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

The Synthesis of Pentacyclosqualene (8,8′-Cycloönocerene) and the α- and β-Onoceradienes[1]

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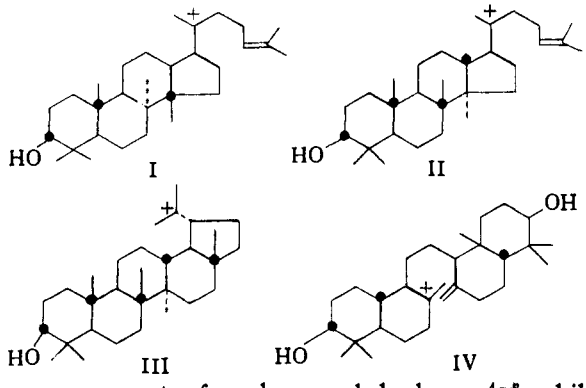
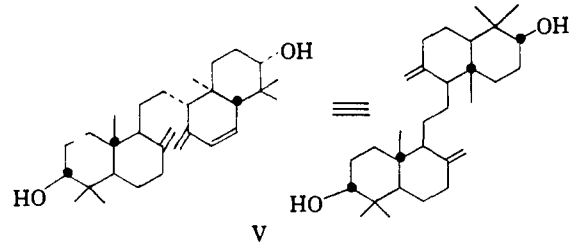
The application of electrolytic oxidation to the synthesis of C_{30}-triterpene structures from C_{16}-carboxylic acids is illustrated by the synthesis of the substances cited above. A proof of the stereochemistry of these substances is presented.

The ingenious suggestions made by Ruzicka, Eschenmoser, *et al.*,[2,3] regarding the pathways of triterpene biosynthesis have provided a straightforward rationale for the diverse structural types encountered in this series and have been of value subsequently in the elucidation of several unknown structures. According to this scheme the acylic triterpene squalene, which serves as a common biosynthetic precursor, may be converted by cation–olefin cyclization to one of four intermediate ions, I–IV, which subsequently lead to the different types of triterpenes. Cation I gives lanosterol after



rearrangement of carbon and hydrogen[4–6] while cation II may form the stereoisomeric euphol[7] and/or tirucallol[8] by rearrangement or may simply combine with hydroxide ion to produce dammarendiol.[9] The pre-lupeol (lupanyl) cation III is regarded as the precursor of the pentacyclic triterpenes lupeol,[10,11] β-amyrin,[10,12] taraxasterol,[13] α-amyrin,[14,15] taraxerol,[16] friedelin[17] and alnusenol[18] (all by rearrangement of carbon and hydrogen) and also their oxygenated derivatives.

The fourth type of cyclization, *via* the preonocerin cation IV, suggested by the structure of onocerin as described by Barton and Overton,[19] is unique in that cyclization is initiated from both ends of the squalene chain and can lead to structures possessing a twofold symmetry axis as in onocerin (V). The present paper describes studies on a synthetic method which takes advantage of their characteristic symmetry.[20]



From the outset one of the main objectives was the development of a practical synthesis of the *pentacyclic* structure XIV which would be formed by cation–olefin cyclization of squalene *via* an intermediate of carbon skeleton IV without rearrangement, and for the sake of operational convenience we chose to deal with substances lacking the hydroxyl functions of the terminal rings. This compound which might, in principle, be formed by acid-catalyzed cyclization of squalene has never been prepared in that way despite numerous attempts to effect such a change (see below), and the only preparative route known is the recent partial synthesis from onocerin.[19] Its synthesis was of interest for this reason and also because of its role as the parent (or precursor) hydrocarbon of naturally occurring triterpenes which might emanate from IV by further cyclization.[21]

The synthesis of pentacyclosqualene (XIV) described herein, which amounts to a total synthesis, was effected starting with the (−)-lactone VII which is easily prepared by oxidation of sclareol

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

(2) L. Ruzicka, A. Eschenmoser and H. Heusser, *Experientia*, **9**, 357 (1953).

(3) A. Eschenmoser, L. Ruzicka, O. Jeger and D. Arigoni, *Helv. Chim. Acta*, **38**, 1890 (1955).

