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Transformations of unsaturated acyclic sugars into enantiomerically pure norbornene derivatives*

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ABSTRACT

The C_7 acyclic unsaturated-sugar ester **1**, derived from L-arabinose, and its enantiomer serve as convenient dieneophiles for chirality transfer for synthesis of optically pure carbocyclic derivatives through cycloaddition reactions. Reaction of **1** with cyclopentadiene may be controlled to give preparative access to the 5,6-disubstituted norbornene adducts **4a**, **5a**, and **7a**, according to the conditions used. The distribution of the four possible isomeric products from this cycloaddition was quantitated, and the effect of substitutional variation on the precursor dienophile **1** was also examined. Adducts **4a** and **5a** were transformed into such substituted carbocycles of known absolute configuration as the methyl esters (**11** and **12**) of norbornene (bicyclo[2.2.1]hept-2-ene)-6-carboxylic acid and nortricyclane (tricyclo[2.2.1.$0^{2,6}$]heptane)-3-carboxylic acid in optically pure form, specifically through decarbonylation reactions using $RhCl(PPh_3)_3$ (Wilkinson's complex) and $[Rh(dppp)_2]Cl$ [dppp = $Ph_2P(CH_2)_3PPh_2$]. The optical purity of **12** was established by the use of a chiral lanthanide shift-reagent.

INTRODUCTION

Such acyclic unsaturated sugar derivatives as the L-arabinose-derived *trans*-C_7 ester **1** have been shown to be useful chiral dienophiles in the Diels–Alder cycloaddition reaction, affording chirally substituted carbocycles[1]. The steric course of cycloaddition of **1** to cyclopentadiene may be controlled. At elevated temperature, the crystalline *re-exo* carboxylate adduct **4a** was isolated in 40% yield, whereas at low temperature in the presence of $AlCl_3$, the crystalline *si-endo* carboxylate adduct **7a** was obtained in 36% yield[1], along with a smaller proportion of the crystalline *re-endo* adduct **5a**. Adduct **7a** has the same absolute and relative stereochemistry at five chiral centers as at corresponding positions of prostaglandin $PGF_{1\alpha}$ and its 9,11-dideoxy-9,11-bis(hydroxymethyl) analog.

Ester **1** is a very useful synthetic intermediate, as it is exclusively obtained as the *E*-alkene by a Wittig reaction from an aldehydo sugar precursor, and in good overall yield from L-arabinose, without any chromatographic separation. Another particular advantage of **1** is that arabinose is readily available as both the D and L enantiomers, thus providing versatility in access to stereochemical variants of target molecules. We were therefore interested in further investigating the synthetic potential of arabinose-derived dienophiles in the Diels–Alder reactions with cyclopentadiene and other dienes.

* Dedicated to Professor Grant Buchanan on the occasion of his 65th birthday.

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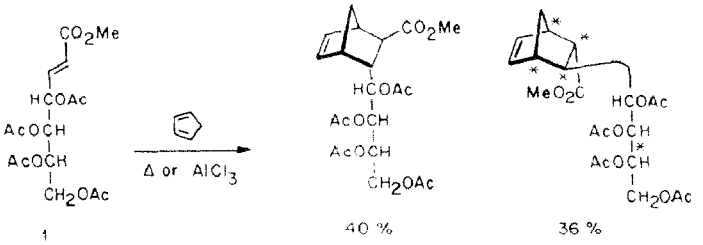
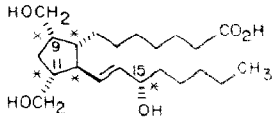


1

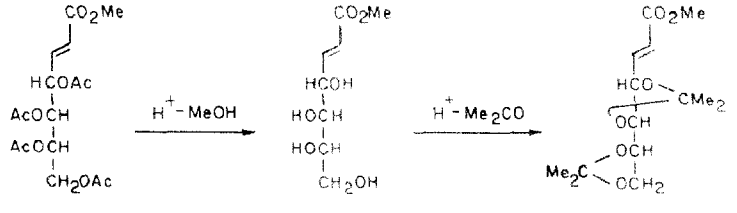


9,11-Dideoxy-9,11-bis(hydroxymethyl)PGF$_{1\alpha}$

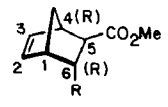
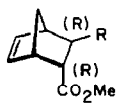
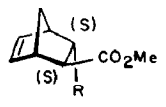
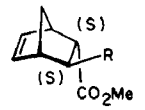
In this paper we report a detailed analysis of the ratios of the four possible stereoisomeric adducts formed from **1** and cyclopentadiene under both thermal and Lewis acid-catalyzed conditions, and also assess the effect of varying the sugar-chain substituents on the dienophile. The potential of the reaction for preparation of any desired stereoisomer of a *trans*-5,6-disubstituted norbornene is demonstrated. The use of organometallic catalysts for decarbonylation of aldehyde groups on a chirally substituted norbornene framework is investigated in detail as a method for obtaining optically pure, defunctionalized products.

RESULTS AND DISCUSSION

Synthesis of dienophiles **2** *and* **3** *from* **1**, *and the Diels–Alder reaction of* **1**, **2**, *and* **3** *with cyclopentadiene.* — For comparative studies in the cycloaddition reaction, analogs of methyl 4,5,6,7-tetra-*O*-acetyl-2,3-dideoxy-L-*arabino*-hept-2-enonate[1] (**1**) having free hydroxyl groups (**2**) and *O*-isopropylidene protecting groups (**3**) were desired. Attempts to deacetylate **1** under basic conditions were unsuccessful; the reaction presumably gave products of conjugate addition. However, acidic transesterification conditions[2] afforded the desired, deacetylated *E*-unsaturated ester **2** as a crystalline solid in 89% yield. Conventional acetonation of **2** gave exclusively the *E*-alkene **3**. Although **3** had previously been prepared by a Wittig reaction from 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose, chromatographic separation of the *E* and *Z* alkenes was necessary[3a].

