T. A. Modro and J. H. Ridd, *J. Chem. Soc. B*, 528 (1968) and earlier papers; W. F. Reynolds, T. A. Modro, and P. G. Mezey, *J. Chem. Soc., Perkin Trans. 2*, 1066 (1977).
(79) General: L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, **1**, 35 (1963), Figures 15, 20, 23. Desilylation: F. B. Deans and C. Eaborn, *J. Chem. Soc.*, 2299 (1959). Degermylation: C. Eaborn and K. C. Pande, *ibid.*, 5082 (1961). Bromination: P. B. D. de la Mare and I. C. Hilton, *ibid.*, 997 (1962); A. Gastaminza, J. H. Ridd, and F. Roy, *J. Chem. Soc. B*, 684 (1969). Nitration: L. M. Stock, *Prog. Phys. Org. Chem.*, **12**, 21 (1976), Figure 5; J. H. Rees, J. H. Ridd, and A. Ricci, *J. Chem. Soc., Perkin Trans. 2*, 294 (1976), and earlier papers. For substitution in $Ph(CH_2)_nSO_3^-$ see H. Cerfontain and Z. R. H. Schaasberg-Nienhuis, *J. Chem. Soc., Perkin Trans. 2*, 1413 (1973) and earlier papers; R. B. Moodie, K. Schofield, and T. Yoshida, *ibid.*, 788 (1975).
(80) A. van Veen, A. J. Hoefnagel, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **90**, 289 (1971).
(81) See M. Salomon in "Physical Chemistry of Organic Solvent Systems", A. K. Covington and T. Dickinson, Ed., Plenum Press, London, 1973.
(82) Cf. E. Larsson and B. Adell, *Z. Phys. Chem., Abt. A*, **156**, 352 (1931); H. S. Dunsmore and J. C. Speakman, *Trans. Faraday Soc.*, **50**, 236 (1954); D. Rosenthal, I. T. Oiwa, A. D. Saxton, and L. R. Lieto, *J. Phys. Chem.*, **69**, 1588 (1965); M. Novak and G. M. Loudon, *J. Am. Chem. Soc.*, **98**, 3591 (1976); ref 80.
(83) G. Åkerlöf, *J. Am. Chem. Soc.*, **54**, 4125 (1932).
(84) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **79**, 1913 (1957), and ref 45.

Absolute Configurations and Absolute Rotations of C_2-Bishomocubane, *ditwist*-Brendane, and Twistane

Masao Nakazaki,* Koichiro Naemura, and Seiichi Nakahara

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

Received May 17, 1978

(+)-*endo*-Dicyclopentadiene-1,8-dione 8-ethylene ketal (**13**), a common synthetic intermediate for both (−)-C_2-bishomocubane (**5**) and (−)-*ditwist*-brendane (**3**), was degraded to (+)-(1*R*,2*S*,4*R*)-methyl 3-(*endo*-2-norbornyl)-propionate (**23**), indicating the (1*S*,2*S*,3*S*,4*S*,5*R*,7*S*,8*S*,9*R*) and (1*R*,2*R*,4*R*,6*R*,7*R*,8*R*) absolute configurations to (−)-**5** and (−)-**3**, respectively. Enantiomer differential shifts observed in NMR spectra of (−)-*exo-ditwist*-brendan-3-ol acetate (**32**) and (−)-twistan-2-ol acetate (**43**) have assigned absolute rotations $[\alpha]_D$ −304°, $[\alpha]_D$ −44°, and $[\alpha]_D$ −440° to (−)-*ditwist*-brendane (**3**), (−)-C_2-bishomocubane (**5**), and (−)-twistane (**2**), respectively.

Preceding papers from our laboratory have reported syntheses and absolute configuration determinations of various gyrochiral[1] cage-shaped hydrocarbons, among which the representatives are (−)-*twist*-brendane (C_2 symmetry) (**1**),[2] (−)-twistane (D_2 symmetry) (**2**),[3] (−)-*ditwist*-brendane (C_2 symmetry) (**3**),[4] (−)-C_2-bishomocubane (C_2 symmetry) (**5**),[5] and (−)-D_3-trishomocubane (D_3 symmetry) (**7**)[4,6] (Chart I). Inspection of their molecular models reveals that all these levorotatory species bear as a common structural unit the bicyclo[2.2.2]octane moiety (**9**) held in the D_3 conformation with *M* helicity (**10**)[7] (Chart II). Although symmetrical C(3)–C(6), C(5)–C(7), and C(2)–C(8) diagonal bridgings with three methylene groups retain the original D_3 symmetry of bicyclo[2.2.2]octane affording chiral D_3-trishomocubane molecule (**7**), direct diagonal bridgings with three single bonds yield cubane (**12**), an achiral molecule with O_h symmetry. Characteristically, this cubane molecule (**12**) can be regarded to be composed of two enantiomeric D_3-bicyclo[2.2.2]octane moieties (**10** and **11**), and which enantiomeric component element is to be expanded determines the chiralities of resulting C_2-bishomocubane (**5**) and D_3-trishomocubane (**7**). Beside the tricyclic members **1** and **2**, whose absolute configurations have been correlated to their synthetic intermediates with known absolute configurations, the absolute configuration determination of the tetracyclic (**3**) and the pentacyclic cage-shaped compounds (**5** and **7**) have been carried out by means of circular dichroism (CD) spectral analyses of the intermediate ketones (−)-**4**, (−)-**6**, and (−)-**8**. Reliability of this CD analysis has been supported by ample examples among which we can cite a recent X-ray crystallographic determination of the absolute configuration of (−)-D_3-trishomocubane (**7**)[8] which eventually verified our result obtained by means of the CD spectral analysis.[4] Nevertheless, attempts have been made in our laboratory to secure another direct and unambiguous experimental evidence to establish the absolute configurations of *ditwist*-brendane (**3**) and C_2-bishomocubane (**5**). In this paper, we report conversion of the (+)-ketone **13**, their common synthetic intermediate, into (+)-(1*R*,2*S*,4*R*)-methyl 3-(*endo*-2-norbornyl)propionate (**23**) to confirm our previous assignments[4,5] of their absolute configurations.

