m.p. 232°(d.) separated directly from the reaction mixture. To 376 mg. of this crude *p*-toluenesulfonyl hydrazone was added a previously prepared solution containing 1.7 g. of sodium in 50 ml. of ethylene glycol, and the reaction mixture was allowed to reflux for 1.5 hours under nitrogen. The reaction mixture was cooled, diluted with water, and extracted exhaustively with ether. The ether layer was washed with dilute aqueous hydrochloric acid and with water. The ether was evaporated *in vacuo* and the residue was crystallized from ethanol–water, yielding 145.5 mg. of Δ^7-cholesten-3β-ol, m.p. 108–115° (43% from 3β-acetoxycholestan-7-one). Purification was effected by chromatography on a column of alumina, Δ^7-cholesten-3β-ol being eluted with 3–2 benzene–ether, m.p. 120–123°, $[\alpha]^{26}D$ −3° (chloroform) (lit.[29] m.p. 123°, $[\alpha]D$ ±0°).

(29) Fr. Schenck, K. Buchholz and O. Wiese, *Ber.*, **69**, 2696 (1936).

Deuterium analyses were performed by combustion of the organic sample and isotopic analysis of the water formed by the "falling drop" method.[30] The isotope position analyses were calculated from the infrared spectrum of the unknown sample and the spectra of 6α- and 6β-deutero-3β-acetoxycholestan-7-one which were obtained from zinc-deuterium bromide reduction of 6α-bromo-3β-acetoxycholestan-7-one and by the synthesis shown in Fig. 2, respectively, using optical densities at ν_{max}. The spectra of these epimeric 6-deutero-7-ketones are recorded in Fig. 4.

(30) A. S. Keston, D. Rittenberg and R. Schoenheimer, *J. Biol. Chem.*, **122**, 227 (1942).

URBANA, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

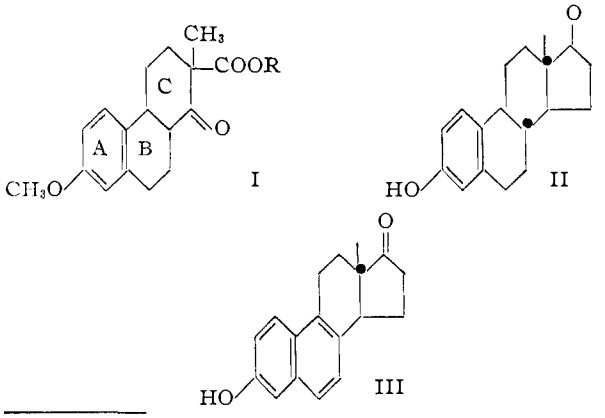
Steroid Total Synthesis—Hydrochrysene Approach. I. General Plan and Summary of Major Objectives

BY WILLIAM S. JOHNSON

RECEIVED MAY 31, 1956

This introductory paper of the series includes a general description of the development of the synthetic plan and a treatment of the major stereochemical problems.

In the early 1930's as the last pieces of the intricate puzzle of the structure of the steroid nucleus were being fitted into place, organic chemists were already initiating studies directed toward the fabrication of this unique honeycomb of carbon atoms with latent physiological potency of wonderful and far-reaching significance. As early as 1936, Robinson and his collaborators[1] had produced a key tricyclic (ring ABC) intermediate I and were clearly already well along toward the completion of the fourth ring D to produce the estrone structure II. But success was not close at hand. The extraordinary difficulties attending the total synthesis of this molecule with four asymmetric centers (*i.e.*, 16 possible isomers) were mainly stereochemical in nature, as emphasized by the fact that a dozen years intervened, during which major contributions were made by various laboratories as described below, before the objective was finally realized.



(1) R. Robinson and E. Schlittler, *J. Chem. Soc.*, 1288 (1935), and R. Robinson and J. Walker, *ibid.*, 747 (1936). For an excellent review of the total synthesis of steroids see J. W. Cornforth, *Prog. Org. Chem.*, **3**, 1 (1955).

Bachmann and his collaborators played a vital role in the early development of the field; indeed Bachmann, Cole and Wilds were the first to accomplish the total synthesis of a natural steroid, equilenin (III), in 1939.[2] This hormone, the simplest of the known steroids, contains one angular methyl group and two centers of asymmetry. All four optical isomers have been prepared.[3] Employing some of the techniques developed in the equilenin synthesis, Bachmann, Kushner and Stevenson[3] turned their hand to the estrone problem and in 1942 published an account of the total synthesis of one of the seven possible unnatural racemates; then the ensuing war years interrupted most of the progress in the field. A relay of efforts to the laboratories of Miescher saw the old keto ester I prepared in quantity, separated into three of its four possible racemic modifications and converted into estrones by the Bachmann sequence for attaching ring D. Thus in 1948, Anner and Miescher[4] announced the total synthesis of estrone and several stereoisomers. Two years later Johnson, Banerjee, Schneider and Gutsche[5] disclosed a fundamentally different synthetic approach which led to the natural hormone as well as to some further stereoisomers. By now seven of the eight possible racemates represented by formula II have been prepared and their configurations proved.[6] A third highly stereoselective approach to estrone was dis-

(2) W. E. Bachmann, W. Cole and A. L. Wilds, THIS JOURNAL, **61**, 974 (1939); **62**, 824 (1940).

