Transposition of Ketones *via* 2-Nitro Ketones[1]

ALFRED HASSNER, JOHN M. LARKIN, AND JAMES E. DOWD

Department of Chemistry, University of Colorado, Boulder, Colorado 80304

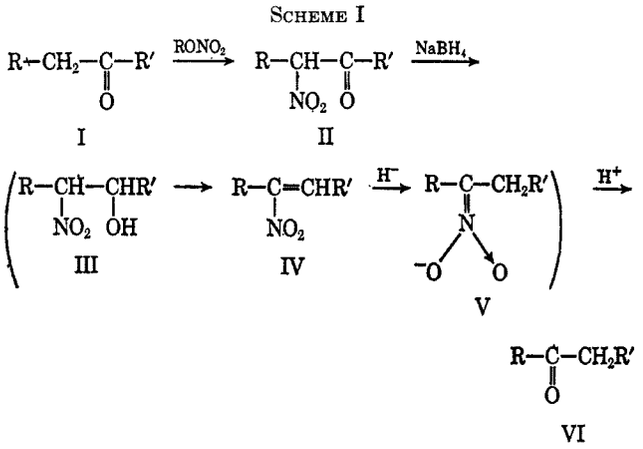
Received November 1, 1966

The reaction of 2-nitro ketones prepared by nitration of some cyclic ketones was investigated with the view toward transposing a carbonyl group to an adjacent carbon. Reduction of these 2-nitro ketones with sodium borohydride leads to 2-nitro alcohols, nitro olefins, or nitroalkanes, which in turn can be converted by various methods into ketones. In this manner cholestan-3-one was converted into cholestan-2-one *via* 2-nitrocholestan-3-one (**2**), its enol acetate (**10**), and 2β-nitrocholestane (**5**). 3β-Hydroxy-5-androsten-16-one was obtained from its 17-keto isomer *via* the 16-nitro 16-olefin. 2,2-Disubstituted cyclopentanones and cyclohexanones were transformed into the corresponding α-nitro ketones and borohydride reduction of the latter was studied. The chemistry of intermediate nitro compounds is discussed.

In synthetic work it is often desirable to shift the position of a ketone carbonyl in cyclic systems by one carbon atom. The following example serves to illustrate the need for a simple method for the transposition of a ketone carbonyl. Djerassi and coworkers recently needed 2-keto steroids for a mass spectral study and were able to prepare these compounds from 3-keto steroids in only 20% over-all yield.[2] Five steps were involved and a mixture requiring purification was obtained in one of the intermediate steps.

The scheme we envisioned for the transposition of a carbonyl group is based on previous experience with steroidal nitro compounds in this laboratory, and involves the reaction sequence in Scheme I. The first

SCHEME I



step, nitration of a ketone with an alkyl nitrate in the presence of potassium *t*-butoxide (I → II), can be carried out in good yield.[3,4] Borohydride reduction of α-nitro ketone II should lead to nitro alcohol III, and it was hoped that dehydration might occur readily under the basic reaction conditions. This elimination should be facilitated by the presence of an acidic proton α to the nitro group. The vinyl nitro compound IV, thus formed, can be reduced further by 1,4 addition of hydride as has been shown by Schechter, *et al.*,[5] and Hassner and Heathcock[6] for systems of this type. The resulting nitronate anion V on acidification with strong acid should produce ketone VI by a Nef reaction.[7] The conversion of ketone I into ketone VI would then occur in essentially two steps, *i.e.*, preparation of the nitro ketone followed by sodium borohydride reduction (I → II → VI).

As will be discussed below, the reaction sequence I → II → VI often is limited by poor yields in the elimination of water from III or by steric hindrance in the reduction of IV, but modifications have been introduced that allow the transposition of the carbonyl group in fair yield.

Steroidal A-Ring Ketones.—The proposed scheme was tested for the isomerization of 3-keto steroids to the more difficultly obtainable 2-keto steroids. 2-Nitrocholestan-3-one (**2**) resulted in good yield from the regiospecific[8a] reaction of cholestan-3-one (**1**) with butyl nitrate in the presence of potassium *t*-butoxide in *t*-butyl alcohol (Scheme II).

This compound exists predominantly in the highly hydrogen-bonded enol form **2a**. This is evidenced by spectral data.[8b] Thus, its infrared spectrum shows very weak carbonyl (1740 cm^{-1}) and nonconjugated nitro absorption (1550 cm^{-1}) but exhibits strong conjugated olefin and nitro absorption at 1610 and 1520 cm^{-1}, respectively. Sodium borohydride reduction of **2a** followed by acidification with dilute acid led to a mixture, separable by chromatography on silica gel into 2-α-nitrocholestan-3β-ol (**3a**, 24%) and 2-nitro-2-cholestene (**4**, 34%). On the other hand chromatography on alumina afforded in addition to **3a** a small amount of cholestan-2-one (**6**). The nitro olefin **4** was identical with that isolated from the addition of nitrosyl chloride to 2-cholestene.[9] Since conversion of **4** into cholestan-2-one **6** in 75% yield by zinc–acetic acid reduction has been demonstrated,[9] this path represents an alternate conversion of **1** into **6**.

It was found that the nitro olefin **4** was reduced by borohydride to give 2β-nitrocholestane (**5**) in excellent yield after acidification with dilute acid. This is in agreement with previous findings[5,6,10] that vinyl nitro compounds undergo 1,4 reduction with sodium borohydride to yield saturated nitro compounds. Protonation of the nitronate anion derived from some nitrocyclohexanes has been shown to lead to the axial nitro

(1) (a) Stereochemistry. XXXI. For paper XXX, see A. Hassner, R. A. Arnold, R. Gault, and A. Terada, *Tetrahedron Lett.*, 1241 (1968). Nitro Compounds. VI. Paper V, A. Hassner, M. J. Haddadin, and P. Catsoulacos, *J. Org. Chem.*, **31**, 1363 (1966). (b) Presented in part before the Colorado–Wyoming Academy of Sciences Meeting, Golden, Colo., April 1964.

(2) J. E. Gurst and C. Djerassi, *J. Amer. Chem. Soc.*, **86**, 5542 (1964).

(3) H. Feuer and R. S. Anderson, *ibid.*, **83**, 2960 (1961); H. Feuer and P. M. Pivawer, *J. Org. Chem.*, **31**, 3152 (1966); N. Kornblum, *Org. Reactions*, **12**, 135 (1962).

(4) A. Hassner and J. M. Larkin, *J. Amer. Chem. Soc.*, **85**, 2181 (1963).

(5) H. Shechter, D. E. Ley, and E. B. Robertson, *ibid.*, **78**, 4984 (1956).

(6) A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 1350 (1964).

