolizidine and indolizine alkaloids.[117] Later on, this procedure was extended to the synthesis of β-lactam carbapenems starting from ω-amido sulfoxides.[118] 4-(Arylthio)-azetidin-2-ones **192**, which were prepared by the reactions of methyl(trimethylsilyl) ketene acetal with amido sulfoxides **193**, were used as the starting compounds. The compounds **192** were oxidised to sulfoxides **194**. Under the action of the same ketene acetal, the latter compounds were transformed into *trans*-disubstituted azetidin-2-ones containing ester groups at the C(4) atom [**195**, the ratio *trans*:*cis* = (89–95):(5–11)], which are the key precursors in the synthesis of β-lactam antibiotics, carbapenems. This procedure was employed for the preparation of racemic carbapenem PS-5 (**196**)[119] and β-methylcarbapenem.[120] The enantioselective synthesis of thienamycin was carried out starting from enantiomerically pure β-amido sulfoxide of the type **193**.[121]

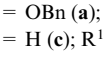


(*a*) , ZnI_2 (cat), MeCN, 20 °C, (*b*) oxidation.

Kita *et al*.[122] demonstrated that (*S*)-(tolylthio)lactams **198a–d** (*ee* 82%–83%) can be prepared in high yields starting from optically active β-amido sulfoxides, for example, from (*R*)-**197a–d**, whereas the corresponding (*R*)-lactams can be prepared with high enantioselectivity from (*S*)-**197a–d**. Hence, the authors of the cited study not only improved the enantioselectivity of this reaction compared to the method proposed by Kaneko,[114] but also proved unambiguously that cyclisation was accompanied by the transfer of the asymmetric centre from the sulfinyl group to the C(4) atom of the lactam ring.

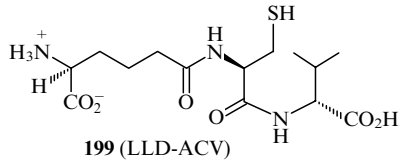


R = MeCHPh (**a**), Bn (**b**), $CHPh_2$ (**c**), 2-$BrC_6H_4CH_2$ (**d**);

(*a*) , ZnI_2 (cat), MeCN, 20 °C.

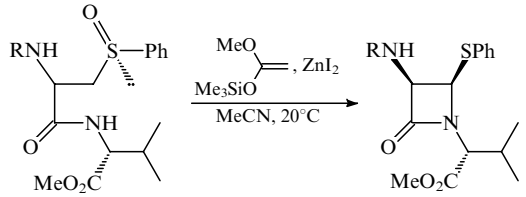
The mechanism of the first stage of the biosynthesis of penicillins consisting in the construction of the *cis*-disubstituted lactam ring by oxidative cyclisation of the tripeptide δ-(L-α-

aminoadipyl)-L-cysteinyl-D-valine (**199**) (LLD-ACV, which was assumed [123] as the direct precursor of isopenicillin N), has long been unknown.



199 (LLD-ACV)

Under the conditions of the sila-Pummerer reaction, amido sulfoxides **200a**,**b**, which contain substituents analogous to those in the compound **199**, were demonstrated [124] to give predominantly *cis*-disubstituted lactams **201a**,**b**. This fact was seemingly evidence in favour of the possible occurrence of the Pummerer sulfenium intermediate in the first stage of the biosynthesis of penicillins.



(*R*)-**200a**,**b** *cis*-**201a**,**b**

R = BnO_2C (**a**); BnO_2CHN (**b**).

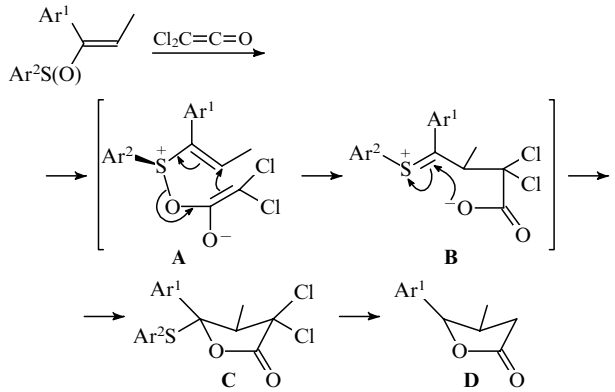


However, the results of the recent investigation performed by Baldwin and coworkers [125] gave conclusive evidence that the biosynthesis of penicillins takes quite a different path. The key stage of this process involves the attack of the Fe-activated enzyme IPNS on the thiol group of LLD-ACV (**199**). When analysing this problem, Shibata and Kita [126] admitted that their strategy [124] has not elucidated the mechanism of the biosynthesis of penicillins, but led to substantial improvement in Pummerer-type asymmetric cyclisation and in the Pummerer reactions of nonracemic sulfoxides. In earlier studies (see the review [14]), high asymmetric induction was not achieved and *ee* was at most 30%.

5. Syntheses involving additive Pummerer reactions

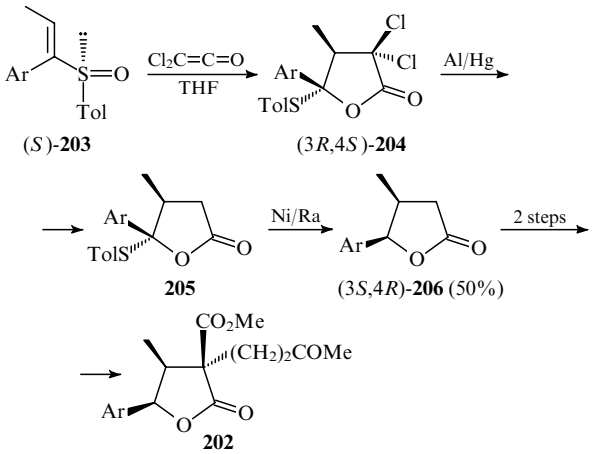
The most interesting results in the field of the asymmetric synthesis of natural compounds were obtained with the so-called additive Pummerer reaction (primarily using the procedure proposed by Marino). These investigations have been considered in detail in a previous review [14] and hence, they are only briefly outlined in the present review .

The mechanism of the additive Pummerer reaction involves the initial attack of electrophilic dichloroketene, which is prepared *in situ* by the reaction of the zinc–copper pair with trichloroacetyl chloride, on the sulfinyl oxygen atom [127, 128] as exemplified below



by disubstituted vinyl sulfoxide. Then the zwitterionic intermediate **A** is converted into the Pummerer sulfenium-cationic intermediate **B** through the [3,3]-sigmatropic rearrangement involving the vinyl C=C bond. The intermediate **B** is stabilised through the intramolecular reaction with the carboxylate anion to give 3-arylthio-5,5-dichloro-γ-lactone **C**.

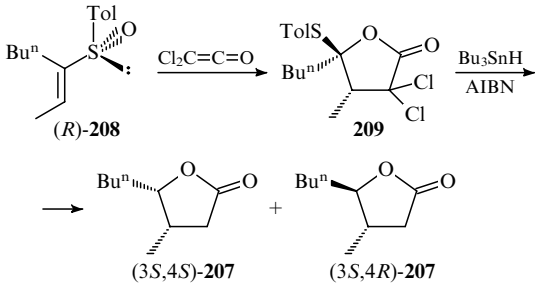
After dechlorination and desulfurisation, 3,4-disubstituted lactone **D** is obtained. The configurations of the chiral centres in the latter compound are completely controlled by the configuration of the chiral sulfinyl group in the initial vinyl sulfoxide. The synthesis of the key precursor of the neolignane porosin **202** starting from (*S*)-(dimethoxyphenyl)prop-1-enyl tolyl sulfoxide (**203**) [128] is an example of the additive Pummerer reaction. Thiosubstituted dichlorolactone **204**, which was obtained in high yield, was dechlorinated with aliminium amalgam to obtain lactone **205**. The latter was desulfurised with freshly prepared Raney nickel at 0 °C. The resulting enantiomerically pure γ-lactone **206** was converted into the target compound (3*S*,4*R*)-**202** in two steps.



(*S*)-**203** (3*R*,4*S*)-**204** **205** (3*S*,4*R*)-**206** (50%) **202**

Ar = 3,4-$(OMe)_2C_6H_3$.

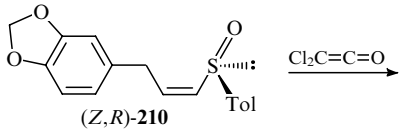
Separation of the dechlorination and desulfation stages is important for a successful synthesis. For example, the synthesis of oak lactones **207** from (*E*,*R*)-3-(tolylsulfinyl)hept-2-ene (**208**),[127] which involved one-step dechlorination–desulfurisation of lactone **209** under the action of tributylstannane, afforded the final product as a mixture of enantiomers.



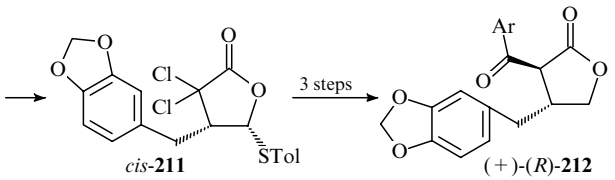
(*R*)-**208** **209** (3*S*,4*S*)-**207** (3*S*,4*R*)-**207**

AIBN is azodiisobutyronitrile.

