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THE PREPARATION AND CHIROPTICAL PROPERTIES OF CAGE-SHAPED PENTACYCLIC HYDROCARBONS; [m.n.0]TRIBLATTANES. HORSE LIVER ALCOHOL DEHYDROGENASE MEDIATED REDUCTION OF PENTACYCLO[5.5.0.$0^{2,6}$.$0^{3,9}$.$0^{5,8}$]DODECAN-4-ONE

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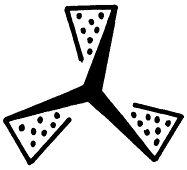
Diazomethane ring expansion of (+)-[1.1.0]triblattan-4-one and (-)-[2.1.0]triblattan-4-one gave [m.1.0]triblattanes (m=3-5) and [m.2.0]triblattanes (m=3-6) respectively, all of which are levorotatory. HLADH mediated reduction of (±)-[3.1.0]triblattan-4-one gave (-)-[3.1.0]triblattan-4-one which was converted into [m.3.0]-triblattanes (m=3,4). These are dextrorotatory in spite of having the central core fixed in an M-helical conformation.

We have been interested in the preparation, stereochemistry, and biological transformation of series of cage-shaped compounds which possess the D_3-twisted bicyclo[2.2.2]octane framework **1** as a common structure. We have coined for them the trivial name [m.n.p]triblattanes,$^{1)}$ where m, n, and p are number of CH_2's in each diagonal bridge. Absolute configurations of triblattanes so far prepared in optically active forms reveal the interesting chiroptical feature that all levorotatory enantiomers possess a central core (shown with dotting) fixed in an M-helical conformation.$^{1,2)}$ In this communication, we wish to report the preparation of series of optically active [m.n.0]triblattanes **4**-**6**, **8**-**13**, some of which are conspicuous for having two long diagonal bridges (m=3, n≥3) and discuss their chiroptical properties.



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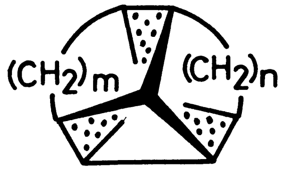
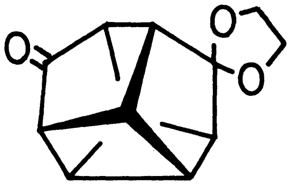
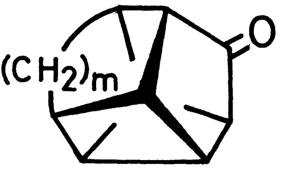


2 m=1 n=1
3 m=1 n=2
4 m=1 n=3
5 m=1 n=4
6 m=1 n=5
7 m=2 n=2
8 m=2 n=3
9 m=2 n=4
10 m=2 n=5
11 m=2 n=6
12 m=3 n=3
13 m=3 n=4

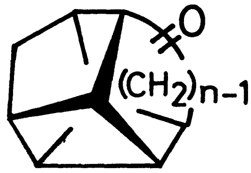
In previous papers,[3] we reported our preparation of (+)-**15** and (-)-**16** from (+)-**14** whose absolute configuration and absolute rotation were established in our laboratory.



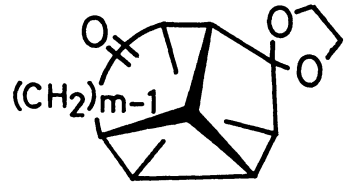
(+)-**14**



(+)-**15** m=1
(-)-**16** m=2
(-)-**17** m=3



18 n=2
19 n=3
20 n=4
21 n=5



22 m=2
23 m=3

An ethereal solution of (+)-**15**, $[\alpha]_D$ +9.36° (72% optical purity), containing of 1 equiv. of BF_3-etherate and 5 equiv. of diazomethane was kept at 0 °C for 30 min to give a mixture of ring-expanded ketones **18**, **19**, **20**, **21**, and additional higher homologs with unknown location of the carbonyl group in the expanded bridge. Wolff-Kishner reduction of the mixture afforded a mixture of [m.1.0]triblattanes[4] which was analyzed by means of GLC and separated by preparative GLC (Table 1).

Table 1. Product ratio and specific rotations of [m.1.0]triblattanes

	3	**4**	**5**	**6**	Higher homologs
Product ratio	44%	13%	25%	11%	7%
$[\alpha]_D$ ($CHCl_3$)	-86.4°	-42.2°	-67.6°	-35.8°	

Ring-expansion of (-)-**16**, $[\alpha]_D$ -27.0° (72% o.p.) was carried out in the same manner as described above and Wolff-Kishner reduction of the ring-expanded ketones followed by separation by preparative GLC gave [m.2.0]triblattanes (Table 2).

Table 2. Product ratio and specific rotations of [m.2.0]triblattanes

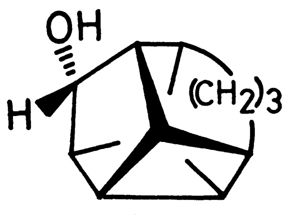
	7	**8**	**9**	**10**	**11**	Higher homologs
Product ratio	11%	6%	39%	13%	18%	13%
$[\alpha]_D$ ($CHCl_3$)	-162°	-65.1°	-69.0°	-52.1°	-57.6°	