(4) T. T. Tchen and K. Bloch, THIS JOURNAL, **78**, 1516 (1955).

(5) R. K. Maudgal, J. T. Tchen and K. Bloch, *ibid.*, **80**, 2589 (1958).

(6) J. W. Cornforth, R. H. Cornforth, A. Pelter, M. G. Horning and G. Popjak, *Proc. Chem. Soc.*, 112 (1958).

(7) D. H. R. Barton, J. F. McGhie, M. K. Pradhan and S. A. Knight, *J. Chem. Soc.*, 876 (1955).

(8) E. Menard, H. Wyler, A. Hiestand, D. Arigoni, O. Jeger and L. Ruzicka, *Helv. Chim. Acta*, **38**, 1517 (1955).

(9) J. S. Mills, *J. Chem. Soc.*, 2196 (1956).

(10) See J. Simonsen and W. C. J. Ross, "The Terpenes," Vol. IV, Cambridge University Press, 1957.

(11) T. R. Ames, T. G. Halsall and E. R. H. Jones, *J. Chem. Soc.*, 450 (1951).

(12) D. H. R. Barton and N. J. Holness, *ibid.*, 78 (1952).

(13) T. R. Ames, T. G. Halsall and E. R. H. Jones, *ibid.*, 1905 (1954).

(14) E. J. Corey and J. J. Ursprung, THIS JOURNAL, **78**, 183 (1956).

(15) E. J. Corey and E. W. Cantrall, *ibid.*, **80**, 499 (1958).

(16) J. M. Beaton, F. S. Spring, R. Stevenson and J. L. Stewart, *J. Chem. Soc.*, 2131 (1955).

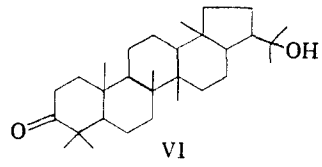
(17) E. J. Corey and J. J. Ursprung, THIS JOURNAL, **78**, 5041 (1956).

(18) F. S. Spring, J. M. Beaton, R. Stevenson and J. M. Stewart, *Chemistry and Industry*, 1054 (1956).

(19) D. H. R. Barton and K. H. Overton, *J. Chem. Soc.*, 2639 (1955).

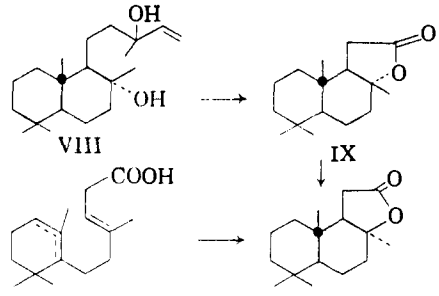
(20) A preliminary announcement of this work appeared in THIS JOURNAL, **79**, 3925 (1957).

(21) Since publication of the preliminary account of this work, evidence has been obtained for the further bio-transformation of the cation IV to pentacyclic triterpenes related to XIV (and fundamentally different from the pentacyclic derivatives formed *via* the pre-lupeol cation III) from the structure of hydroxyhopanone (VI). See W. J. Dunstan, H. Fazakerley, T. G. Halsall and E. R. H. Jones, *Croat. Chem. Acta*, **29**, 173 (1957), and K. Schaffner, L. Cagliotl, D. Arigoni and O. Jeger, *Helv. Chim. Acta*, **41**, 152 (1958).



VI

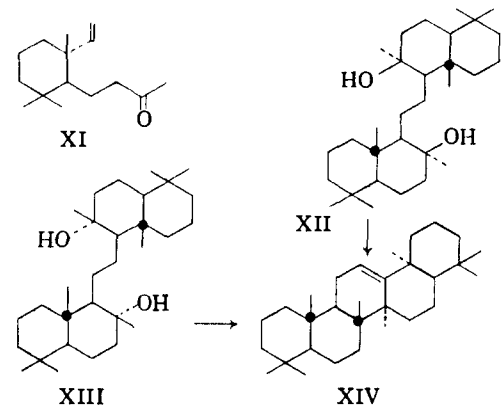
(VIII) to the lactone IX[22] followed by acid-catalyzed isomerization and which has been obtained totally synthetically by Lucius, in racemic admixture with the (+)-antipode, by cyclization of either α- or β-monocyclohomofarnesic acid (X).[23] For the synthesis of a symmetrical C_{30}



