Conformational Preferences of Bridged Aromatic Compounds. III. Ortho-Substituted Acetophenones and Benzophenones

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Abstract: Dipole moments and nmr data are reported for a series of ortho-substituted acetophenones and benzophenones. The nmr data, interpreted on the basis of the ring current and carbonyl shielding effects, have provided useful information about the conformations present in these compounds. The preferred conformations are discussed, and a good agreement is found between dipole moments and nmr data.

In a previous study[1] we used nmr spectra to investigate the conformational preferences induced by ortho substituents in diphenylmethanes. In fact, because of the proximity of the two aromatic rings, the shielding by the ring current[2] of the adjacent nucleus on the ortho positions is a function of the molecular conformation (Figure 1).

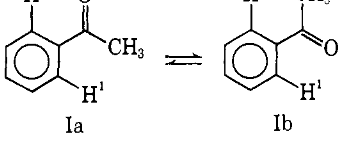
In view of the structural similarity with the diphenylmethanes, we have extended our study to some ortho-substituted benzophenones. Some acetophenones are also discussed. Dipole moment measures are also reported.

The bonding interaction between the π electrons of the aromatic ring and the π electrons of the carbonyl group (conjugation) is well recognized in aromatic ketones.[3] The percentage of double bond character induced by conjugation into the C_{Ar}–CO bond raises the energy barrier to the internal rotation about this bond, and the rotation becomes thermodynamically (but not kinetically) restricted, at room temperature. Conformations where the aromatic ring and the carbonyl group are coplanar (maximum π–π overlap) become strongly preferred whenever structurally possible.[3]

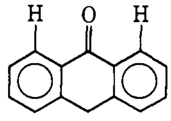
Nuclear Magnetic Resonance

In Table I the nmr chemical shifts of ortho aromatic protons and acetyl groups for a series of acetophenones and benzophenones are reported.

Only one (averaged) nmr signal, at 7.95 ppm, is seen in acetophenone (1) for the two ortho protons marked H and H′ in forms Ia and Ib (planar). Proton H in form Ia experiences the deshielding effect of the carbonyl group;[4] therefore the proton H′ should resonate at higher field values, and *vice versa* in form Ib.

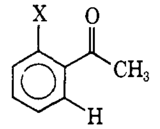


Ia Ib

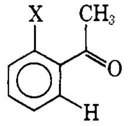


II

Ortho protons in anthrone (II), a structurally rigid molecule, resonate at 8.25 ppm.[5] Assuming this value as valid also for proton H in form Ia, H′ can be calculated[6] to have a chemical-shift value of about 7.65 ppm. Chemical-shift values very close to this figure are found for acetophenones **2** and **4** in Table I (7.64 and 7.70 ppm, respectively), indicating that these molecules exist preferentially in the conformation IIIa, rather than IIIb. These nmr results are in close agreement with dipole moment data in Table II, which will be discussed later.



IIIa



IIIb

Conformations such as IIIb are disfavored in these compounds because the steric hindrance between ortho substituent and $-COCH_3$ methyl would force the molecule out of planarity.[7] Distortion from planarity cannot be avoided in 2,4,6-trimethylacetophenone (**3**) because of the presence of two *o*-methyl groups.[3] Both the acetyl and the *o*-methyl signals appear considerably deshielded (2.16 and 2.10 ppm, respectively) in **3** with respect to the corresponding signals in **2** (2.50 and 2.48 ppm).

These effects can be accounted for considering the magnetic shielding of a proton in the neighborhood of a phenyl ring[2] and of a carbonyl group.[4]

If the theoretical shieldings are mapped[8] as a function of the equilibrium dihedral angle between the phenyl and acetyl planes, this can be calculated by matching the experimental and theoretical shieldings. A value of about 45° is found in this way ($\Delta\nu_{CH_3} = -0.35$ ppm), in good accord with recent estimates from dipole moment data.[3,7,9]

These observations are of value in order to analyze the data concerning the ortho-substituted benzophe-

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(1) (a) G. Montaudo, S. Caccamese, P. Finocchiaro, and F. Bottino, *Tetrahedron Lett.*, 877 (1970); (b) *J. Amer. Chem. Soc.*, **93**, 4208 (1971).

(2) C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, 29, 1012 (1958).