The additive Pummerer reactions can be performed with various nonracemic α,β-unsaturated sulfoxides. Thus lactone (+)-(*R*)-**212**, which is the key intermediate in the syntheses of a broad spectrum of lignane lactones, was derived from (*Z*,*R*)-piperonylvinyl sulfoxide (**210**) *via* lactone **211**.[129]



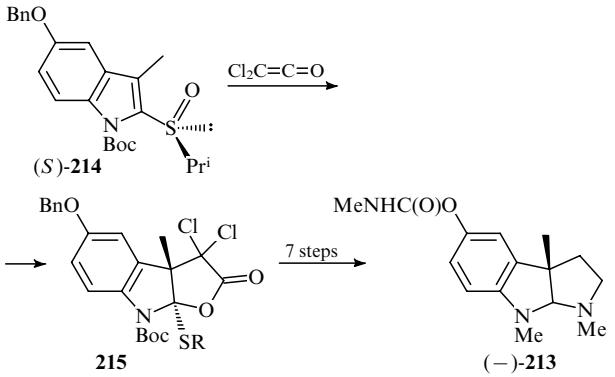
(*Z*,*R*)-**210**



cis-**211** (+)-(*R*)-**212**

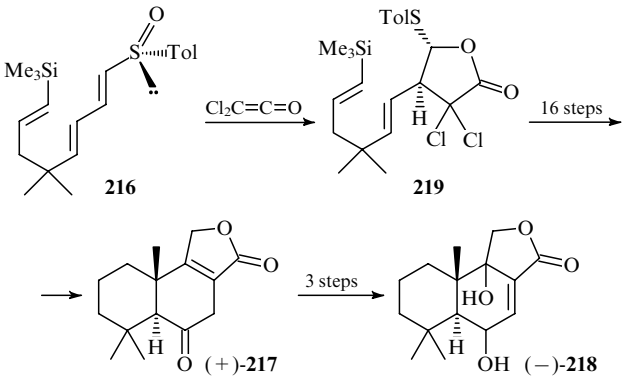
Ar = 3,4,5-$(OMe)_3C_6H_2$.

In the synthesis of (−)-physiostigmine (**213**) (the alkaloid used for the treatment of glaucoma), the reaction pathway was found to depend on the electronic and steric characteristics of the sulfinyl group and on the bulkiness of the protecting group at the nitrogen atom of the initial 2-sulfinylindole.[130] 5-Benzyloxy-3-methyl-2-(isopropylsulfinyl)indole [(*S*)-**214**] containing the protecting Boc group at the nitrogen atom proved to be the starting compound of choice. The reaction involving the above reagent proceeded through the tricyclic adduct with dichloroketene **215** to yield (−)-physiostigmine [(−)-**213**] exhibiting specific optical rotation identical to that of the natural compound.



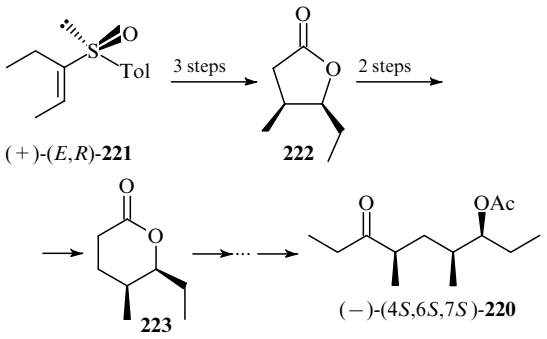
(*S*)-**214** **215** (−)-**213**

Sulfinyl-substituted triene **216** is an example of polyunsaturated sulfinyl precursors. This compound was utilised in the synthesis[131] of drimane-type sesquiterpenoids (+)-fragolide (**217**) and (+)-pereniporin (**218**). The process began with the addition of dichloroketene and the construction of *p*-tolylthiodichloro-γ-lactone fragment in compound **219**. The subsequent multistage transformation involved dechlorination and desulfurisation along with cationic cyclisation with the participation of the vinylsilane group.



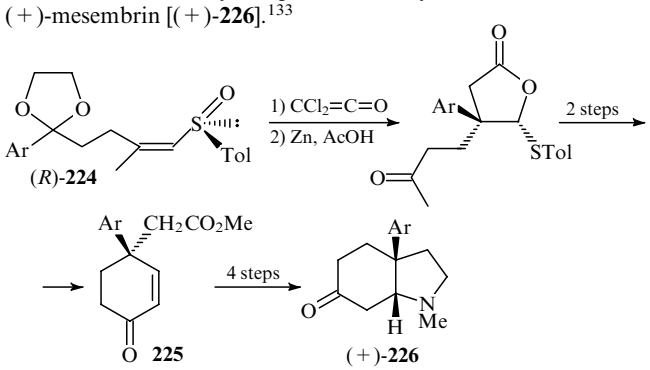
216 **219** (+)-**217** (−)-**218**

The advantages of the additive Pummerer reaction are the possibile subsequent transformations of primary γ-lactones, which can be used in enantioselective syntheses of compounds with various structures. For example, in the facile synthesis of the pheromone with the linear structure, *viz*., (7)-(4*S*,6*S*,7*S*)-serricornin (**220**),[132] starting from (*E*,*R*)-3-(tolylsulfinyl)pent-2-ene (**221**), γ-lactone **222** was converted into the key intermediate, *viz*., 4,5-disubstituted valerolactone **223**, with retention of the chiral centres.



(+)-(*E*,*R*)-**221** **222** **223** (−)-(4*S*,6*S*,7*S*)-**220**

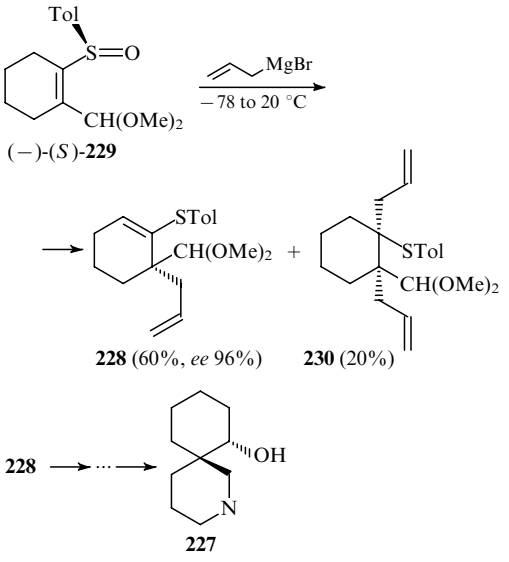
The product of the Pummerer reaction of β,β-disubstituted vinyl disulfoxide (*R*)-**224** with dichloroketene was dechlorinated *in situ* and then converted into 4,4-disubstituted cyclohexenone **225**, which was the key compound in the synthesis of the alkaloid (+)-mesembrin [(+)-**226**].[133]



(*R*)-**224** **225** (+)-**226**

Ar = 3,4-$(OMe)_2C_6H_3$.

Marino's procedure does not exhaust the synthetic possibilities of the additive Pummerer reaction. Iwata *et al.*[134] found that α,β-unsaturated sulfoxides, including cyclic sulfoxides, underwent the Pummerer-like reaction under the action of allylmagnesium bromide and applied this reaction to the enantioselective total synthesis of (−)-sibirine (**227**).[135] The monoallylation product **228** of cyclohexene sulfoxide (−)-(*S*)-**229**, which was readily separated from diallylated compound **230**, already contained the chiral quaternary carbon atom characteristic of (−)-sibirine **227**. The latter was prepared by a multistage transformation; its specific optical rotation corresponded to that of the natural alkaloid.



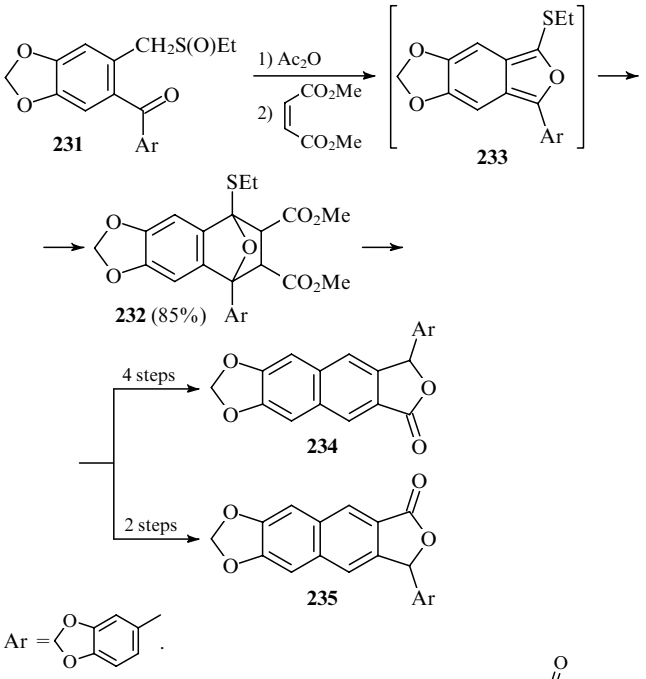
(−)-(*S*)-**229** **228** (60%, *ee* 96%) **230** (20%) **227**

