be of importance for the synthesis of certain natural products, as exemplified by the following communication [17].

REFERENCES

[1] *H. M. R. Hoffmann*, Angew. Chem. *81*, 597 (1969); *ibid.*, Int. Ed. *8*, 556 (1969).
[2] *T. R. Kelly*, Tetrahedron Letters *1973*, 437.
[3] *J. A. Berson, R. G. Wall & H. D. Perlmutter*, J. Amer. chem. Soc. *88*, 187 (1966).
[4] *M. G. Ettlinger & J. E. Hodgkins*, J. Amer. chem. Soc. *77*, 1831 (1955).
[5] *S. F. Reed, Jr.*, J. org. Chemistry *30*, 3258 (1965).
[6] *R. T. Arnold, O. C. Elmer & R. M. Dodson*, J. Amer. chem. Soc. *72*, 4359 (1950).
[7] *A. Sh. Sharifkanov & Sh. S. Skhmedova*, Chem. Abstr. *61*, 13275b (1964).
[8] *T. J. Petcher, Sandoz Ltd.*, unpublished work.
[9] *R. B. Woodward & R. Hoffmann*, Angew. Chem. *81*, 797 (1969); *ibid.*, Int. Ed. *8*, 781 (1969).
[10] *H. Strickler, G. Ohloff & E. Kováts*, Helv. *50*, 759 (1967).
[11] *W. D. Huntsman, P. C. Lang, N. L. Madison & D. A. Uhrick*, J. org. Chemistry *27*, 1983 (1962).
[12] *M. Furdik & E. Sidova*, Chem. Abstr. *63*, 13095a (1965).
[13] *H.-P. Weber, Sandoz Ltd.*, unpublished work.
[14] *K. Taguchi & F. H. Westheimer*, J. org. Chemistry *36*, 1570 (1971).
[15] *N. M. Yoon & H. C. Brown*, J. Amer. chem. Soc. *90*, 2927 (1968).
[16] *W. D. Huntsman & R. P. Hall*, J. org. Chemistry *27*, 1988 (1962).
[17] *W. Oppolzer*, Helv. *56*, 1812 (1973).

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184. The Total Synthesis of (±) β-Acorenol¹)

Preliminary Communication²)

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(4. VI. 73)

Zusammenfassung. Die erste Totalsynthese des Spiro-sesquiterpenes β-Acorenol, ausgehend vom bekannten Cyclohex-1-enylessigsäureäthylester, wird beschrieben. Die Schlüsselstufe **2** → **3** + **4** verläuft über eine thermische intramolekulare En-Reaktion.

β-Acorenol, a spirocyclic sesquiterpene, isolated from the wood of *Juniperus rigida* has been shown by chemical and spectroscopic evidence [1] to have structure **8**³). This communication describes the first total synthesis of racemic β-acorenol **8** and β-acoradiene **9** [1], the key step of which utilizes recent observations on the stereocontrolled synthesis of five-membered ring systems [4]⁴).

The known ethyl cyclohex-1-ene-1-acetate **1** [5] was alkylated [6] with 1-bromo-3-butene to give the oily diene **2**⁵)⁶) (b.p. 91–92°/0.3 Torr; IR.: 1730 cm^{-1}). The latter cyclized in toluene (19% solution in a sealed ampoule) at 280° with 3 days⁷) to a 1:1 mixture (65% yield) of the esters **3**⁵)⁶) and **4**⁵)⁶), which were separated by

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¹) Presented in part at the International Symposium: «Neue Methoden der Organischen Synthese», Basle, Switzerland, May 11, 1973.

²) The content of this communication will appear as part of a full paper in this journal.

³) For isolation and structure of the closely related alaskenes see [2].

