Easy access to *trans*-2,3-disubstituted cyclobutanones, 2,4,5-trisubstituted 3,6-dihydro-2H-pyrans and *cis*-substituted phenylcyclopropylsulfones by using the highly versatile 1-phenylsulfenyl- or 1-phenylsulfonyl-cyclopropylketones†

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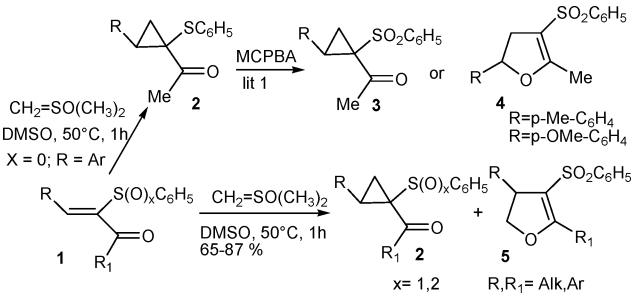
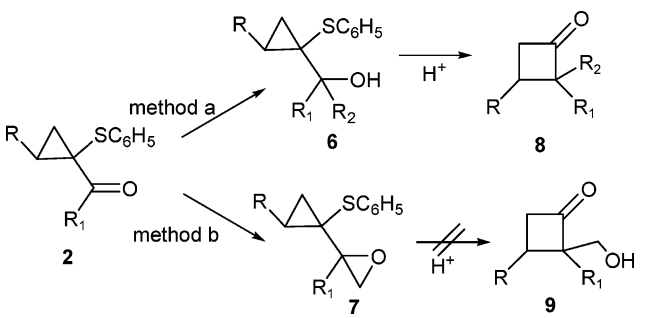
The high versatility of 1-phenylsulfenyl- or 1-phenylsulfonyl-cyclopropylketones has been exploited for the regioselective synthesis of *trans*-2,3-disubstituted cyclobutanones, 2,4,5-trisubstituted 3,6-dihydro-2H-pyrans and *cis*-2-alkyl- or *cis*-2-aryl-cyclopropylphenylsulfones.

Easily obtainable cyclopropyl ketones 1-substituted with an arylthio group, with the sulfur atoms in different oxidation states, are versatile reagents that can be easily prepared stereoselectively by reacting the Corey ylide with the stereochemically defined Z alkenes **1**.[1,2] We recently reported that, by a careful choice of the substituents and by modulation of the oxidation state of the sulfur atom, the alkenes **1** or the cyclopropanes **2** are useful precursors of 2,4,5-trisubstituted- or 3,4,5-trisubstituted-2,3-dihydrofurans **4** and **5** (Scheme 1).[1]



Scheme 1

In order to further study the synthetic potential of cyclopropylketones **2**, we planned the synthesis of 2,3-disubstituted cyclobutanones **8** or **9**, through the intermediacy of the corresponding cyclopropyl carbinols **6** or the oxiranes **7** (Scheme 2). As a matter of fact only two papers have appeared dealing with the chiral synthesis of 2,3-disubstituted cyclobutanones by ring expansion of oxaspiropentanes[3] and one by ring expansion of α-hydroxycyclopropyl carbinols.[4] One previous attempt of preparing these racemic cyclobutanones using 2-pivaloxymethyl-1-(phenylthio)cyclopropyl carbinols led to the corresponding 2,4-disubstituted cyclobutanones[5] by migration of the less substituted cyclopropyl carbon as a consequence of the electron-withdrawing effect of the pivaloxymethyl group. It must be pointed out that, while the synthesis of 1-(phenylthio)cyclopropyl carbinols and their ring expansion to the corresponding 2-substituted cyclobutanones is quite successful,[6] the reaction of 2-methyl-1-(phenylthio)cyclopropyllithium with aldehydes or ketones produced the corresponding alcohols, hypothetical precursors of 2,3-disubstituted cyclobutanones, in a low yield of 30%.[7] In view of these facts, it was of interest to prepare 2-substituted-1-(phenylthio)cyclopropyl carbinols **6** in high yields and to search experimental conditions for their ring expansion to 2,3-disubstituted cyclobutanones in order to overcome the above-mentioned drawbacks (Scheme 2).



Scheme 2

2,3-Disubstituted cyclobutanones 8 (Method a)

For this part of the study the required cyclopropylcarbinols **6** were easily prepared from 1-phenylthiocyclopropyl ketones **2**, either by hydride reduction or by reaction with organolithium derivatives. The reduction of trisubstituted cyclopropyl ketones **2a–g**, carried out with $LiAlH_4$ in THF at −70 °C, gave the alcohols **6a,c,e–g** with modest diastereoselectivity while a good diastereoisomeric excess was obtained when R or R_1 was an aromatic group (**6b**, **6d**). Excellent diastereoselectivity was observed for the alcohols **6h,j** obtained by reaction of the ketone **2b** with methyl- or *n*-butyllithium in THF at −78 °C (Table 1).

As the second part of method "a" involves an acidic treatment of **6** to trigger the ring expansion to the corresponding

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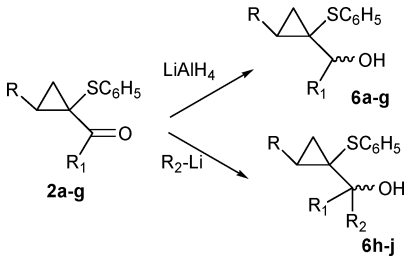
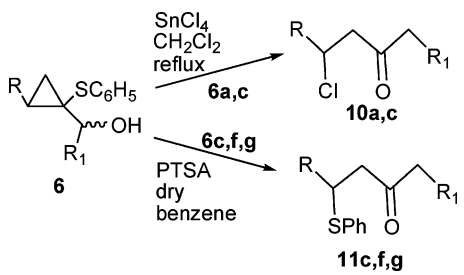
Table 1 Synthesis of the alcohols **6a–j**



Entry	6	R	R_1	R_2	Yield (%)	*Syn:anti* 6[a]
1	**a**	$(CH_3)_2CH$	CH_3	H	96	85:15
2	**b**	$(CH_3)_2CH$	C_6H_5	H	92	94:6
3	**c**	$C_6H_5CH_2CH_2$	CH_3	H	85	70:30
4	**d**	C_6H_5	CH_3	H	80	90:10
5	**e**	$C_6H_5CH_2CH_2$	C_4H_9	H	86	75:25
6	**f**	CH_3	C_4H_9	H	70	60:40
7	**g**	furyl	CH_3	H	94	65:35
8	**h**	$(CH_3)_2CH$	C_6H_5	CH_3	86	94:6
9	**i**	$C_6H_5CH_2CH_2$	CH_3	CH_3	66	
10	**j**	$(CH_3)_2CH$	C_6H_5	C_4H_9	92	>99

[a] The diastereoselectivity was measured by ^{1}H NMR (300 MHz) and GC MS on the crude reaction mixture.