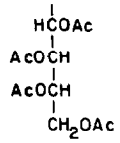
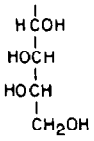
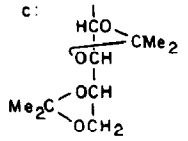


1 2 3

4 5 6 7

δ, CO_2CH_3	a: 3.67	3.61	3.68	3.62
	c: 3.67	3.60	3.68	3.61
δ, $\underline{C}O_2CH_3$	a: 175.0	173.8	175.9	174.4

R = a:  b:  c: 

With the pure *E*-alkenic dienophiles in hand, differing in substitution mode (but not stereochemistry) at C-4, 5, 6, and 7, we analyzed the mixture of their reaction products with cyclopentadiene to determine the ratio of the four possible norbornene adducts formed under both thermal and $AlCl_3$-catalyzed conditions. (The previous study[1] had established preparative conditions, starting from **1**, to afford compound **4a** as the major product under thermal conditions and compound **7a** as the major product under $AlCl_3$-catalyzed conditions). The reactions were conducted in boiling toluene for the acetylated and isopropylidenated dienophiles. For the free-sugar dienophile **2**, DMF was used for the reaction under thermal conditions; the $AlCl_3$-catalyzed reaction in this case was unsuccessful because of limited solubility. The ratio of adducts was determined by the integrated ratio in the ^{1}H-n.m.r. spectra of the Me signals of the CO_2Me groups. For the acetates, the CO signals of the CO_2Me groups in the ^{13}C-n.m.r. spectra were also used to support the quantitations.

Results are summarized in Table I. The acetylated and isopropylidenated dienophiles gave similar results. Furthermore, it is clear that $AlCl_3$ acts to reverse not only the *endo:exo* selectivity, expressed by **5**+**7**:**4**+**6**, but also the diastereofacial selectivity, expressed by **4**+**5**:**6**+**7**. The somewhat lower selectivity observed with the free-hydroxy dienophile **2** may suggest some influence of substituents on the sugar residue, but the difference between the results with the acetylated and isopropylidenated derivatives was not large. The yields from the thermal reaction of **2** and the $AlCl_3$-catalyzed reaction of **3** were low, probably because of the instability of these dienophiles under the reaction conditions. Therefore the acetylated dienophile **1** was selected as the compound of greatest partical value for the remaining studies, and the accessible[1], crystalline adducts **4a** and **5a** were used for this purpose.

Transformation of norbornene adducts **4a** *and* **5a** *into simpler carbocycles.* — With the two norbornene adducts of known absolute configuration in hand, conversions were effected to afford simpler, functionalized carbocycles of known absolute configuration, through removal of the sugar chain by periodate oxidation, and studies were made on decarbonylation of the resultant aldehydes. The scope of the decarbonylation reaction was to be assessed to extend the versatility of the synthetic method[3], and also to clarify

TABLE 1

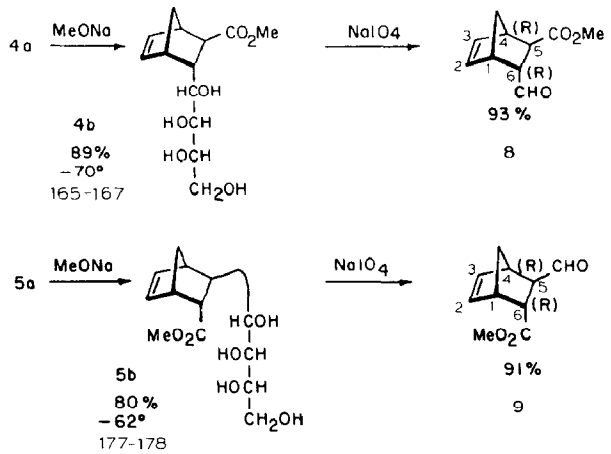
Products of cycloaddition of cyclopentadiene to dienophiles **1**, **2**, and **3**

Entry	*Cond.*	*Dienophile*	*Distribution of isomers (%)*[a]				*Yield (%)*	*Diastereofacial selectivity*	Endo:exo *selectivity*
			4	**5**	**6**	7		**4+5:6+7**	**5+7:4+6**
1[b]	Thermal	**1**	41(46)	18(14)	27(28)	14(13)	Q. [19]	59:41	32:68
2	Thermal	**1**	40(43)	18(16)	28(25)	14(16)	Q. [4]	58:42	32:68
3	Thermal	**3**	42	22	19	17	96 [4]	64:36	39:61
4	Thermal	**2**	33	25	23	19	60[c] [15]	58:42	44:56
5	$AlCl_3$	**1**	9(8)	25(26)	8(8)	58(58)	Q.	34:66	83:17
6	$AlCl_3$	**3**	6	30	9	55	70[c] [14]	36:64	85:15

[a] As determined by ^{13}C-n.m.r. [ ]: Unreacted dienophile. [b] Reactions conducted at reflux temperature; entries 2–4 were conducted in a closed vessel. [c] Yield after acetylation. [d] Including ~10% of unidentified products.

an ambiguity in the result of such a decarbonylation reaction reported in an earlier communication from our laboratory[1b].

Deacetylation of **4a** and **5a** and subsequent periodate oxidation gave the aldehydes **8** and **9** (the racemate of **9** has been prepared[4], but not well characterized), respectively, in >90% yields. Details of the n.m.r. spectra of these aldehydes are recorded in Table II. The ^{13}C-n.m.r. spectra of these products showed doublets of doublets for C-6, even in the off-resonance mode, because of two-bond C–H coupling between the carbon atom bearing an aldehyde group and the aldehyde proton. This coupling was determined from gated decoupling to be 24 and 23 Hz for **8** and **9**, respectively. Although these $^2J_{C\text{-}H}$ couplings are thus of no stereochemical significance, the large value for the carbon atom bearing the aldehyde group may constitute useful diagnostic information (see, for example, ref. 5).



As shown in Fig. 1, starting from D- or L-arabinose and depending on the reaction conditions, any one of the four possible *trans*-disubstituted norbornene derivatives is accessible in optically pure form. These products may be considered as synthetic equivalents of chiral tetrasubstituted cyclopentanes through subsequent application of such well-defined reaction sequences as OsO_4–periodate oxidation[3].

