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Diazomethane Ring-expansion of (−)-D_3-Trishomocubanone. Preparation and Chiroptical Properties of a Series of [*m*.1.1]Triblattanes

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Synopsis. Optically active [3.1.1], [4.1.1], [5.1.1], and [6.1.1]triblattanes were prepared through the diazomethane ring-expansion of (−)-D_3-trishomocubanone. The absolute molecular rotations of [*m*.1.1]triblattanes were found to increase with *m* begining from *m*=0 till *m*=2. On going from *m*=2 to *m*=3, $[M]_{D\,abs.}$ abruptly drops, then the value remains almost constant till *m*=6.

Since our first preparation of twistane (**3**)[1] in an optically active modification, we have been interested in the preparation, stereochemistry, and biological transformations of series of cage-shaped compounds which possess the D_3-twisted bicyclo[2.2.2]octane framework **1** as a common structural feature (Fig. 1). We have classified these hydrocarbons into three categories according to the number of their diagonal bridgings, and have coined for them the generic names [*m*], [*m.n*], and [*m.n.p*]triblattanes,[2] from German, Blatt= leaf, where *m*, *n*, and *p* are the number of CH_2's in each diagonal bridge.

Figure 1[1,3] illustrates the triblattanes so far prepared in optically active forms in our laboratory and reveals the interesting chiroptical feature that all triblattanes having the D_3-twisted bicyclo[2.2.2]octane moiety with M helicity as the central core are levorotatory. Another conspicuous chiroptical property observed in [*m*.2.2], [*m*.2.1], [*m*.1.1], and [*m*]triblattanes having $m<3$ (Fig. 2), is the linear dependence of the absolute molecular rotations ($[M]_{D\,abs.}$) on the bridge span.[4] Owing to their short diagonal bridges ($m<3$), all triblattanes so far prepared in optically active forms are conformationally rigid, and this situation prompted us to prepare a series of optically active [*m*.1.1]triblattanes where *m* is greater than 2.

Results and Discussion

An obvious way for preparing optically active [3.1.1], [4.1.1], [5.1.1], and [6.1.1]triblattanes of known absolute configuration is extention of the diazomethane ring-expansion reaction which has proved successful in our synthesis of (−)-[2.1.1]triblattane (**8**) from (−)-D_3-trishomocubanone (**14**).

Our preliminary experiment utilizing (±)-**14** indicated that when kept at 0 °C an ethereal solution of (±)-**14** containing 10 equiv. of diazomethane gave a mixture of [2.1.1]triblattanone (**15**) and [3.1.1]triblattanones (**16**) with unknown location of the carbonyl group in the expanded bridge (Table 1). Addition of boron trifluoride was found to push the ring-expansion further furnishing a product consisting of higher homologs. An ethereal solution of (±)-**14** containing excess of diazomethane and 1 equiv. of BF_3–etherate was kept at 0 °C for 24 h. The reaction product was a mixture of ring-expanded ketones, again of unknown structure as to the location of the carbonyl group in the expanded bridges. To reveal composition of the mixture, the product was converted into a mixture of hydrocarbons by Wolff-Kishner reduction and the reaction product was analyzed by means of GLC. The results are summerized in Table 2.

We carried out the preparative experiment with a larger amount of (−)-**14**, $[\alpha]_D$ −26.0° (30% optical purity)[3] which was dissolved in an ethereal solution of 3 molar equiv. of diazomethane. The mixture was kept at 0 °C for 8 d, and routine workup furnished a 3 : 2 mixture of **15** and **16**, chromatography of which on alumina provided a 3.5% yield of **16**. Wolff-Kishner reduction of this [3.1.1]triblattanone (**16**) afforded [3.1.1]-triblattane (**20**), $[\alpha]_D$ −46.5°.

