5-ethynyl-5-hydroxycyclopentaneethanol (VIa. R = HC≡C, R′ = H), m.p. 90–93°. Recrystallizations of VIa (R = HC ≡ C, R′ = H) from ether–pentane gave colorless plates, m.p. 97.5–99.5°.

Anal. Calcd. for $C_{16}H_{20}O_3$: C, 73.82; H, 7.75. Found: C, 74.03; H, 7.87.

***trans-anti*-2-(6-Methoxy-2-naphthyl)-5-hydroxy-5-methylcyclopentane-α,α-dimethylethanol (VIc. R = R′ = CH_3).**—To 10 ml. of 3 *M* methylmagnesium bromide in ether stirred and heated under reflux, was added a solution of methyl *trans-anti*-2-(6-methoxy-2-naphthyl)-5-hydroxy-5-methylcyclopentaneacetate, prepared from 0.31 g. (0.000985 mole) of the corresponding acid IVc (R = CH_3), in 35 ml. of anhydrous ether. After the addition was complete, an additional 25 ml. of ether was added. The reaction mixture was stirred and heated under reflux for 3 hr. Then it was decomposed with the successive addition of water and 1.7 *N* hydrochloric acid. The ether phase was separated and washed successively with water, a 5% solution of sodium bicarbonate, water again, and a saturated solution of sodium chloride. After drying over anhydrous sodium sulfate, the ether solution was concentrated to a small volume under reduced pressure. During the concentration, crystallization of the product began. The residue was cooled to 0–5°, and the diol was collected, m.p. 166–170°; yield 0.22 g. (68%). The analytical sample of the *trans-anti*-trimethyldiol VIc (R = R′ = CH_3) was obtained as colorless laths after two more crystallizations from ether, m.p. 170–171°.

Anal. Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 77.32; H, 8.48.

***trans-syn*-2-(6-Methoxy-2-naphthyl)-5-hydroxy-5-methylcyclopentane-α,α-dimethylethanol (Vc. R = R′ = CH_3).**—To a solution of 35 ml. of 1 *M* methylmagnesium bromide in ether, stirred and heated under reflux, was added over a period of 5 min. a solution of 0.14 g. (0.000472 mole) of the *trans-syn*-lactone IIIc (R = CH_3) in 50 ml. of anhydrous ether. After the addition was complete, an additional 25 ml. of ether was added. The reaction mixture was stirred and heated under reflux for 5 hr. Then it was decomposed with the successive addition of water and 1.7 *N* hydrochloric acid. The ether phase was separated and extracted successively with water, a 5% solution of sodium hydroxide, water again, and a saturated solution of sodium chloride. After drying over anhydrous sodium sulfate, the ether solution was distilled to dryness under reduced pressure to yield a semisolid product. Crystallization of the semisolid from ether–pentane gave 0.13 g. (84%) of the *trans-syn*-trimethyldiol Vc (R = R′ = CH_3), m.p. 167–172°. The diol was further crystallized from acetone–pentane to afford colorless rhombs, m.p. 169–171°. Admixed with the *trans-anti*-trimethyldiol VIc (R = R′ = CH_3), it melted at 152–163°. Their infrared spectra were very dissimilar.

Anal. Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.55; H, 8.49.

Reaction of Methyl *trans*-2-(6-Methoxy-2-naphthyl)-5-oxocyclopentaneacetate (IIc, Methyl Ester) with Methylmagnesium Bromide.—To a solution of 70 ml. of 1 *M* methylmagnesium bromide in ether was added over a period of 15 min. a solution of 0.80 g. (0.00268 mole) of the keto ester IIc (methyl ester) in 100 ml. of anhydrous ether. After the addition was complete, an additional 100 ml. of ether was added. The reaction mixture was stirred and heated under reflux for 5 hr. Then it was decomposed with the successive addition of water and 1.7 *N* hydrochloric acid. The ether phase was separated and extracted successively with water, a 5% solution of sodium bicarbonate, water again, and a saturated solution of sodium chloride. The ether solution was dried over anhydrous sodium sulfate and then distilled to dryness under reduced pressure. The semisolid residue was crystallized from acetone–pentane to afford a total of 0.45 g. (51%) of *trans-syn*-2-(6-methoxy-2-naphthyl)-5-hydroxy-5-methylcyclopentaneethanol (Vc. R = R′ = CH_3) melting in the range of 165–167° to 168–170.5°. All fractions melting in this range had identical infrared spectra. The sample melting at 168–170.5° showed no depression in melting point when admixed with an authentic sample of the *trans-syn*-trimethyldiol Vc (R = R′ = CH_3). Their infrared spectra, determined in potassium bromide, were identical.

