221. Asymmetric *Diels-Alder* Reactions of Neopentyl-Ether-Shielded Acrylates and Allenic Esters: Syntheses of (−)-Norbornenone and (−)-β-Santalene

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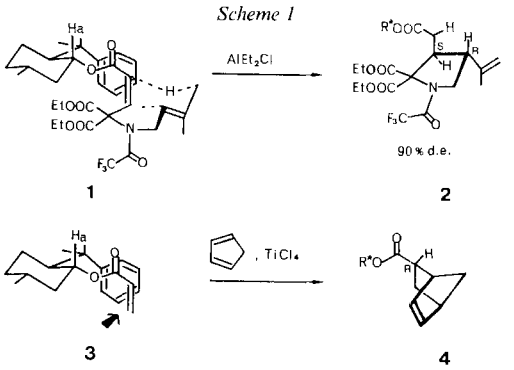
(10.IX.85)

Starting from (+)- or (−)-camphor, the antipodal alcohols **14** and **18**, respectively, have been prepared; the corresponding acrylates **15** and **19** underwent $TiCl_2(i\text{-}PrO)_2$-mediated *Diels-Alder* additions to cyclopentadiene to give adducts **20a** and **22a** respectively, with 95% *endo*- and 99.2% π-face selectivities. Adduct **22a** was converted to enantiomerically pure norbornenone **26**. Addition of 1,3-butadiene to acrylate **15** in the presence of $TiCl_4$ afforded 3-cyclohexenyl carboxylate **29** with > 95.6% stereodifferentiation. The $TiCl_2(i\text{-}PrO)_2$-promoted [4 + 2] cycloaddition of cyclopentadiene to allenic ester **43** proceeding with 99% face differentiation served as the key step for an efficient enantioselective synthesis of (−)-β-santalene ((−)-**41**) with concomitant recovery of the chiral control alcohol **14**.

Introduction. – Given the fundamental role of the *Diels-Alder* reaction in organic synthesis [1], it is without question that the control of its absolute topicity constitutes a topic of pressing importance. It was, however, not until recently that substantial effort has been devoted to and hence significant progress achieved in this area [2].

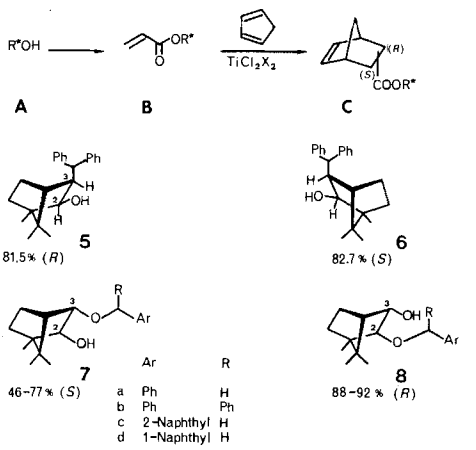
As an extension of a preliminary communication [3], we report here in detail the first successful surmounting of the threshold of 99% face-stereodifferentiation in the *Diels-Alder* process. Its value is illustrated by application to the syntheses of enantiomerically pure building blocks and also of a natural product. The starting point for this work was the encouraging chiral induction observed with *Lewis*-acid-promoted ene-type cyclizations (**1**→**2**) [4] and [4+2] cycloadditions (**3**→**4**) [5] of 8-phenylmenthyl enoates *(Scheme 1)*.

Scheme 1



We attributed this face differentiations to transition states which feature syn-periplanar C=O/C,H_a and antiperiplanar C=O/C_α,C_β bonds resulting in selective C_α-*Re* face shielding by the phenyl group. Prompted by the topological considerations and practical problems encountered here, the design of more efficient and versatile C_α-*Re* and C_α-*Si* directing chiral auxiliaries was undertaken. Our first attempts focussed on monoterpene- or steroid-derived cyclohexanols locked in a chair conformation with both an equatorial OH group and an α-*trans*-positioned aryl-substituted side chain [6]. Exploiting the ready availability of (+)- and (−)-camphor, we then focussed our attention on conformationally rigid *cis*/*endo*- or *cis*/*exo*-bornanols such as **5**–**8** [3] [6].

Scheme 2



To compare the sign and extent of the topological bias provided by each auxiliary **A**, the *Lewis*-acid-promoted addition of acrylates to cyclopentadiene (**B**→**C**) served as a test reaction. However, despite extensive variation of the blocking chain, including the attachment of more or larger aryl groups, *Lewis*-acid-mediated additions **B**→**C** did not exceed 92% asymmetric induction.

Preparation and Acylation of the 3-Hydroxyisobornyl Neopentyl Ethers 14 and 18 (*Schemes 3* and *4*)[1]. – Questioning the hypothetical role of aryl/acrylate π-stacking in π-face differentiation, the effect of steric bulk on acrylate shielding was studied.

Starting from (1*R*)-3,3-(ethylenedioxy)camphor (**10**) [7], readily available from (+)-camphor (**9**), successive reduction with *L*-Selectride (**10**→**11**), *O*-alkylation of deprotonated **11** (NaH) with 1-bromo-2,2-dimethylpropane in *N*-methylpyrrolidone at 130° (→**12**), acetal cleavage with aq. H_2SO_4 (→**13**) and reduction with $NaBH_4$ furnished the *cis*-3-hydroxy-isobornyl neopentyl ether (**14**) in 74% overall yield from **10**. Crystallization of **14** (pentane, −30°) permitted its facile purification.

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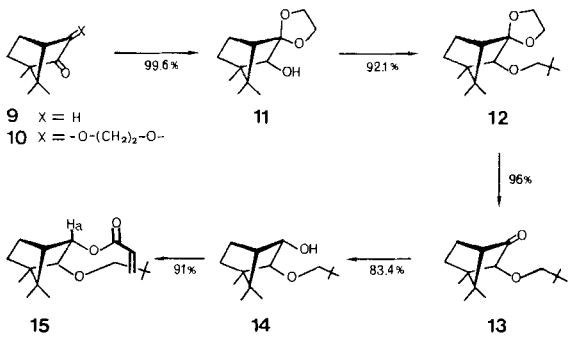
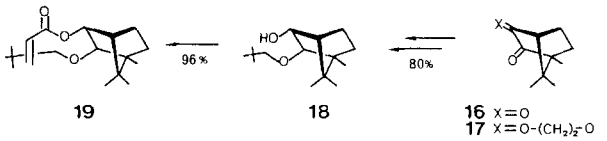
[1]) We thank Dr. *T. Godel* for his contribution to the alkylation step **11**→**12** and Mr. *P. de Kok* (ISEC grantee) for the preparation of alcohol **18**.

Scheme 3



Scheme 4

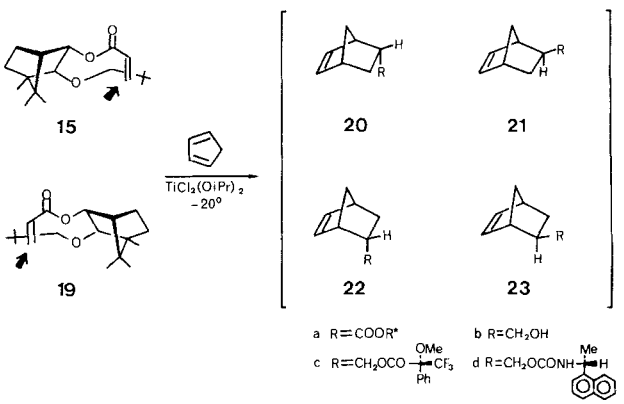


Esterification of **14** by treatment with acryloyl chloride/Et_3N/4-(dimethylamino)pyridine (cat.) at r.t. followed by chromatography afforded acrylate **15** in 91% yield.

To prepare the antipodal dienophile **19**, (−)-camphorquinone (**16**) obtained from (−)-camphor [8] (74%) was converted to acetal **17** (50% overall yield). Analogous to the above protocol, **17** was transformed to auxiliary **18**, which on esterification (acryloyl chloride/AgCN [9]) furnished acrylate **19** *(Scheme 4)*.

Asymmetric [4 + 2] Cycloadditions of Cyclopentadiene to Acrylates 15 and 19 *(Scheme 5)*. – Previous experience has shown that the nature of the *Lewis* acid plays a significant role in asymmetric *Diels-Alder* additions to enoate dienophiles [5b]. Although

Scheme 5



$TiCl_4$ generally led to high face selection, it may promote aryl-ether cleavage or polymerization in the presence of trace amounts of H_2O. We then found that high chemical yields of acrylate/cyclopentadiene adducts were obtained more conveniently and safely using the mild *Lewis* acid $TiCl_2$ (i-PrO)$_2$ [3].

Accordingly, successive treatment of acrylate **15** with a 1:1 mixture of $TiCl_4$/Ti(i-PrO)$_4$ [10] (1.5 mol-equiv.) and cyclopentadiene (3 mol-equiv.) at −20° for 4 h, followed by workup furnished adducts **20a**–**23a** (95%) with stereoisomer **20a** predominating. The isomer ratio as depicted in the *Table* was determined as follows. Non-destructive removal

Table. *Asymmetric* Diels-Alder *Addition of Cyclopentadiene to Acrylates* ***15*** *and* **19**

Entry	Acrylate	$TiCl_2(OR)_2$ R	Reaction temp. [°C]	Yield [%] **20a–23a**	Ratio **20 /22 /21 + 23**	*endo/exo*	d.e. [%][a]) *endo*
1	**15**	i-Pr	−20°	95	95.6: 0.4:4.0	24:1	99.2 (99.4)
2	**19**	i-Pr	−20°	98	0.4:94.6:5.0	19:1	99.1 (99.4)
3	**19**	Et	−30°	97	1.0:96.6:2.4	41:1	98.0 –

[a]) By HPLC of **20d** + **22d** (^{19}F-NMR of **20c** + **22c**).

of auxiliary **14** (recovered in high yield after chromatography) by reduction of the adduct mixture with $LiAlH_4$ gave alcohols **20b**–**23b**. Their GC analysis revealed a 24:1 ratio of the *endo*/*exo*-products **20b** + **22b**/**21b** + **23b**. Removal of the *exo*-isomers by preparative GC, esterification of the *endo*-isomers **20b**/**22b** with (+)-(*R*)-α-methoxy-α-trifluoromethyl-phenylacetic acid (= (+)-(*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid) [11] and analysis of the *Mosher* derivatives **20c**/**22c** by ^{19}F-NMR in the presence of Eu(fod)$_3$ [5b] indicated a ratio of 99.7 (± 0.3) : 0.3 for **20**/**22**. Alternatively, treatment of **20b**/**22b** with (−)-(*R*)-1-(1-naphtyl)ethyl isocyanate 2-(*N*,*N*-dimethylamino)ethanol [12] furnished the *Pirkle* derivatives **20d**/**22d** in a 99.6 (± 0.1) : 0.4 ratio as determined by HPLC.

As expected, equally high but opposite asymmetric induction was achieved in the analogous *Diels-Alder* addition to the antipodal dienophile **19** (*Table, Entry 2*). By using the more reactive *Lewis* acid $TiCl_2(EtO)_2$, the reaction temp. could be lowered to −30° resulting in an improved *endo*/*exo*-ratio (*Entry 3*).