Chart I

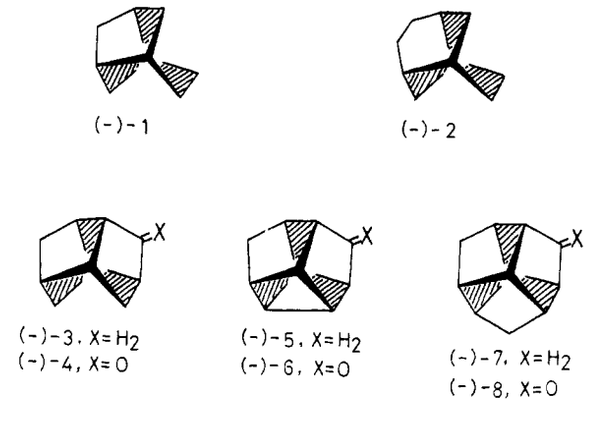
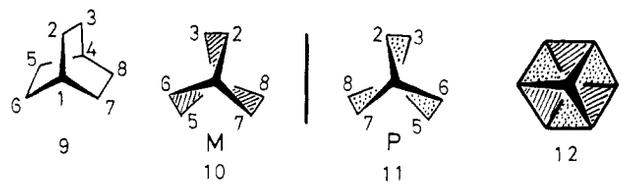


Chart II

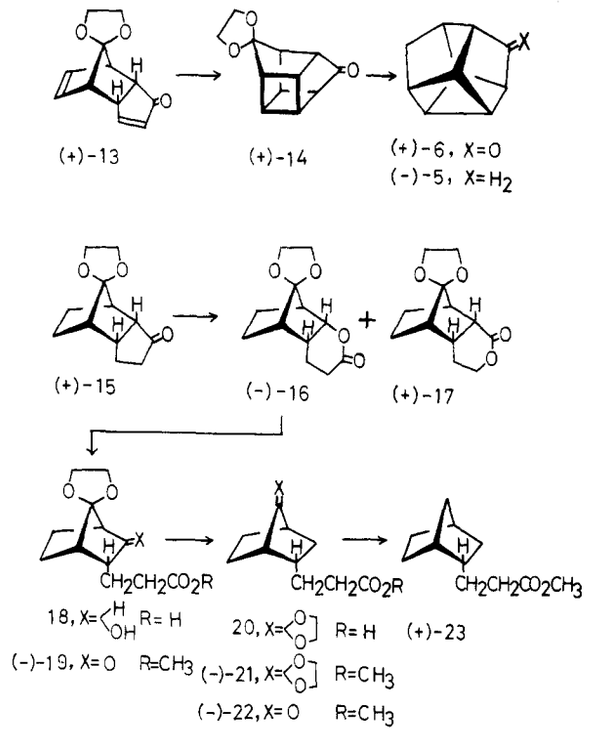


Results and Discussion

Degradation of (+)-*endo*-Dicyclopentadiene-1,8-dione 8-Ethylene Ketal (13) into (+)-(1*R*,2*S*,4*R*)-Methyl 3-(*endo*-2-Norbornyl)propionate (23) (Scheme I).[9] Photocyclization of the (+)-unsaturated ketone **13** to give (−)-

0022-3263/78/1943-4745$01.00/0

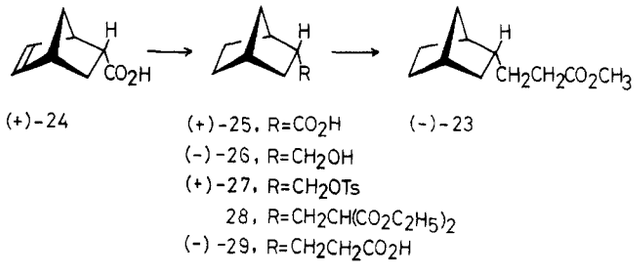
Scheme I



pentacyclic ketone **14** was a stragetic process in our first successful synthesis of optically active C_2-bishomocubane (**5**),[5] whose hydrogenolysis led to the optically active *ditwist*-brendane (**3**).[4] The sequence of conversions which degraded this (+)-unsaturated ketone (**13**) into the (+)-bicyclic carboxylate **23** is illustrated in Scheme I. Catalytic hydrogenation with 5% Pd on carbon converted the (+)-unsaturated ketone **13**, $[\alpha]_D$ +94.0° ($CHCl_3$), into (+)-saturated ketone **15**, $[\alpha]_D$ +173° ($CHCl_3$), whose Baeyer–Villiger oxidation[10] with *m*-chloroperbenzoic acid afforded a 1:1 mixture of two lactones. Careful recrystallization from ether separated the lactones to give a (+)-lactone, mp 113–115 °C, $[\alpha]_D$ +81.9° ($CHCl_3$), and another (−)-lactone, mp 93–96 °C, $[\alpha]_D$ −63.8° ($CHCl_3$), in 25 and 31% yields, respectively. The (−)-isomer exhibited a clearly discernible doublet–doublet signal around δ 4.6–4.8 which could be attributed to the single proton on the methine carbon next to the oxygen atom, indicating the structure **16** to this isomer, while the (+)-isomer showed a broad multiplet at δ 4.1–4.4 corresponding to the structure **17**. These views were found to be supported by eventual conversion of (−)-**16** to the (+)-carboxylate **23**. Alkaline hydrolysis and oxidation of the resulting hydroxy acid **18** followed by esterification with diazomethane yielded the (−)-ketone **19**, whose carbonyl group was removed by the Wolff–Kishner reduction to give the ketal carboxylic acid **20**. This ketal carboxylic acid (**20**) was converted to (+)-**23** by a rather routine procedure comprising: (1) esterification to the (−)-ketal ester **21**; (2) removal of the ketal protective group to afford the keto ester **22**; and (3) the Wolff–Kishner reduction followed by esterification with diazomethane. Distillation of the final product produced the (+)-bicyclic carboxylate **23**, bp 96 °C (bath temperature) (5 mm), $[\alpha]_D$ +8.8° (EtOH), whose identity was established by comparison with an authentic sample prepared from the (+)-endo unsaturated carboxylic acid **24** by the sequence of steps encompassed in Scheme II.

Absolute Configurations of (−)-C_2-Bishomocubane (5) and (−)-*ditwist*-Brendane (3). Preparation of the optically active methyl 3-(*endo*-2-norbornyl)propionate (**23**) with known absolute configuration was again rather straightforwardly accomplished starting from (+)-(1*R*,2*R*,4*R*)-*endo*-

Scheme II



5-norbornene-2-carboxylic acid (**24**), $[\alpha]_D$ +57.2° (EtOH) (Scheme II). Catalytic hydrogenation with 5% Pd on carbon yielded (+)-saturated carboxylic acid **25**, $[\alpha]_D$ +12.1° (EtOH), whose $LiAlH_4$ reduction gave (−)-alcohol **26**, $[\alpha]_D$ −2.15° (EtOH). The malonate **28** secured from the (−)-alcohol **26** via the tosylate **27** was saponified, and decarboxylation of the resulting dicarboxylic acid afforded (−)-carboxylic acid **29**, $[\alpha]_D$ −4.1° (EtOH). Esterification with diazomethane concluded the preparation of (−)-(1*S*,2*R*,4*S*)-methyl 3-(*endo*-2-norbornyl)propionate (**23**), bp 77.5–79 °C (4 mm), $[\alpha]_D$ −4.5° (EtOH), whose NMR, IR, TLC, and VPC were found indistinguishable from those of (+)-**23** obtained by degradation of (+)-**13**.

