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SYNTHESES OF CADINANES. SYNTHETIC CORRELATION OF ABSOLUTE CONFIGURATION BETWEEN THE CADINANE SESQUITERPENES AND MONOTERPENES OF THE *p*-MENTHANE SERIES

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WE wish to report an unambiguous conversion of natural (-)-cryptone (I) to the crystalline dicyclic diketone, II, which is obtained in its dextrorotatory form and is shown to be the enantiomer of the known ozonization product[2] of the native sesquiterpene, ϵ-cadinene (III). The configuration of (-)-cryptone has been correlated previously with that of the natural monoterpenoids (-)-α-phellandrene[3], (-)-piperitol[4], (-)-piperitone[4], (-)-β-phellandrene[5], and (-)-phellandral[5], and the same correlations have been established independently

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[1] M.A., Smith College: (a) 1962; (b) 1960; (c) 1961.

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[3] A. S. Galloway, J. Dewar and J. Read, *J. Chem. Soc.* 1595 (1936).

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among the corresponding enantiomers[4,5]. Similarly, the configuration of ε-cadinene has been correlated, through (−)-cadinene dihydrochloride (IV), with that of the β-, γ-, γ_1-, and δ-cadinenes[6,7], and also with copaene[8], cubeb camphor[8], and α- and δ-cadinol[6,9], and the configuration of (+)-cadinene dihydrochloride has been correlated with that of sesquigoyol[10] and with other natural sesquiterpenoids[11]. The present work links these monoterpenoid and sesquiterpenoid series directly. The results are in accord with the previous determinations of absolute configuration carried out independently on cryptone[5,12,13] and the cadinanes[14].

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(-)-Cryptone[12] ($\lambda_{max}^{CCl_4}$ 5.94 mμ, $[\alpha]_D^{22}$ -115.6°) in the Diels-Alder reaction with 2-ethoxybutadiene-1,3 gave the *anti-cis* enol ether, V (b.p. 134-135°/0.2 mm.; $\lambda_{max}^{CCl_4}$ 5.83 mμ. Found: C, 75.9; H, 9.9; OC_2H_5, 19.3. $C_{15}H_{24}O_2$ requires: C, 76.2; H, 10.2; OC_2H_5, 19.1%), which upon acid hydrolysis[15] and epimerization in alkali[15] afforded as the main product isolated the *anti*-*trans*-diketone, II (m.p. 103-104°, $[\alpha]_D^{22}$ +58.6° ($CHCl_3$). Found: C, 74.9; H, 9.8. $C_{13}H_{20}O_2$ requires: C, 75.0; H, 9.7%). The steric course of these reactions is critically determined in the first step, where the dienophile is attacked mainly from the side of the molecule opposite the bulky (equatorial) isopropyl group. The infrared absorption spectrum is identical in every respect with that of the degradation product[2] from ε-cadinene, m.p. 103-104°, $\lambda_{max}^{CCl_4}$ 5.82 mμ, $[\alpha]_D^{20}$ -54.6° ($CHCl_3$). This product has the complete stereochemistry of all the natural cadinenes.

A total synthesis of the racemic form of this diketone, by a quite different path, has been reported recently[16]. The (±)-diketone was converted further with excess methyllithium to the ditertiary carbinol, which with hydrogen chloride readily gave racemic cadinene dihydrochloride[16]. It might be expected that the overall reaction from the diketone stage would be highly stereospecific since it proceeds through the same carbonium ion intermediate as that involved in the action

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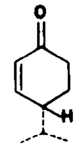

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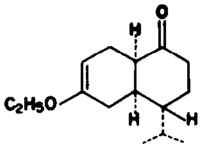

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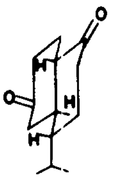

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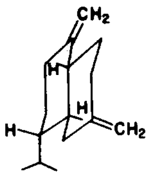

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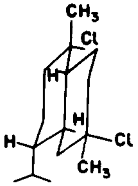

IV

of hydrogen chloride on the various natural cadinanes, which always gives the ditertiary halide of the same relative configuration. The present conversion therefore constitutes in principle a synthesis of (+)-cadinene dihydrochloride, and opens a relatively short and simple route through II and V for the stereospecific syntheses of several naturally occurring members of the cadinane series[17]. We hope to describe in detail later the results of such experiments which are now in progress.

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[17] Both enantiomers of cryptone are available from different botanical sources[8]. A resolution of synthetic (±)-cryptone [M. D. Soffer and M. Jevnik, *J. Amer. Chem. Soc.* **77**, 1003 (1955)], which is required for a formal total synthesis, is underway.

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