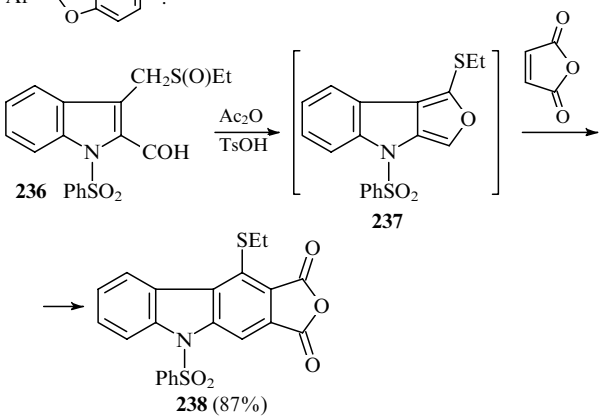
An analogous methodology was employed in the facile synthesis of the spirocyclic alkaloid (−)-perhydrohistrionicotoxin, which also contains the quaternary chiral centre.[136]

6. Syntheses based on cascade processes involving the Pummerer reaction

Examples of application of cascade processes involving the Pummerer reaction to syntheses of natural products were considered above. It should be noted that Padwa and coworkers have obtained particularly impressive results in recent years.[12, 137–139]

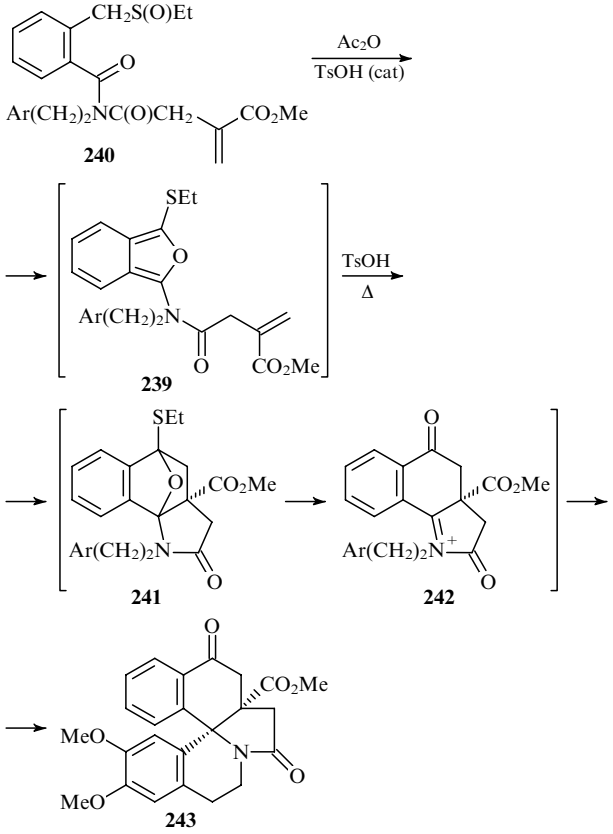
The tandem use of the Pummerer and Diels–Alder reactions made it possible to develop a versatile procedure for the construction of polycyclic molecules. Thus treatment of sulfinylmethyl-substituted diaryl ketone **231** with acetic anhydride and then with dimethyl maleate afforded [137] adduct **232** of the initially formed Pummerer-reaction product, *viz*., α-ethylthioisobenzofuran **233**, in high yield. Simple transformations of the adduct **232** gave rise to natural lactones of the naphthalene series, *viz*., taiwanin **234** and justicidin E **235**.





Kappe and Padwa [138] used *o*-formyl-substituted indole sulfoxide **236** as the starting compound. After the Pummerer reaction, the primary cyclisation product **237** was treated (without isolation) with maleic anhydride to obtain carbazole derivative **238** in high yield. This method can be used for the construction of natural carbazoles, for example, of ellipticine.[12]

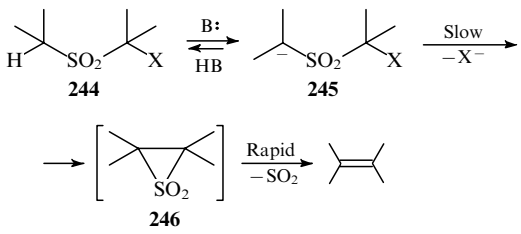
The one-pot synthesis of the five-membered cyclic skeleton of the alkaloid erythrinane is a particularly elegant cascade procedure.[139] For this purpose, compound **239**, which was derived from polysubstituted aromatic sulfoxide **240** under the action of Ac_2O in the presence of a catalytic amount of TsOH, was heated with an additional amount of TsOH. The process involved an intramolecular Diels–Alder reaction giving rise to adduct **241** followed by the oxabicycle opening yielding product **242** and, finally, cyclisation of the latter involving the *N*-acyliminium ion to give 3,4-benzoerythrinane **243** (the total yield was 70%). Padwa *et al*.[139] noted that the tandem process proceeded more or less readily depending on the reaction conditions. The best results were obtained with the use of Ac_2O in toluene in the presence of catalytic amounts of TsOH, which efficiently suppressed the formation of acetoxy sulfide (a normal product of the Pummerer reaction).



Ar = 3,4-$(MeO)_2C_6H_3$.

IV. Use of the Ramberg–Bäcklund rearrangement for the insertion of C=C bonds

The Ramberg–Bäcklund rearrangement (see the reviews [3, 141, 142]), which is the oldest reaction [140] of all known sulfonyl rearrangements, proceeds with the participation of sulfones of type **244** containing a substituent X in the α position as substrates. The substituent can be readily removed in the anionic form once carbanion **245** is generated through α-deprotonation. The mechanism of the process was confirmed by the results of numerous kinetic studies (see the review [3]).



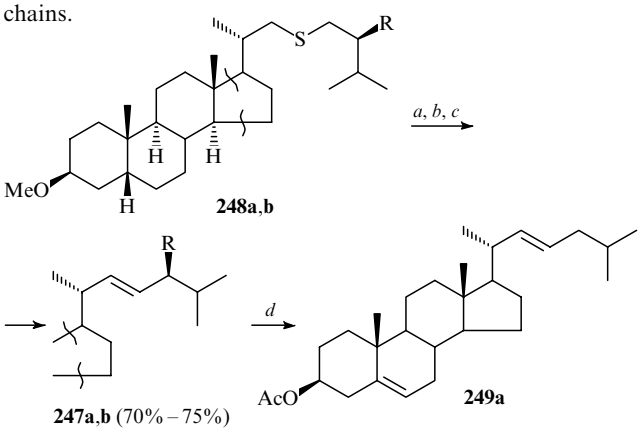
The reaction gives rise to the C=C bond in the strictly fixed site of the molecule through the formation of episulfone **246**, which readily eliminates SO_2. The involvement of the intermediate **246** in the rearrangement was long judged from indirect evidence. Recently, episulfones, which are stable only below −20 °C, were prepared by the reactions of Bu^tOK with some highly reactive α-iodosulfones primarily of the thiolane 1,1-dioxide series.[143]

The Ramberg–Bäcklund reactions are traditionally carried out with the use of α-Cl and α-Br-substituted sulfones as the starting compounds. Halogenation with soft reagents, for example, with *N*-halogenosuccinimides, is often performed at the stage of the initial sulfide before its oxidation to sulfone.

Meyers *et al.*[144] devised a convenient modification of this reaction, which allowed the one-pot preparation of α-chlorosubstituted sulfone and its subsequent rearrangement. In this version, sulfone was treated with powdered KOH in CCl_4–Bu^tOH. Unfortunately, this reaction is sometimes complicated by side processes, such as excessive halogenation or formation of chlorocarbene. To prevent these side reactions, Chen *et al.*[145] used KOH adsorbed on Al_2O_3 in Bu^tOH in the presence of CBr_2F_2, which does not generate carbenes.

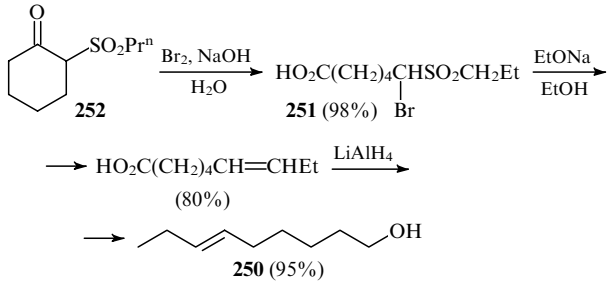
The Ramberg–Bäcklund reaction is actually a versatile procedure for the construction of the C=C bond; the configuration of the latter depends both on the structure of the initial sulfone and the reaction medium; in open-chain compounds, the resulting bond generally has the *E* configuration. The synthetic importance and applications of this reaction were covered in reviews.[141, 142, 146] However, the data on use of this process in syntheses of natural compounds is systematised for the first time in the present review.

Examples of the construction of isolated C=C bonds in open-chain natural compounds or in linear fragments of more complex molecules are considered below. Thus the Bu^tOK-induced rearrangement of α-chlorosulfone was used in the highly *E*-stereoselective synthesis of Δ^{22}-unsaturated steroids of types **247a**,**b** starting from sulfides **248a**,**b**, which were prepared based on 3α,5α-cyclo-6β-methoxypregnane.[147] The structure of the compound **247a** was proved by its conversion into the known steroid **249a**. This synthesis was carried out in view of the fact that many exotic steroids from plants and animals contain unsaturated side chains.

