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THE SULFONATION OF SOME POLYCYCLIC KETONES

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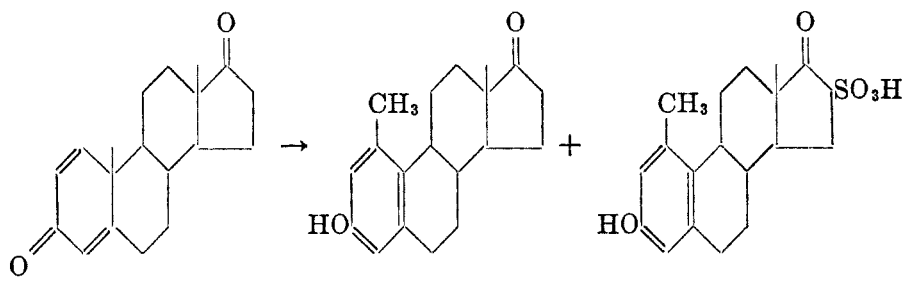
Several years ago Windaus and co-workers (1, 2) showed that saturated 3-keto steroids such as cholestan-3-one and coprostan-3-one were converted to the corresponding β-keto sulfonic acids when treated with equimolar quantities of sulfuric acid in acetic anhydride solution at room temperature or below. The conditions for the sulfonation, therefore, are identical with those employed for dienone-phenol rearrangements except that in the latter case catalytic amounts of sulfuric acid appear to be sufficient.

In a recent synthesis (3) of 1-methylestrone (II) from 1,4-androstadiene-3,17-dione (I) by a dienone-phenol rearrangement in acetic anhydride-sulfuric acid solution, it was noted that the yield of 1-methylestrone (II) dropped markedly with increasing amounts of sulfuric acid, a water-soluble derivative being formed, and that the latter was nearly the sole product when equimolar quantities of sulfuric acid were used. As reviewed in that paper (3), a considerable number of steroid dienones have been rearranged previously to the isomeric phenols, the yield being more or less independent of the amount of sulfuric acid employed. These dienones differed from I only in that the C-17 carbonyl group was replaced by hydroxyl, carbomethoxyl, or hydrocarbon substituents. It was reasonable to assume, therefore, that in the rearrangement of the dienone (I) sulfonation had occurred to form the β-keto sulfonic acid (III).[1] This observation led to the present study of sulfonic acid derivatives of some 17-keto steroids and related compounds.



I II III

With few exceptions, β-keto sulfonic acids do not appear to have been studied (4) and it was of interest to examine some of their properties, particularly in view

[1] Windaus (1, 2) also showed that α,β-unsaturated ketones such as Δ^4-cholesten-3-one could be sulfonated in the 6 position under those conditions and it might be suggested, therefore, that the by-product obtained in the rearrangement of I is due to sulfonation at C-6. If that were true, the same relation between yield and amount of sulfuric acid should have been observed in all the other steroid dienones reviewed in the preceding paper (3), which was not the case.

of their formal resemblance to β-keto acids. As a model ketone, 1-keto-1,2,3,4-tetrahydrophenanthrene (IV) was chosen, since it represented a fairly readily available starting material from which crystalline derivatives could be expected. Furthermore, it resembled the 17-keto steroids to be discussed below in that only one adjacent methylene position was unsubstituted. Some analogies in the behavior of the corresponding sulfonic acids could thus be expected.

