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THE SYNTHESIS AND THE ABSOLUTE CONFIGURATION OF OPTICALLY ACTIVE TRICYCLO[4.4.0.0^{3,8}]DECANE

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In contrast to adamantane which is highly symmetrical and achiral, its isomer tricyclo[4.4.0.0^{3,8}]decane ("twistane")$^{1)}$ $C_{10}H_{16}$ has a unique symmetry (D_2) and is chiral, being composed from five boat-form cyclohexanes which are all twisted in the same sense. Since various derivatives of adamantane have been prepared for the studies of their biological activities, the same line of investigation has been undertaken in this laboratory, and the synthesis as well as the determination of the absolute configuration of optically active "twistane" will be reported in this communication.

The synthetic route of Whitlock, Jr.$^{1a)}$ was modified so as to give the ketocarboxylic acid (IIa)** suitable for the optical resolution as well as the elucidation of the absolute configuration.

The racemic bicyclic glycol (I) prepared following the procedure of Whitlock, Jr.$^{1a)}$ was treated with chromic anhydride in acetic acid to afford the racemic ketocarboxylic acid (IIa), m.p.86-87°. Several trials indicated that the cinchonidine salt was satisfactory for successful optical resolution of (IIa), and the optically active (IIa), so obtained, m.p.81-81.5°, $[\alpha]_D^{25}$ -37.7° (c, 0.850 in EtOH) was converted into the methyl ester (IIb), b.p.120-121°/5 mm, n_D^{14} 1.4883, $[\alpha]_D^{15}$ -29.3° (c, 0.734 in EtOH).

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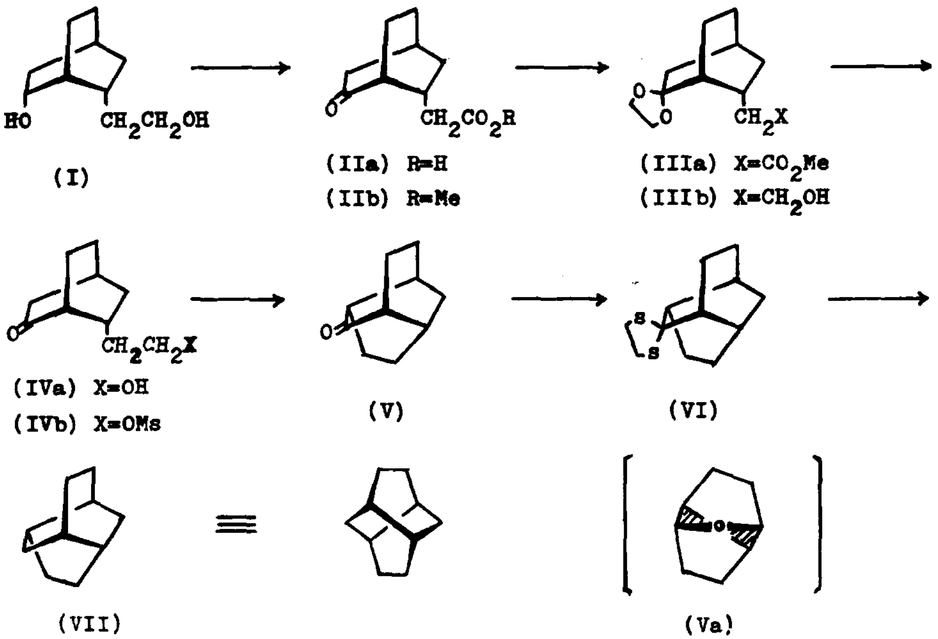
** The racemic series of compounds were prepared by the same procedures, and all new compounds reported in this communication had the requisite spectral and analytical characteristics.



Refluxing with ethylene glycol and p-toluenesulfonic acid in benzene converted (IIb) into the ketal ester (IIIa), b.p.120-121°/2 mm, n_D^{21} 1.4878, $[\alpha]_D^{20}$ -62.9° (c, 0.898 in EtOH), which was reduced with lithium aluminium hydride to give the ketal alcohol (IIIb), b.p.122-123°/2 mm, n_D^{21} 1.4973, $[\alpha]_D^{20}$ -44.5° (c, 0.866 in EtOH).

After the protective group was removed with diluted sulfuric acid, the resulted keto alcohol (IVa), b.p.125°/2 mm, n_D^{20} 1.5032, $[\alpha]_D^{19}$ -44.4° (c, 1.042 in EtOH) was treated with mesyl chloride and pyridine to afford the keto mesylate (IVb) which, without further purification, was refluxed with sodium hydride in dioxane to give the tricyclic ketone (V) (camphor-like odor).

