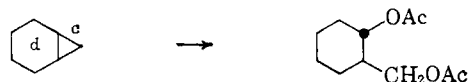


p-Bromophenylcyclopropane yields a higher amount of symmetrical cleavage relative to unsymmetrical cleavage than does phenylcyclopropane. An exact number is not available at this time due to decomposition of the products on the v.p.c. column at the high temperatures necessary for analysis and collection. However, analysis of the n.m.r. spectrum of the crude reaction product indicates that the ratio of cleavage at bond a to bond b is 4. Furthermore *p*-bromophenylcyclopropane reacts slower than phenylcyclopropane by a factor of approximately 2. The kinetics of this system have not been investigated and the order of the reaction is not known. The observations with regard to rates have been made on heterogeneous parallel reactions in which the product composition was determined.

Alkyl-substituted cyclopropanes react slower than phenylcyclopropane. The ratio of unsymmetrical to symmetrical cleavage in ethylcyclopropane is approximately 6. Thus alkyl groups, which are less capable than phenyl of stabilizing an incipient positive charge, allow increased cleavage at bond b. The reactivity of aryl- and alkyl-substituted cyclopropanes and the product composition as a function of substitution will be published in a full paper.

The stereochemistry of the reaction with bicyclic systems is currently under investigation. Criegee² reported that the strained bicyclo[2.1.0]pentane is cleaved by lead tetraacetate. Two fractions were separated by distillation. Saponification of the higher boiling fraction gave *cis*-1,3-cyclopentandiol. We have found that norcarane is cleaved at bonds c and d to yield unsaturated monoacetates and saturated diacetates containing 6- and 7-membered rings. The major product is *trans*-2-acetoxymethylcyclohexyl acetate. The *cis* isomer has not been detected although



the v.p.c. and n.m.r. methods employed do not allow the detection of this substance below 3% of the reaction mixture. The stereochemistry of 1,3-diacetoxycycloheptane which is also obtained has not been established.³

Further experiments to reconcile the differences between the work of Criegee and our observations is underway.

Acknowledgment.—The authors wish to thank Dr. Lloyd Dolby for authentic samples of *cis*- and *trans*-2-acetoxymethylcyclohexyl acetate.

(2) R. Criegee and A. Rimmelin, *Chem. Ber.*, **90**, 417 (1957).

(3) The n.m.r. spectrum of this compound indicates that two equivalent acetate methyl groups of equal intensity are contained in the molecule. This suggests that this product is the *trans* isomer.

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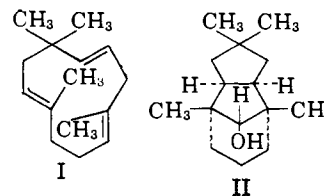
RECEIVED FEBRUARY 8, 1964

Total Synthesis of α -Caryophyllene Alcohol

Sir:

Acid-catalyzed hydration of humulene (I) or commercial "caryophyllene" (which generally contains humulene) under various conditions leads to an interesting and long-known saturated tricyclic alcohol which has been designated as α -caryophyllene alcohol

in the terpene literature.¹ This substance has recently been assigned structure II on the basis of an X-ray diffraction study.² We report here a total synthesis of α -caryophyllene alcohol by a short process consisting of three steps from known compounds.



Slow addition by syringe of a solution of 3-methyl-2-cyclohexenone³ in pentane to a solution of 4,4-dimethylcyclopentene⁴ (*ca.* -10°) under ultraviolet irradiation, using the apparatus previously described,⁵ led to the formation of three isomeric 1:1 adducts of structure III, A, B, and C, in the ratio 74:12:14, respectively, as the only volatile products.⁶ Passage of this mixture in ether through a column of neutral alumina (Woelm, activity I) caused isomerization of C to B and, hence, these ketones differ only in configuration at the methine carbon α to the carbonyl group; isomer C possesses a *trans* 4-6 fusion and B a *cis* 4-6 fusion (see ref. 5). Isomer A was not changed by this treatment and is assigned a *cis* 4-6 fusion. Since isomer A predominates threefold over B plus C, this was taken to be the *cis-anti-cis* adduct and was used for the synthesis of II. The ketone IIIA [b.p. *ca.* 75° (0.08 mm.), infrared maximum 5.88μ (CCl₄), found: C, 81.15; H, 10.69, n.m.r. peaks due to three unsplit methyl groups at 0.80, 1.00, and 1.11 p.p.m. (all shifts are downfield from tetramethylsilane for solutions in CCl₄ at 60 Mc.)], was purified by vapor phase chromatography.⁷

