II and 23% β-bromo ketone IV. After recrystallization from methanol the infrared spectrum was superimposable upon that of an authentic sample of the α,β-unsaturated ketone II, $\gamma_{C=O}$ 1649/91. The melting point was raised to 66–68°.

Product Studies on the Addition of Piperidine to the α,β-Unsaturated Ketone II.—A 1.12-g. sample of the α,β-unsaturated ketone II was dissolved in 10 ml. of piperidine and allowed to stand at room temperature for 25 days. The reaction mixture was poured into water and ether extracted. The ether solution was washed several times with distilled water, dried over anhydr. magnesium sulfate and dry hydrogen chloride was bubbled into the solution. The precipitate formed, 1.18 g., was found to be the hydrochloride of the β-aminoketone III contaminated with about 5% of piperidine hydrochloride, m.p. 192–195° dec. The infrared spectrum showed only one carbonyl peak, $\gamma_{C=O}$ 1669 cm.$^{-1}$.

Anal. Calcd. for $C_{24}H_{30}ONCl$: C, 75.11; H, 7.82; N, 3.65. Calcd. for 95.2% $C_{24}H_{30}ONCl$ and 4.8% $C_5H_{12}NCl$: C, 73.87; H, 7.92; N, 4.04. Found: C, 73.88; H, 7.88; N, 4.04.

A portion of the hydrochloride was dissolved in water and potassium carbonate solution added; a white precipitate was ether extracted. The ether solution was washed several times with distilled water and dried over anhydr. magnesium sulfate. Evaporation of the ether left a white solid, m.p. 105–118°. The infrared spectrum had $\gamma_{C=O}$ 1677/85 due to the β-aminoketone III and $\gamma_{C=O}$ 1649/39 due to a little admixed α,β-unsaturated ketone II, presumably formed by decomposition of the β-aminoketone III during its isolation. A portion of the product was recrystallized from methanol, m.p. 120–123.5°, but was not analyzed.

4-Biphenylyl 2-Bromocyclohexyl Ketone (IV).—A 0.37-g. sample of the α,β-unsaturated ketone II was dissolved in 50 ml. of ether, saturated with dry hydrogen bromide, and then allowed to stand for 48 hours prior to evaporation to dryness. The residue was recrystallized from acetone–water and washed well with water. The crude β-bromoketone IV, 0.32 g. (65% yield), was recrystallized from carbon tetrachloride–petroleum ether solution; m.p. 124°, λ_{max} 287 mμ (ε 23,400), $\gamma_{C=O}$ 1681/82 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{19}BrO$: C, 66.48; H, 5.58; Br, 23.28. Found: C, 66.35; H, 5.90; Br, 23.19.

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[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN, MADISON, WIS., AND OF STANFORD UNIVERSITY, STANFORD, CALIF.]

The Acid-catalyzed Reaction of Diazomethane with Some α,β-Unsaturated Ketones

BY WILLIAM S. JOHNSON, M. NEEMAN, S. P. BIRKELAND AND N. A. FEDORUK

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α,β-Unsaturated ketones have been shown to react with diazomethane, in the presence of either fluoboric acid or boron trifluoride catalyst, to give linear homologation. The main product is that formed by insertion of a methylene group between the carbonyl group and the α-carbon atom holding the double bond to yield a β,γ-unsaturated ketone. Hitherto the uncatalyzed reaction was known either to give pyrazolines or to fail altogether. Thus the following transformations were effected: Δ⁴-cholestene-3-one to A-homocholestenone (I); testosterone propionate to A-homotestosterone propionate (VII). Preliminary studies on the homologation of benzalacetone and benzalacetophenone are also described.

The acid-catalyzed reaction of diazomethane with an α,β-unsaturated ketone to effect linear homologation is new.[1,2] Previously it was known that treatment of α,β-unsaturated ketones with diazomethane gave either pyrazoline derivatives[3] or no reaction at all.[4]

The discovery that fluoboric acid or boron trifluoride catalyzes a reaction of diazomethane with α,β-unsaturated ketones was made in our laboratories inadvertently when testosterone was submitted to the treatment with the view to preparing the 17-methyl ether.[5] The reaction mixture contained, in addition to the expected product,[5] an appreciable amount of material exhibiting unconjugated carbonyl absorption in the infrared spectrum.