structure one clear possibility is the coupling of two of the C_{15} units obtained by removal of the carboxyl function from the acid corresponding to VII. The electrolytic oxidative decarboxylation ("Kolbe coupling") reaction appeared to afford a simple way of generating and coupling such C_{15} units, although none of the previously reported examples of this reaction involve such a complex reactant.[24,25] Despite this fact and the difficulties often encountered in finding suitable reaction conditions for the Kolbe coupling process, it was possible to obtain a fair yield of coupling product without extensive experimentation. The lactone VII was converted to the ammonium salt of the corresponding hydroxy acid and this, in turn, was electrolyzed in refluxing methanol at a smooth platinum anode. Two products were isolated in pure form from the reaction mixture by chromatography, a liquid unsaturated ketone, $C_{15}H_{26}O$ (XI, 34–38% yield),[26] and the expected tetracyclic diol XII in *ca.* 12% yield. Although the yields of the latter probably can be improved by systematic variation of reaction conditions, this was not investigated since, as is described below, the acetyl derivatives of the hydroxy acids are more favorable cases for electrolytic coupling.

Electrolysis of the stereoisomeric ammonium salt derived from the lactone IX under essentially the same conditions described above gave similar results: the liquid ketone $C_{15}H_{26}O$ was obtained in 33–36% yield and the new tetracyclic diol XIII was isolated in *ca.* 17% yield.

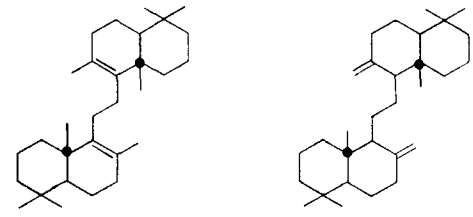
Treatment of either of the tetracyclic diols XII or XIII with perchloric acid in benzene–acetic



acid gave (+)-pentacyclosqualene (XIV) identical in all respects with the substance γ-onocerene (8,8′-cycloönocerene) prepared from onocerin.[19]

Recently the tetracyclic diol XII has also been synthesized by Eschenmoser and co-workers[27] in a very elegant way using a Diels–Alder sort of dimerization of an α-methylene ketone to accomplish the $C_{15}\rightarrow C_{30}$ transformation.

In the present work the tetracyclic diols XII and XIII were also utilized for the synthesis of the α- and β-onoceradienes which are derived from onocerin.[19] Dehydration by means of phosphorus oxychloride–pyridine transformed XII into β-onoceradiene (XV) and XIII into α-onoceradiene (XVI).



XV XVI

These conversions possess considerable stereochemical significance since they provide key data for an unequivocal proof of configuration at all six asymmetric centers of α-onoceradiene—which proceeds as follows. First of all, since the lactones VII and IX are known to have *trans*-interlocked A/B rings with absolute configurations as shown,[28] these configurations must also obtain for the four corresponding centers in the onoceradienes, C_5, C_{10}, C_5' and C_{10}'. The configuration at C_8 (and, of course, C_8') must be the same for diol XII and its precursor lactone VII, and similarly diol XIII and lactone IX also have identical configurations at C_8. From the course of dehydration of diol XII it is clear that the hydroxyl groups must be axially oriented as are the hydrogens at C_9 and C_9' and by the same argument, the hydroxyls of diol XIII are equatorial.[29] Since lactone VII is more stable than lactone IX, as is clear from isomerization data

(22) L. Ruzicka and M. Janot, *Helv. Chim. Acta.*, **14**, 645 (1931).

(23) G. Lucius, *Angew. Chem.*, **68**, 247 (1956); *Archiv. Pharm.*, **63**, 57 (1957).

(24) B. C. L. Weedon, *Quart. Revs.*, **6**, 380 (1952).

(25) Sherlock Swann, Jr., in A. Weissberger "Technique in Organic Chemistry," Vol. II, Interscience Publishers, Inc., New York, N. Y.

(26) The structure of this substance is considered in the accompanying paper, E. J. Corey and R. R. Sauers, THIS JOURNAL, **81**, 1743 (1959).