Decarbonylation studies on aldehydes **8** *and* **9**. — Decarbonylation of the (5*R*,6*R*)-aldehydes **8** (*endo*) and **9** (*exo*) was performed with Wilkinson's complex and also with a cationic rhodium complex having bidentate phosphine ligands. Despite the potential utility of such decarbonylation reactions in synthetic organic chemistry (for a review, see ref. 6), the Wilkinson complex has not received the extent of use that might have been expected. Major drawbacks are that, at relatively low temperatures, this complex works only stoichiometrically; high temperatures, usually >200°, are required for the complex to work catalytically. Inspection of the literature suggested that [Rh(dppp)$_2$]Cl might be more promising in this respect[7]. Reactions were conducted with stoichiometric amounts of Wilkinson's complex in boiling benzene, and with 5 and 7 mol% of [Rh(dppp)$_2$]Cl with respect to the *endo* (**8**) and *exo* (**9**) aldehyde in boiling toluene. Products corre-

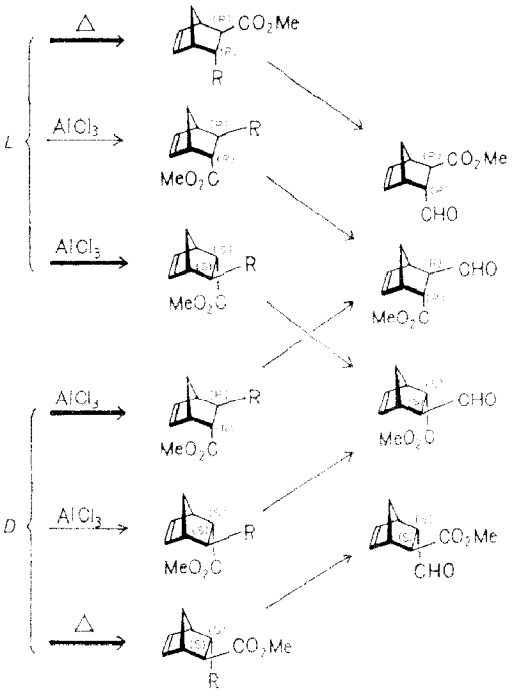


Fig. 1. Synthetic routes to the four 5,6-*trans*-disubstituted norbornenes. [Bold arrows denote the most practical route from the respective D or L dienophile; R = sugar chain from C-2–C-5 of the precursor D- or L-arabinose.]

sponding to simple decarbonylation (**10** and **11**), to decarbonylation with nortricyclane ring-formation (**12**), and decarbonylation with conjugative bond-migration (**13**) were encountered.

The distributions of decarbonylated products are summarized in Table III, and chromatographic characteristics are listed in Table IV. All four products were identified by g.l.c. and by n.m.r.- and mass-spectroscopic comparison with authentic racemic compounds.* There was a clear contrast between reaction with the Wilkinson complex and that with the cationic complex. The Wilkinson complex readily decarbonylates the *endo* aldehyde **8** with concomitant sigma-bond formation to give the nortricyclane **12** in good yield, but it reacts rather sluggishly with the *exo* aldehyde **9** and leads to a mixture of isomeric products in which the decarbonylated norbornene **11** preponderates (a similar difference of reactivity between *endo*- and *exo*-norbornene aldehydes has been reported[9]). In contrast, reaction of [Rh(dppp)$_2$]Cl with the *endo* aldehyde **8** gave the nortricyclane **12** plus a substantial proportion of by-products, including compounds more polar than the starting aldehyde, whereas reaction with the *exo* aldehyde **9** gave **11**, the product of simple decarbonylation, almost exclusively. Furthermore, with this

* A mixture of racemic **10** and **11**, and the racemic free acid of **12**, were prepared according to ref. 8a (for **12**, see also ref. 10c). Racemic **13** was prepared according to ref. 8b. For ^{1}H-n.m.r. data of **13**, see also ref. 8c.

TABLE II

N.m.r. data for compounds **8** and **9**

^{1}H n.m.r.

Compd.		*H-1*	*H-2*	*H-3*	*H-4*	*H-5*endo	*H-6*exo	*H-7*anti	*H-7*syn	*CHO*	CO_2CH_3			
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{1,6}$	$J_{1,7a} \sim J_{4,7a}$ J_{7gem}	$J_{1,7s} \approx J_{4,7s}$ $J_{5,7s}$	J		$J_{1,3}$	$J_{2,4}$	$J_{2,7a} \sim J_{3,7a}$
8	δ	~3.35	6.09	6.27	3.19	2.72	~3.35	1.68 ~1.5	1.52 ~1.5	9.55	3.71			
	J	~2	~5.5	~3	0.6	4.3	—	8.8	1.7	0.6		0.5	<1	~0.5
9	δ	3.29	6.14	6.31	3.21	2.81	3.44	1.34 ~1.5	1.45 ~1.8	9.85	3.65			
	J	2.8	5.5	3.0	~0.8	4.5	3.6	9.0	~1.8	0.8		<1	<1	~0.5

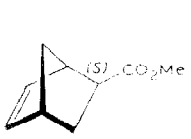
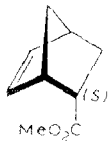
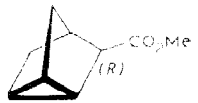
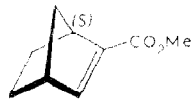
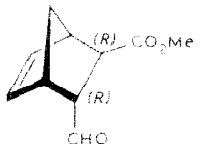
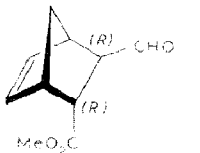
^{13}C n.m.r. (δ)

	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-7*	CO_2CH_3	*CHO*	CO_2CH_3
8	44.2[a]	134.4	137.6	47.5[a]	44.7	56.8	47.3	174.5	201.1	52.0
9	44.5[a]	135.9	137.0	44.5[a]	56.0	45.4[a]	46.7	173.5	200.8	51.8

[a] May be interchanged.

TABLE III

Distribution of decarbonylated isomers[a]

Entry	*Reacting aldehyde*	*Conditions*	 **10**	 **11**	 **12**	 **13**	*Others*	*Yield*
1	 **8**	$RhCl(PPh_3)_3$ 3 h	0.2[b]	0.4[b]	97		2.4	77
2		5 mol % $[Rh(dppp)_2]Cl$ 43 h	5		67	28		60[c]
3	 **9**	$RhCl(PPh_3)_3$ 71 h	2[b]	79	8	7[b]	4	51
4		7 mol % $[Rh(dppp)_2]Cl$ 70 h		>99	<1			62

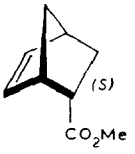
[a] Determined by g.l.c., except for entry 3 which was determined by the integrated ratio of CO_2CH_3 signals in the ^1H-n.m.r. spectrum. [b] Absolute configuration not determined. [c] By g.l.c.

