$J_{A,B}$ = 10.9 Hz, $J_{A,X}$ = 7.3 Hz, $J_{B,X}$ = 7.0 Hz, CH_2-ethyl), 5.40 (1 H, s, 8-H), 6.07 (1 H, s, 2-H), 7.17–7.56 (15 H, m, H-arom); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3-ethyl), 19.3 (9-CH_3), 58.3 (C-8a), 59.4 (C-1a), 61.3 (C-8), 61.5 (CH_2-ethyl), 66.3 (C-2), 122.8 (C-10), 125.5–137.5 (C-arom), 153.1 (C-9), 156.3, 156.5 (CO-4/CO-6), 163.4 (CO-ester). Anal. Calcd for $C_{30}H_{25}N_3O_5$: C, 70.99; H, 4.96; N, 8.28. Found: C, 70.7; H, 5.01; N, 8.4.

Dimethyl 4,6-Dioxo-9-methyl-1a,5,8a-triphenyl-2,8-etheno-1a,2,5,6,8,8a-hexahydro-4*H*-oxireno[*d*][1,2,4]triazolo[1,2-*a*]pyridazine-10-phosphonate (25d). To a solution of 0.74 g (2.0 mmol) of oxepine **14d** in 25 mL of dichloromethane was added dropwise with stirring at room temperature within 30 min a solution of 0.35 g (2.0 mmol) of the triazolinedione **23**[31] in 25 mL of dichloromethane. After 1 h, the mixture was evaporated at 30 °C (15 Torr), and the residue was dissolved in ether. The resultant solution was treated with pentane until a slight cloudiness was observed, and then cooled at −20 °C for 24 h. The adduct **25d** was obtained as colorless crystals: 0.89 g (82%); mp 208 °C; IR (KBr) 1775, 1725 (C=O), 1625 (C=C), 1253 (P=O), 1020 cm^{-1} (POC); ^1H NMR δ 2.42 (3 H, d, $J_{H,P}$ = 3.4 Hz, 9-CH_3), 3.76 (3 H, d, $J_{H,P}$ = 11.3 Hz, $POCH_3$), 3.77 (3 H, d, $J_{H,P}$ = 11.4 Hz, $POCH_3$), 5.38 (1 H, d, $J_{H,P}$ = 5.0 Hz, 8-H), 5.67 (1 H, d, J_{H8P} = 8.4 Hz, 2-H), 7.23–7.50 (15 H, m, H-arom); ^{13}C NMR ($CDCl_3$) δ 19.8 (d, $J_{C,P}$ = 4.2 Hz, 9-CH_3), 52.6 (d, $J_{C,P}$ = 4.8 Hz, $POCH_3$), 52.9 (d, $J_{C,P}$ = 5.9 Hz, $POCH_3$), 57.9 (C-8a), 59.7 (d, $J_{C,P}$ = 4.4 Hz, C-1a), 62.4 (d, $J_{C,P}$ = 13.1 Hz, C-8), 65.3 (d, $J_{C,P}$ = 15.1 Hz, C-2), 119.2 (d, $J_{C,P}$ = 191.2 H, C-10), 125.5–132.3 (C-arom), 152.1 (d, $J_{C,P}$ = 9.3 Hz, C-9), 156.0, 156.4 (CO-4/CO-6). Anal. Calcd for $C_{29}H_{26}N_3O_6P$: C, 64.09; H, 4.82; N, 7.73. Found: C, 63.8; H, 4.92; N, 7.7.