(3) W. E. Bachmann, S. Kushner and A. C. Stevenson, *ibid.*, **64**, 974 (1942).

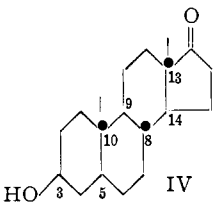
(4) G. Anner and K. Miescher, *Experientia*, **4**, 25 (1948); *Helv. Chim. Acta*, **31**, 2173 (1948); **32**, 1957 (1949).

(5) W. S. Johnson, D. K. Banerjee, W. P. Schneider and C. D. Gutsche, THIS JOURNAL, **72**, 1426 (1950); W. S. Johnson, D. K. Banerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg and L. J. Chinn, *ibid.*, **74**, 2832 (1952).

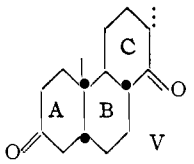
(6) W. S. Johnson, I. A. David and W. F. Johns, unpublished work.

closed by Johnson and Christiansen in 1951.[7] This scheme coupled with the method of Sheehan, Coderre and Cruickshank[8] for the completion of ring D constitutes the most practical totally synthetic approach to this hormone yet developed.

It may be mentioned in passing that a new method for the construction of the ring D system of a 17-keto steroid was developed in 1945 by Johnson, Petersen and Gutsche[9] and applied with singular success to the synthesis of equilenin. Attempts to adapt the method to the synthesis of estrone, however, met with failure.[5]



IV



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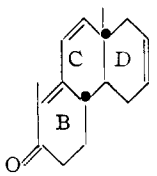
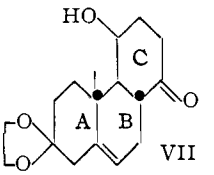


VI

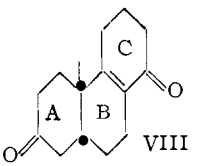
The total synthesis of the non-aromatic steroid with its two angular substituents and multiplicity of asymmetric centers presents a problem of serious complexity. For example, epiandrosterone (IV) has 7 centers of asymmetry (at positions 3, 5, 8, 9, 10, 13 and 14) and is therefore one of 128 possible stereoisomers (64 racemic forms). Progress in the field not only paralleled but was, in fact, largely responsible for the development and understanding of stereoselective reactions of fused ring systems. As this stereoselective art advanced and the stereochemistry of the natural steroids became known,[10] the odds became increasingly favorable for producing the desired isomer by synthesis.

A major development was the announcement of Cornforth and Robinson[11] in 1947 of the synthesis of the tricyclic diketone V identical with a ketone obtained by oxidative degradation of cholesterol and bile acids. In 1951, the coveted goal was reached by Woodward, Sondheimer, Taub, Heusler and McLamore[12] utilizing a completely independent and highly stereoselective approach involving the tricyclic intermediate VI, and by Cardwell, Cornforth, Duff, Holtermann and Robinson[13] who completed the logical development from the tricyclic diketone V.

These first syntheses employed the "relay" technique, *i.e.* supplies of an intermediate for furthering the synthesis were prepared by degradation of a natural product. The result of this approach has been defined[13] as "formal" total synthesis, since the final product is not totally synthetic. The Woodward and the Robinson approaches both thus established totally synthetic pathways to a large number of steroids (including most of the important hormones) that had already been inter-related by a multitude of transformations.



VII



VIII

The next development of major significance was the stereoselective total synthesis of cortisone (employing the intermediate VII) without the use of relays, announced by Sarett and his collaborators in 1952.[14] This achievement was followed closely by the synthesis of epiandrosterone IV,[15] in the first of a group of preliminary announcements of total syntheses from our own laboratory, which represent the subject of the present series of papers. Practically simultaneously, Wilds and his collaborators[16] announced the total synthesis of methyl 3-ketoetiocholanate, utilizing a novel approach involving the tricyclic unsaturated diketone VIII as a key intermediate. In this same year, Barkley, Farrar, Knowles and Raffelson[17] disclosed the utilization of the Woodward intermediates in a total synthesis of cortisone, and Wieland, Ueberwasser, Anner and Miescher[18] announced a synthesis of a D-homo steroid which promises[19] to be convertible into a natural steroid. Recently Schmidlin, Anner, Billeter and Wettstein[20] have utilized the Sarett intermediates[14] in a total synthesis of the difficultly accessible and highly active adrenal hormone, aldosterone; and Stork, Loewenthal and Mukharji[21] have disclosed an original route to 11-oxygenated steroids which shows promise of being applicable to the formation of 18-aldehydo derivatives.

Discussion of Present Work

In contrast with the plans employed by others, we envisaged a three-stage scheme involving (a) initial production of a highly unsaturated tetracyclic molecule which, by virtue of the unsaturation, would contain a minimum of (preferably only one) asymme-

(7) W. S. Johnson and R. G. Christiansen, THIS JOURNAL, **73**, 5511 (1951).