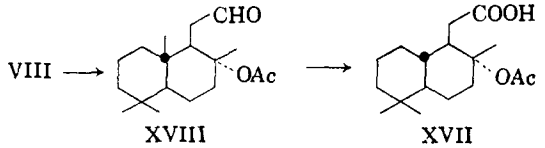
(27) E. Romann, A. J. Frey, P. A. Stadler and A. Eschenmoser, *Helv. Chim. Acta*, **40**, 1900 (1957).

(28) See D. H. R. Barton in E. H. Rodd, "Chemistry of Carbon Compounds," Vol. IIB, Elsevier Publishing Co., Amsterdam, 1953, pp. 723–725 and 764.

(29) See D. H. R. Barton, A. Campos-Neves and R. C. Cookson, *J. Chem. Soc.*, 3500 (1956).

(see Experimental; also *cf.* Stoll and Hinder[30]) and possesses an axial oxygen substituent, it must have a *cis*-fused lactone ring as shown. Further, lactone IX which possesses an equatorial oxygen and which might be either a *trans*-fused lactone with 9α-hydrogen or a *cis*-fused lactone with 9β-hydrogen clearly must be the former to explain the isomerization IX → VII. Since lactone IX and α-onoceradiene must have the same configuration at C_9 (and C_9'), the correct stereoformula of α-onoceradiene is necessarily XVI, and onocerin which is known to possess equatorial hydroxyl functions is given correctly by V as proposed by Barton.[19] The α-orientation of hydrogen at C_9 can now also be considered as proved for the following compounds which have been interrelated via the lactone IX: sclareol, manoöl, ambrein, labdanolic acid[31] and cativic acid.[32,33]

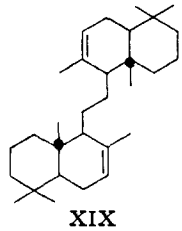
A considerably better route to the onoceran-8,8′ diol XIII and pentacyclosqualene was devised after the nature of the by-product $C_{16}H_{26}O$ had been ascertained, which employed the acetyl derivative XVII of the hydroxy acid derived from IX in the electrolytic coupling. The acetoxy acid was prepared from sclareol (VIII) by a method developed by Dr. S. Proskow in these laboratories which



XVIII XVII

consists of (1) oxidation with osmium tetroxide–sodium metaperiodate to the acetoxy aldehyde XVIII and (2) further oxidation with permanganate to XVII. Electrolytic oxidation of the ammonium salt of XVII in refluxing methanol gave a 34% yield of tetracyclic diacetate, with indications that considerable improvement could result from further experimentation. The yield of coupling product was favored by increasing the concentration of ammonium salt, the current density and temperature (at least up to the b.p. of methanol). None of the unsaturated ketone XI could be detected. Reduction of the tetracyclic diacetate obtained from XVII with lithium aluminum hydride produced the diol XIII in high yield. The tetracyclic diacetate could also be converted to pentacyclosqualene (XIV) by treatment with acid.

In addition to the studies described above a number of experiments were performed on the synthesis of pentacyclosqualene directly from squalene by acid-catalyzed cyclization and, although the results obtained were uniformly unpromising, they are mentioned briefly here because the direct chemical cyclization of squalene is a challenging problem which penetrates many aspects of triterpene synthesis and which deserves continued study. According to Heilbron, *et al.*,[34] treatment of squalene with hot formic acid produces "tetracyclosqualene" as a viscous oil. Since dehydrogenation of this oil, which is probably a complex mixture, with sulfur or selenium affords 1,2,5-trimethylnaphthalene,[35,36] structures such as XIX have been entertained for this substance.[10] Assuming that such structures are present to some extent in the mixture and that a significant fraction of such molecules possess an onocerin-like symmetry and configuration it is possible that Heilbron's "tetracyclosqualene" may, in fact, contain a small amount of pentacyclosqualene or that such can be produced by further treatment with acid, for example under the conditions described above for the synthesis of pentacyclosqualene from the pure tetracyclic diols XII and XIII.