In order to elucidate the nature of this new ketonic product, we first turned our attention to a simpler system, namely Δ⁴-cholestene-3-one. This ketone failed to react with diazomethane under normal conditions, but in the presence of a small amount (about 6 mole % in methylene chloride solution) of fluoboric acid or boron trifluoride, a rapid reaction occurred accompanied by evolution of nitrogen. The extinction coefficient of the ultraviolet absorption maximum due to the α,β-unsaturated ketone at 241 mμ was 6500 for the crude product as compared with 16,600 for the starting ketone. From this mixture there was readily separated a ketone, m.p. 94–95°, $\lambda_{max}^{CH_2Cl_2}$ 5.84 (C=O) and 6.1 μ (weak, C=C). The ultraviolet spectrum of the pure ketone exhibited only end absorption in the short wave length region. This product could be readily isolated in yields as high as 40% when pure cholestenone was used.[6]

(1) W. S. Johnson, M. Neeman and S. P. Birkeland, *Tetrahedron Letters*, **5**, 1 (1960).

(2) H. O. House, E. J. Grubbs and W. F. Cannon, *J. Am. Chem. Soc.*, **82**, 4099 (1960).

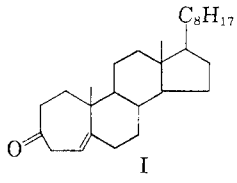
(3) C. D. Gutsche in R. Adams, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 384; R. Huisgen, *Angew. Chem.*, **67**, 439 (1955).

(4) See, for example: A. Wettstein, *Helv. Chim. Acta*, **27**, 1803 (1944); C. Djerassi and C. R. Scholz, *J. Org. Chem.*, **14**, 660 (1949); and A. L. Nussbaum and F. E. Carlon, *J. Am. Chem. Soc.*, **79**, 3831 (1957).

(5) M. Neeman, M. C. Caserio, J. D. Roberts and W. S. Johnson, *Tetrahedron*, **6**, 36 (1959).

(6) Cholestenone was prepared from cholesterol which had been purified as described by L. F. Fieser, *Org. Syntheses*, **35**, 43 (1955). Commercial cholesterol contains significant amounts of cholestanol (L. F. Fieser, *J. Am. Chem. Soc.*, **73**, 5007 (1951); **75**, 4395 (1953)). We have found that cholestenone prepared directly (as recommended by J. F. Eastham and R. Teranishi, *Org. Syntheses*, **35**, 39 (1955)) from commercial cholesterol affords a product which, although not showing a depressed m.p., is contaminated with cholestanone. This fact was first suggested when K. L. Williamson of our laboratories carried out a Wolff–Kishner reduction on ordinary Δ⁴-cholestene-3-one and obtained a mixture from which cholestane was isolated in 2% yield. Moreover, catalytic hydrogenation of (impure) cholestenone had always yielded a mixture of coprostanone and cholestanone, rendering particularly difficult the isolation of the former substance in a pure form. For many years we, as well as others, had regarded the cholestanone thus isolated as being formed by non-stereoselective reduction of the unsaturated ketone; whereas in fact it has now been

Compositional analysis of the new 95° ketone was compatible with either of the two next higher homologs, but by mass spectrometry[7] it was possible to show that the molecular weight was 398, and the formula therefore was $C_{28}H_{46}O$. The 95° ketone gave a yellow color with tetranitromethane, formed a yellow 2,4-dinitrophenylhydrazone, and absorbed 1 mole-equivalent of hydrogen in the presence of palladium catalyst.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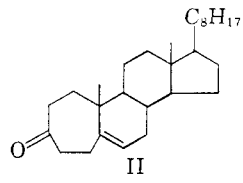
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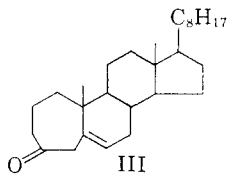

