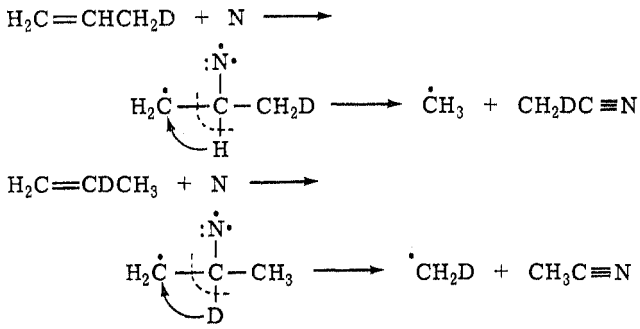
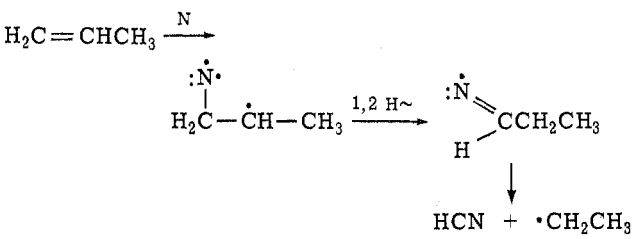
Oka, Suda, Sato Proposal



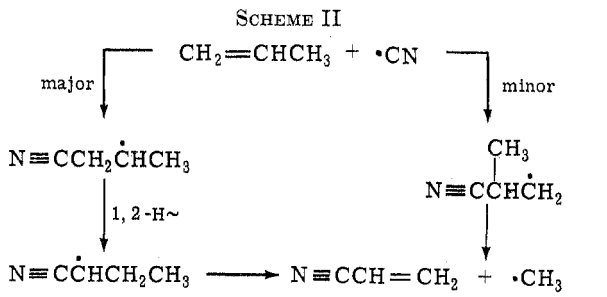
ferred addition of nitrogen atoms to the terminal olefinic carbon of propene.



The deuterium content of the acrylonitrile formed from propene was also studied. The acrylonitrile from 3-deuteriopropene was 97% undeuterated and 3% monodeuterated by mass spectrometric analysis at 14 eV. That formed from 2-deuteriopropene was 9% undeuterated and 91% monodeuterated. These results indicate selective elimination of the methyl group of propene. They can be explained by a mechanism involving cyanogen radicals, which are present in hydrocarbon–atomic nitrogen reactions to a small extent.[9]

Addition of cyanogen radicals to propene can occur in two ways (Scheme II). The major pathway includes

SCHEME II



a 1,2-hydrogen rearrangement, which is uncommon in low temperature condensed phase chemistry. It is possible that this major pathway does not lead to acrylonitrile, but to other products by addition of another molecule of propene (C_4 nitriles were not found). However, the minor pathway is a reasonable one to account for this product.

The reaction of atomic nitrogen with liquid propene closely parallels the gas phase reaction. There is little resemblance between these reactions and the reactions of the reactive species produced by the γ-radiolysis of propene in liquid nitrogen. The active species in the latter reactions cannot be ground state atomic nitrogen.

(9) A. N. Wright and C. A. Winkler, "Active Nitrogen," Academic Press, New York, N. Y., 1968.

Experimental Section

"Active" nitrogen, which is mainly ground state (quartet) atomic nitrogen, was generated by a 2450-Mc microwave discharge through molecular nitrogen. The molecular nitrogen (prepurified grade) was first passed over copper turnings at 500° to remove all but a few ppm of oxygen. Reaction with propene was accomplished by bubbling the atomic nitrogen stream through liquid olefin. Most reaction takes place in the condensed phase, since reaction flames[9] are not seen before the nitrogen reaches substrate, and the yellow nitrogen afterglow does not persist after contact with the substrate. The molar ratio of propene to atomic nitrogen was 120:1. The flow rate of atomic nitrogen (43.8 μmol/min) was determined by a calorimetric method[10] and by the nitric oxide titration method.[11]

2-Deuteriopropene and 3-deuteriopropene were made by D_2O hydrolysis of the corresponding Grignard reagents. Propene was purified by trap-to-trap distillation through a −131° trap. The isotopic purity of the deuterated propenes was determined by mass spectrometry at 11.2 eV. The infrared spectrum of 3-deuteriopropene showed a carbon–deuterium stretch at 2160 cm^{-1}; the carbon–deuterium stretch in 2-deuteriopropene was at 2225 cm^{-1}.

Nitrilic products from the atomic nitrogen reactions were separated from excess propene by trap-to-trap distillation and were analyzed by gas chromatography on a dinonylphthalate column and by comparison of the infrared and mass spectra to those of known samples.

