Bridged Polycyclic Compounds. XLIX. Additions of Acetic Acid to Trimethylenenorbornene[1]

STANLEY J. CRISTOL AND GABRIEL C. FUSCO

Department of Chemistry, University of Colorado, Boulder, Colorado 80302

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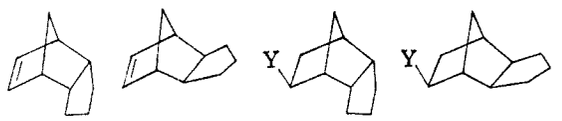
Contrary to earlier reports, addition of acetic acid to *endo*-trimethylenenorbornene (I) gives mixtures substantially richer in *endo*-trimethylene-*exo*-norbornyl acetate (IIIb) and less rich in *exo*-trimethylene-*exo*-norbornyl acetate (IVb) than those obtained in the corresponding additions to *exo*-trimethylenenorbornene (II). It has now been observed that *endo* acetate IIIb rearranges relatively rapidly to a mixture containing 1–2% of IIIb and 98–99% of IVb. Thus addition of acetic acid to I and II resembles that of methanol[2] and several mechanisms or product-determining intermediates are required to rationalize the results.

Several years ago, the additions of acetic acid, formic acid, water, and methanol to *endo*- (I) and *exo*-trimethylenenorbornene (II) to give mixtures of derivatives of *endo*-trimethylene-*exo*-norborneols (III) and *exo*-trimethylene-*exo*-norborneols (IV) were described.[2] In that paper, it was reported that sulfuric acid catalyzed addition of methanol to the *endo* olefin I gave mixtures of IIIa and IVa containing substantially more *endo* IIIa than that from the *exo* isomer II. On the other hand, it was reported that addition of the other addenda (formic acid, acetic acid catalyzed by sulfuric acid, and water catalyzed by sulfuric acid) to I was accompanied by almost complete rearrangement to the *exo* skeletal system IV products. Recent work on additions to norbornadiene[3] and to benzonorbornadiene[4] suggested the possibility that at least some of the products reported earlier were those of thermodynamic rather than those of kinetic control. We now wish to report a reinvestigation and extension of our study of the addition of acetic acid. The present work shows that in fact the products observed earlier were those of thermodynamic control, and that addition of acetic acid, like that of methanol,[2] gives substantially more *endo* IIIb product from I than from II in the first-formed mixture.



I II IIIa, Y = OCH_3 IVa, Y = OCH_3
b, Y = OAc b, Y = OAc
c, Y = OH c, Y = OH

In the previous work,[2] the composition of the mixture of acetate esters was estimated by saponification of the mixture to alcohols, conversion to phenylurethans, and infrared analysis of this mixture. In the present work, we utilized vapor phase chromatographic analysis. When direct analysis of mixtures of IIIb and IVb was attempted, it was observed that the heated inlet of our apparatus converted these substances largely to IVb *via* an internal Wagner–Meerwein rearrangement. The corresponding alcohols IIIc and IVc were stable and resolvable by vpc methods. Accordingly an analytical procedure was developed in which the ester mixture was converted to an alcohol mixture by reduction with lithium aluminum hydride. The resulting mixture of alcohols was then analyzed by quantitative vpc methods.

It has now been found that IIIb rearranges rapidly in acetic acid containing 1.5% sulfuric acid. When the addition to I was carried out for 1 hr at 55°, the product mixture was composed of about 20% of IIIb and 80% of IVb. Treatment for 5 hr gave a mixture containing 15% of IIIb, while treatment for 96 hr gave 3% of IIIb. This latter result is similar to that reported earlier[2] for an addition carried out in refluxing acetic acid. As might be anticipated, both addition and rearrangement occurred more rapidly when more concentrated sulfuric acid was used. Thus addition with 3% sulfuric acid for 10 hr at 55° gave a product mixture containing only 9% of IIIb. When the addition was carried out for 50 hr under these conditions, the mixture was composed of 1.2% of IIIb and 98.8% of IVb.