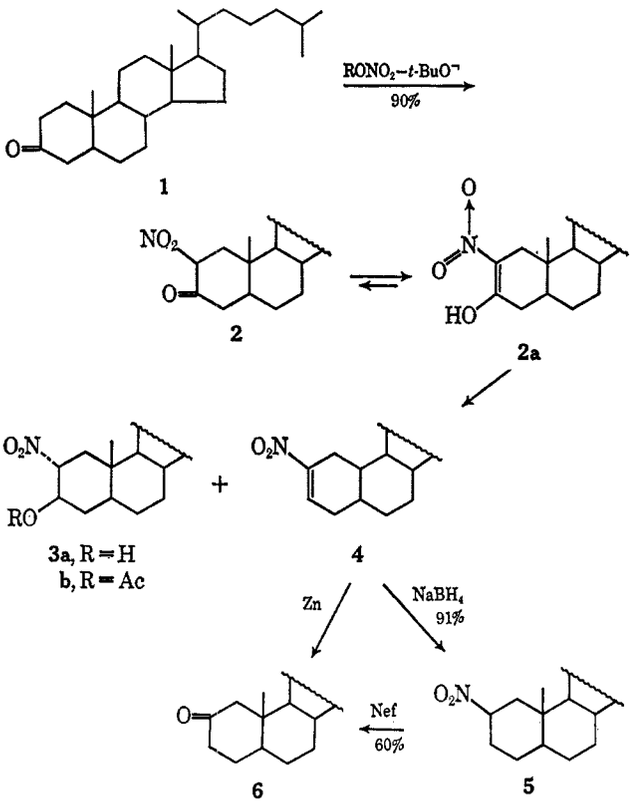
(7) W. E. Noland, *Chem. Rev.*, **55**, 137 (1955); W. E. Noland and R. Libers, *Tetrahedron, Suppl.*, **1**, 23 (1963).

(8) (a) Denotes orientational specificity, A. Hassner, *J. Org. Chem.*, in press. (b) Other steroidal 2-nitro 3-ketones also exist as enols; *cf.* R. E. Schaub, W. Fulmer, and M. J. Weiss, *Tetrahedron*, **20**, 373 (1964).

(9) A. Terada and A. Hassner, *Bull. Chem. Soc. Jap.*, **40**, 1937 (1967).

(10) A. I. Meyers and J. C. Sircar, *J. Org. Chem.*, **32**, 4134 (1967).

SCHEME II



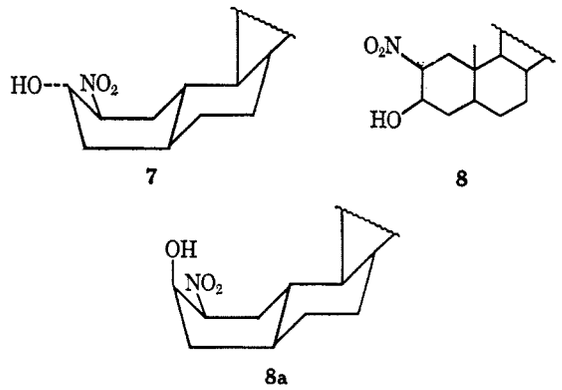
isomer as the kinetic product.[11] Accordingly, it was not surprising that the product of 1,4-hydride reduction of **4** possesses the nitro function in an axial configuration.

2β-Nitrocholestane (**5**) shows saturated nitro absorption at 1550 cm^{-1}, whereas nitro olefin **4** absorbs at 1670 and 1515 cm^{-1}. The half-width of the proton at C-2 of 2β-nitrocholestane (**5**) as measured on an HR-100 instrument is 11 cps, indicative of an equatorial hydrogen. Consistent with this structure assignment is the upfield nmr shift of the C-19 protons to τ 9.32. Shielding of the angular methyl group in steroids by an axial nitro function has been reported[12] and models indictate that the C-19 protons lie in the paramagnetic shielding cone of the N=O bonds. Subtracting the deshielding effect of a 5α-chloro substituent in 5α-chloro-6-nitro steroids[6] one finds a shielding effect of +0.09 ppm for an axial 6β-nitro group on the C-19 methyl group of cholestane.[12] The axial 2β-nitro group in **5** has a similar effect of +0.12 ppm.

When a solution of saturated nitro compound **5** in ethanolic base was acidified with concentrated hydrochloric acid, the ketone **6** was isolated following chromatography in 38% yield, together with its oxime (13%). Oximes have been shown to be occasional by-products in the Nef reaction.[7] If the Nef reaction was carried out by adding the nitronate salt to 17 *N* sulfuric acid in the cold, ketone **6** was isolated pure in 60% yield after chromatography on silica gel.

Nitro alcohol **3a** had major peaks at 3400 (OH) and 1550 cm^{-1} (NO_2). The conformation of the nitro and the alcohol groups in **3a** was shown to be equatorial by an examination of the nmr spectrum. The half-widths of the proton peaks at C-2 and C-3 were each greater than 15 cps indicative of axial protons.[6] The position of the C-19 methyl protons in the nmr spectrum at τ 9.13 also suggested an equatorial (deshielding by −0.08 ppm)[12] rather than an axial nitro function.

On the basis of these data two structures can be considered for the nitro alcohol: 2α-nitrocholestan-3β-ol (**3a**) and 2β-nitrocholestan-3α-ol existing in the boat conformation **7**, as suggested by the referee. Structure **7** is mechanistically easily explained as the minor product resulting from β attack by hydride on **2a** and protonation of the nitronate to yield an axial (2β) nitro function. The boat conformation **7** would allow for relief of 1,3-diaxial NO_2–CH_3 interactions and enable hydrogen bonding between the OH and NO_2 groups. The major products of borohydride reduction of **2a** would then be expected to have been **8** resulting from the more common α attack at C-3 by hydride ion. On work-up or chromatography **8** might have been dehydrated to nitro olefin **4** *via* boat conformation **8a**.



An argument against structure **7** is that there is no obvious reason for **7** to prefer a boat over a chair conformation and the latter is excluded by the nmr data. In fact conformational free energies of a nitro function in cyclohexanes favor the equatorial conformer only by 1 kcal or less,[13] so that relief of the 1,3-nitro–methyl interaction, estimated at 2.5 kcal, is not expected to override the unfavorable boat or twist conformation (ΔG at least 5–6 kcal). If H bonding in **7** plays an important role in favoring this conformation, then its acetate ought to exist as the diaxial conformer. However, acetylation of the nitro alcohol led in good yield to acetate **3b**, the nmr of which indicated equatorial acetate and nitro functions (half-widths of geminal protons = 25 cps). Hence we favor structure **3a** over **7** for the nitro alcohol isolated. The unexpected formation of an equatorial rather than an axial nitro group parallels in this case the borohydride reduction of 6-nitro-5-steroid olefins.[6]

It is obvious that nitro olefin **4** could not have resulted in 40% yield directly by sodium borohydride reduction of **2a** or from nitro alcohol **3a**. When subjected to the conditions of the reduction **3a** gave little nitro olefin, while nitro olefin **4** was shown to be completely converted into **5**. If 1,4 addition of hydride to the conjugated nitro group had less steric requirements than carbonyl reduction, hydride attack at C-3 may have occurred equally well from the β as from the α side.

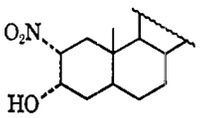
(11) (a) H. E. Zimmerman and T. E. Nevins, *J. Amer. Chem. Soc.*, **79**, 6559 (1957); (b) A. Bowers, M. B. Sanchez, and H. J. Ringold, *ibid.*, **81**, 3702 (1959); see, however, S. K. Malhorta and F. Johnson, *ibid.*, **87**, 5493 (1965).