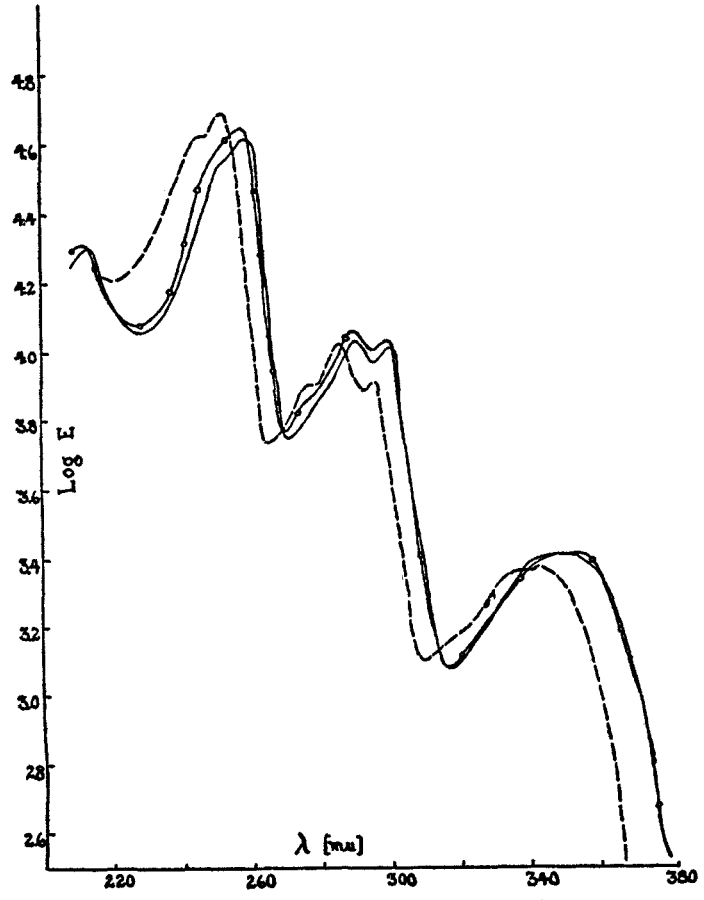


FIG. 1. Ultraviolet absorption spectra (in 95% ethanol solution: – – – 1-ketotetrahydrophenanthrene (IV); ⊖⊖⊖ methyl 1-ketotetrahydrophenanthrene-2-sulfonate (Vb); ——— methyl 1-keto-2-methyltetrahydrophenanthrene-2-sulfonate (VIIIb).

When the ketone IV in acetic anhydride solution was allowed to stand at room temperature for two hours with an equimolar amount of concentrated sulfuric acid, there was obtained in high yield a crystalline, water-soluble sulfonic acid, which could be recovered unchanged on boiling for three hours with dilute hydrochloric acid, thus excluding the possible formation of an enol sulfate. Only two structures remain for consideration, namely an aromatic sulfonic acid (improbable because of the mild reaction conditions) or the β-keto sulfonic acid (Va).

The acid reacted instantaneously with diazomethane to yield a methyl ester, which was soluble in cold 5% sodium hydroxide solution and could be recovered unchanged on acidification. This definitely proved the structure Va for the acid and Vb for the methyl ester. A similar acidity has been demonstrated in certain disulfones (5) and is of course to be expected by analogy to β-keto esters. Attempts to prepare ketone derivatives of the methyl ester failed. For instance,

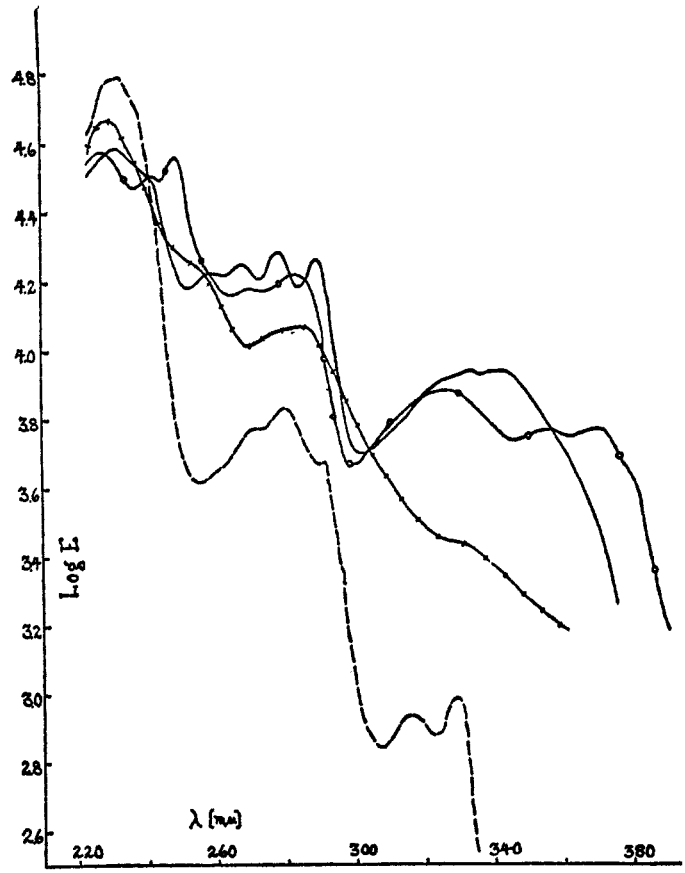
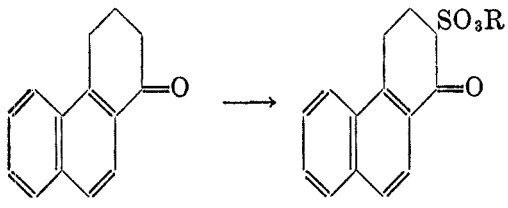