The presence of the epimeric *trans-anti*-trimethyldiol VIc (R = R′ = CH_3) in the reaction mixture could not be established.

Studies in the Total Synthesis of Steroids and Their Analogs. IV. Nonsteroid Mineralcorticoid Antagonists

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The syntheses of two substances, which are not related to the steroidal spirolactones, yet which are capable of blocking the effects of cortexone acetate in adrenalectomized rats, are described.

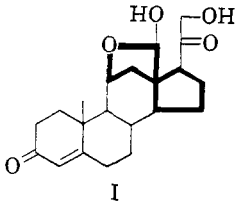
The isolation of aldosterone (I)[1] and the elucidation of its structure[2] have given rise to the hope that an approach based upon the competitive inhibition of this potent mineralcorticoid can be found to alleviate the edematous state of patients suffering from congestive heart failure, nephrosis, or cirrhosis of the liver. As a result of an intensive screening program, steroidal 17-spirolactones II were found to block the sodium-retaining effects of the mineralcorticoids.[3]

These spirolactones bear a superficial resemblance to aldosterone in that in both I and II a

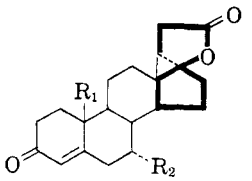
(1) S. A. Simpson, J. F. Tait, A. Wettstein, R. Neher, J. von Euw, and T. Reichstein, *Experientia*, **9**, 333 (1953); S. A. Simpson, J. F. Tait, A. Wettstein, R. Neher, J. von Euw, O. Schindler, and T. Reichstein, *Helv. Chim. Acta*, **37**, 1163 (1954).

(2) S. A. Simpson, J. F. Tait, A. Wettstein, R. Neher, J. von Euw, O. Schindler, and T. Reichstein, *Experientia*, **10**, 132 (1954); *Helv. Chim. Acta*, **37**, 1200 (1954).

(3) (a) J. A. Cella and C. M. Kagawa, *J. Am. Chem. Soc.*, **79**, 4808 (1957); (b) C. M. Kagawa, J. A. Cella, and C. G. Van Arman, *Science*, **126**, 1015 (1957); (c) G. W. Liddle, *ibid.*, **126**, 1016 (1957); (d) C. M. Kagawa. F. M. Sturtevant, and C. G. Van Arman, *J. Pharmacol. and Exp. Therap.*, **126**, 123 (1959); (e) J. A. Cella, *Edema Mechanisms and Management*, J. H. Moyer and M. Fuchs, ed., W. B. Saunders Co., Philadelphia, 1960, p. 303; (f) C. M. Kagawa, *ibid.*, p. 309.



I

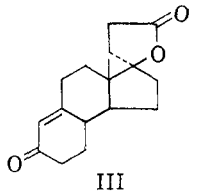


IIa. $R_1 = CH_3$, $R_2 = H$
b. $R_1 = R_2 = H$
c. $R_1 = CH_3$, $R_2 = CH_3\overset{O}{\overset{\|}{C}}S$

tetrahydrofuran ring is joined to ring D with a carbon atom common to both rings.

In his investigation of antimetabolites, Woolley emphasizes the importance of structural similarity between the metabolites and their antagonists.[4] Because of the presence of the oxaspirane system in both I and II, the hypothesis that the spirolactones, which *per se* have no effect on the excretion of the electrolytes, compete reversibly with aldosterone on the receptor sites[3d] is an appealing one, albeit as yet unproven.[5]

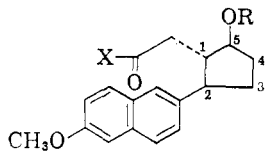
Previously we reported[6] an attempt to assess the extent to which the tetracyclic ring system of the steroid contributes to the biological activities of *inter alia* the spirolactones. We reported that the des-A analog III retains to some degree the capacity to overcome the mineralcortcoids' effect on the electrolytes.