XIX

In the present study squalene, which was purified *via* the thiourea adduct,[37] was subjected to cyclization under a variety of conditions, but in no case could pentacyclosqualene be isolated or detected. Trifluoracetic acid, formic acid, perchloric acid–acetic acid and formic acid–sulfuric acid mixtures were tried at various temperatures. In no case could crystalline material be isolated even after selective destruction of reactive olefinic materials with potassium permanganate and chromatography. The product from formic acid cyclization was investigated further for pentacyclosqualene by oxidation with sodium dichromate and subsequent reduction with lithium aluminum hydride and acid-catalyzed dehydration. This sequence of reagents converts pentacyclosqualene to the Δ^{12}-11-ketone (λ_{max} 241 mμ), the Δ^{12}-11-alcohol and finally the $\Delta^{9:11,12:13}$-diene (λ_{max} 281 mμ).[19] Although a conjugated ketone chromophore was produced in the first step (λ_{max} 246 mμ), the crude product from the three-step sequence did not show any signs of an absorption maximum at or near 281 mμ. It is apparent from these experiments that not more than a very small amount of pentacyclosqualene results from acid treatment of squalene under conditions which are more or less standard for acid-catalyzed cyclization of polyolefins.

It is a pleasure to thank Dr. Sherlock Swann, Jr., and Mr. W. Garrison for valuable aid with the electrolytic experiments and Drs. D. H. R. Barton, M. Stoll and G. Lucius for gifts of onocerin, sclareol and *d,l*-lactone VII, respectively.

Experimental[38]

iso-Norambrienolide (VII).—A solution of 4.00 g. of norambreinolide (IX), prepared[33] from sclareol, in 120 ml. of

(30) M. Stoll and M. Hinder, *Helv. Chim. Acta*, **36**, 1995 (1953); **37**, 1859 (1954).

(31) J. Cocker and T. G. Halsall, *J. Chem. Soc.*, 4262 (1956).

(32) H. Zeiss and F. W. Grant, Jr., THIS JOURNAL, **79**, 1201 (1957).

(33) For additional evidence see D. B. Bigley, N. A. J. Rogers and J. A. Barltrop, *Chemistry and Industry*, 558 (1958).

(34) I. M. Heilbron, E. D. Kamm and W. M. Owens, *J. Chem. Soc.*, **129**, 1630 (1926).

(35) J. Harvey, I. M. Heilbron and E. D. Kamm, *ibid.*, 3136 (1926).

(36) I. M. Heilbron and D. G. Wilkinson, *ibid.*, 2546 (1930).

(37) O. Isler, R. Ruegg, L. Chopard-dit-Jean, H. Werner and K. Bernhard, *Helv. Chim. Acta*, **39**, 897 (1956).

(38) All melting points are corrected; unless otherwise noted they were determined on a micro hot-stage apparatus. All rotations

glacial acetic acid containing 1.0 ml. of concentrated sulfuric acid was heated at *ca.* 85° for 20 minutes. The cooled mixture was poured into 1.2 liters of water and extracted three times with ether. The extracts were washed twice with strong potassium carbonate solution and once with water. Evaporation of the ether *in vacuo* gave 3.56 g. of crude isolactone, m.p. 87–93°. Crystallization from low petroleum ether gave 2.88 g. (72%) of white prisms, m.p. 92–94°; infrared max. (chloroform) 1767 cm.$^{-1}$, identical with an authentic sample of m.p. 91–93°, $[\alpha]^{26}D$ −34.6° (*c* 1.65, in benzene) (lit.[30] m.p. 93°, $[\alpha]^{23}D$ −34.8°, in benzene).

Ammonium Salt from VII.—Hydrolysis of 2.88 g. (0.0115 mole) of isolactone was effected over 12 hours in a refluxing solution of 100 ml. of methanol containing 1.4 g. (0.025 mole) of potassium hydroxide. Evaporation of the methanol gave a gum which was taken up in 200 ml. of ice-water and acidified with ice-cold, dilute hydrochloric acid under a layer of ether. The layers were quickly separated and the aqueous phase extracted once with ether. The combined extracts were washed once with ice-water and poured into a large volume of ammoniacal ether. The precipitated salt was collected and washed with dry ether; yield 3.12 g. (95%), $[\alpha]^{30}D$ 13.3° (*c* 1.95, in methanol).

