ethylene glycol (15 mL). A slow stream of nitrogen was passed over the reaction mixture, and volatile materials were collected in a chilled trap. After the mixture was heated at 140 °C for 1 h, the reaction temperature was gradually raised to 200 °C and kept at this temperature for 3 h. After dilution with water, the mixture was extracted with hexane, and the extract was combined with the hexane solution of an oily product collected in the trap. The combined hexane extracts were washed with 3% HCl solution, 3% $NaHCO_3$ solution, and water and dried over $MgSO_4$. Evaporation of the solvent left an oily product which was stirred with 50% NaOH solution (0.8 mL), $CHCl_3$ (1 mL), and cetyltrimethylammonium chloride (5 mg) at 50 °C for 1 h. After dilution with water, the mixture was extracted with chloroform, and the extract was washed with water and dried over $MgSO_4$. Evaporation of the solvent afforded a residue which on preparative TLC on silicic acid (elution with hexane) gave (-)-**3** (64 mg, 64% yield from **9**): bp 126-128 °C (0.1 mm); $[\alpha]^{24}_D$ -2.3° (*c* 0.60, isooctane); CD (isooctane) $[\theta]_{222.5nm}$ -1.8×10^3; mass spectrum, *m/e* 248 (M^+).

Anal. Calcd for $C_{18}H_{32}$: C, 87.02; H, 12.98. Found: C, 86.78; H, 13.15.

Registry No. (*R*)-**3**, 74080-15-2; **5**, 69416-63-3; **6**, 73986-32-0; **7**, 73986-33-1; **8**, 73986-34-2; **9**, 73986-35-3; (±)-**10**, 73986-36-4; (-)-**10**, 73986-37-5.

Syntheses and Chiroptical Properties of C_2-Bissecocubane (Tricyclo[4.2.0.0^{3,6}]octane) Derivatives

Masao Nakazaki,* Koichiro Naemura, Yasuyoshi Sugano, and Yasuto Kataoka

Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka, 560 Japan

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(+)-2,6-Dioxotricyclo[3.3.2.0^{3,7}]decane-1,5-dicarboxylic acid (**18**) was converted into the dibromo diketone (-)-**10**, whose double Favorskii ring contraction afforded (-)-C_2-bissecocubane-3,6-dicarboxylic acid (**12**). Circular dichroism (CD) spectral comparison of the (-)-diketone **20**, derived from (-)-**10**, with (+)-(1*S*,3*R*,6*R*,8*S*)-homoadamantane-2,7-dione (**31**) assigned the (1*S*,3*R*,5*S*,7*R*) configuration to (-)-**20**, indicating the presence of a D_3-twisted bicyclo[2.2.2]octane moiety with *M*-helicity in (-)-**12**, common to (-)-twistane (**2**) and (-)-*twist*-brendane (**3**).

Diagonal bridging between C(2) and C(5) positions desymmetrizes bicyclo[2.2.2]octane (**1**) to yield a group of tricyclic cage-shaped compounds, (-)-twistane (**2**),[1] (-)-*twist*-brendane (**3**),[2] and tricyclo[4.2.0.0^{3,6}]octane (**4**),[3] all possessing the D_3-twisted bicyclo[2.2.2]octane moiety with *M*-helicity as a common structural unit (see Chart I).

The same (*M*)-D_3-twisted structural feature (**1**) can be found in another group of pentacyclic cage-shaped compounds, (-)-C_2-bismethanotwistane (**6**),[4] (-)-D_3-trishomocubane (**7**),[5] and (-)-C_2-bishomocubane (**8**),[6] all conceptually built by dissymmetrical homologation of cubane molecule (O_h symmetry; **5**), which in turn can be conceived to be constructed by interlocking two D_3-twisted bicyclo[2.2.2]octane units with opposite helicities (see Chart II).

Preparation of these gyrochiral cage-shaped rigid compounds in an optically active modification as well as their absolute configuration determination has been accomplished in our laboratory, except for **4** (see Chart III), which is conspicuous in the following two stereochemical features: (a) this is the only chiral compound among the four possible tricyclic hydrocarbons attainable by two bond fission ("C_2-bissecocubane")[7] of cubane (**5**), and (b) this is the next higher gyrochiral homologue of tricyclo[3.2.0.0^{3,7}]heptane (**9**), the smallest gyrochiral tricyclic hydrocarbon resulting from the diagonal methylene bridging of bicyclo[2.2.0]hexane (the shaped part).

Our continuing interests in gyrochiral cage-shaped molecules prompted us to prepare the C_2-bissecocubane (**4**) derivatives in optically active modification with known

Chart I

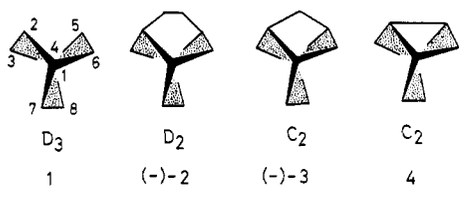


Chart II

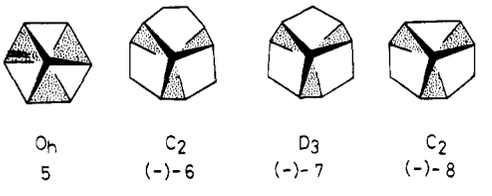
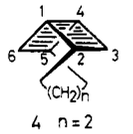
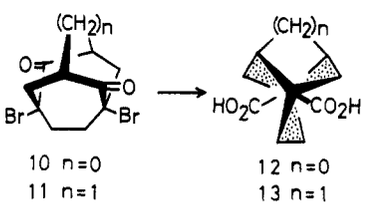


Chart III



Scheme I



(1) Adachi, K.; Naemura, K.; Nakazaki, M. *Tetrahedron Lett.* **1968**, 5467. Tichy, M.; Sicher, J. *Collect. Czech. Chem. Commun.* **1972**, *37*, 3106. In this paper, all structural formulas with (+) or (-) rotational specifications are illustrated in their absolute configurations.