Reaction of the pure ketone IIIA with methyl lithium produced a crystalline tertiary alcohol, m.p. $97-98^\circ$; hydroxyl absorption at 2.67 and 2.84μ in the infrared (CHCl₃), but no carbonyl absorption; n.m.r. peaks due to four methyl groups (all singlets) at 0.81 p.p.m. (one CH₃), 0.90 p.p.m. (one CH₃), and 1.09 p.p.m. (two CH₃); found: C, 81.01; H, 11.85. The same compound was obtained more conveniently from the mixture of isomers IIIA and IIIB by methylation and subsequent recrystallization from pentane. Treatment of the tertiary alcohol in tetrahydrofuran with

(1) See Y. Asahina and T. Tsukamoto, *J. Pharm. Soc. Japan*, **484**, 463 (1922); J. Bell and G. G. Henderson, *J. Chem. Soc.*, 1971 (1930); S. Dev. *Current Sci.* (India), **20**, 296 (1951); A. Nickon, J. R. Mahajan, and F. J. McGuire, *J. Org. Chem.*, **26**, 3617 (1961).

(2) Personal communication from Dr. G. A. Sim, The University, Glasgow; K. W. Gemmill, W. Parker, J. S. Roberts, and G. A. Sim, *J. Am. Chem. Soc.*, **86**, 1438 (1964). Chemical studies leading to II have also been reported by A. Nickon, F. J. McGuire, J. R. Mahajan, B. Umezawa, and S. A. Narang, *ibid.*, **86**, 1437 (1964).

(3) See G. F. Woods, P. H. Griswald, Jr., B. H. Armbrrecht, D. I. Blumenthal, and R. Plapinger, *ibid.*, **71**, 2028 (1949). Methyl lithium was used in the preparation, however.

(4) See H. Kwart and J. A. Ford, Jr., *J. Org. Chem.*, **24**, 2060 (1959).

(5) E. J. Corey, R. B. Mitra, and H. Uda, *J. Am. Chem. Soc.*, **86**, 485 (1964).

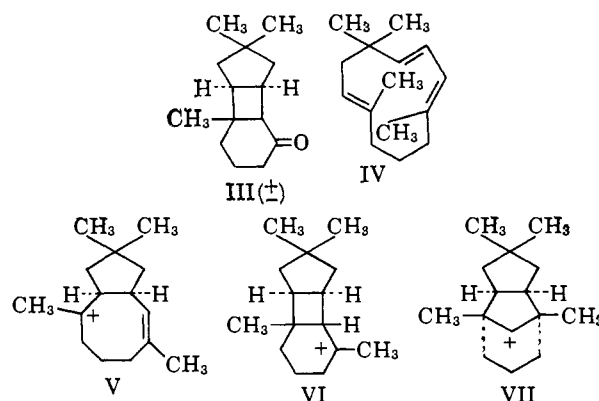
(6) Vapor phase chromatography of this mixture at 185° , using a column of 10% fluorosilicone on Diatoport with a helium flow rate of 50 ml./min., separated A, B, and C; their retention times were 23, 20.3, and 25.5 min., respectively.

(7) The photocondensation of olefins with conjugated ketones has been investigated independently by P. E. Eaton [*J. Am. Chem. Soc.*, **84**, 2554 (1962); Abstracts, American Chemical Society, 145th National Meeting, Sept., 1963, p. 4Q] and in these laboratories by R. B. Mitra, K. Sestanj, and J. D. Bass (to be published). For a previous application to the synthesis of the caryophyllenes see ref. 5 and earlier paper.

40% aqueous sulfuric acid at 0 to -5° for 15 min., and further at 25° for 2 hr., gave synthetic α -caryophyllene alcohol (approximately 50% yield), m.p. $118-118.5^{\circ}$, undepressed upon admixture with authentic material.⁸ *Anal.* Found: C, 81.14; H, 11.77. The n.m.r. and infrared spectra of the synthetic and naturally derived α -caryophyllene alcohol were identical. The former showed peaks due to methyl groups at 0.82 p.p.m. (two CH_3), 0.90 p.p.m. (one CH_3), and 1.03 p.p.m. (one CH_3).