III

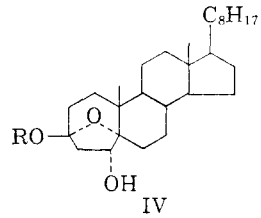
The foregoing facts and the probable mode of formation of the 95° ketone suggested that its structure was either I, II or III. The last two structures could be presumed to arise from the sequence Δ^4-cholestenone $\leftrightarrows$ Δ^5-isomer $\xrightarrow{CH_2N_2}$ II or III, the equilibrium step being catalyzed by the acid. This hypothesis was rendered unlikely, if not altogether untenable, when it was found that the 95° ketone could not be produced in significant amounts from Δ^5-cholestenone.[8] Formula II was unequivocally excluded by the n.m.r. spectrum at 60 mc. (benzene as an external standard) which indicated the partial structure $-CH_2COCH_2CH{=}C$: triplet ($J=6$) at 80 c.p.s. (one vinyl proton, split by two adjacent protons); unresolved multiplet at + 208 c.p.s. (two protons, allylic to double bond and α to carbonyl); multiplets at + 253 and + 266 c.p.s. (two hydrogens, alpha to carbonyl group, one showing axial and the other equatorial properties, both split by adjacent hydrogens). The remaining significant features of the n.m.r. spectrum included sharp signals at + 324 c.p.s. (C_{19}-methyl), + 333 c.p.s. (C_{26}- and C_{27}-methyls), + 339 c.p.s. (C_{21}-methyl) and + 348 c.p.s. (C_{18}-methyl). Confirmation of the β,γ-unsaturated ketone system was afforded by the appearance of a new band at 6.0 μ in the infrared spectrum of the ketone after it was heated overnight in benzene solution containing a trace of *p*-toluenesulfonic acid; thus the olefinic bond apparently was partially isomerized into conjugation with the carbonyl group. It is noteworthy, however, that the equilibrium seems to be in favor of the β,γ-tautomer.

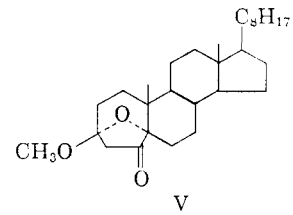
shown (experiments by P. J. Krapp) that the hydrogenation is highly stereoselective, and pure cholestanone is converted into coprostanone in high (89%) yield.

In the present work, the cholestanone-containing cholestenone gave mixtures (undoubtedly containing higher homologs of cholestanone) which were exceedingly difficult to separate, although our first specimen of the 95° ketone was prepared in this way and purified with difficulty only after laborious chromatography and crystallizations.

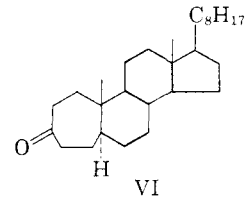
(7) Determination carried out on a Type 21 C.E.C. Mass Spectrometer by Dr. H. Budzikiewicz, to whom we extend our thanks.

(8) Prepared according to L. F. Fieser, *Org. Syntheses*, **35**, 45 (1955).


IV

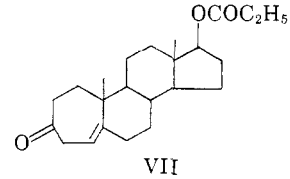

V

Formula III was unequivocally excluded by the following experiments. Hydroxylation with osmium tetroxide gave, in high yield, a semi-crystalline product, which was stable to periodic acid and showed no carbonyl stretching absorption in the infrared spectrum. This hydroxylation product accordingly was formulated as the hemiketal IV (R = H), the α-configurations being preferred for the oxygen atoms introduced by the osmium tetroxide reaction, on the assumption that attack occurred from the less hindered α-side of the molecule. Confirmation of this structure was afforded by its facile conversion, with methanolic hydrogen chloride, into a nicely crystalline hydroxy lactol ether (IV, R = CH_3), m.p. 177.5–178.5°. The hydroxyl group of this derivative was shown to be secondary (rather than tertiary as required by the product derived from III) by oxidation with chromium trioxide in acetic acid to a keto lactol methyl ether (V), m.p. 115–116°.


VI

Finally the hydrogenation product of the 95° ketone was examined. This proved to be a mixture from which a pure substance, m.p. 82–83°, was isolated by chromatography and crystallization. The melting point was undepressed on admixture with an authentic specimen of A-homocholestane-3-one (VI),[9] and the infrared spectra of the two samples were identical.

The 95° ketone may therefore be formulated as A-homo-4a-cholestene-3-one (I).