Registry No.—Atomic nitrogen, 17778-88-0; propene, 115-07-1.

Acknowledgment.—The financial support of the Air Force Office of Scientific Research (Grant. No. 1983) is acknowledged with gratitude.

(10) J. J. Havel and P. S. Skell, *J. Amer. Chem. Soc.*, **94**, 1792 (1972).

(11) P. Harteck, G. Mannella, and R. R. Reeves, *J. Chem. Phys.*, **29**, 608 (1958).

Benzyl Alcohol as Hydrogen Donor in Selective Transfer Hydrogenation of Unsaturated Steroids

R. VITALI, G. CACCIA, AND R. GARDI*

Warner-Vister Steroid Research Institute, Casatenovo (Como), Italy

Received May 2, 1972

In a previous paper[1] we suggested transfer hydrogenation as the first step of the reaction of an α,β-unsaturated ketone with benzyl alcohol under conditions of homogeneous basic catalysis. This prompted us to investigate benzyl alcohol as donor in hydrogen transfer also under conditions of heterogeneous catalysis.[2] To our knowledge, these properties were still unexplored, although some alcohols had been occasionally used to reduce various acceptors in the presence of nickel or palladium.[3]

The present report deals with experiments performed on representative unsaturated steroids as acceptors in order to investigate the scope and limitations of this reaction.

The results obtained by heating solutions of the steroid in benzyl alcohol or other carbinol in the presence of Pd catalyst are summarized in Table I. Benzyl alcohol

(1) R. Vitali, G. Caccia, and P. P. Castelli, *Ann. Chim. (Rome)*, **62**, 315 (1972).

(2) *Cf.* E. A. Braude and R. P. Linstead, *J. Chem. Soc.*, 3544 (1954).

(3) E. C. Kleiderer and E. C. Kornfeld, *J. Org. Chem.*, **13**, 455 (1948). For other references see E. A. Braude, R. P. Linstead, and P. D. W. Mitchel, *J. Chem. Soc.*, 3578 (1954).

TABLE I
TRANSFER HYDROGENATION OF UNSATURATED STEROIDS

Acceptor	Donor	Product	Conversion, %
17β-Hydroxy-5α-androst-1-en-3-one (I)	Benzyl alcohol	17β-Hydroxy-5α-androstan-3-one	100
17β-Hydroxy-5α-androst-1-en-3-one (I)	Cyclohexanol	17β-Hydroxy-5α-androstan-3-one	5
17β-Hydroxy-5α-androst-1-en-3-one (I)	3-Pentanol	17β-Hydroxy-5α-androstan-3-one	5
17β-Hydroxy-5α-androst-1-en-3-one (I)	1-Butanol	No reduction	
17β-Hydroxy-5α-androst-1-en-3-one (I)	Allyl alcohol	No reduction	
17β-Hydroxy-4-androsten-3-one (II)	Benzyl alcohol	17β-Hydroxy-5α-androstan-3-one and	5
		17β-Hydroxy-5β-androstan-3-one	20
17α-Pregn-5-en-20-yne-3β,17-diol (III)	Benzyl alcohol	17α-Pregn-5-ene-3β,17-diol	100
3β-Hydroxy-5,16-pregnadien-20-one (IV)	Benzyl alcohol	3β-Hydroxypregn-5-en-20-one	100
3β-Hydroxy-16-methyl-5,16-pregnadien-20-one (V)	Benzyl alcohol	No reduction	
17β-Hydroxy-1,4-androstadien-3-one (VI)	Benzyl alcohol	17β-Hydroxy-5α-androstan-3-one,	3
		17β-Hydroxy-5β-androstan-3-one,	25
		and 17β-Hydroxy-4-androsten-3-one	72
17β-Hydroxy-4,6-androstadien-3-one (VII)	Benzyl alcohol	17β-Hydroxy-5α-androstan-3-one,	3
		17β-Hydroxy-5β-androstan-3-one,	15
		and 17β-Hydroxy-4-androsten-3-one	82

proved to be by far more effective as hydrogen donor than any other alcohol assayed. Thus, Δ^1-5α-3-ketone I was quantitatively hydrogenated in 3 hr at 80°, while cyclohexanol and 3-pentanol gave rise to only 5% reduction at 100°. Unchanged starting compound was recovered after a similar treatment with 1-butanol and allyl alcohol.

On the contrary, only 25% of the trisubstituted double bond in testosterone (II) was hydrogenated even with benzyl alcohol at 100°. Also the 5,6 double bond survived these reaction conditions. Thus, III and IV were quantitatively converted into 17α-pregn-5-ene-3β,17-diol and 3β-hydroxy-5-pregnen-20-one, respectively, by selective hydrogenation. The role of steric hindrance was further shown by the behavior of tetrasubstituted 16,17-ene in 3β-hydroxy-16-methyl-5,16-pregnadien-20-one (V), which, unlike IV, was recovered unchanged after similar processing.