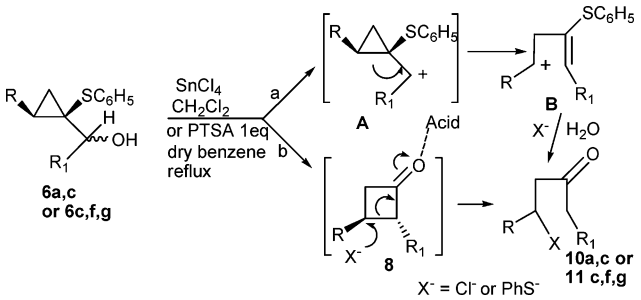
cyclobutanones **8**, we treated the cyclopropylcarbinols **6a**,**c** with anhydrous stannic chloride in methylene chloride at room temperature. We did not obtain the expected cyclobutanones **8** but only the β-chloro-substituted ketones **10a**, **c**, that are extremely useful intermediates in organic synthesis and act as intermediates in the synthesis of enones, annulated compounds, heterocyclic derivatives and dicarbonyl products (Scheme 3).[8]



Scheme 3

We then submitted the cyclopropyl carbinols **6b**,**c**,**f**,**g** to the Trost protocol for this ring expansion, that is the use of *p*-toluenesulfonic acid (PTSA) in refluxing dry benzene.[6b] Also in this case, instead of the expected cyclobutanones **8** we observed the formation of the acyclic ketones **11c**,**f**,**g** and only decomposition products in the case of **6b**.

Concerning the reaction mechanism, the results obtained could suggest two possible pathways as reported in Scheme 4. One could involve the formation of a carbonium ion (A) and its rearrangement to the open chain homoallylic carbocation B, then attack from the nucleophilic species (Cl^- or PhS^-) and final hydrolysis of the so obtained enolthioether to give the final β-substituted ketones **10a**,**c** or **11c**,**f**,**g** (path a). The other possibility could involve the intermediate formation of the cyclobutanone **8** and its ring fission caused by the simultaneous coordination of



Scheme 4 Possible mechanism of substituted ketone formation.

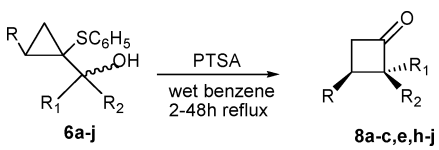
the acid on the carbonyl group and attack of the nucleophile on the 3-carbon (path b).

Changing the reaction conditions again, we were pleased to find that the reaction of **6a–c**,**e**,**h–j** with *p*-toluenesulfonic acid in refluxing benzene, saturated with water,[6b] led to the stereo- and regio-chemically homogeneous corresponding cyclobutanones **8**, while **6d** gave only unidentified decomposition products and **6f**,**g** led to the ring opened derivatives **11f**,**g** (Table 2). The formation of only the *trans*-2,3-disubstituted cyclobutanones **8a–c**,**e**,**h–j** can be attributed to the higher migratory aptitude of the most substituted bond in a cyclopropylcarbinyl-cyclobutyl rearrangement.[9] The assignment of the *trans* stereochemistry was made on the basis of the vicinal coupling constants observed in the ^{1}H NMR spectra[10,11] and by NOE experiments.

Carrying out the reaction of a 70:30 mixture of *syn:anti* **6c** in milder conditions in aqueous benzene with PTSA (1 equiv.) at 70 °C and monitoring the reaction by GS MS, we discovered that a kinetic resolution of the *syn-anti* mixture of **6c** and a *cis-trans* equilibration of **8c** were at work (Table 3).

As a matter of fact we observed that the cyclopropylcarbinyl-cyclobutyl rearrangement was considerably slower and that the major component of the cyclopropylcarbinol mixture reacted faster than the minor one. We observed also that the cyclobutanones initially formed as a roughly 61:39 *cis:trans* mixture

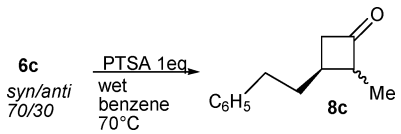
Table 2 Synthesis of 2,3-disubstituted cyclobutanones **8a–c**,**e**,**h–j**



Entry	6	R	R_1	R_2	Time/h	**8** yield (%)[a]
1	**a**	$(CH_3)_2CH$	CH_3	H	1	65
2	**b**	$(CH_3)_2CH$	C_6H_5	H	2	85
3	**c**	$C_6H_5CH_2CH_2$	CH_3	H	2	98[b]
4	**d**	C_6H_5	CH_3	H	2	0
5	**e**	$C_6H_5CH_2CH_2$	C_4H_9	H	2	84
6	**f**	CH_3	C_4H_9	H	4	0[c]
7	**g**	furyl	CH_3	H	1	0[d]
8	**h**	$(CH_3)_2CH$	C_6H_5	CH_3	5	70
9	**i**	$C_6H_5CH_2CH_2$	CH_3	CH_3	48	75
10	**j**	$(CH_3)_2CH$	C_6H_5	C_4H_9	48	75

[a] Isolated yield. [b] **6c** was obtained as a 95/5 mixture of *trans*/*cis* isomers. [c] Only 2-(phenylthio)-nonan-4-one **11f** was isolated. [d] 1-(Furan-2-yl)-1-(phenylthio)pentan-3-one **11g** was isolated.

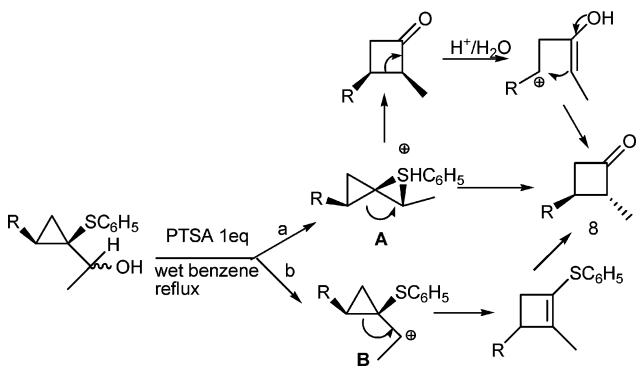
Table 3 Variation of the product distribution with reaction time



Reaction time/h	**6c** (%) (*syn:anti*)	**8c** (%) (*trans:cis*)
0	100 (70:30)	0
16	77 (42:58)	23 (39:61)
23	68 (34:66)	32 (46:54)
40	23 (0:100)	77 (67:33)
49	0	100 (80:20)
64	0	100 (87:13)
80	0	100 (95:5)

changed their relative composition to give, after 70 h, the cyclobutanone *trans*-**8c** as the only product with only traces of the other *cis*-**8c** isomer. The 2,4-disubstituted cyclobutanones, that could have been produced by migration of the less substituted cyclopropyl carbon, were not observed.