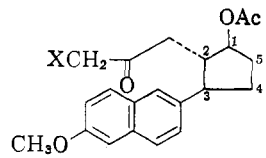
III

As a result of this interesting lead, further modifications of the structures of the steroidal spirolactones were undertaken. This has led to the synthesis of *trans-anti*-2-(2-oxo-3-hydroxypropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol (VIa)[7] and *trans-anti*-2-(2-oxo-3-fluoropropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol (VIc),[7] which are neither steroids nor do they have the spirolactone system incorporated in their structures, yet they have been found to block the activities of cortexone acetate in adrenalectomized rats.[8]

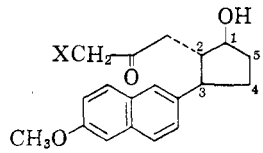
Our syntheses of VIa and VIc proceed from *trans-anti* - 2 - (6 - methoxy - 2 - naphthyl) - 5 - hydroxycyclopentaneacetic acid (IVa).[9] Acetylation of IVa gives IVb, which is converted to the acid chloride IVc by the method of Adams and Ulich.[10]



IV
a. R = H, X = OH
b. R = Ac, X = OH
c. R = Ac, X = Cl



V
a. X = N_2
b. X = OAc
c. X = Cl
d. X = I
e. X = F
f. X = H



VI
a. X = OH
b. X = Cl
c. X = F
d. X = H

Treatment of IVc with diazomethane affords the diazomethyl ketone Va. When Va is heated with acetic acid, *trans-anti*-2-(2-oxo-3-acetoxypropyl)-3-(6 - methoxy - 2 - naphthyl)cyclopentanol 1 - acetate (Vb) is obtained; with hydrochloric acid *trans - anti* - 2 - (2 - oxo - 3 - chloropropyl) - 3-(6-methoxy - 2 - naphthyl)cyclopentanol 1 - acetate (Vc) is the product.

To obtain the fluoromethyl ketone Ve, the chloro group of Vc is replaced first by an iodo and then by a fluoro group with the successive application of sodium iodide and silver fluoride.[11]

In the presence of hydriodic acid (generated *in situ*), the iodomethyl ketone Vd is dehalogenated, and *trans-anti*-2-(2-oxopropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol 1-acetate (Vf) is obtained.

Hydrolysis of the acetate group is accomplished in dilute hydrochloric acid to give VIa and VIc, as well as VIb and VId, from the corresponding acetates.

The hydroxymethyl ketone VIa is effective, both when administered orally and subcutaneously, in off-setting the sodium-retaining effects of cortexone acetate in adrenalectomized rats The subcutaneous medium effective dose (M.E.D.)[12] was established as between 0.36 mg. and 1.0 mg. and the oral M.E.D. value as between 3.0 and 7.8 mg.

(4) D. W. Woodley, "A Study of Antimetabolites," J. Wiley & Sons, Inc., New York, 1952, p. 227.

(5) G. D'Amico and A. Cesana, *Experientia*, **17**, 112 (1961).

(6) L. J. Chinn, H. L. Dryden, Jr., and R. R. Burtner, *J. Org. Chem.*, **26**, 3910 (1961).

(7) The configuration is assigned on the basis of the relative spatial orientation of the methoxynaphthyl group at C-3, the propanone group at C-2 and the hydroxy group at C-1 in that order.

(8) 2,4,7-Triamino-6-phenylpteridine, a non-steroidal substance, has recently been reported to antagonize markedly the effects of aldosterone in man as well as in the rat and the dog; *cf.*, V. D. Wiebelhaus, J. Weinstock, F. T. Brennan, G. Sosnowski, and T. J. Larsen, Abstracts of Federation Proceedings, 45th Annual Meeting, Atlantic City, N. J., April, 1961 (Vol. 20, Part I, p. 409) and J. H. Laragh, E. B. Reilly, T. B. Stites, and M. Angers, *ibid.*, p. 410.

