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.

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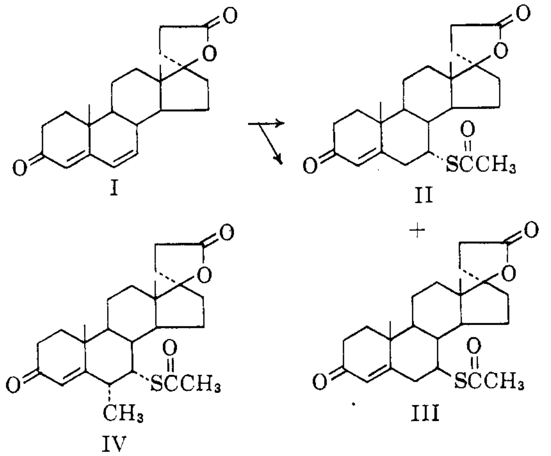
(11) The mid-point of each doublet was taken as the chemical shift, although the intensities implied second order effects; a ratio of 2:1 may be treated as first order since the error would be only about 0.5 c.p.s.

(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).

5.5 to 9.0 μ area but differ in the fingerprint region. Analyses showed that II and III have the same empirical formula.



I

II

+

IV

III

As II had previously been assigned the 7α configuration,[2,3] we felt that III was the 7β isomer. The molecular rotatory contributions of the acetylthio groups (II, −408°; III, +104°) are consistent with the molecular rotatory contributions characteristic of 7-acetoxy groups (7α, −300 to −400°; 7β, +50 to −50°).[4]

Since we desired more evidence to confirm these assignments, we examined the n.m.r. spectra of these two compounds. The spectrum of II contains a peak at 6.08 p.p.m.[5] assigned to the equatorial 7β-hydrogen. In III the axial 7α-proton couples with the 6α-, 6β-, and 8β-hydrogens. A peak at 6.72 p.p.m. in the spectrum of III is assigned to the 7-axial proton since axial protons in general lie at higher fields than equatorial protons.[7] The spin-spin coupling causes it to split into a less distinct multiplet.

The second new compound (IV) mentioned at the beginning was obtained by addition of ethanethiolic acid to 3-(3-oxo-17β-hydroxy-6-methyl-4,6-androstadien-17α-yl)propanoic acid lactone, (V).[1,8] The methyl group at 6 increases the number of possible isomers to four. However, the n.m.r. spectra and optical rotatory dispersion curves prove the structure to be a 6α-methyl-7α-acetylthio steroid. In its n.m.r. spectrum a peak appears at 6.04 p.p.m., indicative of a 7β hydrogen on a carbon attached to an acetylthio group (compare with the value of 6.08 p.p.m. for II). The peak for the 19-methyl appears very close to the value for II and III (see Table I). Slomp and McGarvey[9] have pointed out that introduction of a 6β-methyl group into progesterone shifts the 19-methyl peak downward by 0.05 p.p.m. Introduction of a 6α-methyl group does not shift the 19-methyl peak and our data on the spirolactones agree.

TABLE I

Substituents on the spirolactone	Peaks in the n.m.r spectra C_{10}—CH_3	C_6—CH_3	
none	8.80 p.p.m.		
$7\alpha\text{-S}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{CH}_3$ (II)	8.78		
$7\beta\text{-S}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{CH}_3$ (III)	8.78		
$6\alpha\text{-CH}_3$, $7\alpha\text{-S}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{CH}_3$ (IV)	8.77	8.91	9.00
$6\alpha\text{-CH}_3$ (VI)	8.79	8.87	8.98
$6\beta\text{-CH}_3$ (VII)	8.72	8.75	8.83

The position of the 6-methyl doublet in IV also supports the α-assignment. This doublet is very similar to that of 3-(3-oxo-17β-hydroxy-6α-methyl-4-androsten-17α-yl)propanoic acid lactone (VI), while the corresponding peaks for the 6β-compound (VII) are at definitely lower τ values.[10]

The optical rotatory dispersion curves strongly support the 6α-methyl assignment for IV. As Djerassi indicates,[12] an equatorial 6α-methyl does not change the shape of the curve from that of the parent compound, while an axial 6β-methyl causes an inversion of the curve. Since IV has a negative Cotton effect similar to that given by 3-(3-oxo-17β-

