Cyclopentannulations Leading to the Synthesis of Bicyclic Conjugated Enediones[1]

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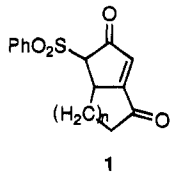
Base-induced reactions of 1-(phenylsulfonyl)-2-methylene-3-bromopropane (**4**) with 2-(phenylsulfonyl)-2-cycloalkenones **8a–d** were investigated with the ultimate purpose to develop a route leading to bicyclic conjugated enediones. Low-temperature, fast-quenched reactions led generally to open-chain adducts, while increase of temperature and addition of HMPA resulted in subsequent ring closure by a tandem Michael–S_N2 process. The stereochemical features of the bicyclo[3.3.0]octanes **11** and **12**, bicyclo[4.3.0]nonanes **18** and **19**, bicyclo[5.3.0]decanes **22** and **23**, and bicyclo[6.3.0]-undecanes **26–28** thus obtained have been determined. Ozonolysis and silica-induced elimination of the tertiary phenylsulfonyl group converted stereoselectively the above products into the desired enediones: pentalenedione **29**, indenedione **30**, azulenedione **32** and cyclopentacyclooctenedione **33**, respectively.

Introduction

There has been in recent years increasing interest in the development of new methods leading to the construction of cyclopentane-containing condensed polycyclic systems. This interest is motivated by the continuing growth in the number of natural compounds, including some of biological interest, which have such a basic framework.[2] In this paper we describe a general approach to conjugated bicyclic enediones **1** which can further serve as versatile intermediates for the synthesis of condensed polycyclic systems containing one or more cyclopentane rings.



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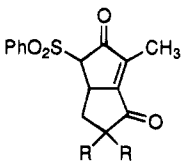
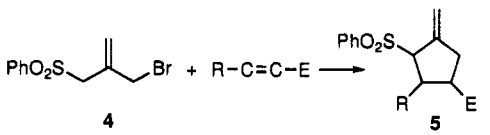


2 R = H

3 R = Me

The effectiveness of methyl-substituted enediones **3** has been demonstrated by Danishevsky in Diels–Alder reactions[3] and in regiospecific Michael additions[4] but the developed methodology for their synthesis was limited to structures **2** and **3**, with methyl substitution on the double bond, and did not provide access to the unsubstituted enediones.[5]

From a survey of available methods of cyclopentannulation of carbocyclic compounds, the transition metal catalyzed [3 + 2] cycloaddition[6] seemed to be appropriate for the proposed targets because the utilization of conjunctive reagents provides annulated methylenecyclopentane derivatives which can be readily converted into the corresponding annulated cyclopentanones. However, a thorough examination revealed that the effectiveness of this methodology depended on the presence of activating groups either on the conjunctive reagent[7] or on the initial carbocycle[8] which delayed a straightforward conversion into the desired enediones. We have therefore preferentially chosen an approach based on an anionic [3 + 2] tandem cyclization recently developed by us as a general route for methylenecyclopentane formation.[9] This process involves reactions of 1-(phenylsulfonyl)-2-methylene-3-bromopropane (**4**), a 1,3-dipole equivalent of trimethylenemethane (TMM), with electrophilic olefins to give products (**5**) in which the stereoselective outcome was found to depend on the electron-withdrawing group (E = COOR′ or NO_2 in eq 1).



4 **5** (1)

Our strategy is based on the use of cyclic enones as acceptors. These enones are additionally activated by a sulfone or a sulfoxide group which, after annulation, would facilitate the introduction of the required double bond (eq 2). The presence of the sulfone in the final product (**1**) could be expected (a) to stabilize the possibly sensitive enedione,[10] (b) to provide an additional center of chemoselective reactivity, and (c) to enable its ready elimination, after performing the required transformations.

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(1) Synthethic Methods. 45. Part 44: Hassner, A.; Belostotskii, A. *Tetrahedron Lett.*, in press.

(2) For pertinent reviews see: Ho, T. L. *Carbocyclic construction in terpene synthesis*; VCH Publ.: New York, 1988. Paquette, L. A.; Doherty, A. M. *Polyquinane Chemistry. Synthesis and Reactions*; Springer Verlag: Berlin, 1987.

(3) Danishevsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3460. Danishevsky, S.; Kahn, M. *Tetrahedron Lett.* **1981**, *22*, 489.

(4) Danishevsky, S.; Kahn. M. *Tetrahedron Lett.* **1981**, *22*, 485.

(5) Danishevsky, S.; Etheredge, S. J. *J. Org. Chem.* **1982**, *47*, 4791.

(6) See, *inter alia*: Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1981**, *103*, 5972. Trost, B. M.; Nanninga T. N. *J. Am. Chem. Soc.* **1985**, *107*, 1293. Binger, P.; Büch, H. M. *Top. Curr. Chem.* **1987**, *135*, 77. Binger, P.; Schäfer, B. *Tetrahedron Lett.* **1988**, *29*, 4539. Shimizu, I.; Ohashi, Y.; Tsuji, J. *Tetrahedron Lett.* **1984**, *25*, 5183. Breuilles, P.; Uguen, D. *Tetrahedron Lett.* **1988**, *29*, 201. Cleary, D. G.; Paquette, L. A. *Synth. Commun.* **1987**, *17*, 497. Heumann, A.; Kaldy, S.; Tenaglia, A. *Chem. Commun.* **1993**, 420.

(7) See, e.g.: Trost, B. M.; Mignani, S. M.; Nanninga, T. N. *J. Am. Chem. Soc.* **1988**, *110*, 1602.

(8) Trost, B. M.; Seoane, P.; Mignani, S.; Acemoglu, M. *J. Am. Chem. Soc.* **1989**, *111*, 7487.

(9) Ghera, E.; Yechezkel, T.; Hassner, A. *Tetrahedron Lett.* **1990**, *25*, 3653. Ghera, E.; Yechezkel, T.; Hassner, A. *J. Org. Chem.* **1993**, *58*, 6717.

(10) For a very sensitive regiomeric bicyclic enedione see: St. Laurent, D. R.; Paquette, L. A. *J. Org. Chem.* **1986**, *51*, 3861.

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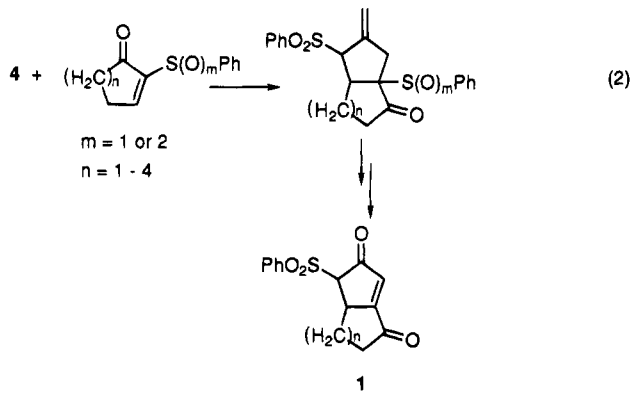
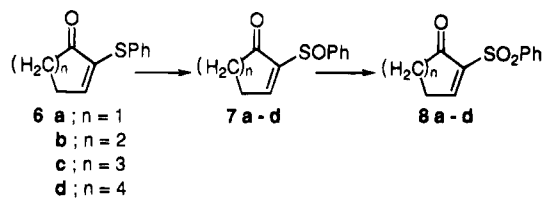


(2)

Results and Discussion

The substrates required as the Michael acceptors were prepared *via* 2-(phenylthio) enones **6a–d**. Direct treatment of cyclopentanone and cyclohexanone, respectively, with phenylsulfenyl chloride,[11] obtained *in situ*,[12] was most effective for the preparation of **6a** and **6b**, while the Pummerer rearrangement of the 2-(phenylsulfinyl)-cycloalkanones[13] was found to be more appropriate for the synthesis of **6c** and **6d**.

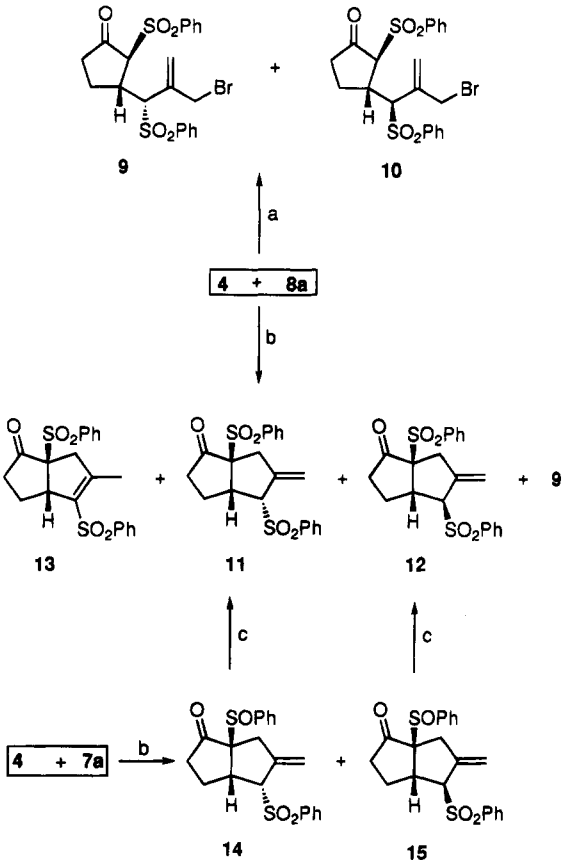
Attempts to chemoselectively oxidize **6a–d** to the corresponding sulfones were, however, unsuccessful: exposure to *m*-chloroperbenzoic acid (*m*-CPBA) or oxone[14] led to partial epoxidation as well. Control of pH during *m*-CPBA oxidation or addition to oxone of borate buffer, which was reported to be helpful in a similar case,[8] did not improve our results. We found, however, that, after oxidation of **6a–d** by $NaIO_4$ to the sulfoxides **7a–d**, the double bond was less prone to oxidation and subsequent exposure to *m*-CPBA afforded the desired unsaturated keto sulfones **8a–d** (eq 3).