The major fraction obtained from the above chromatography was a 1 : 3 mixture of **15** and **16**, and this was dissolved in ether and subjected to further ring-expansion with 10 equiv. of diazomethane and 1 equiv. of BF_3–etherate. The solution was kept at 0 °C for

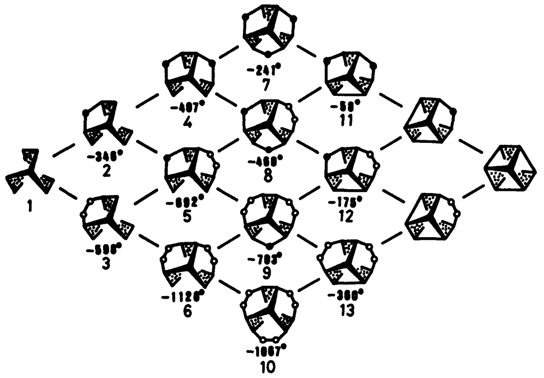


Fig. 1. Absolute configurations and absolute molecular rotations of the levorotatory tri-, tetra-, and pentacyclic hydrocarbons having D_3-twisted bicyclo[2.2.2]octane molecular framework with M helicity.

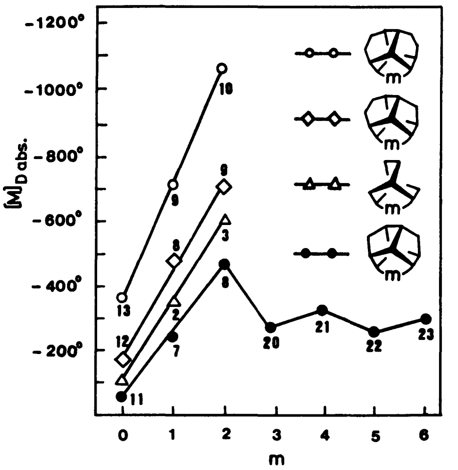


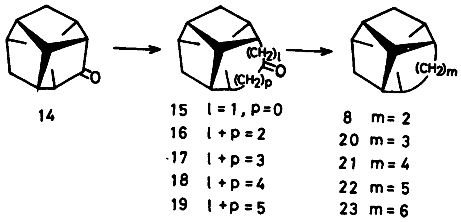
Fig. 2. Correlation between bridge span and absolute molecular rotation ($[M]_{D\,abs.}$) in four series of triblattane.

Table 1. Reaction of (±)-**14** and diazomethane without catalyst

Reaction time	Product ratio		
d	**14**	**15**	**16**
1	2	98	0
3	0	81	19
5	0	73	27
8	0	65	35

Table 2. Product distribution in the ring-expansion product

CH_2N_2 (equiv.)	Product ratio					
	7	**8**	**20**	**21**	**22**	**23**
3	43	45	9	2	1	0
5	6	33	24	28	9	0
10	0	0	11	42	29	18



Scheme 1.

24 h, and routine workup gave a mixture of **16**, **17**, **18**, and **19** from which **16** was removed by alumina chromatography. Wolff-Kishner reduction of the remaining mixture of **17**, **18**, and **19** furnished a 48 : 26 : 26 mixture (by GLC analysis) of **21**, **22**, and **23**. Preparative GLC separated and purified these [*m*.1.1]-triblattanes.

The known optical purity of our starting material (−)-**14** permitted calculation of the absolute molecular rotation of these new hydrocarbons; $[M]_{D\ abs.}$ −268°, −321°, −255°, and −287° for **20**, **21**, **22**, and **23** respectively. These values are plotted in Fig. 2, inspection of which indicates that the $[M]_{D\ abs.}$ of [*m*.1.1]-triblattanes drop abruptly on going from $m=2$ to $m=3$, then remain almost constant till $m=6$. This behavior could be explained in terms of the expected conformational mobility of $(CH_2)_m$ bridge in these higher [*m*.1.1]-triblattanes which should annihilate the $[M]_D$ contribution from this part of molecule.

Experimental

*Product Distribution in the Diazomethane Ring-expansion Product of (±)-D_3-Trishomocuban-4-one (**14**).* *Without Catalyst*: An ethereal solution (100 mL) of diazomethane (1.5 g, 35 mmol) was added with stirring to an ice-cooled solution of (±)-**14**[5)] (500 mg, 3.13 mmol) in dry ether (20 mL). The reaction mixture was allowed to stand at 0 °C, and aliquots were analyzed by GLC at 1, 3, 5, and 8 d period.