The Ammonium Salt from IX was prepared in 93% yield according to the directions given above for the *iso*-salt except that reflux time was cut to 2.5 hours; $[\alpha]^{30}D$ +26.2° (*c* 1.64, in methanol).

Description of Electrolysis Cell.—A 150-ml. electrolytic beaker was fitted with a rubber stopper in which holes were drilled for three electrodes, a reflux condenser and a thermometer. The smooth platinum anode was centered between two smooth platinum cathodes at a distance of *ca.* 0.5 cm. and had a total area of 4.50 cm.^{2}.

General Procedure for Electrolyses.—A solution of the appropriate ammonium salt in 60 ml. of reagent-grade methanol was stirred with a magnetic stirrer and electrolyzed until the current dropped to near zero. Ammoniacal methanol was added periodically to inhibit lactonization.

Isolation of the Tetracyclic Diols XII and XIII.—The isolation of the products from the electrolysis of the ammonium salt from VII involved evaporation of the methanol followed by chromatography on alumina. Elution with low petroleum ether removed only vinyl ketone XI. Subsequent eluates contained uncharacterized oils showing infrared maxima (carbon tetrachloride) at 3620, 3480, 1782, 1647, 924 and 893 cm.$^{-1}$. The diol XII was eluted with 1:1 benzene–ether. Further elution gave only oils.

The pure diol (needles from methanol–water) melted at 185–186.5° and had $[\alpha]^{27}D$ +42.3° (*c* 1.61); infrared max. (carbon disulfide) 3620 and 3480 (broad) cm.$^{-1}$.

Anal. Calcd. for $C_{30}H_{54}O_2$: C, 80.65; H, 12.18. Found: C, 80.58; H, 12.29.

Similar treatment of the reaction mixture from the electrolysis of the hydroxy ammonium salt from IX gave the vinyl ketone in the petroleum ether eluates followed by oils. The diol XIII was removed in 199:1 ether–methanol. Crystallization from methanol afforded colorless needles, m.p. 270–271°, $[\alpha]^{25}D$ +12.5° (*c* 1.44); infrared max. (carbon disulfide) 3356 cm.$^{-1}$.

Anal. Calcd. for $C_{30}H_{54}O_2$: C, 80.65; H, 12.18. Found: C, 80.41; H, 12.34.

The results of several runs are summarized in Tables I and II.

TABLE I

ELECTROLYSIS OF AMMONIUM SALT FROM VII

Salt, mmoles	Initial voltage, v.	Initial current, amps.	Yield of crude diol, %	Yield ketone, %	Temp.
4.71	32	0.8	7.2	38	Reflux
4.80	40	0.5	8.9	38	Reflux
9.63	50	1.7	12.0	34	Reflux

Acetoxy Acid XVII (With Dr. S. Proskow).—To a solution of 30.847 g. (0.1 mole) of sclareol in 900 ml. of purified dioxane was added 300 ml. of water, 117.51 g. (0.55 mole) of sodium metaperiodate and 0.181 g. (0.71 mmole) of osmium tetroxide. The mixture was stirred at 25 to 30° for 5.5 hours and then poured into 3.0 liters of water. The combined extracts from four 400-ml. ether extractions were washed twice with potassium carbonate solution and once with water. Evaporation of the dried extracts gave 22 g. of crude acetoxy aldehyde as a dark, viscous oil. The infrared spectrum in carbon disulfide showed broad absorption at 1725 cm.$^{-1}$ and C–O stretching at 1250 cm.$^{-1}$.

TABLE II

ELECTROLYSIS OF AMMONIUM SALT FROM VIII

Salt, mmoles	Initial voltage, v.	Initial current, amps.	Yield of crude diol, %	Yield ketone, %	Temp., °C.
2.98	70	1.0	1.8	33	*Ca.* 40–50
5.00	26	0.8	17.0	36	Reflux

The crude aldehyde in 1.2 liters of acetone was oxidized with 25 g. of potassium permanganate (5 hours at 26°) with a steady stream of carbon dioxide bubbling through the mixture. Evaporation of the filtered solution gave a dark oil which was taken up in 400 ml. of ether. The ether solution was washed once with dilute sodium sulfite solution and three times with dilute potassium carbonate solutions. The combined aqueous extracts were acidified with 6 *N* hydrochloric acid and extracted with ether. Evaporation of the dried extracts gave 12 g. of crude acetoxy acid. Two crystallizations from ethanol–water gave 4.4 g. (14%) of XVII as white needles, m.p. 158–160° (lit.[39] 157–158°). The infrared spectrum (Nujol) showed strong maxima at 1737, 1705 and 1267 cm.$^{-1}$.

