colorless platelets [11.1 g., m.p. 105.5–107.5°, λ_{max} 281 mμ (ϵ = 3,160) and 287 mμ (ϵ = 3,140), 5.82, 6.18, 6.37, and 7.37 μ (chloroform): $[\alpha]^{25}D$ +122°; calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44; OCH_3, 17.32. Found: C, 73.93; H, 8.43; OCH_3, 17.05]. Compound II formed a bright yellow 2,4-dinitrophenylhydrazone [m.p. 203.5–207.5°, λ_{max} 3.04, 5.83, 6.23, 6.33, and 7.61 μ; calcd. for $C_{28}H_{34}N_4O_7$: C, 62.44; H, 6.36. Found: C, 62.64; H, 6.46].

To confirm the structure assigned to II, methyl O-methyl-7-acetonylpodocarpate was synthesized in the following manner: methyl O-methyl-7-acetylpodocarpate[3] (IV) was converted by a Willgerodt reaction to the corresponding thiomorpholide [V, m.p. 177–180.5°, λ_{max} 281 mμ (ϵ = 17,600), 5.81, 6.20, 6.37 and 6.71 μ (chloroform); $[\alpha]^{25}D$ +101° (ethanol); calcd. for $C_{25}H_{35}NO_4S$: S, 7.20; N, 3.14. Found: S, 7.20; N, 3.17]. Hydrolysis of V with sulfuric acid in acetic acid gave the corresponding monobasic acid [VI, m.p. 144.5–147°, presoftened, λ max 281 mμ (ϵ = 2,690) and 287 mμ (ϵ = 2,630), 5.82, 6.18, 6.35, and 6.66 μ (KBr); calcd. for $C_{21}H_{28}O_5$: C, 69.97; H, 7.83; OCH_3, 17.22; COOH, 12.49. Found: C, 70.23; H, 8.03; OCH_3, 16.87; COOH, 12.33]. Addition of an ether solution of VI to an excess of methylmagnesium bromide gave II which was identical [melting point, no depression on mixing: ultraviolet and infrared spectra] with the compound derived from the Willgerodt reaction on methyl O-methyl-7-propionylpodocarpate.

When heated with sulfur and morpholine, methyl O-methyl-7-acetonylpodocarpate (II) was converted to III (41% yield).

[3] W. P. Campbell and D. Todd, THIS JOURNAL, **62**, 1287 (1940).

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RECEIVED JUNE 3, 1957

THE PREPARATION OF BERYLLIUM AMALGAM[1]

Sir:

The preparation of a beryllium amalgam by electrolysis of concentrated solutions of $BeCl_2$ into a mercury cathode has been claimed by Prytz[2] but this method is not confirmed elsewhere. A new and novel method, involving electrolysis of beryllium from a NaCl–$BeCl_2$ fused salt mixture into a mercury cathode has been developed in this laboratory and applied to the preparation of beryllium metal.[3]

Procedure.—Equimolar quantities of NaCl and $BeCl_2$ are melted together (224°)[4] to form an electrolyte. Beryllium chloride can be prepared by hydrochlorination of beryllium metal at 500°.

The electrolysis cell consists of a 4-liter resin reaction flask with a cylindrical inner sleeve to facilitate removal of the electrolyte at the conclusion of the electrolysis. Heat is supplied by an electric heating mantle.

Mercury (5000 g.) is placed in the cell and chunks of electrolyte are added quickly. The cell is closed and the electrolyte is melted down in an atmosphere of argon. A carbon anode is then inserted and the electrolysis commenced at about 5 volts and 6 amperes at temperatures of 300–350°.

Amalgam tends to climb through the salt to the anode. Therefore it is desirable to stir the cathode during electrolysis to avoid premature termination of the experiment. At the conclusion of the electrolysis (50–100 amp.-hr.) the cell is opened and the inner sleeve removed with the electrolyte within it. The amalgam, which varies in viscosity from a free flowing liquid to a semi-solid paste, depending on beryllium concentration, is found floating on the mercury at the bottom of the cell. The current efficiency of the electrolysis is approximately 65%.

The formation of amalgam evidently is sensitive to small traces of oxygen. Rigorous purification of the argon cover is required and it is essential that the cell be leak tight if amalgam is to be formed.

It is evident from this description that it also might be possible to prepare a beryllium amalgam by a displacement reaction with sodium amalgam and the fused-salt mixture used in electrolysis.

Properties of the Amalgam.—The amalgam is unstable in air, decomposing spontaneously with the formation of a black powder which is approximately 75% Be by weight. Dilute amalgams can be concentrated to about 2% beryllium by pinholing. The 2% amalgam is a thick pasty material from which additional mercury can be removed by such methods as pressing in a die or heating *in vacuo*.

