

TABLE II (Continued)

R	R'	Yield, %	M.P., °C.	Recryst. Solvent <sup>a</sup>	Formula	Analyses, %			
						Calcd.		Found	
						C	H	C	H
2-ClC <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	64	164-166	Dil. ethanol	C <sub>11</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>3</sub> S	45.42	5.20	45.75	5.39
3-ClC <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	60	133-134	Dil. ethanol C <sub>6</sub> H <sub>6</sub> -pet. ether	C <sub>10</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>3</sub> S	43.40	4.73	43.73	4.95
4-ClC <sub>6</sub> H <sub>4</sub>	C <sub>2</sub> H <sub>5</sub>	73	144-146	Dil. ethanol	C <sub>9</sub> H <sub>11</sub> ClN <sub>2</sub> O <sub>3</sub> S	41.16	4.22	41.17	4.25
4-ClC <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	47	127-129	Dil. ethanol	C <sub>10</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>3</sub> S	43.40	4.73	43.48	4.84
4-ClC <sub>6</sub> H <sub>4</sub>	<i>iso</i> -C <sub>3</sub> H <sub>7</sub>	31	155-156	Dil. ethanol	C <sub>10</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>3</sub> S	43.40	4.73	43.56	4.63
4-ClC <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> <sup>e</sup>	54	115-117	Dil. ethanol	C <sub>11</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>3</sub> S	45.42	5.20	45.70	5.23
4-ClC <sub>6</sub> H <sub>4</sub>	3-CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>3</sub>	41	103-105	Dil. ethanol	C <sub>11</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>4</sub> S	43.06	4.93	43.16	5.08
4-ClC <sub>6</sub> H <sub>4</sub>	3-CH <sub>3</sub> S(CH <sub>2</sub> ) <sub>3</sub>	44	135-137	Dil. ethanol	C <sub>11</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>3</sub> S <sub>2</sub>	40.88	4.66	40.84	4.81
2,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	82	171-173	Dil. ethanol	C <sub>11</sub> H <sub>14</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>3</sub> S	40.62	4.34	40.84	3.99
2,5-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	48	201-203	C <sub>6</sub> H <sub>6</sub> -pet. ether	C <sub>10</sub> H <sub>12</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>3</sub> S	38.60	3.89	38.66	3.91
2,5-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	73	194-195	C <sub>6</sub> H <sub>6</sub>	C <sub>11</sub> H <sub>14</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>3</sub> S	40.62	4.34	40.76	4.46
3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	62	144-146	Dil. ethanol	C <sub>10</sub> H <sub>12</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>3</sub> S	38.60	3.89	38.78	3.86
3-Cl-4-CH <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	41	132-133	Dil. ethanol	C <sub>11</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>3</sub> S	45.42	5.20	45.15	5.46
3-Cl-4-CH <sub>3</sub> C <sub>6</sub> H <sub>3</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	41	146-148	Dil. ethanol C <sub>6</sub> H <sub>6</sub> -pet. ether NaHCO <sub>3</sub> rept.	C <sub>12</sub> H <sub>17</sub> ClN <sub>2</sub> O <sub>3</sub> S	47.26	5.62	47.60	5.53
4-Cl-3-CH <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	44	142-144	Dil. ethanol C <sub>6</sub> H <sub>6</sub> -pet. ether	C <sub>11</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>3</sub> S	45.42	5.20	46.04	5.32
4-Cl-3-CH <sub>3</sub> C <sub>6</sub> H <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	30	153-155	Dil. ethanol	C <sub>10</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>3</sub> S	43.40	4.73	43.21	4.71
4-FC <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	43	131-133	Dil. ethanol	C <sub>10</sub> H <sub>13</sub> FN <sub>2</sub> O <sub>3</sub> S	46.11	5.03	46.02	4.98
4-FC <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	52	103-104	Dil. ethanol	C <sub>11</sub> H <sub>15</sub> FN <sub>2</sub> O <sub>3</sub> S	48.16	5.52	48.41	5.75

<sup>a</sup> The petroleum ether used was the fraction boiling at 60-71°. <sup>b</sup> Since prepared in this study, this compound has been reported in Accepted German Patent Specification F 18339 IVb/12o (Dec. 27, 1956). <sup>c</sup> The required amine has been reported by W. Schneider, *Ann.*, **375**, 245 (1910). In this present work it was prepared by lithium aluminum hydride reduction of 3-methylmercaptpropionitrile [C. D. Hurd and L. L. Gershbein, *J. Am. Chem. Soc.*, **69**, 2328 (1947)] by the method of L. H. Amundsen and L. S. Nelson, *J. Am. Chem. Soc.*, **73**, 242 (1951). <sup>d</sup> Since prepared in this present investigation, this compound has been described in Accepted German Patent Specification F 18136 IVb/12o (Sept. 27, 1956). <sup>e</sup> This compound has since been reported independently in Accepted German Patent Specification F 18659 IVb/12o (Dec. 27, 1956).