FIG. 2. Ultraviolet absorption spectra (in 5% sodium hydroxide solution): ——— methyl 1-ketotetrahydrophenanthrene-2-sulfonate (fresh solution); -|-|- same after standing for four weeks; ⊖⊖⊖ 1-phenanthrol; - - - - β-naphthoic acid.

when Vb was treated with dinitrophenylhydrazine, the dinitrophenylhydrazine salt Ve was obtained, identical with a sample prepared from the free acid Va. A similar failure to obtain a phenylhydrazone of acetophenone-ω-sulfonic acid has been mentioned (6). It is likely that the phenylhydrazone obtained by Windaus and Kuhr (1) in the case of cholestanone-2-sulfonic acid actually represented the phenylhydrazine salt of the ketone sulfonic acid. The ultraviolet absorption spectrum (Fig. 1) of the methyl ester Vb in ethanol,

except for a slight bathochromic shift, closely resembles that of the parent ketone IV (7), which would indicate that the compound exists predominantly in the keto form. When measured in sodium hydroxide solution (Fig. 2), the main maximum at 257 mu due to the carbonyl group in conjugation with the aromatic nucleus (7) disappeared, and the spectrum resembled that of 1-phenanthrol taken in sodium hydroxide solution. On prolonged standing, the absorption of the sodium hydroxide solution of Vb changed somewhat, possibly due to ring opening to VI; for comparison with the latter, the ultraviolet absorption spectrum of β-naphthoic acid in sodium hydroxide solution is also reproduced.

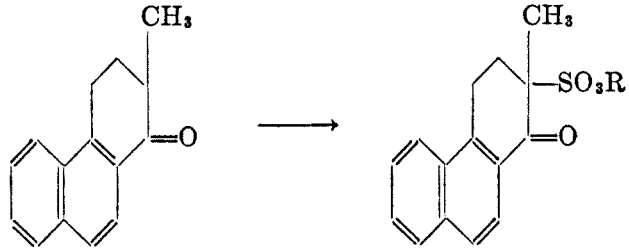


IV

Va R = H
Vb R = CH_3
Vc R = $H \cdot C_5H_5N$
Vd R = $H \cdot NH_3$
Ve R = $H \cdot 2,4—(NO_2)_2C_6H_3NHNH_2$

VI

Attempts to prepare the 2-methyl derivative VIIIb by alkylating the methyl ester Vb with sodium methoxide and methyl iodide failed, possibly due to cleavage to VI, since β-keto sulfonic acids appear to be labile towards alkali (*cf.* 8, 9). The desired compound could be prepared, however, by sulfonation of 1-keto-2-methyl-1,2,3,4-tetrahydrophenanthrene (VII), thus demonstrating that only one free hydrogen atom adjacent to a carbonyl group is necessary for sulfonation under those conditions. In conformance with the assigned structure, the methyl ester VIIIb was insoluble in aqueous alkali and its spectrum in ethanol solution (Fig. 1) was identical with that of Vb.



VII

VIIIa R = H
VIIIb R = CH_3
VIIIc R = $H \cdot C_5H_5N$

Dehydrogenation of the methyl ester Vb with a palladium catalyst in *p*-cymene solution as a possible route to phenolic sulfonic acids was unsuccessful, since the only pure products were 1-phenanthrol and the ketone IV. A some-

what similar hydrogenolysis has been observed with 1-keto-2-hydroxymethylene-1,2,3,4-tetrahydrophenanthrene (10).

The sulfonation procedure was next applied to some 17-keto steroids in order to prepare the corresponding 16-sulfonic acid derivatives, which have not been described hitherto. Isoandrosterone acetate (IX) and its C-3 epimer, androsterone acetate, readily yielded the corresponding sulfonic acid, which in the case of