TABLE II

ROTATORY DISPERSION CURVES[a] OF 3-(3-OXO-17β-HYDROXY-4-ANDROSTEN-17α-YL)PROPANOIC ACID LACTONES

Substituents at C-6 and C-7	Trough (or peak*) [ϕ]	 λ (mμ)
None	− 720	350
$6\alpha\text{-CH}_3$	− 930	345
$6\beta\text{-CH}_3$	+1170*	360
$7\alpha\text{-SCOCH}_3$	−2540	345
$6\alpha\text{-CH}_3$, $7\alpha\text{-SCOCH}_3$	−2320	345
$7\beta\text{-SCOCH}_3$	−1600	350

[a] The curves were of the type characteristic of Δ^4-3-oxosteroids,[12] except for that of the 6β-methyl compound. We are indebted to Miss Jane Jackson for these measurements which were taken in methanol.

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(3) See R. M. Dodson and R. C. Tweit, *J. Am. Chem. Soc.*, **81**, 1224 (1959), for a discussion of the reasons.

(4) R. C. Tweit, A. H. Goldkamp, and R. M. Dodson, *J. Org. Chem.*, **26**, 2856 (1961).

(5) γ-value. The spectra were determined in deuterochloroform relative to tetramethylsilane as an internal standard at 60 Mc.[6]

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

(7) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G Schneider, *J. Am. Chem. Soc.*, **79**, 1005 (1957).

(8) Kindly supplied by Dr. Paul B. Sollman.

(9) G. Slomp, Jr., and B. R. McGarvey, *J. Am. Chem. Soc.*, **81**, 2200 (1959).

(10) Referee II has pointed out that we are assuming the additivity of the contributions of the 6 and 7 substituents to the absorption frequency of the 19-hydrogens. Slomp[11] has recently discussed additivity and the exceptions he has found. These were mostly cases involving multiple bonds where the geometry of the molecule was altered. Since the optical rotatory dispersion curves discussed later do not show any evidence for a change in the shape of the molecule, we feel that the assumption of additivity is valid for compound IV.

(11) G. Slomp, 13th Annual Mid-American Spectroscopy Symposium, Chicago, Illinois, April 30–May 3, 1962, Abstracts, p. 30.

hydroxy-4-androsten-17α-yl)propanoic acid lactone the 6-methyl in IV is in the equatorial (α) configuration, see Table II.

The structure of IV indicates that the predominant reaction of I and V with ethanethiolic acid takes place *via* a trans-diaxial addition to the 6,7 double bond. Although III should be more stable than its isomer II, the product of kinetic control, preliminary efforts to obtain a larger proportion of III by altering the conditions of the addition or by equilibration of II were fruitless.[13] It may be that under conditions necessary to effect equilibration, the addition is reversed and the ethanethiolic acid is lost by side reactions.

The aldosterone blocking potency[14] of IV is the same as that of II (spironolactone) given subcutaneous to adrenalectomized rats. Interestingly the inversion of the 7-acetylthio group lowers both the oral and parenteral activity; thus III has less than 10% of the activity of II.

Experimental[15]

3-(3-Oxo-7β-acetylthio-17β-hydroxy-4-androsten-17α-yl)-propanoic Acid Lactone (III).—A solution of 5.02 g. of 3-(3-oxo-17β-hydroxy-4,6-androstadien-17α-yl)propanoic acid lactone[2] in 5.0 ml. of ethanethiolic acid was heated on a steam bath for 1 hr. The residue, a light yellow gum, was crystallized from 50 ml. of methanol to afford 4.30 g. of material melting at 130–133°, with resolidification and final melting at 203–206°, $[\alpha]_D$ −37°. The infrared spectrum of this material was identical with that of an authentic sample of 3-(3-oxo-7α-acetylthio-17β-hydroxy-4-androsten-17α-yl)propanoic acid lactone.[2]

When the mother liquors from the above crystallization were concentrated to 25 ml. and the solution cooled to 0°, an additional crop of 0.95 g. of material, m.p. 135–137°, with partial resolidification and final melting at 180°, separated. Three crystallizations of this material from methanol afforded 0.204 g. of a substance (III) which melted at 227–230°; $[\alpha]_D$ +88°; $\lambda_{\max}^{CH_3OH}$ 238 mμ, ε 19,100. The infrared spectrum (3% in $CHCl_3$) shows bands at 5.63, 5.91, 6.16, 6.81, 7.00, 7.20, 7.34, 7.49, 7.81, 8.1–8.4, 8.89, 9.29, 9.61, 9.82, 10.51, 10.93, and 11.50 μ.

