Tetrahedron Letters No.26, pp. 2485-2488, 1967. Pergamon Press Ltd. Printed in Great Britain.

DITERPENOID TOTAL SYNTHESIS, AN A→B→C APPROACH. IV.

TOTAL SYNTHESIS OF METHYL dl-DEHYDROABIETATE[1]

Walter L. Meyer and Carl W. Sigel

Department of Chemistry, University of Arkansas, Fayetteville, Arkansas[*] and

Department of Chemistry, Indiana University, Bloomington, Indiana

(Received 17 April 1967)

In an earlier paper[2] we reported the development of a reaction sequence which appeared to have considerable generality for synthesis of a variety of tricyclic diterpenoid types. We now wish to report the total synthesis of a member of the diterpenoid resin acid family, methyl dehydroabietate (XVIII, R = CH_3), by this route.

Alkylation of diethyl α-methylmalonate with δ-bromovaleronitrile affords the cyano diester I, (b.p. 150-165°, 2.5 mm),[**] which is cyclized by potassium t-butoxide in benzene[3] to 2-carbethoxy-2-methyl-6-cyanocyclohexanone (II). Exposure of this cyano ketone to methyl vinyl ketone and sodium ethoxide[4] produces a nearly 50:50 mixture of the bicyclic enones III (m.p. 69-71°) and VI (m.p. 59-60°) in 84% total yield. The double bond of enone III undergoes hydrogenation much more rapidly than does that of VI, and consequently the mixture of enones can be partially reduced over 30% palladium on carbon to a mixture of octalone VI and decalone IV. This mixture is conveniently separated by conversion to the p-carboxyphenylhydrazones, hydrazone exchange with formaldehyde to liberate decalone IV (m.p. 91-92°), and acidic hydrolysis to liberate octalone VI.[5] The latter is hydrogenated to decalone VII (m.p. 85-87°). Thus this sequence makes available intermediates for elaboration to both the podocarpic and the abietic series of resin acids, although our work in the former series is not yet complete.

Alternatively the mixture of octalones III and VI can be hydrogenated until both have been converted to the trans-decalones IV and VII. Treatment of this decalone mixture with 96%