(3) A. G. Pinkus and H. C. Custard *J. Phys. Chem.*, 74, 1042 (1970), and references therein.

(4) J. A. Pople, *J. Chem. Phys.*, 37, 60 (1962); L. M. Jackman and S. Sternhell in "Application of NMR Spectroscopy in Organic Chemistry," 2nd ed, Pergamon, Oxford, 1969, p 88.

(5) R. H. Martin, N. Defay, and F. Geerts-Evrard, *Tetrahedron*, **20**, 1505 (1964).

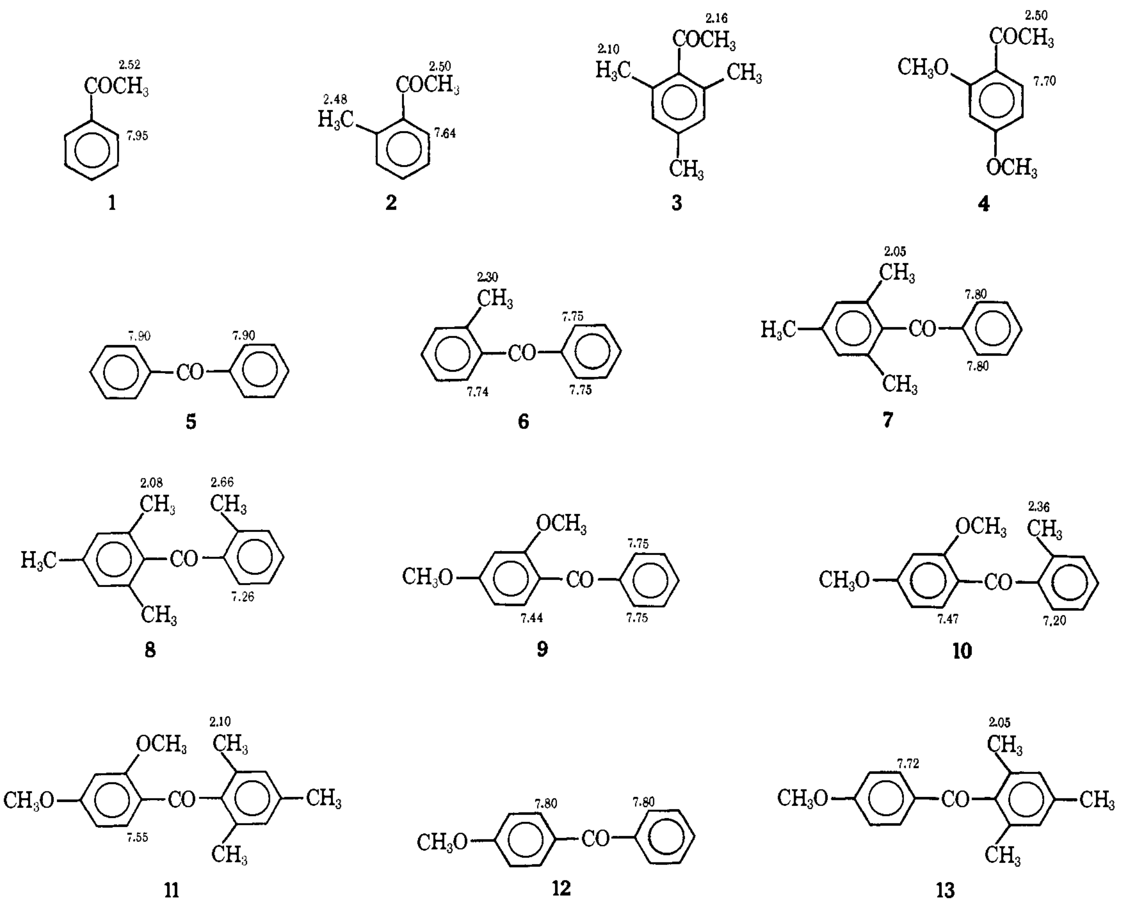
(6) E. L. Eliel and M. H. Gianni, *Tetrahedron Lett.*, 97 (1962).

(7) (a) J. W. Smith, *J. Chem. Soc.*, 4050 (1957); (b) J. B. Bentley, K. E. Everard, R. J. B. Marsden, and L. E. Sutton, *ibid.*, 2957 (1949).

