optically pure *d*-**2** is calculated to be $[\alpha]_D$ +177°. Cyclization of a sample of *d*-**1** derived from *d*-trienynone[1] having $[\alpha]_D$ +58.4°[4] yielded a specimen of *d*-**2** which, after chromatography to remove only the 17α epimer, gave a rotation of $[\alpha]_D$ +161°[4] corresponding to an optical purity of 91%. Similarly *l*-**1** derived from **1**-trienynone,[1] $[\alpha]_D$ −58.0°,[4] afforded *l*-**2**, $[\alpha]_D$ −163° (92% optical purity).

There are a number of variations, involving conventional reactions, that can be envisaged for the transformation of the substance *d*-**2** into useful steroids. We have given preliminary attention to two pathways, which lead to progesterone, but yields have not been optimized. Thus, oxidation of *d*-**2** with *tert*-butyl chromate[7] afforded the enedione **3** (yield *ca.* 60%), which, without purification, was selectively hydrogenated over palladium-on-carbon to give 5β-pregnane-3,20-dione (**4**). Chromatography over Florisil followed by repeated recrystallizations from hexane afforded a pure specimen of the 17β epimer, mp 118.5–120°, undepressed on admixture with authentic, naturally derived 5β-pregnane-3,20-dione,[8] mp 119–120.5°. The ir spectra (KBr) of the two specimens were identical. The conversion of this substance (by bromination followed by dehydrobromination) into progesterone is already known.[8]

An alternative and shorter approach to progesterone which was examined only in the *dl* series consisted of dehydrogenation of *dl*-**3** with dichlorodicyanoquinone[9] to give the dienedione **6**[3] (88% yield by vpc), mp 175–176° after recrystallization from ethyl acetate–hexane (*Anal.* Found: C, 80.7; H, 8.7). Selective hydrogenation of this product in the presence of tris(triphenylphosphine)rhodium(I) iodide[10] gave, after preparative tlc and recrystallization from methanol, *dl*-progesterone. The nmr and solution ir spectra of this sample were identical with the corresponding spectra of naturally derived progesterone as well as of authentic *dl*-progesterone.[2]

Acknowledgment. We are indebted to the National Institutes of Health and the National Science Foundation for support of this research.

(7) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. 1, Wiley, New York, N. Y., 1967, p 86.
(8) See *inter alia* F. Johnson, G. T. Newbold, and F. S. Spring, *J. Chem. Soc.*, 1302 (1954).
(9) *Cf.* A. B. Turner and H. J. Ringold, *J. Chem. Soc. C*, 1720 (1967).
(10) J. F. Young, J. A. Osborne, F. H. Jordine, and G. Wilkinson, *Chem. Commun.*, 131 (1965).

Brian E. McCarry, Ronald L. Markezich, William S. Johnson*
Department of Chemistry, Stanford University
Stanford, California 94305
Received January 31, 1973

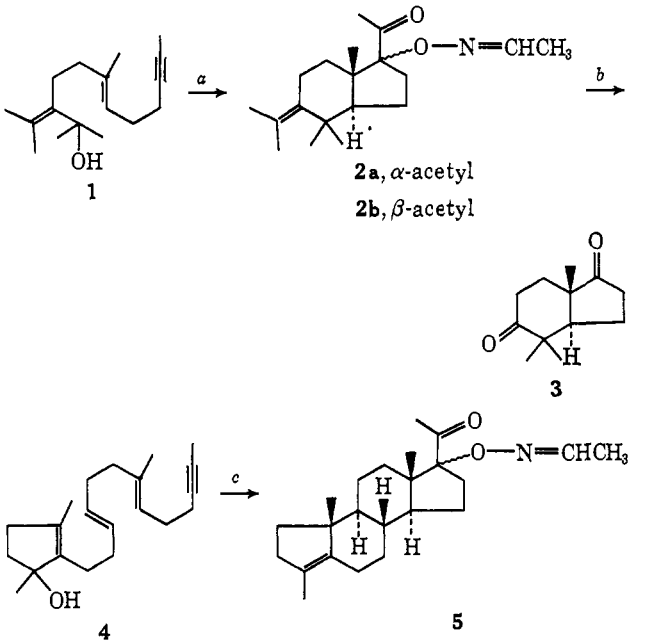
Acetylenic Bond Participation in Biogenetic-Like Olefinic Cyclizations in Nitroalkane Solvents.[1] Synthesis of the 17-Hydroxy-5β-pregnan-20-one System

Sir:

In previous[1-3] communications we have disclosed that allylic alcohols **1**, **4**, and **6** may be induced to undergo stereospecific cyclization to form bicyclic (from **1**) and tetracyclic (from **4** and **6**) products. In each case, an intermediary polycyclic vinyl cation is presumably formed, which is trapped by various nucleophiles (*e.g.*, formic acid, acetonitrile, and ethylene carbonate). In the present communication we report that these reactive vinyl cations may also be trapped by nitroalkanes to afford oxime ethers (*e.g.*, **2**, **5**, and **7**), and that these substances provide an entry into the 17-hydroxypregnan-20-one system.