An especially simple mechanistic explanation for the formation of II from humulene by an acid-catalyzed process involves prototropic rearrangement of humulene to the isomeric conjugated triene IV and protonation of IV with subsequent formation of the carbonium ions V, VI, and VII. On the basis of this hypothesis, it is to be expected that the tertiary alcohol obtained by methylation of the ketone III would give rise to α -

(8) We are indebted to Drs. A. Nickon and J. B. DiGiorgio for providing an authentic sample of naturally derived α -caryophyllene alcohol.



caryophyllene alcohol under acidic conditions, as is indeed the case.⁹

(9) This work was supported by the National Science Foundation, Grant GP-221.

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BOOK REVIEWS

Techniques in Protein Chemistry. By J. LEGGETT BAILEY. American Elsevier Publishing Company, Inc., 52 Vanderbilt Ave., New York, N. Y. 1963. 310 pp. 21.5×14 cm. Price, \$11.66.

A volume of this type seems primarily designed as a textbook for students and research workers concerned with modern techniques for the analysis of protein composition and purity. It covers most of the standard techniques such as paper and column chromatography, electrophoresis, and ion exchange for amino acids and peptides. Techniques such as dialysis and gel filtration, column chromatography, and zone electrophoresis of proteins are also described. Dr. Leggett Bailey includes extensive discussions of reactions used to study the composition of proteins. There are sections dealing with disulfide bonds and selective cleavages of peptides in a framework of sequence determinations. The over-all subject matter is extremely well presented.

I do have some criticism regarding the scope and organization of the book. It is somewhat distressing that a chapter on thin layer chromatography is absent. In addition, since the author stresses techniques in a rather random fashion, it is difficult to follow a logical sequence from the isolation through the analysis of a given protein. Lastly, the title of the work seems too broad. Certainly, ultracentrifugation, X-ray diffraction, light scattering, rotatory dispersion, and salt precipitation are important techniques in protein chemistry which are not included. Perhaps the book should have been called "Chromatography and Sequence Determination in Protein Chemistry." Within these two general areas the book should prove to be a valuable source since it describes the techniques from an experimental point of view.

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Polyanions et Polycations. By P. SOUCHAY, Professeur a la Faculte des Sciences de Paris. Gauthier-Villars, 55 quai des Grands-Augustins, Paris (VI^e), France. 1963. 247 pp. 16.5×25 cm. Price, 42 F.

Interest in the constitution and behavior of the polyions is no new a recent development. The interaction of phosphates with molybdates was indeed observed by Berzelius as early as 1826. It remained, however, for chemists of the modern era to

demonstrate the great generality of the phenomenon of condensation in solution brought about by acidification. The nature of the condensed ionic species in solution is sometimes very difficult to establish with certainty, as the conversion of one form to another may be so slow that true equilibrium is rare even at high temperatures. The newer techniques developed for the study of complex ion equilibria have nonetheless been brought to bear on the problem with fruitful results. Together with X-ray analysis, they have been able to elucidate the structures of many of these remarkably complex inorganic compounds.

In the nine chapters of this book, Professor Souchay has summarized the present knowledge on the structure, behavior, and uses of substances consisting of polycations, isopolyanions, or heteropolyanions. He writes with authority, as one who has contributed to the development of the subject and has observed the work of others with the discernment and perspective that are indispensable to a useful assessment of its value.

In the introductory chapter, the different kinds of polycations and polyanions and the methods by which they are formed are described. Reactions initiated by acidification, dehydration, deamination, and solvolysis are likewise discussed. The isopolyanions formed by polymerization of simple chromates, phosphates, vanadates, silicates, and tungstates are perhaps most familiar to the reader. Chapter 2 is devoted to a discussion of these systems together with the corresponding acids. A brief but rewarding description of the composition of borate solutions is included. A separate chapter, Chapter 7, deals in detail with the polyanions of phosphorus.

Chapter 3 is devoted to heteropolyanions, especially those containing tungsten and molybdenum, which are among the most important and typical of this class. Chapters 4 and 5 describe in some detail the methods that have been used for the study of polyanions in solution and in the solid phase. These include spectrophotometry, polarography, kinetics, cryoscopy, potentiometry, differential thermal analysis, and X-ray methods. Compounds related to the polyanions, for example, peracids and persalts and derivatives containing sulfur and fluorine, are described in Chapter 6.

As polyanions are often formed by the action of a strong mineral acid on certain anions, similarly polycations are formed by the action of hydroxide ion on certain simple cations. The methods of studying these condensed cations, described in Chapter 8, are analogous to those used in the investigation of polyanions. The application of sedimentation and light scattering methods is dis-