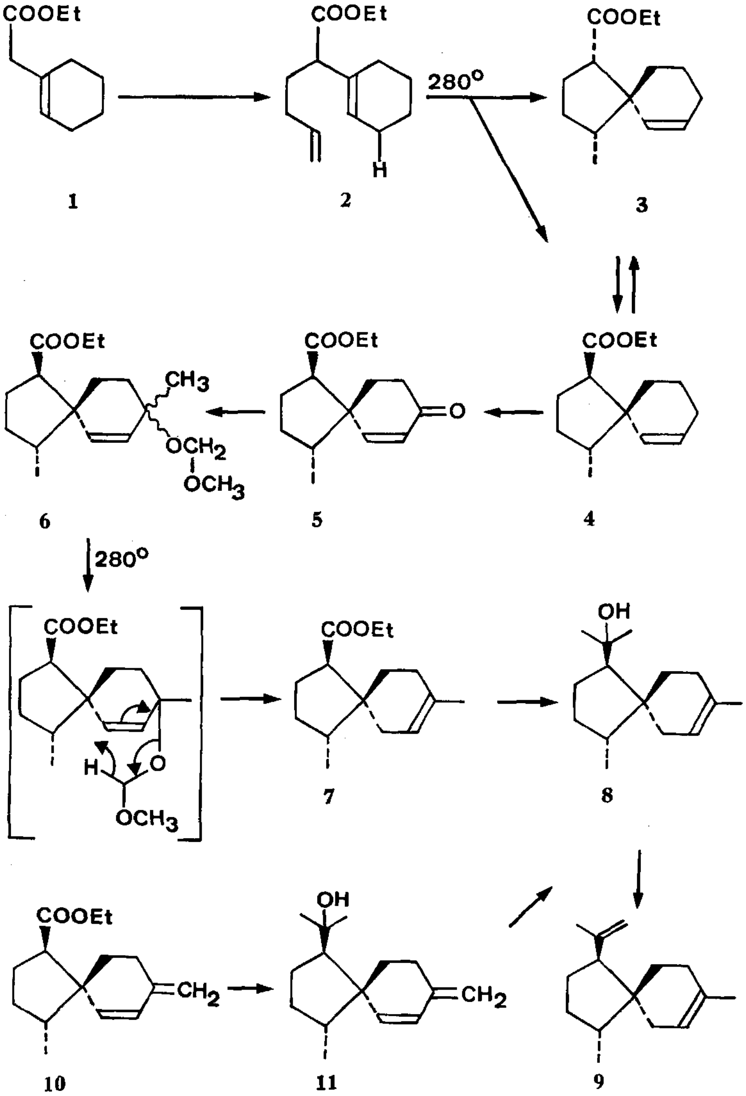
⁴) For previous approaches to acorane-type compounds see [3] [8].

⁵) The IR.- and NMR.-spectra were in agreement with the assigned structure.

⁶) Satisfactory elemental analytical data were obtained for this substance.

⁷) 1-(5-methyl-4-hexenyl)-cyclohexene is reported not to cyclize at temperatures up to 500° [7].

chromatography on silica gel. The esters **3** and **4** could be cleanly interconverted upon exposure to 1 N ethanolic sodium ethoxide at 70° to give a 3:2-equilibrium mixture. In the NMR.-spectrum ($CDCl_3$) the $CHCH_3$-doublet of the more polar ester **3** appears at $\delta = 0.89$ ppm and is shifted to $\delta = 0.96$ ppm on hydrogenation of the olefinic double bond, thus indicating the *cis*-relationship of the double bond and the methyl group. The methylene quartets due to $COOCH_2CH_3$ occur at $\delta = 4{,}07$ ppm in the ester **3** and at $\delta = 4.10$ ppm in the ester **4**[8]).



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[8] This assignment is based on the assumption that the olefinic double bond exerts a weak shielding effect upon the *cis*-carbethoxy group in the ester **3**. In fact, on hydrogenation of the double bond the corresponding CH_2-quartet shifts to $\delta = 4.11$ ppm.