X-ray Analysis of 25d. Crystal data: $C_{29}H_{26}N_3O_6P$, MW 543.5; orthorhombic space group $P2_12_12_1$; a = 7.956 (3), b = 16.370 (3), c = 20.340 (3) Å; Z = 4; D_{calc} = 1.361 g cm^{-3}. Data collection: Enraf-Nonius CAD 4 diffractometer, monochromatized Mo Kα radiation; crystal size 0.55 × 0.24 × 0.24 mm, 2371 unique reflections ($2 \leq \theta \leq 24°$), scan width $(0.90 + 0.35 \tan \theta)°$, scan speed 1.67–5° min^{-1}. Three monitoring reflections gave no hint to systematic changes of intensity. Structure solution and refinement: solution by MULTAN 82, full-matrix least-squares refinement of 456 variables with 1965 observations ($I > 2.2\sigma(I)$, unit weights). Hydrogen atoms were refined with isotropic temperature factors (B = 5.0 Å^2 except for C28 and C29 (B = 8.0 Å^2)). Final values: $R = 0.043$, $R_w = (\sum \Delta^2 F / \sum F_o^2)^{1/2} = 0.040$; maximum shift/error ratio 1.88 for H atoms, 0.60 for heavy atoms. All callculations were carried out on a PDP 11/23 plus computer using the Enraf-Nonius SDP software.

Acknowledgment. We are grateful to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support of this work.

Registry No. **6a**, 773-01-3; **6b**, 2340-23-0; **8a**, 109216-89-9; **8b**, 109216-90-2; **8c**, 109216-91-3; **8d**, 109216-92-4; **13a**, 109216-93-5; **13b**, 109216-94-6; **14a**, 109216-95-7; **14b**, 109216-96-8; **14c**, 109216-97-9; **14d**, 109216-98-0; **18a**, 109216-99-1; **18b**, 109217-00-7; **19a**, 109217-01-8; **19b**, 109217-02-9; **23**, 4233-33-4; **24**, 109241-75-0; **25a**, 109217-05-2; **25b**, 109217-06-3; **25c**, 109217-03-0; **25d**, 109217-04-1; **27c**, 109217-07-4; N_2=$CHCO_2Et$, 623-73-4; N_2=$CHPO(OMe)_2$, 27491-70-9; 2,6-diphenylpyrylium perchlorate, 3558-68-7; 4-methyl-2,6-diphenyl-4*H*-pyran, 55696-71-4.

Supplementary Material Available: ORTEP drawing and tables of positional and thermal parameters, bond distances, bond angles, and general thermal factors for **25d** (8 pages). Ordering information is given on any current masthead page.

Sulfur-33 NMR of Cyclic Sulfides, Sulfoxides, and Sulfones

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Natural abundance sulfur-33 chemical shifts were measured for three-, four-, five-, and six-membered ring sulfides, sulfoxides, and sulfones and the atomic charges at sulfur calculated for all compounds. With increasing oxidation of the sulfur atom there is proportionality between the chemical shift and the atomic charge only for three-membered ring compounds. Thiirane, thiirane 1-oxide, and thiirane 1,1-dioxide are shielded by several tens of ppm with respect to larger rings or the dimethyl analogues. The results are discussed in terms of a balance between the factors contributing to the chemical shift, namely, the atomic charge, the bond-order term, and the mean excitation energy.

Sulfur-containing compounds are useful intermediates in a variety of new syntheses of biologically important products.[1] Sulfur-33 NMR could in principle have a number of chemical applications, such as the identification of conformation or structure of sulfur-containing compounds, since NMR chemical shifts are intimately related to the electronic environment of a given nucleus.[2] Unfortunately, the experimental difficulties associated with sulfur-33 NMR[3] have discouraged organic chemists from exploring this interesting field, and even the chemical shifts of the most common organosulfur compounds are still unknown.

