

CARBON-13 NMR SPECTRA OF STEROIDAL A-RING EPISULFIDES¹

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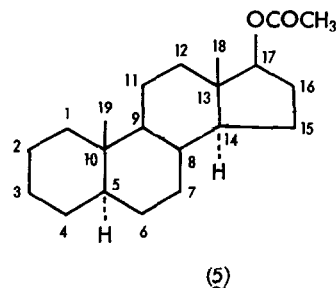
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In a previous paper,² we have reported a ¹³C NMR study of steroidal A-ring epoxides in connection with the configurational assignment of a three-membered ring. Comparisons of the ¹³C NMR spectra of the epoxides with those of the corresponding episulfides have much interested us in the stereochemical correlation with ¹³C chemical shifts in view of the facts that a sulfur atom has a longer van der Waals radius than an oxygen atom has, that a C-S bond of a thiirane ring is longer than a C-O bond of an oxirane ring is,³ and that some of the episulfides show characteristic biological activities.⁴

Thus, the ¹H noise-decoupled natural-abundance ¹³C FT NMR spectra of several epithio derivatives (1-4)⁵ in the A-ring of 17β-acetoxy-5α-androstane (5)² have been examined in CDCl₃.[†] All ¹³C signals were assigned by means of single-frequency off-resonance decoupling (SFORD) techniques,⁷ by applications of known chemical shift rules,⁷ and from comparisons of the spectra from compound to compound. Table 1 lists the chemical shifts δ_C obtained and Table 2 indicates differences in δ_C between epimeric pairs of the episulfides and between those of the corresponding epoxides studied previously,² and methyl substitution effects.

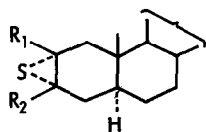
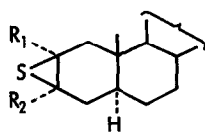
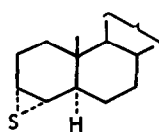


[†] A comprehensive study of ¹H NMR spectra of steroidal episulfides has already been reported.⁶ However, having not been described, ¹H NMR data on 3 are presented here as follows: δ_H (CDCl₃) for H-3β, H-4β, H-18, and H-19 are 3.19, 2.59 (q. J = 6.8 and 3.2 Hz), 0.77, and 0.82, respectively.

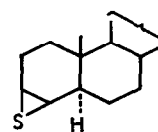
TABLE 1
Carbon-13 Chemical Shift Data on Compounds (1-4) in CDCl_3 (δ_{C})^a

Compounds	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-19	CH_3
<u>1a</u>	40.3	34.6 ^c	37.6 ^c	30.5 ^c	35.4 ^d	28.1	31.0	35.0 ^d	53.6	35.2	20.2	12.6	--
<u>2a</u>	39.3	36.8 ^c	35.2 ^c	30.1 ^c	43.0	28.3	31.3	34.6	56.1	34.6	20.3	14.8	--
<u>1b</u> ^b	47.1 ^d	46.7 ^d	46.7 ^d	31.5 ^f	35.3 ^e	27.9	31.1 ^f	34.8 ^e	53.3	35.7	20.2	12.0	33.3
<u>2b</u> ^b	46.5 ^d	47.3	44.5 ^d	31.1 ^f	43.1	28.2	31.3 ^f	34.6 ^e	56.4	34.8 ^e	20.2	13.9	33.1
<u>1c</u>	41.2	44.3	48.5	37.4	37.0	28.0	31.0	35.3	53.5	35.3	20.3	12.6	30.5
<u>2c</u>	40.1	45.7	46.7	37.5	43.2	28.3	31.3	34.6	56.1	34.1	20.4	14.4	31.9
<u>3</u>	30.4	23.5	36.2	40.5	50.7	28.3	31.4	35.3	52.6	36.2	20.8	12.9	--
<u>4</u>	35.0 ^d	22.5	33.5	43.0	46.4	27.5	31.8	35.3 ^d	55.2	35.7	19.9	14.4	--

^a ^{13}C NMR spectra were taken with a Varian NV-14 FT NMR (at 15.09 MHz) and/or a Bruker HX-90E FT NMR (at 22.63 MHz) spectrometer using TMS as an internal standard ($\delta_{\text{C}} 0$); precision of δ_{C} are about ± 0.1 ppm. Chemical shifts of carbons other than those cited above were only slightly affected by the structural changes in the A-ring,¹⁰ and have already been described in the previous paper.² ^b The spectra of these compounds were not examined by SFORD owing to lack of sufficient materials. ^c These assignments have been confirmed by taking the spectra of the 3-deuterio derivatives (unpublished results). ^{d, e, f} These assignments may be reversed although those given here are preferred.

(1a: $\text{R}_1 = \text{R}_2 = \text{H}$)(1b: $\text{R}_1 = \text{CH}_3$; $\text{R}_2 = \text{H}$)(1c: $\text{R}_1 = \text{H}$; $\text{R}_2 = \text{CH}_3$)(2a: $\text{R}_1 = \text{R}_2 = \text{H}$)(2b: $\text{R}_1 = \text{CH}_3$; $\text{R}_2 = \text{H}$)(2c: $\text{R}_1 = \text{H}$; $\text{R}_2 = \text{CH}_3$)

(3)



(4)

As a whole, spectral features of the episulfides shown in Table 1 are similar to those of the corresponding epoxides previously reported² except for the signal positions of the three-membered ring carbons; an episulfide ring carbon resonates at a higher field as is already known.⁷ However, detailed examinations of the data revealed some interesting differences between them.