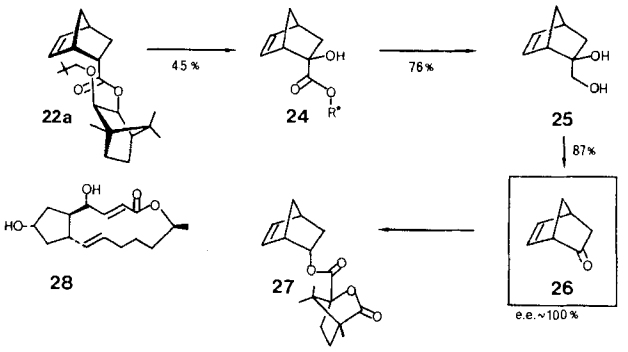
It thus follows that the acrylates **15** and **19** provide the (5*R*)- and (5*S*)-adduct **20a** and **22a**, respectively, in > 94% chemical yield and with over 99% diastereofacial differentiation.

The observed dienophile topicity can be rationalized by a steric shielding of the C_α,C_β face by the *t*-Bu group as depicted in formulas **15** and **19** based on the following assumptions: 1) A synperiplanar C=O/C,H_a and an antiperiplanar C=O/$C_\alpha C_\beta$ acrylate conformation probably reinforced by coordination with the *Lewis* acid [3a]. 2) A staggered neopentyl ether side chain as found by X-ray-diffraction analysis of a carboxylic ester derived from **19** [13].

From the practical standpoint it is worth noting that the auxiliaries are readily attached and regenerated. The relevance of these results is further highlighted by the utility of bicyclo[2.2.1]heptenes as versatile building blocks in natural-product synthesis.

Preparation of Enantiomerically Pure (−)-Norbornen-2-one (26; *Scheme 6*). – In the following we describe the enantioselective preparation of norbornenone **26**, which served as a key intermediate for the synthesis of (+)-brefeldin A (**28**) [14]. α-Hydroxylation of crude adduct **22a** by successive treatment with lithium isopropyl(cyclohexyl)amide and O_2/P(OEt)$_3$ and subsequent crystallization furnished diastereoisomerically pure hydroxy-ester **24** (45%). Hence, the crystalline nature of **24**, imposed by the attached auxiliary, considerably facilitated its separation from even trace amounts of stereoisomers.

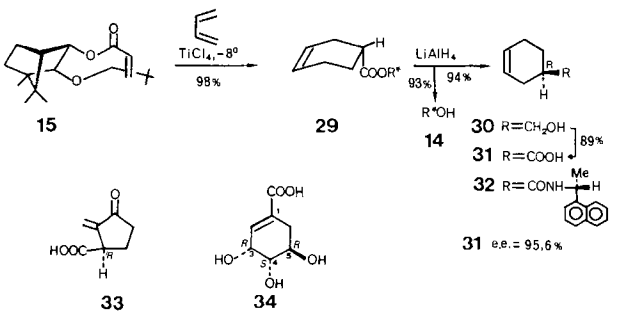
Scheme 6



Reduction of **24** with $LiAlH_4$ gave recovered auxiliary **18** (88%) and crystalline diol **25** (76%). Oxidative cleavage of diol **25** furnished, after distillation, enantiomerically pure norbornenone **26** (87% yield; $[\alpha]_D^{28} = -1152°$ (c = 1.46, isooctane)[2]). The enantiomeric purity of **26** was confirmed to be > 99% by capillary GC analysis of the corresponding camphanate **27** [17].

Asymmetric *Diels-Alder* Addition of 1,3-Butadiene to Acrylate 15 *(Scheme 7).* – To explore the scope of the topological bias displayed by the antipodal dienophile auxiliaries **14** and **18**, we modified the diene and dienophile units. Addition of 1,3-butadiene to **15** proceeded slower (*cf.* cyclopentadiene) even in presence of the more stringent *Lewis* acid

Scheme 7

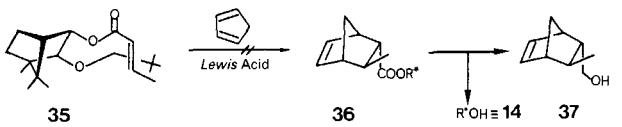


[2]) Based on isotope-dilution techniques, $[\alpha]_D^{28} = +1140°$ (isooctane) has been calculated for the pure antipode of **26** [15]. For further preparations of enantiomerically enriched norbornenones, see [16].

$TiCl_4$ and required 115 h at −8° to reach completion. Nevertheless, the chiral efficiency of the process **15**→**29** was excellent as assessed by the reduction **29**→**30** and the efficient oxidation **30**→**31**. The 3-cyclohexenylcarboxylic acid **31** was shown to be 95.6% enantiomerically pure according to GC and HPLC analyses of its amide **32**. Acide **31** gave a crystalline amidinium salt. These results become even more attractive in view of the potential of alcohol **30** and carboxylic acid **31** as precursors for the enantioselective syntheses of naturally occurring (−)-sarkomycin (**33**)[3]) and (−)-shikimic acid (**34**)[3]), respectively.

Attempted *Diels-Alder* Addition of Cyclopentadiene to Crotonate 35 *(Scheme 8)*. – Modification of the dienophile by attaching a deactivating β-substituent showed, however, a limitation of the above concept. Thus, treatment of crotonate **35** with cyclopentadiene (5 mol-equiv.) in the presence of $TiCl_2(EtO)_2$ or $TiCl_4$ at 0 or 25° failed to give cycloadduct **36** in yields of > 7%[4]). It appears that the cycloaddition of cyclopentadiene

Scheme 8

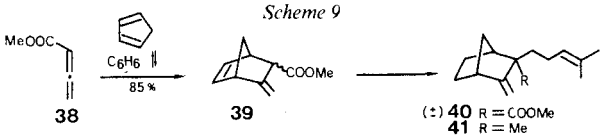


35 **36** **37**

to **35** is slowed down to such an extent that polymerization becomes predominant. Our observation is consistent with the hypothesis that in enoates derived from **14** and **18**, a tetragonalization of the C_α- and C_β-centers is sterically hindered by the neopentyl chain. These considerations led ultimately to the development of 'activating' dienophile auxiliaries thus extending the scope of asymmetric *Diels-Alder* reactions [20].

Enantioselective Synthesis of (−)-β-Santalene (*Schemes 9* and *10*). – Further tempted to combine the exploration of asymmetric *Diels-Alder* reactions with natural-product synthesis, we envisaged the synthesis of the enantiomerically pure, olfactively interesting sandalwood constituent (−)-β-santalene ((−)-**41**)[5]). Its racemate has been elegantly syn-

Scheme 9



38 **39** (±) **40** R = COOMe
41 R = Me

thesized by *Bertrand* [23] *(Scheme 9) via* a thermal allenic ester/cyclopentadiene addition **38**→**39** and intermediate **40.**

Aiming at an efficient π-facial selection in the initial *Diels-Alder* step, the chiral allenic ester **43** was prepared by the following route *(Scheme 10)*. Acylation of chiral alcohol **14**

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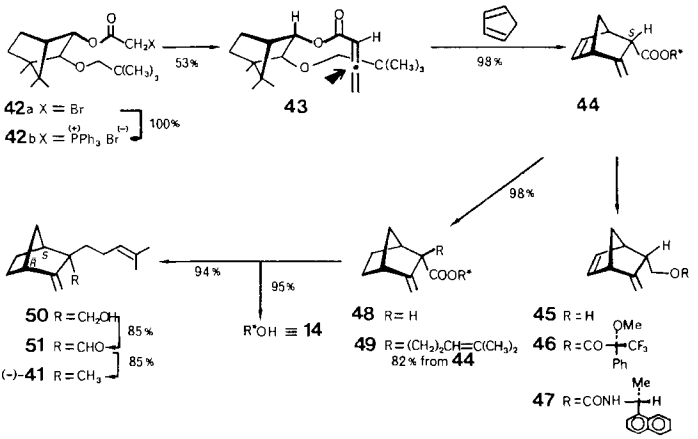
[3]) Compound (±)-**33** [18] as well as (±)-**34** [19] have previously been prepared from (±)-**30** and (±)-**31**, respectively.

[4]) The reaction **35**→**36** was monitored by GC analyzing the crude reaction mixture as well as the alcohols **14** and **37**, obtained therefrom by reduction.

[5]) Structure of **41**, see [21]. Preliminary communication of the following enantioselective synthesis, see [22].

Scheme 10



with bromoacetyl bromide/AgCN followed by treatment of the resulting bromoester **42a** with triphenylphosphine afforded the phosphonium salt **42b** (*ca.* 100% from **14**). *Wittig*-type reaction [24] of **42b** with acetyl chloride/Et_3N gave the allenic ester **43** in 53% yield.

Proceeding to the crucial cycloaddition step, **43** was then treated with $TiCl_2$ (i-PrO)$_2$ (1.5 mol-equiv.) and cyclopentadiene (3 mol-equiv.) at −20° for 6 h affording crude **44** in 98% yield. We were pleased to find that the predominant (98%) *endo*-isomer **44** was formed with 99% diastereofacial differentiation as shown by analysis of derivatives **46** (^{19}F-NMR) and **47** (HPLC)[6]).

The predicted absolute sense of induction follows from the conversion of **44** into (−)-*β*-santalene ((−)-**41**) carried out in analogy to the previous synthesis of racemic **41**. Selective hydrogenation of crude **44** (→**48**) and subsequent ester-dienolate alkylation with 4-methyl-3-pentenyl iodide furnished ester **49**. Traces of isomers were readily removed by crystallization to give pure **49** (100% e.e.)[7]) in 82% overall yield from crude **44**. The auxiliary **14**, having conferred excellent π-facial differentiation to allene **43** as well as convenient crystallinity to intermediate **49**, was then regenerated (95%) by reduction of **49** with $LiAlH_4$.

Chromatography of the reaction mixture furnished a crystalline alcohol **50** which, on successive oxidation (pyridinium chlorochromate) and *Wolff-Kishner* reduction, afforded enantiomerically pure (−)-*β*-santalene ((−)-**41**) in 50% overall yield from allenic ester **43**. Synthetic (−)-**41** was identified by comparison ($[\alpha]_D$, IR, ^{1}H-NMR, ^{13}C-NMR, MS) with (−)-*β*-santalene of natural origin.

Conclusion. – In summary we believe that the π-facially selective cycloadditions of 1,3-dienes to sterically shielded reactive enoates described above constitute a significant advancement in the evolution of asymmetric *Diels-Alder* reactions. Moreover, the neopentyl ether induced face differentiation in esters of auxiliaries **14** and **18** applies also

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[6]) Before the preparation of the *Mosher* and *Pirkle* derivatives, the *endo*- alcohols **45** and antipode were separated from their *exo*-isomers (2%) by prep. GC.

[7]) Ester **49** was assigned to be 100% enantiomerically pure based on capillary GC of the *Mosher* ester of **50**.

to other reactions such as asymmetric 1,4-additions [3b] [25], ene processes [26], and enolate functionalizations [13].

Financial support of this work by the *Swiss National Science Foundation, Sandoz Ltd.*, Basel, and *Givaudan SA*, Vernier, is gratefully acknowledged. We record our gratitude to *Givaudan SA* for kindly providing a sample of (−)-β-santalene of natural origin. We also thank Mr. *D. Reichlin* and Mr. *P. Fantini* for their experimental contributions, and Mr. *J. P. Saulnier*, Mr. *A. Pinto* and Mrs. *D. Clément* for NMR and MS measurements.