(12) K. Tori and K. Kuriyama, *Tetrahedron Lett.*, 3939 (1964).

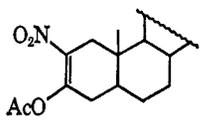
(13) (a) H. Feltkamp and N. C. Franklin, *J. Amer. Chem. Soc.*, **87**, 1616 (1965); (b) W. F. Trager and A. C. Huitric, *J. Org. Chem.*, **30**, 3257 (1965).

β attack would have resulted in the formation of **9** which as an axial alcohol would have lost water on chromatography to give the nitro olefin **4**.

An even better route from **1** to **6** is provided *via* the enol acetate **10**. The latter resulted in quantitative



9

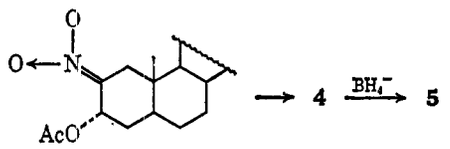


10

yield by treatment of enol **2a** with acetic anhydride–pyridine. The infrared spectrum of **5** is indicative of an enol acetate with strong absorptions at 1770 (C=O of enol acetate), 1660 (conjugated C=C), and 1515 cm^{-1} (unsaturated NO_2). When the nitro enol acetate was treated with sodium borohydride and the mixture acidified, conversion into 2β-nitrocholestane (**5**) was complete. Since cholestan-2-one (**6**) resulted in 60% from a Nef reaction on **5**, this method compares favorably with those developed by others[14] for the synthesis of this 2-keto steroid.

The difference in reactivity toward hydride reduction of enol acetate **10** *vs.* enol **2a** (or ketone **2**) can be rationalized by an increase in positive character at C-3 due to the presence of the electron-withdrawing acetoxy group. On the other hand, the nitro ketone **2** (or its enol **2a**) existing itself as an anion in the alcoholic borohydride solution will certainly be deactivated toward attack by borohydride anion.

Reduction of **10** most likely proceeded *via* an axial acetoxy compound[15] (represented as its anion **11**) from which loss of acetate leading to **4** is expected to be even more facile than loss of water from **9**. When the equatorial 3β-acetoxy-2α-nitrocholestane (**3b**) was treated with sodium borohydride under the conditions of reduction of **10** in the presence or absence of additional base,



11

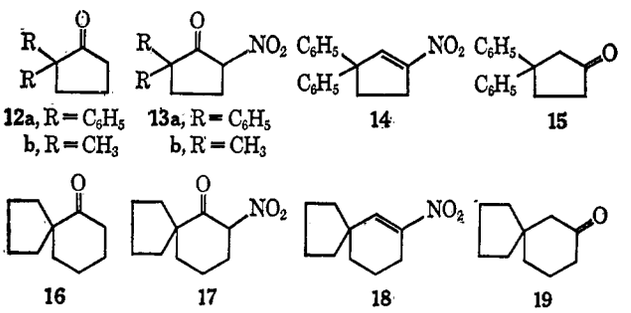
hydrolysis to **3a** occurred but little 2β-nitrocholestane (**5**) was produced. If the structure of the nitro alcohol had been **7** instead of **3a**, its acetate should have been converted quantitatively into **5** *via* **11**. When the reduction of **3b** was conducted in dry tetrahydrofuran, mainly starting material was obtained. These results indicate that the equatorial nitro acetate **3b** or its anion analogous to **11** were not intermediates in the reduction of nitro enol acetate **10** and are consistent with the interpretations made above and with the structure assignment for **3a**. Hydride attack at C-3 on enol acetate **10** apparently occurred preferentially from the β side leading to **11**, because the α side is more shielded by the acetoxy in **10** than by the hydroxy group in **2a**.

Attempts to improve the direct reduction of **2a** to **5** by facilitating elimination from the equatorial alcohol **3a**, *i.e.*, by performing the borohydride reduction at pH 4, met with little success. Warming of 3β-acetoxy-2α-nitrocholestane **3b** with various bases (pyridine, piperidine, collidine) led to elimination product **4** in poor yield—as judged by the appearance of infrared absorption at 1515 cm^{-1} and disappearance of absorption at 1550 cm^{-1}. Less than 50% (by ir spectroscopy) of nitro olefin **4** resulted when a benzene solution of nitro acetate **3b** was allowed to stand over basic alumina for several days. Treatment of nitro alcohol **3a** with *p*-toluenesulfonyl chloride in pyridine resulted in little nitro olefin formation.

Cyclopentanones and Cyclohexanones.—Because eliminations from 3β-hydroxy-2α-nitrocholestane (**3a**) and its derivatives proceeded with difficulty, we subjected some simple cyclic α-nitro ketones to sodium borohydride reduction in the expectation of finding a system in which elimination would occur more readily. In simple cyclopentanes and cyclohexanes, twisting and ring flipping can occur to permit the alcohol to assume an axial conformation (without resorting to boat conformations) even if the initial reduction product is the equatorial alcohol. In basic sodium borohydride solution, the nitro group will presumably exist as a resonance hybrid between the carbanion and its *aci* anion. Elimination of axial hydroxyl ion from this anion might be facile.

2,2-Diphenyl-5-nitrocyclopentanone (**13a**), 2,2-dimethyl-5-nitrocyclopentanone (**13b**), and 7-nitrospiro-[4.5]decan-6-one (**17**) were prepared *via* the potassium *t*-butoxide catalyzed reaction of the ketones **12a**, **12b**, and **16**, respectively, with either isoamyl or *n*-butyl nitrate. The *aci*-nitro salts were first obtained, and acidification gave the nitro ketones (Chart I).

CHART I



12a, R = C_6H_5; **b**, R = CH_3 **13a**, R = C_6H_5; **b**, R = CH_3 **14** **15**

16 **17** **18** **19**

Treatment of these nitro ketones with an excess of sodium borohydride in ethanol, followed by acidification with dilute acid, gave products indicated by infrared spectroscopy to be mixtures of unreacted nitro ketone, nitro alcohols, and nitro olefins. The amount of vinyl nitro compound that could be isolated was always low (about 10%), and no saturated nitro compounds corresponding to **5** were found, even after chromatography. The amount of unreacted spiro nitro ketone **17** after sodium borohydride reduction was considerably less than in the other two cases, indicating the importance of the steric factor in the reduction of the carbonyl group in these neopentyl-type systems. When 3,3-diphenyl-1-nitrocyclopentene (**14**) (isolated by chromatography on alumina) was treated with ethanolic sodium borohydride, no further reaction occurred. This indicates that 1,4 reduction of the vinyl nitro compound is prevented by the bulky groups adjacent to the double bond.

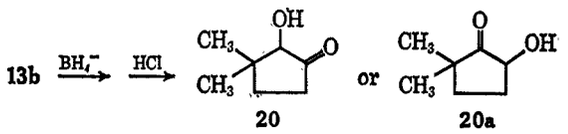
(14) R. L. Clarke, *J. Org. Chem.*, **28**, 2626 (1963).

