N-Carbophenoxyhexamethylenimine.—This compound was prepared from phenyl chloroformate and hexamethylenimine as described above (see N-carbethoxyhexamethylenimine) in 81% yield, b.p. 128–130° (0.60 mm.), n^{25}_{D} 1.5328.

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.82; N, 6.39. Found: C, 71.19; H, 7.82; N, 6.61.

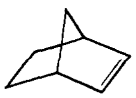
Prins Reaction of Norbornene

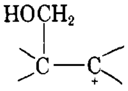
R. R. SAUERS AND P. E. SONNET

School of Chemistry, Rutgers, The State University, New Brunswick, New Jersey

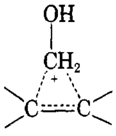
Received August 27, 1963

The course of the Prins reaction of norbornene (I) is of both mechanistic and synthetic interest. Recent work[1] suggests that both open carbonium ions (II) and/or bridged ions (IIIa and/or b) are important intermediates in the reaction. Norbornene, as a substrate in the Prins reaction, offers some interesting possibilities for product formation in view of its facile tendency to rearrange during carbonium ion reactions. Specifically, if any of the reaction proceeds *via* open carbonium ions, the norbornyl cation (IVb) should be created with the concomitant production of rearranged products. Synthetically, simple reactions which lead to 7-carbon substituted norbornane derivatives are rare and hence useful.

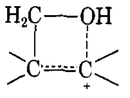

I



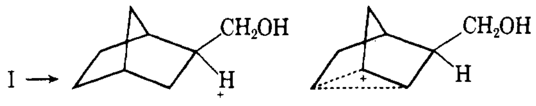
II



IIIa

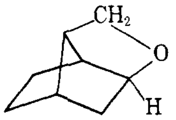


IIIb

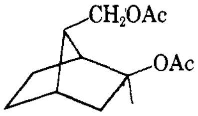


IVa IVb

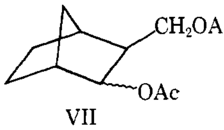
Treatment of norbornene with trioxane in acetic–sulfuric acids led to a complex mixture of products. The low-boiling fraction was shown to contain norbornyl acetate and a new cyclic ether (16%) to which structure V is assigned. The high-boiling fraction (75%) could not be resolved by gas chromatography, but could be shown to contain diacetates VI and VII by further degradation.



V



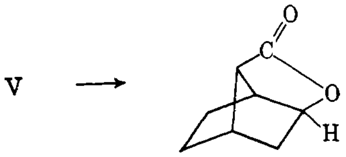
VI



VII

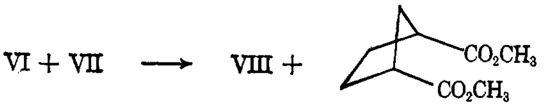
The first clues as to the structures of the $C_8H_{12}O$ ether were provided by the spectral data. No hydroxyl, carbonyl, or unsaturation were evident in the infrared spectrum. The n.m.r. spectrum featured three low-field protons in the ratio of 1:2 centered at 6.0 and 6.4 τ, respectively. The lone proton appeared as a crude triplet with $J = 2.5$ c.p.s. The other two were apparently the AB part of an ABX system in which $J_{AB} = 8.5$ c.p.s., $J_{AX} = 2.5$ c.p.s., and $J_{BX} = 0$ c.p.s.

Since there are several ethers whose spectra could be described by the above data, it was necessary to obtain chemical evidence on this point. This was provided by the fact that oxidation of the ether with chromium trioxide[2] led to a known[3] lactone, VIII.



VIII

The presence of diacetates VI and VII in the high-boiling fraction was demonstrated in the following manner. The crude product was reduced with lithium aluminum hydride to a mixture of diols. Oxidation of this mixture with potassium permanganate followed by esterification of the acidic products showed only two peaks on the gas chromatogram. They were unambiguously identified as lactone VIII and the dimethyl ester of *cis*-cyclopentanedicarboxylic acid (IX) (see the following). Lactone VIII could only have formed from acetate VI by oxidation of the primary function to carboxyl followed by lactonization during the esterification. Diester IX could only have arisen from acetate of structure VII.[4] Unfortunately, the low over-all yield (35%) of the oxidation products precludes exact determination of the relative amounts of VI and VII. The observed molar ratio of VIII to IX was 3:2.



IX

The observed products can be readily rationalized by collapse of ions IVa and/or IVb in unexceptional ways.