(8) A similar analysis is reported, in more detail, for the diphenylmethane case.[1b]

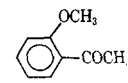
(9) R. G. Kadesch and S. W. Weller, *J. Amer. Chem. Soc.*, **63**, 1310 (1941).

Table I. Chemical Shifts[a] of Relevant Groups in Ortho-Substituted Acetophenones and Benzophenones



[a] Chemical shifts measured in $CDCl_3$ at 30°, in parts per million downfield from TMS as internal standard (60 MHz).

Table II. Experimental and Calculated Values of Dipole Moments of Some Ortho-Substituted Acetophenones and Benzophenones

		Calcd[a]		
Compd	Exptl, D	Form IIIa	Form IIIb	Mixture
2	$2.57 \pm 0.02^{b,c}$	2.56	3.18	2.89
	4.02^{e}	3.80	2.95	3.40
4	4.38 ± 0.02^{b}	3.94	2.83	3.42
6	2.91 ± 0.01^{b}	2.56	3.18	2.89
9	$4.08 \pm 0.01^{b,d}$	3.94	2.83	3.42

[a] Forms IIIa and IIIb (planar) are described in the text. The mixture indicates the value calculated for a 1:1 mixture of IIIa and IIIb. [b] Present work. [c] Smith[7a] reports 2.60 D. [d] Cleverdon and Smith (D. Cleverdon and J. W. Smith, *J. Chem. Soc.*, 2321 (1951)) report 4.16 D. [e] A. E. Lutskii, *Zh. Fiz. Khim.*, **23**, 361 (1949); *Chem. Abstr.*, **43**, 6020*g* (1949).

nones reported in Table I. For benzophenones in the planar conformation, two ortho protons should resonate at 8.25 ppm as in anthrone (II), while the remaining two protons would experience a paramagnetic deshielding from the adjacent phenyl ring of about 1.0 ppm.[1,2] This would shift the signal from 7.65 (acetophenone, form Ia) down to 8.65 ppm.

It follows that ortho hydrogens of benzophenone **5** in the planar conformation should resonate at about 8.45 ppm (averaged value). Coincidence with the experimental value (7.90 ppm) can be obtained, instead, assuming that each phenyl ring is rotated about 20° from the coplanar position, in good agreement with solid-state[10,11] and solution[12] estimates.

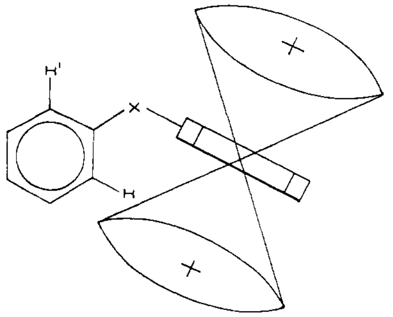


Figure 1. Shielding of the ring current on the ortho protons when the two aromatic rings lie in orthogonal planes. Proton H results diamagnetically shielded, while H' is paramagnetically shielded.

In mesitophenones **7** and **13**, ortho nuclear protons are found at field values very close to those of benzophenone (**5**). Also methyl signals are found at field

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(10) G. M. Lobanova, *Kristallografya*, **13** (6), 984 (1969).

(11) E. B. Fleischer, Nako Sung, and S. Hawkinson, *J. Phys. Chem.*, **72**, 4311 (1968).

(12) (a) R. Bradley and R. J. W. LeFévre, *J. Chem. Soc.*, **56** (1962); (b) P. H. Gore, J. A. Hoskins, R. J. W. LeFévre, L. Radom, and G. L. Ritchie, *ibid.*, *B*, 741 (1967); (c) R. N. Jones, *J. Amer. Chem. Soc.*, **67**, 2127 (1945); (d) R. E. Rekker and W. Th. Nauta, *Recl. Trav. Chim. Pays-Bas*, **80**, 764 (1961); **73**, 969 (1954).

values close to those of methyls in mesitylacetophenone (**3**). This implies that the conformation of **7** and **13** is similar to that of the above parent compounds. Data in Table I also reveal sensible upfield shifts for ortho nuclear protons of benzophenones **4**, **8**, **9**, **10**, and **11**. This, however, should not be interpreted as indicating drastic changes in the molecular (skew) conformation found for benzophenone itself. Several authors[13] have claimed that tri-ortho-substituted benzophenones exist preferentially in a conformation as in Figure 1, where one aromatic ring lies in a plane approximatively at right angles to that of the carbonyl group.