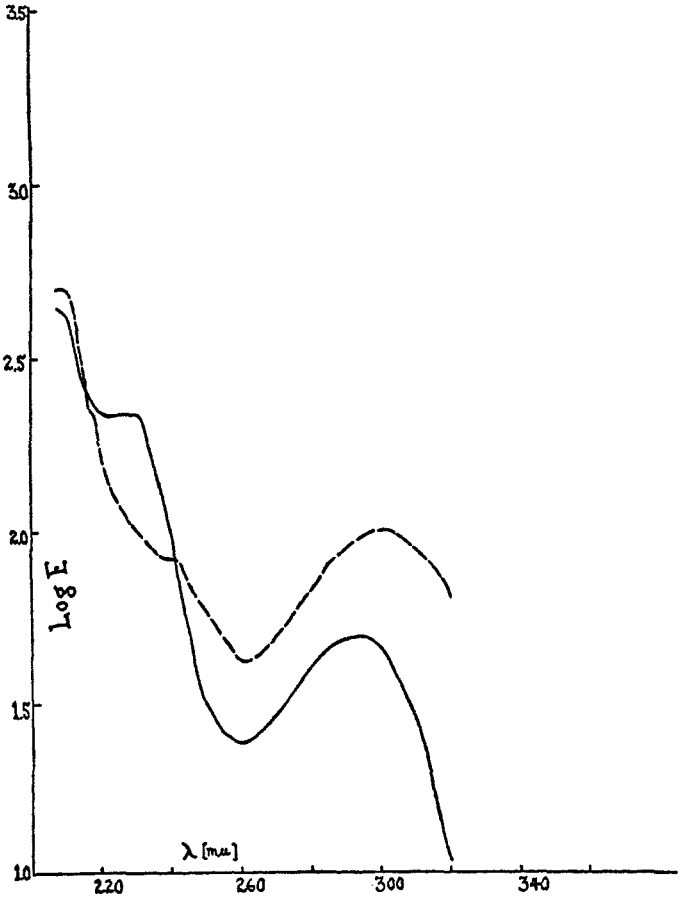
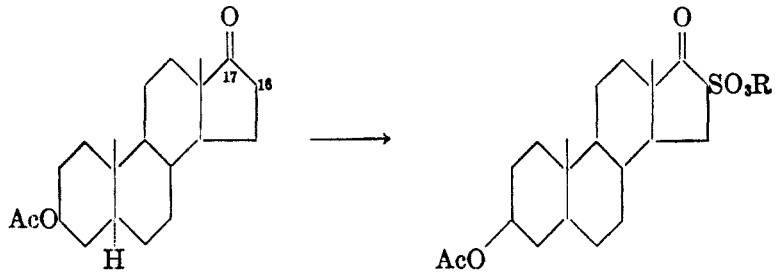


FIG. 3. Ultraviolet absorption spectra (in 95% ethanol solution): ——— isoandrosterone acetate (IX); - - - isoandrosterone acetate 16-sulfonic acid (Xa).

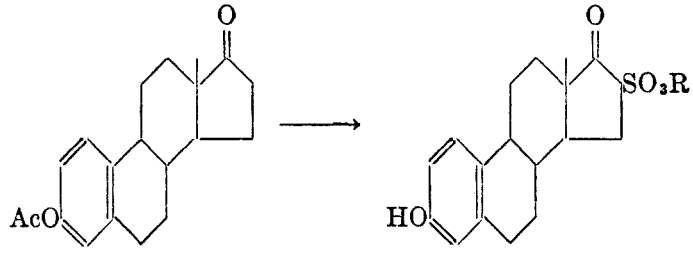
the former could be obtained in crystalline form and which was converted to several derivatives. In this instance also, the ultraviolet absorption spectrum of the sulfonic acid Xa closely resembled that of the parent ketone IX (Fig. 3). It was of particular interest to attempt the sulfonation of estrone acetate (XI), since two derivatives, estrone sulfate and estrone-2 (or 4)-sulfonic acid have already been prepared by Butenandt and Hofstetter (11) by means of chlorosulfonic acid. When the sulfonation was carried out with sulfuric acid in acetic anhydride solution followed by methylation, it was possible to isolate the crys-

talline methyl ester XIIa of estrone-16-sulfonic acid [2] and thence the ammonium salt XIIb.



IX

Xa R = H
Xb R = CH_3
Xc R = H·C_5H_5N



XI

XIIa R = CH_3
XIIb R = H·NH_3

Through the courtesy of Dr. Konrad Dobriner, Sloan-Kettering Institute for Cancer Research, New York, and Dr. R. Norman Jones, National Research Council, Ottawa, the infrared absorption spectra of all of the sulfonic acid methyl esters described in this paper have been determined in nujol mulls. The details will be published elsewhere by them, but it is pertinent to mention at this time that all of the compounds showed a strong carbonyl band which was shifted slightly to lower wave length, probably due to the adjacent sulfonic acid group. These data further confirm that the compounds seem to exist in the keto form as indicated already from the ultraviolet absorption spectra.