(9) L. J. Chinn, E. A. Brown, R. A. Mikulec, and R. B. Garland, *J. Org. Chem.*, **27**, 1733 (1962).

(10) R. Adams and L. H. Ulich, *J. Am. Chem. Soc.*, **42**, 599 (1920).

(11) C. G. Bergstrom, P. B. Sollman, R. T. Nicholson, and R. M. Dodson, *J. Am. Chem. Soc.*, **82**, 2322 (1960).

(12) The M.E.D. value is defined as the "medium effective dose (total mg./rat) which when used with 12 mg. of desoxycorticosterone acetate in adrenalectomized rats produces the same urinary sodium-potassium ratio as that which results from the use of 6 mg. of DOCA alone." E. A. Brown, R. D. Muir, and J. A. Cella, *J. Org. Chem.*, **25**, 96 (1960).

TABLE I

	M.E.D.	
	Subcutaneous	Oral
trans-anti-2-(2-Oxo-3-hydroxypropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol (VIa)	0.36–1.0	3.0–7.8
trans-anti-2-(Oxo-3-chloropropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol (VIb)	>2.4	...
trans-anti-2-(2-Oxo-3-fluoropropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol (VIc)	1.2	>4.8
trans-anti-2-(2-Oxopropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol (VId)	>2.4	...
3-(3-Oxo-17β-hydroxy-4-androsten-17α-yl)propionic acid γ-lactone (IIa)	0.26[a]	19.2[a]
3-(3-Oxo-17β-hydroxy-19-nor-4-androsten-17α-yl)propionic acid γ-lactone (IIb)	0.07[a]	2.2[a]
3-(3-Oxo-17β-hydroxy-7α-acetylthio-4-androsten-17-yl)propionic acid γ-lactone (IIc)	0.26[b]	0.38[b]

[a] Ref. 12. [b] Ref. 3e.

The fluoromethyl ketone VIc shows blocking activities only when given subcutaneously. Its (subcutaneous) M.E.D. value was determined as 1.2 mg.

Replacing the primary hydroxyl group of VIa either with a chloro group or with hydrogen diminishes the antimineralcorticoid effects.[13] The M.E.D. values of these compounds are tabulated. For comparison the values of several steroidal spirolactones, 3-(3-oxo-17β-hydroxy-4-androsten-17α-yl)propionic acid γ-lactone (IIa), 3-(3-oxo-17β-hydroxy-19-nor-4-androsten-17α-yl)propionic acid γ-lactone (IIb), and 3-(3-oxo-17β-hydroxy-7α-acetylthio-4-androsten-17α-yl)-propionic acid γ-lactone (IIc), are included in the Table I.

Experimental[14]

trans-anti-2-(**6-Methoxy-2-naphthyl**)-**5-acetoxycyclopentaneacetic Acid** (**IVb**).—A solution of 15.0 g. (0.05 mole) of *trans-anti*-2-(6-methoxy-2-naphthyl)-5-hydroxycyclopentaneacetic acid (IVa),[9] 150 ml. of pyridine, and 167 ml. (1.77 moles) of acetic anhydride was allowed to stand at room temperature for 17 hr. Then it was carefully diluted with water until turbidity developed. The reaction mixture was warmed on the steam bath, whereupon it became clear. An additional quantity of water was carefully added to the hot reaction mixture until incipient turbidity.[15] The reaction mixture was allowed to stand at room temperature for 1 hr. during which time the product began to crystallize. After the reaction mixture was diluted with a large volume of water, it was cooled to 5°. The colorless solid was collected, washed well with water, and dried; yield 15.2 g. (89%), m.p. 149–151°.

The analytical sample was obtained as colorless laths from a mixture of acetone, benzene, and hexane, m.p. 153–154°; λ_{max}^{KBr} 3.13, 5.75, 5.85, 6.11, 6.22, 8.08 μ.

