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ON THE ABSOLUTE CONFIGURATION OF TRICYCLO($4,4,0,0^{3,8}$)DECANE (TWISTANE)

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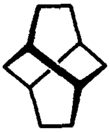
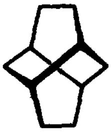
The tricyclo($4,4,0,0^{3,8}$) decane system, first synthesized by Whitlock and Siefken[1], has a remarkable geometry, being composed of boat forms twisted in the same sense and existing in two enantiomeric forms Ia and Ib. This chiral system may be of considerable importance as a valuable model in studies of chiroptical properties of twist-boat structures.



Ia



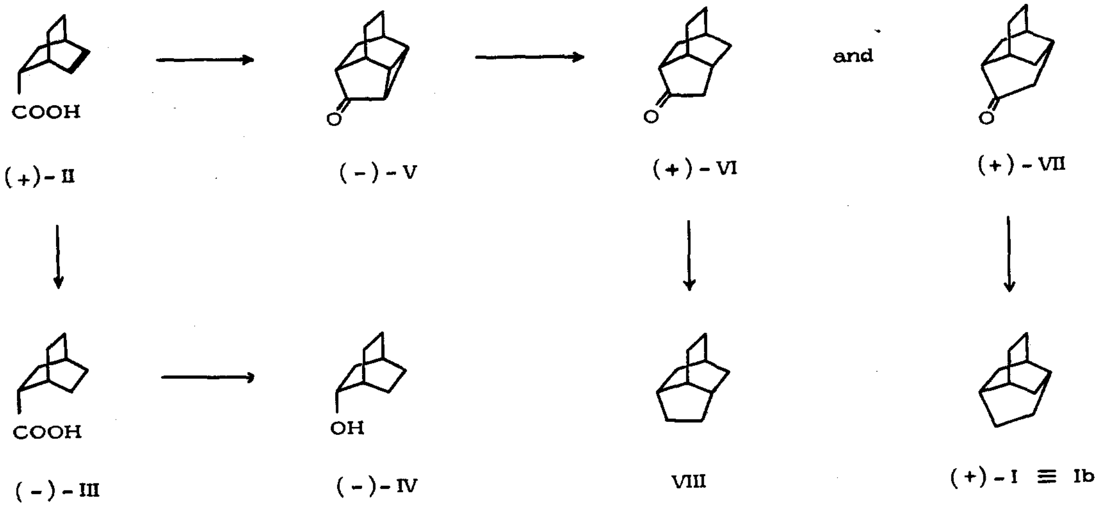
Ib

Adachi, Naemura and Nakazaki[2] applying the Octant rule[3] to endo-5-oxobicyclo(2,2,2) oct-3-ylacetic acid and the Klyne-Djerassi rule[4] to 2-twistanone assigned (+)-twistane the configuration Ia. A similar conclusion was reached on the basis of the observed positive Cotton effect of (+)-4-twistanone[5].

We now present chemical evidence which shows that the assumed absolute configuration of twistane has to be reversed. The correlation sequence is depicted in Scheme 1. The starting acid (+)-II, m.p. 46-47°C, $[\alpha]_D^{20}$ +50.9° (c 0.450, methanol), was obtained by crystallisation of its salt with (+)-2-(1-aminoethyl) naphthalene. On hydrogenation, (+)-II affords the acid (-)-III, $[\alpha]_D^{25}$ -61.6° (c 6.764, chloroform), which was correlated previously with (-)-(2R) -2-hydroxybicyclo(2,2,2) octane (IV) by Berson and collaborators[6]. The acid (+)-II ($[\alpha]_D^{25}$ +48.2°; 95% optical purity) was transformed into the tetracyclic ketone (-) -V, $[\alpha]_D^{25}$ -47.3° (c 0.500, methanol), via diazoketone. Catalytic hydrogenation of (-) -V on Pd/$CaCO_3$ resulted in a mixture of

(+)-VI (87.5%) and (+)-VII (12.5%), according to vpc and IR-spectra. This mixture was transformed into a mixture of VIII and (+)-I (87.3 : 12.7), $[\alpha]_D^{25}$ +52.1° (c 0.501, ethanol); taking for twistane[5] $[\alpha]_D^{25}$ + 434° and assuming the 95% optical purity, the value should be $[\alpha]_D^{25}$ +52.4°. We were moreover able to isolate (+)-VII from the hydrogenation mixture by repeated careful chromatography on silica gel; the compound thus isolated had $[\alpha]_D^{25}$ + 281° (c 0.200, ethanol) and was identical (vpc and IR-spectrum) with authentic (+)-4-twistanone[5], $[\alpha]_D^{25}$ +295° (c 0.518, ethanol).