Experimental Part

General. All reactions were carried out under Ar with magnetic stirring, unless otherwise specified. Solvents were dried by distillation from drying agents as follows: Et_2O; THF (Na-metal)-, toluene (K-metal); $CHCl_3$ (P_2O_5); pyridine, Et_3N, diisopropylamine, and cyclohexylisopropylamine (CaH_2). The organolithium reagents were analyzed by *Gilman*'s titration. 'Workup' denotes extraction with an org. solvent, washing of the org. phase with sat. aq. NaCl soln., drying over anh. $MgSO_4$, and removal of solvent by distillation *in vacuo* using a rotatory evaporator. Column chromatography: SiO_2 (*Merck*, Kieselgel *60*). GC: *Hewlett-Packard 5790A*, integrator *HP 3390*, capillary column (fused silica, 0.2 mm ID), 10 psi H_2, unless otherwise specified; A: *OV-101*, 25 m; C: *OV-1*, 12 m; *Carlo-Erba-Fractovap 2101*, glass column (3 mm ID × 3 m), stationary phase of *Chromosorb W* (acid washed, 80/100 mesh), 1 atm N_2; B: 2% *SE-30; Carlo-Erba Fractovap 2400V* (prep., 15 mm ID × 2 m, *Chromosorb W*); D: 10% *Carbowax*, 1 atm. N_2; E: 10% *OV-225*; F: *Apiezon*, 0.2 atm N_2; retention time in min (area-%). HPLC: *Waters ALC/GPC-244*, UV (254 nm) detector, *Mega/Carlo-Erba* integrator, retention time in min (area-%). M.p.: *Kofler* hot stage; uncorrected. [α]: *Perkin-Elmer-241* polarimeter; in EtOH, unless otherwise specified. IR: in CH_2Cl_2, unless otherwise specified; ν_{max} in cm^{-1}. NMR: in $CDCl_3$, unless otherwise specified; ^{1}H-NMR at 360 MHz, unless otherwise specified; ^{13}C-NMR at 25.2 MHz, unless otherwise specified; standard tetramethylsilane ($\delta = 0$ ppm); *J* in Hz. MS: *m/z* (rel.-%). The antipodal compounds reported here show identical GC, IR, ^{1}H-NMR, and MS.

Preparation and Acylation of Ethers 14 and 18. – *(1S)-1,7,7-Trimethylbicyclo[2.2.1]heptane-2,3-dione* (**16**). Three portions of SeO_2 (3 × 30 g, 0.81 mol) were added in intervals of 1 h each to a stirred soln. of (−)-camphor [8] (70.5 g, 0.46 mol) in Ac_2O (50 ml) under reflux. Heating at reflux for 18 h, cooling, filtration through *Celite*, evaporation of the filtrate, shaking of the crystalline residue with Et_2O/7N aq. NaOH (100 ml) at 0°, extraction with Et_2O (3 ×), washing of the Et_2O soln. with 1N aq. NaOH and H_2O, drying ($MgSO_4$), and evaporation followed by crystallization of the residue (69.3 g) from hexane (800 ml) gave **16** (56.5, 74%), m.p. 197–197.5°. $[\alpha]_D^{23} = +102.9°$; $[\alpha]_{578}^{23} = +113.7°$; $[\alpha]_{546}^{23} = +171.3°$; $[\alpha]_{365}^{23} = -255.4°$ (*c* = 2.47). IR: 2970, 1780, 1760, 1460, 1395, 1375, 1165, 995, 965. ^{1}H-NMR (100 MHz): 0.92 (*s*, 3H); 1.06 (*s*, 3H); 1.10 (*s*, 3H); 1.5–2.3 (4H); 2.62 (*d*, *J* = 4, 1H). ^{13}C-NMR: 204.5 (*s*), 202.4 (*s*), 58.6 (*s*), 58.0 (*d*), 42.5 (*s*), 30.0 (*t*), 22.3 (*t*), 21.0 (*q*), 17.3 (*q*), 8.7 (*q*). MS: 166 (7, $C_{10}H_{14}O_2^+$), 138 (18), 123 (13), 110 (8), 95 (100), 83 (59), 69 (65), 67 (30), 55 (85).

(1S)-3,3-Ethylenedioxy-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (**17**). A mixture of **16** (10.2 g, 61.4 mmol), ethylene glycol (8.5 g, 137 mmol), and TsOH·H_2O (1.1 g, 5.8 mmol) in benzene (100 ml) was heated under reflux using a *Dean-Stark* trap. After 22 h, no **16** was detectable by TLC, and 4 ml of H_2O had been collected. Washing of the soln. with 5% aq. NaOH and workup gave crude **17** (13.6 g) which, on crystallization from EtOH, afforded pure **17** (3.6 g). The mother liquor was chromatographed (hexane/EtOAc 9:1→3:1) to give another crop of **17** (5.2 g; total 68.2%) and the corresponding diacetal (28%) which, on treatment with aq. HCl, refurnished **16**. Yield of **17** based on recovered **16**: 91%. M.p. 87–87.5°. $[\alpha]_D^{25} = -64.8°$; $[\alpha]_{578}^{25} = -68.9°$; $[\alpha]_{546}^{25} = -83.1°$; $[\alpha]_{436}^{25} = -210.0°$; $[\alpha]_{365}^{25} = -811.2°$ (*c* = 2.25). IR: 2970, 2910, 1760, 1320, 1220, 1160, 1130, 1025, 975, 959. ^{1}H-NMR: 0.95 (*s*, 3H); 1.00 (*s*, 3H); 1.20 (*s*, 3H); 1.3–2.1 (5H); 3.8–4.4 (4H). ^{13}C-NMR: 216.8 (*s*), 106.9 (*s*), 66.0 (*t*), 64.4 (*t*), 58.2 (*s*), 51.7 (*d*), 43.6 (*s*), 31.0 (*t*), 21.5 (*t*), 21.4 (*q*), 19.0 (*q*), 9.1 (*q*). MS: 210 (1, $C_{12}H_{18}O_3^+$), 182 (4), 99 (100), 95 (2), 67 (5), 55 (33).

(1R,2S)-3,3-Ethylenedioxy-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (**11**) *and its (1S,2R)-Enantiomer.* A 1M soln. of *L-Selectride* in THF (200 ml, 0.2 mol) was added dropwise at −78° to a soln. of **10** [7] (34.5 g, 164.3 mmol) in THF (210 ml). The mixture was stirred at −78° for 1 h, then allowed to warm up to r.t. overnight, and stirred at r.t. until complete disappearance of **10** (TLC). Successive slow addition of H_2O (10 ml), 4N aq. NaOH (82 ml), and 30% aq. H_2O_2 (92 ml), at 0°, stirring for 1 h at 0°, extraction with Et_2O (3 ×) and workup gave **11** (oil; 36.19 g, 100%). GC (A, 130°): 20.0. IR: 3540, 2960, 2890, 1480, 1460, 1390, 1375, 1095, 1030, 1015, 955. ^{1}H-NMR (100 MHz): 0.84 (*s*, 3H); 0.9 (*s*, 3H); 1.1 (*s*, 3H); 1.45–1.85 (5H); 2.35 (*d*, *J* = 6, 1H; disappears with D_2O); 3.3 (*d*, *J* = 6, 1H; →*s* with D_2O); 3.8–4.1 (4H). ^{13}C-NMR: 115.2 (*s*), 85.5 (*d*), 65.6 (*t*), 63.6 (*t*), 52.8 (*d*), 49.7 (*s*), 47.5 (*s*),

33.6 (*t*), 21.03 (*t*), 21.08 (*q*), 20.8 (*q*), 10.9 (*q*). MS: 212 (3, $C_{12}H_{20}O_3^+$), 197 (11), 141 (24), 127 (100), 109 (6), 99 (21), 95 (10), 83 (27), 73 (24), 69 (17), 55 (43).

Following the above procedure, **17** (22.3 g, 0.106 mol) was reduced to give *(1S,2R)-3,3-ethylenedioxy-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol* (22.43 g, 99.6%). $[\alpha]_D^{22} = -18.5°$; $[\alpha]_{578}^{22} = -19.2°$; $[\alpha]_{546}^{22} = -21.7°$; $[\alpha]_{436}^{22} = -36.4°$; $[\alpha]_{365}^{22} = -56.1°$ ($c = 2.465$).

(1R,2S)-3,3-Ethylenedioxy-2-(2,2-dimethylpropoxy)-1,7,7-trimethylbicyclo[2.2.1]heptane (**12**) *and its (1S,2R)-Enantiomer.* A soln. of **11** (72 g, 0.34 mol) in *N*-methylpyrrolidone (180 ml) was added within 15 min to a suspension of NaH (washed previously with pentane; 12.3 g, 0.513 mol) in *N*-methylpyrrolidone (180 ml) at −15°. The mixture was allowed to warm up to 0° within 50 min and then stirred at 0° for 1 h and at r.t. for 2 h. Neopentyl bromide (132 ml, 1.04 mol) in *N*-methylpyrrolidone (135 ml) was added to this mixture at +110° within 4 h. Heating the mixture at +100° for further 12 h, then at +130° for 18 h, workup, evaporation of the *N*-methylpyrrolidone (b.p. 44°/0.1 Torr), and chromatography of the residue (hexane/EtOAc 39:1) furnished **12** (88.26 g, 92.1%). GC (B, 142°): 13.15. IR: 2960, 2880, 1480, 1465, 1390, 1365, 1320, 1310, 1100, 1040, 1020, 990. ^{1}H-NMR (100 MHz): 0.80 (*s*, 3 H); 0.86 (*s*, 3 H); 0.90 (*s*, 9 H); 1.18 (*s*, 3 H); 1.45–1.75 (5 H); 2.93 (*s*, 1 H); 2.95 (*d*, $J = 8$, 1 H); 3.21 (*d*, $J = 8$, 1 H); 3.7–4.0 (4 H). ^{13}C-NMR: 116.0 (*s*), 93.8 (*d*), 82.5 (*t*), 65.1 (*t*), 63.2 (*t*), 53.4 (*d*), 50.4 (*s*), 47.8 (*s*); 34.2 (*t*), 32.4 (*s*), 26.8 (*q*) 21.1 (*q*), 20.9 (*q*), 20.6 (*t*), 11.7 (*q*). MS: 282 (3, $C_{17}H_{30}O_3^+$), 267 (11), 195 (17), 194 (13), 141 (48), 127 (100), 99 (49), 73 (49), 71 (68), 55 (56).

Following the above procedure, (1*S*,2*R*)-3,3-ethylenedioxy-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (21.3 g, 0.1 mol) was alkylated to afford *(1S,2R)-3,3-ethylenedioxy-2-(2,2-dimethylpropoxy)-1,7,7-trimethylbicyclo-[2.2.1]heptane* (26.2 g 92.3%). $[\alpha]_D^{22} = +21.2°$; $[\alpha]_{578}^{22} = +22.2°$; $[\alpha]_{546}^{22} = +25.2°$; $[\alpha]_{436}^{22} = +42.8°$; $[\alpha]_{365}^{22} = +67.1°$ ($c = 2.675$).