Table 1 shows that the changes in δ_{C} of the allylic carbons (β from sulfur) are smaller upon introduction of an episulfide ring into a six-membered unsaturated ring² than upon introduction of an epoxide ring,²

TABLE 2

Differences in Chemical Shifts between Epimeric Pairs of the Episulfides and the Corresponding Epoxides² (In Parentheses) and Methyl Substitution Effects ($\Delta\delta_C$ in ppm)^a

Compounds to be compared	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-19
Differences in δ_C between epimers												
<u>2a-1a</u>	-1.0 (-0.1)	+2.2 (+2.4)	-2.4 (-0.2)	-0.4 (-0.6)	+7.6 (+5.0)	+0.2 (0.0)	+0.3 (+0.2)	-0.4 (-0.7)	+2.5 (+1.8)	-0.6 (+0.7)	+0.1 (-0.1)	+2.2 (+1.1)
<u>2b-1b</u>	-0.6 (-0.3)	+0.6 (+1.3)	-2.2 (-0.5)	-0.4 (-0.4)	+7.8 (+5.7)	+0.3 (0.0)	+0.2 (+0.2)	-0.2 (-0.7)	+3.1 (+2.0)	-0.9 (+0.7)	0.0 (-0.1)	+1.9 (+0.8)
<u>2c-1c</u>	-1.1 (-0.3)	+1.4 (+1.8)	-1.8 (0.0)	+0.1 (-0.5)	+6.2 (+4.2)	+0.3 (0.0)	+0.3 (+0.2)	-0.7 (-0.6)	+2.6 (+1.8)	-1.2 (-0.2)	+0.1 (0.0)	+1.8 (+0.8)
<u>4-3</u>	+4.6 (+3.2)	-1.0 (-0.1)	-2.7 (-1.6)	+2.5 (+2.0)	-4.3 (-0.5)	-0.8 (-1.4)	+0.4 (+0.4)	0.0 (+0.1)	+2.6 (+2.1)	-0.5 (+1.7)	-0.9 (-0.6)	+1.5 (+0.6)
2-Methyl substitution effects												
<u>1b-1a</u>	+6.9 (+5.5)	+11.9 (+6.6)	+8.9 (+7.7)	+1.3 (+0.7)	-0.3 (-0.3)	-0.2 (-0.1)	-0.1 (+0.1)	-0.2 (+0.1)	-0.4 (+0.1)	+0.5 (+0.5)	0.0 (0.0)	-0.6 (-0.3)
<u>2b-2a</u>	+7.1 (+5.3)	+10.5 (+5.1)	+9.2 (+7.4)	+0.9 (+0.9)	0.0 (+0.4)	-0.2 (-0.1)	-0.1 (+0.1)	-0.2 (+0.1)	+0.1 (+0.3)	+0.2 (+0.5)	-0.1 (0.0)	-1.0 (-0.6)
3-Methyl substitution effects												
<u>1c-1a</u>	+1.0 (+0.9)	+9.5 (+7.9)	+10.7 (+5.5)	+7.2 (+5.2)	+1.4 (+1.1)	-0.1 (0.0)	0.0 (0.0)	+0.3 (0.0)	-0.2 (0.0)	+0.1 (+0.3)	+0.1 (0.0)	0.0 (+0.1)
<u>2c-2a</u>	+0.7 (+0.9)	+8.9 (+7.5)	+11.4 (+5.7)	+7.3 (+5.3)	+0.1 (+0.5)	-0.1 (0.0)	-0.1 (0.0)	-0.2 (+0.1)	-0.1 (0.0)	-0.5 (-0.6)	+0.1 (0.0)	-0.5 (-0.2)

^a Plus sign indicates a downfield shift.

although the C-5 resonances of 3 and 4 were still found at considerably lower fields in comparison with those of their corresponding olefins.²

On inspection of Table 2, the steric γ effects⁷ were found to be produced on carbons bearing an axial hydrogen atom by introducing episulfide rings cis to the hydrogen (C-5 in 1 and C-1 in 3); they are considerably stronger as compared with those exerted by the corresponding epoxide rings.² These stronger effects result evidently from the more bulkiness of the thiirane ring than that of the oxirane ring as expected.

It should be emphasised that the bulkier S-ring also gave stronger long-range δ effects⁸ upon C-19 and C-9 resonances of both 2 and 4; these δ effects resulted in downfield shifts of about +2 and +2.5 ppm, respectively. A longer-range effect⁹ should also be noted to be discernible upon the C-11 resonance of 4.

As can be seen from Table 2, the effects of the methyl substitution at C-2 and C-3 in the episulfides are almost similar to those in the corresponding epoxides; accordingly they do not resemble those observed in the corresponding olefins.² The α , in particular, and β effects were found to be strengthened in the episulfide cases.

The present result that a bulkier substituent exerts stronger steric γ and δ effects appears to be useful in ¹³C NMR spectroscopy. Further studies are in progress in these laboratories.

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