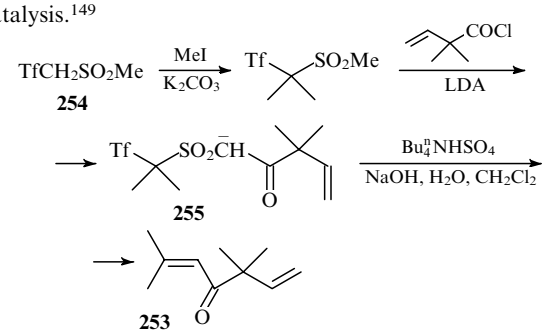


R = H (**a**), Et (**b**); (*a*) NCS, CCl_4; (*b*) MCPBA, $NaHCO_3$; (*c*) 3 equiv. of Bu^tOK; (*d*) R = H, $Zn(OAc)_2$, AcOH.

Non-6-en-1-ol (**250**), which is a pheromone of Mediterranean fruit flies,[148] was synthesised with the use of the rearrangement of linear α-bromosulfone **251**, which was prepared by the reaction of 2-(*n*-propylsulfonyl)cyclohexanone (**252**) with bromine and NaOH. This reaction provided the basis for a general procedure for the synthesis of α-bromosulfones. The scheme of the synthesis ended in reduction of the carboxyl group to the alcoholic group in the initially formed non-6-enoic acid.

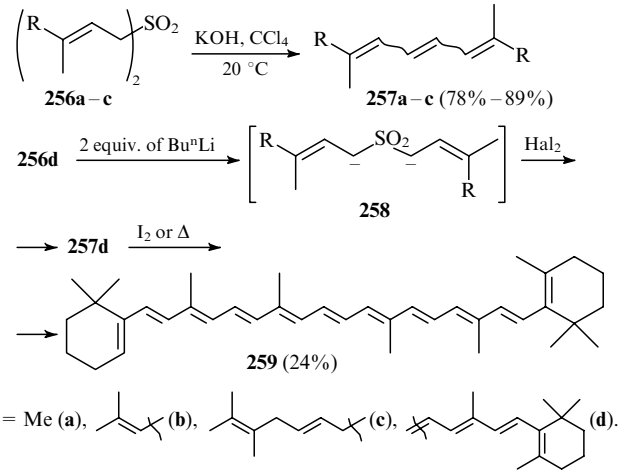


The short synthesis of natural artemisia ketone (**253**) (the total yield was 86%) starting from methyl trifluoromethylsulfonylmethyl sulfone (**254**) demonstrated that the triflate fragment is an excellent leaving group in the Ramberg–Bäcklund reaction. The rearrangement of ketosulfone **255**, which was prepared by alkylation followed by acylation of the sulfone **254**, was carried out at room temperature under conditions of phase transfer catalysis.[149]



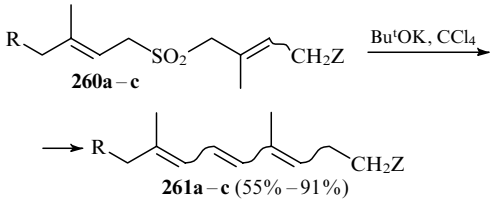
Tf = CF_3SO_2; LDA is lithium diisopropylamide.

Polyenes, including those containing conjugated C=C bonds, can be constructed by the Ramberg–Bäcklund rearrangement starting from substituted diallyl sulfones. In an early study,[150] sulfones **256a**–**d** were used for this purpose. It appeared that treatment of the sulfones **256a**–**c** with KOH and CCl_4 at room temperature afforded mixtures of stereoisomeric polyenes **257a**–**c** in high yields, whereas the retinyl sulfone **256d** did not enter into the reaction under these conditions. To prepare a mixture of polyenes from the latter compound, it was successively treated with butyllithium (it was assumed that dianion **258** was formed) and halogen. Isomerisation of a mixture of the compounds **257d** under the action of iodine or upon heating gave rise to natural all-*trans*-β-carotene (**259**).



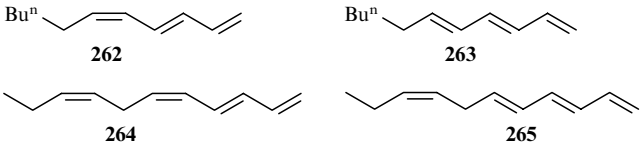
R = Me (**a**), (**b**), (**c**), (**d**).

Later, mixtures of substituted polyisoprenoids **261a**–**c** were obtained from diallyl sulfones **260a**–**c** containing polar substituents Z according to Meyers's procedure.[151]

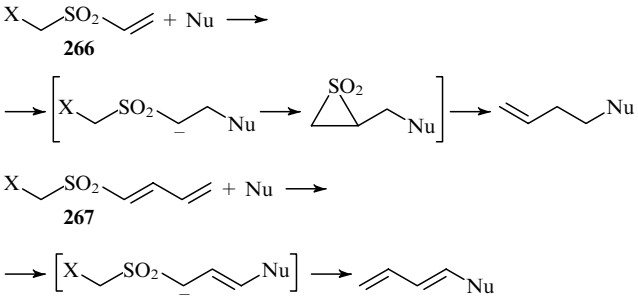


R = H, ; Z = OEt (**a**), CH_2COMe (**b**), $CH_2C(Me)(OH)CH=CH_2$ (**c**).

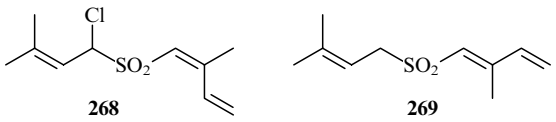
The synthesis of natural undecatrienes **262** and **263** and undecatetraenes **264** and **265** (the compounds **262** and **263** find use in perfumery) from the corresponding diallyl sulfones according to Meyers's procedure [152] also afforded mixtures of geometric isomers.



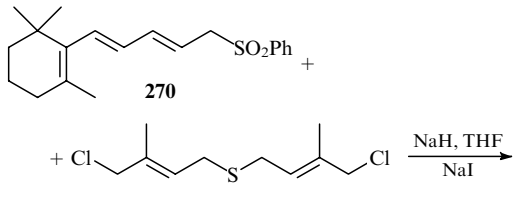
Burger *et al.* [153] failed to elaborate the stereoselective synthesis by decreasing the basicity of the reaction medium through the generation of the required anion by the addition of the sulfinate anion to α-halogenovinyl- (**266**) or butadienyl sulfones **267** [the so-called MIRB process (Michael Induced Ramberg–Bäklund)]. Starting from sulfones **268** and **269**, this procedure also yielded mixtures of stereoisomeric isoprenoinds.[153] The authors of the cited studies [150, 151, 153] did not examine the mechanisms of these processes. Hence, the stage at which *Z*-bonds are formed in the syntheses starting from all-*trans* compounds remains unknown.

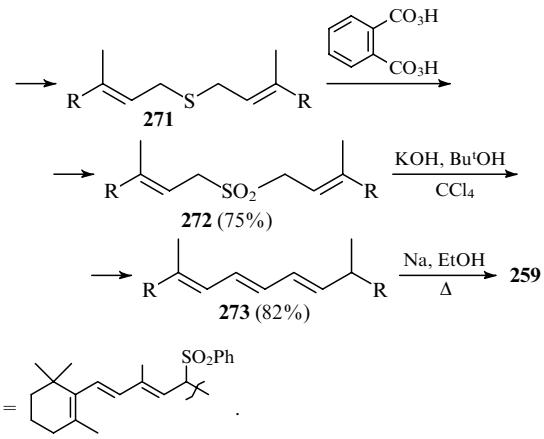


Nu = SO_2Ph; X = Cl, Br.

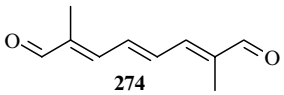


Recently, the problem of the construction of all-*trans*-polyene through the Ramberg–Bäcklund rearrangement has been successfully solved [154] in the synthesis of natural β-carotene **259**, which (along with its analogues) is finding increasing use as a food ingredient possessing simultaneously chemotherapeutic activity against some varieties of cancer. The scheme of the synthesis was based on alkylation of readily accessible sulfone **270** with dichlorodiallyl sulfide, which was prepared from isoprene in four steps. In the alkylation stage, NaI was added to the reaction mixture to form *in situ* more reactive iodide. Then intermediate **271** was converted into sulfone **272** and the latter was subjected to the rearrangement into compound **273** under very mild conditions (oxidation with peroxyphthalic acid formed *in situ* and Meyers's rearrangement under an atmosphere of argon). The sulfonyl groups were removed from the intermediate **273** by reduction. Starting from isoprene, β-carotene **259** (all-*trans*) was obtained in a total yield of 13%. Judging from the results obtained in the cited study, the Ramberg–Bäcklund rearrangement of the sulfone **272** gave rise exclusively to the (*E*)-C=C bond. The presence of sulfonyl groups in the radical R prevents isomerisation of the already existing (*E*)-C=C bonds.



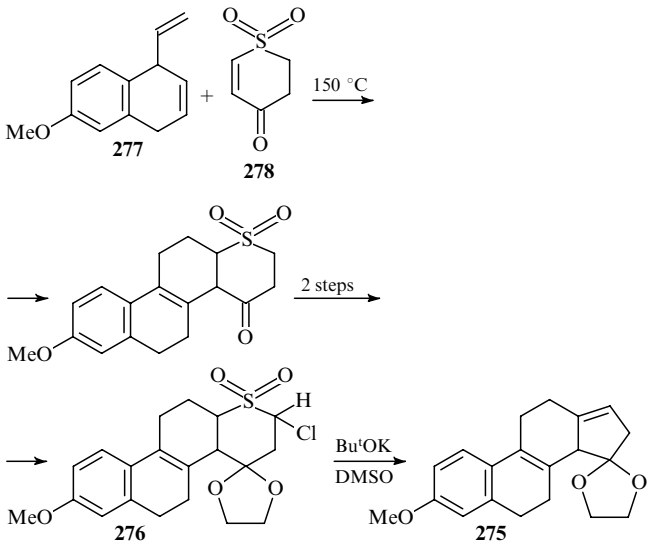


This procedure can also be used for the construction of other natural all-*trans*-polyenes. Thus, this procedure was employed [154] for the preparation of key intermediate **274** in the synthesis of carotenoids by the Wittig method.