Anal. Calcd. for $C_{24}H_{32}O_4S$: C, 69.20; H, 7.74. Found: C, 68.98, 69.20; H, 7.52, 7.56.

3-(3-Oxo-7α-acetylthio-17β-hydroxy-6α-methyl-4-androsten-17α-yl)propanoic Acid Lactone (IV).—3-(3-Oxo-17β-hydroxy-6-methyl-4,6-androstadien-17α-yl)propanoic acid lactone,[1] 224 mg., was dissolved in 0.5 ml. of ethanethiolic acid. The solution was heated for 2 hr. on the steam bath. Most of the excess thiolic acid was removed under vacuum and the residue was crystallized from ether to yield 144 mg. of IV, m.p. 237–240° (dec.), $\lambda_{\max}^{CH_3OH}$ 237.5 mμ, ε 19,400.

Anal. Calcd. for $C_{25}H_{34}O_4S$: C, 69.73; H, 7.96. Found: C, 69.47; H, 8.14.

Acknowledgment.—We wish to thank Mr. T. A. Wittstruck for the determination and preliminary interpretation of some of the n.m.r. spectra.

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[12] C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., New York, 1960, p. 63.

[13] Unpublished work by Mr. R. T. Nicholson.

[14] C. M. Kagawa, *Endocrinology*, **67**, 125 (1960). We are most grateful to Dr. Kagawa and Mr. Robert Jacobs for these results.

[15] Rotations run in chloroform at 24 ± 2°.

Synthesis of Diacrylylmethane[1]

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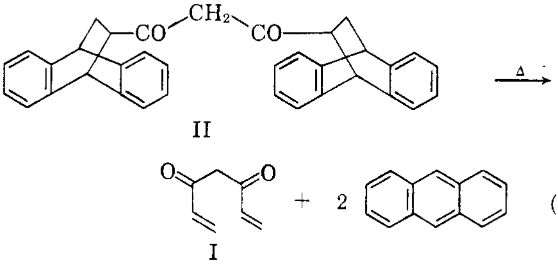
Polydiacrylylmethane prepared by allowing methyl vinyl ketone and methyl acrylate to react in the presence of sodium methoxide,[3] on the basis of microanalytical and infrared data,[4] is not a homopolymer but is apparently a copolymer of diacrylylmethane and methyl vinyl ketone. The expected reaction was

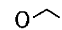
(1)

In order to prepare pure polydiacrylylmethane, which was needed as an intermediate for other studies, it was first necessary to obtain pure diacrylylmethane. This paper reports a successful route to the preparation of this monomer. Unsuccessful reactions are also recorded.

The pyrolytic reverse Diels-Alder reaction of 1,3-di(9,10-dihydro-9,10-ethanoanthracenyl-11)-1,3-propandione,[5] II, in the presence of *p*-terphenyl as an inert, high-boiling diluent produced diacrylylmethane in 47–56% yield. In the absence of *p*-terphenyl the yield averaged about 30%.



(2)

The use of the reverse Diels-Alder reaction to produce chemically unstable compounds is not uncommon. The most recent example is the synthesis, by Field,[6] of 1,3-dioxole, , by pyrolysis of the corresponding anthracene derivative. Another very interesting example is the preparation of cyclopentadienone, also by pyrolysis of the

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[1] This work was supported under contract AF 33(616)7908 with the Nonmetallic Materials Laboratory of Wright Air Development Division, Wright-Patterson Air Force Base, Ohio. This paper may be reproduced for any purpose of the United States Government.

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[3] J. F. Jones, *J. Polymer Sci.*, **33**, 7 (1958).

[4] T. Otsu, J. E. Mulvaney, and C. S. Marvel, *ibid.*, **46**, 546 (1960).

[5] J. J. Bloomfield, *J. Org. Chem.*, **27**, 2742 (1962).

[6] N. D. Field, *J. Am. Chem. Soc.*, **83**, 3504 (1961).