With BF_3-etherate Catalyst: The following experimental procedure is typical. An ethereal solution (100 mL) of diazomethane (1.5 g, 35 mmol) was added to a stirred and chilled (0 °C) solution of (±)-**14** (500 mg, 3.13 mmol) and freshly distilled BF_3–etherate (0.4 mL, 3.2 mmol) in dry ether (20 mL). After the resulting mixture was kept at 0 °C for 24 h, a deposited solid was removed by filtration and the filtrate was washed with aq $NaHCO_3$ and water, dried ($MgSO_4$) and concentrated to give an oily product (460 mg). The product (400 mg) was mixed with 100% hydrazine hydrate (0.35 mL), KOH (190 mg) and triethylene glycol (4 mL) and the mixture was heated for 1 h at 110—120 °C and for an additional 4 h at 190—200 °C. The product (310 mg) was analyzed by GLC.

*Preparation of (−)-[3.1.1]Triblattane (**20**).* An ethereal solution of diazomethane (11 g, 0.26 mol) was added to a stirred and chilled (0 °C) solution of (−)-**14**, $[\alpha]_D$ −26.0°[3)] (13.5 g, 84.4 mmol) in dry ether (100 mL), and the mixture was kept at 0 °C for 8 d. After the remaining diazomethane was destroyed with a small amount of acetic acid, the mixture was washed with aq $NaHCO_3$ and water, and dried ($MgSO_4$). Removal of the solvent left an oily product which was analyzed by GLC and was found to be a 3 : 2 mixture of **15** and **16**. When the mixture was chromatographed on alumina, earlier pentane eluents containing **16** (≥98% estimated by GLC) (550 mg) was followed by fractions containing a 1 : 3 mixture (4.30 g) of **15** and **16** which was reserved for further ring-expansion reaction (*vide infra*). Wolff-Kishner reduction of **16** 240 mg, (1.27 mmol) was carried out by the same procedure described above. The product was chromatographed on alumina and elution with pentane provided **20** (175 mg). The analytical sample was purified by sublimation at 55 °C (15 mm); mp 73—73.5 °C (in a sealed tube); $[\alpha]_D^{22}$ −46.5° (*c* 0.212, $CHCl_3$); MS, *m/e* 174 (M^+); ^{13}C NMR ($CDCl_3$) δ 24.47 (t), 29.32 (t), 35.54 (t), 39.91 (d), 42.31 (d), 46.60 (d), 47.30 (d); GLC, *Rt.* 4′10″ (at 120 °C); Found: C, 89.65; H, 10.36%. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41%.

Preparation of (−)-[4.1.1], (−)-[5.1.1], and (−)-[6.1.1]-Triblattanes. Ring-expansion reaction of the 1 : 3 mixture (4.00 g) of **15** and **16** obtained as described above was carried out with 1 L of ethereal solution of diazomethane (10 g, 0.23 mol) and BF_3–etherate (3.0 mL, 23 mmol) at 0 °C for 24 h. The same workup afforded a mixture (3.50 g) of **16**, **17**, **18**, and **19**. In order to remove **16**, the mixture was chromatographed on alumina, and earlier pentane eluents provided a semi-solid (630 mg) which was found to be free from **16** by GLC. Wolff-Kishner reduction of this fraction (600 mg) was carried out with 100% hydrazine hydrate (0.5 mL), KOH (260 mg), and triethylene glycol (6 mL). The same workup as described above gave a 48 : 26 : 26 mixture (232 mg) of **21**, **22**, and **23**. Preparative GLC (at 140 °C) provided specimens of (−)-**21** (80 mg), *Rt.* 8′20″, (−)-**22** (45 mg), Rt. 12′05″ and (−)-**23** (40 mg), *Rt.* 15′10″. (−)-[4.1.1]Triblattane (**21**); An oil; $[\alpha]_D^{20}$ −51.5° (*c* 0.344, $CHCl_3$); MS, *m/e* 188 (M^+); Found: C, 89.26; H, 10.70%. Calcd for $C_{14}H_{20}$: C, 89.29; H, 10.71%. (−)-[5.1.1]Triblattane (**22**); An oil; $[\alpha]_D^{24}$ −37.9° (*c* 0.796, $CHCl_3$); MS, *m/e* 202 (M^+); Found: C, 88.96; H, 10.97%. Calcd for $C_{15}H_{22}$: C, 89.04; H, 10.96%. (−)-[6.1.1]Triblattane (**23**); mp 64 °C; $[\alpha]_D^{25}$ −39.9° (*c* 1.46, $CHCl_3$); MS, *m/e* 216(M^+); Found: C, 88.67; H, 11.14%. Calcd for $C_{16}H_{24}$: C, 88.82; H, 11.18%.

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