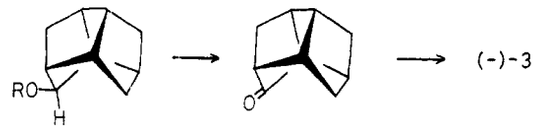
By tracing back the sequence of conversions outlined in Scheme I, this enantiomeric relation between these two bicyclic carboxylates (**23**) immediately indicates the (1*S*,2*S*,3*S*,4*S*,5*R*,7*S*,8*S*,9*R*) absolute configuration to (−)-C_2-bishomocubane (**5**). Since hydrogenolysis of (−)-C_2-bishomocubane (**5**) opens its single bond shared by two cyclobutane moieties to give (−)-*ditwist*-brendane (**3**), these chemical correlations confirmed our previous results based on the CD spectral analyses.[4,5]

Absolute Rotations of *ditwist*-Brendane (3) and C_2-Bishomocubane (5). When we first secured a sample of optically active C_2-bishomocubane (**5**), what surprised us most was a dramatic jump of optical rotations which was observed in hydrogenolysis of (−)-**5**, $[\alpha]_D$ −33.8° ($CHCl_3$), to (−)-*ditwist*-brendane (**3**), $[\alpha]_D$ −233° ($CHCl_3$). And this optical rotation ($[\alpha]_D$ −33.8°) exhibited by (−)-**5** itself is also surprisingly low compared with the rotation $[\alpha]_D$ −165° shown by its next higher homologue (−)-D_3-trishomocubane (**7**) (Chart III). These peculiar chiroptical properties prompted us to seek information about the optical purities of (−)-**3** and (−)-**5**. Guided by our experience on (−)-brexan-2-ol acetate,[11] whose NMR spectrum showed a fairly large enantiomer differential shift on addition of tris[3-(trifluoromethylhydroxymethylene)-*d*-camphorato]europium(III) [Eu(facam)$_3$], we chose optically active *exo-ditwist*-brendan-3-ol acetate (**32**) as a hopeful candidate which should exhibit an observable enantiomer differential shift. Racemic *exo-ditwist*-brendan-3-ol (**30**) prepared by Rothberg's procedure[12] was converted into the hydrogen phthalate **31**, whose resolution was accomplished working with (+)-2-(1-aminoethyl)naphthalene as the resolving agent. Recrystallization of the salt from acetone afforded a sparingly soluble levorotatory salt with $[\alpha]_D$ −30.7° (EtOH) which was treated with diluted HCl to yield (−)-**31**, $[\alpha]_D$ −67.4° (acetone). Alkaline hydrolysis, followed by acetylation of the resulting (−)-alcohol (**30**), $[\alpha]_D$ −171° ($CHCl_3$), with acetic anhydride in pyridine, transformed (−)-**31** into the (−)-acetate **32**, $[\alpha]_D$ −134° ($CHCl_3$). Contrary to our expectation, no enantiomer differential shift was observed in the CH_3CO signal, which only shifted

Chart III

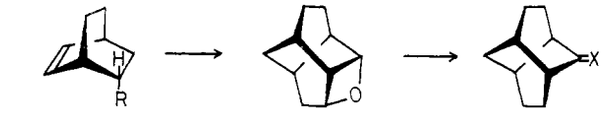
	(−)-1	(−)-2	(−)-3	(−)-5	(−)-7
$[\alpha]_D$	−284°	−440°	−233°	−44°	−165°

Scheme III



(-)-30, R=H (-)-33
(-)-31, R=$COC_6H_4(o)CO_2H$
(-)-32, R=$COCH_3$

Scheme IV



(-)-34, R=CO_2H (-)-41 (-)-42, X= 
(-)-35, R=CH_2OH (-)-43, X= 
(-)-36, R=CH_2OTs (-)-44, X=O
(-)-37, R=CH_2CN (-)-2, X=H_2
(-)-38, R=CH_2CO_2H
(-)-39, R=CH_2CH_2OH
(-)-40, R=CH_2CHO

downfield on addition of Eu(facam)$_3$. Careful examination, however, was rewarded by our discovering a fairly large enantiomer differential shift $\Delta\Delta\delta$ = 0.13 ppm in the broad singlet due to a single proton on the carbon atom carrying the acetoxy group. Integrated intensities indicated an enantiomer ratio 95:5 (optical purity 90%) to this acetate prepared from (−)-**30**, whose oxidation with pyridinium chlorochromate in turn gave (−)-*ditwist*-brendan-3-one (**33**), $[\alpha]_D$ −250° ($CHCl_3$) (Scheme III). Since the Wolff–Kishner reduction converted this ketone into (−)-*ditwist*-brendane (**3**), mp 141–145 °C (in a sealed tube), $[\alpha]_D$ −274° ($CHCl_3$), and whole operations were carried out with precautions not to effect optical purities of all intermediates, these correlations assigned absolute rotation $[\alpha]_D$ −304° to (−)-*ditwist*-brendane (**3**). Combining this value with our reported hydrogenolysis of (−)-C_2-bishomocubane (**5**) with $[\alpha]_D$ −33.8° into (−)-*ditwist*-brendane (**3**), $[\alpha]_D$ −233°,[4] whose optical purity we now know is 75%, we can safely assign absolute rotation $[\alpha]_D$ −44° to (−)-C_2-bishomocubane (**5**).

Absolute Rotations of *twist*-Brendane (1) and Twistane (2). Now that among the five gyrochiral cage-shaped hydrocarbons listed in Chart I three have been known with their absolute rotations, we turn our attention to the absolute rotations of remaining (−)-*twist*-brendane (**1**) and (−)-twistane (**2**). Our previous paper[2] reporting the synthesis of (−)-*twist*-brendane (**1**) with $[\alpha]_D$ −235° (EtOH) from the (−)-unsaturated carboxylic acid **24**, $[\alpha]_D$ −119° (optical purity 83%),[13] with no operations to effect the optical purities of the synthetic intermediates, directly assigns absolute rotation $[\alpha]_D$ −284° to (−)-*twist*-brendane (**1**). To know the absolute rotation of twistane (**2**), however, we had to resort to the NMR enantiomer differential method. Since our experience[11] in the NMR studies of cage-shaped compounds told that optically active 2-twistanol acetate (**43**) could be expected to show a fairly large enantiomer differential shift, we initiated a preparation of this acetate in optically active modification.

The key step in our synthetic approach was the Paterno–Büchi photochemical oxetane cyclization[14] of (−)-bicyclic unsaturated aldehyde (**40**) which was prepared from (−)-*endo*-5-bicyclo[2.2.2]octene-2-carboxylic acid (**34**), $[\alpha]_D$ −14.5° (EtOH), by a routine sequence of conversions shown in Scheme IV. The (−)-alcohol **35** prepared by $LiAlH_4$ reduction of (−)-acid **34** was converted into (−)-tosylate **36**, which in turn afforded (−)-carboxylic acid **38** via (−)-nitrile **37**. Reduction with $LiAlH_4$ followed by pyridinium chlorochromate oxidation converted (−)-**38** into the (−)-unsaturated aldehyde **40**, $[\alpha]_D$ −4.7° (MeOH), in a 36% overall yield based on the acid (**34**) as the starting material. Irradiation of a benzene solution of (−)-**40** with mercury lamp for 6 h led to formation of the oxetane **41** (53% yield), whose reductive cleavage with $LiAlH_4$ yielded (−)-twistan-2-ol (**42**), mp 187–190 °C (in a sealed tube), $[\alpha]_D$ −118° (MeOH). Acetylation with acetic anhydride with pyridine afforded (−)-2-acetoxytwistane (**43**), $[\alpha]_D$ −98.9° (MeOH), which exhibited a singlet signal at δ 4.65 in its NMR spectrum. Addition of Eu(facam)$_3$ (substrate/shift reagent = 1:0.189) split the signal into a doublet at δ 4.43, 4.53 and their integrated intensities indicated an enantiomer ratio 39:80 corresponding to 34.5% optical purity. Finally, this same (−)-twistan-2-ol (**42**) was oxidized with pyridinium chlorochromate to afford (−)-twistan-2-one (**44**), mp 184–188 °C (in a sealed tube), $[\alpha]_D$ −151° (EtOH). Coupled with our early experiment[3] which transformed (+)-twistan-2-one, $[\alpha]_D$ +412° (EtOH), into (+)-twistane (**2**), $[\alpha]_D$ +414° (EtOH), this 34.5% optical purity of (−)-twistan-2-ol with $[\alpha]_D$ −151° indicates absolute rotation of $[\alpha]_D$ −440° to (−)-twistane (**2**).