Concerning the reaction mechanism of this rearrangement, two possible pathways could be at work as reported in Scheme 5. One could involve the formation of an intermediate episulfonium ion A (path a) that, by migration of the more substituted cyclopropyl carbon, can produce either the *cis*- or the *trans*-cyclobutanones, according to the geometry of the starting cyclopropyl carbinol, with final thermodynamic equilibration. Alternatively the formation of the *trans*-cyclobutanone could be justified by the intermediacy of a carbonium ion B, and its subsequent rearrangement to give an intermediate 1-phenylthiocyclobutene intermediate, that can be hydrolyzed to **8** (path b). Further studies are in progress to better understand this mechanistic aspect of the reaction and the results will be published in due course.



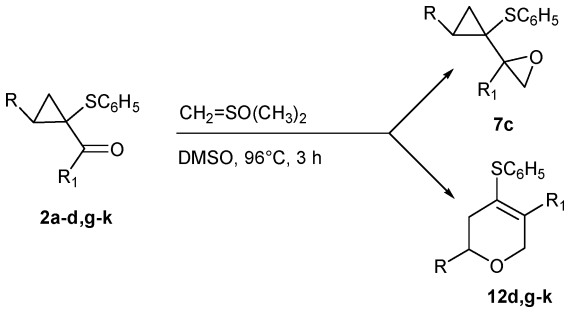
Scheme 5 Possible mechanisms of ring expansion of **6** to give 2,3-disubstituted cyclobutanones **8**.

Failed attempts at synthesizing the 2,3-disubstituted cyclobutanones 9 (Method b). Formation of 2,4,5-trisubstituted 3,6-dihydro-2H-pyrans

At this point we addressed ourselves to the second goal, that is the synthesis of cyclobutanones **9** through the acid catalyzed ring expansion of the oxiranes **7**.

An obvious approach for the synthesis of **7** was the reaction of the cyclopropylketones **2** with the Corey ylide. When we treated

Table 4 Transformation of the 1-phenylthiocyclopropylketones **2** into 3,6-dihydro-2H-pyrans **12**



Entry	**2**	R	R_1	**7** yield (%)	**12** yield (%)
1	**a**	$(CH_3)_2CH$	CH_3		Traces[a]
2	**b**	$(CH_3)_2CH$	C_6H_5		Traces[a]
3	**c**	$C_6H_5CH_2CH_2$	CH_3	65[b]	
4	**d**	C_6H_5	CH_3		86[c]
5	**g**	2-furyl	CH_3		72
6	**h**	*p*-$CH_3C_6H_5$	CH_3		76[d]
7	**i**	*p*-$CH_3C_6H_5$	C_6H_5		82[d]
8	**j**	2-thienyl	CH_3		68
9	**k**	2-naphthyl	CH_3		80

[a] Starting material was recovered together with inseparable traces of the pyrans **12a**,**b** (1%). [b] The oxirane **7c** was obtained as a 75:25 mixture of isomers. [c] When we carried out the same reaction at 60° C the oxirane **7d** was isolated as a mixture of two inseparable diastereoisomers. [d] In a previous work[1] we erroneously assigned the structure of 4,5,6-trisubstituted 3,4-dihydro-2H-pyrans to **12h**,**i**.

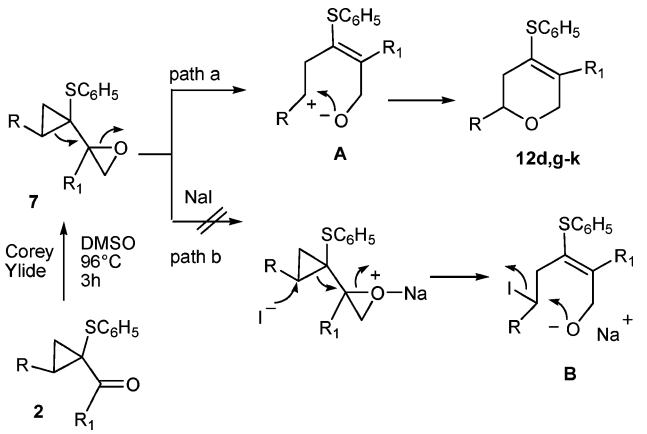
cyclopropylketone **2c** with the Corey ylide in DMSO at 96–97 °C, clean formation of the oxirane **7c** was observed, but with all the other derivatives **2d**,**g–k** we observed, unexpectedly, formation of the 3,6-dihydro-2H-pyrans **12d**,**g–k** instead of the expected cyclopropyl oxiranes **7d**,**g–k**. The important role of the substituent R is clearly indicated by the fact that the reaction of derivatives **2a**,**b** gave only traces of the corresponding pyrans, with almost quantitative recovery of the starting material. Only in the case of cyclopropylketones 2-substituted with an aromatic or heterocyclic substituent, ring expansion occurred cleanly leading to good yields of the corresponding pyrans (Table 4).

This unexpected result was furthermore relevant as pyrans are important synthetic targets due to their frequent occurrence in biologically active natural products and medicinally important molecules.[12]

Our approach for their synthesis constitutes a valid alternative to the classical methods that include the Prins and related cyclization reactions,[13] the hetero-Diels–Alder cyclization and transition-metal-catalysed cyclization of hydroxylated derivatives,[14] cyclization to epoxides[15] and intramolecular oxy-Michael reactions,[16] use of carbohydrate precursors and transition-metal-catalyzed cyclization of allenes.[17]

The structures of derivatives **12d**,**g–k** were determined by ^1H, ^{13}C NMR and GC mass spectroscopies. COSY, GHSQC, GHMQC and ROESY experiments for compound **12d** permitted the unambiguous assignment of all protons and carbon signals.

Concerning the reaction mechanism two possible pathways could be envisioned (Scheme 6). Both paths entail the intermediate



Scheme 6 Mechanism of the formation of the 3,6-dihydro-2H-pyrans.

formation of the corresponding 1-phenylsulfenyl cyclopropyloxirane **7** by addition of the Corey ylide to the carbonyl group.