Experimental

Melting points are corrected and were determined on a Mel-Temp apparatus. Infrared spectra were determined on a Perkin-Elmer Model 21 spectrometer, in carbon tetrachloride unless otherwise noted. N.m.r. spectra were determined on a Varian Model A-60 spectrometer in carbon tetrachloride using tetramethylsilane as internal standard.

Reaction of Norbornene with Trioxane.—To a solution of trioxane (12.0 g., 0.133 mole) in 92 ml. of glacial acetic acid containing 2 ml. of concentrated sulfuric acid was added dropwise a solution of 13.2 g. (0.140 mole) of norbornene in 23 ml. of glacial acetic acid. The temperature was maintained at 65–70° during

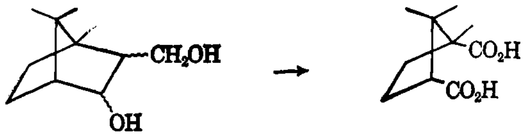
---

[1] (a) L. J. Dolby, C. N. Lieske, D. R. Rosencrantz, and M. J. Schwartz, *J. Am. Chem. Soc.*, **85**, 47 (1963); (b) N. A. LeBel, R. N. Liesemer, and E. Mehmedbasich, *J. Org. Chem.*, **28**, 615 (1963); E. E. Smissman and R. A. Mode, *J. Am. Chem. Soc.*, **79**, 3447 (1957); and A. T. Blomquist and J. Wolinsky, *ibid.*, **79**, 6025 (1957).

[2] H. B. Henbest and B. Nichols, *J. Chem. Soc.*, 227 (1959).

[3] S. Beckmann and H. Geiger, *Ber.*, **94**, 48 (1961).

[4] A similar degradation has been reported by J. Bredt, *Ann.*, **366**, 1 (1909).



the addition (0.5 hr.) and for an additional 0.5 hr. Stirring at *ca.* 28° was maintained for 19 hr. after which time the reaction mixture was quenched with an ice–water mixture. The acetic acid was neutralized with sodium carbonate solution and the aqueous phase was extracted four times with ether. The combined extracts were washed with water and dried over magnesium sulfate.

The ether was carefully removed and a low-boiling fraction (3.4 g.) boiling at 50–65° (25 mm.) was collected. Gas chromatography of this fraction on a 6 ft. × 0.25 in. column of Carbowax 20 *M* at 145° showed three peaks: trioxane, ether V, and norbornyl acetate in the approximate ratios 10:90:10. Trioxane was identified by retention time. Norbornyl acetate was identified by retention time and comparison of infrared spectrum with a known sample. The infrared spectrum of the ether peak showed some weak carbonyl absorption. This impurity was removed by reduction with lithium aluminum hydride followed by gas chromatography. The ether was obtained as a volatile white solid, m.p. 64-65° (sealed capillary, uncor.), in about 16% yield based on the g.c. analysis above.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.27; H, 9.79.

The infrared spectrum was consistent with the assigned structure and showed strong bands at 7.70, 9.15, 9.75, 9.80, 10.35, 10.75, and 11.40 μ. The n.m.r. spectrum exhibited a triplet at 6.1 τ (J = 2.5 c.p.s.) of relative area 1, a multiplet centered at 6.4 τ of area 2, a broad singlet at 7.9 τ of area 3, and a complex absorption of area 6 in the high-field region.

The high-boiling residue (23.8 g.) was essentially a mixture of diacetates VI and VII. The yield calculated on this basis is 75%. The gas chromatogram on a 5 ft. × 0.25 in. column of silicone SE 30 at 170° showed one main broad peak which was collected for analysis.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.93; H, 7.94.

The n.m.r. spectrum of this product showed at least four peaks near 8 τ indicating that this material was a mixture of acetates.

Reduction of Diacetates with Lithium Aluminum Hydride.—The diester fraction (10 g.) was reduced with 3.0 g. of lithium aluminum hydride in ether to give 4.4 g. of a yellow oil. Gas chromatography did not prove feasible due to long retention times.

Oxidation of Diols.—The crude diols (1.0 g., *ca.* 0.007 mole) in 10 ml. of ether was stirred with a solution of 4.45 g. (0.03 mole) of potassium permanganate in 40 ml. of 20% aqueous potassium hydroxide solution. After 1.75 hr. at ice bath temperatures, the excess permanganate and manganese dioxide were destroyed by addition of sodium bisulfite. The reaction mixture was then acidified with hydrochloric acid and extracted with seven 30-ml. portions of ether. The combined extracts were dried and carefully evaporated. Ten milliliters of boron trifluoride–methanol reagent[5] was added and the resulting solution was kept at *ca.* 28° for 1 hr. After dilution with 100 ml. of water, the products were extracted into three 30-ml. portions of ether. The extracts were washed with sodium bicarbonate solution and water and dried. Evaporation of the ether gave 0.38 g. (34%) of the mixture of lactone VIII and diester IX. The yield calculation is based on the results of gas chromatographic analysis of this mixture on a 6 ft. × 0.25 in. column of Craig polyester at 190°. Only two peaks were observed and the retention times corresponded with known samples. Infrared spectra of the collected peaks also corresponded well with those of the authentic materials. The molar ratio of VIII to IX was determined by computation from known mixtures and was 3:2.