We have now measured the sulfur-33 chemical shifts of three-, four-, five-, and six-membered ring systems containing the sulfenyl (–S–), sulfinyl (–SO–), and sulfonyl (–SO_2–), functional groups, i.e., compounds **1**–**5**. Furthermore the charges at the sulfur atom were calculated for these compounds in order to find out whether there

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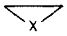
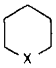
Table I. Sulfur-33 Chemical Shifts[a] and Line Widths[b] of Compounds 1-5

compd		X = S	X = SO	X = SO_2
 **1**	δ	−240	120	245
	$W_{1/2}$	140	215	13
 **2**	δ	31	365	331
	$W_{1/2}$	175	215	10
 **3**	δ	3[c]	360	368[c]
	$W_{1/2}$	239	130	3
 **4**	δ	−30[c]	*d*	321[c]
	$W_{1/2}$	239		4
$(CH_3)_2X$ (**5**)	δ	−95	325[c]	315[c]
	$W_{1/2}$	110	240	2

[a] In ppm with respect to CS_2 as external reference. [b] In ppm. [c] Reference 3c. [d] Not observed.

Table II. Calculated[a] Sulfur Atomic Charges[b] of Compounds 1-5

compd	X = S	X = SO	X = SO_2
1	−1	+280	+347
2	+29	+295	+370
3	+28	+291	+376
4	+32	+286	+374
5	+48	+307	+389

[a] Ab initio STO-3G*. See also: Boyd, R. J.; Szabo, J. P. *Can. J. Chem.* **1982**, *60*, 730. [b] In millielectrons.

is proportionality between the chemical shift and the atomic charge with increasing oxidation of the sulfur atom.

Results and Discussion

The chemical shifts and the line widths of compounds **1**–**5** are given in Table I together with all the available literature information.

The line widths of all sulfones are two orders of magnitude smaller than those of the corresponding sulfides and sulfoxides. This arises from a more symmetric electronic environment of sulfones.[3] No sulfur NMR signal was found for the six-membered ring sulfoxide, probably due to broadening beyond observability arising from the large electric field gradients present at the nucleus in this compound.[3,4]

Two main features are apparent from the data reported in Table I. First, in spite of the fact that a sulfonyl sulfur is always expected to have a greater electropositive character than a sulfinyl sulfur,[5] only the three-membered ring sulfone is largely deshielded with respect to the corresponding sulfoxide. Second, the three-membered ring compounds are markedly shielded compared to the larger rings and the dimethyl analogues, the shielding being more accentuated for thiirane and thiirane 1-oxide than for thiirane 1,1-dioxide.

Table II gives the calculated atomic charges on sulfur for all the compounds reported in Table I. Comparison of these data with those of Table I shows that oxidation of a sulfide to the sulfoxide leads for all compounds to an increase of the charge on sulfur of about 270 millielectrons, in line with an increase of the chemical shift of about 400 ppm. On the contrary, on going from a sulfoxide to the corresponding sulfone there is an increase of the positive charge on sulfur of about 75 millielectrons which does not correspond to a proportional increase of the chemical shift, except for the three-membered ring compound **1**. For **1** and only for it, the increase of the chemical shift following oxidation is proportional to the increase of the positive charge on sulfur. This is clearly shown by Figure 1 which is a plot of the chemical shifts of three-membered ring compounds and the dimethyl analogues against the charge on sulfur. For all remaining compounds, the effect on δ of the increase of the positive charge on sulfur following oxidation of a sulfoxide to the sulfone must be counterbalanced by some other and opposing effect.

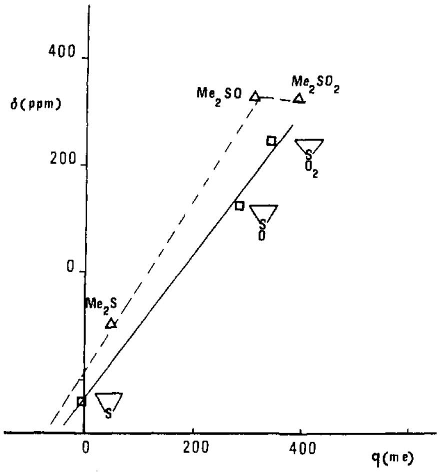


Figure 1. Sulfur-33 chemical shifts of compounds **1** and **5** against the calculated charges on sulfur (STO-3G*).