(1S,3S)3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]heptan-2-one (**13**) *and its (1R,3R)-Enantiomer.* Acetal **12** (17.13 g, 60.75 mmol) was stirred vigorously in 50% aq. H_2SO_4 (200 ml) at +60° for 24 h. Workup gave crude **13** (14.1 g) which was directly converted to **14**. For its characterization, crude **13** was chromatographed (hexane/EtOAc 19:1) to give pure **13** (13.9 g, 96%). IR: 2960, 2880, 1750, 1480, 1120, 1015. ^{1}H-NMR (100 MHz): 0.9 (*s*, 12 H); 1.0 (*s*, 3 H); 1.05 (*s*, 3 H); 1.32–1.92 (4 H); 2.09 (*m*, 1 H); 3.06 (*s*, 1 H); 3.12 (*d*, $J = 8$, 1 H); 3.72 (*d*, $J = 8$, 1 H). ^{13}C-NMR: 217.7 (*s*), 86.6 (*d*), 83.0 (*t*), 59.4 (*d*), 50.0 (*s*), 46.1 (*s*), 33.8 (*t*), 32.3 (*s*), 26.7 (*q*), 21.2 (*q*), 20.9 (*t*), 18.6 (*q*), 10.8 (*q*). MS: 238 (1, $C_{15}H_{26}O_2^+$), 152 (15), 141 (36), 123 (17); 81 (11), 72 (100), 71 (55), 55 (40).

Following the above procedure, (1*S*,2*R*)-3,3-ethylenedioxy-2-(2,2-dimethylpropoxy)-1,7,7-trimethylbicyclo[2.2.1]heptane (26.2 g, 92.8 mmol) was hydrolyzed to give, after chromatography, *(1R,3R)-3-(2,2-dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]heptan-2-one* (20.8 g, 94.1%). $[\alpha]_D^{22} = +169.5°$; $[\alpha]_{578}^{22} = +178.4°$; $[\alpha]_{546}^{22} = +208.3°$; $[\alpha]_{436}^{22} = +430.6°$; $[\alpha]_{365}^{22} = +1135°$ ($c = 2.060$).

(1S,2R,3S)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (**14**). A soln. of **13** (62.18 g, 261 mmol) in MeOH (200 ml) was added during 45 min to a suspension of $NaBH_4$ (9.8 g, 258 mmol) in MeOH (500 ml) at −15°. The mixture was allowed to warm up to 0° during 1 h, then was kept at 0° for 1 more h, and hydrolyzed by addition of 15% aq. HCl until pH 5 was reached. Evaporation of MeOH followed by workup and medium-pressure chromatography (hexane/EtOAc 39:1) afforded pure **14** (52.53 g, 83.4%). M.p. 4–5° (pentane, −30°). GC (C, 110° + 5°/min): 4.81. $[\alpha]_D^{25} = -42.4°$; $[\alpha]_{578}^{25} = -44.3°$; $[\alpha]_{546}^{25} = -50.3°$; $[\alpha]_{436}^{25} = -85.7°$; $[\alpha]_{365}^{25} = -135.4°$ ($c = 1.10$). IR ($CHCl_3$): 3500, 2950, 1480, 1460, 1390, 1130, 1100, 1070. ^{1}H-NMR (100 MHz): 0.8 (*s*, 3 H); 0.94 (*s*, 3 H); 0.96 (*s*, 9 H); 1.1 (*s*, 3 H); 1.2–1.8 (5 H); 3.04 (*d*, $J = 5$, 1 H; disappears with D_2O); 3.22 (*s*, 2 H); 3.24 (*d*, $J = 7$, 1 H); 3.80 (*dd*, $J = 5, 7$, 1 H; *d*, $J = 7$ on exchange with D_2O). ^{13}C-NMR: 88.3 (*d*), 83.9 (*t*), 76.3 (*d*), 51.6 (*d*), 49.3 (*s*), 46.3 (*s*), 33.5 (*t*), 32.4 (*s*), 26.7 (*q*), 24.0 (*t*), 21.7 (*q*), 21.0 (*q*), 11.5 (*q*). MS: 240 (3, $C_{15}H_{28}O_2^+$), 152 (11), 136 (18), 121 (21), 109 (21), 99 (16), 95 (18), 71 (100), 69 (16), 60 (19), 57 (16), 55 (21), 43 (64).

(1R,2S,3R)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (**18**). Following the above procedure, (1*R*,3*R*)-3-(2,2-dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]heptan-2-one (62.18 g, 261 mmol) was reduced to give pure **18** (49.97 g, 79.7%). M.p. 4–5° (pentane, −30°). $[\alpha]_D^{26} = +42.6°$; $[\alpha]_{578}^{26} = +44.4°$; $[\alpha]_{546}^{26} = +50.4°$; $[\alpha]_{436}^{26} = +86.2°$; $[\alpha]_{365}^{26} = +136.2°$ ($c = 2.52$).

(1S,2R,3S)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl Acrylate (**15**). Acryloyl chloride (144 µl, 1.77 mmol) was added slowly to a mixture of **14** (212 mg, 0.883 mmol), Et_3N (245 µl, 1.77 mmol), and 4-(dimethylamino)pyridine (16 mg, 0.13 mmol) in CH_2Cl_2 (9 ml). The mixture was kept at r.t. for 15 h, then washed with 10% aq. NaOH to give, after workup and chromatography (hexane/EtOAc 80:1), pure **15** (237 mg, 91%). IR: 2960, 2889, 1720, 1620, 1475, 1410, 1300, 1290, 1200, 1190, 1135, 1110, 810. IR (after addition of $TiCl_4$ (1 mol-equiv.)): 1640, 1575, 1478, 1420, 1360, 1350, 1135, 1110, 810. ^{1}H-NMR: 0.81 (*s*, 3 H); 0.84 (*s*, 9 H); 0.93 (*s*, 3 H); 1.15 (*s*, 3 H); 1.0–1.83 (5 H); 3.01 (*d*, $J = 7.5$, 1 H); 3.11 (*d*, $J = 7.5$, 1 H); 3.30 (*d*, $J = 7$, 1 H); 4.80 (*d*, $J = 7$, 1 H); 5.80 (*dd*, $J = 2, 10$, 1 H); 5.91 (*dd*, $J = 10, 17$, 1 H); 6.37 (*dd*, $J = 2, 17$, 1 H). MS: 294 (2, $C_{18}H_{30}O_3^+$), 222 (17), 194 (11), 136 (17), 135 (15), 121 (20), 114 (30), 108 (15), 71 (47), 55 (100).

(1R,2S,3R)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl Acrylate (**19**). AgCN (3.9 g, 29.1 mmol) was added to a mixture of **18** (5.0 g, 20.8 mmol) and acryloyl chloride (5.65 g, 62.4 mmol) in benzene (100 ml). Heating under reflux for 18 h, filtration through *Celite*, workup and flash chromatography (hexane/EtOAc 19:1) gave **19** (5.89 g, 96%).

Cycloadditions of Cyclopentadiene to 15 and 19. – Diels-Alder *Reaction of* **15**. A 1M soln. of $TiCl_2$ (i-PrO)$_2$ in CH_2Cl_2 ($TiCl_4$/Ti(i-PrO)$_4$ 1:1; 0.86 ml, 0.86 mmol) was added to a soln of **15** (167 mg, 0.57 mmol) in CH_2Cl_2 (6.5 ml) at −20°. After 1 h, a freshly prepared 1.21M soln. of cyclopentadiene in CH_2Cl_2 (1.41 ml, 1.7 mmol) was added. The mixture was kept at −20° for 4 h, then subjected to workup to give **20a–23a** (193 mg, 94%; containing no starting **15** according to ^{1}H-NMR).

Following the anal. methods described below, the adduct mixture was reduced to give a 96:4 mixture (GC) of alcohols **20b** + **22b**/**21b** + **23b**. ^{19}F-NMR analysis of *Mosher* esters indicated a 99.7:0.3 ratio of **20c**/**22c**. HPLC of *Pirkle* carbamates showed a 99.6:0.4 ratio of **20d**/**22d**.

Diels-Alder *Reaction of* **19**. *Method A* (see *Table, Entry 2*). Acrylate **19** (157 mg, 0.53 mmol) was treated with $TiCl_2$ (i-PrO)$_2$ and cyclopentadiene as described above to give crude **20a–23a** (188.5 mg, 98%; containing no starting **19** according to ^{1}H-NMR). IR ($CHCl_3$): 2958, 2870, 1715, 1270, 1172, 1110. ^{1}H-NMR: 0.76 (*s*, 3 H); 0.8–1.1 (2 H); 0.91 (*s*, 12 H); 1.09 (*s*, 3 H); 1.2–1.35 (2 H); 1.35–1.55 (3 H); 1.6–1.7 (2 H); 1.94 (*m*, 1 H); 2.9 (br. *s*, 1 H); 2.95 (*d*, *J* = 8, 1 H); 3.19 (*d*, *J* = 7, 1 H); 3.21 (*m*, 1 H); 3.25 (*d*, *J* = 8, 1 H); 4.65 (*d*, *J* = 7, 1 H); 6.01 (*m*, 1 H); 6.18 (*m*, 1 H). MS: no $C_{23}H_{36}O_3^+$, 121 (31), 119 (99), 117 (100), 84 (15), 82 (22), 71 (28).

After reduction, GC showed a 95:5 mixture of **20b** + **22b**/**21b** + **23b**. After preparation of the corresponding derivatives, ^{19}F-NMR exhibited a 99.7:0.3 ratio of **20c**/**22c**, and a 99.55:0.45 ratio was determined for the carbamates **20d**/**22d** by HPLC.

Method B (see *Table, Entry 3*). A 2M soln. of $TiCl_2$ (EtO)$_2$ in CH_2Cl_2 ($TiCl_4$/Ti(EtO)$_4$ 1:1; 10.2 ml, 20.4 mmol) was added to a soln. of **19** (2.0 g, 6.79 mmol) in CH_2Cl_2 at −30°. After 30 min at −30°, a 4.84M soln. of cyclopentadiene in CH_2Cl_2 (4.2 ml, 20.4 mmol; precooled to −78°) was added. The mixture was kept at −30° for 4 h to give, after workup, **20a–23a** (2.34 g, 97%). After reduction, GC (C, 40–50°, 1°/min) showed a 97.6:2.4 ratio of **20b** + **22b**/**21b** + **23b**. By means of HPLC, a 99:1 ratio of **20d**/**22d** was determined.

endo-*Bicyclo[2.2.1]hept-5-ene-2-methanol* (**20b**/**22b**). a) *From (±)-Methyl Bicyclo[2.2.1]hept-5-ene-2-carboxylate*. The crude mixture obtained on thermal addition of cyclopentadiene to methyl acrylate [28] (1 g, 6.58 mmol) was stirred with $LiAlH_4$ (250 mg, 6.58 mmol) in Et_2O (70 ml) at r.t. for 1 h. Quenching of the mixture by addition of sat. aq. Na_2SO_4, drying with $MgSO_4$, and bulb-to-bulb distillation afforded a 77:23 mixture of *endo*- and *exo*-bicyclo[2.2.1]hept-5-ene-2-methanols (780 mg, 96%). GC (D, 140°): 13.2 (77), 15.6 (23). GC (E, 120°): 25 (77), 29 (23). Prep. GC (E, 120°) furnished pure (±)-endo-*bicyclo[2.2.1]hept-5-ene-2-methanol*. B.p. (bath) 100°/20 Torr. IR (film): 3350, 2960, 2860, 1345, 1035. ^{1}H-NMR (100 MHz): 0.54 (*m*, 1 H); 1.1–1.6 (3 H); 1.84 (*m*, 1 H); 2.3 (*m*, 1 H); 2.7–3.05 (2 H); 3.1–3.6 (2 H); 5.98 (*dd*, *J* = 2.5, 6, 1 H); 6.16 (*dd*, *J* = 2.5, 6, 1 H). MS: 124 (4, $C_8H_{12}O^+$), 106 (2), 91 (8), 77 (9), 66 (100).

b) *From the Adduct Mixture Obtained from* **15**/*Cyclopentadiene*. Reduction of the mixture (193 mg) as described above gave, according to GC (D, 140°), a 96:4 mixture of **20b** + **22b**/**21b** + **23b** (150 mg, 95%) from which the *endo*-isomers were separated by prep. GC (E, 120°).

c) *From the Adduct Mixture Obtained from* **19**/*Cyclopentadiene*. Reduction of the mixture (300 mg, obtained by *Method B*) with $LiAlH_4$ as described above gave 197 mg (99%) of recovered **18** and, according to GC (C, 40–50°, 1°/min), a 97.6:2.4 mixture of **20b** + **22b**/**21b** + **23b** (95 mg, 92%) from which the *endo*-isomers were separated by prep. GC (D, 120°). $[\alpha]_D^{20} = -80.7°$; $[\alpha]_{578}^{20} = -84.4°$; $[\alpha]_{546}^{20} = -96.4°$; $[\alpha]_{436}^{20} = -168.0°$; $[\alpha]_{365}^{20} = -272.6°$ (*c* = 0.60, EtOH).