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### Steroid Epoxides

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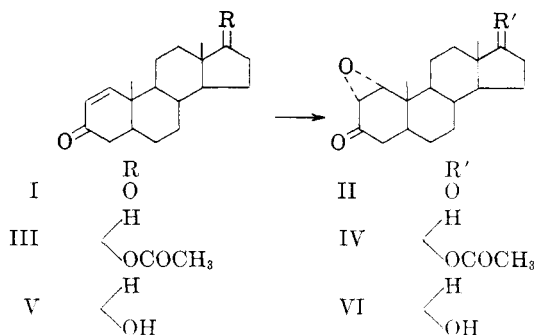
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1 $\alpha$ , 2 $\alpha$ -Epoxyandrostane-3,17-dione (II),<sup>1</sup> a compound useful in the determination of the structure of ruscogenin,<sup>2</sup> was prepared from 1-androstene-3,-

(1) Cf. P. Striebel and C. Tamm, *Helv. Chim. Acta*, **37**, 1094 (1954) for discussion of the configuration of 1,2-epoxides.

(2) W. R. Benn, F. Colton, and R. Pappo, *J. Am. Chem. Soc.*, **79**, 3920 (1957). For other references concerning the structure of ruscogenin see A. L. Nussbaum, F. E. Carlon, D. Gould, E. P. Oliveto, E. B. Hershberg, M. L. Gilmore, and W. Charney, *J. Am. Chem. Soc.*, **79**, 4814 (1957); D. Burn, B. Ellis, and V. Petrow, *Proc. Chem. Soc.*, 119 (1959); H. Lapin and C. Sannie, *Bull. soc. chim.*, 1552 (1955).

17-dione (I)<sup>3</sup> by using alkaline hydrogen peroxide.<sup>4</sup> The same procedure was used in attempt to obtain the corresponding epoxide from 17 $\beta$ -acetoxy-1-androsten-3-one(III), but without success. Further attempts to obtain the epoxide of III were made using perbenzoic acid in chloroform solution and with peracetic acid in benzene. Modification<sup>5</sup> of the method used for the epoxidation of I yielded the



(3) A. Butenandt and H. Dannenberg, *Ber.*, **69**, 1158 (1936).

(4) P. L. Julian, W. Cole, E. W. Meyer, and B. M. Regan, *J. Am. Chem. Soc.*, **77**, 4601 (1955).

(5) The author gratefully acknowledges a suggestion by R. Pappo of our laboratories for this modification.

desired compound. This modified procedure required a relatively short reaction time for the formation of the epoxide, and the alkali concentration was less than that used for the preparation of compound II. 17 $\beta$ -Hydroxy-1 $\alpha$ ,2 $\alpha$ -epoxyandrostan-3-one was obtained by this modified procedure or by the alkaline hydrolysis of the corresponding acetoxy derivative (IV).

The infrared absorption for the epoxide group was at 11.44 and 12.48 for the epoxide II, 11.42 and 12.52 for the epoxide IV, and 11.38 and 12.52 for the 17 $\beta$ -hydroxy-1 $\alpha$ ,2 $\alpha$ -epoxyandrostan-3-one (VI). The ultraviolet spectra of the epoxides exhibited end absorption and at high concentrations the C<sub>3</sub>-ketone group could be demonstrated.

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

*1 $\alpha$ ,2 $\alpha$ -Epoxyandrostan-3,17-dione* (II). To a stirred solution of 1-androstene-3,17-dione (3 g.) in methanol (200 ml.) were added simultaneously and dropwise 4*N* sodium hydroxide (16.2 ml.) and 30% hydrogen peroxide (16.2 ml.). The mixture was maintained at 20° during the addition and stored overnight at 5°. The reaction mixture was diluted with water and extracted with benzene. The benzene solution was washed with 1% sodium hydroxide solution and then with water until the washings were neutral. The benzene solution was dried over anhydrous sodium sulfate, filtered, and the solvent removed under reduced pressure. The crystalline residue, still containing a small amount of benzene was dissolved in methylene chloride. On slow evaporation of the solvent, a crystalline solid was obtained. The solid was separated by filtration and washed with a small amount of methylene chloride. The yield was 2 g.; m.p. 246–247°;  $[\alpha]_D^{20} +189^\circ$  (1% in chloroform).

*Anal.* Calcd. for C<sub>19</sub>H<sub>26</sub>O<sub>3</sub>: C, 75.46; H, 8.67. Found: C, 75.61; H, 8.30;  $\lambda_{\text{max}}^{\text{KBr}}$  5.76, 5.90, 11.42 and 12.48  $\mu$ .

*17 $\beta$ -Acetoxy-1 $\alpha$ ,2 $\alpha$ -epoxyandrostan-3-one* (IV). To a stirred solution of III<sup>7</sup> (1.05 g.; m.p. 128–129°) in methyl alcohol (15 ml.) cooled to 10° was added 30% hydrogen peroxide (1 ml.). Then a 10% solution of sodium hydroxide (0.2 ml.) in methyl alcohol (5 ml.) was added. The temperature was kept between 15–20°. A crystalline precipitate was observed within 3 min. and after the reaction had proceeded for 10 min. the solid was separated by filtration and washed with methanol; yield was 300 mg.; m.p. 160–161°.