(15) An alternate possibility involves hydride attack on the acetate carbonyl function and is based on the work of W. G. Dauben and J. F. Eastham, *J. Amer. Chem. Soc.*, **75**, 1718 (1953).

It was found that the amount of unreacted nitro ketone **17** could be diminished substantially by carrying out the sodium borohydride reductions in methanol or in an aqueous solution of the potassium salt of **17**. Evidently the solvent sphere of sodium borohydride in methanol and in water is smaller than its solvent sphere in ethanol, and attack at the carbonyl is less hindered. Lithium borohydride reductions in ethanol offered no advantage over sodium borohydride reduction in water. Even when the reductions were conducted in water, the yields of vinyl nitro compounds were poor. The nitro-olefins were isolated by chromatography. 3,3-Diphenyl-1-nitrocyclopentene (**14**) was characterized, but **18** was an oil and was identified only by its infrared spectrum.

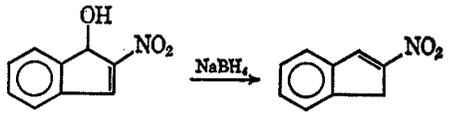
Although sodium borohydride reduction of α-nitro ketones does not directly transpose the carbonyl group as originally envisioned, the desired ketone can be obtained by a two-step process. Reduction of nitro olefins **14** and **18** with zinc in acetic acid gave 3,3-diphenylcyclopentanone (**15**) and spiro[4.5]decan-7-one (**19**), respectively, which were converted into their semicarbazones.

When crude nitro ketone **13b** was treated with sodium borohydride in ethanol, followed by acidification with concentrated hydrochloric acid, the oil which was obtained was shown to be α-ketol **20** (or its isomer **20a**) by its spectra and conversion into the bis-2,4-dinitrophenylhydrazone. Hence, elimination to give a vinyl nitro compound did not occur, but instead the nitro alcohol was converted by a Nef reaction into a ketol. This reaction is probably brought about by the alkaline borohydride reagent.[16] The conversion of α-ketols analogous to **20** with hydriodic acid into 3,3-dimethylcycloalkanones has been reported.[17]



20 **20a**

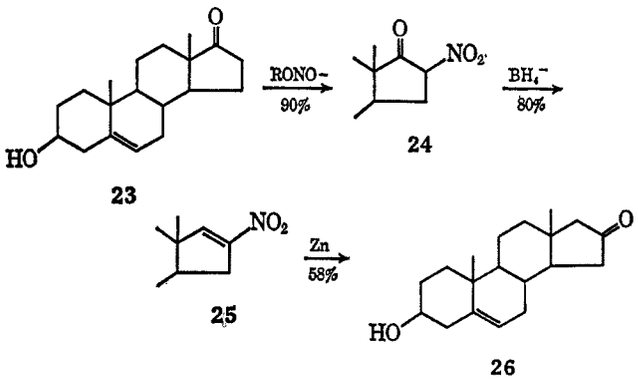
The conversion of 1-indanone into 2-indanone by the route described was not possible because attempts to convert 1-indanone into 2-nitro-1-indanone have been shown to be unsuccessful.[18] 2-Indanone can, however, be obtained from 3-hydroxy-2-nitroindene (**21**). This compound, resulting from condensation of nitromethane with phthalaldehyde, was long thought to be an α-nitro ketone, namely, 2-nitro-1-indanone. Recently, the correct structure was elucidated.[19] Treatment of **21** with sodium borohydride resulted in a 72% yield of 2-nitroindene (**22**). The steps involved are 1,4 reduction of the double bond followed by elimination of water.



21 **22**

2-Nitroindene can be reduced with zinc and acetic acid to 2-indanone.[20]

Steroidal D-Ring Ketones.—The reaction sequence proceeding *via* a nitro olefin was also applied to the transposition of a 17-keto to a 16-keto steroid. Treatment of 3β-hydroxy-16-nitro-5-androsten-17-one (**24**), available from ketone **23** in 90% yield,[4] with excess sodium borohydride in ethanol gave predominantly 3β-hydroxy-16-nitroandrostane-5,16-diene (**25**). Conversion of **25** into 3β-hydroxy-5-androsten-16-one (**26**) was accomplished by zinc–acetic acid reduction. Although the over-all yield from 3β-hydroxy-5-androsten-17-one (**23**) is about 40%, which is slightly lower than the yield claimed by Huffman, *et al.*,[21] the new method is more convenient and requires fewer steps. Here as in **14** hydride reduction of the vinyl nitro compound **25** was sterically unfavorable and no saturated nitro steroid was found. The different reactivity of nitro ketones **24** and **13b** toward borohydride reduction may be attributable to the greater rigidity of the D ring as contrasted to the flexibility of the monocyclic system.



23 **24** **25** **26**

Experimental Section[22]

2-Nitrocholestan-3-one (2) or 2-Nitro-2-cholesten-3-ol (2a).—Potassium metal (1.75 g) was dissolved by heating *t*-butyl alcohol (110 ml) in a nitrogen atmosphere. The potassium *t*-butoxide solution was cooled in a water bath to 17°, and 3.00 g of cholestan-3-one was dissolved in it. *n*-Butyl nitrate (3.1 ml) was added with stirring during a 5-min period. The yellow solution was allowed to stand an additional 3.75 hr in the bath maintained between 17 and 20°. It was diluted with 400 ml of ice water, and after stirring for 10 min the yellow precipitate was filtered off and allowed to air dry. The yield of potassium salt was 3.31 g (90%). The product does not melt below 300°. Major peaks in the infrared spectrum are at 1640 (carbonyl), 1385, broad peak from 1300 to 1220, and 1030 cm^{-1}.

A portion of the potassium salt was dissolved in acetic acid, and the solution was warmed on a steam bath. Warm water was slowly added until the solution became faintly turbid and finally white needles melting at 133.5–136° were obtained. Recrystallization (Skellysolve F) yielded white needles: mp 135–136.5°; ir 1740 (weak), 1610, 1550 (weak), 1520, and 1400 cm^{-1} (lack of a strong carbonyl peak at 1740 suggests that **2** exists mainly in the enol form); nmr τ 9.18 (s, C-19), 9.32 (s, 3, C-18). The compound gives a positive ferric chloride test.

Anal. Calcd for $C_{27}H_{45}NO_3$: C, 75.13; H, 10.51; N, 3.25; O, 11.12. Found: C, 75.35; H, 10.29; N, 3.04; O, 11.10.

(16) S. V. Kessar, Y. P. Gupta, and A. L. Rampal, *Tetrahedron Lett.*, 4319 (1966).

(17) W. Reusch and R. LeMahieu, *J. Amer. Chem. Soc.*, **86**, 3068 (1964).

(18) R. D. Campbell and C. L. Pitzer, *J. Org. Chem.*, **24**, 1531 (1959).

(19) F. W. Lichtenthaler, *Tetrahedron Lett.*, 775 (1963); H. H. Baer and B. Achmatowicz, *Angew. Chem.*, **76**, 50 (1964).

(20) O. Wallach and E. Beschke, *Ann.*, **336**, 1 (1904).