(endo-*Bicyclo[2.2.1]hept-5-en-2-yl)methyl 3,3,3-Trifluoro-2-methoxy-2-phenylpropionates* (= Mosher *Esters;* **20c**/**22c**). Dicyclohexylcarbodiimide (7.5 mg, 0.0363 mmol) was added at r.t. to **20b**/**22b** (3 mg, 0.0242 mmol), (+)-(*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid (8.5 mg, 0.0363 mmol), and 4-(dimethylamino)pyridine (0.4 mg) in CH_2Cl_2 (1 ml). Stirring for 1 h, subsequent filtration, and prep. TLC (hexane/EtOAc 19:1) furnished an inseparable mixture **20c**/**22c** (8 mg, 97%). Data of a 1:1 mixture **20c**/**22c**: IR (CCl_4): 3060, 2970, 2940, 2865, 1755, 1250, 1185, 1170, 1120, 1020. ^{1}H-NMR (100 MHz): 0.4–2.8 (4 H); 2.5 (*m*, 1 H); 2.82 (*m*, 2 H); 3.55 (*s*, 1.5 H); 3.56 (*s*, 1.5 H); 3.9–4.4 (2 H); 5.92 (*m*, 1 H); 6.18 (*m*, 1 H); 7.3–8.2 (5 H). MS: no $C_{18}H_{19}F_3O_3^+$, 275 (32), 243 (15), 189 (48), 79 (16), 66 (100). ^{19}F-NMR (94.1 MHz, C_6F_6): 93.26 (*s*, 3 F); 93.15 (*s*, 3 F). ^{19}F-NMR (Eu(fod)$_3$): 2*s* of equal intensity; signal of **20c** 0.15 ppm upfield from that of **22c**.

Following the same procedure, **20b**/**22b** resulting from the addition of cyclopentadiene to **15** (8 mg, 0.065 mmol) were esterified to give a 99.7:0.3 mixture **20c**/**22c** (21 mg, 96%). The precision of these measurements was tested as follows: To the soln. of virtually pure **20c** (10 mg) in $CDCl_3$ (0.4 ml), aliquots of a soln. of **22c** in $CDCl_3$

(+0.2, 0.4, 0.6, 0.8, 1.6, 3.2%) were added; integration of the major ^{19}F-NMR peak deviated by maximal 0.3% from the theoretical values.

O-*(endo-Bicyclo[2.2.1]hept-5-en-2-yl)methyl N-[(1R)-1-(1-Naphthyl)ethyl] Carbamates* (**20d/22d**). (–)-(*R*)-1-(1-naphthyl)ethyl isocyanate (15 µl, 0.088 mmol) followed by 2-(*N,N*-dimethylamino)ethanol (1 µl) were added to a soln. of **20b/22b** (1:1, 10 mg, 0.08 mmol) in benzene (0.8 ml). Then the mixture was heated in a closed *Pyrex* tube at 80° for 3 d. Evaporation and rapid chromatography of the residue (SiO_2, 0.5 g; hexane/EtOAc 3:1) gave **20d/22d** (1:1; 25 mg, 97%). HPLC: 88 (**20d**, 51.2%), 98 (**22d**, 48.8%). IR: ($CDCl_3$): 3320, 3055, 2980, 1710, 1665, 1520, 1410, 1265. ^{1}H-NMR: 1.68 (*d*, *J* = 8, 3 H); 0.9–1.8 (5 H); 2.35 (*m*, 1 H); 2.8 (*m*, 1 H); 3.65 (*m*, 1 H); 3.89 (*m*, 1 H); 4.98 (*m*, 1 H); 5.67 (*m*, 1 H); 5.96 (*m*, 1 H); 6.14 (*m*, 1 H); 7.41–7.6 (4 H); 7.80 (*d*, *J* = 9, 1 H); 7.88 (*d*, *J* = 9, 1 H); 8.15 (*d*, *J* = 9, 1 H). MS: 321 (8, $C_{21}H_{23}NO_2^+$), 214 (74), 197 (22), 170 (32), 155 (61), 129 (40), 109 (14), 91 (25), 79 (82), 69 (53), 66 (100), 57 (73), 55 (71).

Following the same procedure, **20b/22b** resulting from the addition of cyclopentadiene to **15** (10 mg, 0.08 mmol) gave a 99.55:0.45 mixture (HPLC) **20/22d** (16 mg, 62%). The precision of these measurements was tested as follows: To the soln. of virtually pure **20d** (5 mg) in CH_2Cl_2 (0.4 ml) aliquots of a soln. of **22d** in CH_2Cl_2 (+0.1, 0.2, 0.3, 0.5, 0.8, 1.2%) were added; integration of the major HPLC peak deviated by maximal 0.1% from the theoretical values.

Enantiomerically pure (–)-Norborn-5-en-2-one (**26**). – *(1R,2S,3R)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl (1S,2R)-2-Hydroxybicyclo[2.2.1]hept-5-ene-2-carboxylate* (**24**). A soln. of *N*-(isopropyl)-cyclohexylamine (0.768 g, 5.44 mmol) in THF (5 ml) was added at –78° to 1.6N BuLi in hexane (3.23 ml, 5.17 mmol). After 15 min at –78°, a soln. of **22a** (0.984 g, 2.73 mmol) in THF (8 ml) was added at –78°. The mixture was kept at –15° for 3 h, then cooled to –78°, and added within 15 min at –78° to a soln. of triethyl phosphite (0.96 ml, 5.53 mmol) in THF (15 ml) through which a stream of dry O_2 was passed during the addition process. Stirring the mixture for 2 h at –78°, removal of the cooling bath, further stirring for 30 min, workup and flash chromatography (2×, hexane/EtOAc 19:1, then 39:1) gave crude **24** (0.636 g, 62%) which was recrystallized (EtOH, –25°, 2×) to afford pure **24** (0.431 g, 47%), m.p. 80–81°. IR ($CHCl_3$): 3550, 3060, 2950, 2860, 1705, 1475, 1455, 1390, 1360, 1330, 1302, 1262, 1238, 1110, 1085. ^{1}H-NMR: 0.80 (*s*, 3 H); 0.86 (*s*, 9 H); 0.91 (*s*, 3 H); 1.05 (*s*, 3 H); 0.80–1.10 (2 H); 1.4–1.7 (3 H); 1.70 (*m*, 1 H); 1.72 (*m*, 1 H); 1.97–2.03 (2 H); 2.77 (br. *s*, 1 H); 2.94 (br. *s*, 1 H); 3.02 (*d*, *J* = 8, 1 H); 3.15 (*d*, *J* = 8, 1 H); 3.27 (*s*, 1 H); 3.30 (*d*, *J* = 8, 1 H); 4.73 (*d*, *J* = 8, 1 H); 5.92 (*m*, 1 H); 6.24 (*m*, 1 H). MS: 376 (0.1, $C_{23}H_{36}O_4^+$), 288 (0.2), 260 (1), 223 (5), 154 (9), 153 (37), 135 (16), 130 (11), 121 (9), 109 (36), 108 (14), 95 (18), 94 (12), 83 (9), 81 (15), 79 (14), 72 (8), 71 (100), 70 (9), 69 (11), 67 (14), 66 (98), 60 (18), 57 (18), 55 (28).

(1S,2R)-2-Hydroxybicyclo[2.2.1]hept-5-ene-2-methanol (**25**). A mixture of **24** (431 mg, 1.15 mmol), $LiAlH_4$ (66 mg, 1.74 mmol), and Et_2O (10 ml) was stirred at r.t. for 1 h. Subsequent workup and chromatography (Et_2O/EtOAc 1:1) furnished the auxiliary **18** (243 mg, 88%) and, after crystallization (hexane), pure **25** (122 mg, 76%). M.p. 99–100°. $[\alpha]_D^{25} = -30.6°$; $[\alpha]_{578}^{22} = -32.1°$; $[\alpha]_{546}^{22} = -37.2°$; $[\alpha]_{436}^{22} = -69.8°$; $[\alpha]_{365}^{22} = -126.0°$ (*c* = 3.13, $CHCl_3$). IR ($CHCl_3$): 3570, 3100–3700 (br.), 3060, 2980, 2940, 2870, 1460, 1440, 1330, 1275, 1250, 1085, 1055, 1020, 1000, 885, 855, 660. ^{1}H-NMR: 0.9 (br. *m*, 1 H); 1.20 (*dd*, *J* = 3, 12, 1 H); 1.28 (br. *s*, 1 H); 1.6 (*s*, 1 H); 1.64 (*dd*, *J* = 8, 4, 1 H); 1.94 (*d*, *J* = 8, 1 H); 2.74 (br. *s*, 1 H); 2.88 (br. *s*, 1 H); 3.45 (*d*, *J* = 12, 1 H); 3.50 (*d*, *J* = 12, 1 H); 6.08 (*m*, 1 H); 6.18 (*m*, 1 H). MS: 140 (3, $C_8H_{12}O_2^+$), 122 (3), 109 (16), 81 (9), 79 (12), 78 (61), 77 (7), 74 (6), 67 (19), 66 (100), 65 (12).

(1S,4S)-(–)-Bicyclo[2.2.1]hept-5-en-2-one (**26**). A soln. of **25** (100 mg, 0.71 mmol) in EtOH (1 ml) was added at 0° to a buffered (pH 7.5; Na_2HPO_4) soln. of $NaIO_4$ (158 mg, 0.74 mmol) in H_2O (2 ml). Stirring for 2 h at r.t., addition of another portion of $NaIO_4$ (22 mg, 0.1 mmol), stirring for another 30 min, followed by addition of H_2O (5 ml) and pentane (15 ml), extraction with pentane, drying of the extracts with $MgSO_4$, careful removal of solvent by distillation through a *Vigreux* column, and bulb-to-bulb distillation of the residue at 100° (bath)/50 Torr furnished **26** (67 mg, 87%). $[\alpha]_D^{28} = -1152°$; $[\alpha]_{578}^{28} = -1221°$; $[\alpha]_{546}^{28} = -1449°$; $[\alpha]_{436}^{28} = -3259°$; $[\alpha]_{365}^{28} = -8543°$ (*c* = 1.46, isooctane). IR (film): 3060, 2970, 1755, 1740, 1320, 1220, 1160, 1135, 1120, 985, 855, 765, 735, 705. ^{1}H-NMR: 1.85 (*dd*, *J* = 4.5, 14.5, 1 H); 1.92–2.05 (2 H); 2.20 (*m*, 1 H); 3.02 (*m*, 1 H); 3.20 (br. *s*, 1 H); 6.21 (*m*, 1 H); 6.58 (*dd*, *J* = 2.5, 5.5, 1 H). MS: 108 (17, $C_7H_8^+$), 80 (13), 78 (7), 67 (100).