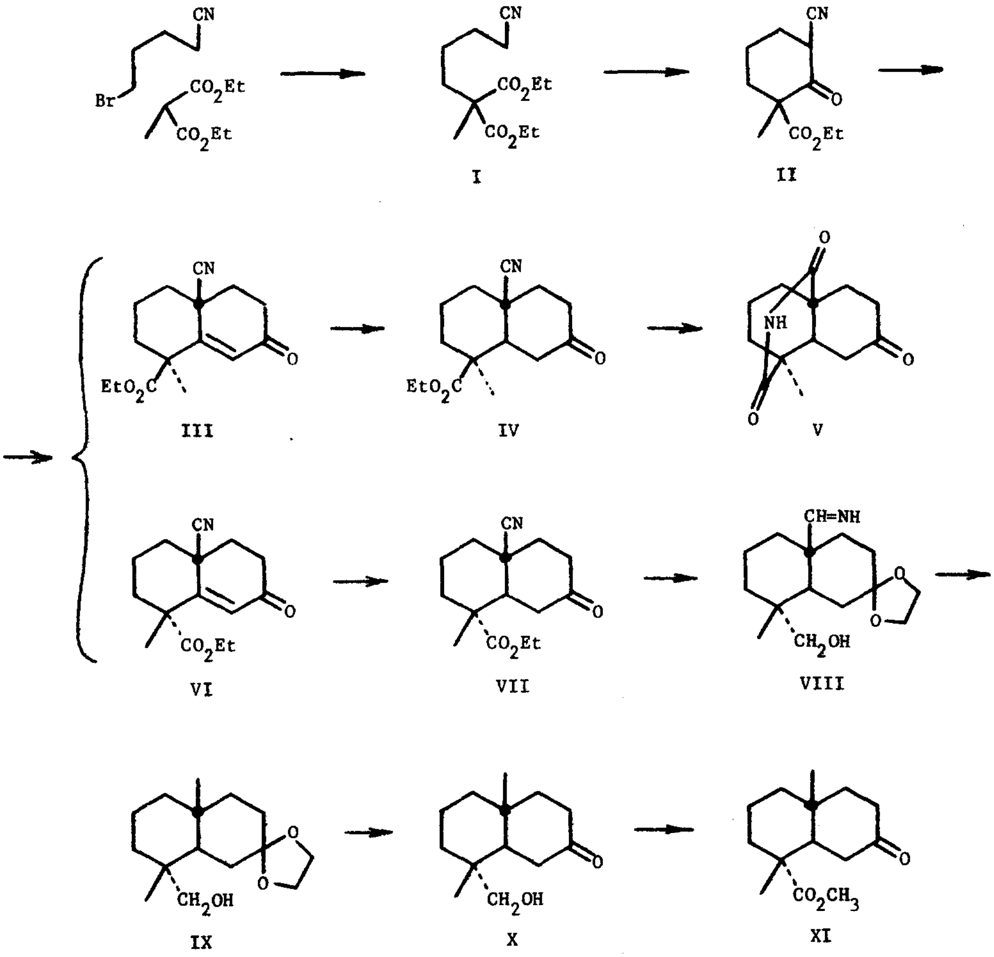
---

[*] Present address

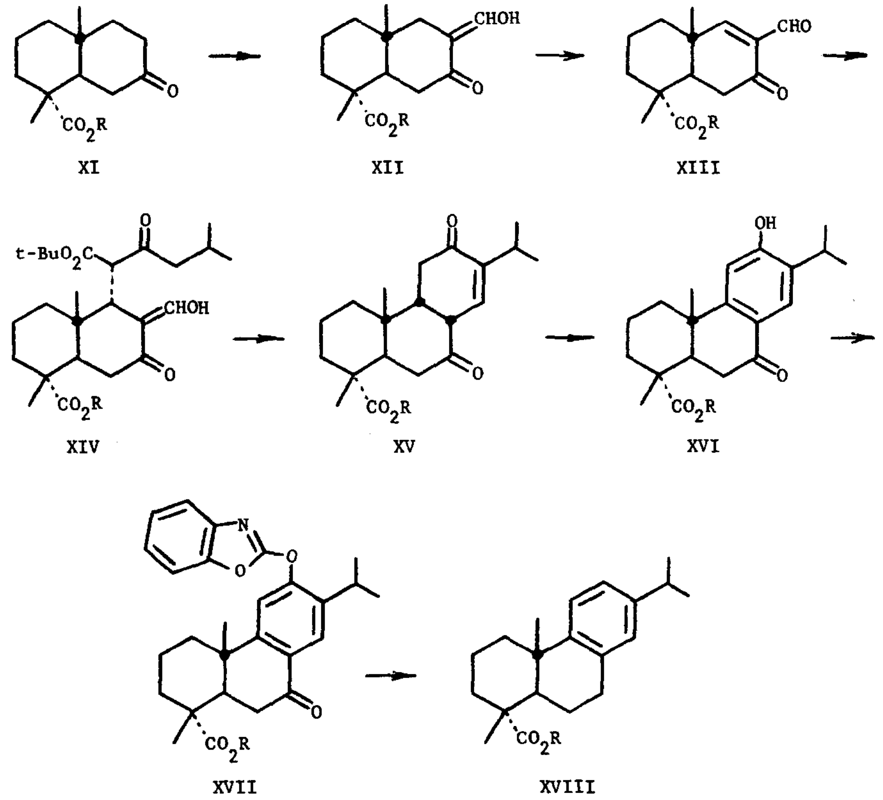
[**] Satisfactory elemental analyses were obtained for all new compounds for which m.p. or b.p. data are reported. Other intermediates were characterized by means of infrared, ultraviolet, and n.m.r. spectra.

sulfuric acid for 15 minutes leaves decalone VII unaltered while transforming decalone IV into the imide V. These two derivatives are readily separated by extraction, affording the cyano keto ester VII for use in the work described below and the imide V (m.p. 167-168°) for future conversion into diterpenoid alkaloids of the aconite-garrya family.

The angular cyano group of decalone VII is converted to methyl by the sequence described in our ferruginol synthesis.[2] Ketalization followed by lithium aluminum hydride reduction produces the hydroxy imino ketal VIII, which upon Huang-Minlon reduction, ketal hydrolysis, Jones oxidation, and diazomethane esterification affords the keto ester XI (m.p. 84-85.5°) in 60% overall yield from cyanodecalone VII.



Condensation with ethyl formate transforms decalone XI into the hydroxymethylene derivative, and this is oxidized by 2,3-dichloro-5,6-dicyanoquinone to the keto aldehyde XIII. Addition of *t*-butyl 5-methyl-3-ketohexanoate followed by treatment with p-toluenesulfonic acid affords the tricyclic enedione XV. Oxidation with pyridinium bromide perbromide affords keto phenol XVI (m.p. 238-240°), the 2-oxazolyl ether of which (XVII) is hydrogenolyzed[6] to remove both the B-ring ketone and the C-ring phenol, thereby producing methyl *dl*-dehydroabietate (XVIII, R = CH_3, m.p. 72-73°; reported[7] m.p. 71.5-73°). Infrared, ultraviolet, and nmr spectra of the latter are identical with those of the authentic *d*-enantiomer.



Acknowledgment. — We are grateful to the National Institute of Arthritis and Metabolic Diseases for support of this work through research grants AM-4215 (Indiana University) and AM-10123 (University of Arkansas), and to the National Institute of General Medical Sciences for a predoctoral fellowship to C. W. S.

REFERENCES

(1) Paper III: W. L. Meyer and E. Schindler, Tetrahedron Letters, 4261 (1966).

(2) W. L. Meyer, G. B. Clemans, and R. W. Huffman, Tetrahedron Letters, 4255 (1966).

(3) S. S. Kulp and S. A. Iobst, J. Med. Chem., **7**, 831 (1964).

(4) W. L. Meyer and A. S. Levinson, J. Org. Chem., **28**, 2184 (1963).

(5) M. Anchel and R. Schoenheimer, J. Biol. Chem., **114**, 539 (1936).

(6) W. J. Musliner and J. W. Gates, Jr., J. Am. Chem. Soc., **88**, 4271 (1966).

(7) G. Stork and J. W. Schulenberg, J. Am. Chem. Soc., **84**, 284 (1962).