The results of preliminary experiments are summarized in Scheme I. Treatment of a solution of the

Scheme I



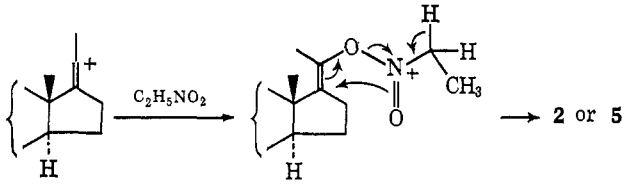
[a] CF_3CO_2H, $CH_3CH_2NO_2$, N_2, −78°, 15 min. [b] RuO_4, CCl_4, 23°, 3 hr. [c] CF_3CO_2H, $(CH_3)_3N$, $CH_3CH_2NO_2$, N_2, −25°, 2 hr.

allylic alcohol **1**[2] in nitroethane at −78° with excess trifluoroacetic acid resulted in the formation of the isomeric oxime ethers **2** (*ca.* 80% yield of a 1:1 mixture of epimers, by vpc). A sample was purified by preparative tlc on silica gel (1:9 ethyl acetate–hexane); mass spectrum *m/e* 305 (M^+); λ_{max}^{film} 5.83 (C=O) and 6.12 (C=N) μ. The nmr spectrum[4] of a chromatography fraction enriched in **2a** included singlets at δ 1.07 (3 H) and 1.20 (6 H) for the three methyl groups attached to quaternary carbon atoms, and at 1.66 (3 H) and 1.80 (3 H) for the isopropylidene methyl groups. In addition, there was a singlet at δ 2.07 (3 H, acetyl methyl), a doublet (J = 6 Hz) at 1.90 (3 H, N=CHCH_3), and a quartet (J = 6 Hz) at 6.83 (1 H, N=CHCH$_3$). The nmr spectrum[4] of another chromatography fraction enriched in **2b** included three-proton singlets at δ 0.70, 1.15, 1.23, 1.70, and 1.82 (see above) in addition to a singlet at 2.03 (3 H, acetyl methyl), a doublet (J = 6

(1) For the previous papers in this series see (a) R. L. Markezich, W. E. Willy, B. E. McCarry, and W. S. Johnson, *J. Amer. Chem. Soc.*, **95**, 4414 (1973); (b) B. E. McCarry, R. L. Markezich, and W. S. Johnson, *ibid.*, **95**, 4416 (1973).
(2) W. S. Johnson, M. B. Gravestock, R. J. Parry, R. F. Myers, T. A. Bryson, and D. H. Miles, *ibid.*, **93**, 4330 (1971).
(3) W. S. Johnson, M. B. Gravestock, and B. E. McCarry, *ibid.*, **93**, 4332 (1971).
(4) The nmr spectrum at 60 MHz (TMS internal standard, $CDCl_3$ solvent) was entirely consistent with the assigned structure. Details are not recorded here, except for absorptions of particular significance.

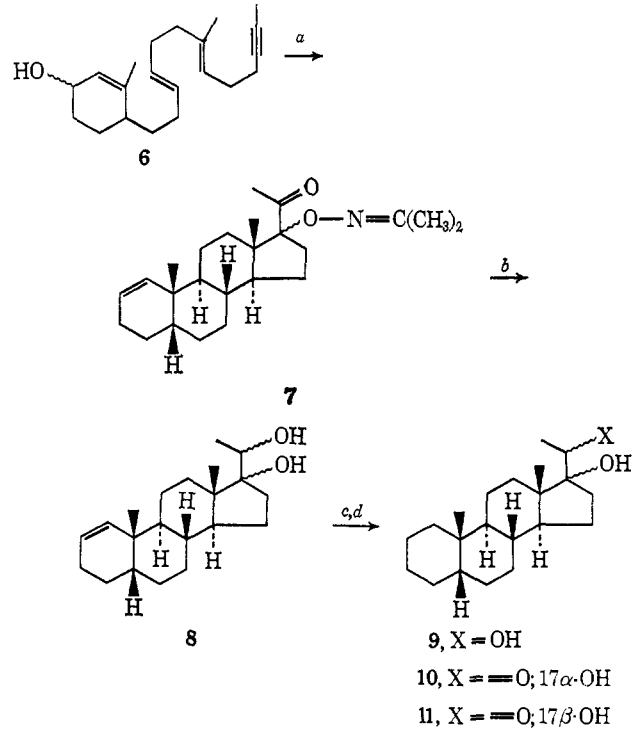
Hz) at 1.90 (3 H, N=CHCH_3), and a quartet (J = 6 Hz) at 6.90 (1 H, N=CHCH$_3$). Degradation of the mixture of **2a** and **2b** with ruthenium tetroxide afforded the hydrindandione **3** identical (by ir, tlc, and vpc coinjection) with authentic material,[2] thereby establishing the trans-fused bicyclic ring structure.