(2) Naemura, K.; Nakazaki, M. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 888. Nakazaki, M.; Naemura, K.; Harita, S. *Ibid.* **1975**, *48*, 1907.

(3) Scherer, K. V., Jr.; Lunt, R. S.; Ungefug, G. A. *Tetrahedron Lett.* **1965**, 1199. Askani, R.; Schwertfeger, W. *Chem. Ber.* **1977**, *110*, 3046.

(4) Nakazaki, M.; Naemura, K.; Arashiba, N.; Iwasaki, M. *J. Org. Chem.* **1979**, *44*, 2433.

(5) (a) Helmchen, G.; Staiger, G. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 116. (b) Nakazaki, M.; Naemura, K.; Arashiba, N. *J. Org. Chem.* **1978**, *43*, 689. (c) Eaton, P. E.; Leipzig, B. *Ibid.* **1978**, *43*, 2483.

(6) Nakazaki, M.; Naemura, K. *J. Org. Chem.* **1977**, *42*, 2985.

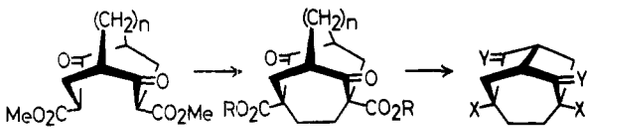
(7) The other three possible bissecocubanes are all achiral: tricyclo[3.1.1.1^{2,4}]octane (D_{2h} symmetry), tricyclo[4.2.0.0^{2,5}]octane[8] (C_{2v} symmetry) and tricyclo[3.1.1.0^{3,6}]heptane[9] (C_s symmetry).

(8) Wristers, J.; Brener, L.; Pettit, R. J. *J. Am. Chem. Soc.* **1970**, *92*, 7499.

(9) Meinwald, J.; Mioduski, J. *Tetrahedron Lett.* **1974**, 4137.

0022-3263/80/1945-3232$01.00/0

Scheme II

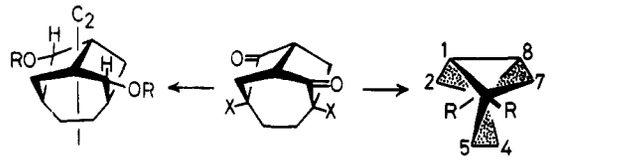


14 n = 0
15 n = 1

16 n=0 R=Me
17 n=1 R=Me
(+)-18 n=0 R=H
19 n=1 R=H

(-)-10 X=Br Y=O
(-)-20 X=H Y=O
21 X=H Y=H_2

Scheme III



(-)-27 R=H
(-)-28 R=Ac

(-)-10 X=Br
(-)-20 X=H

(-)-12 R=CO_2H
(-)-22 R=CO_2Me
23 R=Br
(-)-24 R=CH_2OH
(-)-25 R=CH_2OMs
(-)-26 R=Me

absolute configuration, and in this paper we report their preparations as well as chiroptical properties.

Results and Discussion

Since two methods available in literature[3] for preparing C_2-bissecocubane derivatives appeared unsuitable for our purpose, especially for the assignment of their absolute configurations, we initiated an approach (Scheme I) involving the double Favorskii ring contraction of the tricyclic dibromo diketone **10** to C_2-bissecocubane-3,6-dicarboxylic acid (**12**), which has proved successful for the preparation of *twist*-brendane-3,6-dicarboxylic acid (**13**) from the higher homologous dibromo diketone **11**.[10]

Preparation of (-)-C_2-Bissecocubane-3,6-dicarboxylic Acid (12) by the Double Favorskii Rearrangement of the Dibromo Diketone 10 (Schemes II and III). Condensation of the sodio derivative of dimethyl 2,6-dioxobicyclo[3.3.0]octane-3,7-dicarboxylate (**14**) with ethylene dibromide afforded a reasonable yield (34%)[11] of the diketo dicarboxylate **16** which was hydrolyzed to the diketo dicarboxylic acid **18**. After sterile trials with various optical resolving agents, resolution of (±)-**18** was finally accomplished by working with cinchonidine, providing both enantiomers with $[\alpha]_D$ +13.2° and −12.9° (EtOH), respectively. The Hunsdiecker reaction of (+)-**18**, $[\alpha]_D$ +9.87°, afforded a 78% yield of the dibromo diketone (-)-**10**, $[\alpha]_D$ −67.1°, whose reduction with amalgamated zinc[12] afforded the (-)-diketone **20**, $[\alpha]_D$ −110°, which was proved identical with the specimen secured by direct thermal decarboxylation of the diketo dicarboxylic acid (+)-**18** (vide infra). Observed optical inactivity of the hydrocarbon **21** ($C_{10}H_{16}$), mp 194 °C, obtained by Wolff–Kishner reduction of the (-)-diketone **20**, together with its ^{13}C NMR spectrum exhibiting four groups of signals (see the Experimental Section), was found compatible with C_{2v} symmetry of the tricyclic hydrocarbon **21**, and this directly confirms the skeletal structure of the (-)-diketone **20** as well as that of its dibromide precursor **10**.