VII

The new reaction has also been tried with testosterone propionate. Treatment with diazomethane in the presence of boron trifluoride gave in 20% yield a crystalline homolog, m.p. 112–114° (after purification), which may be formulated as VII. Preliminary physiological tests performed by Dr. Elva G. Shipley indicated that A-homotestosterone propionate has androgenic and myotrophic as well

(9) N. A. Nelson and R. N. Schut, *J. Am. Chem. Soc.*, **81**, 6486 (1959). We wish to thank Dr. Nelson for providing us with comparison specimens of his materials.

as pituitary inhibiting potency. The activity is less than, but of the same order of magnitude as, that of testosterone propionate. It is noteworthy that the ratio of myotrophic to androgenic activity is significantly higher in the case of the A-homo substance than with testosterone propionate.[10]

In order to test further the generality of the acid-catalyzed diazomethane reaction, we have examined in a preliminary way the case of benzalacetone. For a control experiment, this ketone, λ_{max}^{EtOH} 286 mμ (ϵ 23,500), 220 (12,000), $\lambda_{max}^{CHCl_3}$ 5.98 μ (strong C=O), 6.14, 6.20, was treated with 3 mole-equivalents of diazomethane. The significant spectral properties of the crude product were: λ_{max}^{EtOH} 312 mμ (ϵ 8,100); $\lambda_{max}^{CHCl_3}$ 3.04 μ (N—H), 5.98 (strong, C=O), 6.20, which are indicative of the Δ^2-pyrazoline. This spectrum was identical in every detail with that of authentic pyrazoline.[11] When the reaction was repeated as above except that 6 mole % of fluoboric acid was added, the significant spectral properties of the crude product were: λ_{max}^{EtOH} 287 mμ (ϵ 9,600), 255 (8,700); $\lambda_{max}^{CHCl_3}$ 5.85 μ (strong, C=O), 5.98, 6.14, 6.20 μ. It is clear that in the latter experiment, homologation was effected by diazomethane without significant pyrazoline formation. The product clearly contained an unconjugated keto group while the olefinic bond remained in conjugation with the benzene nucleus. Similar infrared and ultraviolet spectroscopic results were obtained with benzalacetophenone. In the fluoboric acid-catalyzed experiment no pyrazoline formation was observed, and the extinction coefficient of the absorption maximum at 308 mμ in the ultraviolet spectrum of the starting material dropped by 25% after the reaction.

When the product from the acid-catalyzed reaction with benzalacetone was hydrogenated over palladium catalyst, a mixture of two ketones was obtained which could be readily separated by vapor phase chromatography and identified as 4-phenylbutanone-2 and 5-phenylpentanone-2 by comparison of the infrared spectra and of the 2,4-dinitrophenylhydrazones with authentic specimens. The former ketone was, of course, derived from starting material, and the latter from the product of homologation.

The generality of the reaction is further supported by the work of House, Grubbs and Cannon[2] who studied the boron trifluoride-catalyzed reaction of diazomethane with mesityl oxide. They observed no pyrazoline formation, but obtained a mixture of two isomeric homologs corresponding to insertion of a methylene group on either side of the carbonyl group. In our study we did not find the product formed by homologation on the saturated side of the carbonyl group.

Acknowledgment.—This work was supported in part by grants from the National Science Foundation, the U. S. Public Health Service and the Wisconsin Alumni Research Foundation.

Experimental[12]

A-Homo-4a-cholestene-3-one (I).—To a stirred solution of 5.6 g. of pure[6] Δ^4-cholestene-3-one in 25 ml. of anhydrous methylene chloride containing 0.3 ml. of *freshly* prepared fluoboric acid catalyst solution[13] was added dropwise over a period of 30 min. 200 ml. of a cold 0.232 *M* solution of diazomethane in anhydrous methylene chloride. Nitrogen evolution began immediately, and after 5 min. the colorless solution became cloudy with precipitated polymethylene. After addition was complete the mixture was stirred for 1 hr., filtered, diluted with ether, washed with saturated sodium bicarbonate solution, then with water, and finally dried over anhydrous sodium sulfate. The residue obtained upon evaporation of the ether amounted to 5.6 g. of an amber oil, $\lambda_{max}^{95\%\ EtOH}$ 241 mμ (ϵ 6,500). This material was dissolved in a small amount of methylene chloride and absorbed on a 200-g. Florisil column. The fractions eluted with 40% benzene in 60–68° petroleum ether amounted to 2.2 g. of crystalline material melting between 90 and 94° and showing no absorption in the 241 mμ region of the ultraviolet spectrum. Repeated recrystallizations from acetone afforded colorless crystals, m.p. 94–95°, $[\alpha]^{25}D$ +47.8° (CCl_4), $\lambda_{max}^{CH_2Cl_2}$ 5.84 μ (C=O), 6.1 μ (C=C).