The lactone (VIII) was prepared according to Beckmann and Geiger[3] from nortricyclene carboxylic acid and had m.p. 118–118.5°, lit.[3] m.p. 120–121°. Diester IX was prepared by esterification of an authentic sample of 1,3-*cis*-cyclopentanedicarboxylic acid[6] with boron trifluoride–methanol reagent,[5] $\lambda_{\max}^{C=O}$ 5.77 μ. The diacid could be regenerated unchanged (infrared) from the ester.

Oxidation of Ether V to Lactone VIII.[3]—A solution of 1.0 g. of crude ether in 60 ml. of acetone was cooled in an ice bath and treated with a solution of 5.0 g. of chromium trioxide in 19 ml. of water containing 4.5 ml. of concentrated sulfuric acid. The resulting mixture was stirred at 28° overnight and then treated with sodium bisulfite to destroy the excess oxidant. Dilution with 500 ml. of water was followed by extraction with five 50-ml. portions of ether. The combined extracts were washed with sodium bicarbonate solution and dried. Evaporation of the ether gave 0.76 g. of an oil whose infrared and n.m.r. spectra were identical with those of the known material. Gas chromatography of the crude product showed starting material as the only other component.

Control Experiment.—A sample of the diacetate mixture was subjected to the Prins reaction conditions (60–70° for 24 hr.) to determine whether ether V is formed as a primary product. The acetates could be recovered in *ca.* quantitative yield. The small amount of V present in the starting mixture was still present at the end of the experiment.

Acknowledgment.—We wish to thank the National Science Foundation for funds toward purchase of the n.m.r. spectrometer and the National Institutes of Health for a research grant, no. R.G. 8701.

---

(5) Obtained from Applied Science Laboratories, State College, Pa.

(6) J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, **76**, 4501 (1954).

Steroid Hormone Analogs. II.[1] Transformations in the C-Nor-D-homosteroid Series[2]

S. MORRIS KUPCHAN, TADASHI MASAMUNE,
AND G. W. A. MILNE

Department of Pharmaceutical Chemistry,
University of Wisconsin, Madison, Wisconsin

Received September 11, 1963

As part of a continuing study of the synthesis of C-nor-D-homosteroid hormone analogs, experiments were carried out, as outlined below, with a view to synthesizing a cortisone analog.

The readily available veratrum alkaloid jervine[3] (I) was the starting material for this investigation. Degradation of jervine to II was effected by the fragmentation reaction developed in the course of the structure elucidation of the alkaloid.[4,1] The secondary alcoholic group in II could not be oxidized without concomitant oxidative cleavage of the 17,20-double bond when chromium trioxide in acetone or pyridine was used. However, Oppenauer oxidation with aluminum isopropoxide in toluene and cyclohexanone afforded an excellent yield of $\Delta^{4,12,17(20)}$-17-ethyletiojervatriene-3,11-dione (IV).

Treatment of the diketone (IV) with a large excess of monoperphthalic acid in ether for 20 hr. at room temperature afforded a 70% yield of the monoepoxide (III). This epoxide did not prove to be of value in the proposed synthesis, because it could not be caused to open with exclusive fission of the C-17 to oxygen bond. Catalytic hydrogenation gave rise to multicomponent mixtures which could be only partially separated by chromatography. Similarly, treatment with lithium aluminum hydride, lithium in liquid ammonia, or boron trifluoride etherate yielded intractable mixtures.

The 3-ethylene ketal derivative (VI) was formed selectively upon treatment of IV with ethylene glycol in the presence of *p*-toluenesulfonic acid, indicative

---

(1) Part I in the series: S. M. Kupchan and S. D. Levine, *J. Am. Chem. Soc.*, **86**, 701 (1964).

(2) This investigation was supported in part by research grants from the Squibb Institute for Medical Research and the National Institutes of Health (H-2275).

(3) We thank Riker Laboratories, Inc., for a generous gift of a jervine-rich alkaloidal extract.

(4) J. Fried and A. Klingsberg, *J. Am. Chem. Soc.*, **75**, 4929 (1953).