The promising selectivity of the procedure is further emphasized by the results obtained on $\Delta^{1,4}$-3-ketone VI and $\Delta^{4,6}$-3-ketone VII, both converted in high yield (70–80%) into Δ^4-3-ketone II. Such separation in reactivity of double bonds in $\Delta^{1,4}$-3-ketones toward heterogeneous catalytic hydrogenation is almost unprecedented and strikingly parallels that observed in homogeneous hydrogenations catalyzed by tris(triphenylphosphine)-chlororhodium.[4,5] However, reduction of Δ^4-3-ketone by benzyl alcohol gave rise to isomeric mixtures mainly compounded by 5β epimer, while homogeneous catalytic hydrogenation has been reported to afford exclusively the 5α epimer.[5,6]

Experimental Section

Uv spectra were determined in 95% EtOH with an Optica CF_4 spectrometer; ir spectra were measured in a Nujol mull on a Perkin-Elmer 457 instrument. Tlc was run with 9:1 benzene–acetone on 250-μ-thick layers of silica gel (Carlo Erba, Milan, Italy), containing 1% fluorescence indicator (S5 grün/1, Leuchstoffwerk Gmbh and Co., Heidelberg, West Germany). After a preliminary examination under short-wave uv light (254 mμ), spots were visualized by spraying with 1:1 H_2SO_4–EtOH and heating at 110° for 10 min. Identification of products relied on tlc behavior, mixture melting point, optical rotation, and superimposable uv and ir spectra. Reduction percentages were calculated by uv analysis and semiquantitative tlc.

General Hydrogenation Procedure.—To a solution of the unsaturated steroid (1 g) in the appropriate carbinol (30 ml), 10% Pd on carbon (0.4 g) was added and the resulting suspension was kept under stirring for 3 hr at 80–100°. After removal of the catalyst by filtration and elimination of the alcohol under reduced pressure, the reaction product was isolated in the conventional manner. Recoveries ranged from 90 to 100%.

Registry No.—Benzyl alcohol, 100-51-6.

(4) See C. Djerassi and J. Gutzwiller, *J. Amer. Chem. Soc.*, **88**, 4537 (1966), and ref 8–11 therein.
(5) A. J. Birch and K. A. M. Walker, *J. Chem. Soc. C*, 1894 (1966).
(6) W. Voelter and C. Djerassi, *Chem. Ber.*, **101**, 58 (1968).

Evidence for a Cationic Imine Intermediate in N,N-Disubstituted α-Aminonitrile Formation[1]

JAMES W. STANLEY,[2] JAMES G. BEASLEY, AND IAN W. MATHISON*

Department of Medicinal Chemistry, College of Pharmacy, University of Tennessee Medical Units, Memphis, Tennessee 38103

Received March 15, 1972

α-Aminonitriles are important intermediates in the synthesis of amino acids[3] and sterically hindered amines.[4–7] They may be prepared in one step by treatment of an aldehyde or ketone with NaCN and NH_4Cl (Strecker synthesis). Salts or primary and secondary amines may be used instead of NH_4^+ to obtain N-substituted and N,N-disubstituted α-aminonitriles (I).[8]

Alternatively, they may be prepared by treating

(1) This investigation was supported by grants from Marion Laboratories, Inc., Kansas City, Mo.; A. H. Robins Co., Richmond, Va.; and the National Science Foundation, Grant B007383.
(2) American Foundation for Pharmaceutical Education Fellow, 1970–1972. The work in this paper constitutes a segment of the thesis to be submitted by James W. Stanley to the Graduate School—Medical Sciences of the University of Tennessee in partial fulfillment of the requirements for the degree of Doctor of Philosophy.
(3) "Organic Syntheses," Wiley, New York, N. Y.: Collect. Vol. I, pp 21, 355; Collect. Vol. III, pp 66, 84, 88, 275; Collect. Vol. IV, pp 25, 43, 274.
(4) J. Sansoulet and C. Tackx, *C. R. Acad. Sci.*, **250**, 4370 (1960).
(5) W. H. Taylor and C. R. Hauser, *J. Amer. Chem. Soc.*, **82**, 1960 (1960).
(6) M. Velghe, *Bull. Sci. Acad. Roy. Belg.*, II, 301 (1925).
(7) P. Bruylants, *ibid.*, II, 261 (1925).
(8) D. B. Luten, *J. Org. Chem.*, **3**, 588 (1938).