white needles. The filtrate was poured into 200 ml. of water and this was followed by ether extraction. The extracts were washed with strong potassium carbonate solution, dried and evaporated to give a clear oil. Filtration in hexane through a column of alumina followed by crystallization from methanol–chloroform gave 11.5 mg. of crystals, m.p. 258–273°. The combined crops were crystallized again to give 14.2 mg. (10%) of pentacyclosqualene (XIV), m.p. (sealed capillary) 275–276.5°, $[\alpha]^{27}D$ +86° (*c* 0.647) identical by infrared spectrum and mixture melting point (274–276.5°) with a sample of γ-onocerene, m.p. 276–277.5°, $[\alpha]^{26}D$ +83° (*c* 1.16) (lit.[19] m.p. 254–256°,[40] $[\alpha]D$ +83°) prepared from α-onoceradiene diol.

B. From Diol XIII.—Under similar conditions 0.192 g. of diol XIII gave 0.017 g. (10%) of pentacyclosqualene, m.p. (sealed capillary) 274–278.5°, $[\alpha]^{28}D$ +84° (*c* 0.753) identical by infrared spectrum and mixture melting point (273–277°) with an authentic sample of γ-onocerene.

C. From Tetracyclic Diacetate of XIII.—Similar treatment of 25 mg. of diacetate of XIII gave 2.0 mg. (10%) of pentacyclosqualene identified by melting point and mixture melting point.

β-Onoceradiene (XV).—A solution of 0.089 g. of diol XII in 6.0 ml. of dry pyridine was treated with 0.6 ml. of freshly distilled phosphorus oxychloride and allowed to stand for 23 hours at room temperature. Pouring into 75 g. of ice was followed by ether extraction. Evaporation of the washed and dried extracts gave 0.076 g. of a white powder, m.p. *ca.* 100–140°. No absorption attributable to exocyclic methylene was present in the infrared spectrum (carbon tetrachloride). Careful chromatography of this material in pentane on freshly activated alumina (4 hours at 250°) followed by crystallization from methanol–chloroform gave 0.222 g. (27%) of β-onoceradiene, m.p. 159–161.5°, $[\alpha]^{27}D$ +140° (*c* 0.522). The infrared spectrum was virtually identical with that of a sample m.p. 155–160°, $[\alpha]^{28}D$ +146° (*c* 0.274) prepared from α-onoceradienediol (lit.[41] m.p. 161–162°, $[\alpha]D$ +153°). A mixture of the two samples melted at 154–162°.

α-Onoceradiene (XVI).—To a solution of 0.122 g. of diol XIII in 8.0 ml. of dry pyridine was added 0.8 ml. of freshly distilled phosphorus oxychloride. The solution was allowed to stand at 27° for 23 hours and then poured slowly onto 100 g. of ice. Extraction with ether followed by a water wash and evaporation gave a solid product which was filtered through a short column of alumina in low petroleum ether. The product melted from 140–186° (0.10 g.) and showed a strong terminal methylene absorption in the infrared (3100, 1646 and 892 cm.$^{-1}$). Fractional crystallization from methanol–chloroform gave 18 mg. (16%) of pure α-onoceradiene, m.p. 199.5–201°, $[\alpha]^{26}D$ +25° (*c* 0.914) infrared max. (carbon tetrachloride) 3105, 1647 and 892 cm.$^{-1}$, identical by infrared and mixture melting point determination with an authentic sample m.p. 199.5–201.5° prepared from α-onoceradienediol (lit.,[19] m.p. 195–197°, $[\alpha]D$ +29°).

(40) We are unable to explain the discrepancy in melting points reported for γ-onocerene. Sometimes melting points on a hot-stage were not obtainable due to sublimation of the sample near 254° although at other times a normal melting point at 276° was observed.

(41) K. Schaffner, R. Viterbo, D. Arigoni and O. Jeger, *Helv. Chim. Acta*, **39**, 174 (1956). See also ref. 31.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

C_β-C_γ Cleavage of a γ-Hydroxy Acid by Electrolytic Oxidation[1]

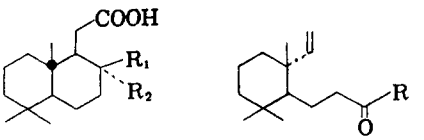
BY E. J. COREY AND R. R. SAUERS

RECEIVED SEPTEMBER 27, 1958

A novel elimination process, which has been observed during anodic reaction of a γ-hydroxy acid, is described.