(8) J. C. Sheehan, R. A. Coderre and P. A. Cruickshank, *ibid.*, **75**, 6231 (1953).

(9) W. S. Johnson, J. W. Petersen and C. D. Gutsche, *ibid.*, **67**, 2274 (1945); **69**, 2942 (1947).

(10) R. B. Turner in L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1949, p. 620.

(11) J. W. Cornforth and R. Robinson, *Nature*, **160**, 737 (1947); *J. Chem. Soc.*, 1855 (1949).

(12) R. B. Woodward, F. Sondheimer, D, Taub, K. Heusler and W. M. McLamore, THIS JOURNAL, **73**, 2403 (1951); **74**, 4223 (1952).

(13) H. M. E. Cardwell, J. W. Cornforth, S. R. Duff, H. Holtermann and R. Robinson, *Chemistry and Industry*, 389 (1951); *J. Chem. Soc.*, 361 (1953).

(14) L. H. Sarett, G. E. Arth, R. M. Lukes, R. E. Beyler, G. I. Poos, W. F. Johns and J. M. Constantin, THIS JOURNAL, **74**, 4974 (1952), *et seq.*

(15) W. S. Johnson, B. Bannister, B. M. Bloom, A. D. Kemp, R. Pappo, E. R. Rogier and J. Szmuszkovicz, *ibid.*, **75**, 2275 (1953).

(16) A. L. Wilds, J. W. Ralls, D. A. Tyner, R. Daniels, S. Kraychy and M. Harnik, *ibid.*, **75**, 4878 (1953).

(17) L. B. Barkley, M. W. Farrar, W. S. Knowles and H. Raffelson, *ibid.*, **75**, 4110 (1953); **76**, 5017 (1954).

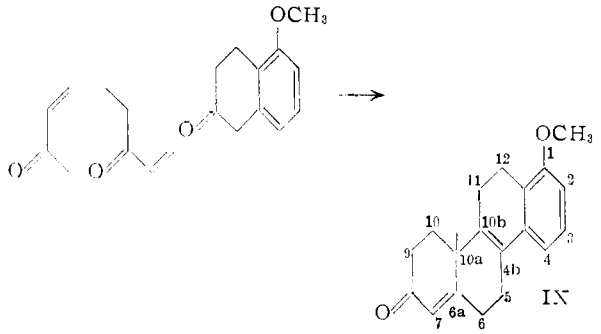
(18) P. Wieland, H. Ueberwasser, G. Anner and K. Miescher, *Helv. Chim. Acta*, **36**, 1231 (1953).

(19) P. Wieland, G. Anner and K. Miescher, *ibid.*, **36**, 1803 (1953).

(20) J. Schmidlin, G. Anner, J. R. Billeter and A. Wettstein, *Experientia*, **11**, 365 (1955).

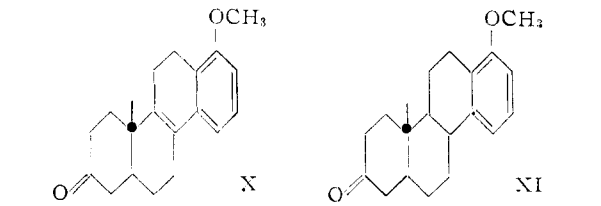
(21) G. Stork, H. J. E. Loewenthal and P. C. Mukharji, THIS JOURNAL, **78**, 501 (1956).

tric centers; (b) reduction of the unsaturated bonds with concomitant introduction of new asymmetric centers by stereoselective processes affording promise of leading to the correct modes of ring fusion, *e.g.*, *trans-anti-trans-anti-trans* as in epiandrosterone IV; (c) appropriate structural modification of the resulting reduced nucleus to produce the natural steroids.



The unsaturated tetracyclic ketone IX with only one asymmetric center (at C_{10a}) was selected as the first objective, since it promised to be readily obtainable from 5-methoxy-2-tetralone by a succession of two Robinson-type ring syntheses. This hope was realized and the crystalline racemate IX thus produced readily. The details of this preparation and the proof of structure are described in part II.