Our next task was the preparation of optically active **17** being the starting material for the synthesis of [m.3.0]triblattanes. Diazomethane ring-expansion of (+)-**14** provided **23** in poor yield. This situation coupled with our interest in biological resolution of a cage-shaped compound prompted us to prepare optically active **17** by HLADH-mediated reduction of (±)-**17**. Ethereal solution of (±)-**14** was treated with 12 equiv. of diazomethane at 0 °C for 11 d to give a mixture of **22** and 23. Wolff-Kishner reduction followed by acid hydrolysis and separation on chromatography (Al_2O_3) furnished (±)-pentacyclo[$5.5.0.0^{2,6}.0^{3,9}.0^{5,8}$]dodecan-4-one (17) as a semi-solid (20% overall yield from 14). The ketone (±)-17 (100 mg) was incubated for 5 min at 25 °C with 1 L of 1/15 M Sørensen phosphate buffer (pH 7.0) containing NAD^+ (45.7 mg), EtOH (1.0 mL), and HLADH (5 mg) and the ether-extracted metabolite was analyzed by means of GLC. Chromatography followed by sublimation gave the recovered 17$^{5)}$ and two diastereoisomeric alcohols 24 and 25 (Table 3).

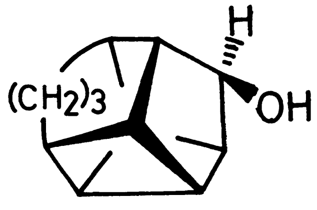
Table 3. Product ratio, specific rotations, and melting points of the metabolites

	Recovered 17	(+)-24	(-)-25
Product ratio	55%	34%	11%
$[\alpha]_D$ ($CHCl_3$)	-5.06°	+40.6°	-27.1°
Mp (in a sealed tube)	58 °C	89-91 °C	111-113 °C

Wolff-Kishner reduction of the recovered (-)-17 to (-)-4, $[\alpha]_D$ -17.1° (29% o.p.) permitted us to assign the M-helicity to the central core of (-)-17 and calculate the absolute rotation of (-)-17, $[\alpha]_D$ $_{abs.}$ -17.4° ($CHCl_3$). Jones oxidation of the metabolite alcohols (+)-24 and (-)-25 to (+)-17, $[\alpha]_D$ +12.1° (70% o.p.) and (-)-17, $[\alpha]_D$ -10.0° (57% o.p.), respectively, allowed us to determine the helicity of the central core of these alcohols and calculate their optical purities. Application of our "quadrant rule"$^{6)}$ to the results led to assume the configuration of the hydroxy group as shown.



(+)-24



(-)-25

After an ethereal solution of (-)-17, $[\alpha]_D$ -5.06° containing 1 equiv. of BF_3-etherate and 3 equiv. of diazomethane was kept at 0 °C for 12 h, the ring-expanded ketones were reduced by Wolff-Kishner reduction to afford a mixture of hydrocarbons which was analyzed by means of GLC and separated by preparative GLC (Table 4).

The known optical purities of our starting materials permitted calculation of the absolute molecular rotations of these new hydrocarbons. These values are plotted in Fig. 1, inspection of which indicates conspicuous features in chiroptical properties; (a) [m.n.0]triblattanes having two short diagonal bridges (n=1 or 2) as well as the twisted bicyclo[2.2.2]octane core with M-helicity are levorotatory and (b) [m.3.0]triblattanes **12** and **13** having two long diagonal bridges are dextrorotatory in spite of possessing the twisted central core with M-helicity.

Table 4. Product ratio and specific rotations of [m.3.0]triblattanes

	8	**12**	**13**	Higher homologs
Product ratio	52%	25%	18%	5%
$[\alpha]_D$ ($CHCl_3$)	-26.3°	+3.00°	+19.2°	

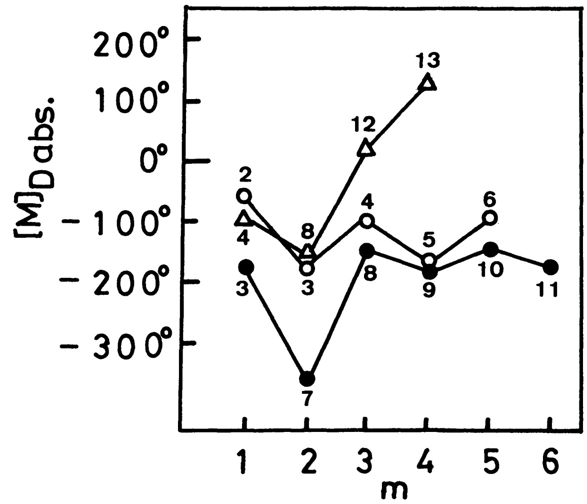


Fig. 1. Correlation between bridge span (m) and absolute molecular rotation ($[M]_{D\ abs.}$) in three series of triblattanes possessing the twisted central core fixed in an M-helical conformation.
○ : [m.1.0]triblattanes,
● : [m.2.0]triblattanes,
△ : [m.3.0]triblattanes.

References

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2) J. A. Jenkins, R. E. Doehner, Jr., and L. A. Paquette, J. Am. Chem. Soc., 102, 2131 (1980); M. Nakazaki and K. Naemura, Yuki Gosei Kagaku Kyokai Shi, 40, 1128 (1982).

3) M. Nakazaki and K. Naemura, J. Org. Chem., 42, 2985 (1977); M. Nakazaki, K. Naemura, Y. Kondo, S. Nakahara, and M. Hashimoto, ibid., 45, 4440 (1980).

4) All new compounds gave satisfactory elemental analyses and mass spectral data.

5) (-)-**17**; circular dichroism (isooctane) [θ] 1.56 x 10^3 (295.5 nm, sh), 1.60 x 10^3 (298.5), 1.50 x 10^3 (302.0, sh), 1.18 x 10^3 (308.0, sh).

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