(1S,2S)-Bicyclo[2.2.1]hept-5-en-2-yl (1S)-3-Oxo-4,7,7-trimethyl-2-oxabicyclo[2.2.1]heptan-1-carboxylate (**27**). $NaBH_4$ (11 mg, 0.25 mmol) was added to a soln. of **26** (27 mg, 0.25 mmol) in MeOH (8 ml) at –78°. Warming up of the mixture to r.t. overnight, addition of aq. 2N HCl (0.3 ml), evaporation of the MeOH, and workup gave *(1S,2S)-bicyclo[2.2.1]hept-5-en-2-ol* (23 mg, 84%). GC (C, 40–220°, 8°/min): 3.06. IR: 3585, 3440, 3060, 2970, 2940, 2870, 1705, 1460, 1445, 1395, 1340, 1110, 1060, 1045, 835. ^{1}H-NMR: 0.77 (*dt*, *J* = 13, 3, 1 H); 1.28 (*d*, *J* = 9, 1 H); 1.48 (*m*, 1 H); 1.5–1.8 (1 H), 2.10 (*ddd*, *J* = 4, 8, 12, 1 H); 2.83 (br. *s*, 1 H); 3.0 (br. *s*, 1 H); 4.48 (*m*, 1 H); 6.04 (*dd*, *J* = 3, 6, 1 H); 6.45 (*dd*, *J* = 3, 6, 1 H). MS: 110 (7, $C_7H_{10}O^+$), 67 (10), 66 (100), 65 (11). AgCN (42 mg, 0.32

mmol) was added to a mixture of (−)-camphanoyl chloride (89 mg, 0.42 mmol) and (1*S*, 2*S*)-bicyclo[2.2.1]hept-5-en-2-ol (23 mg, 0,21 mmol) in benzene (5 ml). Heating of the mixture under reflux for 18 h, filtration through *Celite*, workup and chromatography (hexane/EtOAc 9:1; collecting several fractions before and after elution of **27**) afforded **27** (55 mg, 90%). GC (C, 150°): 13.92 (99.7), 14.19 (0.3). IR ($CHCl_3$): 2970, 2870, 1785, 1740, 1720, 1340, 1312, 1273, 1170, 1105, 1060. ^{1}H-NMR: 0.9–1.2 (1 H); 0.94 (*s*, 3 H); 1.04 (*s*, 3 H); 1.10 (*s*, 3 H); 1.36 (*m*, 1 H); 1.52 (*m*, 1 H); 1.68 (*m*, 1 H); 1.90 (*m*, 1 H); 2.00 (*ddd*, *J* = 4, 10, 12, 1 H); 2.22 (*ddd*, *J* = 4, 8, 12, 1 H); 2.35 (*m*, 1 H); 2.89 (br. *s*, 1 H); 3.22 (*m*, 1 H); 5.40 (*m*, 1 H); 5.98 (*dd*, *J* = 3, 6, 1 H); 6.35 (*dd*, *J* = 4, 6, 1 H). MS: 290 (1, $C_{17}H_{22}O_4^+$), 225 (42), 181 (13), 153 (43), 125 (16), 109 (25), 97 (18), 93 (13), 91 (22), 83 (55), 81 (14), 79 (12), 77 (15), 67 (23), 66 (100), 65 (17), 55 (42).

Analogous esterification of (±)-*endo*-8,9,10-trinorborn-5-en-2-ol with (−)-camphanoyl chloride gave a mixture of diastereoisomers: GC (C, 150°): 13.86 (50.3), 14.26 (49.7).

Asymmetric *Diels-Alder* Addition of 1,3-Butadiene to 15. – *(1S,2R,3S)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl (1R)-Cyclohex-3-ene-1-carboxylate* (**29**). At −20°, 1,3-butadiene (284 mg, 5.2 mmol) was condensed into a 5-ml flask. Successive addition of a soln. of **15** (384 mg, 1.3 mmol) in CH_2Cl_2 (3 ml) and of freshly distilled $TiCl_4$ (346 mg, 1.82 mmol) at −8°, stirring of the mixture at −8° for 112 h, and workup gave **29** (454 mg, 98%). IR (film): 3020, 2950, 2870, 1730, 1475, 1455, 1432, 1220, 1165, 1110. ^{1}H-NMR: 0.80 (*s*, 3 H); 0.89 (*s*, 9 H); 0.93 (*s*, 3 H); 0.8–1.1 (3 H); 1.13 (*s*, 3 H); 1.30 (*m*, 1 H); 1.4–1.8 (3 H); 1.97–2.15 (2 H); 2.22–2.35 (2 H); 2.55 (*m*, 1 H); 2.98 (*d*, *J* = 8, 1 H); 3.15 (*d*, *J* = 8, 1 H); 3.28 (*d*, *J* = 7.5, 1 H); 4.74 (*d*, *J* = 7.5, 1 H); 5.68 (br. *s*, 2 H). MS: 348 (7, $C_{22}H_{36}O_3^+$), 223 (42), 222 (100), 194 (44), 153 (43), 152 (28), 136 (49), 135 (30), 134 (34), 121 (21), 109 (57), 108 (30), 81 (75), 79 (12), 71 (71), 55 (39).

(1R)-(+)-Cyclohex-3-ene-1-methanol (**30**). A mixture of **29** (508 mg, 1.46 mmol) and $LiAlH_4$ (91 mg, 2.4 mmol) in Et_2O (30 ml) was stirrd at r.t. for 18 h. Slow addition of sat. aq. Na_2SO_4, followed by workup and flash chromatography (Et_2O/CH_2Cl_2 1:9) gave recovered auxiliary **14** (153 mg, 93%; fully characterized by IR, ^{1}H-NMR, and MS) and **30** (330 mg, 94%). $[\alpha]_D^{22} = +87.9°$; $[\alpha]_{578}^{22} = +91.3°$; $[\alpha]_{546}^{22} = +103.5°$; $[\alpha]_{436}^{22} = +168.7°$; $[\alpha]_{365}^{22} = +202.4°$ (*c* = 0.904, MeOH). $[\alpha]_D^{22} = +95.9°$; $[\alpha]_{578}^{22} = +106.1°$; $[\alpha]_{546}^{22} = +120.5°$; $[\alpha]_{436}^{22} = +205.4°$; $[\alpha]_{365}^{22} = +324.6°$ (*c* = 6.00, $CHCl_3$). IR (film): 3050–3650, 3020, 2910, 2830, 1430, 1022, 650. ^{1}H-NMR: 1.30 (*m*, 1 H); 1.43 (*s*, 1 H; disappears with D_2O); 1.6–1.9 (3 H); 2.0–2.2 (3 H); 3.45–3.7 (2 H); 5.70 (*s*, 2 H). MS: 112 (2, $C_7H_{12}O^+$), 94 (42), 81 (28), 79 (100), 77 (14), 54 (1), 53 (16).

(1R)-(+)-Cyclohex-3-ene-1-carboxylic Acid (**31**). *Jones'* reagent (2.75 ml, 3.66 mmol) was added to a vigorously stirred *(Vibromix)* soln. of **30** (153 mg, 1.36 mmol) in acetone (30 ml) at r.t. Stirring of the mixture for 4 min, followed by injection of i-PrOH (1 ml), stirring for 1 min, workup and bulb-to-bulb distillation 155° (bath)/15 Torr gave **31** (153 mg, 89%). $[\alpha]_D^{22} = +87.3°$; $[\alpha]_{578}^{22} = +90.0°$; $[\alpha]_{546}^{22} = +103.4°$; $[\alpha]_{436}^{22} = +176.9°$; $[\alpha]_{365}^{22} = +280,2°$ (*c* = 1.60, MeOH). IR (film): 3500–2400 (br.), 3022, 2910, 2840, 1705, 1650, 1455, 1440, 1420, 1240. ^{1}H-NMR: 1.73 (*m*, 1 H); 2.0–2.2 (3 H); 2.25–2.40 (2 H); 2.62 (*m*, 1 H); 5.6–5.8 (2 H); 10.6–11.6 (1 H). MS: 126 (19, $C_7H_{10}O_2^+$), 108 (27), 81 (100), 80 (66), 79 (38), 77 (13), 67 (11), 54 (32), 53 (19), 51 (10).

The amidinium carboxylate, prepared from **31** and 3,3,6,9,9-pentamethyl-2,10-diazabicyclo[4.4.0]dec-1-ene [28] melts at 159° (after 2 crystallizations from hexane/EtOAc 24:1; 88%).

(1R)-N-[(1R)-1-(1-Naphthyl)ethyl]cyclohex-3-ene-carboxamide (**32**). Successive addition of *N*-ethylmorpholine (96 µl, 0.76 mmol), a 50% soln. of propylphosphonic anhydride [29] in CH_2Cl_2 (140 mg, 0.22 mmol) and DMF (1 ml) to a mixture of **31** (20 mg, 0.16 mmol) and (−)-(*S*)-methyl(1-naphthyl)amine (55 mg, 0.32 mmol) in DMF (1 ml) at 0°, followed by stirring of the mixture at 0° and at +20° for 1 h and 18 h, resp., evaporation at 0.5 Torr and workup gave **32** (42 mg, 94%). IR (CCl_4): 3440, 3020, 2925, 2840, 1673, 1600, 1492, 1450, 1220, 1175, 645. ^{1}H-NMR: 1.68 (*d*, *J* = 6, 3 H); 1.6–2.4 (7 H); 5.6–5.75 (2 H); 5.8 (*m*, 1 H); 5.95 (*quint*. *J* = 6, 1 H); 7.4–7.6 (4 H); 7.83 (*d*, *J* = 9, 1 H); 7.88 (*d*, *J* = 9, 1 H); 8.10 (*d*, *J* = 9, 1 H). MS: 279 (44, $C_{19}H_{21}NO^+$), 156 (24), 155 (100). GC (C, 165°): 38.81 (2.2), 39.95 (97.8). HPLC (*µ-Porasil*, hexane/EtOAc 9:1, 1 ml/min): 54.6 (97.5), 59.4 (2.5). Amidation of (±)-cyclohex-3-ene-1-carboxylic acid with (−)-(*S*)-methyl-(1-naphthyl)amine gave a mixture of diastereoisomers. GC (C, 165°): 40.24 (49.9), 41.08 (50.1). HPLC (*µ-Porasil*, hexane/EtOAc 9:1, 0.6 ml/min): 100.2 (49.3), 108.8 (50.7).

