

N, 23.93%. Found<sup>9</sup>: C, 56.64, 56.54%; H, 6.01, 6.06%; N, 23.14, 23.30%. 2,4-Dinitrophenylhydrazone, C<sub>18</sub>H<sub>18</sub>N<sub>4</sub>O<sub>6</sub>, m.p. 156–158°. Calcd.: C, 53.81%, H, 4.20%, N, 19.88%. Found: C, 53.84, 53.76%; H, 4.44, 4.43%; N, 18.80, 19.03%.<sup>10</sup>  
 Derivatives of  $\alpha$ -benzyloximinohydrocinnamaldehyde. Semicarbazone, C<sub>17</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub>, m.p. 180°. Calcd.: C, 65.81%, H, 5.58%, N, 18.06%. Found<sup>10</sup>: C, 65.96, 65.68%; H, 6.27, 6.03%; N, 17.70%.

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(9) Analyses by Micro-Tech Laboratories, Skokie, Ill.

(10) Analyses by Messrs. Weiler and Strauss, Oxford, England.

### Ring A Aromatization of a 19-Norsteroid

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The reactions of 4,5-epoxides of 3-ketosteroids have been studied, *inter alia*, by Camerino *et al.*,<sup>1–3</sup> who found that they led to 4-halo, 4-hydroxy, and 2 $\alpha$ -hydroxy derivatives of 3-keto- $\Delta^4$ -steroids. During the course of an investigation involving the preparation of some esters of 4-chloro-19-nortestosterone (Table I) in this laboratory, another reaction of such 4,5-epoxides was observed.

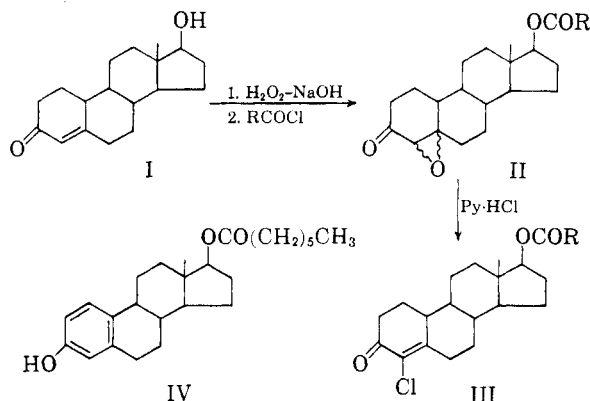
A synthetic scheme similar to that of the Italian workers<sup>3</sup> was employed. 19-Nortestosterone (I) was treated with alkaline peroxide and the oily epoxide was acylated with the appropriate acyl chloride. The crude esters (II) were boiled with pyridinium chloride in chloroform to give the desired 4-chloro compounds (III).

When this sequence was carried out in the case of the heptanoate derivative the expected ester (Table I, No. 1) was obtained as an oil and a second, crystalline, fraction was also isolated. This material had analyses, spectra, and melting point consistent with estradiol 17 $\beta$ -heptanoate (IV).

The mode of formation of IV is unknown. 3-Keto-4 $\beta$ ,5-epoxides are known to rearrange under acid conditions to give stable 2 $\alpha$ -hydroxy-3-keto- $\Delta^4$ -steroids.<sup>2</sup>

The analogous 2 $\beta$ -hydroxy compounds, which could dehydrate to form a 1,4-diene-3-one, are not obtained under these conditions. The corresponding 4 $\alpha$ ,5-epoxides do not undergo such a rearrangement.

Apparently, in the case of the present 19-nor system, a rearrangement of the epoxide, perhaps involving C-10, followed by epoxide cleavage, elimina-



tion, and tautomerization, gives rise to the aromatic product. It is pertinent to note that 5 $\beta$ ,10 $\beta$ -oxido-19-norandrostane-17 $\beta$ -ol-3-one furnishes 10 $\beta$ -hydroxy-19-nortestosterone on treatment with perchloric acid<sup>4</sup> and that the latter compound undergoes acid catalyzed conversion to estradiol.<sup>5</sup> A more detailed formulation of the mechanism cannot be given at this time since the oily intermediates could not be purified and, in particular, because it was necessary to use the oily, mixed 4 $\alpha$ ,5- and 4 $\beta$ ,5-epoxides.