(3)

Tandem Cyclizations to Bicyclo[3.3.0]octane Derivatives. While the first conjugate addition step involving bromo sulfone **4** and cycloalkenones **8a–d** occurred readily and very rapidly with all acceptors, the subsequent ring closure step was found to be significantly dependent on the ring size of the acceptor and on the stereochemical outcome of the initial addition. Thus, low temperature (−100 °C) reaction of lithiated **4** with **8a** resulted in immediate conjugate addition to provide the stereomers **9** and **10** (2:1 ratio) in 82% yield (Scheme 1). It is assumed that protonation affords the less hindered *trans*-disubstituted cyclopentanones in which the stereochemical and conformational assignments in the ring and in the side chain, as shown in Figure 1, are based on ^1H, ^{13}C NMR, and NOE data: in both **9** and **10** the H-3 and H-1′ protons have an *anti* orientation (J = 10 Hz).[15] No NOE enhancement was found between the vinyl proton and the α-phenylsulfonyl proton on the five-membered ring of **9** (5% in **10**), while a 2% NOE was

Scheme 1[a]



[a] Key: (a) LDA, −100 °C; (b) LDA, HMPA, −100 to −40 °C; (c) oxone.

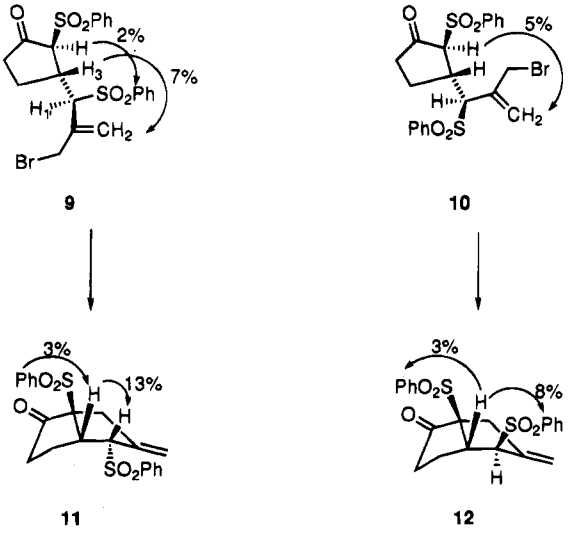


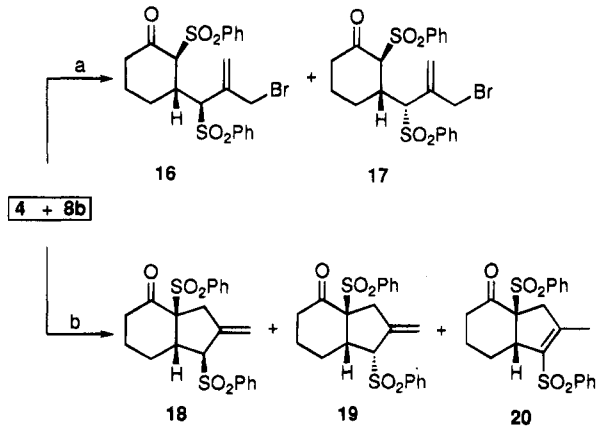
Figure 1.

observed between the latter proton and the ortho-aromatic proton of the phenylsulfonyl group positioned in the side chain of **9** (no equivalent NOE in **10**).

A stepwise increase in reaction temperature (to 0 °C) led to partial cyclization of the conformationally favored adduct **10** to give **12** and olefin-isomerized **13**, while **9** failed to cyclize. In the presence of HMPA, added to the reaction mixture on completion of the addition, the bicyclic products **11**, **12** and **13** were obtained (59%, ratio 9:9:1) along with 34% of the open-chain adduct **9**. The stereochemistry of the cyclized products **11** and **12** was secured by NOE data (Figure 1) and confirms the stereochemical assignments for **9** and **10**. An attempt

(11) Monteiro, H. J. *J. Org. Chem.* **1977**, *42*, 2324.
(12) Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208.
(13) Monteiro, H. J.; Gemal, A. L. *Synthesis* **1975**, 437.
(14) Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, *22*, 1287.
(15) The *anti* orientation of analogous protons has been determined as well in the further described uncyclized **16**, **17**, **21**, and **25**.

Scheme 2[a]



[a] Key: (a) LDA, −100 °C; (b) LDA, −100 to 0 °C.

to cyclize recovered **9** by use of *t*-BuOK in *t*-BuOH[16] at 0 °C resulted in high yield (80%) cyclization to the isomerized **13**, while repeated exposure of **9** to LDA gave only 32% of **11** along with recovered **9** and rearranged **13**. An attempt has been made to improve the cyclization results by influencing the stereochemical outcome of the conjugate addition to favor the formation of stereomer **10**. Addition of hexane to the reaction mixture was expected to slow down the addition rate, thus improving chelation with the counterion in the transition state. Indeed, the presence of cosolvent (hexane/THF 2:1) reversed the adduct ratio (1:2 for **9**/**10**) on early quenching but was detrimental for the ring closure step and therefore was abandoned.

More favorable results were obtained by activating the cyclopentenone with a sulfoxide instead of the sulfone group. Under similar conditions, using **7a** as an acceptor, a 66% yield of **14** and **15** was obtained with improved stereoselectivity (14:86 ratio). The stereochemical assignments, as shown, were deduced by quantitative oxidation of **14** and **15**, using oxone, to sulfones **11** and **12**. This improvement in the stereochemical outcome of conjugate additions involving sulfoxides may tentatively be rationalized by the association of the lithium counterion with a single S−O bond in the transition state while in sulfones both S−O bonds are involved.[17]

Cyclizations to Bicyclo[4.3.0]nonane Derivatives. Bromo sulfone **4** also reacted readily with 2-(phenylsulfonyl)-2-cyclohexenone **8b** to give, after rapid quenching (5 min, −100 °C) the diastereomeric adducts **16** and **17** (Scheme 2, 1:1.5 ratio, 80% yield). The *trans*-diaxial substitution in both stereomers is supported by the coupling constants ($J_{2,3}$ = 1.5 Hz) and the long range diequatorial couplings (*W*) of H-2 and H-3 with H-6 and H-5, respectively (J = 2 Hz), with conformations assigned on the basis of the NOE data, as depicted in Figure 2. In contrast to the five-membered carbocyclic adducts **9** and **10**, a stepwise increase of the reaction temperature to 0 °C was sufficient to produce ring closure of **16** and **17** affording a mixture of bicyclic **18**, **19**, and **20** (ratio 13:1:2) in 71% yield. Addition of HMPA or DMPU did not change these results substantially although the reaction could be then completed at somewhat lower temperature (−20 °C). The *cis* fusion of the rings and the stereochemistry, as shown in Figure 2, was confirmed by NMR data.

(16) Knapp, S.; O'Connor, U.; Mobilio, D. *Tetrahedron Lett.* **1980**, *21*, 4557.
(17) Boche, G. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 277.

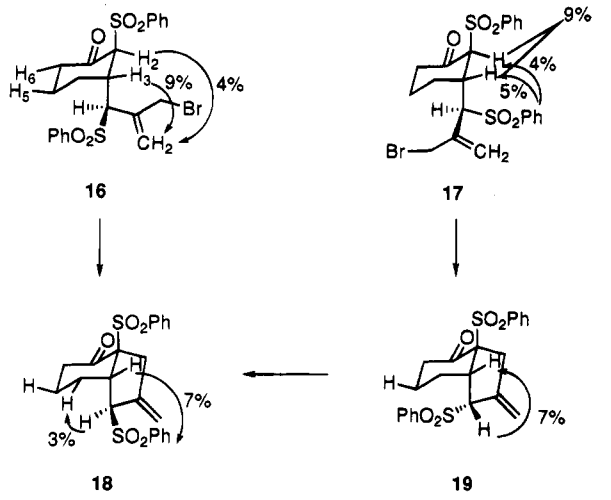


Figure 2.

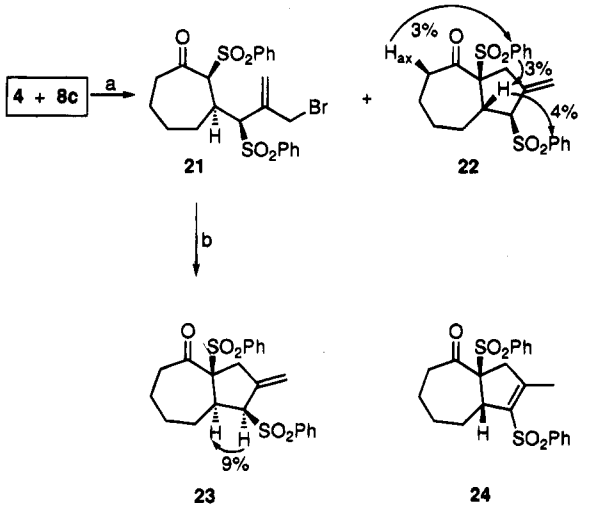
Comparison of the above ratio of cyclized products with the ratio of **16** and **17** obtained on early quenching implies that an epimerization leading to **18** occurred at the allylic α-(phenylsulfonyl) stereogenic center, either before or after cyclization. Indeed, when stereomer **17** was submitted to the ring closure conditions, a mixture of **18** and **19** was obtained. Moreover, partial conversion of **19** to **18** which occurred in the presence of diisopropylamine in THF at 0 °C supports an isomerization of the product after cyclization. This readily occurring epimerization, which has not been observed in the reactions involving **11**, is best rationalized by the hindrance between the secondary phenylsulfonyl group, which is endo and pseudoaxial in **19**, and the six-membered ring endo protons (Figure 2).

Cyclizations to Bicyclo[5.3.0]decane Derivatives. With larger ring acceptors (**8c** and **8d**), the ring closure step occurs even more readily, when the outcome of the initial conjugate addition is stereochemically favorable. Thus, reaction of **8c** with bromo sulfone **4** afforded at low temperature (−85 °C) the bicyclic product **22** (50%) along with the open-chain *cis*-disubstituted adduct **21** (23%). Utilization of a higher reaction temperature (−20 °C) did not induce cyclization of **21** but caused olefin isomerization of **22** to **24**. Separate cyclization of **21**, after its isolation, was ultimately effected by exposure to LDA in presence of HMPA, to afford the *trans*-fused bicyclic product **23** (50%), in which the original stereochemistry of **21** is thus retained (Scheme 3).