Turning again to the construction of the C_2-bissecocubane framework, the double Favorskii ring contraction was carried out by refluxing the dibromo diketone (-)-**10**, $[\alpha]_D$ −67.1°, with potassium hydroxide in aqueous ethanol for 4 h to afford the dicarboxylic acid (-)-**12**, $[\alpha]_D$ −97.9° (37% yield),[13] which was purified as the dimethyl ester (-)-**22**. Beside information from its IR and NMR spectra, convincing evidence supporting C_2 symmetry of the dimethyl ester (-)-**22** was obtained from its ^{13}C NMR spectrum consisting of six groups of signals (C(1), C(2), C(3), C(4), and CO_2CH_3) (see the Experimental Section).

In the final stage of our synthesis of C_2-bissecocubane (**4**) itself, Hunsdiecker reaction of the silver salt of the dicarboxylic acid (-)-**12** was tried in carbon tetrachloride at room temperature, expecting conversion to 3,6-dibromo-C_2-bissecocubane (**23**). This resulted in only a vigorous exothermic reaction from which no traceable products were obtained. Since the Hunsdiecker reaction of the higher homologous dicarboxylic acid **13** smoothly gave the dibromide **32** (70% yield),[14] this anomalous behavior observed in **12** marks an outstanding difference between these dicarboxylic acids, undoubtedly reflecting highly strained structure in C_2-bissecocubane ring system.

Optical Purities. Guided by our previous experience with pentacyclic D_3-trishomocubane derivatives,[5b] our efforts to examine the optical purities of our key intermediates were directed toward the preparation of the diacetate **28** (Scheme III) which could be expected to show a fairly large enantiomer differential shift by an added chiral shift reagent. Lithium aluminum hydride reduction of the (-)-diketone **20**, $[\alpha]_D$ −134°, attainable by thermal decarboxylation of the diketo dicarboxylic acid (+)-**18**, $[\alpha]_D$ +12.0°, yielded the (-)-diol **27**, $[\alpha]_D$ −52.1°, whose acetylation with acetic anhydride in pyridine afforded the (-)-diacetate **28**: mp 74–76 °C, $[\alpha]_D$ −53.9°.

The C_2 symmetrical structure found for the diacetate **28** is supported by the NMR spectrum of the racemic modification which exhibits a singlet at δ 2.01, which, on addition of tris[3-(2,2,2-trifluoro-1-hydroxyethylidene)-*d*-camphorato]europium (Eu(TFC)$_3$) (substrate/shift reagent = 1:0.7 molal ratio), was found to split into two singlets of equal intensity centered at δ 5.81 and 5.96. As for the equatorial stereochemistry[15] of the two homotopic acetate groups, we presently have no solid evidence except to tentatively suggest that a supposedly unhindered hydride attack from the opposite side of the ethano bridge should predominantly give equatorial,equatorial the diol **27**. Addition of Eu(TFC)$_3$ (substrate/shift reagent = 1:0.7 molal ratio) to a specimen of the diacetate **28**, $[\alpha]_D$ −53.9°, split the signal into two singlets at δ 5.83 and 5.99, and their integrated intensities indicate an enantiomeric ratio (9:91) corresponding to 82% optical purity. Correlation of optical purities among the key intermediates assigns 67.6% optical purity to our starting material, the diketo dicarboxylic acid (+)-**18**, $[\alpha]_D$ +9.87°, and this automatically indicates the same optical purity for our sample of (-)-C_2-bissecocubane-3,6-dicarboxylic acid (**12**), $[\alpha]_D$ −97.9°.

Absolute Configuration and Chiroptical Properties. Figure 1 reproduces the CD spectra of (+)-homoadamantane-2,7-dione (**31**) with known (1*S*,3*R*,6*R*,8*S*) configuration and its lower homologous (-)-diketone **20**. Inspection of Figure 1 reveals their pronounced enan-

(10) Vogt, B. R. *Tetrahedron Lett.* **1968**, 1575. Vogt, B. R. *Ibid.* **1968**, 1579.
(11) A 41% yield was observed in the preparation of the higher homologue, **15** → **17**.
(12) Webster, O. W.; Sommer, L. H. *J. Am. Chem. Soc.* **1964**, *86*, 3103.
(13) A doubled yield (82%) was observed in the conversion of the higher homologue, **11** → **13**.
(14) Nakazaki, M.; Naemura, K. *J. Org. Chem.* **1977**, *42*, 4108.
(15) Here, the axial and equatorial bonds refer to the bonds approximately parallel to and perpendicular to the C_2 symmetry axis, respectively.