Attempted *Diels-Alder* Addition of Cyclopentadiene to Crotonate 35. – *(E)-3-(1S,2R,3S)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl Crotonate* (**35**). AgCN (2.34 g, 17.48 mmol) was added to a mixture of **14** (3.0 g, 12.48 mmol) and (*E*)-crotonoyl chloride (3.91 g, 37.44 mmol) in toluene (60 ml). Heating of the mixture at 100° for 18 h, filtration through *Celite*, workup and flash chromatography (hexane/EtOAc, 19:1) gave **35** (3.54 g, 92%). IR (film): 3060, 3040, 2960, 2880, 2820, 1730, 1665, 1480, 1460, 1450, 1180, 1115, 970, 840. ^{1}H-NMR: 0.81 (*s*, 3 H); 0.84 (*s*, 9 H); 0.92 (*s*, 3 H); 1.0–1.15 (2 H); 1.14 (*s*, 3 H); 1.48 (*m*, 1 H); 1.72 (*m*, 1 H); 1.78 (*d*, *J* = 5, 1 H); 1.86 (*dd*, *J* = 1.5, 7, 3 H); 2.99 (*d*, *J* = 8, 1 H); 3.11 (*d*, *J* = 8, 1 H); 3.30 (*d*, *J* = 7, 1 H); 4.79 (*d*,

J = 6.5, 1 H); 5.83 (*dq*, J = 15, 1.5, 1 H); 6.93 (*dq*, J = 15, 7, 1 H). MS: 308 (0.8, $C_{19}H_{32}O_3^+$), 223 (16), 222 (88), 198 (10), 195 (12), 194 (68), 152 (36), 136 (24), 123 (24), 121 (32), 109 (28), 108 (28), 95 (36), 71 (40), 69 (100).

Attempted Cycloadditions of **35** *to Cyclopentadiene.* Crotonate **35** (61 mg, 0.2 mmol) was treated successively with a *Lewis* acid and cyclopentadiene (5 mol-equiv.) in CH_2Cl_2. Periodically samples were submitted to workup and analyzed by GC (C, 110–230°, 10°/min): 6.25 (**35**); 9.93 (**36**, tentatively assigned). Moreover, those samples were reduced with $LiAlH_4$ as described above to give **14**/**37** [20]. GC (C, 40–225°, 10°/min). 4.16 (**37**), 9.56 (**14**). Monitoring the reactions by those two analyses gave the following ratios for **35**/**36**: a) $TiCl_2(EtO)_2$ (3 mol-equiv., 0°) and 4 h: 96.7:3.0; 18 h: 92.0:7.1, polymerization. b) $TiCl_2(EtO)_2$ (3 mol-equiv., +25°) and 3 h: 93.9:4.6; 18 h: 89.7:5.1, polymerization. c) $TiCl_4$ (1.5 mol-equiv., 0°) and 4 h: 99.1:0.4, polymerization.

Enantioselective Synthesis of (−)-β-Santalene. – *(1S,2R,3S)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl Bromoacetate* (**42a**). Bromoacetyl bromide (1.423 ml, 16.34 mmol) was added to **14** (1.961 g, 8.17 mmol) and AgCN (1.533 g, 11.44 mmol) in benzene (47 ml) under reflux. Heating the mixture under reflux for further 20 min, filtration through *Celite* and chromatography (hexane/EtOAc 39:1) gave **42a** (2.95 g, 100%). IR (CCl_4): 2950, 1754, 1730, 1470, 1280, 1110. ^{1}H-NMR (100 MHz): 0.80 (*s*, 3 H); 0.89 (*s*, 9 H); 0.92 (*s*, 3 H); 1.11 (*s*, 3 H); 1.0–1.8 (5 H); 3.02 (*d*, J = 8, 1 H); 3.12 (*d*, J = 8, 1 H); 3.3 (*d*, J = 7, 1 H); 3.84 (*s*, 2 H); 4.74 (*d*, J = 7, 1 H). MS: no $C_{17}H_{29}BrO_3^+$, 222 (20), 194 (11), 182 (12), 180 (12), 153 (13), 152 (18), 137 (17), 136 (31), 135 (22), 134 (22), 130 (31), 121 (46), 119 (95), 117 (100), 109 (19), 108 (24), 95 (25), 71 (62).

[(1S,2R,3S)-(3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-yloxy)carbonylmethyl]triphenylphosphonium Bromide (**42b**). A mixture of **42a** (2.95 g, 8.17 mmol) and Ph_3P (2.28 g, 8.69 mmol) in benzene (10.5 ml) was heated under reflux for 15 h. Evaporation of the mixture and crystallization of the residue from CCl_4 furnished **42b** (5.09 g, 100%). M.p. 185°. IR ($CHCl_3$): 2950, 1725, 1440, 1110. ^{1}H-NMR: 0.71 (*s*, 3 H); 0.83 (*s*, 9 H); 0.87 (*s*, 3 H); 1.0 (*s*, 3 H); 0.9–1.6 (5 H); 2.92 (*d*, J = 8, 1 H); 3.07 (*d*, J = 8, 1 H); 3.2 (*d*, J = 7, 1 H); 4.49 (*d*, J = 7, 1 H); 5.29 (*dd*, J = 13, 17, 1 H); 5.54 (*dd*, J = 13, 17, 1 H); 6.7–8.0 (15 H). MS: no $C_{35}H_{44}BrO_3P^+$, 321 (17), 304 (21), 303 (100), 278 (36), 277 (60), 201 (16), 199 (12), 185 (10), 183 (17), 152 (12), 136 (25), 121 (30), 109 (17), 108 (17), 95 (17), 71 (98).

(1S,2R,3S)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]-hept-2-yl 2,3-Butadienoate (**43**). After successive addition of Et_3N (2.5 ml, 18.0 mmol) and AcCl (0.64 ml, 9.0 mmol) in CH_2Cl_2 (20 ml) to a soln. of **42b** (5.6 g, 9.0 mmol) in CH_2Cl_2 (36 ml) at 0°, the mixture was stirred at 0° for 1 h, then at +40° for 2 h. Evaporation, trituration of the residue with pentane (50 ml), filtration, evaporation of the filtrate, and distillation (145° (bath)/0.15 Torr) afforded **43** (1.46 g, 53%). IR (CCl_4): 2950, 1975, 1940, 1720, 1475, 1260, 1165, 1110, 860, 842. ^{1}H-NMR: 0.79 (*s*, 3 H); 0.86 (*s*, 9 H); 0.91 (*s*, 3 H); 1.0–1.15 (2 H); 1.10 (*s*, 3 H); 1.48 (*m*, 1 H); 1.68 (*m*, 1 H); 1.77 (*d*, J = 5, 1 H); 3.00 (*d*, J = 8, 1 H); 3.11 (*d*, J = 8, 1 H); 3.28 (*d*, J = 7, 1 H); 4.77 (*d*, J = 7, 1 H); 5.15 (*d*, J = 7, 2 H); 5.6 (*t*, J = 7, 1 H). MS: 306 (4, $C_{19}H_{30}O_3^+$), 223 (18), 222 (100), 219 (12), 194 (25), 136 (54), 135 (31), 134 (31), 130 (31), 126 (37), 121 (48), 108 (35), 71 (43).

(1S,2R,3S)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl (1R,2S)-3-Methylidenebicyclo-[2.2.1]hept-5-ene-2-carboxylate (**44**). A 1M soln. of $TiCl_2$ (i-PrO)$_2$ in CH_2Cl_2 (6 ml, 6 mmol) was added at −20° to a soln. of **43** (1.23 g, 4.02 mmol) in CH_2Cl_2 (63 ml). After 15 min, a 1.21M soln. of cyclopentadiene in CH_2Cl_2 (10 ml, 12.1 mmol) was added dropwise. The mixture was kept at −20° for 6 h, then subjected to workup and chromatography (hexane/EtOAc 39:1) to afford **44** (1.46 g, 98%; no trace amount of **43** detected by ^{1}H-NMR). IR (CCl_4): 3060, 2950, 2860, 1730, 1660, 1475, 1310, 1180, 1110, 885. ^{1}H-NMR: 0.8 (*s*, 3 H); 0.9–1.1 (2 H); 0.9 (*s*, 9 H); 0.92 (*s*, 3 H); 1.14 (*s*, 3 H); 1.40–1.55 (2 H); 1.55–1.8 (3 H); 3.02 (*d*, J = 8, 1 H); 3.15 (*d*, J = 8, 1 H); 3.18 (br. *s*, 1 H); 3.22 (br. *s*, 1 H); 3.26 (*d*, J = 7, 1 H); 3.45 (*m*, 1 H); 4.66 (*d*, J = 7, 1 H); 5.05 (br. *s*, 1 H); 5.1 (br. *s*, 1 H); 6.12 (*dd*, J = 3, 5.5, 1 H); 6.32 (*dd*, J = 3, 5.5, 1 H). MS: 372 (20, $C_{24}H_{36}O_3^+$), 224 (20), 223 (100), 222 (60), 194 (21), 154 (10), 153 (87), 135 (32), 133 (32), 71 (63).

Stereochemical Analysis of Cycloadduct **44**. Reduction of **44** (100 mg, 0.56 mmol) with $LiAlH_4$ (50 mg, 1.32 mmol) in Et_2O at r.t. for 30 min gave, after workup, **45**. GC (D, 140°): 14.1 (98.0, *endo*), 15.6 (2.0, *exo*). GC (E, 140°): 28 (98.0), 23 (2.0). After removal of the minor *exo*-alcohol by prep. GC (E, 140°), **45** (5 mg, 0.037 mmol) was esterified with (+)-(*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid, as described for **20c**/**22c**, to give **46** (13 mg, 97%). ^{19}F-NMR (Pr(fod)$_3$): only 1 peak. Analogous reduction of (±)-**39** followed by prep. GC gave (±)-**45** which was acylated with (+)-(*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid to afford the corresponding *Mosher* esters. ^{19}F-NMR (Pr(fod)$_3$): 2 signals, 46:54; the low-field signal corresponds to **46**, derived from adduct **44**. Alcohol **45** derived from **44** (12 mg) was treated with (−)-(*R*)-1-(1-naphthyl)ethyl isocyanate as described for **20d**/**22d** to give **47**. HPLC (*μ-Porasil*, 10 μm, 0.5 × 60 cm, hexane/EtOAc 24:1, 0.8 ml/min): 69 (0.5), 75 (99.5). In analogy, (±)-**45** (12.5 mg, 0.092 mmol) was treated with (−)-(*R*)-1-(1-naphthyl)ethyl isocyanate to give the corresponding carbamates (30 mg, 98%). HPLC (as above): 69 (49.6), 75 (50.4). IR (CCl_4): 3440, 3060, 2980, 1730,

1505, 1335, 1220, 1060, 885. ^{1}H-NMR: 0.8–1.8 (2 H); 1.68 (*m*, 3 H); 2.80 (br. *s*, 1 H); 2.98 (br. *s*, 1 H); 3.17 (br. *s*, 1 H); 3.3–3.7 (2 H); 4.1 (*m*, 1 H); 4.72 (br. *s*, 1 H); 4.9–5.15 (2 H); 5.68 (br. *s*, 1 H); 6.08 (*m*, 1 H); 7.4–7.65 (4 H); 7.8 (*d*, *J* = 9, 1 H); 7.88 (*d*, *J* = 9, 1 H); 8.16 (*d*, *J* = 7, 1 H). MS: 333 (11, $C_{22}H_{23}NO_2^+$), 215 (72), 200 (75), 196 (29), 170 (28), 155 (100), 129 (28), 118 (46), 117 (74), 91 (69).