TABLE IV

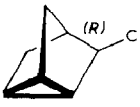
Chromatographic characteristics of compounds **8**, **9**, **10**, **11**, **12**, and **13**

Characteristics	**8**	**9**	**10**	**11**	**12**	**13**
G.l.c.: t_R (min)[a] 120°;	6.63	6.13:90°;	3.9	4.6	5.5	6.9
T.l.c.: R_F, 5:1 hexane–EtOAc	0.34	0.38	0.66	0.57	(0.59)[b]	0.59
Detection[c] u.v. lamp	—	—	—	—	—	+
I_2	+	+	+	+	—	—
H_2SO_4	+	+	—	—	—	—

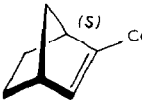
[a] See experimental section for conditions. [b] Estimated, as **12** and **13** had exactly the same mobility on t.l.c. [c] For 10–50 μg of samples.



11 : −137° Entry 4 $[Rh(dppp)_2]Cl$ (lit −141°)



12 : +36.7° Entry 1 $RhCl(PPh_3)_3$: +36° Entry 2 $[Rh(dppp)_2]Cl$

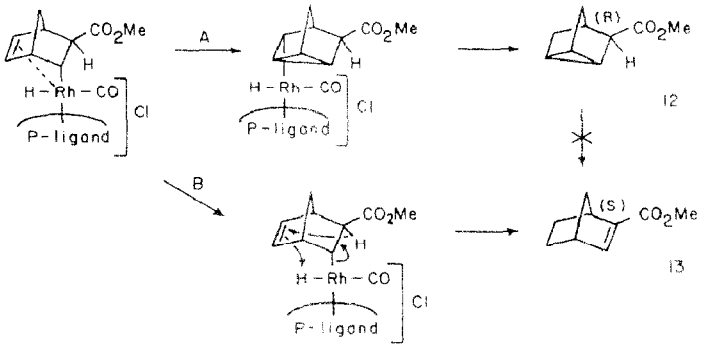


13 : +185° Entry 2 $[Rh(dppp)_2]Cl$

reagent, the difference of reactivity between the *endo* and *exo* aldehydes was not so large as with the Wilkinson complex.

The products obtained here were optically pure and had the correct expected signs of rotation, in accord with literature assignments of configuration (for **11**, see refs. 10a and 10b, for **12** see refs. 10b and 10c). This provides further chemical affirmation for the absolute stereochemistry of the original norbornene adducts, which had independently been determined by X-ray crystallography[1c]. This result establishes also that the decarbonylation reaction proceeds without epimerization at the asymmetric carbon atom adjacent to the reaction site. [It should be noted that prolonged reaction, as shown in the result of entry 3 in Table III, may result in epimerization to some extent (at least 2%)].

Compound **13** was obtained for the first time in optically active form. Although we had no definite proof of its absolute configuration, the 1*S* configuration (from **8**) may be assigned based on a mechanism involving a 1,3-hydrogen shift (path **B**, homoallylic rearrangement; path A would give the nortricyclane[9]). To determine whether **13** was



formed through **12**, compound **12** was heated in the presence of [Rh(dppp)$_2$]Cl, but no trace of **13** was detected, even after 45 h.

For the norbornene derivatives **10** and **11**, epimerization during their formation would have led to the formation of *endo* and *exo* isomers, which are diastereomeric and would be differentiated by conventional methods. In contrast, for the nortricyclane derivative **12**, epimerization during its formation would result in the formation of enantiomers. To rule out the latter possibility, the optical purity of **12** was confirmed by

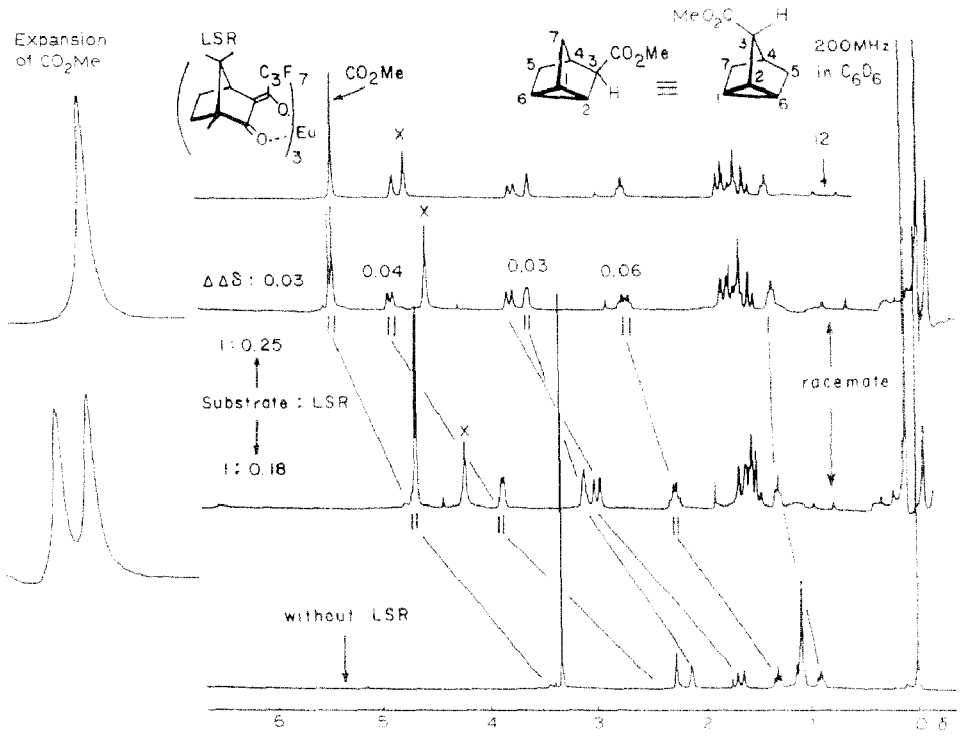


Fig. 2. Use of a chiral shift-reagent to demonstrate the optical purity of compound **12** as obtained by decarbonylation of compound **8**. Top trace is that of **12** prepared from **8**; lower traces are from a sample of racemic **12**.