The intermediate oxirane **7** can undergo (path a) a spontaneous, thermally induced, ring opening of both the oxirane and the cyclopropane rings *via* a concerted mechanism to give the zwitterionic intermediate A, which then undergoes ring closure to generate the pyrans **12**. Alternatively the sodium iodide, generated in the formation of the Corey ylide, can catalyze (path b) the reaction of **7** by the sequence shown in Scheme 6. The relatively weakly basic epoxide oxygen could form a complex with the sodium cation that can undergo fission of the epoxide ring assisted by the contemporaneous nucleophilic attack of the iodide ion at the 2-position of the cyclopropane ring. The so generated sodium alcoholate (intermediate B) can finally lead to the pyrans **12** by intramolecular displacement of the iodide ion.

The most likely mechanism should be the one involved in path a, as treatment of the isolated oxirane **7d** in DMSO in the absence of sodium iodide at 96 °C led cleanly to the expected pyran **12d**.

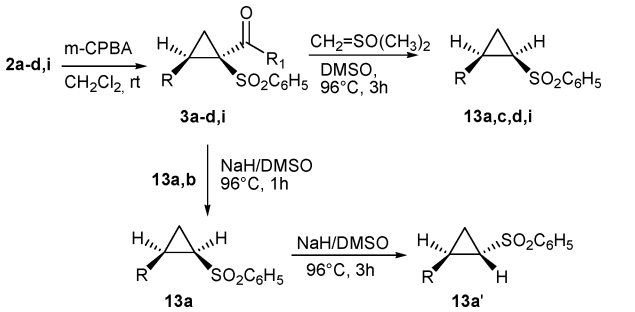
The reaction can also be carried out without isolation of the intermediate cyclopropanes as a one pot, three step reaction. As a matter of fact, treatment of the alkene (Z)-3-(phenylthio)-4-*p*-tolylbut-3-en-2-one[1] (1 equiv.) with the Corey ylide (2.2 equiv) in DMSO at 96–97 °C for 3 h afforded the corresponding pyran **12h** in a reasonably good 70% yield worked out from the GC mass spectrum of the reaction mixture.

cis-Cyclopropylsulfones 13 formation

At this point of the study it was interesting to investigate also the behaviour of the sulfone derivatives **3a–d**,**i** (Table 5) obtained by oxidation of the corresponding sulfides **2a–d**,**i** in CH_2Cl_2 with MCPBA at room temperature (the oxidation of the cyclopropane **2h** gave 2-tolyl-4-phenylsufonyl-5-methyl-2,3-dihydrofuran).[1] When these derivatives were reacted with the Corey ylide, we obtained no detectable amounts of the corresponding expected pyrans, but only good yields of the cyclopropylsulfones **13a**,**c**,**d**,**i** as single *cis*-isomers, whose structures were confirmed by comparison with the analogous known *trans* derivatives (Table 5).

We believe that in the cleavage reaction of the compounds **3a–d**,**i** a mechanism similar to the Haller Bauer reaction[18,19] could occur.

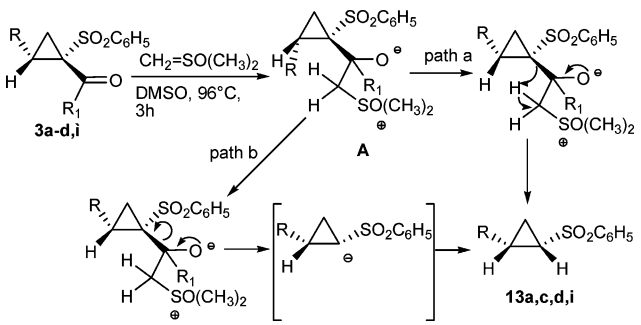
Table 5 Transformation of the 1-phenylsulfonyl cyclopropylketones **3** into *cis*-cyclopropylsulfones **13**



Entry	2	R	R_1	3 yield (%)	13[a] yield (%)
1	**a**	$(CH_3)_2CH$	CH_3	80	72
2	**b**	$(CH_3)_2CH$	C_6H_5	96	82 (**13a**)
3	**c**	$C_6H_5CH_2CH_2$	CH_3	98	96
4	**d**	C_6H_5	CH_3	89	93
5	**i**	*p*-$CH_3C_6H_5$	C_6H_5	94	95

[a] When products **13a**,**c**,**d**,**i** were treated with the Corey ylide for 9 h, *cis-trans* interconversion was not observed. The assignment of the *cis* stereochemistry was determined by comparison with the ^{1}H NMR of the previously reported *trans* derivatives.[21a,b,d,e]

As shown in Scheme 7, it could involve an initial addition of the ylide to the carbonyl group to give a tetrahedral intermediate A that could produce, through a cyclic concerted mechanism (path a), the *cis* cyclopropylsulfone and a new carbonyl-stabilized sulfoxonium ylide. Alternatively, the intermediate A could dissociate into a sulfoxonium ion and a sulfonyl stabilized carbanionic species (path b) that finally could be protonated to give the *cis* cyclopropylsulfones **13a**,**c**,**d**,**i**.



Scheme 7 Proposed mechanism for the *cis*-2-substituted cyclopropylsulfone formation.

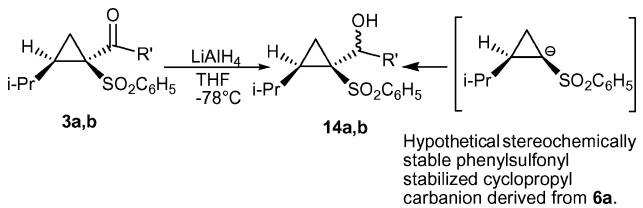
The concerted mechanism (path a) should the most likely because it has been previously found that a sulfonyl stabilized cyclopropyl carbanion should be incapable of retaining its pyramidal configuration giving rise to *cis-trans* interconversion.[19a,20–22] (Scheme 7). This hypothesis is further supported by the fact that, when the sulfones **13a**,**b** were reacted with NaH in DMSO, under the same reaction conditions, the *cis* derivative **13a** was formed within 1 h, but after 3 h the exclusive *trans*-isomer **13a′** was obtained (Table 5)through a thermodynamically controlled process involving the isomerization of the *cis* cyclopropane intermediate **13a** by a deprotonation-protonation sequence. These experimental results further support that the conjugated base of

cis-2-substituted cyclopropylsulfones undergoes an inversion of configuration due to the preference for the *trans* geometry.[21,22]

The most important aspect of this reaction was the exclusive formation of the thermodynamically less stable *cis*-isomer with no detectable amounts of the corresponding *trans*-isomer. As a consequence of the fact that the *trans*-aryl- and alkyl-cyclopropylsulfones have been prepared by different synthetic approaches[21] and only few examples are reported[21b,22] for the synthesis of the corresponding *cis* derivatives, our reaction constitutes a very useful practical access to the latter.