(1S,2R,3S)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl (1R,2S)-3-Methylidenebicyclo[2.2.1]heptane-2-carboxylate (**48**). A 1M soln. of $NaBH_4$ (0.36 ml, 0.36 mmol) in EtOH was added to a suspension of $Ni(OAc)_2$ (89 mg, 0.36 mmol) in EtOH (1.3 ml) under H_2 (1 atm). After 30 min, a soln. of crude **44** (1.063 g, 2.86 mmol) in EtOH (1 ml) was added to the black suspension. The mixture was stirred at r.t. under H_2 (1 atm) until consumption of 71 ml of H_2 (1 mol-equiv. after 3 h). Evaporation of the mixture, trituration of the residue with Et_2O, filtration, and evaporation of the filtrates furnished **48** (1.048 g, 98%). IR (CCl_4): 2960, 2870, 1730, 1660, 1475, 1455, 1160, 1100, 890. ^{1}H-NMR: 0.8 (*s*, 3 H); 0.89 (*s*, 9 H); 0.92 (*s*, 3 H); 1.12 (*s*, 3 H); 1.0–1.7 (10 H); 1.78 (*d*, *J* = 5, 1 H); 2.66 (br. *s*, 1 H); 2.77 (br. *s*, 1 H); 3.0 (*d*, *J* = 8, 1 H); 3.2 (*d*, *J* = 8, 1 H); 3.25 (br. *s*, 1 H); 3.31 (*d*, *J* = 7, 1 H); 4.75 (*d*, *J* = 7, 1 H); 4.94 (*m*, 1 H); 5.0 (*m*, 1 H). MS: 374 (12, $C_{24}H_{38}O_3^+$), 223 (23), 222 (100), 194 (40), 153 (25), 152 (30), 136 (62), 135 (85), 134 (39), 130 (34), 123 (23), 121 (58), 108 (69), 107 (98), 79 (37), 71 (58).

(1S,2R,3S)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl (1S,2S)-3-Methylidene-2-(4-methyl-3-pentenyl)bicyclo[2.2.1]heptane-2-carboxylate (**49**). $(i\text{-}Pr)_2NH$ (0.743 ml, 5.25 mmol) was added dropwise to a mixture 1.4N BuLi in hexane (3.57 ml, 5.0 mmol) and THF (3.2 ml) at −78°. After 5 min, a soln. of **48** (935 mg, 2.5 mmol) in THF (0.36 ml) was added. Stirring at −78° for 5 min, addition of a soln. of 5-iodo-2-methyl-2-pentene (578 mg, 2.75 mmol) in hexamethylphosphorous triamide (0.5 ml), stirring at −78° for 5 h, then at r.t. for 2 h, followed by workup and two crystallizations from EtOH gave pure **49** (958 mg, 84%). M.p. 119–120°. $[\alpha]_D^{22} = -27.62°$; $[\alpha]_{578}^{22} = -28.86°$; $[\alpha]_{546}^{22} = -32.9°$; $[\alpha]_{436}^{22} = -57.97°$; $[\alpha]_{365}^{22} = -95.81°$ (*c* = 1.21, EtOH). IR (CCl_4): 3080, 2950, 2870, 1730, 1660, 1620, 1470, 1460, 1156, 1110. ^{1}H-NMR: 0.79 (*s*, 3 H); 0.9–1.9 (15 H); 0.91 (*s*, 9 H); 0.95 (*s*, 3 H); 1.11 (*s*, 3 H); 1.57 (*s*, 3 H); 1.66 (*s*, 3 H); 2.47 (br. *s*, 1 H); 2.72 (br. *s*, 1 H); 2.85 (*d*, *J* = 8, 1 H); 3.32 (*d*, *J* = 8, 1 H); 3.4 (*d*, *J* = 8, 1 H); 4.77 (*d*, *J* = 8, 1 H); 4.99 (*s*, 1 H); 5.04 (*m*, 1 H); 5.1 (*s*, 1 H). ^{13}C-NMR (90.5 MHz): 174.2 (*s*), 159.7 (*s*), 131.5 (*s*), 124.0 (*d*), 107.2 (*t*), 89.6 (*d*), 83.4 (*t*), 79.2 (*d*), 58.9 (*s*), 50.9 (*d*), 50.1 (*s*), 46.9 (*d*), 46.6 (*s*), 46.5 (*t*), 38.1 (*d*), 36.3 (*t*), 33.7 (*t*), 32.6 (*s*), 29.4 (*q*), 26.9 (*q*), 26.7 (*t*), 25 (*q*), 25.6 (*q*), 24.1 (*t*), 23.5 (*t*), 20.8 (*t*), 17.8 (*q*), 11.8 (*q*). MS: 456 (5, $C_{30}H_{48}O_3^+$), 376 (19), 375 (83), 374 (43), 287 (27), 286 (19), 223 (100), 222 (47), 217 (34), 216 (72), 202 (44), 200 (37), 189 (34), 153 (83), 135 (67), 134 (47). Anal. calc. for $C_{30}H_{48}O_3$ (456.71): C 78.90, H 10.59; found: C 78.81, H 10.35.

(1S,2S)-3-Methylidene-2-(4-methyl-3-pentenyl)bicyclo[2.2.1]heptane-2-methanol (**50**). $LiAlH_4$ (90.5 mg, 2.38 mmol) was added at −30° to a soln. of **49** (362 mg, 0.79 mmol) in Et_2O (8 ml). The mixture was allowed to warm up to r.t. and then stirred for 3 h. Addition of sat. aq. Na_2SO_4, followed by workup and chromatography (hexane/EtOAc 19:1) afforded recovered auxiliary **14** (180 mg, 95%) and **50** (163 mg, 94%). M.p. 38–40° (crystallized from pentane). $[\alpha]_D^{23} = -129.43°$; $[\alpha]_{578}^{23} = -135.86°$; $[\alpha]_{546}^{23} = -156.71°$; $[\alpha]_{436}^{23} = -289.9°$; $[\alpha]_{365}^{23} = -508.0°$ (*c* = 0.7, EtOH). IR (CCl_4): 3630, 3065, 2960, 2920, 2870, 1650, 1570, 1446, 1375, 1025, 885. ^{1}H-NMR: 0.9–2.2 (9 H); 1.61 (*s*, 3 H); 1.68 (*s*, 3 H); 1.93 (*dd*, *J* = 2, 7, 1 H); 2.10 (*m*, 1 H; disappears with D_2O); 2.26 (*m*, 1 H); 2.70 (*m*, 1 H); 3.58 (*d*, *J* = 10, 1 H); 3.62 (*d*, *J* = 10, 1 H); 4.51 (*s*, 1 H), 4.85 (*s*, 1 H); 5.11 (*t*, *J* = 6, 1 H). ^{13}C-NMR (90.5 MHz): 161.6 (*s*), 131.4 (*s*), 124.8 (*d*), 101.9 (*t*), 66.1 (*t*), 50.1 (*s*), 47.0 (*d*), 43.6 (*d*), 37.0 (*t*), 36.3 (*t*), 29.8 (*t*), 25.6 (*q*), 23.7 (*t*), 23.3 (*t*), 17.6 (*q*). MS: 220 (4, $C_{15}H_{24}O^+$), 138 (61), 120 (14), 110 (100), 95 (10), 93 (15), 92 (13), 91 (23), 82 (27). The crude **50** was esterified with (+)-(*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid to give the corresponding *Mosher* ester. GC (C, 185°, 7 psi H_2): 23.25 (100). Analogous esterification of (±)-**50** afforded the corresponding *Mosher* esters. GC (C, 185°, 7 psi H_2): 23.26 (56), 23.78 (44).

(1S,2S)-3-Methylidene-2-(4-methyl-3-pentenyl)bicyclo[2.2.1]heptane-2-carbaldehyde (**51**). A mixture of **50** (136 mg, 0.62 mmol), pyridinium chlorochromate (323 mg, 1.5 mmol), and CH_2Cl_2 (1.3 ml) was stirred at r.t. for 5 h. Dilution with Et_2O, filtration through *Celite*, concentration, filtration through charcoal and prep. TLC (hexane/EtOAc 19:1) gave **51** (115 mg, 85%). $[\alpha]_D^{22} = -11.0°$; $[\alpha]_{578}^{22} = -11.27°$; $[\alpha]_{546}^{22} = -11.91°$; $[\alpha]_{436}^{22} = -5.91°$; $[\alpha]_{365}^{22} = +87.64°$ (*c* = 2.2, $CHCl_3$). IR ($CHCl_3$): 3070, 2960, 2930, 2870, 2710, 1720, 1650, 890. ^{1}H-NMR: 1.2–1.4 (2 H); 1.45–1.75 (6 H); 1.59 (*s*, 3 H); 1.66 (*s*, 3 H); 1.75–2.10 (2 H); 2.52 (br. *s*, 1 H); 2.80 (*m*, 1 H); 4.70 (*s*, 1 H); 5.05 (br. *t*, *J* = 7, 1 H); 5.09 (*s*, 1 H); 9.63 (*s*, 1 H). ^{13}C-NMR (90.5 MHz): 204.1 (*d*), 156.3 (*s*), 132.1 (*s*), 123.9 (*d*), 105.5 (*t*), 61.9 (*s*), 46.6 (*d*), 43.2 (*d*), 37.1 (*t*), 35.7 (*t*), 29.6 (*t*), 25.6 (*q*), 24.2 (*t*), 23.4 (*t*), 17.6 (*q*). MS: 218 (33, $C_{15}H_{22}O^+$), 137 (33), 136 (100), 108 (86), 93 (12), 91 (21), 82 (42), 69 (25).

(−)-β-Santalene ((−)-**41**). Hydrazine (0.22 ml, 4.55 mmol) was added to a mixture of **51** (65 mg, 0.3 mmol) and powdered KOH (220 mg, 3.95 mmol) in ethylene glycol (1.1 ml). The mixture was heated under reflux for 5 h (bath at 160°). Addition of H_2O (2 ml) to the cold soln., extraction with pentane (4 × 5 ml), workup, and chromatography (hexane) gave pure (−)-**41** (52 mg, 85%). $[\alpha]_D^{20} = -108.89°$; $[\alpha]_{578}^{20} = -114.3°$; $[\alpha]_{546}^{20} = -131.83°$; $[\alpha]_{436}^{20} = -247.4°$; $[\alpha]_{365}^{20} = -441.24°$ (*c* = 0.776, $CHCl_3$). IR ($CHCl_3$): 3060, 2960, 2920, 2860, 1655, 1450, 1375,

1107, 878, 835, 820. ^{1}H-NMR: 1.05 (*s*, 3 H); 1.1–1.8 (8 H); 1.62 (*s*, 3 H); 1.69 (*s*, 3 H); 1.85–2.1 (2 H); 2.15 (br. *s*, 1 H); 2.68 (br. *d*, *J* = 3.5, 1 H); 4.48 (*s*, 1 H); 4.75 (*s*, 1 H); 5.12 (br. *t*, *J* = 7, 1 H). ^{13}C-NMR (90.5 MHz): 166.4 (*s*), 131.0 (*s*), 125.1 (*d*), 99.5 (*t*), 46.9 (*d*), 44.8 (*s*), 44.7 (*d*), 41.2 (*t*), 37.1 (*t*), 29.8 (*t*), 25.7 (*q*), 23.7 (*q*), 23.6 (*q*), 22.6 (*t*), 17.5 (*q*). MS: 204 (3, $C_{15}H_{24}^+$), 122 (44), 121 (13), 94 (100), 79 (19).

(−)-*β*-Santalene (92% pure) of natural origin was purified by prep. GC (F, 140°): 62. GC (C, 110°, 6 psi H_2): 10.93 (98). $[\alpha]_D^{20} = -107.8°$; $[\alpha]_{578}^{20} = -113.14°$; $[\alpha]_{546}^{20} = -130.5°$; $[\alpha]_{436}^{20} = -245.92°$; $[\alpha]_{365}^{20} = -438.78°$ (*c* = 0.8, $CHCl_3$).

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