After it had been demonstrated that sulfonation in the 16-position of 17-keto steroids was achieved readily under conditions prevailing in the dienone-phenol rearrangement, attention was directed towards the isolation of the sulfonation product in the rearrangement of 1,4-androstadiene-3,17-dione (I) mentioned in the second paragraph of this discussion. When one mole of sulfuric acid was employed in the rearrangement of I, almost the entire product was water-soluble and on evaporation afforded an amorphous sulfonic acid, which showed the typical ultraviolet absorption spectrum of a phenol, and thus must be 1-methylestrone-16-sulfonic acid (III) rather than the 16-sulfonic acid derivative

[2] Nuclear sulfonation was excluded, since estradiol could be recovered as the diacetate under those conditions.

of the starting material I. An analytically pure, though amorphous methyl ester and pyridinium salt were also prepared. It is interesting to note that steroid sulfonic acids such as isoandrosterone acetate 16-sulfonic acid (Xa) or 1-methylestrone-16-sulfonic acid (III) proved to be excellent catalysts in the dienone-phenol rearrangement of 1,4-androstadiene-3,17-dione, and afforded 70–80% of 1-methylestrone (II).

The author is grateful to the Misses Helen Dudek and Jean Rogers for assistance in the experimental work and to Miss Elizabeth Ryan for the ultraviolet absorption spectra.

EXPERIMENTAL[3]

Sulfonation of 1-keto-1,2,3,4-tetrahldrophenanthrene (IV). A solution of 3.9 g. of the ketone IV in 40 cc. of acetic anhydride was treated dropwise with swirling in an ice-bath with a solution of 2.0 g. of concentrated sulfuric acid in 7 cc. of acetic anhydride and was then allowed to stand at room temperature for two hours. Water was added to hydrolyze the acetic anhydride and the clear solution was evaporated to dryness under reduced pressure, water was added, and the process repeated. The crystalline, very light tan colored residue was triturated with ether-acetone, filtered, and dried in a vacuum desiccator. The yield of *1-ketotetrahydrophenanthrene-2-sulfonic acid hydrate (Va)* was 4.96 g. (85%), with the following melting point behavior, unchanged on recrystallization from acetone: partly melting at 154°, solidifying at 158°, darkening at 187°, and decomposing at 194–195°. The acid was recovered unchanged after refluxing for three hours in 5% hydrochloric acid solution. It formed a water-insoluble barium salt.

Anal. Calc'd for $C_{14}H_{12}O_4S \cdot H_2O$: C, 57.13; H, 4.79; S, 10.89; neut. equivalent, 294.
Found: C, 56.80; H, 4.87; S, 10.85; neut. equivalent, 288.

Instantaneous nitrogen evolution was observed when a solution of 2.5 g. of the above sulfonic acid in methanol was treated with excess ethereal diazomethane. After two minutes, the solution was evaporated to dryness, yielding 2.32 g. (94%) of colorless crystals of *methyl 1-keto-1,2,3,4-tetrahydrophenanthrene-2-sulfonate (Vb)* melting at 101–105°. The analytical sample was recrystallized from ether, and melted at 104–106°. The compound gave no color with alcoholic ferric chloride solution. It was readily soluble in 5% sodium hydroxide solution and was recovered unchanged on acidification. The ultraviolet absorption spectra in 95% ethanol and in 5% sodium hydroxide solution are reproduced in Figs. 1 and 2.

Anal. Calc'd for $C_{15}H_{14}O_4S$: C, 62.05; H, 4.86; S, 11.04; methoxyl, 10.69.
Found: C, 62.38; H, 5.28; S, 10.75; methoxyl, 10.44.

1-Keto-1,2,3,4-tetrahydrophenanthrene-2-sulfonic acid pyridinium salt (Vc). A solution of 100 mg. of the sulfonic acid Va in 1 cc. of methanol was treated with three drops of pyridine and the solution was diluted with absolute ether. The fluffy, colorless needles of the pyridinium salt were filtered, washed well with ether, and dried in a vacuum desiccator; yield, 110 mg., m.p. 199–201°. It gave no color with 5% sodium hydroxide solution.

Anal. Calc'd for $C_{19}H_{17}NO_4S$: N, 3.94; S, 9.02.
Found: N, 3.75; S, 9.45.

1-Keto-1,2,3,4-tetrahydrophenanthrene-2-sulfonic acid ammonium salt (Vd). A solution of 100 mg. of the sulfonic acid Va in 3 cc. of water was treated with one drop of concentrated ammonium hydroxide and the solution was evaporated to dryness. Recrystallization from

[3] All melting points are corrected unless noted otherwise. The specific rotations were determined on 5–10 mg. of sample in a 1 dcm. tube of 1 cc. capacity. All microanalyses were carried out by Mr. Joseph Alicino, Metuchen, New Jersey and Mr. George L. Stragand, Microchemical Laboratory, University of Pittsburgh.

methanol gave colorless, glistening plates melting at 268° (dec. uncorr.) with softening at about 260°. The same product was obtained when 200 mg. of the methyl ester Vb was heated on the steam-bath with 10 cc. of ammonium hydroxide solution and evaporated to dryness.

