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The Magnetic Anisotropy of the Aromatic Ring, Aryl Thioethers and Sulfones

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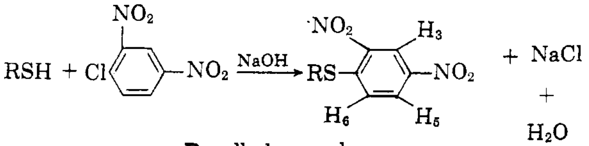
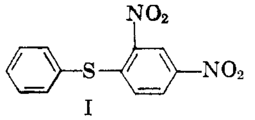
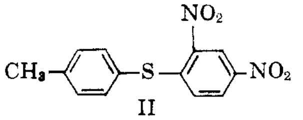
During a study[1] of thioethers prepared[2,3] by the reaction of 2,4-dinitrochlorobenzene and the desired thiol, the n.m.r. spectra of those derivatives which were synthesized from the aromatic thiols exhibited an apparent anomaly—the position of the proton (H_6) *ortho* to the thioether group was displaced to high field. Examination of the aromatic protons in the spectra of the 2,4-dinitrophenyl alkyl thioethers showed the chemical shifts and the coupling constants were consistent with what might be expected, and the τ values[4] for the aromatic protons of similar trisubstituted aromatics are shown in Table I as well as the typical thioethers. The spectra of the alkyl thioethers in the aromatic region are simple first order and the proton *ortho* to thioether group (H_6) has its resonance of 2.41 τ (*ortho* coupled). However, the (H_6) resonance of the aryl thioethers (I, II, III, and IV) were 3.00 τ, 3.00 τ, 3.00 τ, and 3.18 τ, respectively. In addition, it is not surprising that the spectrum of 2,4-dinitrophenyl benzyl thioether exhibited no anisotropic effect on the protons—*i.e.*, similar to an aliphatic derivative. The magnetic anisotropy of the benzene ring has been discussed[5] and its effect on the chemical shift of protons has been reported[6]—*i.e.*, a high or low field displacement of a proton in the vicinity of the aromatic ring, depending on the relative geometry of the system. Diphenyl ether has been discussed[7] and the possibility of calculation of the shielding of each individual proton of the diphenyl ether may be established in this manner. However, with the use of non-equivalent rings, gross changes can be observed as long as one of the rings has its electron current altered by withdrawing groups and as a result, the spectral analysis is limited to first order treatment. The aromatic protons of the thiols exhibited little or no effect due to the anisotropy of the ring containing the nitro groups.



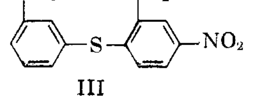
R = alkyl or aryl



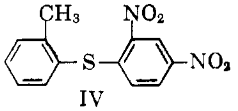
I



II



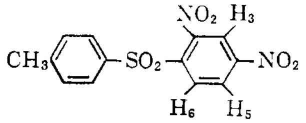
III



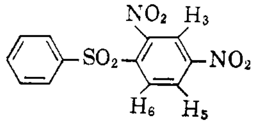
IV

In addition, the evaluation of the relative roles of resonance effects and inductive effect have also been discussed,[8] and it appears unlikely the high field shift is caused by either of these. A steric interaction might alter the coplanarity[9] of the nitro group with the aromatic ring. Since the resonance position of proton (H_3) is essentially unchanged, a steric effect appears to make little or no contribution. Therefore, the anisotropic effect of the phenyl ring must cause the observed displacement. Many examples of this shielding effect[10] exist in the literature, but the aryl thioethers and sulfones have not been studied.

The oxidation of the thioether to the sulfone[2] would introduce a group which would yield a system that tended toward coplanarity. The n.m.r. spectrum of the sulfone (V), in addition to a multiplet centered at 1.45 τ (H_3, H_5, and H_6), contained a typical AB-type spectrum at higher field (2.11 τ and 2.60 τ).[11]



V



VI

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(1) R. Rittner, G. Tilley, A. Mayer, Jr., and S. Siggia, *Anal. Chem.*, **34**, 237 (1962).

(2) N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," Crowell Co., New York, 1947, p. 321.

(3) R. W. Bost, J. O. Turner, and R. D. Norton, *J. Am. Chem. Soc.*, **54**, 1985 (1932).

(4) G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

(5)(a) J. A. Pople, *J. Chem. Phys.*, **24**, 1111 (1956). (b) H. M. McConnell, *ibid.*, **27**, 226 (1957). (c) H. Conroy, "Advances in Organic Chemistry," Vol. II, Interscience Publishers, Inc., New York 1960, pp. 281–283.

(6)(a) J. S. Waugh and R. W. Fessenden, *J. Am. Chem. Soc.*, **79**, 846 (1957). (b) H. Conroy, "Advances in Organic Chemistry," Vol. II, Interscience Publishers, Inc., New York, 1960, pp. 284–285. (c) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York (1959), pp. 180–183. (d) S. Brownstein, *J. Am. Chem. Soc.*, **83**, 2300 (1958). (e) C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958).

(7) H. Shimizu, S. Fujiwara, and Y. Morino, *J. Chem. Phys.*, **34**, 1467 (1961).

(8) P. L. Corio and B. P. Dailey, *J. Am. Chem. Soc.*, **78**, 3043 (1956).

(9) E. R. Alexander, "Principles of Ionic Organic Reactions," John Wiley & Sons, Inc., New York, 1950, p. 20.