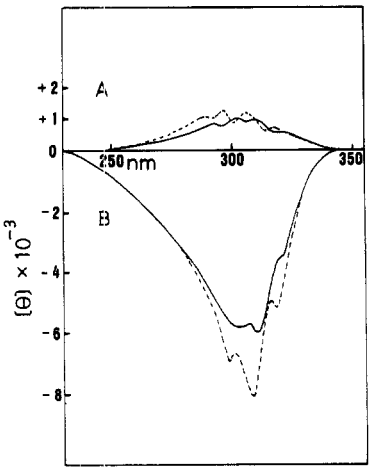
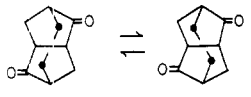


Figure 1. Temperature-dependent CD spectra (in EPA) of (A) (+)-homoadamantane-2,7-dione (**31**) and (B) (−)-tricyclo-[3.3.2.0^{3,7}]decane-2,6-dione (**20**), both corrected to 100% optical purity [(—) at +25 °C, (- - -) at −190 °C].

Chart IV



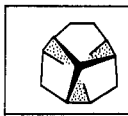
29 30

tiomeric nature except for the higher rotatory strength in the lower homologue **20**, presumably attributable to a more rigid molecular geometry of **20** which would bring two interacting carbonyl chromophores much closer than those in the higher homologue **31**. This constrained stereochemistry in the lower homologue **21** also is reflected in its temperature-dependent CD spectrum (Figure 1), which, contrary to that of **31**, shows almost no shift of peaks, excluding a possible conformational mobility between **29** and **30** (Chart IV).

These CD spectral analyses eventually led to the assignment of the 1*S*,3*R*,5*S*,7*R* configuration to (−)-tricyclo[3.3.2.0^{3,7}]decane-2,6-dione (**20**), ultimately demonstrating the 1*R*,3*R*,6*R*,8*R* configuration of the dicarboxylic acid (−)-**12** with a D_3-twisted bicyclo[2.2.2]octane moiety of *M*-helicity.

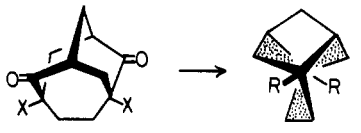
Our failure to secure C_2-bissecocubane (**4**) itself prevents us from knowing whether the interesting decreasing order of $[M]_{D,abs}$ with decreasing bridge length exhibited by the pentacyclic hydrocarbons **6**, **7**, and **8** (Table I) could also be demonstrated in the parallel members of the tricyclic hydrocarbons **2**, **3**, and **4**. To circumvent this difficulty, we converted two homologous dicarboxylic acids, **12** and **13**, with C_2-bissecocubane and *twist*-brendane frameworks, respectively, into their dimethyl derivatives **26** and **36** via the parallel sequence of transformations comprising (a) esterification, (b) $LiAlH_4$ reduction, (c) mesylation, followed by (d) final $LiAlH_4$ reduction of the mesylates to dimethyl derivatives **26** and **36** (see Scheme IV). Knowledge of the optical purity of their starting materials enabled us to calculate the absolute molecular rotations $[M]_{D,abs}$ +254° and −171° for (+)-3,6-dimethyl-*twist*-brendane (**36**) and (−)-3,6-dimethyl-C_2-bissecocubane (**26**), respectively. Since location of the methyl groups in **26** and **36** is similar, we could plausibly assume that the contributions of the methyl groups to the molecular rotations are approximately same, and the known $[M]_{D,abs}$ −346° of (−)-*twist*-brendane (**2**) provides $[M]_D$ ~+100° for the rotational increment of the methyl groups. Taking account of this value, we have a provisional $[M]_{D,abs}$ −270° for (−)-C_2-bissecocubane (**4**) itself, and Table I summarizes the $[M]_{D,abs}$ of various gyrochiral penta- and tricyclic hydrocarbons with an (*M*)-D_3-twisted bicyclo[2.2.2]octane moiety. Conspicuous features common to these gyrochiral cage-shaped hydrocarbons are the following: (a) all compounds with a D_3-twisted bicyclo[2.2.2]octane framework of *M*-helicity are levorotatory, and (b) rotatory strengths decrease with decreasing bridge lengths.

Table I. Absolute $[M]_D$ of the Gyrochiral Penta- and Tricyclic Hydrocarbons with an (*M*)-Bicyclo[2.2.2]octane Moiety

		
−469°[a]	−241°[a]	−58°[a]
		
−598°[b]	R=H −346°[b] R=Me −254°[b]	(R=H −270°)[b] R=Me −171°[b]

[a] Chloroform solvent. [b] Ethanol solvent.

Scheme IV



(+)-**11** X=Br
(+)-**31** X=H

(+)-**13** R=CO_2H
(+)-**32** R=Br
(+)-**33** R=CO_2Me
(+)-**34** R=CH_2OH
(+)-**35** R=CH_2OMs
(+)-**36** R=Me

Experimental Section

Infrared spectra were taken with a Hitachi EPI-S2 spectrometer. ^1H NMR spectra were recorded on a JNM-C-60 HL and ^{13}C NMR spectra were recorded on a JNM FX-100. Chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane. Optical rotations were measured with a JASCO-DIP-SL automatic polarimeter. Circular dichroism (CD) data were recorded on a JASCO-J-40 spectropolarimeter. Elemental analyses were determined on a Yanagimoto CHN-Corder, Type II. All boiling and melting points are uncorrected.