It is generally held[2] that for all nuclei but hydrogen the variations of the chemical shift within a series of related compounds are mainly determined by variations of the "local paramagnetic term", σ_p. In the framework of Pople's MO theory of the chemical shift,[2,6] for a nucleus A $\sigma_p{}^A(\mathrm{loc})$ is given by the expression in eq. 1. $\langle r^{-3}\rangle_{np}$ is the mean

$$\sigma_p{}^A(\mathrm{loc}) = -\frac{\mu_0 e^2 \hbar}{8m^2}\langle r^{-3}\rangle_{np}(\Delta E^{-1})\sum_B Q_{AB} \qquad (1)$$

inverse cube of the distance between the nucleus and its valence electrons and is proportional to the charge; ΔE is the average excitation energy, often approximated to the lowest singlet excitation energy and related to the wavelength of the appropriate UV transition; $\sum_B Q_{AB}$ is the bond-order term which increases with increasing the double bond character between A and the neighboring nuclei. According to the scale chosen (CS_2 as external reference), sulfur chemical shifts increase when $\langle r^{-3}\rangle_{np}$ and $\sum_B Q_{AB}$ increase and when ΔE decreases. The three terms upon which the chemical shift depends are interrelated; however, one of them may be predominant, cf. the correlations found between oxygen-17 chemical shifts and the low-lying n → π^* transitions of a variety of compounds[7] or between carbon-13 chemical shifts and the atomic charges for several classes of organic compounds.[8] In this respect it is worth recalling that for a given series of compounds a linear relationship between the chemical shift

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Table III. First Ionization Energies[a] (UPS) and Electron Affinities[a] (ETS) of $(CH_3)_2S$, $(CH_3)_2SO$, and $(CH_3)_2SO_2$

compd	IE	EA
$(CH_3)_2S$	8.67[b]	−3.3[e]
$(CH_3)_2SO$	9.01[c]	−2.1[f]
$(CH_3)_2SO_2$	10.65[d]	−3.1[f]

[a] In eV. [b] Reference 23. [c] Reference 24. [d] Reference 25. [e] Reference 26. [f] Modelli, A., private communication.

and the atomic charge can only be observed if the ratio between the bond-order term and the mean excitation energy remains constant within the series;[2] neglecting this fact may lead to misinterpretation of chemical shift variations.

In view of the fact that (i) sulfides and sulfoxides give very similar UV spectra[9] and that (ii) the C–S bond lengths of sulfides are very close to those of the corresponding sulfoxides,[10] it appears that oxidation of a sulfide to the corresponding sulfoxide leads to a variation of the chemical shift which is mainly determined by the increase of the positive charge on sulfur, in agreement with the data reported in Tables I and II.

Oxidation of a sulfoxide to the corresponding sulfone leads to the decrease of both S–O and C–S bond lengths, implying an increase of the bond-order term in Pople's expression for σ_p and a positive increment of δ. However, contrary to sulfoxides, sulfones show no absorption in the UV region,[9] suggesting that the lowest singlet excitation energy is higher for sulfones than for sulfoxides. Within the limits of Koopmann's theorem this is in agreement with the data reported in Table III, showing that the energy difference between the lowest electron affinity and ionization potential is higher for dimethyl sulfone than for dimethyl sulfoxide. Therefore, since the ΔE term of Pople's expression increases on going from a sulfoxide to the corresponding sulfone, its contribution to the variation of the chemical shift counterbalances those arising from the atomic charge and the bond-order term. When the contribution to δ arising from ΔE overwhelms those arising from the charge on sulfur and the bond-order term, the chemical shift of the sulfone will be *smaller* than that of the sulfoxide, as is apparently the case of the four-membered ring compound **2**.[11]