Anal. Calcd. for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.04; H, 6.41.

trans-anti-2-(**6-Methoxy-2-naphthyl**)-**5-acetoxycyclopentaneacetyl Chloride** (**IVc**).—A mixture of 0.330 g. (0.000964 mole) of IVb and 1.0 ml. (0.01488 mole) of oxalyl chloride[10] was warmed on the steam bath for 2 min. and then allowed to stand at room temperature for 2 hr. The orange-red solution was evaporated to dryness under reduced pressure to yield a yellow crystalline product, m.p. 104.5–114.5°; λ_{max}^{KBr} 5.51, 5.75, 6.10, 6.21, 8.00 μ. Crystallization from anhydrous benzene–hexane gave the acid chloride as nearly colorless plates, m.p. 111.5–115°.

trans-anti-2-(**2-Oxo-3-diazopropyl**)-**3-(6-methoxy-2-naphthyl)cyclopentanol 1-Acetate** (**Va**).—The crude acid chloride IVc prepared from 4.2 g. (0.0123 mole) of the acetoxy acid IVb was dissolved in 20 ml. of anhydrous benzene. The solution was cooled in an ice bath, and then it was carefully added to an ethereal solution of diazomethane cooled to 5°. The diazomethane solution was prepared from 18 g. of *N*-nitrosomethylurea (0.175 mole), 36 g. of potassium hydroxide, and 36 ml. of water in 180 ml. of ether.[16] The reaction mixture was allowed to stand at 5° for 2 hr. after which it was filtered. The filtrate was evaporated to dryness under reduced pressure to yield a viscous oil. On standing at 5° the oil solidified. A sample of the yellow crystalline product was washed with ether–pentane, m.p. 93–98°, presoftening at 90° and melting with evolution of gas; λ_{max}^{KBr} 4.68, 5.73, 6.05, 6.18, 7.95, 8.05 μ.

trans-anti-2-(**2-Oxo-3-acetoxypropyl**)-**3-(6-methoxy-2-naphthyl)cyclopentanol 1-Acetate** (**Vb**).—The crude diazomethyl ketone Va prepared from 4.2 g. (0.0123 mole) of the acetoxy acid IVb as described above was dissolved in 120 ml. of glacial acetic acid, and the solution was quickly brought to reflux. After 5 min. of heating under reflux the reaction mixture was distilled nearly to dryness under reduced pressure. The residue was diluted with a large volume of water. On cooling to 5°, the resulting oil solidified. The solid was collected, washed well with water, and dried. It was chromatographed on 300 g. of silica gel, and the column was eluted with varying proportions of benzene–ethyl acetate. Elution with 5% ethyl acetate in benzene gave a total of 3.26 g. (67% from IVb) of Vb melting from 93–97.5° to 104–112°. A sample melting at 109.5–111.5° was obtained as colorless platelets from ether. The analysis, however, was performed on a sample obtained as colorless nondescript crystals from ether–pentane, m.p. 94.5–98.5°, clearing 104.5°; λ_{max}^{KBr} *ca.* 5.73, 6.10, 6.20, *ca.* 7.9, *ca.* 8.02 μ.

Anal. Calcd. for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 68.95; H, 6.61.

The crude acetoxymethyl ketone Vb obtained after chromatography was satisfactory for subsequent use.

trans-anti-2-(**2-Oxo-3-chloropropyl**)-**3-(6-methoxy-2-naphthyl)cyclopentanol 1-Acetate** (**Vc**).—The crude diazomethyl ketone Va prepared as described above from 5.0 g. (0.0146 mole) of the acetoxy acid IVb and the proportionate amounts of oxalyl chloride and *N*-nitrosomethylurea was dissolved in 30 ml. of purified dioxane. To this solution was added 10 ml. of 12 *N* hydrochloric acid. The reaction mixture was warmed on the steam bath for 1 min., and then it was diluted with a large volume of water. On cooling to 5°, the resulting oil solidified. The solid was collected washed well with water, and dried; yield 2.8 g. (52% from IVb), m.p. 98–100°. Extraction of the filtrate with ether gave an additional 2 g. (37%) of oil, which solidified on standing. The chloromethyl ketone was difficult to purify. The analytical sample was obtained as colorless, nondescript crystals from ether–pentane, m.p. 96–104.5°; λ_{max}^{KBr} 5.75, 5.78, 6.12, 6.22, *ca.* 8.0 μ.