The accompanying paper[2] describes the conversion of salts of the stereoisomeric hydroxy acids I and II to tetracyclic triterpenes of the onocerane series by electrolytic oxidation. The present paper concerns a noteworthy elimination process which occurs concurrently with the previously described coupling during the electrolysis of I and which leads to a liquid unsaturated ketone $C_{15}H_{26}O$. In particular the experimental observations leading to the formulation of the ketone as III are detailed.[3]

The ketonic cleavage product was separated from the other products of the electrolysis using chromatography and distillation and was easily obtained in *ca.* 97% purity as determined by vapor chromatographic analysis. The contaminant appeared to be a single substance and to be approximately as volatile as III since the two could not be separated by careful distillation in a Holzmann semi-micro column. Analytical data on III indicated the formula $C_{15}H_{26}O$ and it was apparent from the absorption at 1722 cm.$^{-1}$ (CCl_4 as solvent) and the lack of hydroxyl absorption that the oxygen is present in a carbonyl function. This was shown to be ketonic by conversion of III to a semicarbazone, m.p. 175.5–178°, and by other evidence given below. The infrared spectrum of the ketone indicated the presence of carbon-atom unsaturation in the form of a vinyl



I, R_1 = CH_3, R_2 = OH III, R = CH_3
II, R_1 = OH, R_2 = CH_3 IV, R = OH
V, R_1 = CH_3, R_2 = OAc

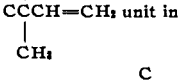
group since bands of moderate intensity were observed at 1637 cm.$^{-1}$ (C=C stretching) and 1008, 917 cm.$^{-1}$ (-CH=CH_2 out-of-plane C—H bending)[4] and this was confirmed by hydrogenation with palladium–charcoal in methanol to a dihydroketone which showed no absorption at *ca.* 1637, 1008 and 917 cm.$^{-1}$ and which was characterized

(1) This investigation was supported by a fellowship (AF-6570 for R.R.S.) from the National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service.

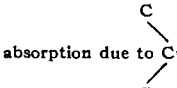
(2) E. J. Corey and R. R. Sauers, THIS JOURNAL, **81**, 1739 (1959).

(3) Preliminary report: E. J. Corey, R. R. Sauers and S. Swann, Jr., *ibid.*, **79**, 5826 (1957).

(4) These bands are very similar to those observed for the similar



unit in elemol (906 and 1010 cm.$^{-1}$) and differs from the



absorption due to C=CH_2 in elemol which occurs at 892 cm.$^{-1}$. See W. Wicki, J. Kalvoda and O. Jeger, *Croat. Chem. Acta*, **29**, 263 (1957).

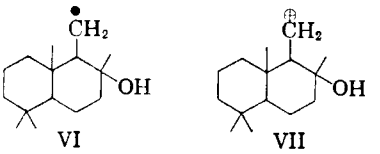
as the crystalline semicarbazone derivative. The proton magnetic resonance spectrum of III (in $CDCl_3$ and relative to external CH_2Cl_2 as reference[5]) indicated the presence of three olefinic hydrogens (−20 to +30 c.p.s., multiplet), one methyl attached to carbonyl (+131 c.p.s, sharp; *cf.* acetone in $CDCl_3$ at +133 c.p.s.) and three other methyl groups (+174 and +179 c.p.s., signal ratio 1:2). In accord with this physical evidence for the structural feature $RCOCH_3$, reaction of the unsaturated ketone with sodium hypobromite afforded a nor-acid (IV, liquid) which was characterized as the crystalline benzylisothiouronium salt. The infrared spectrum of the nor-acid IV indicated that the vinyl group had been retained. These facts would seem to be reasonably accommodated only by structure III.

Electrolytic oxidation of the C_8-epimer of I (II) also produces the cleavage product III, but in addition considerable amounts (20–30% of total) of two impurities as determined by vapor chromatography. The major impurity is more rapidly eluted than III and corresponds to the contaminant mentioned above; the other is eluted more slowly (elution times under standard conditions were 6.6, 9.2 and 12.6 minutes, respectively). Although these by-products are of considerable interest, we prefer to defer a structural discussion until they have been characterized as pure substances and investigated in detail.