(21) M. N. Huffman, M. H. Lott, and A. Tillotson, *J. Biol. Chem.*, **218**, 565 (1956).

(22) All melting points were taken on a Fisher-Johns melting point block and are uncorrected. Infrared spectra were obtained in KBr disks on a Beckman IR-5 spectrometer, whereas nmr spectra were run in 10% solutions of chloroform on a Varian A-60 spectrometer using tetramethylsilane as an internal standard. Elemental analysis were performed by A. Bernhardt, Mülheim, Germany, and Huffman Laboratories, Denver, Colo.

2α-Nitrocholestan-3β-ol (3a).—To a suspension of 0.50 g of 2-nitro-2-cholesten-3-ol (**2a**) in 40 ml of 95% ethanol, there was added 0.65 g of sodium borohydride. The mixture was stirred occasionally and allowed to stand for 1 hr. The solution was acidified dropwise with 1.5 *N* hydrochloric acid. The white precipitate was removed by filtration and washed (H_2O): yield 0.5 g; mp 104–126°. The infrared spectrum was indicative of a nitro alcohol.

The material was chromatographed on 12.5 g of Woelm neutral alumina, activity grade I, and eluted with solvents of successively increasing polarity. A few milligrams of 2-cholestanone (**6**) (by infrared), mp 115–122°, was eluted with 30% ether–70% benzene. The only other material, 2α-nitrocholestan-3β-ol (**3a**), was obtained on terminal elution with 1% methanol–99% ether. The waxy solid was recrystallized three times from 95% ethanol to give white crystals: mp 140–141.5°; ir 3400, 1550, and 1350 cm^{-1}; nmr broad peaks centered at 5.5 (triplet of doublets, 1, J = 10 and 4 cps), 5.9 (t, 1, $W_{1/2}$ = 20 cps), 7.37 (s, 1, OH), 9.13 (s, C-19), 9.36 (s, 3, C-18).

Anal. Calcd for $C_{27}H_{47}NO_3$: C, 74.78; H, 10.92; N, 3.23. Found: C, 74.63; H, 11.00; N, 3.40.

2α-Nitro-3β-acetoxycholestane (3b).—Acetic anhydride (3 ml) was added to a solution of 2α-nitrocholestan-3β-ol (**3a**, 0.40 g) in 1.5 ml of dry pyridine. The solution was allowed to stand at room temperature for 16 hr, after which time it was diluted with 40 ml of cold water. A precipitate (0.42 g) of **3b**, mp 61–121°, was obtained. A portion of the white solid was recrystallized from methanol to yield white crystals: mp 139–140°; ir 1740, 1550, 1375, and 1230 cm^{-1}; nmr broad multiplets centered at τ 4.8 ($W_{1/2}$ = 25 cps) and 5.2 ($W_{1/2}$ = 25 cps), 8.01 (s, 3, OCO-CH_3), 9.11 (s, C-19 CH_3), 9.36 (s, 3, C-18).

Anal. Calcd for $C_{29}H_{49}NO_4$: C, 73.22; H, 10.38; N, 2.94. Found: C, 73.45; H, 10.61; N, 3.11.

2-Nitro-3-acetoxy-2-cholestene (10).—To a suspension of 0.48 g of 2-nitro-2-cholesten-3-ol (**2a**) in 8 ml of acetic anhydride, there was added 1.2 ml of pyridine. The stoppered flask was shaken for 10 min. A white crystalline solid precipitated. It was filtered off, washed with a little acetic anhydride, and allowed to air dry: yield 0.34 g; mp 147–148°.

The filtrate was poured into 60 ml of ice water. After the acetic anhydride had hydrolyzed, the precipitated white solid was collected by filtration and washed with water. The product (mp 112–120°) weighed 0.17 g. The infrared spectrum of this product was virtually identical with that of the above product. The total yield was 0.51 g (97%): ir 1770, (C=O), 1660, (C=C), 1515, (conjugated NO_2), 1330 (NO_2), and 1178 cm^{-1} (C—O).

Anal. Calcd for $C_{29}H_{47}NO_4$: C, 73.53; H, 10.00; N, 2.96. Found: C, 73.58; H, 10.14; N, 3.11.

2β-Nitrocholestane (5). A. From 2-Nitro-3-acetoxy-2-cholestene (10).—To a suspension of 0.32 g of 2-nitro-3-acetoxy-2-cholestene (**10**) in 20 ml of ethanol, there was added 0.30 g of sodium borohydride. Gas evolution commenced and material rapidly dissolved. The solution was allowed to stand at room temperature for 15 hr and was then diluted with 60 ml of water. The faintly turbid solution was slowly acidified with 2 *N* HCl. The white solid that precipitated was washed (H_2O) and allowed to air dry, yield 0.30 g (100%). One crystallization from aqueous ethanol and another from methanol yielded white crystals: mp 116–117.5°; ir 1540 and 1380 cm^{-1}; nmr broad peak at 5.60 ($W_{1/2}$ = 11 cps), 9.32 (s, 3, C-19), 9.37 (s, 3, C-18).

Anal. Calcd for $C_{27}H_{47}NO_2$: C, 77.64; H, 11.34; N, 3.35. Found: C, 77.55; H, 11.26; N, 3.51.

B. From 2-Nitro-2-cholestene (4).—To a suspension of 0.12 g of 2-nitro-2-cholestene (**4**) in 10 ml of ethanol, there was added 0.12 g of sodium borohydride. Complete solution was rapidly achieved. The solution was allowed to stand at room temperature for 24 hr, and was then diluted with 75 ml of water. Dropwise acidification (2 *N* HCl) precipitated a white solid, yield 0.11 g (91%). Recrystallization from methanol gave white crystals, mp 119–122°. The infrared spectrum is identical with that of material prepared by procedure A above.

2-Nitro-2-cholestene (4). A. From 2-Nitro-2-cholesten-3-ol (2a).—To a suspension of 3.0 g of enol **2a** in 120 ml of 95% ethanol was added 1.95 g of sodium borohydride and the mixture stirred for 1.5 hr at room temperature. The solution was then carefully acidified to pH 3–4 (1.0 *N* HCl) and the resulting precipitate was filtered off, washed (H_2O), and air dried: yield 3.1 g; ir 3300, 1670, 1545, and 1520 cm^{-1}, indicating a mixture of nitro alcohol and nitro olefin.

This material was chromatographed on silica gel (Grace, grade 62, 60–200 mesh) with a ratio of 1.0 g of material to 20 g of silica gel. With benzene as eluent, the first material to come off the column was 2-nitro-2-cholestene (**4**) (recrystallized from methanol, mp 129–132°), followed by 2α-nitro-3β-cholestanol (**3a**) (mp 138–140°). A trace of the enol **2a** was obtained along with a contaminant of a saturated nitro compound in the nitro-olefin. Recovery from the column was 65%, with a yield of 1.072 g of 2-nitro-2-cholestene (34%) and 0.735 g of 2α-nitro-3β-cholestanol (24%), based on starting material. The infrared spectrum of **4** shows peaks at 1670, 1515, and 1335 cm^{-1}, and was identical with that of authentic **4**.