### EXPERIMENTAL<sup>6</sup>

*Esters of 4-chloro-19-nortestosterone* (Table I). To a stirred solution of 5.0 g. (0.018 mole) of 19-nortestosterone<sup>7</sup> in 300 ml. of methanol maintained at  $-5^{\circ}$  to  $0^{\circ}$  there were added, dropwise and simultaneously during 8–10 min., 10 ml. of 4*N* sodium hydroxide solution and 37.5 ml. of 30% hydrogen peroxide solution. The resulting solution was stirred at  $0^{\circ}$  for an additional 50 min., treated with 2.5 ml. of glacial acetic acid, and poured into 2 l. of brine. The resulting suspension was extracted with ethyl acetate ( $5 \times 400$  ml.) and the united extracts were dried with sodium sulfate, filtered, and concentrated *in vacuo* to give 6.1–6.6 g. of a gum with no selective ultraviolet absorption.

A stirred solution of the crude epoxide in 55 ml. of dry pyridine was chilled to below  $-5^{\circ}$  and treated with 0.0549–0.0915 mole of the requisite acid chloride. The mixture was allowed to stand at  $5$ – $27^{\circ}$  for 18 hr., cooled in ice, and then decomposed by cautious addition of 60 ml. of water. The resulting solution was poured into 1 l. of brine and extracted with chloroform ( $5 \times 200$  ml.). The combined organic extract was washed with 5% sodium bicarbonate solution and water, and then dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and evaporated *in vacuo*. The residue was a brown gum.

A solution of the crude ester in 120 ml. of chloroform containing 21.2 g. (0.183 mole) of distilled pyridinium chloride was refluxed for 18 hr. The cooled brown solution was diluted with 150 ml. of chloroform, washed with 1% hydrochloric acid and then with water, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated *in vacuo*. The residue was purified by recrystallization or chromatography.

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(6) All melting points are corrected. Microanalyses were performed under the supervision of Mr. W. F. Ellenbogen, Analytical Section. Spectral determinations and interpretations were made by Dr. Walter Thompson.

(7) Purchased from Schering, A. G., m.p. 122.5–123.5 $^{\circ}$ .

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TABLE I  
 ESTERS OF 4-CHLORO-19-NORTESTOSTERONE (III)

No.	R	M.P.	Yield, % <sup>a</sup>	Recryst. Solv.	Formula	Analyses			
						Calcd.		Found	
						C	H	C	H
1	CH <sub>2</sub> (CH <sub>2</sub> ) <sub>6</sub>	Oil	13	<sup>b</sup>	C <sub>26</sub> H <sub>37</sub> O <sub>3</sub> Cl	71.32	8.86	71.48	9.19
2	CH <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub> CH—CH <sub>2</sub> —CH <sub>2</sub> <sup>c</sup>	88–89	17	Et <sub>2</sub> O-PE <sup>d</sup>	C <sub>26</sub> H <sub>37</sub> O <sub>3</sub> Cl	72.11	8.61	72.27	8.70
3	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub>	127–130	17	Et <sub>2</sub> O <sup>e</sup>	C <sub>27</sub> H <sub>35</sub> O <sub>3</sub> Cl	73.53	7.54	73.39	7.77
4	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> OCH <sub>2</sub> <sup>f</sup>	167–168	37	MeCOEt	C <sub>26</sub> H <sub>30</sub> O <sub>4</sub> Cl <sub>2</sub>	65.41	6.33	65.28	6.37
5	C <sub>6</sub> H <sub>5</sub>	192–196	12	Et <sub>2</sub> O <sup>g</sup>	C <sub>26</sub> H <sub>29</sub> O <sub>3</sub> Cl	72.71	7.08	72.47	7.37

<sup>a</sup> Yields are of pure product based on 19-nortestosterone. <sup>b</sup> Eluted by benzene and 1:1 benzene-ether. <sup>c</sup> B. Camerino, B. Patelli, and A. Vercellone, *J. Am. Chem. Soc.*, **28**, 3540 (1956) disclosed the biological activity of this compound but not the physical properties. <sup>d</sup> Eluted by 1:1 benzene-ether. <sup>e</sup> Eluted by 1:1 petroleum ether-benzene and benzene. <sup>f</sup>  $[\alpha]_D^{25} +60.5^\circ$  (1% in chloroform). <sup>g</sup> Decolorized by passage through alumina in benzene.