(10) D. Y. Curtin, H. Gruen and B. A. Shoulders, *Chem. Ind.* (London), 1205 (1958).

The n.m.r. spectrum of the phenyl sulfone (VI), also contained the same multiplet at 1.41 τ as well as two sets of lines in a ratio of 3:2, 2.32 and 1.99 τ, respectively. The alkyl sulfones in the aromatic region exhibited resonances at 1.58, 1.42, and 1.38 τ, (H_6, H_5, and H_3, respectively). The difference in shifts from the aryl sulfones may be due to resonance effects. The high field displacement of the (H_3) proton (both aryl and alkyl sulfones) suggests a steric interaction of the sulfone and the nitro group. The lack of coplanarity of the nitro group would shield the proton *ortho* to the nitro group, causing the shift to higher field.

The spectrum of the benzyl sulfone, on the other hand, was a typical first-order spectrum; (H_6), 2.24 τ (*ortho* coupled), (H_5), 1.70 τ [*ortho* and *meta* coupled, (H_3), 1.40 τ (*meta* coupled)]. Since the (H_3) resonance position is unchanged, the high field position of (H_5) and (H_6) in this derivative can be explained only by assuming the phenyl ring is so oriented that there is a shielding effect on protons (H_5) and (H_6). The magnitude of the shifts suggests the anisotropy of the phenyl ring is a reasonable explanation and molecular models indicate that this is feasible.

TABLE I

	δ-shift in τ values		
	H_3	H_5	H_6
2,4-Dinitrochlorobenzene	1.23	1.55	2.15
2,4-Dinitrotoluene	1.19	1.62	2.37
2,4-Dinitrophenyl thioethers			
Methyl	0.88	1.56	2.45
Ethyl	0.94	1.64	2.45
Propyl	0.90	1.62	2.42
Isoamyl	0.90	1.61	2.41
Decyl	0.90	1.61	2.44
Benzyl	0.90	1.65	2.38
Phenyl	0.90	1.86	3.00
o-Tolyl	0.90	1.90	3.18
m-Tolyl	0.94	1.90	3.00
p-Tolyl	0.92	1.88	3.00
Sulfones			
Ethyl	1.38	1.44	1.58
Propyl	1.35	1.40	1.60
Isoamyl	1.36	1.41	1.62
Benzyl	1.42	1.74	2.26
Decyl	1.37	1.41	1.61
Phenyl	1.45[a]		
Tolyl	1.41		

[a] Multiplet whose integral is equivalent to three protons (H_3, H_5, and H_6).

Experimental

Preparation of the Thioethers.—The thiols used were Eastman White Label reagents, and they were reacted with 2,4-dinitrochlorobenzene in the following manner, using the method of Cheronis and Entrikin.[2] A methanolic solution of the mercaptan was treated with sodium hydroxide and then added to a methanolic solution of 2,4-dinitrochlorobenzene. The solution was refluxed for a few minutes and filtered while hot. The filtrate was then cooled and the precipitate was filtered. The aliphatic derivatives were recrystallized from methanol–water and the aromatic derivatives from methanol alone. The sulfones were prepared according to the method described in Cheronis and Entrikin[2] with slight modifications.

N.m.r. Spectra.—The H^1 spectra were obtained from samples in deuterochloroform solution at 60 Mc. The chemical shifts were obtained, using the side band technique. Three readings were taken for each peak, and the chemical shift was obtained by averaging these values. Tetramethylsilane was used as the internal standard.

The aromatic protons of the alkyl sulfone derivatives were treated as an ABC system. The observed spectrum and the calculated spectrum were compared, the best fit made, and the chemical shifts were obtained in this manner.

Acknowledgment.—The authors are grateful to Dr. Robert Rittner and Mr. Albert Mayer for the compounds used in this study. The authors are also indebted to Mr. Henry Gauthier for comparing data obtained by the HR-60 on the A-60 n.m.r. spectrometer.

(11) The mid-point of each doublet was taken as the chemical shift, although the intensities implied second order effects; a ratio of 2:1 may be treated as first order since the error would be only about 0.5 c.p.s.

Steroidal Aldosterone Blockers. V. Stereochemistry of the Addition of Ethanethiolic Acid to $\Delta^{4,6}$-3-Oxosteroids

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In continuation of previous work on steroidal spirolactones,[1] we have now prepared two additional acetylthiospirolactones. The newer physical methods now available have enabled us to prove the structures unequivocally as well as to provide conclusive evidence for the structure of a compound reported previously.

In an earlier paper,[2] the addition of ethanethiolic acid to 3-(3-oxo-17β-hydroxy-4,6-androstadien-17-α-yl)propanoic acid lactone (I) was reported to yield the 7α-acetylthio derivative (II). When this reaction was repeated on a larger scale using carefully purified I, a second, higher melting isomer (III) was found as well as the predominant product (II).

The ultraviolet spectrum of III is the same as II and an ultraviolet spectrum of III in *N* methanolic potassium hydroxide shifted very rapidly from 238 mμ to 284 mμ, ϵ 29,500. This elimination of ethanethiolic acid to give I also occurs with II. The infrared spectra of II and III are similar in the

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(1) Paper IV, N. W. Atwater, R. H. Bible, Jr., E. A. Brown, R. R. Burtner, J. S. Mihina, L. N. Nysted, and P. B. Sollman, *J. Org. Chem.*, **26**, 3077 (1961).

(2) J. A. Cella and R. C. Tweit, *ibid.*, **24**, 1109 (1959).