264–272° dec., $\nu_{max.}^{KBr}$ 3400, 3200, 1660, 1630, 1595, 1540 cm.$^{-1}$, λ_{max}^{EtOH} 246, 302, 385 mμ (ε 5400, 3000, 10800) and was identical with natural holomycin (infrared and ultraviolet spectra, mixture m.p. determination and R_f value in paper chromatography[10]).

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(10) The authors wish to thank Professor V. Prelog and Dr. W. Keller for having performed this comparison.

(11) National Institutes of Health Predoctoral Fellow 1961–1963.

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RECEIVED JANUARY 21, 1963

METAL–AMMONIA REDUCTION OF ALLENES[1]

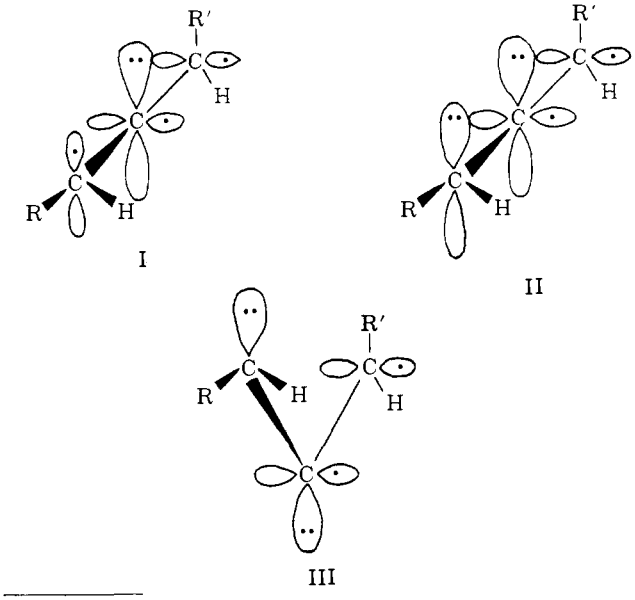
Sir:

The sodium–ammonia reduction of 1,2-cyclononadiene to *cis*-cyclononene was described recently.[2,3] Subsequent examination of additional members—both cyclic and acyclic—of the allene family has shown the reaction to be completely general and not peculiar to strained medium-rings. Moreover, it appears to be rapid and quantitative[4] and the product mixtures are free of rearrangement products.

The reduction of 2,3-nonadiene afforded *cis*- and *trans*-2-nonene (50/50) and less than 1% of two other substances, assumed to be *cis*- and *trans*-3-nonene. Similarly, 2-methyl-2,3-pentadiene gave rise to *trans*-4-methyl-2-pentene (48%), *cis*-4-methyl-2-pentene (34%) and 2-methyl-2-pentene (18%). 1,2-Cyclodecadiene gave only *cis*-cyclodecene while 1,2-cyclotridecadiene[5] afforded equal amounts of *cis*- and *trans*-cyclotridecene. The synthetic utility of the method is illustrated in the reduction of readily available[6] 1,2,6-cyclononatriene to pure *cis,cis*-1,5-cyclononadiene.[5] Finally, the reduction of 1,2-nonadiene, the only terminal allene studied, gave *cis*-2-nonene (85%), *trans*-2-nonene (8%) and 1-nonene (6%).

Excluding for the moment 1,2-nonadiene, these reductions share one very important feature; the most hindered double bond is reduced. The attack of an electron on the allene linkage is electrophilic and therefore probably occurs at the central atom[7] giving rise to intermediate radical-ion I. It is important to note that this species (and those formed from it) does not approach pi-symmetry (*i.e.*, become an allyl radical or allyl anion) as such symmetry would leave only the substituent effects of alkyl groups to dictate the site of protonation by solvent. It is clear that I retains the configurational identity of the allene and that the direction of approach taken by the electron in the formation of I determines which double bond is reduced. This direction appears to be determined by the relative magnitude of steric interaction of the enlarged pi-orbital containing the extra electron with R and R′. Thus, in representation I, R would be larger than R′. The attack of a second electron then precedes protonation (which would give an allyl radical) with consequent formation of dianion II. The configurational geometry of II must be as shown for reasons pointed out in the description of I; a 90° twist between the two charged atoms would give a species having symmetrical pi geometry. The rehybridized dianion (III)[8] in which coulombic repulsions are minimized at the expense of overlap energy cannot be discarded.[9] Structure II would appear to be more consistent with the observed *cis/trans* ratios of products.

The anomalous reduction of 1,2-nonadiene suggests that terminal allenes react by a different mechanism. This possibility is under investigation.



I II III

(1) Supported by The Robert A. Welch Foundation.

(2) P. D. Gardner and M. Narayana, *J. Org. Chem.*, **26**, 3518 (1961).

(3) The reduction of tetraphenylpropadiene to 1,1,3,3-tetraphenylpropane [C. B. Wooster and J. F. Ryan, *J. Am. Chem. Soc.*, **56**, 1133 (1934)] is best considered in context, "The Reduction of Phenylated Olefins with Alkali Metals in Liquid Ammonia."