By allylic oxidation [8] the isomer **4** was converted in 64% yield to the unsaturated ketone **5**⁵)⁶) (UV.(MeOH) $\lambda_{\max}$: 230 nm ($\log\varepsilon = 4.05$), 317 nm ($\log\varepsilon = 1{,}48$)). Reaction of the ketone **5** with 1.0 mol of methyllithium in ether at –70° and subsequent treatment of the reaction mixture with an excess of chlorodimethyl ether in ether/hexamethylphosphoramide 1:1 for 1 h. at 25°⁹) afforded the acetal **6**⁵) as a mixture of epimers. The crude acetal **6** on thermolysis in heptane at 270° (sealed ampoule) within two h. underwent a retro-ene-reaction¹⁰) to give in 30% yield the ester **7**⁵)¹¹). This compound was also obtained from the isomer **3**, using the same reaction sequence, followed by epimerization of the reaction mixture with sodium ethylate. Finally, exposure of the ester **7** to an excess of methyllithium in ether at 25° for 40 min, followed by aqueous work-up, led quantitatively to (±) β-acorenol **8**, with IR.-(KBr) and NMR.-(CCl_4) spectra identical to those of the natural β-acorenol. Further evidence for the assigned structure was provided by dehydration [1] of the synthetic β-acorenol **8** to (±) β-acoradiene **9**, identified by comparison of its IR.-(KBr) and NMR.-(CCl_4) spectra with those of natural β-acoradiene.

An alternative, more efficient synthesis of β-acorenol **8** from the crude acetal **6** involved thermolysis of the latter at 195° for 16 h. This gave in 84% yield a 3:1 mixture of the diene **10**⁵) (UV.(MeOH) $\lambda_{\max}$ 223 nm ($\log\varepsilon \sim 4.3$)) and the monoene **7**. Treatment of this mixture with methyllithium at 25°, followed by reduction of the diene **11**⁵), using excess sodium in ammonia/ethanol [10], gave (±) β-acorenol **8** in 60% overall yield from the acetal **6**.

IR.- and NMR.-spectra of various spiro-sesquiterpenes, provided by Professors *B. Tomita* and *N. H. Anderson*, are gratefully acknowledged.

REFERENCES

[1] *B. Tomita, T. Isono & Y. Hirose*, Tetrahedron Letters *1970*, 1371.
[2] *N. H. Andersen & D. D. Syrdal*, Tetrahedron Letters *1972*, 899.
[3] *E. J. Corey, N. N. Girotra & C. T. Mathew*, J. Amer. chem. Soc. *91*, 1557 (1969); *T. G. Crandall & R. G. Lawton, ibid. 91*, 2127 (1969); *J. A. Marshall & S. F. Brady*, Tetrahedron Letters *1969*, 1387; *J. M. Conia, J. P. Drouet & J. Gore*, Tetrahedron *27*, 2481 (1971); *P. Naegeli & R. Kaiser*, Tetrahedron Letters *1972*, 2013.
[4] *W. Oppolzer*, Helv. *56*, 1807 (1973).
[5] *J. W. Cook & A. Dansi*, J. chem. Soc. *1935*, 500.
[6] *M. W. Rathke & D. Sullivan*, Tetrahedron Letters *1972*, 4249.
[7] *W. D. Huntsman, P. C. Lang, N. L. Madison & D. A. Uhrick*, J. org. Chemistry *27*, 1983 (1962).
[8] *J. A. Marshall & P. C. Johnson*, J. org. Chemistry *35*, 192 (1970).
[9] *F. Mutterer, J. M. Morgen, J. M. Biedermann, J. P. Fleury & F. Weiss*, Tetrahedron *26*, 477 (1970).
[10] *A. J. Birch & H. Smith*, Quarterly Reviews *12*, 17 (1958).

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⁹) This reaction has to be performed under rigorous exclusion of moisture and removal of the excess of chlorodimethylether by distillation before aqueous work-up.

¹⁰) The thermal retro-ene-reactions of various allyl acetals have been described by *Fleury et al.* [9]. The specific use of the methoxymethylene group has been studied independently by *Q. Branca*, ETH, Zurich (private communication by Prof. *D. Arigoni*).

¹¹) Satisfactory high-resolution mass-spectra were obtained, using a *CEC*-21-110 B spectrometer.