Anyway because of the stereochemical instability of the sulfonyl stabilized cyclopropyl carbanion, even a deprotonation of a *cis*-2-substituted cyclopropylsulfone and subsequent reaction with an electrophile should give only the corresponding *trans* derivative with loss of stereochemical integrity.[21e,22b]

On the other hand the stereoselective preparation of the alkenes **1** by Knoevenagel reaction and their stereoselective cyclopropanation offers a means to circumvent the above mentioned difficulty. As a matter of fact, by reducing the derivatives **3a**,**b** with $LiAlH_4$ we obtained the *cis* cyclopropyl carbinols **14a**,**b** as a *syn:anti* mixture that can be considered as formally derived by reaction of the anion of the cyclopropyl sulfone **3a** (hypothetically capable of retaining its stereochemistry) with acetaldehyde or benzaldehyde (Scheme 8).



Scheme 8 Synthesis of *syn:anti cis*-cyclopropyl carbinols.

Use of cyclopropylsulfones like **3** carrying different keto groups will give ready access to this class of compounds with the above reported stereochemistry.

Conclusions

In summary we have reported that 1-phenylsulfenyl cyclopropylketones bearing C-2 alkyl substituents, easily reduced to the corresponding cyclopropylcarbinols, can be the starting materials for the synthesis of *trans*-2,3-disubstituted cyclobutanones. On the other hand by a careful choice of the substituents on the cyclopropane ring and a careful control of the reaction temperature, the synthesis of 2,4,5- trisubstituted 3,6-dihydro-2H-pyrans can be easily performed by the reaction of the same cyclopropylketones with the Corey ylide. Furthermore, upon changing the oxidation state of the sulfur atom of the cyclopropyl ketones, the same reaction with the Corey ylide gives a useful and remarkably easy access to the *cis*-2-alkyl- or 2-aryl-1-phenylsulfonyl cyclopropanes.

Experimental

^{1}H NMR spectra were recorded using 300 and 400 MHz VARIAN spectrometers at ambient temperature with $CDCl_3$ as solvent and TMS as internal standard. ^{13}C NMR spectra were recorded at 75 or 100 MHz at ambient temperature with $CDCl_3$ as solvent unless otherwise stated. Chemical shifts are reported as follows: chemical shifts, integration, multiplicity and coupling constants.

Infrared spectra were recorded on a Nicolet Nexus 670 FT-IR spectrophotometer. Microanalyses were carried out on a Carlo Erba 1106 element analyzer.

Mass spectra analyses were recorded on an Agilent 5973 N (Cpsil 32 m) and a Nermag R10-10 (quartz-Cpsil 5.25 m) (E.I. 70eV, C.I. NH_3). Analytical thin layer chromatography was performed using 0.25 mm silica gel 60-F plates. Flash chromatography was performed using 0.040–0.063 mesh silica gel (Merk KGaA). Yields refer to chromatography and spectroscopically pure materials, unless otherwise stated.

THF and diethyl ether were freshly distilled from sodium/benzophenone. DMSO was dried over 2 Å molecular sieves. Reactions requiring anhydrous conditions were performed in oven dried glassware under argon atmosphere.

Compounds **1a–i** and **2a–k** were prepared according to the previously reported procedure.[1]

Spectral data of the compounds **1a**,**d**,**h**,**i**[1,2] and **1g**[23], **2a**,**d**,**h**,**i**[1] has been previously reported.

Analytical data for **1b**, **1c**, **1e**, **1f**, **1j**, **1k**, **2b**, **2c**, **2e**, **2f**, **2g**, **2j**, **2k**, **6a–j**, **10a**,**c**, **11c**,**f**,**g**, **3b**,**c** and **14a**,**b** can be found in the Electronic Supplementary Information (ESI†).

Rearrangement of cyclopropylcarbinols 6a–j to cyclobutanones 8c–j. General procedure

A stirred solution of cyclopropylcarbinol **6a–j** (1.2 mmol) and *p*-toluenesulfonic acid (20 mg, 1,2 mmol,) in wet benzene (10 mL) was refluxed for 2 h. The reaction mixture was then washed with 10% $NaHCO_3$ and brine, dried (Na_2SO_4) and evaporated to remove the solvent. The residue was chromatographed on silica gel with diethyl ether-light petroleum 1:1 as eluent. Spectral data of the compounds **8b** have been previously reported.[11]

(2*R*,3*R*)-2-Methyl-3-isopropylcyclobutanone 8a

Characterization of this volatile cyclobutanone was not pursued and it was identified by GC MS m/z: 126 (M^+ (4)), 108 (5), 84 (42), 69 (100), 53 (40). It was isolated as the non-volatile 2,4-dinitrophenylhydrazone derivative and spectroscopic data were identical to the previously reported compound.[11]

(2*S**,2*R**)-2-Methyl-3-phenylethylcyclobutanone 8c

The assignment of *trans* stereochemistry for the substituents in the major isomer was determined by comparison with the ^{1}H NMR of the previously reported analogous *trans* and *cis* compounds.[10,11] Mixture 95:5 of two *trans:cis* isomers. Yield 98%. IR (neat): 1781 cm^{-1}. Major isomer: ^{1}H NMR ($CDCl_3$) δ: 1.16 (d, 3H, J = 7.2 Hz), 1.88–2.06 (m, 3H), 2.59–2.70 (m, 3H), 2.86–2.90 (m, 1H), 3.00 (ddd, 1H, J = 17.1 Hz, J = 8.1 Hz, J = 2.4 Hz), 7.17–7.32 (m, 5H). ^{13}C NMR δ:7.49, 33.00, 36.34, 36.53, 43.35, 47.73, 125.83, 128.28, 128.86, 132.25, 209.89. MS m/z: 188 (M^+ (15)), 146 (51), 131 (15), 115 (14), 91 (100), 77 (14). Anal. Calcd. for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.84; H, 8.52%. Minor *cis* isomer. Spectral data worked out by reaction mixture: ^{1}H NMR ($CDCl_3$) δ: 1.7 (d, 3H, J = 7.5 Hz), 1.52–1.64 (m, 3H), 2.38–2.44 (m, 3H), 2.86–2.90 (m, 1H), 3.40 (ddd, 1H, J = 16.8 Hz, J = 9.0 Hz,

J = 3.3 Hz), 7.17–7.32 (m, 5H). MS m/z: 188 (M^+ (3)), 146 (14), 131 (10), 115 (12), 91 (100), 77 (14).

(2*S,2*R**)-2-Butyl-3-phenylethylcyclobutanone 8e**

Yield 84%. IR (neat): 1760 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.88 (t, 3H, J = 7.2 Hz), 1.16–1.71 (m, 7H), 1.76–2.10 (m, 2H), 2.52–2.88 (m, 4H), 2.96–3.05 (m, 1H), 7.14–7.32 (m, 5H).^{13}C NMR δ: 13.85, 22.59, 28.87, 29.39, 30.99, 34.67, 38.38, 49.77, 65.62, 125.98, 128.28, 128.44, 132.36, 210.96. MS m/z: 230 (M^+ (14)), 188 (62), 146 (15), 117 (24), 105 (94), 91 (100). Anal. Calcd. for $C_{16}H_{22}O$: C,83.43; H, 9.63. Found: C, 83.41; H, 9.72%.