Chiroptical Properties. Chart III listed the absolute rotation values of the cage-shaped compounds discussed in this paper together with their absolute configurations. The conspicuously small rotation observed in (−)-C_2-bishomocubane (**5**) undoubtly reflects its characteristic molecular structure, which deviates least from the achiral cubane molecular framework with O_h symmetry. Lastly, Table I records the CD spectrum of newly prepared (−)-*ditwist*-brendan-3-one (**33**). Examination of the octant projections (Chart IV) of tricyclic (−)-*twist*-brendan-2-one (**45**) and tetracyclic (−)-*ditwist*-brendan-3-one (**33**) predicts negative Cotton effects of these ketones which were found to be consistent with their observed CD spectra, suggesting the extra methylene bridge (broken line) in **33** exerts little influence on the Cotton curve.

Experimental Section

Infrared spectral data were obtained from a Hitachi-EPI-S2 spectrophotometer. Nuclear magnetic resonance spectra were obtained from a JNM-C-60HL spectrometer. Ultraviolet spectra were recorded on a Beckman DB spectrometer. Optical rotations were measured with a JASCO-DPI-SL automatic polarimeter. Circular dichroism data were measured on a JASCO-J-40 spectropolarimeter. Elemental analyses were performed on a Yanagimoto CHN-Corder type II. All melting points and boiling points are uncorrected.

(+)-*endo*-Tetrahydrodicyclopentadiene-1,8-dione 8-Ethylene Ketal (15). The ethylene ketal **15** was prepared from (+)-**13**, $[\alpha]^{12}_D$ +94.0°, by the same method reported previously for the (−)-enantiomer:[5] bp 110–114 °C (0.6 mm); $[\alpha]^{29}_D$ +173° (*c* 0.342, $CHCl_3$).

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.05; H, 7.72.

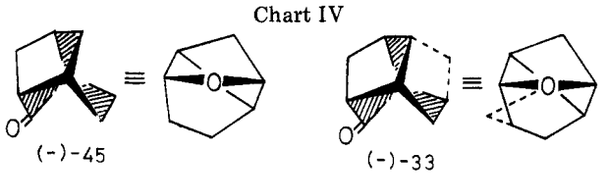
The Baeyer–Villiger Oxidation of (+)-15. After a mixture of (+)-**15**, $[\alpha]^{29}_D$ +173° (11.5 g, 55.4 mmol), *m*-chloroperbenzoic acid (11.7 g, 67.5 mmol), *p*-toluenesulfonic acid (4.24 g), and dry benzene (1.1 L) was stirred for 36 h at room temperature, the mixture was poured into water (1.1 L). Separation of the organic phase was followed by benzene extraction of the aqueous phase. Combined organic solutions were washed with saturated $NaHCO_3$ solution and water

Table I. CD Spectrum of (−)-*ditwist*-Brendan-3-one (33) [b]

$[\theta]$[a]	nm
-9.42×10^3	286.5 (sh)
-1.06×10^4	290 (sh)
-1.18×10^4	295.5
-1.16×10^4	298.5
-9.18×10^3	305.5 (sh)
-7.31×10^3	310 (sh)

[a] Corrected to 100% optical purity. [b] *c* 2.74×10^{-2} in isooctane.

Chart IV



(-)-45 (-)-33

and dried ($MgSO_4$). Evaporation of the solvent gave an oily product, to which was added pentane–ether (1:1 v/v). The mixture was allowed to stand overnight in a refrigerator to deposit crystals which were collected to yield 10.2 g of a mixture of **16** and **17** (**16/17** = 1:1). Fractional recrystallization of the mixture from ether afforded 3.51 g of **17**, whose further recrystallization from the same solvent gave 3.11 g of the lactone **17** (25% yield): mp 113–115 °C; $[\alpha]^{29}_D$ +81.9° (*c* 0.608, $CHCl_3$); IR (KBr) 1732, 1398, 1332, 1200, 1180, 1113, 1075, 1060, 950 cm^{-1}; NMR ($CDCl_3$) δ 1.41–1.95 (m, 7 H), 2.05–2.25 (br s, 1 H), 2.5–3.3 (m, 2 H), 3.93 (s, 4 H), 4.1–4.4 (m, 2 H).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.09; H, 7.24.

Concentration and cooling of the mother liquor yielded 3.87 g of crystals which were recrystallized from ether to give 2.15 g of the isomeric lactone **16** (31% yield): mp 93–96 °C; $[\alpha]^{29}_D$ −63.8° (*c* 0.437, $CHCl_3$); IR (KBr) 1723, 1325, 1280, 1252, 1190, 1130, 1072, 1040, 1000, 950 cm^{-1}; NMR ($CDCl_3$) δ 1.5–2.3 (m, 9 H), 2.4–2.8 (m, 2 H), 3.92 (s, 4 H), 4.71 (d, d, *J* = 11, 5 Hz, 1 H).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.09; H, 7.23.

(−)-Methyl 3-(7,7-Ethylenedioxy-3-oxo-*endo*-2-norbornyl)-propionate (19). A mixture of (−)-**16**, $[\alpha]^{29}_D$ −63.8° (3.36 g, 15.0 mmol), and 2 N NaOH solution (50 mL) was stirred for 48 h at room temperature. The reaction mixture was made acidic with HCl and extracted with ether. The extract was washed with water and dried ($MgSO_4$). After evaporation of the solvent, the residue was dissolved in KOH solution (KOH 1.40 g, water 30 mL). A solution of potassium permanganate (1.90 g) in water (25 mL) was added to the alkaline solution and the mixture was stirred for 1 h at 30–35 °C. After being freed of manganese dioxide, the filtrate was made acidic with dilute sulfuric acid and extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated to give 2.90 g of an oily product, which was dissolved in ether (50 mL). The ether solution was esterified with an ethereal solution of diazomethane. Distillation of the product afforded 2.75 g of **19** (72% yield): bp 143–145 °C (0.5 mm); $[\alpha]^{30}_D$ −1.8° (*c* 1.51, $CHCl_3$); IR (neat film) 1735, 1330, 1205, 1080, 950 cm^{-1}.

Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.04; H, 7.14. Found: C, 60.19; H, 7.22.