At the reflux temperature, with 1.5% sulfuric acid, addition for 1 hr gave a mixture containing 1.5% of IIIb, and the composition was similar after 2.2 hr at which time addition had proceeded to about 54%. The *endo* olefin I which was recovered was not perceivably isomerized, as has been noted before.[2]

Several experiments were conducted to show that the above-described experiments reflected rearrangements of first-formed products under acid catalysis. A mixture of 48% of IIIb and 52% of IVb was heated for 12 hr at 55° in the presence of 1.5% sulfuric acid in acetic acid and was converted to a mixture containing 58% of IVb. A similar mixture containg 3% sulfuric acid as catalyst led to mixtures containing 31% of IIIb after 10 hr, 16% of IIIb after 24 hr, and 2–3% of IIIb after 50 hr.

When acetic acid was added to the *exo* olefin II (1.5% sulfuric acid, 55°), product mixtures composed of 1–2% of IIIb and 98–99% of IVb were obtained.

Addition of acetic acid to *endo* olefin I in the absence of mineral acid was carried out at 85° for times varying from 46 to 107 hr. The composition of the mixture of acetates varied from 52% of IIIb at the shorter time to 46% at 107 hr. About 2.6% conversion had occurred in 107 hr. Analogous results were observed at 55 and at 100°.

Results and Discussion

In our earlier paper on additions to norbornenes,[2] we pointed out that at least two different mechanisms or product-determining intermediates were required to

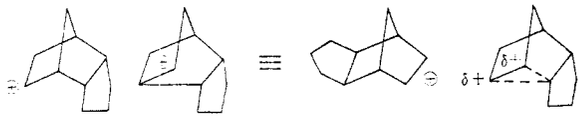
(1) Paper XLVIII: S. J. Cristol and G. W. Nachtigall. *J. Org. Chem.*, **32**, 3738 (1967). The authors are indebted to the National Science Foundation for generous support of this work.

(2) S. J. Cristol, W. K. Seifert, D. W. Johnson, and J. B. Jurale, *J. Am. Chem. Soc.*, **84**, 3918 (1962), and references cited therein.

(3) (a) S. J. Cristol, T. C. Morrill, and R. A. Sanchez, *J. Org. Chem.*, **31**, 2719 (1966); (b) *ibid.*, **31**, 2726 (1966); (c) *ibid.*, **31**, 2733 (1966).

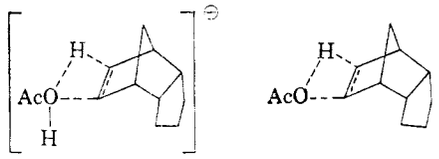
(4) S. J. Cristol and R. Caple, *ibid.*, **31**, 2741 (1966).

account for the results, and, in subsequent papers,[3,5] we were able to rule out certain possibilities and discuss others in more detail. It seemed possible from the initial report[2] regarding the product mixture ratios with methanol and with acetic acid that two of these product-determining intermediates could be the classical ions V and VI, (associated with a gegenion or gegen molecule and related to each other *via* a Wagner–Meerwein rearrangement), or they could be one of these and the nonclassical ion VII, and that the difference between the sets of results reflected the better ability of methanol to capture the initially formed cation produced by protonation of I before it rearranged more or less completely to the other cation or to the equilibrium mixture of cations. The results which we are now reporting, in which as much as 20% of IIIb has been observed in the acid-catalyzed additions and 50% of IIIb in the uncatalyzed additions, make it clear that methanol has no particular ability in this system to intercept a cationic intermediate before rearrangement.