B. From Treatment of 2α-Nitro-3β-acetoxycholestane (3b) with Alumina.—2α-Nitro-3β-acetoxycholestane (**3b**) was prepared by treatment of 1.17 g of 2α-nitrocholestan-3β-ol with 7 ml of acetic anhydride and 5 ml of pyridine on a steam bath for 0.5 hr and at room temperature for 13 hr. The product so obtained contained approximately 10% of the vinyl nitro compound **4** as indicated by the relative magnitude of the peaks at 1550 (saturated nitro), and 1515 cm^{-1} (vinyl nitro).

This material was dissolved in 20 ml of dry benzene, and 6.5 g of Merck alumina was added. The brown solution was allowed to stand over alumina for 70 hr. The alumina was filtered off, and the filtrate was evaporated to dryness *in vacuo* at 40°. The amount of vinyl nitro compound in the yellow oil which remained was increased considerably, as indicated by the increase in the absorption at 1515 cm^{-1}. Chromatography on alumina afforded 2-nitro-2-cholestene with an infrared spectrum identical with that of **4** prepared by procedure A. Recrystallization from methanol gave white crystals, mp 119–125°.

Cholestan-2-one (6). A. From 2-Nitro-2-cholesten-3-ol (2a).—To a suspension of 2.25 g of nitro enol **2a** in 60 ml of ethanol, there was added 3.25 g of sodium borohydride. The mixture was allowed to stand at room temperature for 24 hr, and then was diluted with excess water. Concentrated hydrochloric acid was added, and the resulting sticky tan solid was removed by filtration and washed with water. The yield of this material was 2.10 g. A portion (1.23 g) of the material was chromatographed on 30 g of Woelm neutral alumina, activity grade I. Elution with 45% Skellysolve F–55% benzene gave a few milligrams of a saturated nitro compound, mp 150–153°. It had a strong infrared absorption peak at 1560 cm^{-1}, but was not identical with 2β-nitrocholestane. This material was not further identified.

From benzene–ether fractions, there was eluted a total of 0.17 g (13%) of cholestan-2-one (**6**). Recrystallization from methanol gave a product melting at 127–129°. When mixed with 3-cholestanone, mp 127–129°, it melted at 103–124°. The reported melting point of 2-cholestanone[23] is 130.5–131.5°. The infrared spectrum shows a strong carbonyl peak at 1710 cm^{-1}.

B. By the Nef Reaction of 2β-Nitrocholestane (5). I.—To a solution of 0.22 g of potassium hydroxide in 18 ml of 95% ethanol and 2 ml of water, there was added 0.33 g of 2β-nitrocholestane (**5**). The suspension was warmed briefly and allowed to stand for 0.5 hr in order to completely dissolve the solid. After the addition of 15 ml of water, the solution remained clear. Hydrochloric acid (11 ml) was added in one portion. The white flocculant solid which precipitated was removed by filtration and washed with water. When dry, the solid, 0.24 g, was light green in color.

Chromatography of 0.17 g of the product on 4.8 g of Woelm neutral alumina, activity grade I, resulted in the isolation of 3 mg of the same saturated nitro compound as was obtained in procedure A above, as well as 83 mg (38%) of 2-cholestanone (**6**). The melting point of the largest fraction (80 mg) was 129–130°.

When elution was continued with 3% methanol–97% ether, 29 mg of 2-cholestanone oxime was obtained. The melting point was 174–178°. Recrystallization from aqueous ethanol and then from methanol–chloroform gave a product melting at 196–198° (lit.[24] mp 200°). On admixture with a sample prepared from 2-cholestanone and hydroxylamine, no melting point depression was noted.

II.—A solution of 0.07 g of potassium hydroxide in 5.5 ml of 95% ethanol and 1.0 ml of water was added to 93.4 mg of 2β-nitrocholestane (**5**) and stirring was continued with some warming for 40 min. No solid remained after this time. This was

(23) L. Ruzicka, Pl. A. Plattner, and M. Furrer, *Helv. Chim. Acta*, **27**, 524 (1944).

(24) A. Furst and Pl. A. Plattner, *ibid.*, **32**, 275 (1949).

cooled to −15° and added dropwise with stirring to 10.5 ml of 17 *N* sulfuric acid (5.5 ml of water and 5.0 ml of concentrated H_2SO_4). The precipitate was filtered, washed (H_2O, CH_3OH), and dried under vacuum at 25°.

The material was chromatographed on 4 g of Grace silica gel and eluted with 50% petroleum ether (bp 40–60°)–benzene. Nitro-containing material came off first, followed by 2-cholestanone (**6**). The yield of the latter was 52 mg (60%), mp 129–130°. Its ir spectrum was identical with that of **6** prepared as described above.

Reaction of 2α-Nitrocholestan-3β-ol (3a) with *p*-Toluenesulfonyl Chloride. Attempted Elimination of the Resulting Tosylate.—Crude 2α-nitrocholestan-3β-ol (**3a**, 0.50 g) was exposed to 3.2 ml of dry pyridine and 0.40 g of *p*-toluenesulfonyl chloride at room temperature for 12 hr; the mixture was then diluted with 70 ml of water. The crude product (0.5 g) showed no hydroxy peak in the infrared spectrum. There was a strong peak at 1545 cm^{-1} (saturated nitro) and a peak about half as intense at 1515 cm^{-1} (vinyl nitro). No further reaction occurred on exposure of the above product to collidine for 17 hr.

When 0.36 g of the above mixture was stirred at 30° for 44 hr in a solution of 12 ml of dimethyl sulfoxide and 0.5 ml of collidine, 0.10 g of crude 2-nitro-2-cholestene (**4**), mp 120–125°, precipitated. Dilution of the filtrate with excess water resulted in isolation of a gummy solid containing a preponderance of saturated nitro compound as indicated by the strong infrared absorption at 1550 cm^{-1}.

When a solution of 0.40 g of the crude tosylate (prepared as above) dissolved in a solution of 0.2 ml of concentrated hydrochloric acid and 10 ml of glacial acetic acid was allowed to stand for 8 days, the product obtained consisted of a mixture of 2α-nitro-3β-acetoxycholestane (**3b**) and 2-nitro-2-cholestene (**4**). The infrared absorption at 1515 (conjugated nitro) was small compared with that at 1550 (saturated nitro) and 1740 cm^{-1} (acetoxy carbonyl).

Attempted Reaction of 2α-Nitro-3β-acetoxycholestene (3b) with Bases.—2α-Nitrocholestan-3β-ol (**3a**) was treated with acetic anhydride and pyridine either at room temperature for 68 hr, or at 90° for 4 hr. Treatment of the resulting 2α-nitro-3β-acetoxycholestane (**3b**) for 71 hr with piperidine followed by acidification and chromatography on neutral alumina failed to give any 2-nitro-2-cholestene. Acetate **3b** was recovered largely unchanged on attempted sodium borohydride reduction in dry tetrahydrofuran.