As far as the chemical shift of thiirane and its derivatives is concerned, it is known that nuclei belonging to three-membered rings are always shielded with respect to the corresponding six-membered rings or open-chain compounds.[13] For nuclei other than proton,[13a] no interpretation of the phenomenon was given. The present results show that for sulfur the shielding is one order of magnitude larger than that observed for first-row nuclei. The data of Table II indicate that for three-membered ring compounds the positive charge on sulfur is always smaller than for the larger rings or the dimethyl analogues. However, as shown by comparison of the data reported in Tables I and II, the variation of the atomic charge on sulfur may account only for a small part of the large upfield effects observed on thiirane and its derivatives. It can be assumed that owing to the large strain of three-membered ring compounds,[14] the bond-order term must play an important role in determining the chemical shift of nuclei belonging to the molecular skeleton. However large upfield effects are also observed on the oxygen atoms of thiirane 1,1-dioxide[15] which are outside the ring skeleton, suggesting that the factors which are at the origin of the shieldings observed are complex and related to the very peculiar electronic properties of these compounds.[16,10c] We believe that only detailed calculations will account for the chemical shifts of three-membered ring compounds, and we are currently investigating in this direction.

Experimental Section

All sulfides are commercial products. Sulfoxides and sulfones were obtained by oxidation of the corresponding sulfides, either with *m*-chloroperbenzoic acid at 0–4 °C (ice bath) using $CHCl_3$ as the solvent or with hydrogen peroxide using acetone as the solvent.[17–20]

Sulfur-33 NMR spectra were run with a Bruker CXP-300 spectrometer at the probe temperature (ca. 30 °C). A high-power probe system equipped with a solenoid insert operating at 23.03 MHz and 15-mm horizontal glass tubes was used. No frequency-field lock was needed. With our equipment the ringing[21] decays to zero in approximately 60 μs, as measured with a sample of neat $CHCl_3$. Thus an equivalent time was allowed after the pulse before accumulation. Typical conditions were pulse width 90°, spectral width 40 kHz, and 4K data points. All spectra were obtained in $CHCl_3$. For sulfones the concentration was 0.1–0.5 M, and the accumulation time required to obtain a good signal-to-noise ratio never exceeded 2 h. For sulfoxides the concentration was 2–3 M and for sulfides solutions of about 80% in $CHCl_3$ were employed. For these compounds a much longer accumulation time was required, i.e., 30–50 h. The absolute frequency of the signal of neat CS_2 was measured, and the chemical shifts of all samples were calculated with respect to this frequency. Compounds resonating at low field with respect to CS_2 were considered to have positive chemical shifts.

Sulfur charges were calculated at the STO-3G* level, which includes d orbitals, on the CRAY computer in Bologna using a Gaussian 82 program option. For compounds **1** microwave geometries[10c,d] and for compounds **2**–**5** the geometries optimized with force field MM2 calculations[22] were employed.

Registry No. **1** (X = S), 420-12-2; **1** (X = SO), 7117-41-1; **1** (X = SO_2), 1782-89-4; **2** (X = S), 287-27-4; **2** (X = SO), 13153-11-2;

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2 ($X = SO_2$), 5687-92-3; **3** ($X = S$), 110-01-0; **3** ($X = SO$), 1600-44-8; **3** ($X = SO_2$), 126-33-0; **4** ($X = S$), 1613-51-0; **4** ($X = SO_2$), 4988-33-4; **5** ($X = S$), 75-18-3; **5** ($X = SO$), 67-68-5; **5** ($X = SO_2$), 67-71-0.

Supplementary Material Available: Table IV, giving the bond lengths and bond angles of compounds **2**–**5** from the geometries optimized with force-field MM2 calculations, and Table V, giving the calculated (ab initio STO-3G*) atomic charges on sulfur and α carbons, the overlap populations of S–O and C–S bonds, and the HOMO–LUMO energy differences for compounds **1**–**5** (2 pages). Ordering information is given on any current masthead page.