(13) We are indebted to Drs. V. A. Drill, C. M. Kagawa, Mr. R. S. Jacobs, and their associates for determining the biological activities.

(14) Melting points were taken on a Fisher-Johns melting block. Compounds possessing centers of asymmetry are racemic.

(15) In a previous run it was found that the crude acetylated mixture showed a band at 5.47 μ in its infrared spectrum (determined in potassium bromide) which indicated the presence of an anhydride. By so treating the reaction mixture, the anhydride was selectively hydrolyzed.

(16) W. E. Bachmann and W. S. Struve, *Org. Reactions*, **1**, 50 (1942).

Anal. Calcd. for $C_{21}H_{23}ClO_4$: Cl, 9.46. Found: Cl, 9.25.

trans-anti-**2-(2-Oxo-3-fluoropropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol 1-acetate (Vc).**[11]—A mixture of 1.5 g. (0.004 mole) of the chloromethyl ketone Vc, 7.8 g. (0.052 mole) of sodium iodide, and 150 ml. of acetone was heated under reflux for 1.25 hr. and then distilled nearly to dryness under reduced pressure. The residue was extracted with a mixture of ethyl acetate and water. The ethyl acetate phase was separated, washed in succession with water and a saturated solution of sodium chloride, dried over anhydrous sodium sulfate, and distilled to dryness under reduced pressure. The residual, viscous, reddish brown oil was dissolved in 150 ml. of acetonitrile (freshly distilled after drying over calcium chloride) and treated with 9 g. of a commercial grade of silver fluoride.[17] After the reaction mixture was heated under reflux for 16 hr. the insoluble material was removed by filtration, and the filtrate was concentrated to a small volume by distillation under reduced pressure. The residue was dissolved in ethyl acetate, and the ethyl acetate solution was washed with water, dried over anhydrous sodium sulfate, and distilled to dryness under reduced pressure. The dark brown, viscous oil which remained was chromatographed on 60 g. of silica gel. The column was eluted with varying proportions of benzene–ethyl acetate. Elution with 10% ethyl acetate in benzene gave 0.38 g. (22% from Vc) of Ve, m.p. 108.5–113.5°. It gave a positive fluorine test. The analytical sample was obtained from ether–pentane as colorless, densely packed platelets, m.p. 109.5–113°; λ_{max}^{KBr} *ca.* 5.73 (shoulder), 5.76, 6.11, 6.21, 7.87 μ.

Anal. Calcd. for $C_{21}H_{23}FO_4$: C, 70.37; H, 6.46. Found: C, 70.16; H, 6.34.

trans-anti-**2-(2-Oxopropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol 1-Acetate (Vf).**—A mixture of 1.0 g. (0.00267 mole) of chloromethyl ketone Vc, 4 g. (0.0267 mole) of sodium iodide and 75 ml. of acetone was heated under reflux for 1.5 hr. and then distilled nearly to dryness under reduced pressure. After the residue was treated with 15 ml. of glacial acetic acid and stirred at room temperature for 1 hr., the reaction mixture was poured into 500 ml. of water containing 30 g. of sodium bicarbonate and 6 g. of sodium thiosulfate pentahydrate. The mixture was extracted with chloroform. The chloroform extracts were washed successively with a dilute solution of sodium thiosulfate and water, dried over anhydrous sodium sulfate, and distilled to dryness under reduced pressure to yield 0.91 g. (100% from Vc) of a pale yellow semisolid. The semisolid was crystallized three times from ether–pentane to yield 0.19 g (21%) of Vf as colorless dense crystals, m.p. 96.5–99.5°; λ_{max}^{KBr} 5.77, 6.10, 6.21, 7.93 μ. It gave a negative Beilstein test.

Anal. Calcd. for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.35; H, 7.00.

From the combined mother liquors an additional 0.51 g. (56%) of Vf, m.p. 89.5–98.5°, was obtained.