TABLE V

^{1}H-N.m.r. data of **12** with and without Eu(hfc)$_3$ in C_6D_6

Molar ratio of Eu(hfc)$_3$	*Substrate*	*Chemical shifts*									
		H-1	*H-2*	*H-3*	*H-4*	*H-5a*	*H-5b*	*H-6*	*H-7*syn	*H-7*anti	CO_2CH_3
0	(±)-**12** =(+)-**12**	1.09	1.31	2.26	2.12	~1.1	~1.1	0.91	1.66	1.11	3.34
0.18	(±)-**12**	~1.45	2.18	3.81	3.03	~1.45	1.38	1.19	2.96	1.54	4.62
			2.15	3.78							4.60
0.25	(±)-**12**	~1.7	2.70	4.80	3.627	~1.7	1.57	1.39	3.74	1.82	5.45
			2.76	4.84	3.652						5.48
0.25	(±)-**12**	~1.65	2.73	4.87	3.60	~1.65	1.55	1.37	3.75	1.80	5.44

measuring its ^{1}H-n.m.r. spectrum in the presence of a chiral lanthanide-shift reagent[11], tris(3-heptafluorobutanoyl-*d*-camphorato)europium(III), Eu(hfc)$_3$. In this study, the use of C_6D_6 as solvent gave much better results than those obtained with $CDCl_3$.

With a reference sample of racemic **12** and with a molar ratio of shift reagent to substrate of 0.25, four sets of signals appeared that showed clear distinction between the enantiomers (Fig. 2, Table V), and the singlet of CO_2Me was selected as a good standard to establish the optical purity. Under the same conditions, the spectrum of compound **12** as obtained by decarbonylation showed a single peak for the CO_2Me group, and the product was thus considered to be optically pure by these criteria.

In summary, this work shows that chiral dienophiles derived from sugar precursors constitute useful and versatile synthetic intermediates for the preparation of such optically pure, chirally substituted carbocycles as the norbornene and nortricyclane derivatives demonstrated here, through Diels–Alder cycloaddition with cyclopentadiene. A following paper[5] presents further transformations of the norbornene derivatives through cleavage of the double bond to generate chiral, tetrasubstituted cyclopentane derivatives that can further be transformed through selective defunctionalization.

EXPERIMENTAL

General methods. — Melting points were determined with a Thomas–Hoover capillary melting-point apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 polarimeter using a 1-dm cell (volume, ~1 mL). T.l.c. was performed on precoated glass plates (0.25 mm) coated with Silica Gel 60 F-254 (E. Merck); components were detected by a u.v. lamp (short wave), by I_2 vapor, and by 10% H_2SO_4 with subsequent heating. Silica Gel 60, 230–400 mesh (E. Merck) was used for column separations. Gas chromatographic (g.l.c.) analyses were performed with a Hewlett–Packard 5720A gas chromatograph equipped with a flame-ionization detector, using He as carrier gas (~30 mL/min). Retention times (t_R) were recorded using a 6 ft. × 1/8 in. glass column packed with 3% OV-17 on GasChrom Q. G.l.c.–m.s. was performed at the Campus Chemical Instrumental Center (The Ohio State University) on a Finnigan 4021 g.l.c.–m.s. system using the same column as that used for analytical g.l.c. Preparative g.l.c. was performed on a Varian Model 3700 instrument using a 6 ft. × 1/4 in. stainless-steel column packed with 10% OV-17, with He as carrier gas (~30 mL/min), and detection with a thermal-conductivity detector. I.r. spectra were recorded with a Perkin–Elmer 283B spectrophotometer. ^{1}H-N.m.r. spectra were recorded, unless otherwise noted, at 200 MHz with a Bruker WP-200 spectrometer in $CDCl_3$ solutions. ^{13}C-N.m.r. spectra were recorded at 50.3 MHz with a Bruker WP-200 spectrometer. N.m.r. spectra were recorded by P. Bhaté, A. Thomas, and Dr. O. Mols. Chemical shifts refer to internal Me_4Si ($\delta = 0.0$). Mass spectra were recorded by C. R. Weisenberger with a Kratos MS-30 double-focusing spectrometer at 70 eV with a direct-inlet probe. Elemental analyses were performed by Atlantic Microlab, Inc. (Atlanta, GA).

Methyl (E)-*2,3-dideoxy*-L-arabino-*hept-2-enonate* (**2**) *and methyl* (E)-*2,3-dide-*

oxy-4,5:6,7-isopropylidene-L-arabino-*hept-2-enonate* (**3**). — To a suspension of compound[1a] **1** (4.24 g, 11.3 mmol) in dry MeOH (120 mL) was added AcCl (1 mL) dropwise with stirring under ice-bath cooling. The mixture was stirred for 10 min at this temperature and then heated at 50–55°. Soon it became a homogeneous solution, and after 4 h, t.l.c. showed a single spot of **2** (R_F 0.39, 5:1 $CHCl_3$–MeOH). The solution was evaporated to one-half of the original volume and refrigerated for a few h. Crystals of **2** which formed were filtered and washed with cold MeOH, and then with ether; yield, 1.88 g (80%). The filtrate and MeOH washings were combined, evaporated to dryness, toluene was twice evaporated from the residue, and the crystalline residue was recrystallized from MeOH, giving an additional crop of **2**; 210 mg, total yield 89%, m.p. 168–169°, $[\alpha]_D^{26}$ −17° (*c* 1, MeOH); i.r. (KBr) *v* 3300 (br), 1720 (C–O), 1665 (C=C), 1440, 1165, 1085, 1030, 920 cm^{-1}; ^{1}H-n.m.r. (C_5D_5N + D_2O ~4:1): δ 7.48 (dd, 1 H, $J_{3,4}$ 4.2 Hz, H-3), 6.49 (dd, 1 H, $J_{2,3}$ 15.6 Hz, $J_{2,4}$ 1.9 Hz, H-2), 5.17 (ddd, apparent quintet, $J_{4,5}$ ~2.5 Hz, H-4), 4.2–4.5 (m, 4 H, H-5,6,7a,b), 3.66 (s, 3 H, CO_2CH_3); ^{13}C-n.m.r. (C_5D_5N): δ 167.1 (CO_2CH_3), 152.1 (C-3), 120.9 (C-2), 74.8 73.3 72.0 (C-4,5,6), 65.1 (C-7), 51.2 (CO_2CH_3).