Anal. Calcd. for $C_{28}H_{46}O$: C, 84.36; H, 11.63. Found: C, 84.4; H, 11.6.

The 2,4-dinitrophenylhydrazone was obtained from chloroform–95% ethanol as yellow plates, m.p. 189–190°.

Anal. Calcd. for $C_{34}H_{50}O_4N_4$: C, 70.55; H, 8.71. Found: C, 70.3; H, 8.8.

In another experiment the homocholestenone was prepared by the procedure described above except that the fluoboric acid catalyst was replaced by 0.3 ml. of a solution of 1 ml. of freshly distilled boron trifluoride etherate in 25 ml. of the anhydrous 3:1 ether–methylene chloride solution. The yield of product was the same as described above.

3β-Methoxy-3α,5α-oxido-4aα-hydroxy-A-homocholestane (IV, R = CH_3).—A solution of 0.23 g. of osmium tetroxide in 2.3 ml. of tetrahydrofuran was added with stirring to a cooled (Dry Ice) solution of 0.318 g. of the aforementioned homocholestenone, m.p. 90–94°, in 10 ml. of tetrahydrofuran containing 0.15 ml. of anhydrous pyridine. After the addition was complete, the cooling bath was removed and the mixture allowed to stir at room temperature for 48 hr. After the addition of 8 ml. of anhydrous ether, gaseous hydrogen sulfide was introduced, and the black precipitate that formed was removed by filtration. Evaporation of the combined filtrates and washings gave 0.3 g. of a glassy residue, λ_{max}^{KBr} 3.0 μ (OH), of crude 3β-hydroxy-3α,5α-oxido-4aα-hydroxy-A-homocholestane (IV, R = H). Material of this quality from other experiments was obtained as a partly crystalline gel on attempted recrystallization. A satisfactory analytical specimen was not obtained.

The 0.3 g. of crude hemiketal was dissolved in 20 ml. of anhydrous methanol containing 0.5 ml. of methanolic hydrogen chloride and heated under reflux for 1 hr. Another 0.5 ml. of methanolic hydrogen chloride was added and heating continued for 30 min. The mixture was cooled, solid ammonium carbonate and 50 ml. of methylene chloride were added, and the mixture was filtered. The residue obtained upon evaporation of the filtrates under reduced pressure was dissolved in 25 ml. of methylene chloride and filtered through 1.5 g. of neutral Woelm alumina (activity I) to give 0.263 g. of material, m.p. 170–173°. Recrystallization from methylcyclohexane gave 0.198 g. of colorless plates, m.p. 177.5–178.5°, $[\alpha]^{25}D$ + 37.2° (CH_2Cl_2), $\lambda_{max}^{CH_2Cl_2}$ 2.8 μ (OH).

Anal. Calcd. for $C_{29}H_{50}O_3$: C, 77.97; H, 11.28; OCH_3, 6.95. Found: C, 77.75; H, 11.2; OCH_3, 6.9.

(10) This opportunity is taken to give a preliminary report on the physiological tests carried out, also by Dr. Shipley, on testosterone methyl ether (ref. 5) which exhibited activity comparable to, but somewhat less than, that of testosterone propionate. The methyl ether, moreover, appeared to be somewhat longer-acting than the natural hormone. The high potency of testosterone methyl ether is interesting in connection with the problem of the mechanism of hormone action. Unless the methyl ether is unexpectedly susceptible to cleavage in biological systems, our results suggest that the androgenic and myotrophic action of testosterone is not associated with a trans-hydrogenation process involving the oxygen function at the 17-position; *cf.* P. Talalay, B. Hurlock and H. G. Williams-Ashman, *Proc. Natl. Acad. Sci.*, **44**, 862 (1958).

(11) E. Azzarello, *Gazz. chim. ital.*, **36, II,** 50 (1906); L. I. Smith and K. L. Howard, *J. Am. Chem. Soc.*, **65**, 165 (1943).

(12) All melting points are corrected for stem exposure.

(13) Prepared by dissolving 1 ml. of concentrated (ref. 5) fluoboric acid (*ca.* 19 *N*) in 100 ml. of an anhydrous 3:1 diethyl ether–methylene chloride solution.