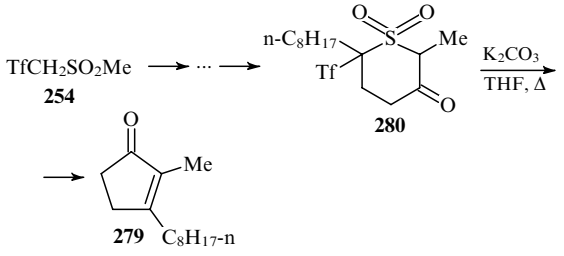


In his review, Paquette [141] emphasised that the construction of unsaturated rings of different sizes is one of the problems, which can be solved by applying the Ramberg–Bäcklund rearrangement. Examples of the use of this rearrangement in the synthesis of natural compounds are the preparation of both unsaturated carbocycles and oxygen-containing heterocycles.

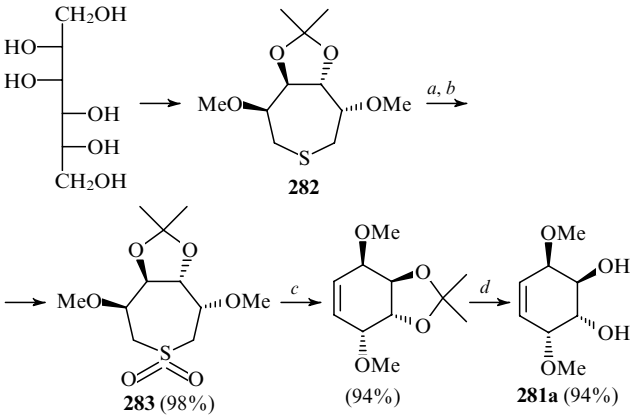
In the study,[155] the cyclopentene ring in steroid **275** was formed starting from tetracyclic α-chloro-substituted sulfone **276**, which was synthesised in two steps from the adduct of diene **277** and 2,3-dihydrothiopyran-4-one *S*,*S*-dioxide (**278**).



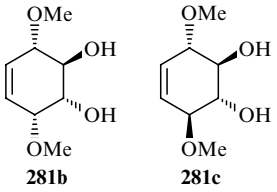
Dehydrojasmone **279** was synthesised starting from (trifluoromethylsulfonylmethyl)sulfone **254**. The latter compound was converted into cyclic ketosulfone **280** containing the triflate group, which was eliminated to give the target product **279**.[156]



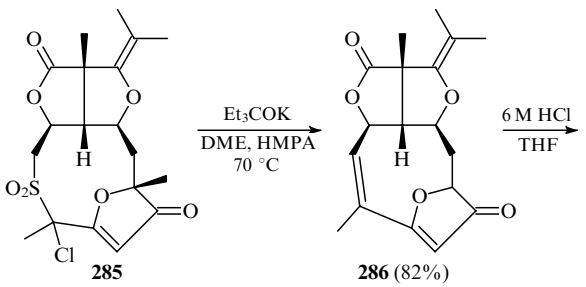
An interesting procedure was developed [157, 158] for the synthesis of enantiomerically pure cyclohexene alcohols of type **281a**–**c**, *viz*., conduritols containing four chiral alcoholic centres. These compounds are inhibitors of glycosidases and also serve as the key compounds in the preparation of agents, which show promise for AIDS treatment. These alcohols were synthesised starting from sugar derivatives containing the required chiral centres. The latter compounds were converted into thiepanes whose oxidation to sulfones followed by the rearrangement under Meyers's conditions gave rise to conduritols in high yields. This procedure was used for the preparation of (−)-conduritol E derivative (**281a**) [157] from Δ-mannitol through thiepane **282** and its sulfone **283**. All reactions proceeded in quantitative yields, the starting chiral centres remaining intact. Later, this procedure was extended [158] to the synthesis of derivatives of (−)-conduritol F (**281b**) and (+)-conduritol B (**281c**) starting from Δ-sorbitol and L-iditol, respectively. Conduritols (−)-F and (−)-E containing four unprotected hydroxy groups were obtained in 83% and 79% total yields, respectively, using readily removable benzyl instead of methyl as protecting groups.[158]

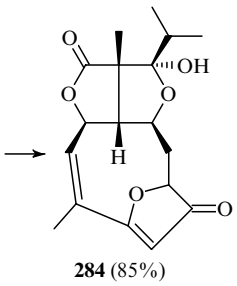


(*a*) MCPBA, 0 °C; (*b*) $Na_2S_2O_5$, CCl_4, 20 °C; (*c*) KOH, Bu^tOH, CCl_4, H_2O, 20 °C; (*d*) 0.1 N H_2SO_4.

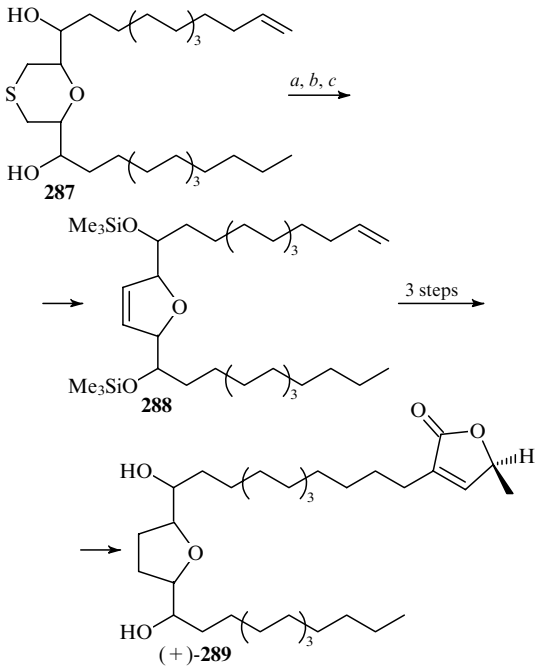


In the synthesis of the strained nine-membered oxygen-containing ring of (+)-eremantholide (**284**), which exhibits antitumour activity *in vitro*, the final stages were carried out with the use of α-chloro-substituted sulfone **285**.[159] The latter was unstable in the presence of strong bases due to which the rearrangement was performed under the action of the weakly basic alkoxide of 3-ethylpentan-3-ol. Under these conditions, intermediate **286** was obtained in quantitative yield and was converted into the final product in one step.



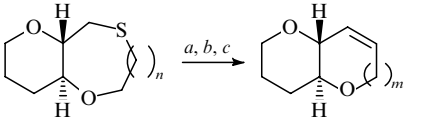


Meyers's method was successfully used [160] for the conversion of 1,4-oxathiane fragment of compound **287** (after oxidation of sulfide sulfur to sulfonyl sulfur) into the dihydrofuran fragment of compound **288**. The latter compound was converted in three steps into acetogenin (+)-solamine (**289**). This procedure is applicable to syntheses of other acetogenins possessing various biological activities.

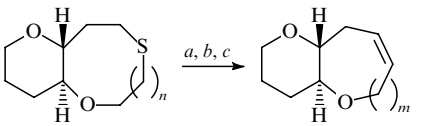


(*a*) MCPBA; (*b*) Me_3SiCl, Et_3N; (*c*) Bu^tOK, Bu^tOH, CCl_4.

In the course of the studies aimed at preparing polycyclic ciguatoxin, an efficient procedure was devised [161] for the preparation of dioxabicyclic systems. For this purpose, *trans*-fused bicyclic intermediates **290a**,**b** and **291a**,**b** generated by thioannelation were successively subjected to α-chlorination, oxidation to sulfones and rearrangement without isolation of intermediates. The resulting oxabicyclic compounds **292a**,**b** and **293a** containing



n = 2 (**290a**), 3 (**290b**); m = 1 (**292a**), 2 (**292b**).



n = 3 (**291a**), 4 (**291b**); m = 2 (**293a**), 3 (**293b**).
(*a*) NCS, CCl_4; (*b*) MCPBA; (*c*) Bu^tOK, THF.

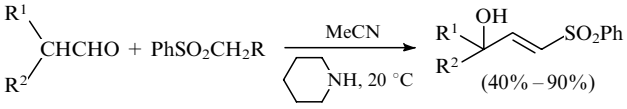
the newly formed six-, seven or eight-membered rings occurred as individual *trans*-fused molecules. Only compound **293b** with the nine-membered ring was obtained as a mixture of *cis* and *trans* isomers.

V. Conclusion

The data surveyed in the present review show that rearrangements of sulfoxides and, to a lesser extent, of sulfones find many varied applications in the total syntheses of natural compounds, including enantioselective processes.

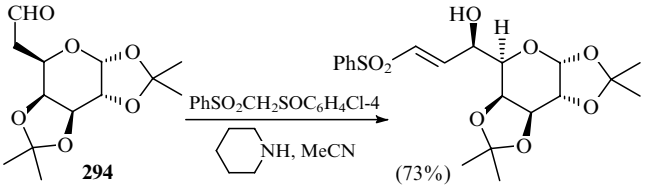
In the coming years, one would expect the wider use of cascade processes involving these rearrangements.