Anal. Calc. for $C_8H_{14}O_6$ (206.2): C, 46.40; H, 6.84. Found: C, 46.67; H, 6.84.

Isopropylidenation of **2** *to give* **3**. — To a cooled (ice bath) suspension of **2** (1.80 g, 8.73 mmol) in dry acetone (30 mL) was added conc. H_2SO_4 (0.3 mL), and the mixture was shaken well. The resulting solution was kept for 16 h at room temperature, whereupon it was neutralized with 28% NH_4OH under ice-bath cooling. The resulting precipitate was filtered off, and the filtrate was evaporated. The residual oil (2.50 g) was passed through a short column of silica gel (12 g, 5:1 hexane–EtOAc) giving pure **3** as an oil; yield 2.17 g (87%); $[\alpha]_D^{27}$ +1° (*c* 1, $CHCl_3$) (lit.[1a] $[\alpha]_D^{25}$ +5°. The spectral properties were identical with those of a specimen prepared through a Wittig reaction from 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose[1a].

Anal. Calc. for $C_{14}H_{22}O_6$ (286.16): C, 58.73; H, 7.75. Found C, 58.78; H, 7.79.

Diels–Alder reaction of **1**, **2**, *and* **3** *with cyclopentadiene (Table I).* — *A. Thermal conditions. Entry 1.* The reaction was conducted as described in the previous paper[1a]. The crude product obtained after processing of the reaction mixture was passed through a short column of silica gel (first with toluene and then 2:1 toluene–EtOAc) to give a mixture of adducts (**4a** + **5a** + **6a** + **7a**) in near-quantitative yield.

Entries 2, 3, and 4. These reactions were conducted as for entry 1, but using a glass pressure-bottle heated at 115–120° with the initial addition of 15 mmol equivalents of cyclopentadiene. (Entries 2 and 3 in toluene, 75 and 50 h, respectively; entry **4**, in DMF, 95 h). Up to ~12 g of the dienophile could be reacted in this manner, eliminating the repeated addition of cyclopentadiene necessary when reactions at reflux were conducted in an open vessel. The crude product obtained from the reaction of **2** was acetylated with Ac_2O and pyridine to give a mixture of acetylated adducts (60% overall yield based on **2**), which was then analyzed.

B. $AlCl_3$-catalyzed conditions. Entry 5. This experiment was conducted as described in the previous paper[1a]. The crude product obtained after processing was applied onto a short column of silica gel (~15 parts by weight of dienophile). After washing out

most of the cyclopentadiene-related side-products with toluene, the adducts were first eluted with 8:1 toluene–EtOAc and then with the same solvent (2:1 ratio). This pre-column treatment was also useful for preparative purposes, as it permitted the separation of adducts by successive use of a large medium-pressure column (Ace Glass, Inc. Michel–Miller type, packed with 1.2 kg of Silica Gel 60), to which up to ~10 g of the adduct mixture could be applied.

Entry 6. To a cooled (ice bath) mixture of **3** (186 mg, 0.649 mmol) and $AlCl_3$ (85 mg, 0.64 mmol) in dry toluene, was added freshly distilled cyclopentadiene (0.27 mL, ~3.3 mmol) in an atmosphere of nitrogen. The mixture was stirred for 3 h at this temperature and then poured into ice-cold water (10 mL) containing Na_2CO_3 (150 mg), which was stirred vigorously for 0.5 h. The mixture was passed through a bed of Celite that was then washed with toluene. The separated organic layer was washed successively with saturated aqueous $NaHCO_3$, water, 0.1M HCl, saturated brine, and then dried (Na_2SO_4). The solution was evaporated to ~3 mL and applied onto a column of silica gel (5 g) that was then washed with toluene (~50 mL) and eluted with 5:1 toluene–EtOAc. The product mixture was further purified on a column of silica gel (10 g, 5:1 hexane–EtOAc), giving 161 mg of adducts (70%). This mixture contained ~10% of unidentified by-products along with 14% of unreacted dienophile, as analyzed by ^{1}H-n.m.r. spectroscopy.

*Methyl (5*R*,6*R*)-6*-endo-(L-arabino-*tetritol-1-yl)bicyclo[2.2.1]hept-2-eno-5*-exo-*carboxylate* (**4b**) *and methyl (5*R*,6*R*)-5*-exo-(L-arabino-*tetritol-1-yl)bicyclo[2.2.1]hept-2-eno-6*-endo-*carboxylate* (**5b**). — These products were prepared by deacetylation of **4a** and **5a** as described[13] for the D enantiomer of **4b** in 89 and 80% yields, respectively.

Compound **4b**: m.p. 165–167° (after three recrystallizations), $[\alpha]_D^{25}$ −70 (*c* 1, MeOH) (lit.[13a] for the D enantiomer, m.p. 156–158°; $[\alpha]_D^{25}$ +71°); the i.r. and ^{1}H-n.m.r. spectra were identical with those of the D enantiomer.

Anal. Calc. for $C_{13}H_{20}O_6$ (272.3): C, 57.34; H, 7.40. Found: C, 57.42; H, 7.41.