Electrolysis of the acetoxy acid V derived from II proceeds smoothly and gives the corresponding Kolbe coupling product in substantially higher yield than is obtained from the salts of I or II. However, no cleavage product, neither III nor the corresponding enol acetate, was detectable by infrared analysis of the material remaining after removal of the coupling product. Vinyl absorption at *ca.* 1637, 1008 and 917 cm.$^{-1}$ was completely absent as was absorption for ketone carbonyl (1700–1720) and C=C of enol acetate (1650–1700). It is clear, therefore, that the acetoxy acid V does not undergo cleavage to an appreciable extent.

Present evidence does not provide a basis for favoring one of the several mechanisms which appear moderately reasonable for the electrolytic cleavage process considered herein. Although all of our findings are consistent with the view that formation of III occurs simply by hydrogen atom discharge from VI with carbon–carbon cleavage it is entirely possible that the cation VII may be an intermediate.[6] The former possibility, however, affords a more straightforward explanation for the lack of cleavage during electrolysis of the acetoxy acid V.

It is clear that a satisfactory understanding of the cleavage process observed with I and II demands further study of these and related systems and we are now addressing ourselves to this task. Although we are not aware of any comparable electrolytic cleavage reactions in the literature, it



VI VII

seems likely from work in progress that the scope of the process is fairly broad and that other unusual changes can also occur.

Experimental[7]

4-[1,3,3-Trimethyl-1-vinylcyclohexyl]-butan-2-one (III).—The vinyl ketone from the hydroxy ammonium salt corresponding to I (isolated by chromatography as described in ref. 2) was distilled at 95–96° (0.4 mm.) to give a colorless oil, $n^{21}D$ 1.4857, $[\alpha]^{26}D$ −10.4° (*c* 1.06): infrared max. (carbon tetrachloride) 3110, 1722, 1637, 1008 and 917 cm.$^{-1}$; ultraviolet max. (95% ethanol) 272 mμ (log ε 1.89).

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.88; H, 11.80.

The vapor chromatogram of this material showed a strong peak at 9 minutes and a very weak peak at 6.2 minutes corresponding to about 3% impurity.

The semicarbazone melted at 175.5–178.5° and crystallized as plates from ethanol–water.

Anal. Calcd. for $C_{16}H_{29}N_3O$: C, 68.77; H, 10.46. Found: C, 68.71; H, 10.33.

The vinyl ketone prepared from the isohydroxyammonium salt corresponding to II was distilled from 93–100° (0.3 mm.), $n^{24.5}D$ 1.4834. The infrared spectrum (carbon tetrachloride) showed the same maxima as the product described above but with diminished intensities (by *ca.* 20%) for the carbonyl and vinyl groups. A vapor chromatogram showed a strong peak at 9.2 minutes and weaker ones at 6.6 minutes, and a very weak peak at 12.6 minutes.

The semicarbazone melted at 173–174° after one crystallization from ethanol–water; a mixture melting point with the pure derivative (above) was 173.5–176°.

Unsaturated Nor-acid IV.—A solution of sodium hypobromite was make by adding 0.8 ml. of bromine to an ice-cold solution of 1.8 g. of sodium hydroxide in 14 ml. of water. To a solution of 0.204 g. of ketone in 4 ml. of dioxane was added 2.9 ml. of the hypobromite solution and the mixture was stirred for 12 hours at room temperature. After heating for 15 minutes on the steam-bath, the mixture was poured into 25 ml. of water and extracted with ether. Acidification with dilute hydrochloric acid followed by ether extraction gave 0.150 g. (73%) of the nor-acid as a viscous oil; infrared max. (chloroform) 1707, 1635, 1009 and 918 cm.$^{-1}$.

The benzylisothiouronium salt[8] crystallized as plates from ethanol–water and melted at 143–145°.

Anal.. Calcd. $C_{22}H_{34}N_2SO_2$: C, 67.65; H, 8.77. Found: C, 67.46; H, 8.80.