Cyclizations to Bicyclo[6.3.0]undecane Derivatives. A less favorable stereochemical outcome of the addition step involving the cyclooctenone acceptor **8d** resulted in ring closure to **26** and **27** (30%), along with the *cis* disubstituted open-chain adduct **25**, obtained in 45% yield (Scheme 4). On fast quenching (5 min, −100 °C), **27** (endo sulfone) was the major cyclized product (**27**:**26** 5:1) which converted fully into the thermodynamically favored exo **26** on increasing the reaction time and temperature (2.5 h, −40 °C). As opposed to other ring-size cyclized products, no olefin isomerization leading to an endocyclic double bond has been observed here. Furthermore, an effective ring closure of the open-chain **25** to the *trans*-fused product **28** (80%) was achieved using *t*-BuOK in 2-methyl-2-propanol and THF, thus raising the yield of the bicyclic products to 65%.

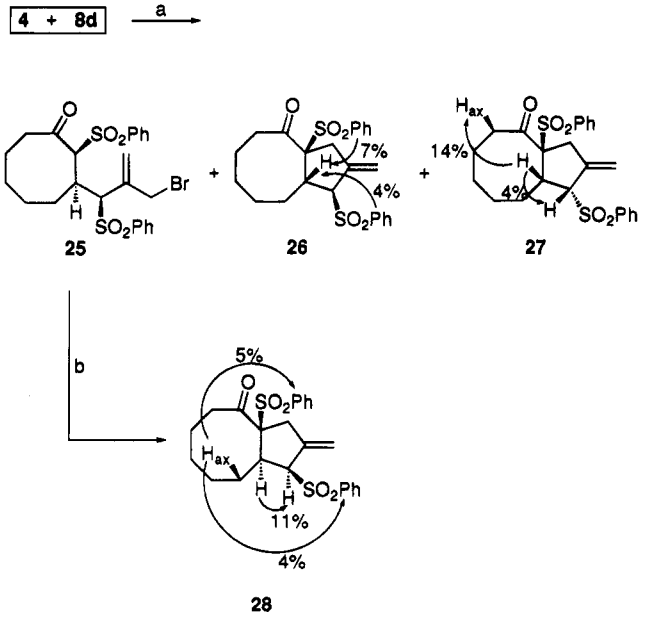
Stereochemical Preferences. In the conjugate additions involving the flattened five- and six-membered ring acceptors (**8a**,**b**) the stereoselective attack of lithi-

Scheme 3[a]



[a] Key: (a) LDA, −100 to −85 °C; (b) LDA, HMPA, −100 to −50 °C.

Scheme 4[a]



[a] Key: (a) LDA, −100 °C; (b) *t*-BuOK, *t*-BuOH/THF, 0 °C to rt.

ated **4** results solely in *trans*-disubstitution with a preference for axial (or pseudoaxial) orientation of the phenylsulfonyl group, after the occurrence of protonation. In larger ring acceptors (**8c,d**) the conjugate attack is not stereoselective due to the steric shielding of the vinyl sulfone moiety by the remainder of the seven- or eight-membered ring.[18] The ^{1}H NMR and NOE-based assignments for the uncyclized **25** (Figure 3) imply a boat−chair conformation of the eight-membered ring in which the phenylsulfonyl group vicinal to the ketone adopts a pseudoaxial position, resulting in *cis*-disubstitution. By analogy, a pseudoaxial orientation is tentatively assigned to the phenylsulfonyl group vicinal to the ketone in **21** as well. This preference for an axially oriented α-(phenylsulfonyl) substituent in all our cycloalkanones parallels the previously observed α-halo effect in cyclohexanones[19] also in those substituted with an α-(phenylthio)

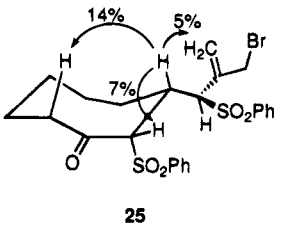


Figure 3.

group.[20] While information on conformational preferences of the phenylsulfonyl group in such compounds appears to be lacking, molecular mechanics calculations indicate that an α-(methylsulfonyl) group in cyclohexanones prefers the axial over the equatorial orientation by 1.54 kcal/mol.[21]

While the *trans* disubstituted adducts derived from the more flexible seven- and eight-membered rings, **8c** and **8d**, were not isolable but underwent at once ring closure below −85 °C to *cis*-fused products **22**, **26**, and **27**, the cyclization of the *cis* disubstituted adducts **21** and **25** was achieved in a separate step, as indicated. Cyclization of the *trans* adducts **9**, **10**, **16**, and **17** derived from five- and six-membered rings, required higher temperature or solvating agents (HMPA).

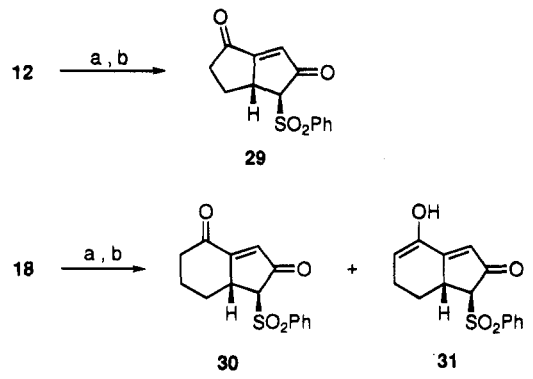
NMR Correlations. An examination of ^{1}H NMR spectra of the bicyclic products indicates that the chemical shift of the α-(phenylsulfonyl) proton in the five-membered ring is characteristic of the stereochemical relationships in the molecule. Thus, in the *cis*-fused compounds **11**, **19**, and **27** the above proton is *cis* related to the hydrogen at the ring junction and absorbs at δ 4.52, 4.30, and 4.45, respectively. When the configuration of the phenylsulfonyl group in the *cis*-fused systems is reversed (*trans* hydrogens), the chemical shift of the α-sulfonyl proton appears at a much higher field: δ 3.73 (in **12**), 3.78 (in **18**), 3.96 (in **22**), and 3.93 (in **26**). In *trans*-fused products (obtained with seven- and eight-membered ring acceptors) a downfield shift for the same proton is observed: δ 5.23 in **23** and 5.21 in **28**.

Formation of Enediones. The diquinane derivative **12**, obtained as the major cyclization product (via **15**), was exposed to ozone in methylene chloride solution at −78 °C. Addition of dimethyl sulfide, to decompose the ozonide, gave bests results when left at ambient temperature, under argon. The crude product was very sensitive to acid or base and treatment with base, to eliminate the tertiary sulfone, led to decomposition. We found that argon-protected column chromatography on neutral silica gel[22] of the crude product, obtained after decomposition of the ozonide, led to effective desulfonylation to afford crystalline enedione **29** (Scheme 5).

A similar ozonolysis−desulfonylation route converted **18** into a 3:1 mixture of **30** and its stable enol form **31** (80% overall yield) from which pure **30** was obtained by crystallization (Scheme 5). The latter, on standing in chloroform solution or by repeated filtration through silica, is again converted into the equilibrium 3:1 ketone−enol mixture, as determined by ^{1}H NMR spectroscopy. This partial enolization on equilibration was not observed in the enediones with other size rings. The initial

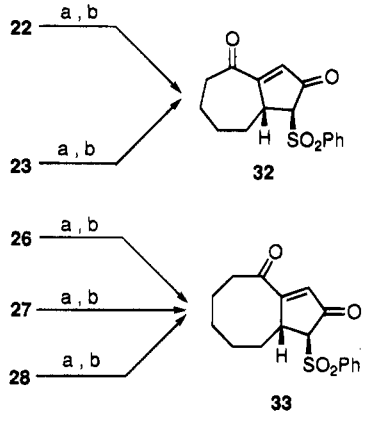
(18) Hardinger, A. S.; Fuchs, P. L. *J. Org. Chem.* **1987**, *52*, 2739.
(19) Cantacuzene, J.; Jantzen, R.; Ricard, D. *Tetrahedron* **1972**, *28*, 717.
(20) Trost, B. H.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.
(21) To be published.
(22) Desulfonylation results seem to be sensitive to the neutrality of the silica gel used; optimal results for **29** and **30**, respectively, were obtained on Riedel-de-haën silica gel S (pH = 7); the use of a Merck silica gel G (pH = 6.5−7.5) column caused decomposition of products.

Scheme 5[a]



[a] Key: (a) O_3, Me_2S; (b) silica gel column (pH = 7).

Scheme 6[a]



[a] Key: O_3, Me_2S; (b) silica gel column (Merck, pH = 6.5–7.5).

(favored) *exo*-configuration of the sulfone groups is preserved in both **29** and **30**.

Ozonolysis of bicyclo[5.3.0]decane derivatives **22** and **23** followed by desulfonylation on a silica column[23] provided a single enedione **32** from both precursors, with the less hindered *exo*-(phenylsulfonyl) group (Scheme 6).

Similarly, each of the available stereomers in the bicyclo[6.3.0]undecane series, namely **26**, **27**, and **28**, afforded the same enedione **33**, the isomerization to the more stable stereomer occurring probably after desulfonylation, on the column.

In summary, we have shown that 1-(phenylsulfonyl)-2-methylene-3-bromopropane (**4**) reacts with cycloalkenones, additionally activated by a phenylsulfonyl (or phenylsulfinyl) group, in a tandem Michael–S_N2 ring closure to give bicyclic systems with three stereocenters of defined stereochemistry. These products can be readily and stereoselectively converted into stable bicyclic conjugated 2-ene-1,4-diones in which a cyclopentenone is fused to a cycloalkanone of various ring sizes. Further utilization of these compounds as intermediates for specific syntheses of natural compounds will be explored.

Experimental Section

General experimental techniques and analytical measurements were applied as previously described.[24] Melting points are uncorrected. Mass spectra (CI in isobutane or NH_3) were recorded at 60 eV. Anhydrous lithium bromide[25] was additionally flame-dried in the reaction flask under argon, prior to introduction of other reagents.