Surprisingly, the room temperature X-ray diffraction pattern of the amalgam is the same as solid (−78°) mercury. The exact nature of the amalgam is not known. By analogy with the Mg–Hg system the compound $BeHg_2$ (2.2% Be) is suspected. It is hoped this information will assist in further investigation of the Be–Hg system.

[1] Presented at Miami meeting of American Chemical Society April 7–12, 1957. Research supported by the Atomic Energy Commission.

[2] M. Prytz, *Z. anorg. allgem. Chem.*, **193**, 113 (1930).

[3] M. C. Kells, R. B. Holden, C. I. Whitman, AEC report SEP-207 (1956).

[4] J. M. Schmidt, *Bull. soc. chim.*, **39**, 1686–1703 (1926).

[5] Stanford Research Institute, Menlo Park, California.

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RECEIVED JUNE 10, 1957

TOTAL SYNTHESIS OF PENTACYCLOSQUALENE[1]

Sir:

Despite the probable genesis of the pentacyclic hydropicene triterpenes[2] from squalene by cation-olefin cyclization with subsequent rearrangement of carbon and hydrogen,[3,4,5] the pentacyclic substance I which would be formed from squalene by

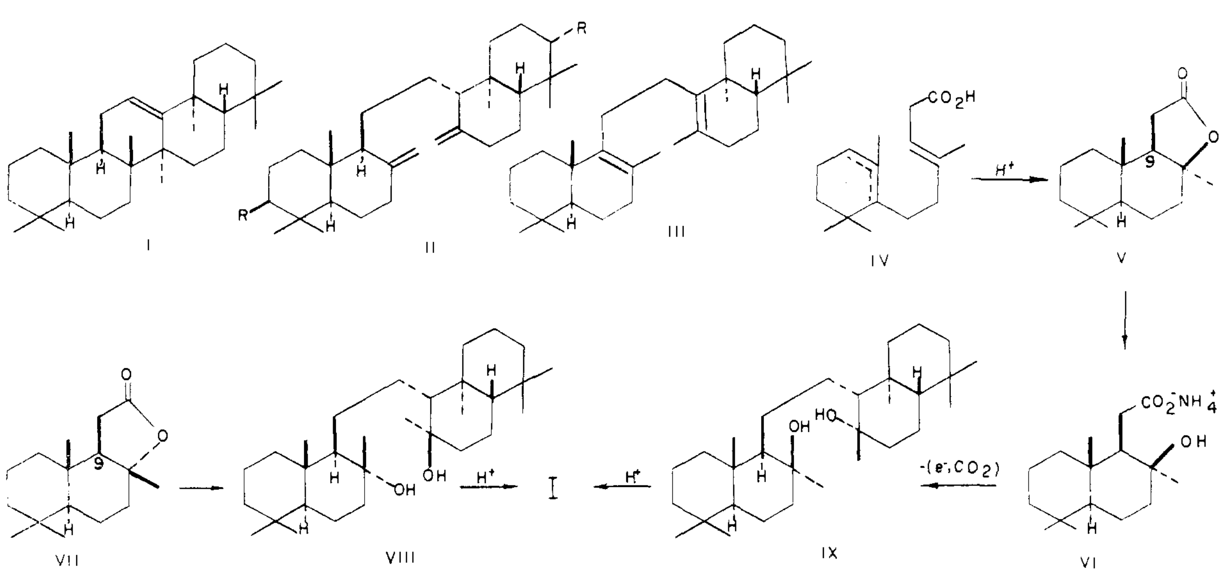
[1] This investigation was supported by a fellowship (AF-6570) from the National Institute of Arthritis and Metabolic Diseases, Public Health Service.

[2] α-Amyrin, β-amyrin, taraxerol, taraxasterol, friedelin, alnusenol and their oxygenated derivatives.

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

[4] E. J. Corey and J. J. Ursprung, THIS JOURNAL, **78**, 183 (1956).