Hydrogenation of III.—A solution of 0.432 g. (1.953 mmoles) of vinyl ketone III (from isohydroxyammonium salt II) in 10 ml. of reagent grade methanol was hydrogenated in the presence of 39 mg. of 5% palladium-on-charcoal. Rapid uptake of 0.76 mole of hydrogen was followed by slow uptake of 0.12 mole. Addition of fresh catalyst and changing the solvent to glacial acetic acid did not increase the amount of uptake beyond this point. Evaporation of the acetic acid *in vacuo* was followed by dilution with water and ether extraction. Evaporation of the ether gave an oil which was filtered through a short column of alumina in low petroleum ether. A clear oil weighing 0.286 g. (65%) was obtained from the eluate; infrared max. 1718 cm.$^{-1}$ and no absorption attributable to vinyl unsaturation. This product gave a positive tetranitromethane test and showed three peaks on a vapor chromatogram: 7.2(w), 10(s) and 12.4(w) minutes.

(5) The spectrum was obtained at 40 mc. with a Varian Model V-4300B high-resolution spectrometer fitted with a field-sensing stabilizer. A concentric tube cell [Wilmad Glass Co.] was employed.

(6) Carbon–carbon cleavage of a γ-hydroxylated cation has been reported recently by R. R. Burford, F. R. Hewgill and P. R. Jefferies, *J. Chem. Soc.*, 2937 (1957); see also C. A. Grob, *Experientia*, **13**, 126 (1957).

(7) We are indebted to Mr. James Brader for the infrared spectra and to Mr. Jozsef Nemeth and associates for microanalyses. The vapor chromatograms were obtained at 222–224° with a Perkin–Elmer Vapor Fractometer (model 154B) using column "C" (silicone liquid phase) and a column pressure of 25 p.s.i. (flow rate 55 ml./min.) using 0.002-ml. samples.

(8) R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 202.

The semicarbazone melted at 156.5–158.5° and a mixture melting point with the semicarbazone of the vinyl ketone was 154–162°.

Anal. Calcd. for $C_{16}H_{31}N_3O$: C, 68.28; H, 11.10. Found: C, 68.56; H, 10.91.

URBANA, ILL.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Proof of the Structure and Stereochemistry of α-Amyrin by Synthesis from a β-Amyrin Derivative, Glycyrrhetic Acid[1,2]

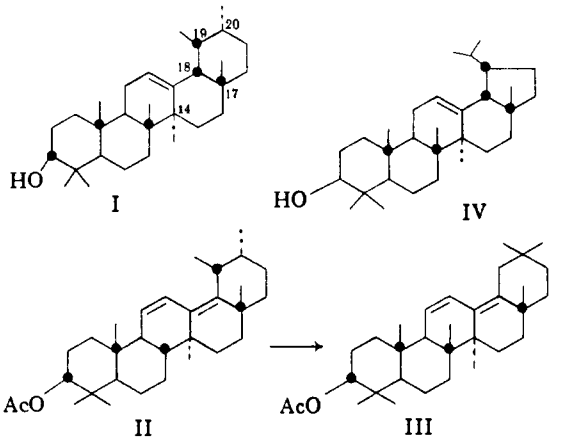
BY E. J. COREY AND E. W. CANTRALL

RECEIVED SEPTEMBER 27, 1958

A partial synthesis of α-amyrin according to the following sequence is described. Methyl glycyrrhetate → desoxoglycyrrhetic acid (VIb) → acetyl desoxoglycyrrhetic acid chloride (VIc) → 29-nor-20β-methylaminoölean-12-en-3β-ol (VIf) → 29-nor-20β-trimethylammonoiumolean-12-en-3-β-ol iodide (VIg) → 29-norolean-12:20(30)-dien-3β-yl acetate (VIIb) → 29,30-bisnorolean-12-en-20-on-3β-yl benzoate (VIIIb) → 30-norurs-12-en-20-on-3β-yl benzoate (IX) → ursa-12:20(30)-dien-3β-yl benzoate (X) → α-amyrin.

The gross structure of α-amyrin which had been determined by Ruzicka, Jeger and co-workers[3] (I without stereochemical connotations) was elaborated to the complete sterochemical description I, in 1954, on the basis of extensive chemical and physical data.[4] This stereoformula provided for the first time a reasonable explanation of several aspects of the chemistry of α-amyrin which had been puzzling (*e.g.*, the unreactivity of the $\Delta^{12,13}$ double bond in comparison with that in β-amyrin). In addition the considerations leading to the assignment of I focused attention on the fact that the D and E rings comprise a *cis*-decalin system which is more stable than the corresponding *trans*-decalin system formed by epimerization of C_{18}, an inversion in the usual order of stability. It is also noteworthy that formula I for α-amyrin agrees nicely with the Ruzicka–Eschenmoser scheme for triterpene biosynthesis and permits additional conclusions regarding the stereochemistry of hydrogen migration.[4b]