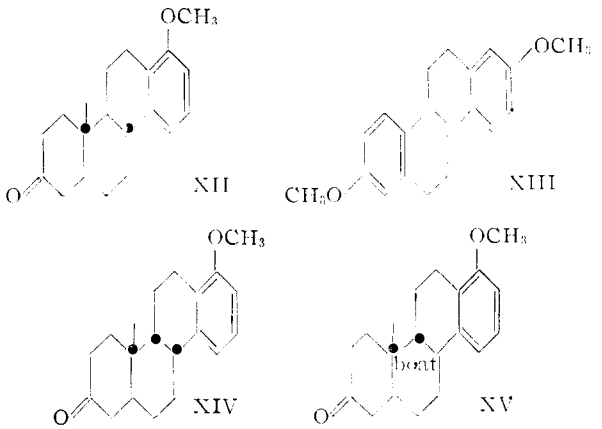
The second and most difficult stage of the scheme was initiated by a study of the reduction of the two ethylenic bonds (at 6a, 7 and 4b, 10b) of the tetracyclic ketone IX. The details of this work appear in parts III and IV where the synthesis and configurational assignment of 6 of the 8 possible tetrahydro forms of IX are described. Catalytic hydrogenation of IX over 10% palladium-on-carbon stopped after the absorption of 1 mole-equivalent of hydrogen giving a dihydro compound, m.p. 121°. Another dihydro ketone, m.p. 176°, was produced *via* selective hydrogenation of the enol ether—a method known to give cholestanone (A/B *trans*) from cholestenone.[22] The ultraviolet spectra of the two dihydro ketones were identical and typical of the *m*-methoxystyrene chromophore, showing that the α,β-unsaturated ketone system (responsible for the strong absorption of IX in the 240 mμ region) had indeed been reduced and that the two products were, in fact, stereoisomeric forms of 6a,7-dihydro IX. Since catalytic hydrogenation of cholestenone is known to give predominantly coprostanone (A/B *cis*),[23] while reduction *via* the enol ether gives A/B *trans*,[22] the 121 and 176° dihydro ketones were analogously assigned the A/B *cis* and A/B *trans* configurations.



(22) H. H. Inhoffen, G. Stoeck, G. Kölling and U. Stoeck, *Ann.*, **568**, 52 (1950).

(23) H. Grasshof, *Z. physiol. Chem.*, **223**, 249 (1934).

When the A/B *trans*-dihydro ketone X was hydrogenated over 30% palladium hydroxide-on-strontium carbonate, the 4b,10b (styrene) bond was stereoselectively reduced as evidenced by the disappearance of the *m*-methoxystyrene absorption and the appearance of the anisole spectrum in the ultraviolet region. The resulting tetrahydro compound, m.p. 187°, produced stereoselectively, was assigned the *trans-anti-cis* configuration (formula XI) on the basis of the Linstead concept[24] of *cis* addition of hydrogen to that side of the molecule most readily adsorbed on the surface of the catalyst. The molecular model suggests that adsorption and hence hydrogenation of the flat molecule would occur preferably on the face (α) opposite to that (β) carrying the axially attached angular methyl group at C_{10a}.



When the dihydro ketone X was reduced by sodium or lithium and alcohol in ammonia, the keto group being protected from reduction as the ethylene ketal, a new tetrahydro ketone, m.p. 211°, was produced stereoselectively. The ultraviolet spectrum of this substance was identical with that of XI and clearly showed that the styrene bond had been reduced. A precedent is found in the work of Birch and Smith[25] who thus reduced the tetracyclic compound XIII to yield a mixture of *cis*- and *trans*-dihydro isomers in about equal amounts. Since there was some suggestion that such carbanion reductions are thermodynamically controlled processes,[26] it seemed reasonable to assume that this 211° tetrahydro ketone was the desired *trans-anti-trans* compound XII, because this configuration is undoubtedly more stable than the other two possibilities, namely, the *trans-syn-cis* (XIV) and the *trans-syn-trans* (XV).[27] On the basis of this hypothesis, the 211° tetrahydro ketone was selected for the first studies of the reduction of the aromatic nucleus which are described in detail in part VI.

Treatment of the 211° tetrahydro compound with lithium aluminum hydride effected stereoselective reduction of the keto to hydroxyl group, which was undoubtedly β-oriented (equatorial) be-

(24) R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine and R. R. Whetstone, THIS JOURNAL, **64**, 1985 (1942).

(25) A. J. Birch and H. Smith, *J. Chem. Soc.*, 1882 (1951).

(26) For a recent summary see D. H. R. Barton and C. H. Robinson, *ibid.*, 3045 (1954).

(27) *Cf.* W. S. Johnson, *Experientia*, **7**, 315 (1951); THIS JOURNAL, **75**, 1498 (1953).