Anal. Calc'd for $C_{14}H_{15}NO_4S$: C, 57.32; H, 5.15; N, 4.78; S, 10.93.
Found: C, 57.92; H, 5.56; N, 4.65; S, 11.18.

1-Keto-1,2,3,4-tetrahydrophenanthrene-2-sulfonic acid 2,4-dinitrophenylhydrazinium salt (Ve). To a warm solution of 100 mg. of 2,4-dinitrophenylhydrazine in 5 cc. of ethanol and 0.2 cc. of concentrated hydrochloric acid was added 50 mg. of the methyl ester Vb in an attempt to prepare the phenylhydrazone. After heating for two minutes, a precipitate appeared, whereupon the solution was cooled and the light yellow crystals were filtered and washed; yield, 40 mg., m.p. 213–215° (dec.); found: methoxyl, 0.00. The dinitrophenylhydrazine salt thus produced gave no depression in melting point on admixture with a sample (m.p. 215–216° dec.) prepared by crystallizing equimolar quantities of sulfonic acid Va and dinitrophenylhydrazine from ethanol.

Anal. Calc'd for $C_{20}H_{18}N_4O_8S$: C, 50.63; H, 3.82; N, 11.81; S, 6.74.
Found: C, 50.27; H, 3.87; N, 11.51; S, 6.99.

When a mixture of 70 mg. of the above salt Ve was shaken at room temperature overnight with a few cc. of water and 7 drops of acetone, filtration gave 30 mg. (85%) of acetone dinitrophenylhydrazone of m.p. 124–125°.

Dehydrogenation of methyl 1-keto-1,2,3,4-tetrahydrophenanthrene-2-sulfonate. A mixture of 200 mg. of the methyl ester Vb, 40 mg. of 5% palladized charcoal, and 4 cc. of *p*-cymene was refluxed in an atmosphere of nitrogen for twenty hours. The solution was diluted with ether, the catalyst removed by filtration, and the filtrate was extracted four times with 5% sodium hydroxide solution. Acidification of the extracts gave 20 mg. (15%) of 1-phenanthrol of m.p. 151–153° which on admixture with authentic 1-phenanthrol (m.p. 154–155°) melted at 151–154°. From the neutral fraction, after evaporative distillation under reduced pressure, there was obtained 30% of 1-ketotetrahydrophenanthrene (IV).

Sulfonation of 1-keto-2-methyl-1,2,3,4-tetrahydrophenanthrene (VII). The sulfonation of VII was carried out exactly as described for the non-methylated derivative IV and afforded 10% of recovered ketone and 71% of *1-keto-2-methyl-1,2,3,4-tetrahydrophenanthrene-2-sulfonic acid hydrate*, which started to melt at 108° solidified at 115° and decomposed at 145–147°.

Anal. Calc'd for $C_{15}H_{14}O_4S \cdot H_2O$: S, 10.40; neut. equivalent, 308.
Found: S, 10.26; neut. equivalent, 303.

Methylation with diazomethane and recrystallization from hexane-acetone gave colorless, shiny crystals of the *methyl ester* VIIIb melting at 105–106°. The compound was insoluble in 5% sodium hydroxide solution; its absorption spectrum in ethanol solution is shown in Fig. 2.

Anal. Calc'd for $C_{13}H_{14}O_4S$: C, 63.14; H, 5.30; S, 10.53; methoxyl, 10.20.
Found: C, 62.90; H, 5.27; S, 10.93; methoxyl, 10.36.

The *pyridinium salt* VIIIc was prepared in the usual manner, and melted at 99–100° (sealed capillary).

Anal. Calc'd for $C_{20}H_{19}NO_4S$: N, 3.79; S, 8.68.
Found: N, 3.57; S, 8.32.