Based on the experimental data in Table I and on the theoretical shielding[1,2] maps discussed above, we calculate that if compound **8** existed in such a conformation the ortho hydrogen would resonate at about 6.75 ppm, too far away from the value (7.26 ppm) actually found.

Recently it has been pointed out[3,14,15] that in 2,4,6-trimethylacetophenones, similar to biphenyls, overlap of π orbitals is possible even though the aromatic ring may be twisted from coplanarity with the carbonyl group. A twist angle of 45° would still allow 50% resonance to be present, while releasing most of the steric hindrance. The same rationalization should apply to ortho-substituted benzophenones. A conformation as in Figure 1 becomes preferred in a system where there is no conjugation between the bridged group and the phenyl ring, and the molecular conformation is a function only of the steric repulsion forces among nonbonded atoms. This is the case of tri-ortho-substituted diphenylmethanes, as we have shown elsewhere.[1]

Dipole Moment Data

Dipole moments, being conformation dependent, have been widely used in the study of aromatic ketones.[3,7,9,16] However, due to their angular geometry, these molecules may happen to have two or more different conformations with the same calculated dipole moment.

The inspection of contour maps of calculated dipole moments reveals that for several of the compounds in Table I it is difficult to assign conformational preferences on the basis of experimental values. For this reason, dipole moment measurements were restricted to a few cases (Table II). The values for conformations in Table II were calculated on the following assumptions. (a) The valence angle of acetophenone C_{Ar}–C–CH_3 and of benzophenone C_{Ar}–C–C_{Ar} is 120° (according to X-ray data[10,11]). (b) The dipole moment of acetophenone and benzophenone is 2.96 D.[16] (c) The individual moments contributed by each group are 0.43 D as in toluene[16] and 1.25 D as in anisol.[16] (d) The contribution of the methoxy group to the molecular dipole moment is computed considering it freely rotating.

Experimental values for the three acetophenones in Table II are in good agreement with those calculated for conformation IIIa, confirming our interpretation of the nmr data. The fact that conformation IIIa was actually preferred in **3** had been previously realized.[7]

Although formally incorrect, notations IIIa and IIIb may also be used to indicate conformations of benzophenones as **6** and **9**, substituted only in one ring. For compound **9** the experimental value is in excellent agreement with that calculated for form IIIa. The accord is only fair in the case of **6**, due to the little individual moment of the methyl group. Also, these results confirm our interpretation of the nmr data for ortho-substituted benzophenones, indicating that a skew conformation (with an equilibrium dihedral angle subject to vary according to the substitution pattern) is preferred in all the cases discussed.

Experimental Section

Known compounds discussed in this paper were prepared as described previously.[17]

2,4-Dimethoxy-2′-methylbenzophenone. 2-Methylbenzoyl chloride (10 g, 0.065 mol) was dissolved in $EtNO_2$ and added to 9.5 g (0.0715 mol) of $AlCl_3$. The clear solution was added under stirring at 20° to a solution of 1,3-dimethoxybenzene in $EtNO_2$. After 1 hr the mixture was poured into 5% HCl–water, extracted with $CHCl_3$, dried (Na_2SO_4), and distilled under vacuum ($K_{p7} \simeq 190°$). The white solid obtained (yield 75%) was crystallized from CH_3OH: mp 46–47°; nmr ($CDCl_3$) 2.36 (3), 3.58 (3), 3.75 (3), 6.43 (1), 6.51 (1), 7.20 (4) 7.47 (1).

Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.97; H, 6.29; mol wt 256.29. Found: C, 75.02; H, 6.24; mol wt (dichloroethane 50°) 257.5.