V VI VII

Instead it is clear that additions of methanol and of acetic acid to trimethylenenorbornene are very similar to those to norbornadiene,[2,3] and that the mechanisms are also similar. Unfortunately, however, we are yet unable[3] to distinguish among a variety of mechanisms. These include cyclic processes without cationic intermediates but instead involving transition states such as VIII and IX, and those with cationic species such as V, VI, and VII involved in ion pairs with acetate or other ions, or similar cationic species involved in ion-dipole complexes with acetic acid.[6]



VIII IX

Experimental Section

***exo*-5,6-Trimethylene-2-norbornene** was prepared as described earlier.[10] Analysis by vpc indicated the product consisted of 90.8% *exo* olefin II, 8.2% *endo* olefin I, and 1% dicyclopentadiene.

Preparation of *endo*-5,6-Trimethylene-2-norbornene.—A mixture of 204 g (3.08 moles) of freshly distilled cyclopentadiene and 613 g (9.0 moles) of cyclopentene was placed in a 2-l. stainless steel autoclave and heated at 190–195° for 4 days. The unreacted cyclopentene was removed by distillation and the desired olefin I, 164 g (26%), was distilled at 44° (0.7 mm), $n^{25}D$ 1.5006.

Vapor phase chromatography showed that the product was composed of 93.3% *endo* olefin I, 2.8% *exo* olefin II, and 3.8% dicyclopentadiene.

This mixture was used for all of the work herein described. Repeated analysis during several years showed the same composition of materials.

Preparation of *endo*-5,6-Trimethylene-*exo*-2-norbornyl Alcohol (IIIc).—This alcohol was prepared by oxidative hydroboration as described earlier.[10] An oil was obtained which was crystallized from *n*-pentane with cooling. A yield of 49.1 g (64.5%) (mp 62–64°, lit.[10] mp 81.5–82.5°) was observed. Vapor phase chromatography showed the material to be composed of 92.3% *endo*-skeleton alcohol IIIc and 7.7% *exo*-skeleton alcohol IVc.

Preparation of *endo*-5,6-Trimethylene-2-*exo*-norbornyl Acetate (IIIb).—To 195 ml of reagent grade acetic anhydride was added 5.0 g (0.033 mole) of the IIIc described above and 2.6 g (0.033 mole) of dry pyridine. The resulting solution was allowed to stand at room temperature for 12 hr and was then poured into ice water and extracted with ether. The ethereal solution was washed with 5% sodium bicarbonate solution, 5% hydrochloric acid solution and finally with water until neutral. The ether solution was dried over anhydrous magnesium sulfate, and the solvent was removed by distillation to yield 3.0 g (47%) of IIIb, bp 60° (3.0 mm), $n^{25}D$ 1.4869. The sample showed no hydroxyl absorption in the infrared analysis, but had peaks at 8.07 and 15.6 μ indicative of an acetate.

Hydrolysis of the acetate with ethanolic potassium hydroxide solution, or reduction with lithium aluminum hydride in ether, showed the product to contain 92.3% *endo*-skeleton alcohol IIIc and 7.7% *exo*-skeleton alcohol IVc. The nuclear magnetic resonance spectrum had a broad doublet centering at τ 5.29 (J = 6.4 cps) for the *endo*-2 proton.

Preparation of *exo*-5,6-Trimethylene-*exo*-norbornyl Acetate (IVb).—This acetate was prepared from 5.0 g (0.033 mole) of IVc, 2.6 g (0.033 mole) of pyridine, and 150 ml of acetic anhydride. A liquid weighing 5.6 g (80%) and distilling at 80° (1.5 mm) was obtained, $n^{25}D$ 1.4824. Infrared analysis showed no hydroxyl absorption and showed absorptions at 8.07 and 15.6 μ indicative of an acetate.

Hydrolysis employing alcoholic potassium hydroxide or reduction with lithium aluminum hydride in ether afforded an alcohol mixture which, when analyzed by vpc, was shown to be 95.5% *exo*-skeleton alcohol IVc and 4.5% *endo*-skeleton alcohol IIIc.

The nmr spectrum showed a symmetrical quartet at τ 6.45 (J = 6.0, 2.5 cps) for the *endo*-2 proton.