Subsequent to the proposal of stereoformula I two alternative formulations were advanced. The first of these, in which configurations opposite to those in I had been assigned to C_{17}, C_{19} and C_{20},[5] soon had to be discarded since it was discovered that acid-catalyzed isomerization of ursa-11:13-(18)-dien-3β-yl acetate (II) produces olean-11:13-(18)-dien-3β-yl acetate (known to be III),[6] a change which almost certainly does not affect the configuration at C_{17}. The other formulation[6,7] for α-amyrin (IV), which adopted the ring system of lupeol, seemed unlikely from the outset for reasons outlined previously (footnote 4, reference 2), and has now been exlcuded rigorously by the synthesis reported herein, which was commenced



in 1954, and by evidence presented in the interim by the Zurich group.[8]

Our work started with the view that since β-amyrin and I differ only with regard to substitution at C_{19} and C_{20}, a partial synthesis of α-amyrin could probably be achieved from a β-amyrin derivative possessing functionality at or near these centers by suitable degradation and reconstruction. The most advantageous starting material from this standpoint and because of its availability to us in the form of the glycoside was the substance glycyrrhetic acid (V), the structure[9] and stereochemistry[10] of which had been established.

It was soon apparent that the first task, the conversion of the glycoside, glycyrrhizinic acid,[11,12]

(1) Preliminary communication, THIS JOURNAL, **80**, 499 (1958).

(2) Taken fron the Ph.D. dissertation of E. W. Cantrall, University of Illinois, 1957.

(3) A. Meisels, O. Jeger and L. Ruzicka, *Helv. Chem. Acta*, **32**, 1075 (1949); see also O. Jeger, *Forts. Chem. Org. Naturs.*, **7**, 1 (1950).

(4) (a) E. J. Corey and J. J. Ursprung, *Chemistry & Industry*, 1387 (1954); (b) THIS JOURNAL, **78**, 183 (1956); (c) previously the configurations at C_8, C_{14}, C_{17}, C_{18}, C_{19} and C_{20} were unknown, although the configuration at C_{17} opposite to that in I had been considered as proved on the basis of lengthy degradative sequences [O. Jeger, *Angew. Chem.*, 196 (1951); see also *Ann. Rep.*, **48**, 198 (1951)].

(5) J. L. Beton and T. G. Halsall, *Chemistry & Industry*, 1560 (1954).

(6) G. G. Allen, J. M. Beaton, J. I. Shaw, F. S. Spring, R. Stevenson, J. L. Stewart and W. S. Strachan, *ibid.*, 281 (1955).

(7) F. A. Spring and co-workers, *J. Chem. Soc.*, 2606, 2610, 3072, 3371, 3378, 3992 (1955); 456, 465 (1956); see also D. D. Phillips and D. E. Tuites, THIS JOURNAL, **78**, 5438 (1956) and G. D. Meakins, *Chemistry & Industry*, 1353 (1955).

(8) A. Malera, D. Arigoni, A. Eschenmoser, O. Jeger and L. Ruzicka, *Helv. Chim. Acta*, **39**, 441 (1956), succeeded in dissecting ring E from α-amyrin and in converting the fragment so obtained into a 2,3,6-trimethylcyclohexanone of known absolute configuration thereby establishing unambiguously the configuration at C_{20} in α-amyrin and the fact that the E ring is six membered.

(9) L. Ruzicka and A. Marxer, *ibid.*, **22**, 195 (1939).

(10) (a) D. H. R. Barton and N. J. Holness, *J. Chem. Soc.*, 78 (1952); (b) J. M. Beaton and F. S. Spring, *ibid.*, 3126 (1955).

(11) Glycyrrhizinic acid, $C_{42}H_{62}O_{16}$, is a β-glycoside containing two hexuronic acid units: (a) A. Tschirch and H. Cederberg, *Arch. Pharm.*, **245**, 97 (1907); (b) W. Voss, P. Klein and H. Sauer, *Ber.*, **70**, 122 (1937); (c) C. Norman, *Chem. Weekblad*, **48**, 213 (1952).

(12) We are indebted to Dr. C. K. Swift of the MacAndrews-Forbes Co. for generous supplies of glycyrrhizinic acid as the monoammonium salt.