Synthesis of Cembrane Natural Products via [2,3] Wittig Ring Contraction of Propargylic Ethers

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A new route to the cembranoid carbon skeleton has been devised. Accordingly, the 17-membered ether **15** underwent facile [2,3] Wittig rearrangement to the $1R^*,2R^*$ 14-membered carbocycle **16** upon treatment with *n*-BuLi in THF–hexanes at −78 °C. In THF–HMPA the rearrangement of **15** gave mainly the isomeric $1R^*,2S^*$ carbocycle **17**. Directed hydroalanation of **16** followed by trapping with I_2 yielded the (*Z*)-vinyl iodide **21**. This was further elaborated via Pd-catalyzed carbonylation to the butenolide **28**, which was reduced to diol **29**. The monoacetate **30** underwent hydrogenolysis with Li/NH$_3$ to give epimukulol **18**. Hydromagnesiation of the alkynol **16** followed by carboxylation and reduction afforded (±)-desoxyasperdiol (**34**).

In recent years the cembrane diterpenes have emerged as a major class of natural products.[1] Of widespread occurrence in marine and terrestrial organisms this structurally diverse family of 14-membered carbocycles has increasingly attracted the attention of synthetic organic chemists. A major problem in cembrane synthesis centers about the efficient construction of the carbocyclic ring with control of sp^2 and sp^3 stereochemistry. Although carbocyclization has been successfully employed in several total syntheses, the efficiency and stereoselectivity of such processes are highly substrate dependent.[2]

As an alternative to direct carbocyclization we formulated a strategy based upon ring contraction of heteromacrocyclic intermediates as a possible route to the cembrane skeleton.[3] The [2,3] Wittig rearrangement (Figure 1) of allylic ethers seemed well suited to this end as previous studies on acyclic systems had established that a high degree of regio- and stereoselectivity was possible for such reactions.[4] The additional constraints engendered by the macrocyclic ring were expected to facilitate the rearrangement by holding the reacting centers in close proximity. The advantages of the approach would derive from the expectedly greater ease of heterocyclic over carbocyclic ring formation and the ensuing direct and stereocontrolled formation of the β-isopropenyl alcohol moiety on the ring-contracted product.

To test the proposed synthetic strategy we selected the 17-membered ether **15** for initial study. A propargylic rather than an allylic ether was chosen for two reasons. (1) Propargylic ethers are known to rearrange with high regio- and stereoselectivity in acyclic systems.[4] (2) The resulting propargylic alcohol offers the potential for conversion to a variety of cembranes through appropriate manipulation of the acetylenic grouping.

The synthesis of ether **15** was readily accomplished from the acetate **2** of *trans,trans*-farnesol (**1**).[5] Selective allylic oxidation of the *E*-isopropylidene methyl group was effected with SeO$_2$–TBHP[6] according to the procedure developed by Sharpless for the analogous oxidation of geranyl

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(4) For recent work on the [2,3] Wittig rearrangement, see: (a) Mikami, K.; Azuma, K.; Nakai, T. *Tetrahedron* **1984**, *40*, 2303 and references therein. (b) Marshall, J. A.; Jenson, T. M. *J. Org. Chem.* **1984**, *49*, 1707. (c) Midland, M. M.; Kwon, Y. C. *Tetrahedron Lett.* **1985**, *26*, 5017 and references therein.

(5) *trans,trans*-Farnesol was obtained from Aldrich Chemical Co., Milwaukee, WI.

(6) Abbreviations: DIBAH = diisobutylaluminum hydride; DMAP = 4-(*N,N*-dimethylamino)pyridine; HMPA = hexamethylphosphoric triamide; KHMDS = potassium bis(trimethylsilyl)amide; Red-Al = sodium bis(2-methoxyethoxy)aluminum hydride; TBHP = *tert*-butyl hydroperoxide; TBS = *tert*-butyldimethylsilyl; THF = tetrahydrofuran.

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