*Anal.* Calcd. for C<sub>21</sub>H<sub>30</sub>O<sub>4</sub>: C, 72.80; H, 8.73. Found: C, 72.61; H, 9.04;  $\lambda_{\text{max}}^{\text{KBr}}$  5.74; 5.78 (sh), 7.26, 9.56, 9.72, 11.42 and 12.52  $\mu$ .

The mother liquor was allowed to stand at 15–20° for 45 min. and diluted with water. The solid which deposited, was filtered, dried to constant weight (400 mg.) in a vacuum oven, and recrystallized from methanol. The yield from the latter material was 250 mg.; m.p. 157–158°.

*Hydrolysis of 17 $\beta$ -acetoxy 1 $\alpha$ ,2 $\alpha$ -epoxyandrostan-3-one* (IV). To a solution of IV (250 mg.) in ethyl alcohol (10 ml.; 2B) was added 5*N* sodium hydroxide (0.5 ml.) and the solution heated to gentle reflux for 10 min. The reaction mixture became slightly turbid during the treatment. The mixture was cooled, diluted with water (50 ml.) and the aqueous layer decanted from the gummy residue which deposited

on the sides of the flask. The gum was dissolved in methyl alcohol (5 ml.) and diluted with water (15 ml.). The filtered solid was dried to constant weight (220 mg.; m.p. 120–123°). The product was chromatographed over silica (45 g.). Elution was begun with benzene and followed by an ethyl acetate-benzene mixture (5.0-ml. fractions were collected). The first material eluted with 20% ethyl acetate was IV (70 mg.; m.p. 158–159.5°) followed by VI (90 mg.; m.p. 140–165°). Recrystallized from aqueous methyl alcohol gave pure IV (m.p. 160–161°); VI (m.p. 156–158°).

*Anal.* (VI) Calcd. for C<sub>19</sub>H<sub>26</sub>O<sub>3</sub>: C, 74.96; H, 9.27. Found: C, 75.09; H, 9.46;  $\lambda_{\text{max}}^{\text{KBr}}$  2.87, 5.82, 9.43, 9.6, 10.78, 11.38, 12.51  $\mu$ .

*17 $\beta$ -Hydroxy-1 $\alpha$ ,2 $\alpha$ -epoxyandrostan-3-one* (VI). To a stirred solution of V<sup>7b</sup> (0.9 g.; m.p. 152–153°) in methyl alcohol cooled to 10° was added 30% hydrogen peroxide (1 ml.). Then a 10% solution of sodium hydroxide in methyl alcohol (0.2 ml.) was added. The temperature was kept between 14–18°. After 10 min., the reaction mixture was diluted with water (45 ml.) and the solid that crystallized from the solution was separated by filtration and dried. The product (m.p. 157–158°) weighed about 700 mg. and was crystallized to constant m.p. from 90% methyl alcohol (m.p. 161–162°). This product showed no absorption in the 220–300  $\mu$  region.

*Anal.* Calcd. for C<sub>19</sub>H<sub>26</sub>O<sub>3</sub>: C, 74.96; H, 9.27. Found: C, 74.95; H, 9.17;  $\lambda_{\text{max}}^{\text{KBr}}$  2.86, 5.83, 9.44, 9.51, 10.78, 11.38 and 12.52  $\mu$ .

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### Isomeric 2-Phenoxypropylcarboxylic Acids<sup>1</sup>

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Recently, a series of 2-aryloxypropylcarboxylic acids was prepared by hydrolysis of the ethyl esters, initially formed through reaction of ethyl diazoacetate with a suitable arylvinyl ether.<sup>2</sup> In all cases only one acid was reported. The present communication describes the two theoretically possible diastereomeric 2-phenoxypropylcarboxylic acids, as well as infrared spectra of the isomeric acids.

Although we employed the same reactants as Julia and Tchernoff,<sup>2</sup> our experimental procedure (similar to that of Burger and Yost<sup>3</sup>) differed from that of the French workers in several respects: reaction period, absence of copper catalyst, method for isolation of the ester, hydrolysis medium, and purification procedure. No attempt was made to obtain the pure diastereomeric ethyl esters, which were hydrolyzed in ethanolic sodium hydroxide.

(1) Abstracted from a portion of a thesis submitted by Loren L. Braun in partial fulfillment of the requirements for the Ph.D. degree, University of Nebraska, 1956.

(2) M. Julia and C. Tchernoff, *Bull. soc. chim. France*, 181 (1956).

(3) A. Burger and W. L. Yost, *J. Am. Chem. Soc.*, **70**, 2198 (1948).

(6) The author expresses his appreciation to Dr. R. T. Dillon and his staff on the analytical department of the G. D. Searle and Co. for the analytical data presented in this paper. The melting point determinations were observed on a Fischer-Johns block.

(7) (a) A. Butenandt and H. Dannenberg [*Ber.*, **71**, 1681 (1938)] describe this compound with a melting point 117–118°. (b) *Ber.*, **73**, 206 (1940).