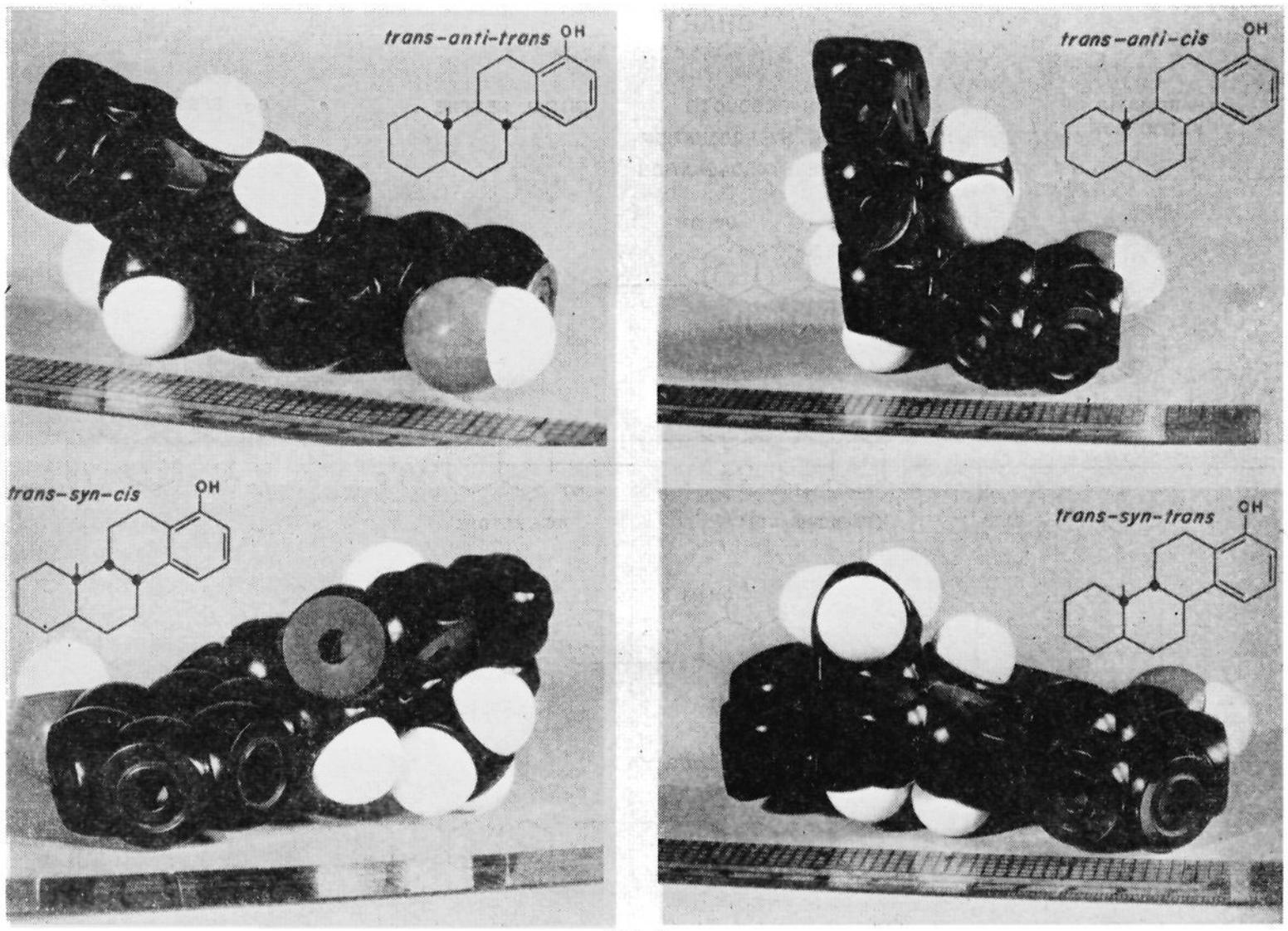


Fig. 1.

cause of the *trans* fusion of rings A and B.[28] Demethylation to the phenolic alcohol (Ia, R = H, Chart 1) followed by selective acetylation of the alcoholic hydroxyl group yielded the half acetate (Ia, R = Ac, Chart 1). Catalytic hydrogenation over a highly active platinum oxide in acetic acid gave, in addition to some hydrogenolyzed material, a mixture of saturated carbinols which appeared to consist of only two stereoisomers—an expected event considering that the reaction conditions were those known to favor one-sided (all *cis*) hydrogenation of the aromatic nucleus.[24] On the assumption that the configuration of rings A/B/C was *trans-anti-trans*, the two hydrogenation products would be represented by formulas IIa (R = Ac, Chart 1) and Va (R = Ac, Chart 1) in which the B/C/D configuration is *trans-anti-cis* and *trans-syn-cis*, respectively.