(4) Yields of *distilled* products were usually in the 80% range but no pot-residues were found; the loss is assumed to be manipulative. Analyses of alkene or cycloalkene mixtures were made by vapor–liquid chromatography on silver nitrate columns using authentic samples for retention time comparisons. Identity of products was established in some cases by comparing chromatogram charts of different runs. Product ratios described were obtained with sodium as the reductant although a brief study with lithium gave identical results.

(5) This substance gave satisfactory analytical data. Its asssignment of structure satisfies numerous items of chemical and physical data.

(6) L. Skätteböl, *Tetrahedron Letters*, **5**, 167 (1961).

(7) D. Devaprabhakara and P. D. Gardner, *J. Am. Chem. Soc.*, in press.

(8) *Cf.* A. J. Birch and H. Smith, *Quart. Rev.*, **12**, 17 (1958), and references cited therein.

(9) Likewise, orbital geometry analogous to that in II cannot be ruled out as a representation of the dianion formed in the reduction of a disubstituted acetylene. The observed *trans* geometry[8] of the resulting olefin would seem consistent with the type of orbital geometry shown in either II or III.

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RECEIVED JANUARY 28, 1963

BICYCLIC ENAMINES. I. THE FORMATION OF A SUBSTITUTED NORTRICYCLENE FROM A BICYCLIC ENAMINE[1]

Sir:

It has been noted previously that the addition of a proton to an enamine takes place at the β-carbon atom to form an iminium salt[2] unless protonation at the β-carbon atom is sterically prohibited, in which case N-protonation takes place.[2,3] Iminium salts possessing endocyclic double bonds[2,4,5] and exocyclic double bonds[6–8] have been synthesized previously. It has been found in this laboratory that protonation of certain bicyclic enamines resulted in the formation of substituted nortricyclenes. The production of sub-

(1) Support of this work by a Frederick Gardner Cottrell Grant from the Research Corporation is gratefully acknowledged.

(2) N. J. Leonard and V. W. Gash, *J. Am. Chem. Soc.*, **76**, 2781 (1954).

(3) C. A. Grob, A. Kaiser and E. Renk, *Chem. Ind.* (London), 598 (1957).

(4) N. J. Leonard and A. G. Cook, *J. Am. Chem. Soc.*, **81**, 5627 (1959), previous papers and references cited therein.

(5) N. J. Doorenbos and C. L. Huang, *J. Org. Chem.*, **26**, 4106 (1961).

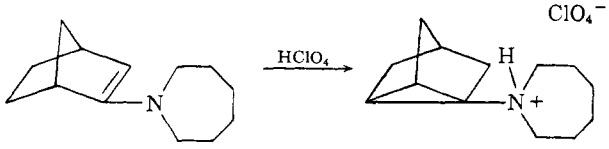
(6) N. J. Leonard and K. Jann, *J. Am. Chem. Soc.*, **82**, 6418 (1960), and references cited therein.

(7) G. Opitz and W. Merz, *Ann.*, **652**, 139 (1962).

(8) A. T. Blomquist and E. J. Moriconi, *J. Org. Chem.*, **26**, 3761 (1961).

stituted nortricyclenes by the attack of electrophilic reagents on norbornene has been observed before.[9-13] However, the electrophilic reagents used previously did not possess the simplicity of the proton, nor did the reactions proceed in such a quantitative and readily reversed manner as the reaction described here.

2-N-Hexamethyleniminebicyclo[2.2.1]heptene (I), b.p. 92–93° (0.9 mm.), $n^{20}D$ 1.5000, ν_{max}^{film} 1685 cm.$^{-1}$, was prepared in the usual manner[14] from hexamethylenimine and norcamphor in a 33% yield. Treatment of an ether solution of compound I with perchloric acid in ethanol quantitatively produced N-tricyclo-



I II

[2.2.1.$0^{2,6}$]heptane-2-hexamethyleniminium perchlorate (II), m.p. 311–312° dec. (Calcd. for $C_{13}H_{22}ClNO_4$: C, 53.51; H, 7.60; N, 4.80. Found: C, 53.66; H, 7.68; N, 4.91.) The nortricyclene type structure of compound II was suggested by analysis, an infrared spectrum maximum at 3150 cm.$^{-1}$ due to $\geqslant \overset{+}{N}H$ stretch and the absence of any maxima in the 1500 to 1800 cm.$^{-1}$ region which might correspond to $\diagdown\!\overset{+}{\diagup}C{=}N\diagdown\!\diagup$ or $\diagdown\!\diagup C{=}C\diagdown\!\diagup$. The presence of an unshifted carbon–carbon double bond is further excluded by the absence of a vinyl proton peak in the n.m.r. spectrum.[15] Chemical evidence supporting the indicated structure of compound II is shown by the inability of 98–100% formic acid to reduce compound I under the usual conditions[16-18] (as shown by the lack of evolution of carbon dioxide and product analysis). Upon basification of the reaction mixture with aqueous sodium hydroxide, then extraction and distillation, the reactant, compound I, was recovered in a 62% yield with the balance of the material being the enamine hydrolysis products, namely, norcamphor and hexamethylenimine. The possibility that the tricyclic amine corresponding to II was liberated in the cold and that heat from distillation caused the opening of the three-membered ring to form compound I is eliminated by a study of the residual oil resulting from the basification of perchlorate salt II in the cold with aqueous sodium hydroxide in the presence of diethyl ether followed by drying of the ether extract and removal of the solvent *in vacuo* at a temperature no higher than 35°. The infrared spectrum of this product was identical with that of enamine I except for a weak band at 1750 cm.$^{-1}$ (norcamphor impurity). Alternatively, enamine I may have been produced by the nucleophilic attack of hydroxide ion on the alpha carbon atom of the freed tricyclic amine corresponding to II to form a bicyclic pseudobase followed by elimination of water. The norcamphor and hexamethylenimine by-products could have been formed from the same intermediate.