2,2-Diphenyl-5-nitrocyclopentanone (13a).—2,2-Diphenylcyclopentanone (**12a**) was prepared by the method of Kulp, *et al.*[25] Potassium metal (1.25 g) was dissolved in 55 ml of *t*-butyl alcohol by heating under nitrogen. The solution was cooled to room temperature, and 2.5 g of 2,2-diphenylcyclopentaone (**12a**) was added. When the latter had nearly dissolved (15 min), the nitrogen flow was stopped, and 2.2 ml of isoamyl nitrate was added. The straw yellow solution was allowed to stand at room temperature for 9 hr. It was diluted with 200 ml of water, and the resultant solution was extracted with three 50-ml portions of chloroform. Partial evaporation of the chloroform gave crops of 1.15 g and 0.48 g of the *aci*-nitro ketone salt, mp 270–285° dec. Complete evaporation of the solvent gave an additional 1.69 g of the salt. The infrared spectrum shows strong absorption at 1650 and a shoulder at 1600 cm^{-1}.

To a solution of 1.03 g of the above potassium salt in 25 ml of water, there was added 16 ml of 20% sodium potassium tartrate. Addition of 1 ml of concentrated HCl resulted in the precipitation of 1.0 g of a white solid; the ir spectrum was indicative of a nitro ketone (1740 and 1540 cm^{-1}).

A portion of this crude product was boiled in 95% ethanol for 5 min, and material which remained insoluble (tartaric acid residue) was removed by filtration. The filtrate deposited colorless needles of **13a**: mp 125–126°; ir 1740, 1545, 1365, as well as strong peaks in the 650–820-cm^{-1} region.

Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.48; ; H, 5.41; N, 5.11.

1-Nitro-3,3-diphenylcyclopentene (14).—Sodium borohydride (1.25 g) was added to a suspension of 0.65 g of 2,2-diphenyl-5-nitrocyclopenanone (**13a**) in 35 ml of ethanol. Gas began evolving, and complete solution was rapidly achieved. The solution was allowed to stand at room temperature for 37 hr. It was diluted with 75 ml of water and acidified dropwise with dilute hydrochloric acid. The turbid suspension was extracted with ether, and the ether solution was dried ($MgSO_4$). A viscous yellow oil was obtained after evaporation of the solvent. The ir spectrum showed peaks characteristic of a ketone, an alcohol, a conjugated nitro, and a saturated nitro compound.

The oil was dissolved in 8 ml of 60% benzene–40% Skellysolve F, and adsorbed on 12.5 g of Woelm neutral alumina, activity grade I. Elution with mixtures of Skellysolve F (bp 30–60°) and benzene, and with 10% ether–90% benzene, gave 67 mg of oils which later solidified. A portion was crystallized from aqueous ethanol to give pale yellow crystals of 1-nitro-3,3-diphenylcyclopentene (**14**): mp 75–76°; ir 1640 (C=C), 1595 (phenyl), 1510 and 1350 cm^{-1} (vinyl NO_2).

Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.21; H, 5.72; N, 5.17.

3,3-Diphenylcyclopentanone (15).—To a solution of 50 mg of 1-nitro-3,3-diphenylcyclopentene (**14**) in 5 ml of 90% aqueous acetic acid, there was added 250 mg of zinc dust. The mixture was refluxed for 7 hr. While the solution was hot, unreacted zinc and zinc acetate were removed by filtration. The filtrate was diluted with 20 ml of water. The resulting suspension was extracted with two 25-ml portions of ether and the combined ethereal extracts were washed with saturated Na_2CO_3 until gas effervescence ceased. The solvent was removed from the dried ($MgSO_4$) solution by evaporation on a steam bath. A yellow oil (30 mg) remained; the ir spectrum at 1735 and 1595 cm^{-1} was indicative of 3,3-diphenylcyclopentanone (**15**); there was no nitro absorption.

From the oil and semicarbazide hydrochloride in the presence of sodium acetate, there was prepared the semicarbazone of **15**, mp 201–203°. (The melting point of 2,2-diphenylcyclopentanone semicarbazone is 245°.)[25]

Anal. Calcd for $C_{18}H_{19}N_3O$: C, 73.69; H, 6.53; N, 14.33. Found: C, 73.64; H, 6.54; H, 6.54; N, 13.91.

7-Nitrospiro[4.5]decan-6-one (17).—Treatment of 2.5 g of potassium metal in 160 ml of *t*-butyl alcohol with 7.3 g of spiro[4.5]decan-6-one (**16**)[26] and 7.9 ml of isoamyl nitrate for 4 hr at 25°, as described for **13a**, led to 8.09 g of the potassium salt of *aci*-7-nitrospiro[4.5]decan-6-one, washed with ether.

A portion of the salt was dissolved in water and then acidified with 6 *N* hydrochloric acid. The resulting suspension was extracted with chloroform, and the chloroform solution was dried ($MgSO_4$). After the solvent was evaporated at room temperature, a crystalline solid, mp 80–83°, remained. It was crystallized (CCl_4) to give white crystals of **17**: mp 80–81.5°; ir 1710, 1545, and 1395 cm^{-1}.

Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.89; H, 7.67; N, 7.10. Found: C, 61.04; H, 7.58; N, 7.21.

Spiro[4.5]decan-7-one (19).—A solution of 4.00 g of the potassium salt of **17** and 2.2 g of sodium borohydride in 75 ml of water was kept at room temperature for 36 hr and worked up as described for **14**. Chromatography on 11.5 g of Merck acid-washed alumina and elution with 25 ml of 90% benzene–10% Skellysolve F gave 2.45 g of a yellow oil the infrared spectrum of which indicated it to be a mixture of a nitro alcohol and a nitro olefin. The oil thus obtained was adsorbed on 16.5 g of Woelm neutral alumina, activity grade I, and rechromatographed. Elution with 25 ml of 60% benzene–40% Skellysolve F gave 1.07 g of an oil indicated by infrared spectroscopy to be much richer in vinyl nitro compound (1515 cm^{-1}).

This oil was rechromatographed on 16.5 g of Woelm neutral alumina, activity grade I. From the first 50 ml of 82% Skellysolve F–18% benzene there was obtained 220 mg (7.2%) of a colorless oil, indicated by infrared spectroscopy to be 7-nitrospiro[4.5]-6-decene (**18**). Principal absorption peaks were at 1650 (C=C), 1515 (vinyl NO_2), and 1335 cm^{-1}.

Later eluents of all three chromatographies gave predominantly a nitro alcohol (by infrared spectroscopy) presumed to be 7-nitrospiro[4.5]decan-6-ol. Room temperature acetylation of the latter with acetic anhydride and pyridine resulted in the formation of a nitro acetate (by infrared spectroscopy), also as an oil. Treatment with base gave no olefin.

A solution of 225 mg of crude 7-nitrospiro[4.5]6-decene (**18**), obtained as described above, in 10 ml of 90% acetic acid was refluxed for 11 hr with 750 mg of zinc dust and worked up as

(25) S. S. Kulp, V. B. Fish, and N. R. Easton, *J. Med. Chem.*, **6**, 516 (1963).

(26) M. Mousseron, H. Christol, and F. Plenat, *Compt. Rend.*, **245**, 1281 (1957).

described for **15**. A yellow-brown oil of ketone **19** (150 mg, 80%) resulted: ir 1705 and 1225 cm^{-1} (weak).