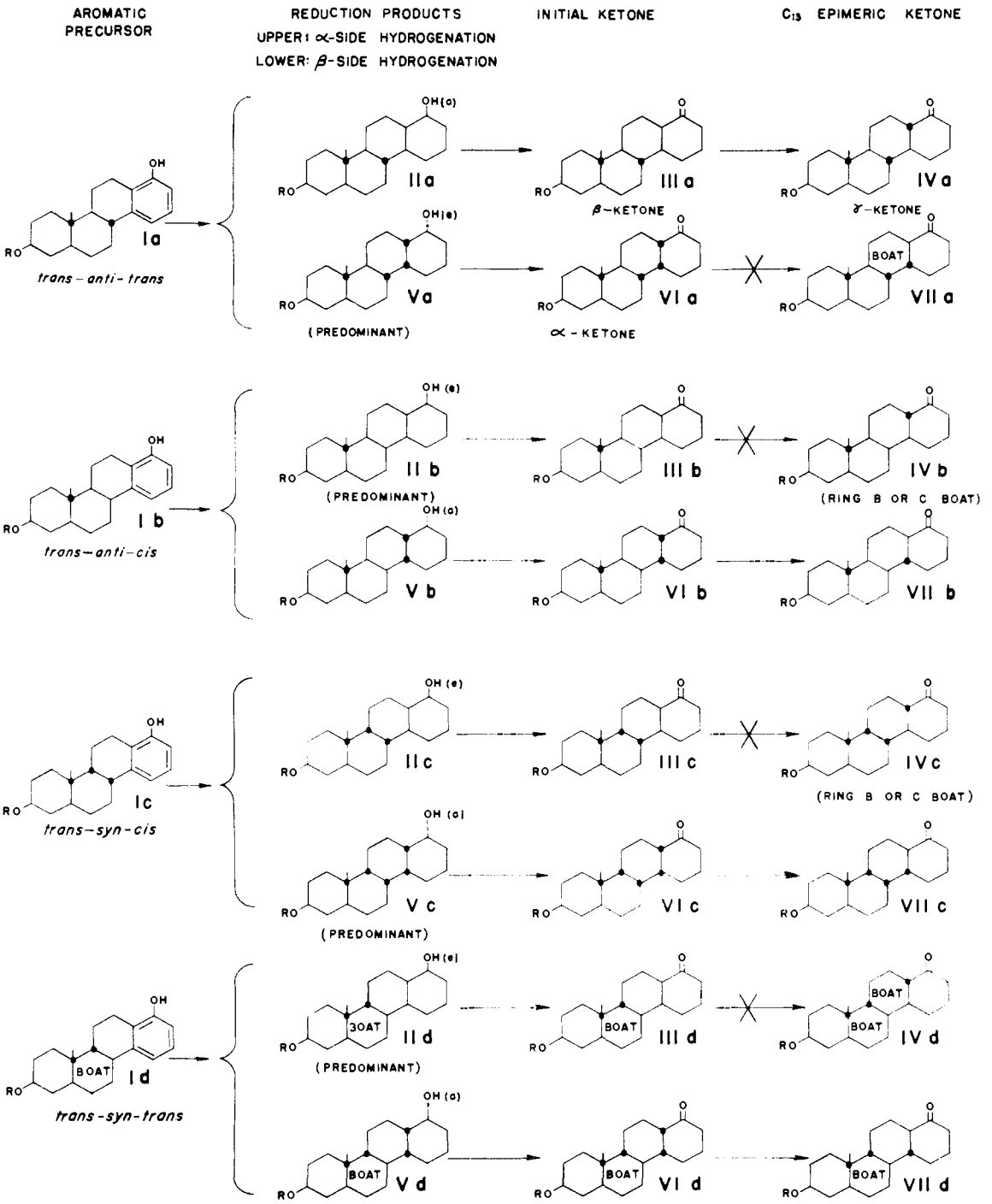
Chromic acid oxidation of the saturated carbinols proceeded much more slowly with the predominant form than with its companion stereoisomer which suggests[28] that the hydroxyl group is equatorial (e) in the former and axial (a) in the latter. Conformational analysis[28] shows that the hydroxyl of Va is equatorial and that of IIa is axial, hence on the A/B/C *trans-anti-trans* postulate these configurations would represent the major and minor hydrogenation products, respectively. This formulation is also consistent with the behavior of the resulting ketones: that one, the "α-ketone" derived from the major (slow-oxidizing) carbinol was stable to alkali. This is the expected behavior of the B/C/D *trans-syn-cis* ketone (VIa) which would not isomerize to the less stable B/C/D *trans-syn-trans* form (VIIa) because this change requires the conversion of ring C into the boat conformation.[27] The "β-ketone" derived from the minor (fast-oxidizing) carbinol, on the contrary, was unstable and readily isomerized into a new stereoisomer, the "γ-ketone," a behavior consistent with the expected epimerization of the B/C/D *trans-anti-cis* (IIIa) to the more stable *trans-anti-trans* form (IVa).[27]

Considering the matter of the proportion of saturated isomeric carbinols formed on hydrogenation of the aromatic nucleus, examination of molecular models shows (see Fig. 1) that the aromatic nucleus of the *trans-anti-trans* form Ia can approach the catalyst surface (represented in Fig. 1 by the surface holding the ruler) more readily on the front (β) face holding the angular methyl group; hence the expected result is a predominance of the product of addition of hydrogen to the β face, namely, Va.

The above interpretation provides a consistent rationalization predicated on the assumption that the 211° tetrahydro compound has the *trans-anti-trans* configuration (Ia). Since the A/B *trans* fusion is undoubtedly correct (see above), only three other possibilities need to be considered and these are summarized in Chart 1. The A/B/C *trans-anti-cis* series Ib → VIIb also gives a consistent interpretation of the facts. However, this formulation almost certainly corresponds to a different series (described also in part VI) that is derived from the tetrahydro ketone (m.p. 187°) obtained by the catalytic hydrogenation of the styrene bond of X (see above). The A/B/C

(28) D. H. R. Barton, *Experientia*, **6**, 316 (1950).