2,4-Dimethoxy-2′,4′,6′-trimethylbenzophenone. Mesitoyl chloride (10 g, 0.055 mol) (obtained according to literature[18]) was dissolved in $EtNO_2$ and added to 8.20 g (0.0615 mol) of $AlCl_3$. The clear solution was added dropwise under stirring at 20° to a solution

Table III. Dielectric Constant Data[a]

Compd	w_2	ϵ_{12}	Δn_D
2	0.00000	2.2725	0.000000
$a_\epsilon = 5.435$	0.00313	2.2895	0.000079
$a_n = 0.072$	0.00547	2.3001	0.000139
	0.00838	2.3162	0.000204
	0.01054	2.3281	0.000264
	0.01284	2.3432	0.000312
4	0.00000	2.2725	0.000000
$a_\epsilon = 11.699$	0.00154	2.2906	0.000073
$a_n = 0.137$	0.00405	2.3202	0.000186
	0.00461	2.3243	0.000226
	0.00553	2.3375	0.000254
	0.00824	2.3686	0.000388
6	0.00000	2.2725	0.000000
$a_\epsilon = 4.952$	0.00308	2.2880	0.000255
$a_n = 0.245$	0.00582	2.3017	0.000457
	0.00849	2.3150	0.000696
	0.01192	2.3322	0.000979
	0.01611	2.3520	0.001325
9	0.00000	2.2725	0.000000
$a_\epsilon = 7.740$	0.00209	2.2890	0.000183
$a_n = 0.255$	0.00698	2.3270	0.000600
	0.00966	2.3470	0.000827
	0.01004	2.3507	0.000872
	0.01407	2.3812	0.001202

[a] $a_\epsilon = [(\epsilon_{12} - \epsilon_1)/w_2]_{w_2\to 0}$, $a_n = [(n_{12}^2 - n_1^2)/w_2]_{w_2\to 0}$; ϵ_1 = dielectric constant of solvent; ϵ_{12} = dielectric constant of solution; w_2, weight fraction of solute; n_1, refractive index of solvent; n_{12}, refractive index of solution.

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[13] (a) K. Maruyama, *Bull. Chem. Soc. Jap.*, **39**, 2772 (1966); (b) N. E. Alexandrou, *J. Chem. Soc. C*, 536 (1969); (c) E. J. Moriconi, W. F. O'Connor, and W. F. Forbes, *J. Amer. Chem. Soc.*, **84**, 3928 (1962).

[14] L. L. Ingraham in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley New York, N. Y., 1956, Chapter 11, p 479 ff.

[15] W. M. Schubert and W. A. Sweeney, *J. Amer. Chem. Soc.*, **77**, 4172 (1955).

[16] A. L. McClellan, "Tables of Experimental Dipole Moments," W. H. Freeman, San Francisco, Calif., 1963.

[17] G. A. Olah in "Friedel-Crafts and Related Reactions," Vol. III, Part 1, Interscience, New York, N. Y., 1964.

[18] R. W. Hufferd and W. A. Noyes, *J. Amer. Chem. Soc.*, **43**, 925 (1921).

of 7.6 g (0.055 mol) of 1,3-dimethoxybenzene in $EtNO_2$. After 1 hr the mixture was poured into 5% HCl–water, extracted with $CHCl_3$, and dried (Na_2SO_4), and the solvent was removed under vacuum. The crude product was crystallized from EtOH: mp 91–92°; yield 85%; nmr ($CDCl_3$) 2.10 (6), 2.26 (3), 3.68 (3), 3.76 (3), 6.46 (2), 6.80 (2), 7.55 (1).

Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.02; H, 7.09; mol wt 284.34. Found: C, 75.88; H, 7.16; mol wt (dichloroethane 50°) 283.4.

Nmr. ^1H nmr spectra were obtained using a Varian A-60 spectrometer (60 MHz). Spectra of aromatic ketones examined consist of two types of signals corresponding to methyl and nuclear protons, respectively. Methyl peaks appear as sharp singlets. Aromatic protons have various appearances according to nuclear substitution patterns. However, nuclear protons in positions ortho to the carbonyl group resonate at lower field values with respect to those meta and para. This makes straightforward the assignment of ortho nuclear protons.

Dipole Moments. Purification of solvent, the apparatus used for the measurements of dielectric constants and refractive indices differences, and the Guggenheim procedure for the calculation of μ were described in a previous paper.[1] The dielectric constant data (Table III) were measured in benzene at 25 ± 0.01°.