[5] T. T. Tchen and K. Bloch, *ibid.*, **78**, 1516 (1956).



cyclization,[6] *without rearrangement*, has not yet been detected in nature. In addition, numerous attempts to effect the synthesis of pentacyclosqualene by acid-catalyzed cyclization of squalene have failed.[7]

We outline here a total synthesis of this substance, heretofore obtained only by partial synthesis from α-onoceradienediol[8] (II, R = OH), and, incidentally, the synthesis of both α-onoceradiene (II, R = H)[8] and β-onoceradiene (III).[8,9]

Acid-catalyzed cyclization of either α- or β-monocyclohomofarnesic acid (IV) leads to a mixture of lactones from which the (±)-lactone V has been isolated.[10,11] Hydrolysis of the (−)-lactone in methanolic potassium hydroxide followed by careful acidification and ammonolysis gave the ammonium salt VI in high yield. Oxidative electrolytic coupling of VI in refluxing methanol at a smooth platinum anode[12] gave after chromatography the diol IX (m.p. 185–186.5°, $[\alpha]_D$ +420; found: C, 80.58; H, 12.29). Cyclization of IX with perchloric acid in benzene-acetic acid yielded (+)-pentacyclosqualene, I (m.p. 275–276.5° (sealed capillary), $[\alpha]_D$ +86°) identical in all respects with "γ-onocerene" prepared from α-onoceradienediol (II, R = OH).[8] Dehydration of the diol IX with phosphorus oxychloride–pyridine gave β-onoceradiene (m.p. 159–161°, $[\alpha]_D$ +140°) identical with an authentic sample.

Similarly, the (+)-lactone VII led to the diol VIII (m.p. 270–271°, $[\alpha]_D$ +13°; found: C, 80.41; H, 12.34) which on cyclization also gave (+)-pentacyclosqualene (I). α-Onoceradiene (II, R = H; m.p. 199.5–201°, $[\alpha]_D$ +25°) was obtained from VIII by $POCl_3$ dehydration.[13]

It is a pleasure to thank Drs. D. H. R. Barton, G. Lucius and M. Stoll for gifts of materials and Dr. Sherlock Swann, Jr., and Mr. W. Garrison for valuable aid with the electrolytic experiments.

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[6] Following the same stereocourse which leads to the triterpenes cited in ref. 2.

[7] See L. Ruzicka, *Experientia*, **9**, 359 (1953).

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

[9] J. D. Cocker and T. G. Halsall, *ibid.*, 4262 (1956); K. Schaffner, R. Viterbo, D. Arigoni and O. Jeger, *Helv. Chim. Acta*, **39**, 174 (1956).

[10] G. Lucius, *Angew. Chemie*, **68**, 257 (1956); G. Lucius, private communication.

[11] Mild acid treatment of the (+)-*trans*-lactone VII obtained from sclareol served as a convenient source of the epimeric *cis*-lactone V; *cf.* L. Ruzicka and M. Janot, *Helv. Chim. Acta*, **14**, 645 (1931), and M. Stoll and M. Hinder, *Helv. Chim. Acta*, **36**, 1995 (1953). The lactone of L. Ruzicka, C. F. Seidel and L. L. Engel, *Helv. Chim. Acta*, **25**, 621 (1942), was shown by its characteristic infrared spectrum to correspond to the third lactone of Lucius[10] and is probably the C_9 epimer of VII since it can be prepared from *either* V or VII by acid-catalyzed isomerization. Further data on the sterochemistry and interconversions of these lactones will be reported later.

[12] The best yields of coupled material were obtained with high current density, refluxing methanol, and high salt concentrations. Ammonia was added periodically to inhibit lactonization.

[13] The dehydration products of the two epimeric diols IX and VII confirm, respectively, the diaxial and diequatorial orientations of the hydroxyl groups; *cf.* D. H. R. Barton, A. Campos-Neves and R. C. Cookson, *J. Chem. Soc.*, 3500 (1956).

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RECEIVED JUNE 17, 1957

MACROLIDE ANTIBIOTICS. VI. A STANDARD OF ABSOLUTE CONFIGURATION AMONG MACROLIDE ANTIBIOTICS

Sir:

As pointed out in a recent review,[1] the macrolide group of antibiotics represents a therapeutically and biogenetically important class of natural products. Knowledge concerning the absolute configuration of these substances is limited to a single center (C-10) of magnamycin[1] and this is of no direct applicability to the other antibiotics of this class since magnamycin follows the "acetate" rather than "propionate" pattern so common among macrolide antibiotics. Attempts to use rotation rules such as Hudson's lactone rule for the determination of the absolute configuration in the erythromycin series[2] have led to ambiguous results. We should now like to report certain reactions with neomethymycin (Ia)[3] which establish the absolute

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[1] R. B. Woodward "Festschrift Arthur Stoll," Birkhäuser, Basel, 1957, pp. 524–544; *Angew. Chem.*, **69**, 50 (1957).

[2] K. Gerzon, E. H. Flynn, M. V. Sigal, P. F. Wiley, R. Monahan and U. C. Quarck, THIS JOURNAL, **78**, 6396 (1956), footnote 21.

[3] Paper V, C. Djerassi and O. Halpern, *ibid.*, **79**, 2022 (1957)