Preparation of *exo*-5,6-Trimethylene-*exo*-2-norbornyl Alcohol (IVc).—This alcohol was prepared from the corresponding formate as described earlier.[10] A viscous oil was obtained which distilled at 80° (1 mm) and which was crystallized from *n*-pentane to give a product melting at 55°. Analysis by vpc showed this material to contain 94.9% *exo*-skeleton alcohol IVc and 5.1% *endo*-skeleton alcohol IIIc.

Reduction of Mixtures of IIIb and IVb.—The acetates were dissolved in 25 ml of ether and placed in a flask containing a drying tube filled with Drierite. An excess of lithium aluminum hydride was added to the ether solution and the resulting mixture was kept at room temperature for 16 hr.

The excess hydride was destroyed by careful addition of wet ether. The mixture was filtered and dried over anhydrous magnesium sulfate. The solvent was then removed by distillation. The resulting alcohols were analyzed by vpc. Calculated and observed results generally agreed within 0.5%.

Catalytic Addition of Acetic Acid to I.—The additions were conducted at three temperatures (room temperature, 55°, and reflux) and at two concentrations of sulfuric acid (1.5 and 3.0%). The following is a generalized procedure describing the way in which the reactions were performed.

One gram (7.4 mmoles) of *endo* olefin I was dissolved in a 70-ml solution of glacial acetic acid containing 1.5% by weight of 96% sulfuric acid. The solution was placed in a one-neck, 200-ml, round bottom flask fitted with a condenser and equipped with a drying tube filled with anhydrous calcium sulfate. The flask was heated at 55 ± 1°.

From time to time two 5-ml aliquots were removed. The 5-ml aliquots were poured into ice water and extracted with ether. The ether solution was washed with water, 5% sodium bicarbonate solution, and again with water until the aqueous

(5) S. J. Cristol, L. K. Gaston, and D. W. Johnson, *Tetrahedron Letters*, 185 (1963).

(6) It has recently been proposed[7] that the classical ions V and VI are involved in the methanolysis of the *p*-toluenesulfonates of IIIc and IVc. This proposal was based upon the observation that the IIIa–IVa mixture contained more IIIa when the sulfonate ester of IIIc was used than did the mixture resulting from methanolysis of the ester of IVc. Similarly, decomposition of the chlorosulfinate ester of IIIc led to more *endo* ring-skeleton chloride than did the corresponding decomposition of the ester of IVc,[8] and classical ions V and VI were similarly proposed as intermediates. We have noted[9] analogous results in a number of solvolytic reactions.

(7) K. Takeuchi, T. Oshika, and Y. Koga, *Bull. Chem. Soc. Japan*, **38**, 1318 (1965).

(8) D. Cash and P. Wilder, Jr., *Chem. Commun.*, 662 (1966).

(9) G. C. Fusco, Ph.D. Dissertation, University of Colorado, Boulder, Colo., 1965.

(10) S. J. Cristol, W. K. Seifert, and S. B. Soloway, *J. Am. Chem. Soc.*, **82**, 2351 (1960).

wash was neutral. The solution was dried over anhydrous magnesium sulfate and filtered. An excess of lithium aluminum hydride was then added.

The mixture was allowed to stand for 17 hr, the excess hydride was decomposed by ice-wet ether, and the ether suspension was filtered to remove inorganic materials. The ethereal solution was dried over anhydrous magnesium sulfate and filtered, and the ether was recovered by distillation.

The residual oil was dissolved in distilled *n*-pentane and analyzed by vpc.

The data are reported in Tables I–IV.