From 3 drops of the ketone **19** there was prepared a semicarbazone, using 100 mg of semicarbazide hydrochloride and 150 mg of sodium acetate. The resulting product, 66 mg, mp 208–210°, was recrystallized from 80% aqueous ethanol, white crystals, mp 215–217°. The semicarbazone of spiro[4.5]decan-6-one (**16**) melts at 190–193°.[27]

Anal. Calcd for $C_{11}H_{19}N_3O$: C, 63.13; H, 9.15; N, 20.08. Found: C, 63.90; H, 9.13; N, 20.01.

Reaction of 2,2-Dimethylcyclopentanone (12b) with Isoamyl Nitrate. Sodium Borohydride Reduction of the Resultant Product.—The solution obtained on nitration of 3.6 g of 2,2-dimethylcyclopentanone (**12b**)[28] with 8.0 ml of isoamyl nitrate and potassium *t*-butoxide at 0° (see preparation of **2a**) was acidified with dilute hydrochloric acid. A green oil separated and was withdrawn. The yellow aqueous solution was extracted with three 30-ml portions of chloroform and the combined chloroform extracts were extracted with three 35-ml portions of 5% KOH. The basic solution was acidified (HCl) and extracted with three 30-ml portions of ether. The ether solution was dried ($MgSO_4$) and the solvent was removed *in vacuo*. An orange oil, showing nitro absorption at 1550 cm^{-1} and carbonyl absorption at 1730 cm^{-1}, remained.

The oil was dissolved in 15 ml of ethanol, and reduced with 1.75 g of sodium borohydride at 25° for 18 hr. Work-up with hydrochloric acid yielded a yellow-orange oil, 0.8 g; ir ($CHCl_3$) showed a broad –OH absorption, a strong carbonyl peak at 1725 cm^{-1}, but no nitro absorption. It is presumed to be a mixture of 2,2-dimethyl-5-hydroxycyclopentanone (**20**), and 3,3-dimethyl-2-hydroxycyclopentanone (**20a**) or the corresponding diosphenol. The product showed no appreciable absorption in the ultraviolet.

From the above product and 2,4-dinitrophenylhydrazine, there was prepared the bis-2,4-dinitrophenylhydrazone of 3,3-dimethylcyclopentane-1,2-dione as red-orange crystals, mp 294–295°, after successive recrystallizations from 95% ethanol and from chloroform.

Anal. Calcd for $C_{19}H_{18}N_8O_8$: C, 46.91; H, 3.73; N, 23.04. Found: C, 46.96; H, 4.11; N, 22.81.

2-Nitroindene (22).—To a solution of 0.12 g of 2-nitro-2-inden-1-ol (**21**)[18] in 7 ml of ethanol, there was added 0.15 g of sodium borohydride. The yellow color of the solution rapidly disappeared, and gas evolved as the reaction proceeded. After 25 hr at room temperature, the mixture was acidified with 4 ml of concentrated hydrochloric acid. Excess water was added, whereupon 0.08 g (72%) of **22** as a yellow solid, mp 141–143°, was deposited (lit.[18] mp 140–141°): uv max (C_2H_5OH) 337 mμ (ε 11,200) and 240 mμ (ε 6500) [lit.[18] uv max (C_2H_5OH) 337 mμ (ε 11,000), 239 mμ (ε 6200), and 233 mμ (ε 6300)].

3β-Hydroxy-16-nitro-5,16-androstadiene (25).—To a solution of 2.00 g of 3β-hydroxy-16-nitro-5-androsten-17-one (**24**)[4] in 50 ml of ethanol, there was added 1.0 g of sodium borohydride. A gelatinous slurry resulted. The mixture was allowed to stand for 14 hr, at which time another 25 ml of ethanol and 0.75 g of sodium borohydride were added. The slurry was allowed to stand for an additional 52 hr. Water (125 ml) was added, and the white material which remained insoluble was removed by filtration. This material decomposed at 215–220°, but never completely melted even at 300°.

The aqueous filtrate was acidified dropwise with 1 *N* hydrochloric acid. A white solid precipitated: 1.12 g; mp 176°; ir 3400, 1615, 1512, and 1350 cm^{-1}. Recrystallization from cyclohexane–benzene gave white crystals of **25**, mp 187–189°.

Anal. Calcd for $C_{19}H_{27}NO_3$: C, 71.89; H, 8.57; N, 4.41. Found: C, 72.37; H, 8.53; N, 4.36.

An additional 0.12 g of crude **25** was obtained as a second crop from the filtrate; however, this material also showed weak infrared absorption at 1545 cm^{-1}.

The high melting material which was first removed from the aqueous solution was dissolved in water, and dilute hydrochloric acid was added. The solution was allowed to stand overnight, and the pink solid (0.5 g) was removed by filtration. The infrared spectrum was identical with that of **25** obtained above.

3β-Hydroxy-5-androsten-16-one (26).—Zinc dust (0.75 g) was added to a solution of 0.62 g of 3 β-hydroxy-16-nitroandrosta-5,16-diene (**25**) in 12 ml of 90% acetic acid. The mixture was refluxed for 1.5 hr, and the solution was filtered hot to remove unreacted zinc and zinc acetate. The filtrate was diluted with 50 ml of water. After 2 hr, a brown solid had precipitated. The yield of material indicated by infrared to be 3β-hydroxy-5-androsten-16-one (**26**) was 0.28 g, mp 104–113°. From the filtrate there was obtained a second crop (0.06 g) of **26**, mp 125–134°.

Two recrystallizations from aqueous methanol gave ketone **26**, mp 159–161°, identical with authentic material (lit.[21] mp 163.5–165°).

From 0.10 g of crude **26** and acetic anhydride and pyridine, there was prepared 0.10 g of 3β-acetoxy-5-androsten-16-one. It was dissolved in 50% benzene–50% hexane and filtered through 1.5 g of Woelm neutral alumina, activity grade I. Removal of the solvent resulted in material melting at 103–120°. Recrystallization from aqueous methanol gave crystals, mp 124–126° (lit.[21] mp 127.5–128°).

(27) F. Salmon-Legagneur and C. Neveu, *Bull. Soc. Chim. Fr.*, 929 (1956).
(28) C. F. Wilcox, Jr., and M. Mesirov, *J. Org. Chem.*, **25**, 1841 (1960).

Registry No.—2, 16020-88-5; **3a**, 16020-89-6; **3b**, 16020-90-9; **4**, 16020-91-0; **5**, 16020-92-1; **6**, 16020-93-2; **10**, 16020-94-3; **13a**, 16020-95-4; **14**, 16020-96-5; **15**, 16020-97-6; **17**, 16020-98-7; semicarbazone of **19**, 16020-99-8; bis-2,4-dinitrophenylhydrazone of 3,3-dimethylcyclopentane-1,2-dione, 16021-00-4; **22**, 16021-01-5; **25**, 16021-03-7; **26**, 5088-64-2.

Acknowledgment.—This investigation was supported by U. S. Public Health Service Grant CA-04474 from the National Cancer Institute.