4-Chloro-19-nortestosterone-17 $\beta$ -benzoate (Table I, No. 5). The preparation of this substance differed from the other esters in that 19-nortestosterone-17 $\beta$ -benzoate<sup>8</sup> was epoxidized using the same general procedure as for 19-nortestosterone. The remainder of the sequence was unchanged.

Isolation of estradiol 17 $\beta$ -heptanoate. The preparation of 4-chloro-19-nortestosterone-17 $\beta$ -heptanoate, starting from 10.0 g. (0.0366 mole) of 19-nortestosterone was carried out as described above. The total crude final product was chromatographed on 770 g. of ethyl acetate washed alumina. After elution of the desired oily ester with a total of 5000 ml. of petroleum ether, benzene and ether mixtures, the estradiol ester was eluted by 1:1 benzene:ether and ether and recrystallized from ligroin to give 2.35 g. (18% from 19-nortestosterone) of colorless plates, m.p. 94–96° (lit.<sup>9</sup> 96–98°),  $\epsilon_{281}^{C_2H_5OH}$  2000 (shoulder at 286 m $\mu$ ),  $\mu^{Nujol}$  2.9, 5.9, 6.2, 6.3, 6.7, 7.8, 8.1, 8.7, 11.5, 12.3, 12.8.

Anal. Calcd. for C<sub>25</sub>H<sub>36</sub>O<sub>3</sub>: C, 78.08; H, 9.44; mol. wt. 384. Found: C, 78.21; H, 9.64; mol. wt. 370 (camphor).

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## The Dipole Moment of Norbornylene. Use of the IBM 650 Computer for Dipole Moment Calculations<sup>1</sup>

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Norbornylene (bicyclo[2.2.1]hept-2-ene) is known to contain a "strained" olefinic linkage by the usual chemical test of phenyl azide addition.<sup>2</sup> A comparison of the infrared spectrum of norbornylene<sup>3</sup> with other *cis* olefins<sup>4</sup> showed the olefinic

(1) This work was supported by a grant from the Sloan Foundation.

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hydrogen stretching band of the former at 3070 cm.<sup>-1</sup>, considerably higher than the usual value (3010 cm.<sup>-1</sup>). It was shown that the corresponding absorption was found at 3000 cm.<sup>-1</sup> for *trans*-cyclooctene, another strained olefin, which indicated the strain in this case was quite different from that found in norbornylene.<sup>5</sup> The dipole moment of *trans*-cyclooctene was found to have the unusually large value of 0.8 D, and a unique strained geometry about the double bond was proposed<sup>5</sup> to account for this large moment.

TABLE I  
INFRARED ABSORPTION MAXIMA, CM.<sup>-1</sup>

	=C—H	C=C
<i>cis</i> -4-Octene	3010	1650
<i>cis</i> -Cyclooctene	3010	1664
<i>trans</i> -Cyclooctene	3000	1658
Cyclohexene	3020	1650
Norbornylene	3070	1575
1-Butyne	3300	—

Norbornylene is strained in quite a different way from *trans*-cyclooctene as is indicated by the infrared spectrum. Some pertinent infrared data are summarized in Table I. In norbornylene, the C—C=C bond angles are reduced below the preferred value of 120° by the geometrical requirements of the ring system. There is a consequent increase in the *p* character in the C—C bonds of the olefinic system, and a corresponding increase in *s* character in the olefinic C—H bond. These effects increase the =C—H stretching frequency considerably, and simultaneously reduce the C=C stretching frequency. A quantitative relationship exists<sup>6</sup> between the C—H stretching frequency and the amount of *s* character in the bond, and from the position of the norbornylene band relative to the corresponding bands in an ordinary *cis* olefin and a terminal acetylene (Table I), the appreciable strain is apparent.

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