(2*S,3*R**)-3-Isopropyl-2-methyl-2-phenylcyclobutanone 8h**

Yield 70%. IR (neat): 1781 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.00 (d, 3H, J = 6.3 Hz), 1.10 (d, 3H, J = 6.3 Hz), 1.52 (s, 3H), 1.87–1.96 (m, 1H), 2.41–2.48 (m, 1H), 2.89 (dd, 1H, J = 17.6 Hz, J = 8.4 Hz), 3.06 (dd, 1H, J = 17.6 Hz, J = 9.6 Hz), 7.18–7.38 (m, 5H). ^{13}C NMR δ: 19.49, 21.36, 22.75, 30.07, 43.04, 47.46, 67.80, 126.08, 126.53, 128.44, 142.94, 211.97. MS m/z: 160 (M^+ – 42 (22)), 145 (100), 130 (26), 115 (48), 91 (48), 77 (44). The stereochemistry of the *trans* isomer was confirmed by a strong nuclear Overhauser effect (NOE) between the methyl group (s, 1.52 ppm), and the proton of the isopropyl group (m, 1.87–1.96 ppm). Anal. Calcd. for $C_{14}H_{18}O$: C,83.12; H, 8.97. Found: C, 83.21; H, 9.02%.

2,2-Dimethyl-3-phenethylcyclobutanone 8i

Yellow oil. Yield 75%. IR (neat): 1781 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.11 (s, 3H), 1.19 (s, 3H), 1.68–1.77 (m, 1H), 1.93–2.10 (m, 2H), 2.61–2.66 (m, 2H), 2.69 (dd, 1H, J = 17.4 Hz, J = 6.9 Hz), 3.12 (dd, 1H, J = 17.4 Hz, J = 9.0 Hz), 7.17–7.32 (m, 5H). ^{13}C NMR δ: 17.11, 23.61, 32.82, 34.77, 35.99, 48.48, 60.76, 125.97, 128.31, 128.43, 141.71, 214.85. MS m/z: 160 (M^+– 44 (58)), 145 (2), 129 (6), 115 (12), 91 (100), 77 (20), 69 (82). Anal. Calcd. for $C_{14}H_{18}O$: C,83.12; H, 8.97. Found: C, 83.28; H, 9.12%.

(2*S,3*R**)-2-Butyl-3-isopropyl-2-phenylcyclobutanone 8j**

Yield 75%. IR (neat): 1780 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.81 (t, 3H, J = 7.2 Hz), 0.95 (d, 3H, J = 6.6 Hz), 1.16 (d, 3H, J = 6.6 Hz), 1.19–1.48 (m, 7H), 1.92–1.98 (m, 1H), 2.18–2.24 (m, 1H), 2.86 (dd, 1H, J = 17.7 Hz, J = 8.7 Hz), 3.02 (dd, 1H, J = 17.7 Hz, J = 9.3 Hz), 7.08–7.49 (m, 5H). ^{13}C NMR δ: 21.44, 22.19, 22.95, 26.92, 32.13, 39.95, 45.64, 47.55, 71.56, 128.26, 128.53, 128.23, 141.76, 211.81. MS m/z: 244 (M^+ (1)), 202 (38), 187 (14), 160 (8), 145 (100), 118 (28), 91 (24), 77 (8). Anal. Calcd. for $C_{17}H_{24}O$: C,83.55; H, 9.90. Found: C, 83.51; H, 9.82%.

General method for the synthesis of the cyclopropyl oxirane 7c and the 3,6-dihydro-2H-pyrans 12d,g–k

Trimethylsulfoxonium iodide (960 mg, 4.36 mmol) was rapidly added to a stirred suspension of pentane-washed NaH (179 mg, 4.36 mmol, 60% in mineral oil) in DMSO (5 mL) under an argon atmosphere. After keeping the reaction mixture at room temperature for 2h, a solution of the cyclopropanes **2a–i** (2.9 mmol) was added and the reaction mixture was heated at 96 °C for 3h. The mixture was diluted with diethyl ether, washed with brine and dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue purified by chromatography on silica gel (light petroleum-diethyl ether 10:1) gave **7c** and **12d**, **g–k**. When we carried out the same reaction at 60 °C with the cyclopropane **2d** we isolated the oxirane **7d** as mixture of two inseparable diastereoisomers.

2-Methyl-2-(2-phenethyl-1-(phenylthio)cyclopropyl)oxirane 7c

Inseparable 75:25 mixture of two diastereoisomers. Yellow oil. Yield 65%. Spectral data worked out by reaction mixture. Major isomer: ^1H NMR ($CDCl_3$) δ: 0.59 (dd, 1H, J = 6.6 Hz, J = 4.5 Hz), 1.06 (dd, 1H, J = 4.5 Hz, J = 9.0 Hz), 1.19–1.27 (m, 1H), 1.56 (s, 3H), 1.99 (q, 2H, J = 7.5 Hz), 2.26 (d, 1H, J = 4.8 Hz), 2.42 (d, 1H, J = 4.8 Hz), 2.70–2.81 (m, 2H), 7.17–7.47 (m, 10H). MS m/z: 201 (M^+-109 (18)), 183 (4), 143 (16), 128 (8), 110 (26), 91 (100). Minor isomer: H NMR ($CDCl_3$) δ: 0.55 (dd, 1H, J = 6.0 Hz, J = 5.1 Hz), 1.06 (dd, 1H, J = 5.1 Hz, J = 9.3 Hz), 1.25–1.31 (m, 1H), 1.54 (s, 3H), 1.95–2.03 (m, 2H), 2.45 (d, 1H, J = 5.7 Hz), 2.50 (d, 1H, J = 4.8 Hz), 2.69 (t, 2H, J = 8.1 Hz), 7.17–7.47 (m, 10H). MS m/z: 280 (M^+ – 30 (10)), 189 (14), 171 (32), 155 (13), 128 (8), 109 (20), 91 (100).