2-(Phenylthio)-2-cyclopentenone (6a). A reported procedure[11] was improved by utilization of a freshly prepared solution of PhSCl in CH_2Cl_2[12] (33 mmol) which is added to cyclopentanone (840 mg, 10 mmol) in CH_3CN (15 mL). Workup and chromatographic purification gave **6a** (1.4 gr, 74%): mp 63–65 °C; (lit.[11] mp 64–65 °C); ^1H NMR δ 7.52–7.31 (m, 5H), 6.94 (t, J = 3 Hz, 1H), 2.64–2.49 (m, 4H).

2-(Phenylthio)-2-cyclohexenone (6b) was prepared as shown for **6a**, with the reaction time increased from 2 to 24 h. Chromatographic purification gave **6b** (84%): mp 46–48 °C (lit.[13] mp 50–51 °C); ^1H NMR δ 7.50–7.31 (m, 5H), 6.47 (t, J = 4.5 Hz, 1H), 2.62–2.51 (m, 2H), 2.44–2.30 (m, 2H), 2.10–1.95 (m, 2H).

2-(Phenylthio)-2-cycloheptenone (6c). To crude 2-(phenylsulfinyl)cycloheptanone[26] (4 mmol in 3 mL CH_2Cl_2) was added acetic anhydride (0.5 mL, 5.3 mmol) and methanesulfonic acid (2 drops) following a reported general procedure.[13] Flash column chromatography yielded **6c** (750 mg, 86%) as a pale yellow oil: ^1H NMR δ 7.52–7.20 (m, 5H), 6.63 (t, J = 5 Hz, 1H), 2.72–2.61 (m, 2H), 2.49–2.37 (m, 2H), 1.90–1.72 (m, 4H).

2-(Phenylthio)-2-cyclooctenone (6d) was prepared as reported[13] in 94% yield and was used without purification for the next step: ^1H NMR δ 7.55–7.20 (m, 5H), 6.42 (t, J = 6 Hz, 1H) 2.49–2.27 (m, 4H), 1.92–1.53 (m, 6H).

General Procedure for the Preparation of 2-(Phenylsulfinyl)-2-cycloalkenones 7a–d. A mixture of sodium periodate (4.4 mmol), water (6 mL), methanol (6 mL), and 2-(phenylthio)-2-cycloalkenone (2.2 mmol) was stirred at room temperature for 16 h. The white precipitate was removed by suction filtration and washed with a small amount of methanol. The combined filtrates were concentrated *in vacuo*, diluted with water, and extracted with CH_2Cl_2, and the extracts were dried ($MgSO_4$) and evaporated under reduced pressure.

2-(Phenylsulfinyl)-2-cyclopentenone (7a)[27] was purified by chromatography (EtOAc) (87%): mp 72–74 °C; ^1H NMR δ 8.15 (t, J = 3 Hz, 1H), 7.84–7.72 (m, 2H), 7.54–7.45 (m, 3H), 2.96–2.41 (m, 4H).

2-(Phenylsulfinyl)-2-cyclohexenone (7b). Purification by chromatography (Et_2O) gave an oil, (80%): ^1H NMR δ 7.79–7.67 (m, 3H), 7.48–7.38 (m, 3H), 2.67–2.30 (m, 4H), 2.10–1.95 (m, 2H).

2-(Phenylsulfinyl)-2-cycloheptenone (7c): yellow oil, 98%, was suitable for conversion to sulfone **7d** without purification; ^1H NMR δ 7.73–7.64 (m, 2H), 7.47–7.39 (m, 3H), 7.33 (t, J = 5 Hz, 1H), 2.82–2.55 (m, 3H), 2.48–2.32 (m, 1H), 1.93–1.69 (m, 4H).

2-(Phenylsulfinyl)-2-cyclooctenone (7d). Flash chromatography (petroleum ether/Et_2O 1:1) provided **7d** as an oil (83%): ^1H NMR δ 7.73–7.55 (m, 2H), 7.54–7.38 (m, 3H), 6.93 (t, J = 6 Hz, 1H), 2.85–2.18 (m, 3H), 1.86–1.40 (m, 7H).

General Procedure for the Preparation of 2-(Phenylsulfonyl)-2-cycloalkenones (8a–d). To an ice-cooled stirred solution of 2-(phenylsulfinyl)-2-cycloalkenone (11 mmol) in CH_2Cl_2 (130 mL) was added a solution of *m*-CPBA (7 mmol) in CH_2Cl_2 (20 mL), and the reaction mixture was stirred at room temperature. Additional portions of *m*-CPBA were added to complete the oxidation, 2 mmol after 8 h and 2 mmol after an additional 12 h (TLC). After 3 h of additional stirring, the reaction mixture was washed with aqueous $NaHCO_3$, and the resulting aqueous layer was washed again with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure.

(23) In the bicyclo [5.3.0] and [6.3.0] series desulfonylation was successful on a silica gel G (Merck) column. See: Yoshida, T.; Saito, S. *Chem. Lett.* **1982**, 165 for an example of acid-catalyzed desulfonylation of a γ-ketosulfonyl group.

(24) Ghera, E.; Yechezkel, T.; Hassner, A. *J. Org. Chem.* **1990**, *55*, 5977.

(25) The use of LiBr in 1,4 additions provided cleaner reaction results; for a recent example of LiBr added to a lithium base in Michael addition see: Lambs, L.; Singh, N. P. Biellmann, J. F. *J. Org. Chem.* **1992**, *57*, 6301.

(26) For the general preparation method see: Monteiro, H.; De Souza, J. P. *Tetrahedron Lett.* **1975**, 921.

(27) Compound **7a** was previously mentioned but not characterized: Ono, N.; Kamimura, A.; Miyake, H.; Hamamoto, I.; Kaji, A. *J. Org. Chem.* **1985**, *50*, 3692.

2-(Phenylsulfonyl)-2-cyclopentenone (8a) was directly crystallized (CH_2Cl_2/Et_2O, 85%) because on chromatography some decomposition occurs: mp 113–114 °C; ^1H NMR δ 8.49 (t, J = 3 Hz, 1H), 8.12–8.03 (m, 2H), 7.69–7.48 (m, 3H), 2.88–2.77 (m, 2H), 2.65–2.52 (m, 2H); ^{13}C NMR δ 198.76 (s), 171.01 (d), 146.65 (s), 138.92 (s), 133.92 (d), 128.94 (d, 2 × CH), 128.44 (d, 2 × CH), 35.83 (t), 26.72 (t); MS m/z 240 (MNH_4^+, 100), 223 (MH^+, 2).

2-(Phenylsulfonyl)-2-cyclohexenone (8b). Flash column chromatography (petroleum ether/EtOAc 1:1) gave **8b** (80%): mp 110–112 °C; ^1H NMR δ 8.22, (t, J = 5 Hz, 1H), 8.06–7.97 (m, 2H), 7.67–7.45 (m, 3H), 2.73–2.61 (m, 2H), 2.49–2.39 (m, 2H), 2.11–1.97 (m, 2H); ^{13}C NMR δ 191.25 (s), 158.39 (d), 140.44 (s), 139.74 (s), 133.35 (d), 128.69 (d, 2 × CH), 128.59 (d, 2 × CH), 38.51 (t), 26.40 (t), 21.57 (t); MS m/z 254 (MNH_4^+, 100), 237 (MH^+, 3).

2-(Phenylsulfonyl)-2-cycloheptenone (8c). Crystallization (ether) produced **8c** (70%): mp 81–82 °C; ^1H NMR δ 7.99–7.90 (m, 3H), 7.62–7.45 (m, 3H), 2.74–2.63 (m, 4H), 1.88–1.74 (m, 4H); ^{13}C NMR δ 197.26 (s), 153.11 (d), 144.01 (s), 140.66 (s), 132.93 (d), 128.47 (d, 2 × CH), 128.17 (d, 2 × CH), 43.79 (t), 29.01 (t), 24.24 (t), 21.45 (t); MS m/z 268 (MNH_4^+, 100), 251 (MH^+, 5).

2-(Phenylsulfonyl)-2-cyclooctenone (8d). Flash chromatography (ether) provided **8d** (95%): mp 76–78 °C; ^1H NMR δ 7.87–7.77 (m, 2H), 7.66–7.45 (m, 3H), 7.38 (t, J = 6 Hz, 1H), 2.61–2.48 (m, 4H), 1.98–1.82 (m, 2H), 1.69–1.53 (m, 4H); ^{13}C NMR δ 204.17 (s), 146.88 (d), 139.63 (s), 138.94 (s), 133.32 (d), 128.76 (d, 2 × CH), 128.16 (d, 2 × CH), 44.79 (t), 30.25 (t), 28.68 (t), 21.26 (t), 21.03 (t); MS m/z 282 (MNH_4^+, 100), 265 (MH^+, 3).