From the mother liquor of the analytical specimen an additional 0.033 g., m.p. 175.5–178°, was obtained, making the total yield of purified material 65%.

Further elution of the alumina column described above with 100 ml. of 7% methanol in methylene chloride gave 0.028 g. of starting material.

3β-Methoxy-3α,5α-oxido-A-homocholestane-4a-one (V).—To a suspension of 0.038 g. of the aforementioned oxido ether (IV, R = CH_3), m.p. 177.5–178.5°, in 2 ml. of glacial acetic acid was added 8 ml. of a 0.05 *N* solution of chromium trioxide in glacial acetic acid. The suspension was shaken until dissolution was complete (15 min.). Aliquots of 2.0 ml. were titrated by the potassium iodide–sodium thiosulfate method after 1 hr. and after 3.8 hr. The consumption of chromic anhydride was 0.9 and 1.0 mole equivalent, respectively. The oxidation mixture was diluted with ice-water, sodium bisulfite solution was added, and the mixture extracted with methylene chloride. The combined extracts were washed with water, with sodium carbonate, again with water and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave 0.023 g. of crude product which crystallized spontaneously, m.p. 103–106°, $\lambda_{max}^{CH_2Cl_2}$ 5.71 μ (C=O in a strained ring). This material was combined with 0.063 g. of comparable material from another run and chromatographed on 0.8 g. of Woelm neutral alumina (activity I). Elution with 50% benzene in methylene chloride, methylene chloride, and 50% methylene chloride in ethyl acetate afforded a total of 0.082 g., m.p. 113–115°. Recrystallization from absolute ethanol gave 0.071 g. of colorless plates, m.p. 115–116°, $[\alpha]^{25}D$ + 9.8° (CH_2Cl_2), $\lambda_{max}^{CH_2Cl_2}$ 5.71 μ.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.33; H, 10.88; OCH_3, 6.98. Found: C, 78.7; H, 10.8; OCH_3, 7.4.

Hydrogenation of A-Homo-4a-cholestene-3-one (I).—A solution of 0.50 g. of homocholestenone, m.p. 90–94°, in 40 ml. of 95% ethanol was hydrogenated over 0.1 g. of 10% palladium-on-carbon (Engelhard Industries, Inc.) at atmospheric pressure and room temperature. After 50 min., 1 mole-equivalent of hydrogen had been absorbed and reaction had ceased. The mixture was filtered and the filtrate evaporated to give 0.5 g. of an oil which gave two distinct peaks (ratio 3:2) on vapor phase chromatography.[14] The crude product was chromatographed on 65 g. of Florisil. A large (0.3-g.) oily fraction was obtained from the early petroleum ether–benzene eluates. Elution with pure benzene afforded 0.16 g. of crystalline material, which on recrystallization from methanol afforded 0.11 g. of colorless plates, m.p. 82–83°, $\lambda_{max}^{CCl_4}$ 5.85 μ (C=O). The melting point was undepressed on admixture with an authentic specimen of A-homocholestane-3-one, m.p. 82–83°,[9] but was depressed to 77–81° on admixture with A-homocholestane-4-one, m.p. 86–87°.[9] The infrared spectra of our material and of the authentic 3-one were identical and different from that of the 4-one. The retention times on vapor phase chromatography of all three homoketones were identical and corresponded to that of the substances present in higher proportion in the crude product. The material present in lesser amounts (shorter retention time) was presumed to be A-homocoprostane-3-one.

A-Homotestosterone Propionate (VII).—A 4.0-g. sample of testosterone propionate, m.p. 119–120°, in 25 ml. of methylene chloride was treated as described above for cholestenone with 1.0 ml. of boron trifluoride catalyst solution (see above), followed by 100 ml. of 0.33 M solution of diazomethane in methylene chloride. After all of the diazomethane was added (30 min.), an additional 1.0 ml. of catalyst solution was introduced and stirring continued for 2 hr. The product was isolated as described above, giving 4.0 g. of an amber oil, $\lambda_{max}^{95\% EtOH}$ 241 mμ (ε 3,700). A solution of this material in a small volume of methylene chloride was adsorbed on 100 g. of Woelm neutral alumina (activity II). The fractions eluted with 1–2% acetone in benzene amounted to 1.7 g., showing no significant absorption in the 240 mμ region of the ultraviolet spectrum. Crystallization was induced by trituration with petroleum ether. However this material had a broad melting range (95–100°) and could not be recrystallized satisfactorily. Purification was effected by conversion to the **2,4-dinitrophenylhydrazone** which crystallized from chloroform–95% ethanol as bright yellow plates, m.p. 192.5–193.5°, $\lambda_{max}^{95\% EtOH}$ 363 mμ (ε 26,500).