(−)-Methyl 3-(7,7-Ethylenedioxy-*endo*-2-norbornyl)propionate (21). A mixture of (−)-**19**, $[\alpha]^{30}_D$ −1.8° (2.66 g, 10.5 mmol), KOH (1.52 g), 80% hydrazine hydrate (1.71 mL), and triethylene glycol (14 mL) was heated for 1.5 h at 120 °C and then for an additional 3 h at 190–200 °C. After cooling to room temperature, the reaction mixture was diluted with water, made acidic with HCl, and extracted with ether. The extract was washed with water and dried ($MgSO_4$). Evaporation of the solvent gave 2.17 g of a crude product, which was dissolved in ether (50 mL) and esterified with an ethereal solution of diazomethane. When the product was chromatographed on silica gel, fractions eluted with chloroform gave **21**, which was distilled to afford 640 mg of **21** (25% yield): bp 150 °C (bath temperature) (5 mm); $[\alpha]^{30}_D$ −3.0° (*c* 2.13, $CHCl_3$); IR (neat film) 1735, 1335, 1200, 1100, 950 cm^{-1}; NMR ($CDCl_3$) δ 0.6–1.3 (m, 2 H), 1.4–2.0 (m, 8 H), 2.1–2.4 (m, 3 H), 3.63 (s, 3 H), 3.89 (s, 4 H).

Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.69; H, 8.42.

(−)-Methyl 3-(7-Oxo-*endo*-2-norbornyl)propionate (22). A mixture of (−)-**21**, $[\alpha]^{30}_D$ −3.0° (560 mg, 2.33 mmol), and 10% sulfuric acid (10 mL) was stirred for 5 days at room temperature. After extraction with chloroform, the extract was washed with water, dried ($MgSO_4$), and condensed to give an oily product, which was dissolved in ether (20 mL). The solution was esterified with an ethereal solution of diazomethane. Evaporation of the solvent and distillation of the residue gave 382 mg of **22** (83% yield): bp 135 °C (bath temperature) (5 mm); $[\alpha]^{30}_D$ −23.9° (*c* 1.30, $CHCl_3$); IR (neat film) 1765, 1735, 1260, 1200, 1175 cm^{-1}.

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.02; H, 8.30.

(+)-Methyl 3-(*endo*-2-Norbornyl)propionate (23). A mixture of (−)-**22**, $[\alpha]^{30}_D$ −23.9° (327 mg, 1.67 mmol), KOH (0.25 g), 80% hydrazine hydrate (0.27 mL), and triethylene glycol (3 mL) was heated for 1.5 h at 120 °C and then for an additional 3 h at 200 °C. After cooling, the reaction mixture was diluted with water, made acidic with HCl, and extracted with ether. The extract was washed with water and dried ($MgSO_4$). After removal of the solvent, the residue was dissolved in ether (20 mL) and esterified with an ethereal solution of diazomethane. Distillation of the product gave 240 mg of **23** (79% yield): bp 96 °C (bath temperature) (5 mm); $[\alpha]^{30}_D$ +8.8° (*c* 1.02, EtOH). IR and NMR spectra of (+)-**23** are identical with those of (−)-**23**.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.19; H, 9.89.

(+)-*endo*-Norbornane-2-carboxylic Acid (25). (+)-*endo*-5-Norbornene-2-carboxylic acid (**24**), $[\alpha]^{20}_D$ +57.2° (EtOH) (6.70 g, 0.0485 mol), prepared by the same method reported previously[2] was dissolved in 200 mL of ethanol and the mixture was shaken at room temperature in a hydrogenation flask with 300 mg of 5% Pd on carbon at 1 atm of hydrogen. After the hydrogen absorption had ceased, the catalyst was filtered off. The filtrate was condensed and the residue was distilled to give 6.51 g of **25** (96% yield): bp 140 °C (20 mm); $[\alpha]^{22}_D$ +12.1° (*c* 0.865, EtOH) [lit.[15] mp 25.5–26.5 °C; $[\alpha]_D$ −30.6° (EtOH)].

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.33; H, 8.70.

(−)-*endo*-2-(Hydroxymethyl)norbornane (26). A solution of (+)-**25**, $[\alpha]^{22}_D$ +12.1° (3.28 g, 0.0234 mol), in dry ether (50 mL) was added to a suspension of $LiAlH_4$ (1.14 g, 0.0300 mol) in dry ether (50 mL) and the mixture was refluxed for 4 h. After cooling with ice, to the chilled reaction mixture was added 5% sulfuric acid. Separation of the organic phase was followed by ether extraction of the aqueous phase. Combined organic solutions were washed with 5% sulfuric acid, saturated $NaHCO_3$ solution, and water and dried ($MgSO_4$). After evaporation of the solvent, the residue was distilled to give 2.53 g of **26** (85% yield): bp 101–102 °C (20 mm); $[\alpha]^{25}_D$ −2.15° (*c* 0.606, EtOH) [lit.[13] $[\alpha]_D$ −4.04° (EtOH)].

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 75.97; H, 11.23.

(+)-(*endo*-2-Norbornyl)methyl *p*-Toluenesulfonate (27). To a chilled solution of (−)-**26**, $[\alpha]^{25}_D$ −2.15° (2.53 g, 20.0 mmol), in pyridine (12 mL) was added *p*-toluenesulfonyl chloride (5.00 g, 26.1 mmol) at 0–5 °C and the mixture was stirred for 6 h at this temperature. After being allowed to stand overnight at room temperature, the reaction mixture was poured onto ice and made acidic with HCl. It was extracted with ether and the extract was washed with saturated $NaHCO_3$ solution and water and dried ($MgSO_4$). Removal of the solvent gave a solid which was recrystallized from pentane to yield 3.25 g of **27** (58% yield): mp 42–45 °C; $[\alpha]^{26}_D$ +2.3° (*c* 0.633, $CHCl_3$); IR (KBr) 1595, 1360, 1190, 970, 952 cm^{-1}.

Anal. Calcd for $C_{15}H_{20}O_3S$: C, 64.26; H, 7.19. Found: C, 64.23; H, 7.20.

(−)-3-(*endo*-2-Norbornyl)propionic Acid (29). Ethyl malonate (8.00 g, 50.0 mmol) was added to a solution of sodium ethoxide prepared from sodium (0.80 g, 34.8 mmol) and 20 mL of absolute ethanol, and the mixture was refluxed for 1 h. To the mixture was added a solution of (+)-**27**, $[\alpha]^{26}_D$ +2.3° (3.00 g, 10.7 mmol), in absolute ethanol (30 mL), and the resulting mixture was refluxed for 14 h. The mixture was poured into ice–water (100 mL) and extracted with ether. The extract was washed with water and dried ($MgSO_4$). Evaporation of the solvent left a residue to which was added methanolic KOH (KOH 1.8 g, MeOH 30 mL, water 10 mL). The mixture was refluxed for 2 h, then cooled to room temperature. The mixture was poured into water and made acidic with HCl. It was extracted with ether and the extract was washed with water and dried ($MgSO_4$). Evaporation of the solvent gave a solid, which was put into a small distilling flask and heated under reduced pressure (20 mm). When the bath temperature raised to 170 °C, carbon dioxide evolved vigorously. After heating for 30 min at this temperature, the decarboxylated product was distilled to give 1.20 g of **29** (65% yield): bp 101–104 °C (0.8 mm); $[\alpha]^{22}_D$ −4.1° (*c* 0.758, EtOH); IR (neat film) 1708 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.01; H, 9.65.