(2*S,3*S**,1′*R**)-2-(Phenylsulfonyl)-3-[3′-bromo-2′-methylene-1′-(phenylsulfonyl)propyl]cyclopentan-1-one (9) and (2*S**,3*S**,1′*S**)-2-(Phenylsulfonyl)-3-[3′-bromo-2′-methylene-1′-(phenyl-sulfonyl)propyl]cyclopentan-1-one (10).** To a stirred solution of LDA, prepared from 0.08 mL (0.56 mmol) of diisopropylamine, 0.36 mL of n-BuLi (0.54 mmol, 1.54 M in hexane), and LiBr (40 mg) in 4 mL of THF was added dropwise at −100 °C a solution of **4** (110 mg, 0.4mmol) in 2 mL of THF. After being stirred for 10 min at the above temperature, the ketosulfone **8a** (97 mg, 0.44 mmol) in 2 mL of THF was added dropwise. After 5 min the reaction mixture was quenched with aqueous (20%) AcOH, poured into water, and extracted with CH_2Cl_2. The extracts were washed successively with saturated $NaHCO_3$ solution and water, dried ($MgSO_4$), and evaporated under reduced pressure. The diastereomeric ratio (**9**/**10**, 2:1) was established by integrated ^1H NMR spectra of the crude mixture. Chromatographic purification (EtOAc/petroleum ether 1:2) gave first **9** (107 mg, 54%) and then **10** (56 mg, 28%). **9**: mp 167–168 °C; ^1H NMR δ 8.00–7.94 (m, 2H), 7.93–7.87 (m, 2H), 7.75–7.66 (m, 2H), 7.65–7.55 (m, 4H), 5.68 (bs, 1H), 5.15 (s, 1H), 4.63 (bd, J = 5 Hz, 1H), 4.09 (d, J = 9 Hz, 1H), 3.99 (d, J = 11 Hz, 1H), 3.91 (dd, J = 11, 1 Hz, 1H), 3.74–3.62 (m, 1H), 2.67–2.51 (m, 1H), 2.48–2.37 (m, 2H), 2.13 (quintet, J = 6 Hz, 1H); ^{13}C NMR δ 205.46 (s), 137.76 (s), 136.14 (s), 135.90 (s), 134.41 (d), 134.35 (d), 130.09 (d, 2 × CH), 129.25 (d, 2 × CH), 129.20 (d, 2 × CH), 129.06 (d, 2 × CH), 126.06 (t), 72.06 (d), 68.52 (d), 37.21 (t), 37.09 (t), 36.72 (d), 23.97 (t); MS m/z 499, 497 (MH^+, 100, 84), 434 (54), 417 (75), 275 (52), 143 (85). Anal. Calcd for $C_{21}H_{21}BrO_5S_2$: C, 50.81; H, 4.06; S, 12.91. Found: C, 50.89; H, 4.25; S, 12.43. **10**: mp 133–134 °C; ^1H NMR δ 7.90–7.81 (m, 4H), 7.75–7.66 (m, 2H), 7.63–7.53 (m, 4H), 5.60 (q, J = 1 Hz, 1H), 5.43 (s, 1H), 4.34 (d, J = 5 Hz, 1H), 4.19 (d, J = 8 Hz, 1H), 3.85 (dd, J = 11, 1 Hz, 1H), 3.64 (dd, J = 11, 1 Hz, 1H), 3.60 (dtd, J = 8, 5, 2 Hz, 1H), 2.86 (dt, J = 12, 6 Hz, 1H), 2.63–2.43 (m, 2H); ^{13}C NMR δ 205.30 (s), 137.82 (s), 137.12 (s), 134.45 (d), 134.34 (d), 129.63 (d, 2 × CH), 129.19 (d, 2 × CH), 129.16 (d, 2 × CH), 129.05 (d, 2 × CH), 124.26 (t), 72.66 (d), 67.37 (d), 39.14 (d), 37.30 (t), 36.84 (t); MS m/z 500 ((M + 3)$^+$, 36), 498 (MH^+, 24), 417 (82), 357, 355 (100, 95), 133 (81).

(3aβ,4α,6aβ)-5-Methylene-[4,6a-bis(phenylsulfonyl)-hexahydro-1(2*H*)-pentalenone (11) and (3aβ,4β,6aβ)-5-Methylene-[4,6a-bis(phenylsulfonyl)-hexahydro-1(2*H*)-pentalenone (12). Lithiated **4** was reacted with ketosulfone **8a** under the conditions and in the amounts shown for the preparation of **9** and **10**. To the stirred reaction mixture was added HMPA (0.5 mL) dropwise at −100 °C. The reaction mixture was allowed to warm to −40 °C (30 min) and was stirred at this temperature for an additional 1 h. Workup as before and chromatography (EtOAc/petroleum ether 2:3) gave by order of elution **9** (67 mg, 34%), **11** + **13** (54 mg, 28% + 5%), and **12** (43 mg, 26%). Crystallization (EtOAc/petroleum ether) gave pure **11**: mp 181–182 °C; ^1H NMR δ 7.94–7.88 (m, 2H), 7.83–7.77 (m, 2H), 7.75–7.53 (m, 6H), 5.09 (q, J = 2 Hz, 1H), 4.92 (q, J = 2 Hz, 1H), 4.52 (dq, J = 8, 1.5 Hz, 1H), 3.87 (qd, J = 8, 1.5 Hz, 1H), 2.87 (dt, J = 18, 2 Hz, 1H), 2.77 (dq, J = 18, 2 Hz, 1H), 2.69–2.34 (m, 4H); ^{13}C NMR δ 208.38 (s), 139.47 (s), 138.83 (s), 134.95 (s), 134.60 (d), 134.07 (d), 130.44 (d, 2 × CH), 129.22 (d, 2 × CH), 128.95 (d, 2 × CH), 128.36 (d, 2 × CH), 115.56 (t), 78.80 (s), 70.29 (d), 46.04 (d), 39.26 (t), 37.53 (t), 20.47 (t); MS m/z 417 (MH^+, 31), 275 (40), 133 (100). Anal. Calcd for $C_{21}H_{20}S_2O_5$: C, 60.55; H, 4.84; S, 15.39. Found: C, 60.25, H, 4.79; S, 14.90.

12: mp 176–177 °C; ^1H NMR δ 7.98–7.90 (m, 2H), 7.77–7.52 (m, 8H), 5.12 (dt, J = 1.5, 1 Hz, 1H), 5.06 (dt, J = 1.5, 1 Hz, 1H), 4.11 (td, J = 6, 2 Hz, 1H), 3.73 (dq, J = 6, 1.5 Hz, 1H), 2.76–2.68 (m, 1H), 2.65 (dt, J = 14, 1.5 Hz, 1H), 2.53 (dddd, J = 17.5, 13.5, 10, 7 Hz, 1H), 2.43 (d, J = 15 Hz, 1H), 2.21 (ddd, J = 19, 10, 8 Hz, 1H), 1.88 (dd, J = 13, 9 Hz, 1H); ^{13}C NMR δ 210.50 (s), 138.10 (s), 136.32 (s), 136.13 (s), 134.53 (d), 134.21 (d), 129.94 (d, 2 × CH), 129.76 (d, 2 × CH), 129.24 (d, 2 × CH), 128.95 (d, 2 × CH), 117.84 (t), 79.00 (s), 75.72 (d), 45.17 (d), 40.94 (t), 36.74 (dd) 26.44 (dd); MS m/z 434 ($[MH_2O]^+$, 59), 417 (MH^+, 100), 275 (25), 143 (24).

The double bond isomer (**13**, 5%) could not be obtained in pure form but was characterized (from the mixture with **11**) by ^1H NMR: δ 7.95–7.86 (m, 2H), 7.76–7.50 (m, 8H), 4.35–4.25 (m, 1H), 3.07 (bd, J = 19 Hz, 1H), 2.67 (bd, J = 19 Hz, 1H), 2.60 (ddd, J = 18.5, 9.5, 6 Hz, 1H), 2.46–2.33 (m, 2H), 2.20 (ddd, J = 18.5, 9, 8 Hz, 1H), 2.10 (bs, 3H).

(3aβ,4α,6aβ)-5-Methylene-6a-(phenylsulfinyl)-4-(phenylsulfonyl)hexahydro-1(2*H*)-pentalenone (14) and (3aβ,4β,6aβ)-5-Methylene-6a-(phenylsulfinyl)-4-(phenylsulfonyl)hexahydro-1(2*H*)-pentalenone (15). Lithiated **4** was reacted with keto sulfone **7a** under the conditions and amounts given for the preparation of **9** and **10**. To the stirred solution was added HMPA (0.8 mL) dropwise at −85 °C. The reaction mixture was allowed to warm to −40 °C during 1.5 h; workup as described earlier and chromatographic purification (petroleum ether/EtOAc 1:1) gave, by order of elution, a small amount (~5%) of unstable, uncharacterized open-chain adduct followed by **15** (91 mg, 57%) and **14** (14 mg, 9%).

14: ^1H NMR δ 7.90–7.82 (m, 2H), 7.73–7.48 (m, 8H), 5.13 (dt, J = 3, 1 Hz, 1H), 4.83 (dt, J = 3.5, 1 Hz, 1H), 3.70 (dq, J = 4.5, 1.5 Hz, 1H), 3.65–3.57 (m, 1H), 2.85 (dtd, J = 15.5, 3, 2 Hz, 1H), 2.63 (bd, J = 15.5 Hz, 1H), 2.17–1.97 (m, 3H), 1.78–1.64 (m, 1H); ^{13}C NMR δ 211.94 (s), 139.12 (s), 136.29 (s), 134.18 (d), 132.44 (d), 129.52 (d, 2 × CH), 129.16 (d, 4 × CH), 128.90 (s), 125.72 (d, 2 × CH), 117.43 (t), 77,23 (s), 75.95 (d), 43.10 (d), 38.49 (t), 37.44 (d), 25.96 (d); MS m/z 401 (MH^+, 23), 275 (42), 133 (100), 125 (58), 78 (50).

15: mp 133–134 °C; ^1H NMR δ 8.01–7.93 (m, 2H), 7.76–7.68 (m, 1H), 7.66–7.46 (m, 7H), 5.14 (dd, J = 2.5, 1 Hz, 1H), 4.95 (dt, J = 3, 1 Hz, 1H), 3.97 (dt, J = 8.5, 3.5 Hz, 1H), 3.78 (dq, J = 3.5, 1.5 Hz, 1H), 2.80 (dtd, J = 15.5, 3, 2 Hz, 1H), 2.44 (bd, J = 15.5 Hz, 1H), 2.33–2.10 (m, 2H), 1.91 (dddd, J = 13.5, 10, 8.5, 7.5 Hz, 1H), 1.60–1.46 (m, 1H); ^{13}C NMR δ 211.48 (s), 139.56 (s), 139.13 (s), 136.33 (s), 134.15 (d), 132.13 (d), 129.54 (d, 2 × CH), 129.15 (d, 2 × CH), 128.84 (d, 2 × CH), 125.10 (d, 2 × CH), 117.68 (t), 77.00 (d), 76.86 (s), 43.87 (d), 39.48 (t), 38.42 (t), 26.43 (t); MS m/z 401 (MH^+, 58), 275 (82), 235 (65), 134 (90), 126 (100); MS m/z 401 (MH^+, 55), 275 (83), 126 (100), 77 (35).