Sulfonation of isoandrosterone acetate (IX). An ice-cold solution of 665 mg. of isoandrosterone acetate (IX) in 3 cc. of acetic anhydride was treated dropwise with a solution of 200 mg. of sulfuric acid in 3 cc. of acetic anhydride. The dark green solution was allowed to stand at room temperature for two hours, at which time crystals of the sulfonic acid had appeared. After cooling in ice for one-half hour, the colorless crystals were filtered on sintered glass, washed with acetic anhydride and ether, and dried in a vacuum desiccator. The *isoandrosterone acetate 16-sulfonic acid* (Xa) thus obtained was dissolved in acetone and precipitated with ether; yield 520 mg. (63%), m.p. 169–172° (dec.), $[\alpha]_D^{25}$ +33.5° (ethanol). The acid was quite soluble in water, but formed an insoluble barium salt. The ultraviolet

absorption spectrum (Fig. 3) was determined in ethanol solution and showed a maximum at 300 mμ, log E 1.99 and a minimum at 261 mμ, log E 1.62.

Anal. Calc'd for $C_{21}H_{32}O_6S$: C, 61.14; H, 7.82; S, 7.77; acetyl, 10.43.
Found: C, 60.72; H, 7.71; S. 7.42; acetyl, 10.01.

The *methyl ester Xb*, prepared by two minutes treatment with diazomethane, crystallized as rosettes of colorless needles from hexane-acetone or from ethanol, m.p. 189–190°, $[\alpha]_D^{25}$ +53.3° (acetone).

Anal. Calc'd for $C_{22}H_{34}O_6S$: C, 61.94; H, 8.03; S, 7.52; methoxyl, 7.28.
Found: C, 62.02; H, 7.64; S, 7.49; methoxyl, 7.08.

The *pyridinium salt Xc* formed colorless glistening crystals with m.p. 246–248° (dec. uncorr.), $[\alpha]_D^{25}$ +32.3° (ethanol).

Anal. Calc'd for $C_{26}H_{37}NO_6S$: N, 2.85; S, 6.52.
Found: N, 3.15; S, 6.38.

Oxidation of isoandrosterone acetate 16-sulfonic acid (Xa). By analogy to the oxidation of cholestanone-2-sulfonic acid (1), 0.4 g. of the above sulfonic acid Xa in 10 cc. of 90% acetic acid was heated for 2 hours at 60° with a solution of 0.38 g. of chromic anhydride in 5 cc. of 90% acetic acid. After diluting with water and shaking with ether, the latter was extracted with sodium hydroxide solution, the basic extracts were acidified and the precipitated acid was extracted with ether. Evaporation of the dried ether solution and recrystallization from a mixture of hexane and acetone gave 0.09 g. (24%) of colorless crystals of 3(β)-acetoxy*allo*etiobilianic acid with m.p. 229–232°, $[\alpha]_D^{29}$ −10.3° (acetone), thus affording further evidence for the 16-position of the sulfonic acid group.

Anal. Calc'd for $C_{21}H_{32}O_6$: C, 66.29; H, 8.48; neut. equiv., 190.
Found: C, 66.68; H, 8.60; neut. equiv., 184.

Sulfonation of androsterone acetate. The reaction was carried out as above, except that 10 cc. of acetic anhydride was necessary to dissolve the ketone. The sulfonic acid did not crystallize out and the reaction mixture was therefore diluted with water, evaporated to dryness under reduced pressure (the acetoxy group being hydrolyzed during this treatment) and the residue in methanol solution was treated with ethereal diazomethane. *Methyl androsterone-16-sulfonate* crystallized as colorless needles from methanol with m.p. 176–178°, $[\alpha]_D^{25}$ +80° (acetone).

Anal. Calc'd for $C_{20}H_{32}O_5S$: C, 62.47; H, 8.39; S, 8.34; methoxyl, 8.07.
Found: C, 62.38; H, 8.25; S, 8.55; methoxyl, 7.84; acetyl, 0.00.

Sulfonation of estrone acetate (XI). The sulfonation[2] was carried out in the usual manner with 624 mg. of estrone acetate, 200 mg. of concentrated sulfuric acid, and 5 cc. of acetic anhydride. After two hours, the solution was diluted with water and evaporated to dryness under reduced pressure, hydrolysis of the acetate group occurring during that treatment. The residue in methanol solution was treated for a few minutes with diazomethane and evaporated. On careful cooling of a hexane-acetone solution of the residue, decanting twice from oily impurities and scratching, there was obtained 400 mg. (55%) of nearly colorless crystals of *methyl estrone-16-sulfonate* (XIIa) of m.p. 188–194° (dec.) and an additional 135 mg. (18.5%) from the mother liquors, which melted at 180–185°. Several recrystallizations led to colorless blades with m.p. 199–200° (dec.), $[\alpha]_D^{25}$ +139° (acetone). The ultraviolet absorption spectrum in ethanol showed a maximum at 281 mμ, log E 3.37 and a minimum at 251 mμ, log E 2.92, characteristic for phenols.