(−)-Methyl 3-(*endo*-2-Norbornyl)propionate (23). To a solution of (−)-**29**, $[\alpha]^{22}_D$ −4.1° (1.02 g, 7.14 mmol), in ether (100 mL) was added an excess of diazomethane in ether at 0–5 °C, and the mixture was stirred for 2 h at this temperature. After addition of a small amount of acetic acid to decompose the remaining diazomethane, the mixture was washed with saturated $NaHCO_3$ solution and water and dried ($MgSO_4$). After evaporation of the solvent, the residue was distilled to give 1.10 g of **23** (86% yield): bp 77.5–79 °C (4 mm); $[\alpha]^{25}_D$ −4.5° (*c* 0.953, EtOH); IR (neat film) 1740, 1430, 1345, 1245, 1195, 1170 cm^{-1} NMR ($CDCl_3$) δ 0.55–0.68 (m, 1 H), 1.0–1.8 (m, 10 H), 2.00–2.35 (m, 4 H), 3.62 (s, 3 H).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.20; H, 9.98.

(±)-*exo*-3-Tetracyclo[5.2.1.0^{2,6}.0^{4,8}]decyl Hydrogen Phthalate (31). To a solution of (±)-*exo-ditwist*-brendan-3-ol [(±)-*exo*-tetracyclo[5.2.1.0^{2,6}.0^{4,8}]decan-3-ol] (**30**) (8.00 g, 53.3 mmol), prepared according to Rothberg's method,[12] in dry pyridine (30 mL) was added phthalic anhydride (7.89 g, 53.3 mmol) at 0–5 °C. The mixture was stirred for 3 h at this temperature and then allowed to stand overnight at room temperature. The reaction mixture was poured into ice-water, made acidic with HCl, and extracted with ether. The extract was washed with dilute HCl and water and dried ($MgSO_4$). After evaporation of the solvent, the residue was triturated with hexane to give a solid, which was recrystallized from benzene–hexane to afford 13.1 g of **31** (82% yield), mp 163.5–164 °C.

Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.46; H, 6.08. Found: C, 72.54; H, 6.07.

Optical Resolution of 31. A mixture of **31** (12.7 g, 42.5 mmol), (+)-2-(1-aminoethyl)naphthalene (7.27 g, 42.5 mmol), and acetone (200 mL) was refluxed for 5 h. Standing overnight at room temperature deposited a solid which was collected to give 15.2 g of a salt, $[\alpha]^{23}_D$ + 7.5° (*c* 0.224, EtOH). Fractional recrystallization of the salt from acetone (seven times) afforded 5.79 g of the levorotatory salt, mp 182–184 °C dec, $[\alpha]^{25}_D$ −30.7° (*c* 0.338, EtOH). After the levorotatory salt was stirred with 10% HCl (120 mL) for 5 h at room temperature, an insoluble solid was collected. The solid was washed with 10% HCl and water and dried ($CaCl_2$) to give 3.62 g of (−)-**31**, $[\alpha]^{21}_D$ −67.2° (*c* 0.460, acetone). Recrystallization of this from benzene–hexane (1:1 v/v) afforded 3.42 g of (−)-**31**, mp 153–154.5 °C, $[\alpha]^{23}_D$ −67.4° (*c* 0.506, acetone).

Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.46; H, 6.08. Found: C, 72.52; H, 6.16.

(−)-*exo-ditwist*-Brendan-3-ol (30). A mixture of (−)-**31** (3.40 g, 11.4 mmol) and 5% KOH solution (50 mL) was stirred for 12 h at room temperature. A deposited solid was collected and washed with water. The solid was recrystallized from pentane to give 1.10 g of (−)-**30** (64% yield): mp 178.5–179.5 °C (in a sealed tube); $[\alpha]^{26}_D$ −171° (*c* 0.393, $CHCl_3$); IR (KBr) 3300, 1075, 1022, 998, 940 cm^{-1}.

Anal. Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 79.70; H, 9.28.

(−)-*exo*-3-Acetoxy-*ditwist*-brendane (32). To a solution of (−)-**30**, $[\alpha]^{26}_D$ −171° (76 mg, 0.508 mmol), in pyridine (7 mL) was added acetic anhydride (180 mg, 1.76 mmol) and the mixture was stirred for 3 h with ice cooling. After being allowed to stand overnight at room temperature, the mixture was poured into ice–water and extracted with pentane. The extract was washed with diluted HCl, saturated $NaHCO_3$ solution, and water, and dried ($MgSO_4$). After evaporation of the solvent, the residue was distilled to give 82 mg of (−)-**32** (85% yield): bp 148–150 °C (bath temperature) (20 mm), $[\alpha]^{25}_D$ −134° (*c* 0.292, $CHCl_3$); IR (neat film) 1735, 1250, 1230, 1058, 1030 cm^{-1}; NMR (CCl_4) δ 0.6–1.6 (m, 6 H), 1.7–2.0 (m, 1 H), 2.88 (s, 3 H), 2.05–2.50 (m, 5 H), 4.72–4.82 (br s, 1 H); NMR (CCl_4; (−)-**32**/Eu(facam)$_3$ = 1:0.22) δ 8.83 (br s, half-band width 4.5 Hz) and 8.96 (br s, half-band width 4.5 Hz) (anisochronous endo proton at C-3).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.91; H, 8.31.

(−)-*ditwist*-Brendan-3-one (33). A solution of (−)-30, $[\alpha]^{26}_D$ −171° (1.00 g, 6.67 mmol), in methylene chloride (10 mL) was added to a suspension of pyridinium chlorochromate[16] (2.15 g, 10.0 mmol) in methylene chloride (13 mL) and then the mixture was stirred for 1.5 h at room temperature. The organic phase was separated by decantation and an inorganic residue was rinsed with methylene chloride. Combined solutions were washed with dilute HCl, saturated $NaHCO_3$ solution, and water, and dried ($MgSO_4$). After evaporation of the solvent, the residue was chromatographed on neutral alumina (Woelm, activity III). Fractions eluted with pentane gave a solid which was sublimed at 85–90 °C (20 mm) to give 502 mg of (−)-**33** (51% yield): mp 180–181.5 °C (in a sealed tube); $[\alpha]^{25}_D$ −250° (*c* 0.245, $CHCl_3$); IR (KBr) 1762 cm^{-1}; UV λ_{max} (isooctane) 296 nm (ε 28.5), 306 (sh) (ε 20.8).

Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.01; H, 8.25.

(−)-*ditwist*-Brendane (3). A mixture of (−)-**33**, $[\alpha]^{25}_D$ −250° (148 mg, 1.00 mmol), KOH (65 mg), 80% hydrazine hydrate (0.12 mL), and triethylene glycol (1.5 mL) was heated for 1 h at 110–120 °C and then for an additional 4 h at 190–200 °C. During this period, a white solid condensed on the inner wall of the condenser. After cooling, the solid was dissolved in pentane and the pentane solution was washed with water and dried ($MgSO_4$). After evaporation of the solvent, the residual solid was chromatographed on neutral alumina (Woelm, activity III). Fractions eluted with pentane gave a solid which was sublimed at 70 °C (20 mm) to yield 44 mg of (−)-**3** (33% yield), mp 141–145 °C (in a sealed tube), $[\alpha]^{25}_D$ −274° (*c* 0.302, $CHCl_3$). IR spectrum of this compound is identical with that of (−)-**3** reported previously.[4]

Anal. Calcd for $C_{10}H_{14}$: C, 89.49; H, 10.51. Found: C, 89.26; H, 10.61.