Oxidation of 15 to 12. To a stirred solution of **15** (30 mg, 0.075 mmol) in MeOH (3 mL) and water (2.5 mL) at 0 °C was added oxone (150 mg). After the reaction mixture was stirred overnight, TLC analysis showed complete conversion. Dilution with water and extraction with CH_2Cl_2 afforded, after usual workup, a crystalline residue (30 mg, 98%) identical (^1H NMR) with **12**. A similar oxidation of **14** gave the sulfone **11** in quantitative yield.

(2S*,3S*,1′S*)-2-(Phenylsulfonyl)-3-[3′-bromo-2′-methylene-1′-(phenylsulfonyl)propyl]cyclohexan-1-one (16)

and (2S*,3S*,1'R*)-2-(Phenylsulfonyl)-3-[3'-bromo-2'-methylene-1'-(phenylsulfonyl)propyl]cyclohexane-1-one (17). The reaction of **4** with keto sulfone **8b** following the procedure and amounts as described for obtaining **9** and **10** gave the ratio 1.5:1 for **16/17**. Chromatography, using the same eluents, gave, in order of elution, **17** (98 mg, 48%) and **16** (65 mg, 32%).

16: ^{1}H NMR δ 7.84–7.80 (m, 2H), 7.77–7.72 (m, 2H), 7.71–7.64 (m, 1H), 7.60–7.50 (m, 5H), 5.53 (bs, 1H), 5.34 (s, 1H), 4.04 (q, J = 2 Hz, 1H), 3.94 (d, J = 10.5 Hz, 1H), 3.72–3.65 (m, 1H), 3.63 (dd, J = 11, 1 Hz, 1H), 3.39 (dd, J = 11, 1 Hz, 1H), 2.89 (ddd, J = 15.5, 12, 7 Hz, 1H), 2.77–2.58 (m, 2H), 2.53 (dtd, J = 16, 4, 2 Hz, 1H), 2.16–1.93 (m, 2H); ^{13}C NMR δ 200.55 (s), 137.67 (s), 136.99 (s), 134.28 (d, 2 × CH), 129.81 (s), 129.55 (d, 2 × CH), 129.23 (d, 2 × CH), 129.07 (d, 2 × CH), 128.52 (d, 2 × CH), 124.02 (t), 73.90 (d), 67.29 (d), 40.55 (t), 37.25 (d), 35.69 (t), 23.84 (t), 20.68 (t); MS m/z 514, 512 ((MH$^+$, 23, 18), 371, 369 (39, 36), 147 (100).

17: mp 152–153 °C; ^{1}H NMR δ 7.93–7.86 (m, 2H), 7.83–7.78 (m, 2H), 7.74–7.50 (m, 6H), 5.65 (s, 1H), 5.19 (q, J = 1 Hz, 1H), 5.08 (q, J = 1 Hz, 1H), 3.93 (d, J = 10 Hz, 1H), 3.84 (d, J = 12 Hz, 1H), 3.82–3.75 (m, 1H), 3.73 (d, J = 12 Hz, 1H), 2.97 (ddd, J = 16, 11, 8 Hz, 1H), 2.57 (tt, J = 10, 5 Hz, 1H), 2.48 (dt, J = 16, 4 Hz, 1H), 2.04–1.75 (m, 3H); ^{13}C NMR δ 201.43 (s), 138.04 (s), 136.43 (s), 136.06 (s), 134.3 (d, 2 × CH), 129.67 (d, 2 × CH), 129.27 (d, 2 × CH), 129.01 (d, 2 × CH), 128.61 (d, 2 × CH), 126.32 (t), 73.75 (d), 69.23 (d), 39.66 (t), 36.01 (d), 35.07 (t), 23.64 (dd), 21.16 (t); MS m/z 513, 511, (MH$^+$, 65, 52), 431 (50), 371 (100, 81). Anal. Calcd for $C_{22}H_{23}BrS_2O_5$: C, 51.76; H 4.34; S, 12.56. Found: C, 51.50; H, 4.47; S, 12.20.

(1β,3aβ,7aβ)-2-Methylene-[1,3a-bis(phenylsulfonyl)]octahydro-4*H*-inden-4-one (18) and (1α,3aβ,7aβ)-2-Methylene-[1,3a-bis(phenylsulfonyl)]-octahydro-4H-inden-4-one (19). Lithiated **4** was reacted with keto sulfone **8b** under conditions and amounts as described for **8a**. The reaction mixture was then allowed to warm from −100 to 0 °C (30 min) and stirred for an additional 2 h at the above temperature. Quenching and workup as shown before were followed by chromatographic purification (EtOAc/petroleum ether 1:1) to give, by order of elution, **19** (8 mg, 4.5%) and a mixture of **18** and **20** (98 mg, 57% and 16 mg, 9%, respectively); crystallization (EtOAc/petroleum ether) afforded pure **18**: mp 202–203 °C; ^{1}H NMR δ 7.96–7.89 (m, 2H), 7.76–7.47 (m, 8H), 5.13 (ddd, J = 2, 1.5, 0.5 Hz, 1H), 5.11 (ddd, J = 2, 1.5, 0.5 Hz, 1H), 4.04 (ddt, J = 7.5, 5.5, 2 Hz, 1H), 3.80, (dq, J = 8, 2 Hz, 1H), 3.07 (ddd, J = 15, 14, 6 Hz, 1H), 2.62 (d, J = 14 Hz, 1H), 2.52 (bdd, J = 15, 3.5 Hz, 1H), 2.48 (tdd, J = 14, 5, 3.5 Hz, 1H), 2.23 (dq, J = 14, 3 Hz, 1H), 2.15–2.02 (m, 1H), 1.87 (ddd, J = 14, 3.5, 2 Hz, 1H), 1.74 (qt, J = 14, 3.5 Hz, 1H); ^{13} C NMR δ 202.52 (s), 137.34 (s), 136.03 (s), 135.47 (s), 134.48 (d), 134.18 (d), 129.95 (d, 2 × CH), 129.51 (d, 2 × CH), 129.16 (d, 2 × CH), 128.92 (d, 2 × CH), 117.53 (t), 78.03 (s), 70.50 (d), 43.22 (d), 41.18 (t), 40.58 (t), 25.46 (dd), 21.38 (t); MS m/z 431 (MH$^+$, 100), 289 (93), 147 (76). Anal. Calcd for $C_{22}H_{22}S_2O_5$: C, 61.37; H, 5.15; S, 14.89. Found: C, 61.19; H, 5.04; S, 14.40.

19: mp 172–174 °C; ^{1}H NMR δ 7.85–7.77 (m, 2H), 7.73–7.48 (m, 8H), 4.89 (dt, J = 3, 1.5 Hz, 1H), 4.30 (bd, J = 8 Hz, 1H), 4.20 (dt, J = 3, 1.5 Hz, 1H), 4.06 (q, J = 8 Hz, 1H), 3.26 (dt, J = 18, 3 Hz, 1H), 3.01 (dt, J = 17.5, 7.5 Hz, 1H), 2.75–2.60 (m, 1H), 2.60 (d, J = 17.5, 5 Hz, 1H), 2.55 (dd, J = 17.5, 6.5 Hz, 1H), 2.48–2.27 (m, 2H), 2.25–2.12 (m, 1H); ^{13}C NMR δ 204.23 (s), 139.51 (s), 137.93 (s), 134.63 (s), 134.56 (d), 133.93 (d), 130.29 (d, 2 × CH), 129.05 (d, 2 × CH), 128.93 (d, 2 × CH), 128.85 (d, 2 × CH), 115.99 (dd), 80.28 (s), 72.71 (d), 44.42 (d), 39.01 (t), 38.82 (t), 23.59 (t), 21.90 (t); MS m/z 431 (MH$^+$, 36), 289 (100), 147 (77).

The double bond isomer (**20**) was not obtained in pure form but was characterized from the mixture with **18**: ^{1}H NMR δ 7.93–7.85 (m, 2H), 7.73–7.48 (m, 8H), 4.26–4.14 (m, 1H), 3.08 (dq, J = 18, 1Hz, 1H), 2.92 (dt, J = 17, 8 Hz, 1H), 2.90 (d, J = 18 Hz, 1H), 2.57–2.36 (m, 2H), 2.09 (bs, 3H), 2.01–1.87 (m, 1H), 1.85–1.63 (m, 2H); ^{13}C NMR δ 204.24 (s), 152.37 (s), 141.16 (s), 134.98 (s), 134.55 (d), 134.17 (s), 133.49 (d), 129.94 (d, 2 × CH), 129.53 (d, 2 × CH), 129.27 (d, 2 × CH), 127.14 (d, 2 × CH), 78.30 (s), 50.20 (d), 44.91 (t), 39.41 (t), 26.76 (dd), 20.60 (t), 15.55 (q); MS DCI/NH$_3$ m/z 448 (MNH$_4^+$, 100), 308 (10).

(2S*,3R*,1'S*)-2-(Phenylsulfonyl)-3-[3'-bromo-2'-methylene-1'-(phenylsulfonyl)propyl]cycloheptan-1-one (21) and (1β,3aβ,8aβ)-2-Methylene-[1,3a-bis(phenylsulfonyl)-octahydro-1*H*-azulen-4-one (22). Lithiated **4** was reacted with **8c** under conditions and amounts as described for **8a**, and the reaction mixture was stirred at −85 °C for 1 h. Workup as usual and chromatography (EtOAc/petroleum ether 2:3) gave **21** (48 mg, 23%) and **22** (105 mg, 50%). **21**: mp 157–158 °C; ^{1}H NMR δ 7.96–7.87 (m, 2H), 7.79–7.48 (m, 8H), 5.80 (q, J = 1 Hz, 1H), 5.59 (s, 1H), 4.84 (d, J = 3 Hz, 1H), 4.11 (d, J = 10 Hz, 1H), 4.06 (dd, J = 12, 1 Hz, 1H), 3.97 (dd, J = 12, 1 Hz, 1H), 3.62 (tdd, J = 11, 3.5, 1 Hz, 1H), 3.09 (td, J = 12, 3 Hz, 1H), 2.93 (bdd, J = 15, 6 Hz, 1H), 2.32 (ddd, J = 13, 8, 3 Hz, 1H), 2.13–1.93 (m, 2H), 1.67 (qdd, J = 13, 4, 2 Hz, 1H), 1.43 (tt, J = 12, 3 Hz, 1H), 1.27 (dtd, J = 15, 11, 2 Hz, 1H); ^{13} C NMR δ 203.05 (s), 137.96 (s), 137.51 (s), 134.61 (s), 134.61 (d), 134.13 (d), 129.38 (d, 4 × CH), 129.21 (t), 129.01 (d, 2 × CH), 128.49 (d, 2 × CH), 79.20 (d), 69.38 (d), 41.72 (dd), 35.48 (d), 34.55 (t), 29.69 (t), 29.35 (t), 27.19 (t); MS m/z 527, 525 (MH$^+$, 23, 18), 445 (98), 385, 383 (100, 84).