Studies are now in progress on the generality of this reaction and similar electrophilic reactions in other bicyclic enamine systems such as the substituted norbornadiene enamine system. These results will be reported in subsequent publications.

(9) J. D. Roberts, E. R. Trumbull, Jr., W. Bennett and R. Armstrong, *J. Am. Chem. Soc.*, **72**, 3116 (1950).
(10) J. D. Roberts, F. O. Johnson and R. A. Carboni, *ibid.*, **76**, 5692 (1954).
(11) H. Kwart and R. K. Miller, *ibid.*, **78**, 5678 (1956).
(12) K. Alder, F. H. Flock and H. Wirtz, *Chem. Ber.*, **91**, 609 (1958).
(13) H. Krieger, *Suomen Kemistilehti*, **33B**, 127 (1960).
(14) F. W. Heyl and M. E. Herr, *J. Am. Chem. Soc.*, **75**, 1918 (1953).
(15) The author expresses his sincere appreciation to Dr. John Ferraro, Argonne National Laboratories, Argonne, Ill., for the determination of this spectrum.
(16) P. L. deBenneville and J. H. Macartney, *J. Am. Chem. Soc.*, **72**, 3073 (1950).
(17) P. L. deBenneville, U. S. Patent 2,578,787 (1951).
(18) N. J. Leonard and R. R. Sauers, *J. Am. Chem. Soc.*, **79**, 6210 (1957).

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RECEIVED DECEMBER 3, 1962

BOOK REVIEWS

Analyse des Stéroïdes Hormonaux. Tome I. Méthodes Générales. Par M. F. JAYLE, Professeur de Chimie biologique á la Faculté de Médecine de Paris. Avec la collaboration de E. E. BAULIEU, O. CRÉPY, J. POLONOVSKI et S. H. WEINMANN. Masson et Cie., 120, Boulevard Saint-Germain, Paris 6, France. 1961. 275 pp. 16.5 × 24.5 cm. Price, 45 NF.

Analyse des Stéroïdes Hormonaux. Tome II. Méthodes de Dosage. Par M. F. JAYLE, Professeur de Chimie biologique à la Faculté de Medécine de Paris. Avec la collaboration de E. E. BAULIEU, O. CRÉPY, P. DESGREZ, R. HENRY et R. SCHOLLER. Masson et Cie., 120, Boulevard Saint-Germain, Paris 6, France. 1962. 497 pp. 16.5 × 24.5 cm. Price, 80 NF.

The two volumes contain an authoritative review and exposition on procedures for the qualitative and quantitative analyses of the steroid hormones and their metabolites. The first volume contains the theory and technical aspects of the general procedures that have been employed for steroid analysis. The second volume describes in detail many analytical procedures for the separation and measurement of individual steroids or of specific groups of steroids. A third volume, not yet published, is intended to review the application of these analytical procedures for the investigation of the functioning steroid-producing endocrine glands.

Volume I, "Méthodes Générales," consists of six chapters, beginning with a brief but adequate discussion of the nomenclature and stereoisomerism of steroid compounds. The second chapter treats in detail the techniques for the separation, isolation and identification of the conjugate forms of the steroids. This chapter will be particularly welcome and useful for the reader since it contains, in addition to the work of other investigators, a complete description of the techniques evolved in the authors' own laboratories, where initial pioneering efforts and subsequent advances in this area have been developed. The volume contains separate chapters on the procedures for the hydrolysis and extraction of steroids, counter-current distribution, paper and column chromatography, and spectrophotometric analyses of the steroids. There are many valuable tables of physical constants including: absorption minima and maxima in the ultraviolet and visible regions for steroids dissolved in sulfuric acid and in phosphoric acid; the wave numbers in the infrared region for steroid functional groups; and the optical rotation, melting point and molecular weight of a comprehensive list of steroids.

Volume II, "Méthodes de Dosage," is divided into four large chapters which faithfully reproduce in great detail the published methods for the individual as well as group measurements of 17-ketosteroids, adrenocortical compounds, pregnanediol, pregnanetriol and related compounds, and the phenolic steroids. In addition, there is an appendix which contains procedures for the purification of solvents and reagents including possible dangers of usage and toxicity.

The two volumes will be valuable additions to the reference shelf for laboratories engaged in research and in routine clinical analysis, since both aspects of steroid analysis are discussed. A most attractive feature of the presentation is the liberal use of illustrations which, along with a precise and detailed exposition