(−)-*endo*-2-(Hydroxymethyl)bicyclo[2.2.2]oct-5-ene (35). An ethereal solution of (−)-*endo*-5-bicyclo[2.2.2]octene-2-carboxylic acid, $[\alpha]^{25}_D$ −14.5° (EtOH) (17.0 g, 0.112 mol), prepared by the method reported previously[14b] was added to a suspension of $LiAlH_4$ (4.25 g, 0.112 mol) in ether (100 mL) at room temperature and the mixture was refluxed for 4 h. After cooling with ice, dilute sulfuric acid was carefully added to the chilled reaction mixture. The mixture was extracted with ether and the extract was washed with saturated $NaHCO_3$ solution and water and dried ($MgSO_4$). Removal of the solvent and distillation of the product afforded 14.1 g of (−)-**35** (91% yield), bp 91–92 °C (5 mm), $[\alpha]^{21}_D$ −3.3° (*c* 0.510, MeOH).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.35; H, 10.36.

(−)-*endo*-2-(Cyanomethyl)bicyclo[2.2.2]oct-5-ene (37). To a solution of (−)-**35**, $[\alpha]^{21}_D$ −3.3° (13.8 g, 0.100 mol), in pyridine (40 mL) was added *p*-toluenesulfonyl chloride (23.5 g, 0.123 mol) and the mixture was stirred for 6 h with ice cooling. After being allowed to stand overnight, the mixture was poured onto ice, made acidic with HCl, and extracted with ether. The extract was washed with saturated $NaHCO_3$ solution and water, and dried ($MgSO_4$). After evaporation of the solvent, the crude tosylate (**36**), without further purification, was dissolved in dimethylformamide (200 mL). After addition of sodium cyanide (16.0 g, 0.326 mol), the mixture was heated for 12 h at 120–130 °C with stirring. An inorganic solid was filtered off and the filtrate was condensed under reduced pressure. To the residue was added water and the mixture was extracted with ether. The extract was washed with dilute HCl, saturated $NaHCO_3$ solution, and water and dried ($MgSO_4$). After evaporation of the solvent, the residue was distilled to yield 12.7 g of (−)-**37** (86% yield), bp 83–84 °C (2 mm), $[\alpha]^{22}_D$ −6.0° (*c* 0.782, MeOH).

Anal. Calcd for $C_{10}H_{13}N$: C, 81.58; H, 8.90; N, 9.52. Found: C, 81.38; H, 9.03; N, 9.36.

(−)-*endo*-2-(Carboxymethyl)bicyclo[2.2.2]oct-5-ene (38). A mixture of (−)-**37**, $[\alpha]^{22}_D$ −6.0° (12.0 g, 0.0816 mol), KOH (14.5 g), and ethylene glycol (140 mL) was heated for 8 h at 150–160 °C with stirring and then poured into ice–water. The mixture was washed with ether to remove neutral substances and made acidic with HCl. The acidic mixture was extracted with ether and the extract was washed with water and dried ($MgSO_4$). Removal of the solvent and distillation of the product gave 12.5 g of (−)-**38** (92% yield), bp 160–163 °C (5 mm), $[\alpha]^{20}_D$ −5.1° (*c* 0.400, MeOH).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.27; H, 8.50.

(−)-*endo*-2-(2-Hydroxyethyl)bicyclo[2.2.2]oct-5-ene (39). Reduction of (−)-**38**, $[\alpha]^{20}_D$ −5.1° (12.3 g, 0.0741 mol), with $LiAlH_4$ (2.90 g, 0.0771 mol) in ether was carried out by routine procedure to give 10.4 g of (−)-**39** (93% yield), bp 105–109 °C (5 mm), $[\alpha]^{23}_D$ −0.97° (*c* 0.876, MeOH).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.86; H, 10.68.

(−)-*endo*-2-(Formylmethyl)bicyclo[2.2.2]oct-5-ene (40). To a suspension of pyridinium chlorochromate[16] (33.7 g, 0.157 mol) in methylene chloride (160 mL) was added a solution of (−)-**39**, $[\alpha]^{23}_D$ −0.97° (10.0 g, 0.0658 mol), in methylene chloride (20 mL) and the mixture was stirred for 1.5 h at room temperature. Usual working up gave a product which was distilled to afford 5.30 g of (−)-**40** (54% yield): bp 100–101 °C (20 mm); $[\alpha]^{23}_D$ −4.7° (*c* 0.815, MeOH); IR (neat film) 2950, 2700, 1720, 720 cm^{-1}.

Anal. Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 80.14; H, 9.28.

(−)-Twistan-2-ol (42). A solution of (−)-**40**, $[\alpha]^{23}_D$ −4.7° (2.80 g, 0.0187 mol), in benzene (300 mL) was irradiated for 6 h with a mercury lamp (Toshiba, SHL-100 UV). During this period, the reaction mixture was cooled with running water (20 °C). After evaporation of benzene, the residue was chromatographed on neutral alumina (Woelm, activity III). Fractions eluted with pentane gave a solid which was sublimed at 65 °C (30 mm) to afford 1.49 g of the oxetane (**41**; 53% yield), $[\alpha]^{23}_D$ −74.4° (*c* 0.650, MeOH). To a solution of (−)-**41** (1.20 g, 8.00 mmol) in *N*-methylmorpholine (80 mL) was added $LiAlH_4$ (2.40 g, 0.00632 mol) and the mixture was refluxed for 80 h with stirring. After cooling with ice, the reaction mixture was carefully poured into ice–water, made acidic with HCl, and extracted with ether. The extract was washed with dilute HCl, saturated $NaHCO_3$ solution, and water and dried ($MgSO_4$). Evaporation of the solvent gave a solid (1.10 g), which was recrystallized twice from pentane to yield 330 mg of (−)-**42** (27% yield): mp 187–190

°C (in a sealed tube); $[\alpha]^{20}_D$ −118° (c 0.340, MeOH); IR (KBr) 3300, 1080, 1010 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.74; H, 10.65.

(−)-2-Acetoxytwistane (43). To a solution of (−)-**42**, $[\alpha]^{20}_D$ −118° (170 mg, 1.12 mmol), in pyridine (2 mL) was added acetic anhydride (0.3 mL) and the mixture was stirred for 6 h with ice cooling. After being allowed to stand overnight at room temperature, the mixture was poured into ice–water and extracted with ether. The extract was washed with dilute HCl, saturated $NaHCO_3$ solution, and water and dried ($MgSO_4$). After evaporation of the solvent, the residue was distilled to give 150 mg of (−)-**43** (69% yield): bp 130–135 °C (bath temperature) (20 mm); $[\alpha]^{25}_D$ −98.9° (c 0.527, MeOH); IR (neat film) 1730, 1365, 1250, 1240, 1230, 1055 cm^{-1}; NMR (CCl_4) δ 1.2–2.2 (m, 14 H), 2.93 (s, 3 H), 4.65 (d, J = 6 Hz 1 H); NMR (CCl_4; (−)-**43**/Eu(facam)$_3$ = 1:0.189) δ 4.43 and 4.53 ($OCOCH_3$).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.01; H, 9.40.