The extension of tandem processes, for example, the Diels–Alder reaction followed by the sulfoxide–sulfenate rearrangement involving enantiomerically pure sulfinyl-substituted dienes, to the synthesis of natural compounds has considerable promise.[162] The SPAC cascade process, which has been developed recently (by two research groups [163, 164] virtually simultaneously) and which provides a route to the synthesis of γ-hydroxy-α,β-unsaturated sulfones, can find application in functionalisation of natural compounds.

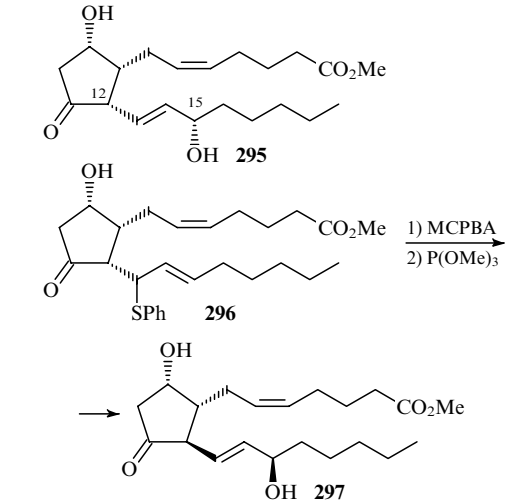


R = 4-MeC_6H_4, 4-ClC_6H_4.

In particular, Trost and Grese [164] demonstrated that this process occurred under very mild conditions, which allow the successful use of even such a labile compound, as galactose derivative **294**, as an aldehyde component.



However, the reagents used in a particular stage of the tandem process must be chosen with caution. Thus attempt was made to synthesise the ethyl ester of 15-D_{2c}-isoprostane (**295**) (which belongs to compounds structurally related to prostaglandins) starting from sulfide **296** through the Mislow–Evans rearrangement.[165] Generally (see Refs 23–26), the oxidation–rearrangement tandem processes give rise to the 'lower branch' of the product with correct stereochemistry. However, the last-mentioned process afforded C(12)-,C(15)-epimer **297** rather than isoprostane **295**.

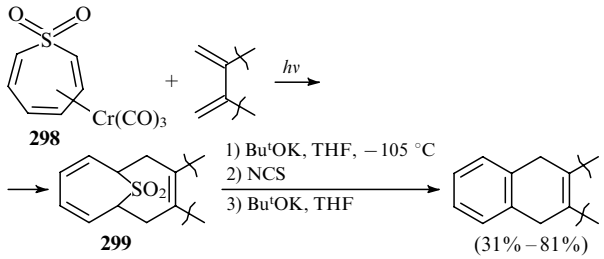


The authors believed that epimerisation was preceded by rearrangement under the action of residual amounts of *m*-chloroperbenzoic acid.

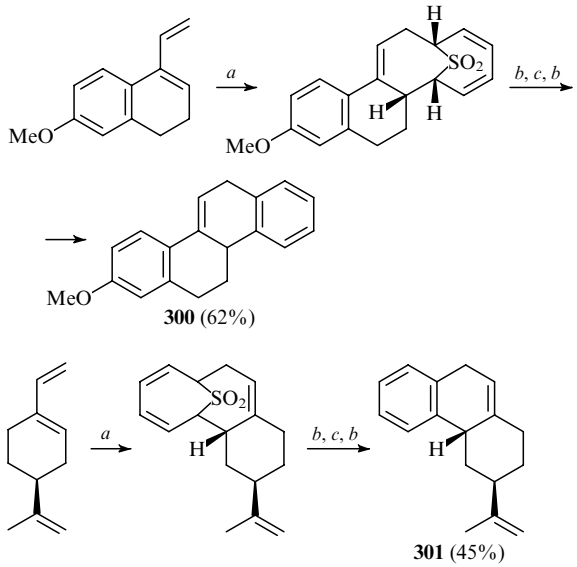
As for the Pummerer reaction, one would expect new examples of its application to the asymmetric synthesis of natural compounds both involving novel efficient inducing agents (for example, vinyl esters containing the ethoxy group in the α position proposed in recent years [166]) and by designing new reagents for the additive Pummerer process. Investigations carried out by Padwa and coworkers with the aim of devising new cascade processes hold much promise. For example, the tandem use of the Pummerer reaction and subsequent intramolecular [3 + 2]-cycloaddition has been applied.[167]

One would expect that the Ramberg–Bäcklund reaction will continue in use for the construction of unsaturated natural cyclic molecules.

It is likely that the recent cascade process,[168] which readily affords benzoannelated polycyclic molecules, will be extended to the synthesis of natural compounds. The process starts with the photochemical [6π + 4π]-cycloaddition of various dienes to the chromium tricarbonyl complex of 1,1-thiepin dioxide (**298**) and ends in the Ramberg–Bäcklund rearrangement of the resulting adduct **299**.



The characteristic feature of this process is that it makes possible both rapid assembly of the final polycyclic product (for example, in the synthesis of compound **300**) and the stereospecific synthesis (for example, in the synthesis of compound **301**) with the use of chiral nonracemic dienes.



(*a*) **298**, *hv*; (*b*) ButOK, THF, −105 °C; (*c*) *N*-iodosuccinimide, THF.

The investigations published in the very recent past [169–175] (after the present review had already been written) demonstrated that the rearrangements of sulfones and sulfoxides continue in use in syntheses of natural products. The investigations of Padwa and coworkers devoted to the application of cascade Pummerer cyclisation–deprotonation–cycloaddition processes to syntheses of alkaloids were summarised in a review.[169] Intramolecular Pummerer cyclisation was used as the key stage in the synthesis of bicyclic precursors for anthracyclinones.[170] The Pummerer

reaction was employed[171] in the stereoselective synthesis of 4β-thioribonucleosides. The procedure for the construction of the oxathiazepine ring using the modified Pummerer cyclisation[111] was extended to the synthesis of (−)-eudistamines C, E, F, K and L.[172]

Other rearrangements were used more rarely. Thus the Mislow–Evans reaction was employed in the synthesis of enantiomerically pure diastereomers of 8-F_{2t} isoprostane.[173] The Ramberg–Bäcklund reaction was utilised in the syntheses of (+)-estradiol[174] and exocylcic cisoid dienes, which served as the starting compounds for the preparation of natural substances.[175]

In conclusion, it should be emphasised that rearrangements of sulfoxides and sulfones other than the above-considered three processes were also described in the literature (see, for example, the reviews [2, 3]). There is still room for progress in the applications of these reactions to syntheses of natural molecules. This review will hopefully be found interesting and useful by chemists and contribute to progress in this field of chemistry.