Dimethyl 2,6-Dioxotricyclo[3.3.2.0^{3,7}]decane-1,5-dicarboxylate (16). Dimethyl 2,6-dioxobicyclo[3.3.0]octane-3,7-dicarboxylate (**14**), mp 92–93 °C (lit.[16] mp 91 °C), was prepared according to Blood's procedure.[16]

To a suspension of sodium hydride (8.6 g, 0.358 mol) in dry 1,2-dimethoxyethane (95 mL) was added **14** (24.2 g, 0.0953 mol), and the mixture was stirred for 10 min at room temperature. Distillation of the solvent afforded a residue which was stirred with 1,2-dibromoethane (162 g, 0.863 mol) at 115–120 °C for 25 h. After aqueous acetic acid was added to quench the reaction, the reaction mixture was made acidic with aqueous HCl and extracted with $CHCl_3$. The extract was washed with water and dried ($MgSO_4$). The solvent was removed to give a semisolid, which was chromatographed on silica gel. Fractions eluted with $CHCl_3$ gave a white solid, which was recrystallized from benzene to furnish 10.5 g of **16** (39% yield): mp 193–194 °C; IR (KBr) 1748, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3–2.1 (m, 4 H), 2.5–3.2 (m, 6 H), 3.72 (s, 6 H).

Anal. Calcd for $C_{14}H_{16}O_6$: C, 59.99; H, 5.75. Found: C, 59.91; H, 5.66.

2,6-Dioxotricyclo[3.3.2.0^{3,7}]decane-1,5-dicarboxylic Acid (18). A mixture of **16** (3.55 g, 0.0127 mol), concentrated HCl (14

(16) Blood, C. T.; Linstead, R. P. *J. Chem. Soc.* **1952**, 2255.

mL), acetic acid (60 mL), and water (40 mL) was heated under reflux for 8 h. Evaporation of the solvent afforded a solid, which was recrystallized from ethyl acetate to give 2.86 g of **18** (89% yield): mp 255 °C dec; IR (KBr) 1725, 1235 cm^{-1}.

Anal. Calcd for $C_{12}H_{12}O_6$: C, 57.14; H, 4.80. Found: C, 57.05; H, 4.82.

Optical Resolution of (±)-18. A mixture of (±)-**18** (21.3 g, 0.0845 mol) and cinchonidine (49.8 g, 0.169 mol) in 95% ethanol (500 mL) was refluxed for 8.5 h and allowed to stand overnight at room temperature. The deposited cinchonidine salt (44.7 g), $[\alpha]^{24}_D$ −92.9° (*c* 0.549, EtOH), was freed from the mother liquor which was reserved for isolation of the enantiomeric dicarboxylic acid **18**. Five recrystallizations of the salt from ethanol furnished 6.44 g of the salt, $[\alpha]^{25}_D$ −97.0° (*c* 0.344, EtOH), which was stirred for 6 h with 5% HCl (80 mL) at room temperature. The acidic solution was extracted continuously for 3 days with ether, and removal of the solvent from the extract afforded 1.70 g of (+)-**18**, $[\alpha]^{27}_D$ +11.5° (*c* 0.738, EtOH), which was recrystallized three times from ethyl acetate to give 335 mg of (+)-**18**: $[\alpha]^{27}_D$ +13.2° (*c* 0.791, EtOH); mp 259 °C dec. The mother liquor containing the salt of (−)-**18** was condensed to give a viscous oil which was diluted with 5% HCl. The same workup described for (+)-**18** afforded 4.33 g of (−)-**18**, $[\alpha]^{26}_D$ −10.0° (*c* 0.720, EtOH), which was recrystallized four times from ethyl acetate to give (−)-**18**: $[\alpha]^{25}_D$ −12.9° (*c* 0.650, EtOH); mp 258 °C dec.

(−)-1,5-Dibromotricyclo[3.3.2.0^{3,7}]decane-2,6-dione (10). A solution of (+)-**18** (1.20 g, 4.76 mmol), $[\alpha]_D$ +9.87°, in methanol (11 mL) was neutralized with 1 N aqueous KOH solution and made slightly acidic with diluted nitric acid. To the solution was added a solution of silver nitrate (1.62 g, 9.52 mmol) in methanol (5 mL) and water (4 mL), and the mixture was stirred for 30 min at room temperature. A deposited solid was collected, washed with water and methanol, and dried over phosphorus pentoxide at 70 °C in vacuo for 3 days to yield 1.93 g of the silver dicarboxylate. To a solution of bromine (1.70 g, 10.6 mmol) in dry CCl_4 (6 mL) was added the silver dicarboxylate (1.93 g, 4.11 mmol) with stirring, and the mixture was stirred for 30 min at room temperature followed by refluxing for 3 h. After the mixture cooled, a solid was collected and boiled under reflux with $CHCl_3$ to extract an organic substance. The extract was washed with aqueous $NaHCO_3$ solution and water and dried ($MgSO_4$). Removal of the solvent gave 1.20 g of (−)-**10** (78% yield): $[\alpha]^{25}_D$ −67.1° (*c* 0.939, $CHCl_3$); mp 199 °C dec; IR (KBr) 1755 cm^{-1}.