(−)-Twistan-2-one (44). To a suspension of pyridinium chlorochromate[16] (310 mg, 1.44 mmol) in methylene chloride (6 mL) was added (−)-**42**, $[\alpha]^{20}_D$ −118° (90 mg, 0.592 mmol), and the mixture was stirred for 2.5 h at room temperature. An organic phase was separated and the residue was rinsed with ether. Combined organic solutions were washed with dilute HCl, saturated $NaHCO_3$ solution, and water and dried ($MgSO_4$). After evaporation of the solvent, the residue was chromatographed on neutral alumina (Woelm, activity III). Fractions eluted with pentane gave a white solid which was sublimed at 80 °C (30 mm) to give 50 mg of (−)-**44** (56% yield), mp 184–188 °C (in a sealed tube), $[\alpha]^{22}_D$ −151° (c 0.405, EtOH). IR spectrum and VPC (stationary phase PEG-20M 10% 2 m, column temperature 180 °C) behaviors were identical with those of (+)-twistan-2-one.[3]

Anal. Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 79.70; H, 9.35.

Registry No.—**1**, 42070-69-9; **2**, 37165-27-8; **3**, 64727-80-6; **5**, 62928-75-0; **13**, 62928-79-4; **15**, 67844-29-5; **16**, 67815-16-1; **17**, 67815-17-2; **18**, 67815-18-3; **19**, 67815-19-4; **20**, 67815-20-7; **21**, 67815-21-8; **22**, 67815-22-9; (+)-**23**, 67815-23-0; (−)-**23**, 67844-30-8; **24**, 58001-99-3; **25**, 2566-59-8; **26**, 67844-31-9; **27**, 67844-32-0; **28**, 67844-33-1; **29**, 67844-34-2; (−)-**30**, 67844-35-3; (+−)-**30**, 67844-36-4; (−)-**31**, 67815-24-1; (+−)-**31**, 67844-37-5; **32**, 67815-25-2; **33**, 67844-38-6; **34**, 20507-57-7; **35**, 54515-89-8; **36**, 67815-26-3; **37**, 67844-39-7; **38**, 54515-90-1; **39**, 67815-27-4; **40**, 67815-28-5; **41**, 67815-29-6; **42**, 67844-40-0; **43**, 67815-30-9; **44**, 37165-26-7; (−)-*exo*-3-tetracyclo[5.2.1.0^{2,6}.0^{4,8}]decyl hydrogen phthalate, (+)-2-(1-aminoethyl)naphthalene salt, 67844-41-1; ethyl malonate, 105-53-3; phthalic anhydride, 85-44-9; (+)-2-(1-aminoethyl)naphthalene, 3886-70-2; sodium cyanide, 143-33-9.

References and Note

(1) M. Nakazaki, K. Naemura, and H. Kadowaki, *J. Org. Chem.*, **41**, 3725 (1976).
(2) K. Naemura and M. Nakazaki, *Bull. Chem. Soc. Jpn.*, **46**, 888 (1973).
(3) K. Adachi, K. Naemura, and M. Nakazaki, *Tetrahedron Lett.*, 5467 (1968). For other syntheses of optically active twistane see M. Tichy and J. Sicher, *Tetrahedron Lett.*, 4609 (1969); M. Tichy, *ibid.*, 2001 (1972).
(4) M. Nakazaki, K. Naemura, and N. Arashiba, *J. Org. Chem.*, in press.
(5) M. Nakazaki and K. Naemura, *J. Org. Chem.*, **42**, 2985 (1977).
(6) M. Nakazaki, K. Naemura, and N. Arashiba, *J. Chem. Soc., Chem. Commun.*, 678 (1976).
(7) R. S. Cahn, C. K. Ingold, and V. Prelog, *Angew. Chem., Int. Ed. Engl.*, **5**, 385 (1966).
(8) G. Helmchen and G. Staiger, *Angew. Chem., Int. Ed. Engl.*, **16**, 117 (1977).
(9) All structural formulas in this paper are presented in their absolute configurations.
(10) C. H. Hassall, *Org. React.*, **9**, 73 (1957).
(11) M. Nakazaki, K. Naemura, and H. Kadowaki, *J. Org. Chem.*, submitted for publication.
(12) I. Rothberg, J. Fraser, R. Garnick, J. C. King, S. Kirsch, and H. Skidanow, *J. Org. Chem.*, **39**, 870 (1974).
(13) J. A. Berson, J. S. Walia, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff, and D. Willner, *J. Am. Chem. Soc.*, **83**, 3986 (1961).
(14) (a) R. R. Sauers and K. W. Kelly, *J. Org. Chem.*, **35**, 498 (1970); (b) M. Nakazaki, K. Naemura, and S. Harita, *Bull. Chem. Soc. Jpn.*, **48**, 1907 (1975).
(15) J. A. Berson and D. A. Ben-Efrain, *J. Am. Chem. Soc.*, **81**, 4083 (1959).
(16) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).

A New, Convenient, and Stereospecific Method for the Conversion of Secondary Amines to Primary Amines and Olefins. Thermal Decomposition of Magnesium, Zinc, and Aluminum Amides

E. C. Ashby* and G. Fred Willard

School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332

Received May 16, 1978

Magnesium, zinc, and aluminum amides of the general formula $RMNR'_2$ thermally decompose at 150–250 °C to give hydrocarbon (RH), an olefin (from R'), and a residue of empirical formula $(MNR')_x$, which can be hydrolyzed to a primary amine. Kinetic and stereochemical studies indicate that a cyclic, unimolecular six-center transition state is involved. This reaction represents the conversion of a secondary amine to a primary amine and an olefin in a syn stereochemical manner and compares favorably as an alternative to the Hoffman elimination and Cope elimination reactions.

Several methods are known for the preparation of olefins from amines.[1] These methods include the pyrolysis of quaternary ammonium hydroxides[2] (Hoffman elimination reaction) and the pyrolysis of amine oxides[3] (Cope elimination reaction). The Hoffman elimination reaction involves the thermal decomposition of a quaternary ammonium hydroxide to give an olefin, a tertiary amine, and water. The reaction usually occurs by an E_2 mechanism in an anti stereochemical manner. The yield is quite dependent upon the particular compound being decomposed with an average yield in the range 50–75%. The disadvantages of the Hoffman elimination reaction include (1) the necessity of having a tertiary amine in order to convert it to the quaternary ammonium hydroxide, (2) separation of the olefin product from the tertiary amine and water byproducts, and (3) a competing side reaction to produce an alcohol and tertiary amine due to a displacement reaction at the carbon atom.

The Cope elimination reaction involves the thermal decomposition of tertiary amine oxides to yield an olefin and a derivative of hydroxylamine in a syn stereochemical manner. The amine oxides are prepared by treating the tertiary amine with 35% aqueous hydrogen peroxide at room temperature or with stronger reagents, e.g., 40% peroxyacetic acid or monoperoxyphthalic acid. It is necessary to destroy excess peroxide

0022-3263/78/1943-4750$01.00/0