References

1. E N Prilezhaeva *Usp. Khim.* **69** 403 (2000) [*Russ. Chem. Rev.* **69** 367 (2000)]
2. S Braverman, in *The Chemistry of Sulfones and Sulfoxides* (Eds S Patai, Z Rappoport, C J M Stirling) (New York: Wiley, 1988) p. 717
3. S Braverman, in *The Chemistry of Sulfones and Sulfoxides* (Eds S Patai, Z Rappoport, C J M Stirling) (New York: Wiley, 1988) p. 665
4. R Pummerer *Berichte* **43** 1401 (1910)
5. L Horner, P Kaiser *Liebigs Ann. Chem.* **626** 19 (1959)
6. L Horner *Liebigs Ann. Chem.* **631** 198 (1960)
7. S Oae, T Numata, in *Isotopes in Organic Chemistry* Vol. 5 (Eds E Bunce, C C Lee) (New York: Elsevier, 1980) p. 45
8. S Oae, T Numata, T Ioshimura *The Chemistry of Sulphonium Group* (Eds C J M Stirling, S Patai) (New York: Wiley, 1981)
9. A M Moiseenkov, V A Dragan, V V Veselovskii *Usp. Khim.* **60** 1255 (1991) [*Russ. Chem. Rev.* **60** 643 (1991)]
10. O De Lucci, U Miotti, G Modena *Org. React.* **40** 147 (1991)
11. D S Grierson, H P Husson, in *Comprehensive Organic Synthesis* Vol. 6 (Eds B M Trost, J E Fleming) (Oxford: Pergamon Press, 1991) p. 910
12. A Padwa, D E Gunn Jr, M H Osterhout *Synthesis* 1353 (1997)
13. E N Prilezhaeva, in *Poluchenie i Svoistva Organicheskikh Soedinenii Sery* (Preparation and Properties of Organic Compounds of Sulfur) (Ed. L I Belen'kii) (Moscow: Khimiya, 1998) p. 209
14. M S Carreño *Chem. Rev.* **95** 1717 (1995)
15. P Bickart, F W Carson, J Jacobus, E G Miller, K Mislow *J. Am. Chem. Soc.* **90** 4869 (1968)
16. D A Evans, G C Andrews *Acc. Chem. Res.* **7** 147 (1974)
17. Y Masaki, K Sakuma, K Kaji *Chem. Pharm. Bull.* **33** 2531 (1985)
18. D K Jones-Hertzog, W L Jorgensen *J. Org. Chem.* **60** 6682 (1995)
19. T Sato, J Otera, H Nozaki *J. Org. Chem.* **54** 2779 (1989)
20. T Sato, J Otera *Tetrahedron Lett.* **35** 6701 (1994)
21. R W Hoffmann *Angew. Chem., Int. Ed. Engl.* **18** 563 (1979)
22. D R Evans, T C Crawford, T T Fujimoto, A C Thomas *J. Org. Chem.* **39** 3176 (1974)
23. D F Taber *J. Am. Chem. Soc.* **99** 3513 (1977)
24. K Kondo, T Umemoto, K Yako, D Tunemoto *Tetrahedron Lett.* 3927 (1978)
25. K Kondo, T Umemoto, Y Takahatake, D Tunemoto *Tetrahedron Lett.* 113 (1977)
26. K Bannai, T Toru, T Oba, T Tanaka, N Okamura, K Watanabe, S Kurozumi *Tetrahedron Lett.* **22** 1417 (1981)
27. J G Miller, W Kurz, K G Untch, G Stork *J. Am. Chem. Soc.* **96** 6774 (1974)
28. K Mori, H Ueda *Tetrahedron* **37** 2581 (1981)
29. Y Masaki, K Hashimoto, K Kaji *Tetrahedron Lett.* 5123 (1978)
30. Y Masaki, K Hashimoto, K Sakuma, K Kaji *Chem. Pharm. Bull.* **32** 3952 (1984)
31. Y Masaki, K Hashimoto, K Kaji *Chem. Pharm. Bull.* **32** 3959 (1984)
32. E Morera, G Octar *J. Org. Chem.* **48** 119 (1983)
33. K Tanikaga, Y Nozaki, T Tamura, A Kaji *Synthesis* 134 (1983)
34. E J Corey, P Carpino *Tetrahedron Lett.* **31** 7555 (1990)
35. J Nokami, M Ohkura, Y Dan-oh, Y Sakamoto *Tetrahedron Lett.* **32** 2409 (1990)
36. G Solladie, C Gerber *Synlett* 449 (1992)
37. J Nokami, T Taniguchi, S Gomyo, T Kakihara *Chem. Lett.* 1103 (1994)
38. K Neuschuetz, J Velker, K Neier *Synthesis* 227 (1998)
39. D A Evans, C A Bryan, C L Sims *J. Am. Chem. Soc.* **94** 2891 (1972)
40. G H Posner, A Haces, W Harrison, C M Kinter *J. Org. Chem.* **52** 4836 (1987)
41. V V Veselovskii, Z G Makarova, A I Lutsenko, N A Shapiro, V M Zhulin, A M Moiseenkov *Izv. Akad Nauk SSSR, Ser. Khim.* 810 (1988) [a]
42. M C Carreño, M B Cid, J L Garcia-Ruano, M Santos *Tetrahedron Lett.* **39** 1405 (1998)
43. M Kodama, K Shimada, S Ito *Tetrahedron Lett.* 2763 (1977)
44. B M Trost, J H Rigby *J. Org. Chem.* **43** 2938 (1978)
45. J-P Corbet, C Bezra *J. Org. Chem.* **46** 1141 (1981)
46. P J Parsons, M Stefinovic *Synlett* 931 (1993)
47. V van Reenen, K P Shephard *J. Org. Chem.* **44** 1582 (1979)
48. G Neef, U Eder, A Seeger *Tetrahedron Lett.* **21** 903 (1980)
49. A Haces, M G A van Kruchten, W H Okamura *Tetrahedron Lett.* **23** 2707 (1982)
50. H J Altenbach, H Soike *Tetrahedron Lett.* **27** 1561 (1986)
51. R A Gibbs, K Bartels, R W K Lee, W H Okamura *J. Am. Chem. Soc.* **111** 3717 (1989)
52. W H Okamura *Acc. Chem. Res.* **16** 81 (1983)
53. T Durst, in *Comprehensive Organic Chemistry* Vol. 3 (Eds D Barton, W D Ollis) (Oxford: Pergamon Press, 1979)
54. S Lane, S J Quick, R J K Taylor *Tetrahedron Lett.* **25** 1039 (1984)
55. D Craig, K Daniels, A R McKenzie *Tetrahedron Lett.* **31** 6441 (1990)
56. J P Marino, M Neisser *J. Am. Chem. Soc.* **103** 7687 (1981)
57. M A Tius, M A Terr *Synth. Commun.* **18** 1905 (1988)
58. J M Akkerman, H de Koning, H O Huisman *J. Chem. Soc., Perkin Trans. 1* 2124 (1979)
59. E J Corey, D J Hoover *Tetrahedron Lett.* **23** 3463 (1982)
60. S L Schrieber, K Satake *J. Am. Chem. Soc.* **106** 4186 (1984)
61. F M Houser, S R Ellenberger, J P Glusker, C J Smart, H L Carrell *J. Org. Chem.* **51** 50 (1986)
62. T Takai, H Kotsubo, T Koizumi *J. Chem. Soc., Perkin Trans. 1* 1667 (1991)
63. H Takayama, A Iyobe, T Koizumi *J. Chem. Soc., Chem. Commun.* 771 (1986)
64. R Baker, R B Keen, M D Morris, R W Turner *J. Chem. Soc., Chem. Commun.* 987 (1984)
65. T Mandai, K Mizobuchi, M Kawada, J Otera *J. Org. Chem.* **49** 3403 (1984)
66. T Mandai, K Kawada, J Otera *J. Org. Chem.* **48** 5183 (1983)
67. G Solladié, J Hutt, C Frechou *Tetrahedron Lett.* **28** 61 (1987)
68. G Solladié, A Almario *Tetrahedron Asymmetry* **5** 1717 (1994)
69. G Solladié, N Wilb, C Bauder, C Bonini, L Viggiani, L Chiummiento *J. Org. Chem.* **64** 5447 (1999)
70. K Konno, K Hashimoto, H Shirahama, T Matsumoto *Tetrahedron Lett.* **27** 3865 (1986)
71. K Konno, K Hashimoto, Y Ohfune, H Shirahama, T Matsumoto *Tetrahedron Lett.* **27** 607 (1986)
72. K Hashimoto, K Konno, H Shirahama, T Matsumoto *Chem. Lett.* 1399 (1986)
73. Y Tamura, H Maeda, H D Choi, H Ishibashi *Synthesis* 56 (1982)
74. H Ishibashi, M Ohnishi, T Senda, M Ikeda *Synth. Commun.* **19** 857 (1989)
75. H Ishibashi, H Komatsu, K Maruyama, M Ikeda *Tetrahedron Lett.* **26** 5791 (1985)
76. H Ishibashi, H Komatsu, M Ikeda *J. Chem. Res. (S)* 296 (1987)
77. H Ishibashi, C Uehara, H Komatsu, M Ikeda *Chem. Pharm. Bull.* **35** 2750 (1987)
78. T H Kim, K M Park *Tetrahedron Lett.* **36** 4833 (1995)
79. Y Oikawa, O Yonemitsu *J. Chem. Soc., Perkin Trans. 1* 1479 (1976)
80. P Magnus, T Gallagher, P Brown, P Pappalardo *Acc. Chem. Res.* **17** 35 (1984)
81. T Gallagher, P Magnus, J C Huffman *J. Am. Chem. Soc.* **105** 4750 (1983)
82. K Cordwell, B Hewitt, P Magnus *Tetrahedron Lett.* **28** 3303 (1987)
83. R Z Andriamialisoa, N Langlois, Y Langlois *J. Org. Chem.* **50** 961 (1985)