Compound **5b**: m.p. 178–180°, $[\alpha]_D^{25}$ −62° (*c* 1, MeOH); i.r. (KBr) ν 3350 (br), 2500 (br, C=O–H-O), 1740 (C=O), 1445, 1165, 1075, 1020, 720 cm^{-1}; ^{1}H-n.m.r. (~6:1 C_5D_5N + D_2O): δ 6.29 (dd, 1 H, $J_{2,3}$ 5.6, $J_{3,4}$ 3.2 Hz, H-3), 6.08 (dd, 1 H, $J_{1,2}$ 2.7 Hz, H-2), 4.53 (ddd, 1 H, $J_{2',3'}$ 8.3, $J_{3',4'a}$ 5.7, $J_{3',4'b}$ 3.7 Hz, H-3'), 4.42 (dd, 1 H, J_{gem} 11.2 Hz, H-4'b), 4.33 (dd, 1 H, $J_{1',2'}$ 0.8 Hz, H-1'), 4.27 (dd, 1 H, H-4'a), 4.22 (dd, 1 H, H-2'), 3.60 (s, 3 H, CO_2Me), 3.43 (m, 1 H, $J_{3,4}$ 3.2, $J_{4,5}$ ~0 Hz, H-4), 3.14 (m, 1 H, $J_{1,2}$ 2.7, $J_{1,6}$ ~4 Hz, H-1), 2.88 (apparent t, 1 H, $J_{5,6}$ 4.7 Hz, H-6), 2.55 (ddd, 1 H, $J_{5,7syn}$ 1.5 Hz, H-5*endo*), 1.67 (dt, 1 H, J_{gem} ~8.5, $J_{1,7anti}$ $J_{4,7anti}$ ~1 Hz, H-7*anti*), 1.34 (dq, 1 H, $J_{1,7syn}$ ~ $J_{4,7syn}$ ~ 1.5 Hz, H-7*syn*); ^{13}C n.m.r. (~6:1 C_5D_5N + D_2O): δ 175.8 (CO_2Me), 138.9 (C-3), 134.0 (C-2), 73.1 (C-1'), 72.6 (C-2'), 72.2 (C-3'), 64.3 (C-4'), 51.6 (CO_2Me), 47.7 (C-6), 46.9 (C-5), 45.9 (C-1 and 7, double intensity), 44.4 (C-4).

Anal. Calc. for $C_{13}H_{20}O_6$ (272.3): C, 57.34; H, 7.40. Found: C, 57.18; H, 7.40.

*Methyl (5*R*,6*R*)-6*-endo-*formylbicyclo[2.2.1]hept-2-eno-5*-exo-*carboxylate* (**8**). — To a solution of **4b** (678 mg, 2.49 mmol) in MeOH (23 mL) was added an aqueous solution (14 mL) of $NaIO_4$ (1.76 g, 8.22 mmol), and the mixture was stirred at room temperature for 0.5 h. The solid that formed was filtered off, and the filtrate was

concentrated to an aqueous mixture (~10 mL). This was extracted with CH_2Cl_2 (30 mL + 10 mL), and the extract was washed with water (~10 mL), dried (Na_2SO_4) and evaporated. The residual oil was dried briefly (~2 min) using a rotary vacuum pump (<1 mm Hg) to give pure **8** as an oil; yield 416 mg (93%). Although the oil was distillable (~95°/0.7 mmHg, Kugelrohr), the oil as directly obtained showed satisfactory analytical and spectral data and was directly used in the next decarbonylation reaction. Care had to be exercised when drying, so as not to cause unnecessary loss of **8** through its volatility; $[\alpha]_D^{26}$ −93.5° (*c* 1.5, $CHCl_3$); i.r. (neat) *v* 2950, 1710–1740 (C=0), 1430, 1330, 1250 (br.), 1170 (br.), 1020, 920, 720 cm^{-1}; *m/z* (rel. intensity, composition): 180.0808 (3. M^+ calc. 180.0787), 151 (14, $C_9H_{11}O_2$), 121 (28, C_8H_9O), 119 (17, C_8H_7O), 115 (19, $C_5H_7O_3$), 91 (24, C_7H_7), 83 (32, $C_4H_3O_2$), 66 (100, C_5H_6). For n.m.r. data see Table II.

Anal. Calc. for $C_{10}H_{12}O_3$ (180.2): C, 66.65; H, 6.71. Found: C, 66.69; H, 6.71.

*Methyl (5*R,6R*)-5-*exo-*formylbicyclo[2.2.1]hept-2-eno-6-*endo-*carboxylate (***9***).* — This compound was prepared from **5b**, in 91% yield, in the same manner as just described for compound **8**; $[\alpha]_D^{26}$ −93° (*c* 1.5, $CHCl_3$); i.r. (neat) *v* 2950, 1720 (br.), 1440, 1305, 1265 (br.), 1200 (br.) 1115, 1020, 905, 720 cm^{-1}; *m/z* (rel. intensity): 180.0802 (1, M^+ calc. 180.0787), 151 (5), 121 (23), 119 (11), 115 (12), 91 (20), 83 (21), 66 (100) (the composition of each fragment ion was the same as that observed for compound **8**). For n.m.r. data see Table II.

Anal. Calc. for $C_{10}H_{12}O_3$ (180.2): C, 66.65; H, 6.71. Found: C, 66.47; H, 6.76.

Decarbonylation reaction of **8** *and* **9** *with* $RhCl(PPh_3)_3$ *and* $[Rh(dppp)_2]Cl$. — *General.* Solvents used for the reaction (benzene and toluene) were freshly distilled over CaH_2 under nitrogen after refluxing at least one day. Nitrogen was a pre-purified grade and was passed through a column packed with molecular sieve 4A pellets. $RhCl(PPh_3)_3$ was purchased from Aldrich Chemical Co. $[Rh(dppp)_2]Cl$ was prepared by the procedure of James and Mahajan[12], but starting from commercially available (Aldrich) $[RhCl(C_2H_4)_2]_2$ instead of $[RhCl(cyclooctene)_2]_2$. 1,3-Bis(diphenylphosphino)propane was purchased from Strem Chemicals, Inc.

Reaction of **8** *with* $RhCl(PPh_3)_3$. *Methyl (*R*)-(+)-tricyclo[2.2.1.0*^{2,6}*]heptane-3-carboxylate* (**12**). — A solution of **8** (300 mg, 1.66 mmol) in benzene (20 mL) was boiled under reflux for 5 min, while nitrogen was bubbled through the solution. Heating was terminated, and $RhCl(PPh_3)_3$ (1.81 g, 1.95 mmol) was added to the solution. The deep wine-red mixture was boiled under reflux for 3 h under a slight overpressure of nitrogen, during which time the red solid of $RhCl(PPh_3)_3$ disappeared, and a yellow solid $[RhCl(CO)(PPh_3)_2]$ appeared instead. T.l.c. of the mixture showed the disappearance of aldehyde **8**, but the products of decarbonylation were not detectable by t.l.c. either by u.v., I_2 vapor, or H_2SO_4. The mixture was filtered to give 932 mg of yellow powder $[RhCl(CO)(PPh_3)_2$, 81% of the theoretical amount], and the filtrate was passed through a short column of silica gel (~6 g) with the aid of CH_2Cl_2. The eluate containing **12**, as checked by g.l.c., was collected and evaporated to remove most of the solvent. Distillation (~100°/6 mmHg, Kugelrohr) gave **12** as an oil; yield 195 mg (77%) that was 97% pure by g.l.c.; $[\alpha]_D^{28}$ +36.5° (*c* 1, 95% EtOH); *m/z* (rel. intensity, composition): 152.0820 (22, M^+ calc. 152.0837), 137 (10, $M^+ - CH_3$), 120 (25, $C_8H_8O_1$), 111 (15, $C_6H_7O_2$), 93 (100, C_7H_9), 77 (52, C_6H_5), 74 (39, $C_3H_6O_2$), 66 (56, C_5H_6).