Initial efforts to extend this reaction to the tetracyclic series involved similar cyclization of the allylic alcohol **4**,[3] which gave, after preparative tlc on silica gel (4:6 ethyl acetate–pentane) and short-path distillation, a 55:45 mixture of the β-acetyl:α-acetyl oxime ethers **5** in *ca.* 30% yield; mass spectrum *m/e* 357 (M^+). The infrared and nmr spectra were similar to those for **2** and were in complete accord with structure **5**. A possible mechanism for the formation of the oxime ethers is suggested by the following equation.



Attention was next turned to a detailed study of the cyclization of trienynol **6**[1a] (Scheme II). By analogy

Scheme II



[a] Cl_3CCO_2H, $(CH_3)_2CHNO_2$, N_2, 0°, 4 hr. [b] $LiAlH_4$, THF, N_2, reflux, 2 hr. [c] To give **9**: H_2, 10% Pd/C, EtOAc, 23°. [d] To give **10** and **11**: NBS, dioxane, H_2O, 23°, 5 hr.

to this work (see below) we feel that the structural assignments **2** and **5** in the preliminary studies are now secure. 2-Nitropropane was used instead of nitroethane as the cyclization solvent for **6** in the hope that the elimination of the possibility of syn and anti forms of the oxime ethers would simplify the nature and characterization of the product. Thus, treatment of a solution of **6** in 2-nitropropane at 0° with trichloroacetic acid gave, after preparative tlc on silica gel (1% ethyl acetate in hexane), the isomeric oxime ethers **7** in 45% yield (1:1 mixture of 17α-acetyl:17β-acetyl isomers as determined by nmr). Short-path distillation at 190° (0.01 mm) afforded a colorless oil (*Anal.* Found: C, 77.8; H, 10.0; N, 3.7): $\lambda_{max}^{CCl_4}$ 5.84 (C=O), 6.10 (C=N) μ. The nmr spectrum[4] included singlets at δ 0.64 (3 H, C-18 of β-acetyl isomer), 0.97 (3, H, C-18 of α-acetyl isomer), 1.00 (6 H, C-19, both isomers), and at 1.83, 1.87, 1.90, 1.99, 2.03, and 2.06 (18 H total) for the methyl groups adjacent to the carbonyl and oxime groups. In addition there were two singlets at 5.54 and 5.60 (4 H total) for the olefinic protons in ring A. Attempts to separate the isomeric oxime ethers by tlc or high-pressure liquid chromatography were unsuccessful.

Treatment of the unpurified mixture of oxime ethers **7** with excess lithium aluminum hydride in refluxing tetrahydrofuran effected hydrogenolysis of the N–O bond in addition to reducing the carbonyl group to give an isomeric mixture of diols **8** in 54% yield after preparative tlc on silica gel (3:7 ethyl acetate–hexane). Since **8** can exist in four possible stereoisomeric forms it was not fully characterized; however, its nmr and infrared spectra were entirely consistent with the assigned structure. Hydrogenation of the olefinic bond gave diol **9** as a mixture of stereoisomers in 98% yield. The nmr spectrum indicated the absence of olefinic protons. Oxidation of **9** with *N*-bromosuccinimide followed by preparative tlc on silica gel (1:20 ethyl acetate–hexane; continuous elution for 6 hr) effected separation of the hydroxy ketones **10** and **11** which were thus obtained in *ca.* 69% combined yield from **9** correcting for about 11% of recovered diol. Recrystallization of **10** from hexane gave colorless needles, mp 148–49°, identical by nmr, infrared, tlc, and mixture melting point with an authentic sample of *dl*-17α-hydroxy-5β,17β-pregnan-20-one (*Anal.* Found: C, 79.4; H, 11.0) synthesized[5] from *dl*-5β-pregnan-20-one.[1b] Recrystallization of **11** from hexane gave colorless needles, mp 159–164°, identical by nmr, solution ir, tlc, and vpc coinjection with an authentic sample of *l*-17β-hydroxy-5β,17α-pregnan-20-one.[6]

The attractiveness of the method described above for the total synthesis of 17α-hydroxyprogesterone is somewhat diminished by the fact that a mixture of C-17 epimers (**7**) is formed in the cyclization of **6**. However, further study, *e.g.*, with hindered nitroalkanes, hopefully may reveal a method of realizing stereoselectivity.

Acknowledgment. We are indebted to the National Institutes of Health and the National Science Foundation for support of this research.

(5) The method of synthesis followed the known conversion of pregnan-20-ones to the $\Delta^{17,20}$-enol acetate followed by selective α epoxidation and rearrangement of the epoxy acetate in aqueous alkali to give the 17α-hydroxypregnan-20-one; see E. P. Oliveto in "Organic Reactions in Steroid Chemistry," Vol. 2, J. Fried and J. A. Edwards, Ed., Van Nostrand Reinhold, New York, N. Y., 1972, pp 185–195, and references cited therein.

(6) C. W. Shoppee, N. W. Hughes, and B. C. Newman, *J. Chem. Soc. C*, 558 (1970).

Douglas R. Morton, Michael B. Gravestock
Ronald J. Parry, William S. Johnson*
Department of Chemistry, Stanford University
Stanford, California 94305
Received December 27, 1972