TABLE I

ADDITION OF ACETIC ACID CATALYZED BY SULFURIC ACID TO *endo* OLEFIN I AT 55°

	Time, hr	H_2SO_4, %	IIIb, %	IVb, %
Run 1		1.5		
	10		15.3	84.7
	12		13.1	86.9
	36		11.0	89.0
	48		8.2	91.8
	96		4.4	95.6
	200		0.0	100.0
Run 2		1.5		
	10		14.9	85.1
	20		11.0	89.0
	33		11.9	88.1
	96		3.2	96.8
Run 3		1.5		
	1		19.9	80.1
	2.25		17.7	82.3
	3.5		17.7	82.3
	5		17.0	83.0
	6		16.1	83.9
	8		15.5	84.5
	9		16.5	83.5
	10		15.3	84.7
	11.25		16.0	84.0
	12.5		16.5	83.5
Run 4		3.0		
	10		8.9	91.1
	24		4.4	95.6
	50		1.2	98.8
	95		1.2	98.8

TABLE II

ADDITION OF ACETIC ACID TO I CATALYZED BY 1.5% SULFURIC ACID

	Time	Temp, °C	IIIb, %	IVb, %
Run 1		110		
	1.0 hr		1.6	98.2
	2.2 hr		1.2	98.8
Run 2		25		
	57 days		20	80
	201 days		0	100

TABLE III

ADDITION OF ACETIC ACID TO *exo* OLEFIN II CATALYZED BY 1.5% SULFURIC ACID AT 55°

Time, hr	IIIb, %	IVb, %
2	1.8	98.2
4	1.8	98.2
6	1.1	98.9
8	1.3	98.7
10	1.2	98.8
24	1.3	98.7
49	1.0	99.0

Stability of IIIb and IVb in Acetic Acid Containing Sulfuric Acid.—Several reactions were performed employing varying concentrations of sulfuric acid (1.5 and 3.0%) and at various temperatures.

TABLE IV

THE UNCATALYZED ADDITION OF ACETIC ACID TO I

	Time, days	Temp, °C	IIIb, %	IVb, %
Run 1		87		
	46		51.8	48.2
	55.5		50.2	49.8
	64.5		47.3	52.7
	107		45.9	54.1
Run 2		100		
	13		40.5	59.5
Run 3		55		
	150		46.5	53.3

The acetates were placed in acetic acid containing a specific amount of sulfuric acid. The solution was heated and aliquots were removed from time to time. These were worked up and analyzed as described for the addition reactions. The results are described in Tables V and VI.

TABLE V

STABILITY OF IIIb AND IVb IN ACETIC ACID CONTAINING SULFURIC ACID AT 55°

	Time, hr	H_2SO_4, %	IIIb, %	IVb, %
Run 1		1.5		
	0		50.4	49.6
	10		43.0	57.0
Run 2		1.5		
	0		47.9	52.1
	1		47.8	51.7
	2.5		48.4	51.6
	3.5		45.7	54.3
	5		47.1	52.9
	6		46.8	53.2
	8		45.2	54.8
	9		45.6	54.4
	10		44.9	55.1
	11.3		44.1	55.9
	12.5		42.6	57.4
Run 3		3.0		
	0		53.1	46.9
	10		31.2	68.8
	24		16.2	83.8
	33		13.8	86.2
	50		2.8	97.2
	95		1.5	98.5

TABLE VI

STABILITY OF IIIb AND IVb IN UNCATALYZED ACETIC ACID

Time, days	Temp, °C	IIIb, %	IVb, %
0	55	93	7
27		93	7
0	90	93	7
24		93	7

Vapor Phase Chromatography.—Vapor phase chromatographic determinations were performed on a Perkin-Elmer vapor fractometer, Model 154-C, using helium as carrier gas.

The isomeric alcohols were analyzed on a 1 m by 0.25 in. copper column packed with Carbowax 20M on Chromosorb W, regular 60–80 mesh (approximately 30%). Analysis was conducted at 150° at a flow rate of 108 cc/min. The retention volume of *exo*-5,6-trimethylene-*exo*-2-norbornyl alcohol (IVc) was 3240 ml, and that of *endo*-5,6-trimethylene-*exo*-2-norbornyl alcohol (IIIc) was 3888 ml.