Anal. Calc. for $C_9H_{12}O_2$ (152.2): C, 71.02; H, 7.95. Found: C, 70.96; H, 7.98.

A portion of the foregoing sample was purified by preparative g.l.c. to give a sample of >99.5% purity by analytical g.l.c.: $[\alpha]_D^{26}$ + 36.7° (*c* 1.3, 95% EtOH).

Reaction of **8** *with* [*Rh*(*dppp*)$_2$]*Cl. Compound* **12** *and methyl* (1*S*)-*bicyclo*[*2.2.1*]*hept-2-eno-2-carboxylate* (**13**). — A solution of **8** (380 mg, 2.11 mmol) in toluene (25 mL) was boiled under reflux for ~5 min, while nitrogen was bubbled through the solution. Heating was terminated and [Rh(dppp)$_2$]Cl (100 mg, 0.1 mmol) was added. The mixture was heated (bath temp. ~120°) while nitrogen was bubbled through it during the whole reaction period at such a rate that the gentle refluxing of the mixture was maintained. (In some instances, a considerable decrease of the volume of the solvent was observed after conducting the reaction overnight. In such cases, toluene was added to restore the original volume.) The reaction was monitored by t.l.c.: after 43 h the spot of **8** disappeared, and a major spot of an unidentified product was observed (R_f ~0.2, 5:1 hexane–EtOAc), which was not detected in the reaction with RhCl(PPh$_3$)$_3$. The whole mixture was passed through a short column of silica gel (~10 g, dry column) with the aid of CH_2Cl_2. The eluate was fractionated (~3 mL) and monitored by t.l.c. and g.l.c. Fractions containing **10**, **12**, and **13** were collected and quantified by using a racemic mixture of **10** and **11** (ref. 8a) as an external standard. A portion of the mixture was subjected to preparative g.l.c. to give pure **12** and **13**. Compound **12**: $[\alpha]_D^{25}$ +36° (*c* 0.4, 95% EtOH); **13**: $[\alpha]_D^{25}$ + 185° (*c* 0.4, 95% EtOH); *m/z* (rel. intensity, composition): 152.0830 (9, M^+ calc. 152.0837), 124 (100, M – C_2H_4), 96 (20, C_5H_8O), 93 (26, C_7H_9 and C_6H_5O), 79 (19, C_6H_7), 65 (23, C_5H_5).

After elution of the foregoing fractions (**10**, **12**, and **13**), compounds of a more polar nature than the starting aldehyde (R_f ~0.2) were eluted from the silica gel column; these amounted to 152 mg after removal of solvent.

Reaction of **9** *with RhCl*(*PPh*$_3$)$_3$. — Compound **9** (173 mg, 0.960 mmol) was treated with RhCl(PPh$_3$)$_3$ (980 mg, 1.06 mmol) in the manner described for **8**. The reaction was monitored by t.l.c. and after 71 h the spot of **9** disappeared. Processing as described for **8** and final distillation (65–70°/5 mmHg, Kugelrohr) gave a mixture of products (75 mg, 51%), which consisted mainly (79%) of the 6-*endo* ester **11**: $[\alpha]_D^{25}$ −113° (*c* 1, 95% EtOH). G.l.c.–m.s. and ^{1}H-n.m.r. spectroscopy of the mixture revealed the presence of **10** (2%), **12** (8%), and **13** (7%) (the absolute configuration of these is not established), and an unidentified compound (4%).

Reaction of **9** *with* [*Rh*(*dppp*)$_2$]*Cl. Methyl* (6*S*)-*bicyclo*[*2.2.1*]*hept-2-eno-6-endo-carboxylate* (**11**). — Compound **9** (165 mg, 0.916 mmol) was treated with [Rh(dppp)$_2$]Cl (43 mg, 0.045 mmol) in the manner described for **8**. After 22 h and 45 h, ~1:10 aliquots of the mixture were withdrawn, passed through a small column of silica gel with CH_2Cl_2, and the eluates were analyzed by g.l.c. The reaction remained incomplete after 22 and 45 h; at the latter time ~13% of starting aldehyde remaining unreacted. Additional [Rh(dppp)$_2$]Cl (~12 mg) was added and heating was continued for 25 h, after which time the aldehyde **9** was no longer detected by t.l.c. The entire mixture was applied to a column (~1.5 g, dry column) of silica gel that was eluted with CH_2Cl_2. Evaporation and final distillation (~85°/7 mm Hg, Kugelrohr) gave **11**: 68 mg,

~62% (estimated yield). It was >99% pure and contained <1% of the nortricyclane ester **12**. The distribution of the products at 22 h and 45 h of reaction was the same as that in the final mixture. Compound **11** had $[\alpha]_D^{25}$ −137° (*c* 1, 95% EtOH); *m/z* (rel. intensity, composition): 152.0830 (5, M^+ calc. 152.0837), 121 (4, $M^+ - CH_3O$), 91 (7, C_7H_7), 87 (9, $C_4H_7O_2$), 77 (6, C_6H_5), 66 (100, C_5H_6).

Anal. Calc. for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 70.98; H, 7.98.

Attempted conversion of **12** *into* **13**. — A mixture of **12** (racemate, 30 mg) and $[Rh(dppp)_2]Cl$ in toluene (2 mL) was heated at 115–120° and stirred in a closed vessel under an N_2 atmosphere. After 45 h an ~0.7-mL portion of the mixture was withdrawn and g.l.c. analysis, after bulb-to-bulb distillation, showed that the starting material **12** remained unchanged. To the rest of the mixture ~15 mg of benzaldehyde was added, and heating was continued for 47 h. G.l.c. analysis showed the formation of benzene, along with unreacted benzaldehyde, but compound **12** still remained intact, and no trace of **13** was detected.

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