After purification by chromatography and sublimation, the ketone (V) melted at 186-188° (racemic: m.p.198-199.5°)[1a], and showed a positive optical rotation, $[\alpha]_D^{23}$ +412° (c, 0.656 in EtOH). Reaction of the ketone (V) with ethanedithiol and boron trifluoride yielded the thioketal (VI), $[\alpha]_D^{23}$ +308° (c, 0.536 in $CHCl_3$), the desulfurization of which with Raney nickel in refluxing ethyl acetate gave crystalline (+)-twistane (VII), m.p.162-163° (racemic: m.p.163-164.8°)[1a], $[\alpha]_D^{22}$ +414° (c, 0.489 in EtOH) whose camphor-like odor and great

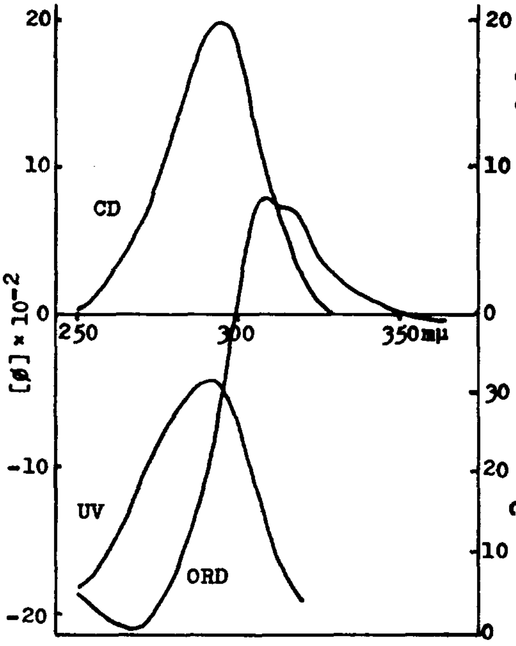


Fig. 1

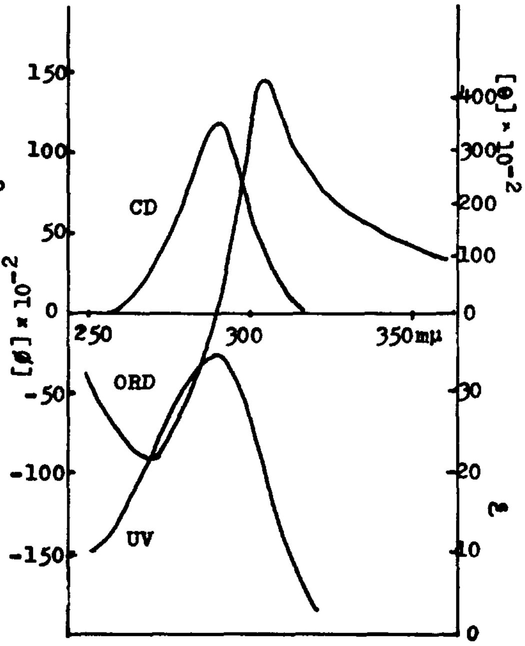


Fig. 2

volatility are very characteristic.

Application of the Octant rule[2] to the intermediate bicyclic keto carboxylic acid (IIa) which shows strongly positive Cotton effect (Fig. 1) assigns the absolute configuration (IIa) to this keto carboxylic acid. This is further supported by the positive Cotton curve with extraordinarily large amplitude (Fig. 2) exhibited by the tricyclic ketone (V). The cyclohexanone moiety which is indicated by shadow in the projection formula (Va) has a typical "right-handed" twist boat form and is expected to show dispersion curve of distinctive amplitude according to the empirical rule of Djerassi and Klyne[3),4)].

These findings indicate that (+)-twistane has the absolute configuration (VII) and four equivalent asymmetrical carbon atoms have the S-configurations[5].

As a hydrocarbon, optically active twistane shows an abnormally large optical rotation ([ϕ] +570°), and the large discrepansy between the observed value and the value ([ϕ] +140°) calculated according to the Brewster's asymmetric conformation model[6] suggests the importance of the "permolecular effects"[7] in assigning the absolute configuration in rigid system e.g.,norbornane[7] and twistane on the basis of the conformational asymmetry rule.

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