(−)-Tricyclo[3.3.2.0^{3,7}]decane-2,6-dione (20). A mixture of (−)-**10** (1.11 g, 3.45 mmol), $[\alpha]_D$ −67.1°, amalgamated zinc (20.0 g), water (1 mL), and acetic acid (78 mL) was refluxed with stirring for 30 h. The reaction mixture freed from zinc was diluted with water and extracted continuously with ether. The extract was washed with 2% aqueous NaOH solution and water and dried ($MgSO_4$). After evaporation of the solvent, a residual solid was sublimed at 60–80 °C (5 mm) to furnish 180 mg of (−)-**20** (33% yield): $[\alpha]^{22}_D$ −110° (*c* 0.660, $CHCl_3$); mp 233–235 °C (sealed tube); IR (KBr) 1738 cm^{-1}; CD (*c* 1.67 × 10^{-2}, isooctane, at 25 °C) [θ] (nm) −2.67 × 10^3 (sh, 281.5), −4.88 × 10^3 (sh, 291), −7.22 × 10^3 (300.5), −7.80 × 10^3 (311), −4.85 × 10^3 (323); CD (*c* 8.72 × 10^{-3}, EPA, at 25 °C) [θ] (nm) −5.94 × 10^3 (300), −6.05 × 10^3 (309), −3.50 × 10^3 (sh, 320); CD (EPA, at −68 °C) [θ] (nm) −4.47 × 10^3 (sh, 290), −6.12 × 10^3 (299), −5.21 × 10^3 (311.5), −3.89 × 10^3 (320.5); CD (EPA, at −190 °C) [θ] (nm) −6.95 × 10^3 (297), −8.11 × 10^3 (307.5), −5.17 × 10^3 (318.5).

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.11; H, 7.38. Found: C, 73.14; H, 7.37.

Tricyclo[3.3.2.0^{3,7}]decane (21). A mixture of (−)-**20** (150 mg, 0.915 mmol), $[\alpha]_D$ −110°, KOH (130 mg), 80% hydrazine hydrate (0.24 mL), and triethylene glycol (3 mL) was heated in an oil bath. During 1.5 h, the bath temperature was gradually raised to 190–200 °C and then this temperature was kept for a further 4 h, during which a white solid condensed on the inner wall of the condenser. After the mixture cooled, the solid was dissolved in pentane and the reaction mixture was diluted with water and extracted with pentane. Combined pentane extracts were washed with water and dried ($MgSO_4$). Evaporation of the solvent gave a solid, which was sublimed at 50 °C (30 mm) to yield 60 mg of **21** (48% yield): mp 194–196 °C (sealed tube); $[\alpha]^{25}_D$ 0° (*c* 0.311, EtOH); IR (KBr) 2925, 2870, 1455 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 30.29 (CH_2), 36.82 (CH), 41.54 (CH), 42.28 (CH_2).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.25; H, 11.69.

Decarboxylation of (+)-18. Dicarboxylic acid (+)-**18** (650 mg, 2.58 mmol), $[\alpha]_D$ +12.0°, was directly heated with a small flame in a test tube provided with a cold finger, and heating was continued until evolution of carbon dioxide ceased. A white solid which condensed on the cold finger was dissolved in ether, and the ethereal solution was washed with aqueous $NaHCO_3$ solution and water and dried ($MgSO_4$). Evaporation of the solvent afforded a solid which was sublimed at 70–80 °C (5 mm) to give 142 mg of **20** (33% yield): mp 232–234 °C (sealed tube); $[\alpha]^{22}_D$ −134° (*c* 0.235, $CHCl_3$). An IR spectrum indicated its identity with the diketone **20** prepared from the dibromo diketone **10**.

(−)-Tricyclo[3.3.2.0^{3,7}]decane-2,6-diol (27). A solution of (−)-**20** (120 mg, 0.732 mmol), $[\alpha]_D$ −134°, in dry ether (30 mL) was added to a suspension of $LiAlH_4$ (40 mg, 1.03 mmol) in dry ether (20 mL) and the mixture was refluxed for 6 h. After the mixture cooled, diluted sulfuric acid was added to the chilled reaction mixture. An inorganic solid was filtered off and the filtrate was washed with aqueous $NaHCO_3$ solution and water and dried ($MgSO_4$). After removal of the solvent, a white solid was purified by sublimation at 120–130 °C (5 mm) to afford 110 mg of **27** (89% yield): mp 303–305 °C (sealed tube); $[\alpha]^{22}_D$ −52.1° (*c* 0.494, EtOH).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.11, H, 9.56.

(−)-2,6-Diacetoxytricyclo[3.3.2.0^{3,7}]decane (28). To a solution of (−)-**27** (90 mg, 0.536 mmol), $[\alpha]_D$ −52.1°, in dry pyridine (2 mL) was added acetic anhydride (370 mg, 3.63 mmol) with ice cooling. After standing for 24 h at room temperature, the reaction mixture was poured into ice water and extracted with ether. The extract was washed with 5% HCl, aqueous $NaHCO_3$ solution, and water and dried ($MgSO_4$). Evaporation of the solvent afforded a solid, whose distillation under vacuum gave 115 mg of **28** (85% yield), bp 110–115 °C (air bath temperature) (5 mm). The distillate solidified and melted at 74–76 °C: $[\alpha]^{20}_D$ −53.9° (*c* 0.383, EtOH); IR (KBr) 1730, 1250, 1240 cm^{-1}; ^1H NMR (CCl_4) δ 1.1–1.9 (m, 8 H), 2.01 (s, 6 H), 2.1–2.7 (m, 4 H), 4.8 (d,d, *J* = 5.3, 7.2 Hz, 2 H).

Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.71; H, 7.93.

(−)-Dimethyl Tricyclo[4.2.0.0^{3,8}]octane-3,6-dicarboxylate (22). A mixture of (−)-**10** (1.30 g, 4.04 mmol), $[\alpha]_D$ −67.1°, KOH (3.04 g), ethanol (7.5 mL), and water (7.5 mL) was refluxed for 4 h. The chilled reaction mixture was made acidic with HCl and concentrated to give a solid, which was extracted with boiling acetone. An insoluble solid was filtered off and the filtrate was treated with Norit followed by concentration to afford 293 mg of **12** (37% yield). This was esterified with ethereal CH_2N_2 by the usual method. The crude ester **22** was chromatographed on silica gel and fractions eluted with $CHCl_3$ afforded a solid, which was sublimed to give 234 mg of (−)-**22** (70% yield): mp 79–80 °C (sealed tube); $[\alpha]^{25}_D$ −90.2° (*c* 0.467, MeOH); IR (KBr) 1725, 1100 cm^{-1}; ^1H NMR (CCl_4) δ 1.9–2.4 (m, 8 H), 2.8–2.9 (m, 2 H), 3.59 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 24.07 (CH_2), 30.94 (CH_2), 39.57 (CH), 45.38 (CCO_2CH_3), 51.55 (CH_3), 175.43 (CO_2CH_3).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.12; H, 7.23.

Hydrolysis of (−)-22. After a mixture of (−)-**22** (400 mg, 1.79 mmol), $[\alpha]_D$ −90.2°, KOH (560 mg), and 50% aqueous methanol (10 mL) was refluxed for 3 h, methanol was distilled in vacuo to give a residue which was diluted with water. The mixture was made acidic with HCl to precipitate a solid which was collected on a filter, washed with water, and dried over $CaCl_2$ to yield 255 mg of (−)-**12** (73% yield). A part of the solid was sublimed at 180–190 °C (0.5 mm) to furnish an analytical sample: mp 243 °C dec; $[\alpha]^{24}_D$ −97.9° (*c* 0.493, EtOH); IR (KBr) 1695 cm^{-1}.

Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.24; H, 6.28.

(−)-3,6-Bis(hydroxymethyl)tricyclo[4.2.0.0^{3,8}]octane (24). To a suspension of $LiAlH_4$ (126 mg, 3.30 mmol) in dry tetrahydrofuran (THF; 15 mL) was added a solution of (−)-**12** (250 mg, 1.32 mmol), $[\alpha]_D$ −97.9°, in dry THF (15 mL) and the mixture was refluxed for 3 h. Then, just enough diluted sulfuric acid was added to precipitate an inorganic solid with ice cooling. The filtrate freed from the solid was dried ($MgSO_4$) and concentrated. The residue was chromatographed on neutral alumina (Woelm, activity III) and fractions eluted with ether gave 110 mg of (−)-**24**

(50% yield) as a colorless oil: $[\alpha]^{26}_D$ -94.5° (c 0.308, EtOH); IR (neat film) 3400, 1025 cm^{-1}.

Methanesulfonate of (-)-24. To a chilled solution of (-)-**24** (100 mg, 0.595 mmol), $[\alpha]_D$ -94.5°, in dry pyridine (3 mL) was added methanesulfonyl chloride (205 mg, 1.78 mmol). The mixture was stirred for 3 h with ice cooling, allowed to stand overnight at room temperature, poured into ice-water, and extracted with $CHCl_3$. The extract was washed with 5% HCl, aqueous $NaHCO_3$ solution, and water and dried ($MgSO_4$). Removal of the solvent gave 130 mg of (-)-**25** (67% yield): mp 132-134 °C; $[\alpha]^{26}_D$ -35.7° (c 0.291, $CHCl_3$); IR (KBr) 1340, 1320, 1165, 930 cm^{-1}.

Anal. Calcd for $C_{12}H_{20}O_6S_2$: C, 44.44; H, 6.22. Found: C, 44.25; H, 6.30.

(-)-3,6-Dimethyltricyclo[4.2.0.0^{3,8}]octane (26). To a suspension of (-)-**25** (120 mg, 0.370 mmol), $[\alpha]_D$ -35.7°, in dry ether (20 mL) was added $LiAlH_4$ (160 mg, 4.20 mmol) and then the mixture was refluxed for 20 h. Saturated aqueous NH_4Cl solution was added, the deposited inorganic solid was filtered, and the filtrate was dried ($MgSO_4$). After evaporation of the solvent, the residue was chromatographed on neutral alumina (Woelm, activity II) and fractions eluted with pentane afforded a colorless oil, which was distilled to furnish 23 mg of (-)-**26** (46% yield): bp 75-80 °C (air bath temperature) (30 mm); $[\alpha]^{26}_D$ -85.0° (c 0.178, EtOH); IR (neat film) 2940, 2870, 1450 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 87.88; H, 11.70.

(+)-Dimethyl *twist*-Brendane-3,6-dicarboxylate (33). Esterification of (+)-**13** (70 mg, 0.333 mmol), $[\alpha]_D$ +135° (c 0.610, MeOH) (optical purity 80%), with ethereal CH_2N_2 gave a solid product which was sublimed to furnish 56 mg of (+)-**33** (71% yield): mp 62-63 °C (sealed tube); $[\alpha]^{23}_D$ +113° (c 0.252, MeOH); IR (KBr) 1720, 1290, 1272, 1253, 1098 cm^{-1}.