TABLE III

ELECTROLYSIS OF ACETOXY ACID XVII

Acid,[a] mmoles	Initial voltage, v.	Initial current, amps.	Yield coupled product (% crude)	Temp., °C.
3.86	65	1.0	7.5	37–50
6.63	62	1.3	6.2	Reflux
4.83	35	.4	21	Reflux
5.00	34	.3	23	Reflux
5.57	30	.4	26	Reflux
5.48	40	.4	30	Reflux
5.61	45	.6	34.5	Reflux

[a] The ammonium salt of the acetoxy acid was not isolated but made *in situ* by adding ammoniacal methanol at the beginning of the run.

Electrolysis of the Acetoxy Acid XVII.—Table III summarizes the various electrolytic experiments with XVII.

The work-up procedure for the acetoxy acid coupling reaction was simply to filter off the product at the end of the electrolysis. No further product was obtained on subsequent chromatography; only an oil showing strong carbonyl absorption at 1738 cm.$^{-1}$ (carbon tetrachloride) and acetate C–O stretching at 1252 cm.$^{-1}$ was obtained.

The tetracyclic diacetate was purified by crystallization from acetone (needles) and had m.p. 189–191.5° $[\alpha]^{26}D$ −18.3° (*c* 1.36); infrared max. (carbon tetrachloride) 1729 and 1255 cm.$^{-1}$.

Anal. Calcd. for $C_{34}H_{58}O_4$: C, 76.93; H, 11.01. Found: C, 76.70; H, 10.95.

Lithium Aluminum Hydride Reduction of the Diacetate of XIII.—To a slurry of 0.063 g. of lithium aluminum hydride in 25 ml. of dry ether was added 0.050 g. of tetracyclic diacetate from XVII. After stirring for 1.5 hours at room temperature, the reaction was treated cautiously with water and dilute hydrochloric acid. Extraction with ether followed by drying and evaporation gave 0.039 g. (93%) of diol XIII, m.p. 267–269.5°, identical by infrared spectrum and mixture melting point with the diol XIII prepared from the lactone IX.

Pentacyclosqualene XIV. A. From Diol XII.—A solution of 0.150 g. of diol in 12 ml. of benzene was added to 30 ml. of acetic acid containing 3 ml. of perchloric acid and 18 drops of acetic anhydride and allowed to stand at room temperature for 27 hours. The benzene was allowed to evaporate during another 18 hours. Filtration afforded 9.5 mg. of

were determined in chloroform unless otherwise noted. The alumina used for chromatography was Merck reagent aluminum oxide and was not further treated except where noted. We are indebted to Mr. James Brader and associates for the infrared spectra and to Mr. Jozsef Nemeth and associates for microanalyses.

(39) L. Ruzicka, C. F. Seidel and L. L. Engel, *Helv. Chim. Acta*, **25**, 621 (1942).

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°, $[\alpha]^{25}D$ +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°, $[\alpha]^{26}D$ +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

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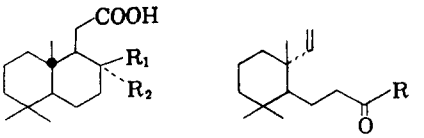
A novel elimination process, which has been observed during anodic reaction of a γ-hydroxy acid, is described.

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

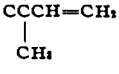
group since bands of moderate intensity were observed at 1637 cm.$^{-1}$ (C=C stretching) and 1008, 917 cm.$^{-1}$ (-CH=CH_2 out-of-plane C—H bending)[4] and this was confirmed by hydrogenation with palladium–charcoal in methanol to a dihydroketone which showed no absorption at *ca.* 1637, 1008 and 917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

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