22: mp 187–188 °C; ^{1}H NMR δ 7.97–7.88 (m, 2H), 7.78–7.48 (m, 8H), 5.17 (dt, J = 2.5, 1.5 Hz, 1H). 5.10 (dt, J = 2.5, 1.5 Hz, 1H), 3.96 (dq, J = 8, 1.5 Hz, 1H), 3.87 (ddd, J = 8, 5.5, 2.5 Hz, 1H), 3.20 (ddd, J = 13, 10, 3.5 Hz, 1H), 2.60 (d, J = 13 Hz, 1H), 2.53 (dq, J = 13, 1.5 Hz, 1H), 2.36 (ddd, J = 13, 11, 3 Hz, 1H), 1.96 (dtd, J = 16, 5.5, 3 Hz, 1H), 1.89–1.67 (m, 3H), 1.64–1.43 (m, 2H); ^{13}C NMR δ 203.49 (s), 137.97 (s), 137.03 (s), 136.29 (s), 134.22 (d), 134.15 (d), 129.91 (d, 2 × CH), 129.85 (d, 2 × CH), 129.15 (d, 2 × CH), 128.79 (d, 2 × CH), 117.17 (t), 82.90 (s), 69.69 (d), 41.89 (t), 41.87 (d), 41.43 (t), 27.05 (t), 21.79 (t), 21.61 (t); MS m/z 445 (MH$^+$, 100), 303 (48), 161 (38). Anal Calcd for $C_{23}H_{24}O_5S_2$: C, 62.14; H, 5.44. Found: C, 62.07; H, 5.55.

(1β,3aβ,8aα)-2-Methylene-[1,3a-bis(phenylsulfonyl)-octahydro-1*H*-azulen-4-one (23) and (3aβ,8aβ)-1,3-Bis-(phenylsulfonyl)]-3a,5,6,7,8,8a-hexahydro-1*H*-azulen-4-one (24). To a solution of **21** (120 mg, 0.24 mmol) in 8 mL of THF at −100 °C was added dropwise a solution of LDA (0.32 mmol, containing 20 mg LiBr) in 8 mL of THF. After the solution was stirred for 5 min at the above temperature, HMPA (2 mL) was added dropwise, and the reaction mixture was allowed to warm to −50 °C (30 min) and was stirred at this temperature for 40 min. Workup as shown earlier and chromatography (EtOAc/petroleum ether 2:3) gave **21** (28 mg, 23%), **23** (52 mg, 51%), and **24** (6 mg, 5%).

23: mp 152–153 °C; ^{1}H NMR δ 8.03–7.96 (m, 2H), 7.74–7.58 (m, 6H), 7.56–7.47 (m, 2H), 5.23 (dq, J = 7, 2 Hz, 1H), 5.21 (q, J = 2.5 Hz, 1H), 5.10 (q, J = 2.5 Hz, 1H), 3.54 (bdd, J = 11, 7 Hz, 1H), 3.41 (ddd, J = 12.5, 11.5, 3 Hz, 1H), 3.18 (dq, J = 19, 2 Hz, 1H), 2.94 (dd, J = 16, 6 Hz, 1H), 2.77 (dq, J = 19, 2 Hz, 1H), 2.60–2.50 (m, 1H), 2.08–1.93 (m, 2H) 1.55–1.30 (m, 2H), 1.06 (dt, J = 16, 11 Hz, 1H); ^{13} C NMR δ 204.27 (s), 140.45 (s), 137.57 (s), 134.90 (s), 134.72 (d), 133.87 (d), 129.59 (d, 2 × CH), 129.45 (d, 2 × CH), 129.13 (d, 2 × CH), 128.06 (d, 2 × CH), 113.07 (t), 85.47 (s), 69.62 (d), 45.14 (d), 43.34 (dd), 36.67 (t), 29.31 (t), 28.07 (t), 27.82 (t); MS m/z 445 (MH$^+$, 100), 303 (40), 160 (53), 77 (32).

24: mp 182–184 °C; ^{1}H NMR δ 7.95–7.92 (m, 2H), 7.71–7.56 (m, 6H), 7.52–7.44 (m, 2H), 3.98 (dq, J = 11, 1.5 Hz, 1H), 3.41 (dt, J = 20, 1.5 Hz, 1H), 3.38 (td, J = 11, 3 Hz, 1H), 2.60 (dd, J = 20, 1 Hz, 1H), 2.60–2.51 (m, 1H), 2.45 (ddq, J = 15, 6.5, 1.5 Hz, 1H), 2.07–1.88 (bs, 3H), 1.67 (qdd, J = 13, 3.5, 1.5 Hz, 1H), 1.43 (qt, J = 12.5, 3.5 Hz, 1H), 1.17–1.02 (m, 1H); ^{13} C NMR δ 203.27 (s), 150.93 (s), 136.34 (s), 136.07 (s), 134.42 (d), 133.46 (d), 129.95 (s), 129.71 (d, 2 × CH), 129.15 (d, 4 × CH), 127.60 (d, 2 × CH), 86.70 (s), 50.49 (d), 43.24 (dd), 42.46 (dd), 32.33 (dd), 28.26 (t), 27.15 (t), 15.17 (q); MS m/z 445 (MH$^+$, 24), 302 (41), 161 (100).

(2S*,3R*,1'S*)-2-(Phenylsulfonyl)-3-[3'-bromo-2'-methylene-1'-(phenylsulfonyl)propyl]cyclooctan-1-one (25), (1β,3aβ,9aβ)-2-Methylene-[1,3a-bis(phenylsulfonyl)decahydro-4*H*-cyclopentacycloocten-4-one (26), and (1α,3aβ,-9aβ)-2-Methylene-[1,3a-bis(phenylsulfonyl)decahydro-4*H*-cyclopentacyclooctene-4-one (27). Bromo sulfone **4** was reacted with the keto sulfone **8d** under the conditions and amounts given for the preparation of **11** and **12**, and the reaction mixture was stirred at −40 °C for 2.5 h. Usual

workup and chromatography (EtOAc/petroleum ether 1:2) gave **25** (97 mg, 45%) and **26** (55 mg, 30%).

25: mp 175–176 °C; ^{1}H NMR δ 8.35–8.24 (m, 2H), 8.00–7.89 (m, 2H), 7.74–7.52 (m, 6H), 5.82 (bs, 1H), 5.77 (bs, 1H), 5.70 (bs, 1H), 5.40 (bd, J = 10 Hz, 1H), 3.86 (tt, J = 10, 2 Hz, 1H), 3.43 (bd, J = 12 Hz, 1H), 3.10 (bd, J = 12 Hz, 1H), 2.92 (td, J = 12, 4 Hz, 1H), 2.42–2.26 (m, 2H), 2.08–1.92 (m, 3H), 1.84–1.65 (m, 2H), 1.47–1.07 (m, 2H); ^{13} C NMR δ 205.29 (s), 142.63 (s), 137.85 (s), 134.20 (d), 133.33 (d), 129.88 (s), 129.15 (d, 4 × CH), 129.01 (d, 4 × CH), 122.81 (t), 73.27 (d), 67.40 (d), 40.68 (dd), 37.29 (d), 36.17 (t), 30.52 (t), 29.85 (t), 26.04 (t), 24.13 (t); MS m/z 540, 538 (MH^+, 22, 18), 459 (20), 399, 397 (100, 86), 175 (63). Anal. Calcd for $C_{24}H_{27}BrO_5S_2$: C, 53.43; H, 5.04. Found: C, 53.30; H, 5.03.

26: mp 199–200 °C; ^{1}H NMR δ 8.46–8.39 (m, 2H), 8.29–8.03 (m, 8H), 5.78 (ddd, J = 2, 1.5, 1 Hz, 1H), 5.50 (ddd, J = 2, 1.5, 1 Hz, 1H), 3.97–3.82 (m, 3H), 2.88 (d, J = 14 Hz, 1H), 2.70–2.55 (m, 1H), 2.45 (dtd, J = 14, 3, 1.5 Hz, 1H), 2.35 (dt, J = 13, 5 Hz, 1H), 2.09 (dq, J = 16, 6.5 Hz, 1H), 2.02–1.89 (m, 1H), 1.86–1.58 (m, 4H), 1.54–1.40 (m, 1H); ^{13}C NMR δ 206.47 (s), 138.68 (s), 136.47 (s), 136.39 (s), 134.60 (d), 134.14 (d), 129.75 (d, 2 × CH), 129.52 (d, 2 × CH), 129.23 (d, 2 × CH), 129.15 (d, 2 × CH), 116.39 (t), 82.32 (s), 69.68 (d), 44.85 (d), 39.91 (t), 39.67 (t), 28.21 (t), 27.07 (t), 25.87 (t), 22.38 (t); MS m/z 459 (MH^+, 42), 317 (52), 175 (100). Anal. Calcd for $C_{24}H_{26}O_5S_2$: C, 62.86; H, 5.72. Found: C, 63.15; H, 5.79.

On quenching the above reaction after 5 min at −100 °C (like for **9** and **10**), chromatography afforded compound **27** (46 mg, 25%) along with **25** (90 mg, 42%) and a small amount of **26** (9 mg, 5%).