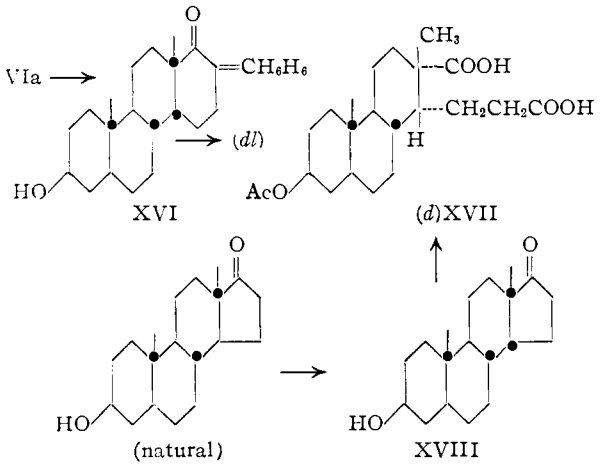
CHART I



trans-syn-cis series Ic → VIIc provides a consistent picture except for the isomer ratios. Examination of the molecular model (Fig. 1) suggests that the predominant saturated carbinol would be the one (Vc) that is oxidized more (instead of less) rapidly and gives an isomerizable (instead of stable) ketone (VIc). This series accordingly may be considered a less likely possibility. The A/B/C *trans-syn-trans* series Id → VIId provides a completely consistent rationalization of the facts, and the basis for considering it less attractive than the *trans-anti-trans* series is the expected mode of reduction of the styrene bond (see above).

Even though the analysis presented above favored the Ia → VIIa interpretation, it was considered desirable to establish the point unequivocally before investing more effort toward the ultimate synthetic targets. Unfortunately the γ-ketone IVa, which would be expected to lead to a natural steroid, was not available from the hydro-

genation study in sufficient quantity to carry on with the synthesis. The most practical approach toward the immediate objective was to attempt to establish a tie-up between a natural steroid and the predominant α-ketone VIa.



With this end in view, the α-ketone was condensed with benzaldehyde, the resulting benzylidene derivative methylated and the major product (presumably C/D *cis*, formula XVI) acetylated and oxidized to the dibasic acid XVII.[29] The infrared spectrum of the dimethyl ester of this racemic diacid was identical with that of authentic *d*-dimethyl 3-acetoxy 14-isoetioallohomobilianate prepared from epiandrosterone *via* the 14-iso ketone XVIII, the details of which are disclosed in part IX. The identity of the synthetic material with the 14-iso steroid series thus proved that the presumed configurations (Ia → VIa, Chart 1) for the intermediates were correct and that the γ-ketone was, in fact, the desired *trans-anti-trans-anti-trans* form (IVa) that was required for synthesis of a natural steroid. We turned our attention, therefore, to the matter of producing this substance more readily.

In view of the stereoselective reduction of cholestenone to β-cholestanol (A/B *trans*) with sodium and amyl alcohol,[30] it was hoped that lithium and alcohol in liquid ammonia would similarly effect reduction of the α,β-unsaturated ketone system of the tetracyclic ketone IX, as well as of the styrene double bond to give the *trans-anti-trans*-carbinol XIX. This indeed proved to be the case, XIX being produced directly from IX in a single stereoselective operation, and a major improvement in the scheme was thus realized. The details of this work are described in part III.

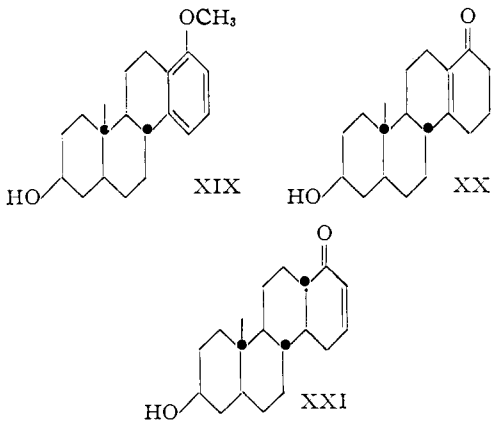
The original conception of the synthetic scheme envisaged metal-in-ammonia reduction[31] of the aromatic nucleus of, for example, compound XIX. Numerous preliminary experiments employing conventional procedures were totally unsuccessful and the approach was temporarily abandoned. Eventually appropriate modification of conditions spelled success and the details are disclosed in part VII.

(29) *Cf.* W. S. Johnson, THIS JOURNAL, **66**, 215 (1944); W. S. Johnson, D. K. Banerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg and L. J. Chinn, *ibid.*, **74**, 2832 (1952).

(30) O. Diels and E. Abderhalden, *Ber.*, **39**, 884 (1906).

(31) A. J. Birch, *Quart. Rev.*, **4**, 69 (1950).

The reduction product, after the usual acid treatment, afforded both possible α,β-unsaturated ketones XX and XXI. The latter on catalytic hydrogenation gave the γ-ketone directly, while the former thus yielded the unstable β-ketone which is readily isomerized with alkali to the γ-ketone (see above). For preparative purposes it was, therefore, unnecessary to separate the mixture of α,β-unsaturated ketones which, by hydrogenation in the presence of alkali, could be converted directly into the desired γ-ketone. Since the conditions for reduction of the aromatic nucleus of XIX were similar to



those used to produce this intermediate stereoselectively from the tetracyclic ketone IX, consolidation of the steps was indicated. It was gratifying to find that the modified reduction conditions applied to the tetracyclic ketone IX gave directly the mixture of α,β-unsaturated ketones that is reducible to the γ-ketone. The two combined reduction steps thus constitute a stereoselective synthesis of the γ-ketone from IX (see Chart 2), a process involving the introduction of no less than six new asymmetric centers.