The composition of the isomeric olefins was determined on two separate columns. One column separated *exo*-skeleton olefin from *endo*-skeleton olefin, while the second column separated the mixture of monoolefins from dicyclopentadiene.

The isomeric olefins were analyzed on a 4 m by 0.25 in. copper column packed with "Ucon" polyglycol LB-550-X (approxi-

mately 30% by weight). Analyses were conducted at 113° at a flow rate of 86 cc/min. The retention volume of *exo*-5,6-trimethylene-2-norbornene was 11,000 ml and that of *endo*-5,6-trimethylene-2-norbornene was 11,524 ml.

The isomeric olefins were separated from *endo*-dicyclopentadiene on a 2 m by 0.25 in. copper column packed with Apiezon L on Chromosorb W 60–80 mesh (approximately 30% by weight). Analyses were conducted at 125° at a flow rate of 78 cc/min. The retention volume of dicyclopentadiene was 3634 ml, and that of the mixture of monoolefins was 4056 ml.

Registry No.—I, 2826-19-9; II, 10466-50-9; IIIb, 14362-73-3; IVb, 14362-74-4; acetic acid, 64-19-7.

The Partial Synthesis of 18,19-Dinor Steroids

WILLIAM F. JOHNS

Division of Chemical Research, G. D. Searle & Co., Chicago, Illinois 60680

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The synthesis of 18-norestrone and the 18,19-dinor analogs of testosterone, progesterone, and desoxycorticosterone is described starting from 3-methoxy-17-acetylgona-1,3,5(10),16-tetraene (**4a**). Reduction of the carbonyl group of 18-nor-13α-estrone methyl ether (**3a**) with lithium aluminum hydride gave preponderantly the axial (17β) alcohol **3b**, with sodium–propanol the equatorial (17α) epimer **3c**, and with sodium borohydride–sodium hydroxide the 17β alcohol of the *trans*-C/D series (**2b**).

The preparation of 18-nor steroids, both with and without the 19-methyl group, has been reported by several groups of investigators, using either partial or total syntheses.[1] The present communication describes the partial synthesis of the 18,19-dinor steroids from the 17-acetylgonatetraene **4a**, an intermediate available from estradiol methyl ether by an eight-step reaction sequence.[2,3] (See Scheme I.)

The first phase of the investigation, the synthesis of several gonane derivatives, was initiated by Beckmann rearrangement[4] of the oxime **4b**. To preclude isomerization at C-13 in the expected *trans* ketone **2a**, the phosphorous oxychloride reaction mixture was poured directly into cold aqueous acid. Instead of ketonic product, the intermediate enamide **1** was isolated. Although the enamide showed the expected NH absorption in the infrared (3.02 μ), overlapping aromatic absorptions in both ultraviolet[5] and nmr spectra precluded further support for this structure as opposed to the alternative imine structure.

Hydrolysis of the purified enamide **1** was accompanied by isomerization at C-13. In contrast, direct acid hydrolysis of the phosphorous oxychloride reaction mixture at room temperature afforded in good yield the *trans* ketone, 18-norestrone methyl ether (**2a**). The configuration of the 13 proton in **2a** was assigned from mechanistic considerations: lithium–ammonia reduction of the 13,17a double bond in its chrysenone antecedent[3b] would afford the *trans* (13-β) isomer; no change in this configuration would occur in the subsequent production of **2a**. In agreement with this expectation, the ORD curve of the *trans* ketone (**2a**)[6] (as well as of its D-homo precursor) shows a strong positive Cotton effect, analogous to the *trans*-hydrindan-1-ones. Esr data are also in accord with this assignment.[7] Since the configuration of the 14-hydrogen (α) remains unchanged in the synthesis, the transfusion of the C/D ring juncture is established.