27: mp 197–198 °C; ^{1}H NMR δ 8.14–8.07 (m, 2H), 8.00–7.92 (m, 2H), 7.75–7.47 (m, 6H), 5.24 (t, J = 2 Hz, 1H), 5.10 (t, J = 2 Hz, 1H), 4.45 (dq, J = 9.5, 2 Hz, 1H), 3.77 (ddd, J = 13, 9.5, 4 Hz, 1H), 2.65 (td, J = 12, 4 Hz, 1H), 2.58 (dq, J = 17, 2 Hz, 1H), 2.51 (tt, J = 13, 3 Hz, 1H), 2.24 (d, J = 17 Hz, 1H), 2.26–2.20 (m, 1H), 2.15–1.89 (m, 3H), 1.85–1.64 (m, 2H), 1.58–1.25 (m, 2H); ^{13}C NMR δ 207.27 (s), 139.65 (s), 138.65 (s), 138.62 (s), 137.08 (s), 134.23 (d), 133.89 (d), 130.70 (d, 2 × CH), 129.53 (d, 2 × CH), 129.22 (d, 2 × CH), 128.41 (d, 2 × CH), 116.12 (t), 83.75 (s), 71.27 (d), 46.42 (d), 42.58 (t), 39.39 (t), 31.17 (t), 29.45 (dd), 26.09 (t), 25.86 (t); MS m/z 459 (MH^+, 14), 317 (47), 175 (100).

(1β,3aβ,9aα)-2-Methylene-[1,3a-bis(phenylsulfonyl)]-decahydro-4*H*-cyclopentacycloocten-4-one (28). To a solution of **25** (30 mg, 0.056 mmol) in 1.5 mL of THF at 0 °C was added dropwise a solution of potassium *tert*-butoxide (9.5 mg, 0.084 mmol) in 1 mL of 2-methyl-2-propanol and 0.5 mL of THF. The reaction mixture was stirred for 2 h at 0 °C and 1 h at room temperature. Usual workup and chromatographic purification (EtOAc/petroleum ether 1:2) yielded **28** (20 mg, 79%): mp 202–203 °C; ^{1}H NMR δ 8.04–7.96 (m, 2H), 7.80–7.46 (m, 8H), 5.25 (q, J = 2 Hz, 1H), 5.22 (dqd, J = 7, 2.5, 1 Hz, 1H), 5.17 (q, J = 2 Hz, 1H), 3.79 (tt, J = 7, 1.5 Hz, 1H), 3.38 (ddd, J = 13.5, 11, 3 Hz, 1H), 3.35 (dq, J = 19, 2.5 Hz, 1H), 2.85 (dqd, J = 19, 2, 1 Hz, 1H), 2.64 (dquintet, J = 16, 3 Hz, 1H), 2.40 (dddd, J = 13, 11, 8, 3 Hz, 1H), 2.00–1.85 (m, 1H), 1.75–1.42 (m, 5H), 1.15–1.00 (m, 1H); ^{13}C NMR δ 205.06 (s), 141.06 (s), 138.03 (s), 136.44 (s), 134.69 (d), 133.85 (d), 129.48 (d, 2 × CH), 129.25 (d, 2 × CH), 127.93 (d, 2 × CH), 113.31 (t), 87.01 (s), 70.11 (d), 44.04 (d), 42.45 (dd), 36.44 (t), 26.68 (t), 25.78 (t), 25.11 (d), 24.81 (t); Ms m/z 459 (MH^+, 7), 317 (31), 175 (100). Anal. Calcd for $C_{24}H_{26}O_5S_2$: C, 62.86; H, 5.72. Found: C, 62.78; H, 5.76

4β-(Phenylsulfonyl)-2,3,3aβ,4-tetrahydropentalene-1,5-dione (29). Ozone was bubbled through a solution of **12** (30 mg, 0.07 mmol) in CH_2Cl_2 (6 mL) at −78 °C until the blue color persisted for 15 min. After argon purging and addition of dimethyl sulfide (0.5 mL), the reaction mixture was allowed to warm slowly to room temperature under argon during 2 h by decreasing the cooling, and the stirring was continued for additional 30 min at ambient temperature. Evaporation of solvent under reduced pressure and chromatography[23] (silica gel S 0.032–0.063 mm, pH = 7, Riedel-de-haën, EtOAc/petroleum ether 1:1) gave 14.5 mg of **29** (75%): ^{1}H NMR δ 8.03–7.95 (m, 2H), 7.76–7.68 (m, 1H), 7.65–7.57 (m, 2H), 6.43 (d, J = 3 Hz, 1H), 3.97 (d, J = 4 Hz, 1H), 3.86 (dddd, J = 11.5, 6.5, 4, 3 Hz, 1H), 2.75–2.60 (m, 2H), 1.85–1.69 (m, 2H); ^{13}C NMR δ 199.5, (s) 196.86 (s), 171.23 (s), 134.93 (s), 134.48 (d), 129.29 (d, 4 × CH), 127.07 (d), 75.81 (d), 44.71 (d), 39.97 (t), 27.47 (t); MS CI/CH_4 m/z 277 (MH^+, 33), 60 (100).

1β-(Phenylsulfonyl)-5,6,7,7aβ-tetrahydro-1*H*-indene-2,4-dione (30). Compund **18** (30 mg, 0.07 mmol) in CH_2Cl_2 (6 mL) was submitted to ozonolysis following the above procedure to give 16.2 mg (80%) of **30** and its enol **31**. The ratio 3:1 was determined by integration of the ^{1}H NMR spectrum and pure **30** was obtained by crystallization (EtOAc/petroleum ether).

30: mp 150–153 °C; ^{1}H NMR δ 7.98–7.90 (m, 2H), 7.76–7.68 (m, 1H), 7.65–7.55 (m, 2H), 6.34 (d, J = 2.5 Hz, 1H), 3.85 (d, J = 4 Hz, 1H), 3.70 (dddd, J = 12.5, 5.5, 4, 2.5 Hz, 1H), 2.81 (ddt, J = 17, 4, 2 Hz, 1H), 2.53 (d quintet, J = 13, 3 Hz, 1H), 2.42 (dddd, J = 19, 13, 6.5, 3 Hz, 1H), 2.24, (dtd, J = 14, 6, 3 Hz, 1H), 2.00 (qt, J = 14, 4 Hz, 1H), 1.63 (qd, J = 13, 3.5 Hz, 1H); ^{13}C NMR δ 196.94 (s), 194.87 (s), 169.31 (s), 137.79 (s), 134.42 (d), 130.26 (d), 129.36 (d, 2 × CH), 129.20 (d, 2 × CH), 74.06 (d), 44.82 (d), 41.35 (dd), 30.87 (dd), 23.22 (t); MS m/z 291 (MH^+, 100), 149 (65), 141 (16), 121 (15).

31: ^{1}H NMR (from a mixture with **30**) δ 7.98–7.55 (m, 5H), 6.05 (bd, J = 1.5 Hz, 1H), 5.56 (dd, J = 6, 3 Hz, 1H), 3.75 (d, J = 4 Hz, 1H), 3.47 (dtd, J = 14, 4, 2 Hz, 1H). The other peaks are overlapping with the peaks of **30**.

1,5,6,7,8,8aβ-Hexahydro-1β-(phenylsulfonyl)azulene-2,4-dione (32). Compound **22** (30 mg 0.067 mmol) was ozonized following the same procedure as above. Chromatography using silica gel 60 Merck (0.04–0.063 mm, pH 6.5–7.5, EtOAc/petroleum ether, 2:3) gave 17.5 mg of **32** (85%). The latter was obtained also from **23** using the same conditions in 73% yield: mp 135–137 °C; ^{1}H NMR δ 7.95–7.87 (m, 2H), 7.77–7.69 (m, 1H), 7.65–7.56 (m, 2H), 6.68 (d, J = 2 Hz, 1H), 3.76 (d, J = 2 Hz, 1H), 3.76 (d quintet, J = 10, 2.5 Hz, 1H), 2.88–2.80 (m, 1H), 2.76 (ddd, J = 16, 14, 2.5 Hz, 1H), 2.41 (d quintet, J = 14, 3 Hz, 1H), 2.21–2.09 (m, 2H), 1.78 (qd, J = 12, 3 Hz, 1H), 1.51 (qd, J = 13, 2.5 Hz, 1H), 1.47 (qd, J = 12, 2 Hz, 1H); ^{13}C NMR δ 198.09 (s), 195.54 (s), 170.77 (s), 137.33 (s), 134.99 (d), 134.50 (d), 129.27 (d, 2 × CH), 129.18 (d, 2 × CH), 75.30 (d), 44.11 (t), 42.95 (d), 36.43 (dd), 30.16 (t), 24.50 (dd); MS m/z 322 (MNH_4^+, 100), 305 (MH^+, 20).

5,6,7,8,9,9aβ-Hexahydro-1β-(phenylsulfonyl)-1*H*-cyclopentacyclooctene-2,4-dione (33). Compound **26** (30 mg, 0.065 mmol) was ozonized by the same procedure and the product was chromatographed with the silica and eluents as for **32**, to give 19.5 mg (93%) of enedione **33**; the latter was obtained, using the same procedure, also from **28** (60%) and from **27** (75%). In the last case more time was required for ozonolysis (2.5 h): mp 119–121 °C; ^{1}H NMR δ 7.91–7.83 (m, 2H), 7.75–7.67 (m, 1H), 7.64–7.55 (m, 2H), 6.32 (d, J = 2 Hz, 1H), 4.03 (ddt, J = 12, 6, 2 Hz, 1H), 3.72 (d, J = 2 Hz, 1H), 2.85 (td, J = 13, 4 Hz, 1H), 2.58 (ddd, J = 13, 5.5, 4 Hz, 1H), 2.27 (tdd, J = 11, 5.5, 2 Hz, 1H), 2.05–1.60 (m, 5H), 1.53–1.33 (m, 2H); ^{13}C NMR δ 203.88 (s), 197.50 (s), 174.10 (s), 136.80 (s), 134.52 (d), 131.89 (d), 129.26 (d, 2 × CH), 129.19 (d, 2 × CH), 75.16 (d), 42.87 (d), 40.55 (t), 35.35 (dd), 27.02 (t), 26.26 (t), 24.67 (t); MS m/z 317 (MH^+, 100), 175 (40).

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