84. P L Feldman, H Rapoport *J. Org. Chem.* **51** 3882 (1986)
85. D Genin, R Z Andriamialisoa, N Langlois, Y Langlois *Heterocycles* **26** 377 (1987)
86. M Dardaine, N Langlois *Tetrahedron Lett.* **33** 3641 (1992)
87. M Ladlow, P M Cairns, P Magnus *J. Chem. Soc., Chem. Commun.* 1756 (1986)
88. P Magnus, T Gallagher, P Brown, J C Hoffman *J. Am. Chem. Soc.* **106** 2105 (1984)
89. P Magnus, P Brown *J. Chem. Soc., Chem. Commun.* 184 (1985)
90. P Magnus, N L Sear, C S Kim, N Vicker *J. Org. Chem.* **57** 70 (1992)
91. M Amat, J Bosch *J. Org. Chem.* **57** 5792 (1992)
92. M Amat, A Linares, J Bosch *J. Org. Chem.* **55** 6299 (1990)
93. J Catena, N Valls, J Bosch, J Bonjoch *Tetrahedron Lett.* **35** 4433 (1994)
94. M-L Bannasar, J-M Jimenez, B A Sufi, J Bosch *Tetrahedron Lett.* **37** 9105 (1996)
95. M Amat, M L Bennasar, S Hadida, B A Sufi, E Zulaica, J Bosch *Tetrahedron Lett.* **37** 5217 (1996)
96. M L Bennasar, E Zulaica, A Ramirez, J Bosch *Tetrahedron Lett.* **37** 6611 (1996)
97. H Ishibashi, T Sato, M Takahashi, M Hayashi, M Ikeda *Heterocycles* **27** 2787 (1988)
98. A Barco, S Benetti, A Casolari, S Manfredini, G P Pollini, E Polo, V Zanirato *Tetrahedron* **45** 3935 (1989)
99. H Ishibashi, K Sato, K Maruyama, M Ikeda, Y Tamura *Chem. Pharm. Bull.* **33** 4593 (1985)
100. H Ishibashi, H Ozaki, M Ikeda *J. Chem. Soc., Chem. Commun.* 654 (1986)
101. A W Lee, W H Chan, E T T Chan *J. Chem. Soc., Perkin Trans. 1* 309 (1992)
102. S Takano, H Iida, K Inomata, K Ogasawara *Heterocycles* **35** 47 (1993)
103. H Ishibashi, H Kawanami, H Irigyama, M Ikeda *Tetrahedron Lett.* **36** 6733 (1995)
104. S Takano, K Inomata, T Sato, K Ogasawara *J. Chem. Soc., Chem. Commun.* 1591 (1989)
105. A B Hughes, M V Sargent *J. Chem. Soc., Perkin Tarans. 1* 1787 (1987)
106. A de Groot, B J M Jansen *J. Org. Chem.* **49** 2034 (1984)
107. B J M Jansen, C T Bouwman, A de Groot *Tetrahedron Lett.* **35** 2977 (1994)
108. V V Veselovskii, A I Moiseenkov *Izv. Akad. Nauk, Ser. Khim.* 113 (1993) [a]
109. S D Burke, K W Jung, R E Perri *Tetrahedron Lett.* **35** 5841 (1994)
110. T Ikeda, C R Hutchinson *J. Org. Chem.* **49** 2837 (1984)
111. M Nakagawa, J-J Liu, T Hino *J. Am. Chem. Soc.* **111** 2721 (1989)
112. C U Kim, P F Misco, D N McGregor *J. Org. Chem.* **47** 170 (1982)
113. J E Baldwin, A K Forrest, S Ko, L Sheppard *J. Chem. Soc., Chem. Commun.* 81 (1987)
114. T Kaneko *J. Am. Chem. Soc.* **107** 5490 (1985)
115. T Kaneko, Y Okamoto, K Hatada *J. Chem. Soc., Chem. Commun.* 1511 (1987)
116. Y Kita, H Yasuda, O Tamura, F Itoh, Y Tamura *Tetrahedron Lett.* **25** 4681 (1984)
117. Y Kita, O Tamura, T Miki, Y Tamura *Tetrahedron Lett.* **28** 6479 (1987)
118. Y Kita, N Shibata *Synlett* 289 (1996)
119. Y Kita, N Shibata, O Tamura, T Miki *Chem. Pharm. Bull.* **39** 2225 (1991)
120. Y Kita, N Shibata, T Tojho, N Yoshida *J. Chem. Soc., Perkin Trans. 1* 1795 (1992)
121. Y Kita, N Shibata, T Miki, Y Takemura, O Tamura *Chem. Pharm. Bull.* **40** 12 (1992)
122. Y Kita, N Shibata, N Kawano, T Tohjo, C Fujimori, K Matsumoto *Tetrahedron Lett.* **36** 115 (1995)
123. J E Baldwin, M Bradley *Chem. Rev.* **90** 1079 (1990)
124. Y Kita, N Shibata, N Kawano, T Tohjo, C Fugimori, H Ohishi *J. Am. Chem. Soc.* **116** 5116 (1994)
125. P L Roach, I J Clifton, C M H Hensgens, N Shibata, C Shofield, J Hajdu, J E Baldwin *Nature (London)* **387** 827 (1997)
126. N Shibata, Y Kita *Khim. Geterotsikl. Soedin.* 1463 (1998) [b]
127. J P Marino, R Fernandez de la Pradilla *Tetrahedron Lett.* **26** 5381 (1985)
128. J P Marino, R Fernandez de la Pradilla, E Laborde *Synthesis* 1088 (1987)
129. H Kosugi, K Tagami, A Takahashi, H Kanna, H Uda *J. Chem. Soc., Perkin Trans. 1* 935 (1989)
130. J P Marino, S Bogdan, K Kimura *J. Am. Chem. Soc.* **114** 5566 (1992)
131. S D Burke, K Shankaran, M J Helber *Tetrahedron Lett.* **32** 4655 (1991)
132. J T B Ferreira, J A Marques, J P Marino *Tetrahedron Asymmetry* **5** 641 (1994)
133. H Kosugi, Y Miura, H Kanna, H Uda *Tetrahedron Asymmetry* **4** 1409 (1993)
134. C Iwata, N Maezaki, T Kurumada, H Fukuyama, K Sugiyama, T Imanishi *J. Chem. Soc., Chem. Commun.* 1408 (1991)
135. T Imanishi, T Kurumada, N Maezaki, K Sugiyama, C Iwata *J. Chem. Soc., Chem. Commun.* 1409 (1991)
136. N Maezaki, H Fukuyama, S Yagi, T Tanaka, C Iwata *J. Am. Chem. Soc., Chem. Commun.* 1835 (1994)
137. A Padwa, J E Kochran, C O Kappe *J. Org. Chem.* **61** 3706 (1996)
138. C O Kappe, A Padwa *J. Org. Chem.* **61** 6166 (1996)
139. A Padwa, C O Kappe, T S Reger *J. Org. Chem.* **61** 4888 (1996)
140. L Ramberg, B Bäklund *Arkiv Kemi, Mineral., Geol.* **A13** 27 (1940); *Chem. Abstr.* **34** 4725 (1940)
141. L A Paquette *Org. React.* **25** 1 (1977)
142. J N Clough, in *Comprehensive Organic Synthesis* Vol. 3 (Eds B M Trost, J Fleming, G Pattenden) (New York: Pergamon Press, 1991) p. 861
143. R A Ewin, W A Loughlin, S M Pyke, J C Morales, R J K Taylor *Synlett* 660 (1993)
144. C Y Meyers, A M Malte, W S Matthews *J. Am. Chem. Soc.* **91** 7510 (1969)
145. T L Chen, S Fong, Y Li, C D Poon *J. Chem. Soc., Chem. Commun.* 1771 (1994)
146. J March, in *Advanced Organic Chemistry* (New York: Wiley, 1985) p. 921
147. T Schmittberger, D Uguen *Tetrahedron Lett.* **37** 29 (1996)
148. D Scholz *Liebigs Ann. Chem.* 98 (1983)
149. J B Hendrickson, G J Boudreaux, P S Palumbo *J. Am. Chem. Soc.* **108** 2358 (1986)
150. G Büchi, R M Freidinger *J. Am. Chem. Soc.* **96** 3332 (1974)
151. M Julia, D Lave, M Mulhauser, M Ramirez-Munoz, D Uguen *Tetrahedron Lett.* **24** 1783 (1983)
152. F Nef, R Decorzant, S D Esher *Tetrahedron Lett.* **23** 5043 (1982)
153. J J Burger, T B R A Chen, E R de Waard, H O Huisman *Tetrahedron* **37** 417 (1981)
154. H Choi, M Ji, M Park, I-K Yun, S-S Oh, W Baik, S Koo *J. Org. Chem.* **64** 8051 (1999)
155. J Kattenberg, E R de Waard, H O Huisman *Tetrahedron Lett.* 1173 (1977)
156. J B Hendrickson, P S Palumbo *J. Org. Chem.* **50** 2110 (1985)
157. V Cere, F Peri, S Pollicino *Tetrahedron Lett.* **38** 7797 (1997)
158. V Cere, G Montovani, F Peri, S Pollicino, A Ricci *Tetrahedron* **56** 1225 (2000)
159. R K Boeckman Jr, S K Yoon, D K Heckendorn *J. Am. Chem. Soc.* **113** 9682 (1991)
160. B M Trost, Z Shi *J. Am. Chem. Soc.* **116** 7459 (1994)
161. E Alvarez, M Delgado, M T Diaz, L Hanxing, R Perez, J D Martin *Tetrahedron Lett.* **37** 2865 (1996)
162. E Arce, M C Carreno, M B Cid, J L G Ruano *J. Org. Chem.* **59** 3421 (1994)
163. E Dominguez, J C Carretero *Tetrahedron Lett.* **31** 2487 (1990)
164. B M Trost, T A Grese *J. Org. Chem.* **56** 3189 (1991)
165. D F Taber, K Kanai *J. Org. Chem.* **63** 6607 (1998)
166. N Shibata, M Matsugi, N Kawano, S Fukui, C Fujimori, K Gotanda, K Murata, Y Kita *Tetrahedron Assymetry* **8** 303 (1997)
167. J T Kuethe, A Padwa *J. Org. Chem.* **62** 774 (1997)
168. J H Rigby, N C Warshakoon *J. Org. Chem.* **61** 7644 (1996)
169. A Padwa, T M Heidelbaugh, J T Kuehte *J. Org. Chem.* **65** 2368 (2000)
170. J L G Ruano, C Garcia Peredes *Tetrahedron Lett.* **41** 261 (2000)
171. T Naka, N Minakawa, H Abe, D Kaga, A Matsuda *J. Am. Chem. Soc.* **122** 7233 (2000)
172. J-J Liu, T Hino, A Tsuruoka, N Harada, M Nakagawa *J. Chem. Soc., Perkin Trans. 1* 3487 (2000)
173. D F Taber, Q Jiang *J. Org. Chem.* **66** 1876 (2001)
174. J H Rigby, N C Warshakoon, A J Payen *J. Am. Chem. Soc.* **121** 8237 (1999)
175. C P Raj, T Pichnit, S Braverman *Tetrahedron Lett.* **41** 1501 (2000)

[a] — *Russ. Chem. Bull., Int. Ed. (Engl. Transl.)*
[b] — *Chem. Heterocycl. Compd. (Engl. Transl.)*