Base-catalyzed equilibration of the *trans* ketone ([α]D +188°) gave a mixture ([α]D +11°) from which the *cis* ketone **3a** ([α]D −66°) could be isolated. The *cis* ketone, obtained previously from ozonolysis of a mixture containing the exocyclic olefin **3d**,[3a] exhibits a negative Cotton effect in its ORD spectrum as expected for a *cis*-hydrindanone structure.[6b] In addition, the *cis* ketone was readily converted with acid or base to the same mixture of ketones obtained from the *trans* ketone, establishing that the two compounds are an epimeric pair. The ratio of 13β/13α epimers at equilibrium calculated from the specific rotations is approximately 7:3.[8]

Lithium aluminum hydride reduction of the *trans* ketone **2a** provided mainly a single compound, 18-norestradiol methyl ether (**2b**, [α]D +76°). The configuration of the 17-hydroxyl was assigned in analogy to the comparable reduction in the 13-methyl steroids[9] and was supported by rotational data.[10] The axial character of the 17 proton in the nmr, masked by the 3-methoxyl signal in the free alcohol, was seen clearly in the corresponding 17-acetate and supported the configurational assignment.[11] The anal-

(1) W. L. Meyer, D. D. Cameron, and W. S. Johnson, *J. Org. Chem.*, **27**, 1130 (1962), and references cited therein; D. H. R. Barton, A. da S. Campos-Neves and A. I. Scott, *J. Chem. Soc.*, 2698 (1957); L. Velluz, G. Amiard, R. Heymes, and B. Goffinet, *Bull. Soc. Chim. France*, 2166 (1961); R. Anliker, M. Muller, M. Perelman, J. Wohlfahrt, and H. Heuser, *Helv. Chim. Acta*, **42**, 1071 (1958); G. Stork, H. N. Khastgir and A. J. Solo, *J. Am. Chem. Soc.*, **80**, 6458 (1958).

(2) See W. F. Johns, *J. Am. Chem. Soc.*, **80**, 6456 (1958), for an initial report of this work.

(3) (a) W. F. Johns, *J. Org. Chem.*, **26**, 4583 (1961); (b) *ibid.*, **28**, 1856 (1963).

(4) Application of this rearrangement to pregnane degradation as well as isolation and characterization of the intermediate enamide was reported by G. Rosenkranz, O. Mancera, F. Sondheimer, and C. Djerassi, *J. Org. Chem.*, **21**, 520 (1956). See also E. Testa and F. Fava, *Gazz. Chim. Ital.*, **87**, 971 (1957).

(5) The acetamidoandrostene was reported in footnote 4 to exhibit λ_{max} 240 mμ (ϵ 6600).

(6) (a) This ORD allows calculation of the insertion value of the 13-methyl group: $\Delta a = -31$. We are indebted to Professor W. Klyne, Westfield College, University of London, for both the ORD curve and the insertion value. (b) For a discussion of the ORD values of the hydrindanones, see C. Djerassi and W. Klyne, *J. Chem. Soc.*, 2390 (1963), and references cited.

(7) E. R. Talaty and G. A. Russell, *J. Am. Chem. Soc.*, **87**, 4867 (1965).

(8) For a discussion of hydrindan-1-one stabilities, see H. O. House and G. H. Rasmusson, *J. Org. Chem.*, **28**, 31 (1963), and references cited therein; N. L. Allinger, R. B. Hermann, and C. Djerassi, *ibid.*, **25**, 922 (1960). The latter report a different equilibrium value (55/45) for this equilibrium mixture, the discrepancy presumably being due to the inherently greater accuracy of the ORD method employed by them.

(9) L. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p 467.

(10) For the values of estrone methyl ether (+169°) and estradiol methyl ether (+78°), see J. Jacques, H. Kagan, and G. Ourisson, "Pouvoir Rotatoire Naturel," Pergamon Press Inc., New York, N. Y., 1965.

(11) E. L. Eliel, M. H. Gianni, and Th. H. Williams, *Tetrahedron Letters*, 741 (1962); Y. Kawazoa, Y. Sato, T. Okamoto, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **11**, 328 (1963).