2-Methyl-2-(2-phenyl-1-(phenylthio)cyclopropyl)oxirane 7d

Inseparable 70:30 mixture of two diastereoisomers. Yellow oil. Yield 65%. ^1H NMR ($CDCl_3$) δ: 1.42–1.53 (m, 4H), 1.70 (s, 3H), 1.71 (s, 3H), 2.39 (dd, 1H, J = 15.6 Hz, J = 5.1 Hz), 2.53 (dd, 1H, J = 18.3 Hz, J = 5.1 Hz), 2.54–2.62 (m, 2H), 6.97–7.45 (m, 10H). ^{13}C NMR δ: 16.74, 17.01, 19.96, 20.05, 26.84, 28.59, 39.14, 39.80, 53.49, 53.84, 57.59, 57.99, 126.30, 126.56, 127.27, 127.40, 127.58, 127.86, 128.22, 128.62, 128.94, 128.02, 132.50, 133.18, 134.14, 137.01, 137.09. Major isomer: MS m/z: 282 (M^+ (48)), 267 (2), 191 (4), 173 (80), 145 (37), 105 (100), 77 (51). Minor isomer: MS m/z: 282 (M^+ (15)), 267 (2), 191 (8), 173 (100), 145 (92), 105 (38), 77 (24).

3,6-Dihydro-5-methyl-2-phenyl-4-(phenylthio)-2H-pyran 12d

Yellow oil. Yield 86%. ^1H NMR ($CDCl_3$) δ: 1.93 (s, 3H), 2.29–2.36(m, 1H), 2.43–2.52 (m, 1H), 4.31–4.42 (m, 2H), 4.59 (dd, 1H, J = 3.3 Hz, J = 10.5 Hz) 7.15–7.31 (m, 10H). ^{13}C NMR δ: 16.21, 38.05, 70.77, 77.00, 121.64, 125.79, 126.12, 127.62, 128.35, 128.96, 129.40, 134.82, 138.48, 141.44. MS m/z: 282 (M^+ (60)), 267 (3), 249 (3), 191 (5), 173 (100), 161 (64), 143 (49), 129 (58), 105 (54), 91 (54), 77 (71). Anal. Calcd. for $C_{18}H_{18}OS$: C, 76.56; H, 6.42; S, 11.35. Found: C, 76.74; H, 6.52; S, 11.56%.

2-(Furan-2-yl)-3,6-dihydro-5-methyl-4-(phenylthio)-2H-pyran 12g

Yellow oil. Yield 72%. ^1H NMR ($CDCl_3$) δ: 1.91 (s, 3H), 2.32–2.42 (m, 1H), 2.67–2.78 (m, 1H), 4.24, 4.39 (ABq, 2H, J = 16.5 Hz),), 4.68 (dd, 1H, J = 3.6 Hz, J = 9.9 Hz), 6.23 (d, 1H, J = 3.0 Hz), 6.30 (dd, J = 3.3 Hz, J = 1.8 Hz), 7.14–7.28 (m, 5H), 7.36 (dd, 1H, J = 0.6 Hz, J = 1.8 Hz).^{13}C NMR δ: 16.28, 33.89, 70.07, 70.12, 107.12, 110.10, 120.36, 126.14, 128.97, 129.32, 138.56, 139.40, 142.39, 153.39. MS m/z: 272 (M^+ (38)), 242 (4), 204 (6), 163 (38), 135 (37), 109 (81), 95 (100), 77 (62). Anal. Calcd. for $C_{16}H_{16}O_2S$: C, 70.56; H, 5.92; S, 11.77. Found: C, 70.52; H, 5.88; S, 11.65%.

3,6-Dihydro-5-methyl-4-(phenylthio)-2-*p*-tolyl-2H-pyran 12h

Orange oil. Yield 76%. ^{1}H NMR ($CDCl_3$) δ: 1.91 (s, 3H), 2.27–2.33 (m, 1H), 2.29 (s, 3H), 2.43–2.53 (m, 1H), 4.34–4.35 (m, 2H), 4.53 (dd,1H, J = 3.6 Hz, J = 10.5 Hz), 7.08–7.27 (m, 9H).^{13}C NMR δ: 16.21, 21.06, 38.03, 70.74, 77.43, 121.67, 125.73, 126.07, 128.91, 128.97, 129.41, 134.82, 137.21, 138.38, 138.47. MS m/z: 296 (M^+ (55)), 281 (12), 207 (45), 187 (71), 176 (100), 161 (96), 143 (75), 129 (54), 105 (50), 91 (61), 77 (24). Anal. Calcd. for $C_{19}H_{20}OS$: C, 76.99; H, 6.80; S, 10.82. Found: C, 76.74; H, 6.72; S, 11.66%.

3,6-Dihydro-5-phenyl-4-(phenylthio)-2-*p*-tolyl-2H-pyran 12i

Brown crystals, mp 96–98°C. Yield 82%. H NMR ($CDCl_3$) δ: 2.31 (s, 3H), 2.38–2.60 (m, 2H), 4.59–4.62 (m, 2H), 4.68 (dd,1H, J = 3.3 Hz, J = 9.9 Hz), 7.11–7.37 (m, 14H). ^{13}C NMR δ: 21.11, 37.42, 71.14, 76.58, 125.07, 125.84, 126.66, 127.86, 128.29, 128.44, 126.91, 129.07, 130.80, 134.04, 137.44, 137.76, 138.33. 140.95. MS m/z: 358 (M^+ (20)), 281 (8), 238 (75), 205 (58), 191 (10), 147 (51), 128 (100), 109 (24), 91 (82),77 (39). Anal. Calcd. for $C_{24}H_{22}OS$: C, 80.41; H, 6.19; S, 8.94. Found: C, 80.52; H, 6.12; S, 8.79%.

3,6-Dihydro-5-methyl-4-(phenylthio)–2-(thiophen-2-yl)-2H-pyran 12j

Red oil. Yield 68%. ^{1}H NMR ($CDCl_3$) δ: 1.91 (s, 3H), 2.42–2.48 (m, 1H), 2.58–2.69 (m, 1H), 4.30, 4.38 (ABq, 2H, J = 16.5 Hz), 4.86 (dd,1H, J = 3.3 Hz, J = 9.9 Hz), 6.91–6.94 (m, 2H), 7.15–7.28 (m, 6H). ^{13}C NMR δ: 16.23, 37.78, 70.38, 72.76, 121.06, 124.00, 124.88, 126.16, 128.98, 129.37, 134.67, 138.51, 144.32. MS m/z: 288 (M^+ (88)), 255 (6), 204 (16), 176 (95), 161 (100), 135 (57), 111 (71), 85 (81), 65 (46). Anal. Calcd. for $C_{16}H_{16}OS_2$: C, 66.63; H, 5.59; S, 22.23. Found: C, 66.54; H, 5.37; S, 22.38%.