With a good method for the production of the γ-ketone at hand, attention was turned to completion of the synthesis. The over-all scheme is summarized in Chart 2. The angular methylation–ring contraction sequence for the transformation of the α-decalone ring system into the C/D ring moiety of a 17-keto steroid[29] was applied to the γ-ketone. Condensation with furfuraldehyde followed by methylation of the resulting furfurylidene derivative afforded the expected mixture of C_{13}-epimers, which was readily separated by chromatography. The less preponderant isomer (C/D *trans*) was ozonized to the dibasic acid which, in turn, was cyclized to *dl*-epiandrosterone, identified by infrared spectroscopy. Since many transformations from partial synthesis studies link epiandrosterone to other members of the steroid group,[13] this synthesis like others mentioned in the intro-

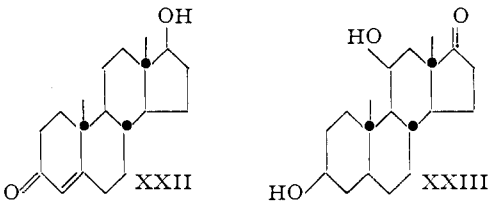
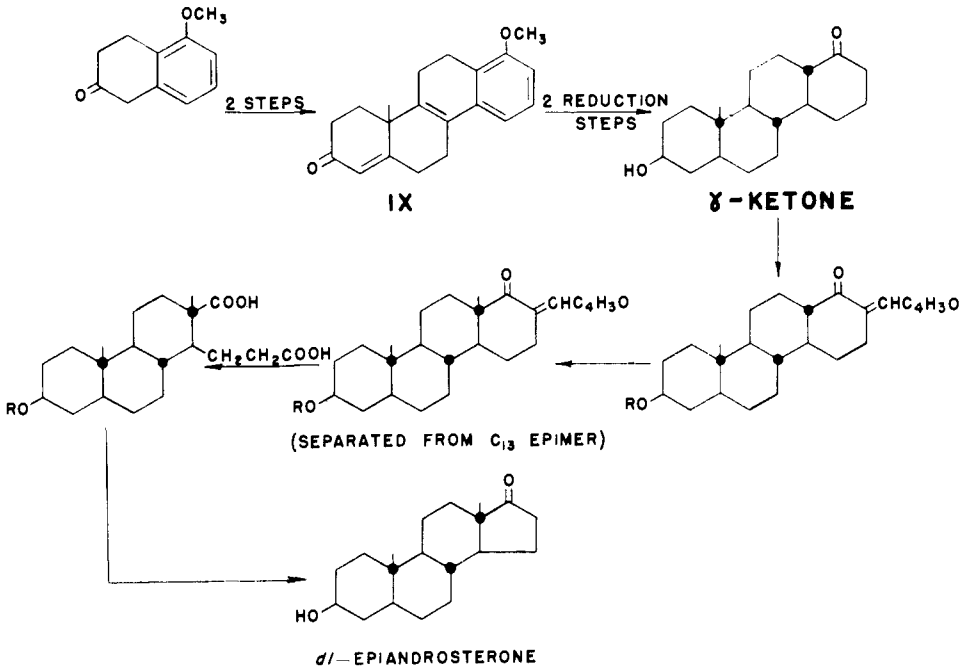


CHART 2



duction constitutes a formal total synthesis of many important steroids, *e.g.*, cholesterol, cortisone and testosterone.

Now that the feasibility of the scheme was demonstrated by the successful synthesis of epiandrosterone described above, we turned our attention to the matter of the direct total synthesis of some of the other steroids. The obvious approach, *i.e.*, to synthesize *dl*-epiandrosterone in quantity and to utilize it as an intermediate following pathways already defined by formal total syntheses (see above), was considered circuitous and uninspired, not to mention impractical. Our studies, therefore, have taken the form of modification of our scheme at the appropriate stage to open up more direct routes to other steroids. Some of this work is reported in the present series of papers. One of our objectives, the total synthesis of testosterone XXII, has been realized and the details are set forth in paper X. In this case the general scheme for epiandrosterone (Chart 2) was modified by preservation of the α,β-unsaturated ketone system of ring A by protection as the cyclic ethylene ketal. A number of new difficulties were thus introduced, but these problems were amenable to solution and the hitherto unknown *dl*-testosterone was produced.

Significant progress also has been made toward the total synthesis of 11-oxygenated steroids. A method has been developed for the introduction of oxygen at C_{11} at an early stage of the synthesis, and this study is described in part V. The intermediate XIX has thus been oxygenated, and, as described in part VIII, carried through the general scheme analogous to that represented in Chart 2 to yield the *dl*-form of 3β,11β-dihydroxyandrostane-17-one (XXIII), a naturally occurring steroid. The synthesis of other steroids is under investigation.

Acknowledgment.—I am deeply grateful to my collaborators who, through skill and determined effort, were largely responsible for this work. I am also indebted to the foundations and industrial organizations mentioned in the following papers who have generously supported our program and in turn the educational process. Thanks are also due to my many friends who have given helpful advice, and to Patricia Barth Davis for technical assistance.

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