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.82; H, 7.63.

(+)-3,6-Bis(hydroxymethyl)-*twist*-brendane (34). Reduction of (+)-**33** (420 mg, 2.00 mmol), $[\alpha]_D$ +135°, with $LiAlH_4$ (114 mg, 3.00 mmol) was carried out as described for the preparation of (-)-**24**. Routine workup gave 330 mg of (+)-**34** (90% yield) as a white solid: mp 116-118 °C; $[\alpha]^{25}_D$ +134° (c 0.453, EtOH); IR (KBr) 3300, 1040 cm^{-1}.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.21; H, 9.97.

(+)-3,6-Dimethyl-*twist*-brendane (36). A pyridine solution of (+)-**34** (453 mg, 2.39 mmol), $[\alpha]_D$ +134°, was treated with methanesulfonyl chloride (890 mg, 7.74 mmol) by the same manner described for the preparation of (-)-**25**, and 590 mg of (+)-**35** (73% yield) was obtained as a solid: $[\alpha]^{22}_D$ +60.3° (c 0.300, $CHCl_3$); IR (KBr) 1345, 1170, 945 cm^{-1}.

To a suspension of $LiAlH_4$ (715 mg, 18.8 mmol) in dry ether (80 mL) was added the dimesylate **35** (560 mg, 1.66 mmol), and the mixture was refluxed for 24 h. After workup as described for (-)-**26**, the crude product was chromatographed on neutral alumina (Woelm, activity III) and fractions eluted with pentane gave a colorless oil, which was distilled to furnish 70 mg of (+)-**36** (28% yield): bp 70-73 °C (air bath temperature) (20 mm); $[\alpha]^{25}_D$ +135° (c 0.241, EtOH); IR (neat film) 2940, 2870, 1450, 1375, 1335 cm^{-1}; ^1H NMR (CCl_4) δ 0.7-0.9 (m, 2 H), 0.95 (s, 6 H), 1.1-1.6 (m, 8 H), 1.7-1.9 (m, 2 H).

Anal. Calcd for $C_{11}H_{18}$: C, 87.92; H, 12.08. Found: C, 87.79; H, 12.04.

Registry No. (-)-**10**, 73986-08-0; (+)-**11**, 63903-40-2; (-)-**12**, 73986-09-1; (+)-**13**, 63902-02-3; **14**, 74034-31-4; **15**, 74007-19-5; **16**, 73986-10-4; **17**, 63833-61-4; (±)-**18**, 73986-11-5; (-)-**18**, 74034-32-5; (+)-**18**, 74034-33-6; (-)-**20**, 73986-12-6; **21**, 49700-60-9; (-)-**22**, 74034-34-7; (-)-**24**, 73986-13-7; (-)-**25**, 73986-14-8; (-)-**26**, 73986-15-9; (-)-**27**, 73986-16-0; (-)-**28**, 73986-17-1; (+)-**31**, 63902-06-7; (+)-**33**, 73986-18-2; (+)-**34**, 73986-19-3; (+)-**35**, 73986-20-6; (+)-**36**, 73986-21-7.

Stereochemistry of Alkylation of Carboxylic Acid Salt and Ester α Anions Derived from Cyclic Systems

A. Paul Krapcho* and Edward A. Dundulis[1]

Department of Chemistry, The University of Vermont, Burlington, Vermont 05401

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A stereochemical study of the alkylation of α-lithiated carboxylate salts and esters has been performed. The α anions derived from the bicyclic acids *exo*-**1**, *endo*-**1**, and **7** (R = H) and the esters **4** and **7** (R = CH_3) yield predominantly exo alkylation. As an example, the α anion derived from ester **7** (R = CH_3) on treatment with CH_3I yields *exo*-**8** (R = R′ = CH_3) and *endo*-**9** (R = R′ = CH_3) in a 97:3 ratio, a highly stereoselective reaction. Addition of TMEDA to the reactions involving the α anions derived from *exo*- or *endo*-**1** did not change the stereochemical alkylation results. The α anions derived from the substituted cyclohexanecarboxylic acids **10**, **13**, **16**, **19**, or **22** (where R = H in each case) on methylation yield more axial methylation (axial/equatorial ratios of 0.4-2.7) than the α anions derived from the methyl esters corresponding to these acids. The α anions from the esters yield predominantly equatorial methylated products (e/a ratios varying from 4 to 9). The reasons for the different stereochemical results are discussed.

Many alkylations and other synthetic applications of α-metalated carboxylate salts[2] and esters[3] have appeared in recent literature. However, no studies of any depth have been reported which deal with the factors which might control the stereochemistry of alkylation of these reactive species.

Several reports dealing with the stereoselective methylations of ester enolates formed by Li/NH_3 reduction of substituted α,β-unsaturated esters have appeared.[4] High stereoselectivity was found in the Li/NH_3 reductive methylation of α anions of carboxylic acid salts in model studies of systems directed toward a synthesis of the gibberellins.[5] The Li/NH_3 reductive alkylations of 4-*tert*-

(1) Fellow of the Humphrey Chemical Co., North Haven, CT.

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