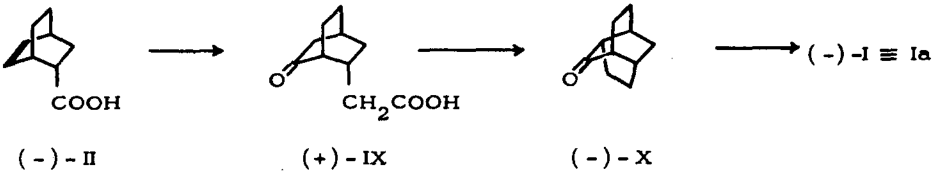
Now, if the acid (+)-II has the R-configuration as depicted in Scheme 1, the (+)-twistane obtained by the shown reaction sequence must have the configuration Ib and not Ia as anticipated previously.



Scheme 1

In order to verify this unexpected finding we carried out another sequence of reactions based on the work of Whitlock[1] (Scheme 2) which correlates the acid II with the acid IX of Adachi[2]. The acid (-)-II (46% optical purity) afforded the dextrorotatory keto-acid (+)-IX, m.p. 64-65.5°C, $[\alpha]_D^{25}$ + 16.4° (c 0.603, ethanol), $\Delta\varepsilon_{295}$ -0.25, which was obtained by the Japanese authors as the laevorotatory enantiomer. In accord with their work[2], the (+)-IX afforded laevorotatory 2-twistanone (-)-X, $[\alpha]_D^{25}$ -205.6° (c 0.600, ethanol), which was converted to (-)-twistane,

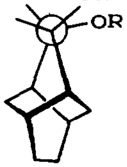
$[\alpha]_D^{25}$ -183.0° (c 0.500, EtOH). Thus, we obtained the same result as in the first correlation, the (-) -II being related to (-)-I.



Scheme 2

The absolute configuration of (-)-2-hydroxybicyclo(2,2,2) octane - and hence of the acid (+)-II - seems to be firmly established[7-9]. As previous assignments of absolute configuration rest on the ORD and CD measurements we suppose that the application of these optical methods to the boat structures studied failed for some unexpected reason.

Measurements of the CD curves[10] of some other derivatives belonging to the (+)-twistane series afforded results contradictory to that obtained from the ORD and CD measurements[2,5] on ketones. Thus, the CD-curve of (+)-cis-4,5-twistanediol dibenzoate, m.p. 85°C ((+) -XII) exhibits in ethanol two maxima, the first being positive ($\Delta\varepsilon_{236}$ 10.0) and the second negative ($\Delta\varepsilon_{221}$ -3.2). The same result was obtained with an equimolar mixture of the (+)-4,5-diol (+)-XI and $(DPM)_3Eu$ in CCl_4 ($\Delta\varepsilon_{312}$ +4.2, $\Delta\varepsilon_{288}$ -2.3) and with the thiocarbonyl derivative (+) -XIII (dioxan , $\Delta\varepsilon_{311}$ + 1.0,



(+)-XI ; R = H

(+)-XII ; R = C_6H_5CO-

(+)-XIII ; R,R = -CS-

$\Delta\varepsilon_{255}$ -0.5). The results of all these measurements are in accord with such arrangement of the -O-C-C-O- segment[11-13] which is present in the twistane system of absolute configuration Ib.

We are at present investigating this problem more closely and shall publish the results elsewhere.

REFERENCES

1. H.W. Whitlock Jr. and H.W. Siefken, *J. Am. Chem. Soc.* **90**, 4929 (1968).
2. K. Adachi, K. Naemura, and M. Nakazaki, *Tetrahedron Letters* 1968, 5467.
3. W. Moffitt, R.B. Woodward, A. Moscowitz, W. Klyne, and C. Djerassi, *J. Am. Chem. Soc.* **83**, 4013 (1961).
4. C. Djerassi and W. Klyne, *Proc. Natl. Acad. Sci. US* **48**, 1093 (1962).
5. M. Tichý and J. Sicher, *Tetrahedron Letters* 1969, 4609.
6. J.A. Berson, R.T. Luibrand, N.G. Kundu, and D.G. Morris, *J. Am. Chem. Soc.* **93**, 3075 (1971). The author is greatly indebted to Professor Berson for furnishing the details of the correlation (-)-III → (-)-IV.
7. H.M. Walborski, M.E. Baum, and A.A. Yousseff, *J. Am. Chem. Soc.* **83**, 988 (1961).
8. J.A. Berson and D. Willner, *J. Am. Chem. Soc.* **84**, 675 (1962).
9. K. Mislow and J.G. Berger, *J. Am. Chem. Soc.* **84**, 1956 (1962).
10. The author is indebted to Dr S. Vašíčková for the CD measurements.
11. N. Harada and K. Nakanishi, *J. Am. Chem. Soc.* **91**, 3989 (1969).
12. K. Nakanishi and J. Dillon, *J. Am. Chem. Soc.* **93**, 4058 (1971).
13. A.N. Haines, C.S.P. Jenkins, *Chem. Commun.* 1969, 350.