Hydrolysis of Acetates. A. Preparation of *trans-anti*-**2-(2-Oxo-3-hydroxypropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol (VIa).**—A mixture of 1.25 g. (0.00313 mole) of Vb, 60 ml. of 95% ethanol, 60 ml. of water, and 6 ml. of 12 *N* hydrochloric acid was heated under reflux for 2.25 hr. in an atmosphere of nitrogen. After 6 ml. of pyridine was added to the reaction mixture, it was distilled under reduced pressure to remove the alcohol. The residue was diluted with water, saturated with sodium chloride, and cooled to 5°. The colorless crystalline product VIa was collected, washed well with water, and dried, m.p. 126–129°, yield 0.90 g. (91%). The analytical sample was obtained as colorless plates, m.p. 130–131°, after several crystallizations from acetone–ether; λ_{max}^{KBr} 2.83, 2.98, 5.83, 6.21, 6.22 μ.

Anal. Calcd. for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.45; H, 6.93.

A 0.100-g. sample of VIa was reacetylated with acetic anhydride and pyridine in the usual manner to yield after crystallization from ether–pentane 0.117 g. (92%) of the diacetate Vb, m.p. 95.5–98.5°. The identity of the product was established through mixed melting point and a comparison of its infrared spectrum (determined in potassium bromide) with that of an authentic sample. Hence, no rearrangement occurred during the hydrolysis of Vb.

B. Preparation of *trans-anti*-**2-(3-Oxo-3-chloropropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol (VIb).**—A 0.221-g. sample (0.00059 mole) of Vc was hydrolyzed in a solution of 13 ml. of 95% ethanol, 13 ml. of water, and 1.3 ml. of 12 *N* hydrochloric acid as described in A. After 1.5 ml. of pyridine was added, the reaction mixture was worked up as before. The product proved to be an oil. It was extracted with ethyl acetate. The ethyl acetate extracts were washed with a saturated solution of sodium chloride, dried over anhydrous sodium sulfate, and evaporated to dryness. The residual oil was chromatographed on 10 g. of silica gel, and the column was eluted with varying proportions of benzene–ethyl acetate. Elution with 10% ethyl acetate in benzene gave a colorless crystalline product, which was crystallized several times from ether–pentane to afford 0.065 g. (33%) of VIb as colorless platelets, m.p. 84–87°; λ_{max}^{KBr} 2.86, 2.97, 5.75, 5.81, 6.12, 6.24 μ.

Anal. Calcd. for $C_{19}H_{21}ClO_3$: C, 68.56; H, 6.36. Found: C, 68.28; H, 6.51.

From the combined mother liquors an additional 0.063 g. (32%) of VIb, m.p. 83.5–86°, was obtained.

C. Preparation of *trans-anti*-**2-(2-Oxo-3-fluoropropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol (VIc).**—A 0.200-g. sample (0.00056 mole) of Ve was hydrolyzed using the quantities of the reagent as described in **B**. The crude solid product worked up as described in A melted at 100.5–104.5°. Two crystallizations from ether–pentane gave VIc as colorless flat needles, yield 0.124 g. (70%), m.p. 106.5–107°; λ_{max}^{KBr} 2.86, 5.78, 6.12, 6.23 μ.

Anal. Calcd. for $C_{19}H_{21}FO_3$: C, 72.13; H, 6.69. Found: C, 72.20; H, 6.50.

From the combined mother liquors an additional 0.028 g. (16%) of VIc, m.p. 99.5–101.5°, was obtained.

D. Preparation of *trans-anti*-**2-(2-Oxopropyl)-3-(6-methoxy-2-naphthyl)cyclopentanol (VId).**—A 0.300-g. sample (0.00088 mole) of Vf was hydrolyzed in a solution of 20 ml. of 95% ethanol, 20 ml. of water, and 2 ml. of 12 *N* hydrochloric acid as described in **A**. After 2 ml. of pyridine was added, the reaction mixture was worked up as previously described to yield 0.215 g. (82%) of VId, m.p. 89–92°. Two crystallizations from ether–pentane gave VId as colorless plates, m.p. 89.5–92.5°; λ_{max}^{KBr} 2.82, 5.85, 6.10, 6.22 μ.

Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.78; H, 7.59.

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