Anal. Calc'd for $C_{19}H_{24}O_5S$: C, 62.61; H, 6.64; S, 8.80; methoxyl, 8.51.
Found: C, 62.77; H, 6.77; S, 8.67; methoxyl, 8.06; acetyl, 0.00

In an attempt to prepare the acetate, the above methyl ester was heated under nitrogen with acetic anhydride for two and one-half hours. After the usual work-up, there was obtained a viscous oil, which could not be induced to crystallize. The ultraviolet absorption spectrum showed maxima at 267.5 mμ, log E 3.09 and 275 mμ, log E 3.06, and minima at 251 mμ, log E 2.97 and 272.5 mμ, log E 3.02. Judging from the analytical figures, the oil appears to be contaminated by some acetic anhydride.

Anal. Calc'd for $C_{21}H_{26}O_6S$: S, 7.89; methoxyl, 7.63; acetyl, 10.59.
Found: S, 6.21; methoxyl, 6.23; acetyl, 11.93.

The methyl ester XIIa was converted to the *ammonium salt* XIIb by heating 50 mg. with 5 cc. of concentrated ammonium hydroxide solution for one hour and evaporating to dryness. The residue was digested with acetone, filtered, and the precipitate was washed well with acetone; yield 40 mg., m.p. (inserted at 260° in sealed capillary) sintering at 270° with decomposition at 320–323° (uncorr.), $[\alpha]_D^{26}$ +124° (ethanol). The ultraviolet absorption spectrum was identical with that of the methyl ester.

Anal. Calc'd for $C_{18}H_{25}NO_5S$: N, 3.81; S, 8.73.
Found: N, 3.93; S, 8.90.

Dienone-phenol rearrangement of 1,4-androstadiene-3,17-dione (I). (*a*) *With one mole of sulfuric acid.* The dienone-phenol rearrangement was carried out with 285 mg. of the ketone I and 100 mg. of sulfuric acid in the usual manner (3). After dilution with water, ether extraction, and saponification, there was obtained 20 mg. (7%) of 1-methylestrone (II). The aqueous solution was evaporated to dryness under reduced pressure, water was added, the solution again evaporated, and this process repeated several times. The purplish amorphous residue was then dried in a vacuum desiccator for twenty hours and weighed 230 mg. (63%). It melted at 125–138° with previous softening and since its ultraviolet absorption spectrum showed a maximum at 283 mμ, log E 3.69 and a minimum at 246 mμ, log E 3.27, it is considered to be *1-methylestrone-16-sulfonic acid* (III).

Anal. Calc'd for $C_{19}H_{24}O_5S$: S, 8.80.
Found: S, 8.63.

Treatment of the above acid with pyridine and precipitation with ether gave an apparently microcrystalline, light tan precipitate of the *pyridinium salt* melting with decomposition at 150° (previous softening).

Anal. Calc'd for $C_{24}H_{29}NO_5S$: N, 3.16; S, 7.23.
Found: N, 2.97; S, 7.15.

The sulfonic acid reacted immediately with diazomethane to give a colorless, amorphous *methyl ester* with m.p. 90–104°.

Anal. Calc'd for $C_{20}H_{26}O_5S$: S, 8.47; methoxyl, 8.20.
Found: S, 8.27; methoxyl, 8.51.

(*b*) *With 1-methylestrone-16-sulfonic acid (III).* To demonstrate that 1-methylestrone-16-sulfonic acid itself could be a catalyst in the rearrangement in (*a*), 100 mg. of the dienone I in 2.5 cc. of acetic anhydride was treated with 25 mg. of the amorphous sulfonic acid described above for five hours at room temperature. After working up as usual, there was isolated 70 mg. of 1-methylestrone, m.p. 249–251°.

(*c*) *With isoandrosterone acetate 16-sulfonic acid (Xa).* The reaction was carried out as above, except that 25 mg. of crystalline isoandrosterone acetate 16-sulfonic acid (Xa) was used and the reaction was carried out on the steam-bath. The yield of 1-methylestrone (II) was 80 mg.

SUMMARY

This paper deals with the preparation and properties of β-keto sulfonic acids derived from 1-ketotetrahydrophenanthrene, its 2-methyl derivative, estrone, androsterone, and isoandrosterone acetate. On the basis of the ready sulfonation of the 17-keto steroids at room temperature with sulfuric acid-acetic anhydride, it was shown that the by-product in the dienone-phenol rearrangement of 1,4-androstadiene-3,17-dione (3) was 1-methylestrone-16-sulfonic acid.

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