Sulfonate Leaving Groups, Structure and Reactivity. 2,2,2-Trifluoroethanesulfonate

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Abstract: An easily synthesized reactive new leaving group, 2,2,2-trifluoroethanesulfonate (tresylate), is described. Preparations of tresyl chloride and tresylate esters have been developed. Solvolysis rates of several tresylate esters have been determined and typically appear to be about 100 times *larger* than those of the corresponding *p*-toluenesulfonates (tosylates) and 400 times *smaller* than those of the corresponding trifluoromethanesulfonates (triflates). A linear free energy relationship is shown to correlate limiting solvolysis rates of $X–SO_3R$ esters and σ_m of X with a ρ of +10.3. Convenient solvolysis rates for a wide range of R groups and solvents are obtainable with these leaving groups.

Since the introduction of the Tipson procedure for the synthesis of tosylates,[3] synthetic and especially physical organic chemistry has been well served by arenesulfonate leaving groups.[4] The recent introduction of trifluoromethanesulfonates (triflates)[5,6] has increased the solvolytic reactivity spread between various sulfonate esters to about 80,000.[7,8] However, the reactivity spread is not gradual; the commonly used leaving groups (mesylate, tosylate, brosylate) differ in reactivity by only a factor of ten[9] while triflate is about 8000 times more reactive than brosylate, the most reactive of these groups. Thus, a considerable reactivity gap exists between triflate and other sulfonate esters.

Recently, the synthetic advantages of preparing sulfonate esters by the addition of alcohols to the appropriate sulfene[10] have been pointed out.[11] This method requires precursor sulfonyl halides possessing at least one hydrogen α to the sulfonyl group. As a part of a continuing investigation of leaving groups we have sought to develop new sulfonate esters of intermediate solvolytic reactivity which may be prepared using the sulfene mechanism. In this paper we report the synthesis and characterization of 2,2,2-trifluoroethanesulfonates (tresylates, –OTr) and present a new linear free energy correlation which approximately correlates the rates of solvolysis of sulfonate esters with the substituent on sulfur.

Based on a patent description[12] the first detailed synthesis of 2,2,2-trifluoroethanesulfonyl chloride (tresyl chloride) was published by Truce.[13] The low overall yield of this method (6.7%) clearly renders it unsuitable for preparative scale procedures. Our procedure differs from that of Truce in that the starting material was 2,2,2-trifluoroethyl mesylate instead of the corresponding tosylate and the displacement reaction with a sulfur nucleophile was carried out with thiocyanate instead of disulfide. The starting mesylate was readily available in high yield from trifluoroethanol.[11] Displacement of mesylate by thiocyanate was accomplished in dimethylformamide solution. The resulting alkyl thiocyanate was then oxidized to tresyl chloride with chlorine in wet trifluoroacetic acid to give an overall yield, based on 2,2,2-trifluoroethyl mesylate, of 41%. Tresylate esters may be prepared from alcohols by procedures analogous to those used to prepare mesylates.[11] However, in this case, the sulfene is more readily generated due to activation of the system toward dehydro-

$$CF_3CH_2OH \longrightarrow CF_3CH_2OMs \longrightarrow CF_3CH_2SCN \longrightarrow CF_3CH_2SO_2Cl$$

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[2] Undergraduate Research Participant, 1970.

[3] R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

[4] For a survey of newer methods of preparing arenesulfonates, see R. M. Coates and J. P. Chen, *Tetrahedron Lett.*, 2705 (1969).

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[6] R. L. Hansen, *J. Org. Chem.*, **30**, 4322 (1965).

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[9] R. E. Robertson, *Progr. Phys. Org. Chem.*, **4**, 213 (1967).

[10] For a review of sulfenes as reaction intermediates, see G. Opitz, *Angew. Chem., Int. Ed. Engl.*, **6**, 107 (1967).

[11] R. K. Crossland and K. L. Servis, *J. Org. Chem.*, **35**, 3195 (1970).

[12] R. E. Oesterling, U. S. Patent 3,006,964 (Oct 31, 1961). Note: as pointed out by Truce (ref 13), the *Chemical Abstracts* reference [*Chem. Abstr.*, **56**, 9967c (1962)] is in error.

[13] W. E. Truce and J. R. Norell, *J. Amer. Chem. Soc.*, **85**, 3231 (1963).