3,6-Dihydro-5-methyl-2-(naphthalen-2-yl)-4-(phenylthio)-2H-pyran 12k

Red oil. Yield 80%. H NMR ($CDCl_3$) δ: 1.96 (s, 3H), 2.52–2.62 (m, 2H), 4.41 (m, 2H), 4.77 (dd, 1H, J = 3.3 Hz, J = 10.2 Hz), 7.08–7.80 (m, 12H). ^{13}C NMR δ: 16.31, 38.08, 70.78, 77.08 121.66, 123.96, 124.44, 125.82, 126.05, 126.12, 127.60, 127.96, 128.12, 129.01, 129.43, 132.91, 133.20, 134.82, 138.57, 138.87. MS m/z: 332 (M^+ (45)), 257 (6), 223 (26), 193 14), 178 (42), 155 (78), 127 (100), 109 (70), 85 (28), 77 (34). Anal. Calcd. for $C_{22}H_{20}OS$: C, 79.48; H, 6.06; S, 9.64. Found: C, 79.34; H, 6.19; S, 9.52%.

General method for the synthesis of the *cis*-cyclopropanes 13a,c,d,i

Trimethylsulfoxonium iodide (960 mg, 4.36 mmol) was rapidly added to a stirred suspension of pentane-washed NaH (179 mg, 4.36 mmol, 60% in mineral oil) in DMSO (5 mL) under an argon atmosphere. After keeping the reaction mixture at room temperature for 2h, a solution of the cyclopropanes **3a–d,i** (2.9 mmol) was added and the reaction mixture was heated at 96 °C for 3h. The mixture was diluted with diethyl ether, washed with brine and dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue purified by chromatography on silica gel (light petroleum-diethyl ether 10:1) gave **13a**,**c**,**d**,**i**.

1-((1*R,2*R**)-2-Isopropylcyclopropylsulfonyl)benzene 13a**

Colourless oil. Yield 82%. IR (neat): 1150, 1310 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.04 (d, 6H, J = 6.6 Hz), 1.17–1.21 (m, 2H), 1.26–1.31 (m, 1H), 2.13–2.18 (m, 1H), 2.43 (ddd, 1H, J = 5.7 Hz, J = 8.4 H, J = 14.1 Hz), 7.51–7.94 (m, 5H). ^{13}C NMR δ: 12.14, 22.99, 26.39, 31.31, 38.78, 127.17, 129.03, 133.06, 141.99. MS m/z: 224 (M^+ (2)), 209 (3), 169 (100), 143 (15), 125 (22), 77 (96), 55 (60). Anal. Calcd. for $C_{12}H_{16}O_2S$: C, 64.25; H, 7.19; S, 14.29. Found: C, 64.32; H, 7.12; S, 14.36%.

1-((1*S,2*R**)-2-Isopropylcyclopropylsulfonyl)benzene 13a′**

Yellow oil. Yield 80%. IR (neat): 1150, 1310 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 0.746 (d, 3H, J = 6.3 Hz), 0.89–0.94 (m, 1H), 0.94 (d, 3H, J = 6.3 Hz), 1.03–1.10 (m, 1H), 1.47–1.52 (m, 2H), 2.20 (ddd, 1H, J = 4.5 Hz, J = 9.0 Hz, J = 8.4 Hz), 7.52–7.91 (m, 5H).). ^{13}C NMR δ: 12.01, 21.26, 21.36, 27.99, 31.07, 38.57, 127.52, 129.04, 133.20, 139.43. MS m/z: 224 (M^+ (1)), 169 (38), 143 (15), 125 (18), 77 (90), 55 (100). Anal. Calcd. for $C_{12}H_{16}O_2S$: C, 64.25; H, 7.19; S, 14.29. Found: C, 64.28; H, 7.15; S, 14.33%.

1-((1*R,2*S**)-2-Phenethylcyclopropylsulfonyl)benzene 13c**

Yellow oil. Yield 96%. IR (neat): 1150, 1310 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.19–1.28 (m, 1H), 1.28–1.39 (m, 2H), 2.11–2-19 (m, 2H), 2.42 (dt, 1H, J = 7.8 Hz, J = 8.4 Hz), 2.76 (t, 2H, J = 7.2 Hz),7.17–7.94 (m, 10H). ^{13}C NMR δ: 12.30, 21.72, 28.21, 35.80, 38.12, 125.87, 127.21, 128.30, 128.52, 129.14, 133.17, 141.36, 141.84. MS m/z: 286 (M^+ (10)), 195 (3), 169 (10), 144 (54), 129 (50), 109 (12), 91 (100), 77 (54). Anal. Calcd. for $C_{17}H_{18}O_2S$: C, 71.30; H, 6.34; S, 11.19. Found: C, 71.38; H, 6.22; S, 11.12%.

1-(1*R,2*R**)-2-(Phenylcyclopropylsulfonyl)benzene 13d**

Colourless oil. Yield 93%. IR (neat): 1150, 1310 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.57 (ddd, 1H, J = 5.7 Hz, J = 8.4 Hz, J = 8.7 Hz), 2.17 (ddd, 1H, J = 5.7 Hz, J = 8.4 Hz, J = 5.4 Hz), 2.34 (s, 3H), 2.59 (dt, 1H, J = 5.7 Hz, J = 8.4 Hz), 2.78 (ddd, 1H, J = 5.7 Hz, J = 8.4 Hz, J = 5.4 Hz), 7.03–7.52 (m, 10H). ^{13}C NMR δ: 9.16, 24.94, 39.57, 126.99, 127.16, 127.65, 128.51, 129.53, 132.18, 132.81, 140.47. Anal. Calcd. for $C_{15}H_{14}O_2S$: C, 69.74; H, 5.46; S, 12.41. Found: C, 69.52; H, 5.54; S, 12.36%.

1-((1*R,2*R**)-2-*p*-Tolylcyclopropylsulfonyl)benzene 13i**

Yellow oil. Yield 95%. IR (neat): 1140, 1310 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.57 (ddd, 1H, J = 5.7 Hz, J = 14.1 Hz, J = 8.7 Hz), 2.17 (ddd, 1H, J = 5.7 Hz, J = 8.1 Hz, J = 5.4 Hz), 2.34 (s, 3H), 2.59 (q, 1H, J = 8.4 Hz), 2.78 (ddd, 1H, J = 13.8 Hz, J = 8.4 Hz, J = 5.4 Hz), 7.03–7.52 (m, 10H). ^{13}C NMR δ: 9.33, 21.04, 24.79, 39.62, 127.31, 128.44, 128.56, 129.43, 132.83, 136.70, 140.68. MS m/z: 272 (M^+ (1)), 131 (100), 115 (30), 91 (24), 77 (32). Anal. Calcd. for $C_{16}H_{16}O_2S$: C, 70.56; H, 5.92; S, 11.77. Found: C, 70.52; H, 5.89; S, 11.70%.

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