Anal. Calcd. for $C_{29}H_{38}O_6N_4$: C, 64.66; H, 7.11; N, 10.40. Found: C, 64.7; H, 7.2; N, 10.4.

A 0.47-g. sample of crude A-homotestosterone propionate 2,4-dinitrophenylhydrazone, m.p. 180–185° (prepared in 71% yield), was hydrolyzed[15] by treatment with 20 ml. of levulinic acid, 10 ml. of chloroform and 3 ml. of 1 *N* hydrochloric acid by warming for 30 min. on a steam-bath. After the reaction mixture had stood overnight at room temperature, ether was added and the organic layer washed with water, followed by 5% sodium carbonate solution. The ether layer was then shaken with Norit and anhydrous sodium sulfate. The residue obtained upon evaporation of the filtrates amounted to 0.24 g. of crystalline material which was recrystallized from aqueous methanol to give 0.15 g. of colorless plates of A-homotestosterone propionate, m.p. 112–114°, $\lambda_{max}^{CHCl_3}$ 5.83 μ.

Anal. Calcd. for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 76.9; H, 9.7.

Homologation of Benzalacetone.—A 0.52-g. specimen of benzalacetone, m.p. 40–41°, in 15 ml. of methylene chloride was treated as described above for cholestenone with 0.3 ml. of the boron trifluoride catalyst solution (see above), followed by 35 ml. of 0.38 *M* solution of diazomethane in methylene chloride. After the addition of diazomethane was complete, the mixture was stirred for an additional hour and the product isolated as described above to give 0.5 g. of an oily residue. A solution of this crude product in 25 ml. of 95% ethanol was hydrogenated over 0.1 g. of 10% palladium-on-carbon (Engelhard Industries, Inc.) at atmospheric pressure and room temperature. After 1.0 hr., 1 mole-equivalent of hydrogen had been absorbed and reaction had ceased. The residue obtained upon evaporation of the solvent from the filtered solution was separated by vapor phase chromatography on a 4-ft. Surf-packed column heated to 210°. The first eluate, which amounted to about 40% of the total, was recognized as 4-phenylbutanone-2 by the identity of its V.P.C. retention time and its infrared spectrum with that of authentic material prepared by the hydrogenation of benzalacetone. The second fraction eluted, which accounted for the remaining 60%, was recognized as 5-phenylpentanone-2 by the identity of its V.P.C. retention time and infrared spectrum with that of authentic material.[16] The **2,4-dinitrophenylhydrazone** prepared from this second fraction was obtained as an oil which was purified by filtration through neutral Woelm alumina (activity II). Two recrystallizations from 95% ethanol gave yellow needles, m.p. 87.5–88.5°, undepressed on admixture with the derivative prepared from authentic 5-phenylpentanone-2.

Anal. Calcd. for $C_{17}H_{18}O_4N_4$: C, 59.64; H, 5.30. Found: C, 59.4; H, 5.4.

(14) Vapor phase chromatographs were carried out on an Aerograph Gas Chromatography Instrument at 280° with a flame ionization detector and a 5-ft. 5% S.E. 30 column.

(15) C. H. DePuy and B. W. Ponder, *J. Am. Chem. Soc.*, **81**, 4629 (1959).

(16) 5-Phenylpentanone-2 was prepared from γ-phenylbutyric acid (E. L. Martin, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 499) which was converted to the acid chloride (W. E. Hanford and R. Adams, *J. Am. Chem. Soc.*, **57**, 921 (1935)) which was in turn treated with dimethylcadmium (*cf.* J. Cason, *J. Am. Chem. Soc.*, **68**, 2078 (1946)). The ketone boiled at 74–76° (0.5 mm.); reported, 128–130° (15 mm.) (I. M. Heilbron, R. N. Heslop, F. Irving and J. S. Wilson, *J. Chem. Soc.*, 1336 (1931).