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4-Hydroxycyclopent-2-en-1-one and Derivatives as Chiral Synthetic Equivalents of Cyclopentadienone in Asymmetric Diels-Alder reactions

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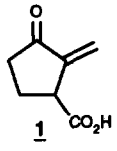
Abstract: Endo-*tricyclodecadienone* ***8a*** *and related annelated cyclopentenones (****8b****,* ***20****,* ***21a-c*** *and* ***22****) are synthesized in good chemical yield by a Diels-Alder reaction of 4-hydroxycyclopent-2-en-1-one* ***12a*** *and derivatives* ***12b-h*** *with an appropriate diene. These additions are considerably accelerated by Lewis catalysts, high pressure and by using water as solvent. Due to opposing steric and electronic effects the diastereofacial selectivity of the asymmetric cycloadditions is moderate. By carefully choosing the substrate and reaction conditions an acceptable π-facial selectivity can be achieved.*

INTRODUCTION

Since the early 1960s, when prostaglandins were isolated and their crucial role in controlling a multitude of physiologically important processes was discovered[1], cyclopentenoids constitute a rapidly growing class among the numerous biologically active natural products. In addition, related structures such as sarkomycin **1**, methylenomycin A **2** and B **3**, pentenomycin **4** and the marine eicosanoids, such as clavulone **5** and punaglandin **6** are of pharmacological and synthetic interest, because of their antibiotic and/or antitumor activity[2]. Considerable effort has therefore been devoted to designing stereo- and enantioselective total



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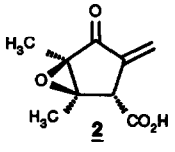

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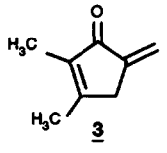

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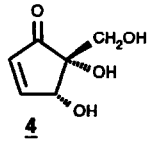

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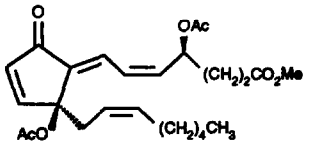

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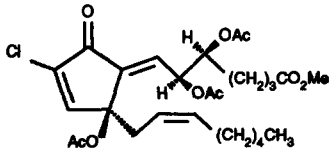

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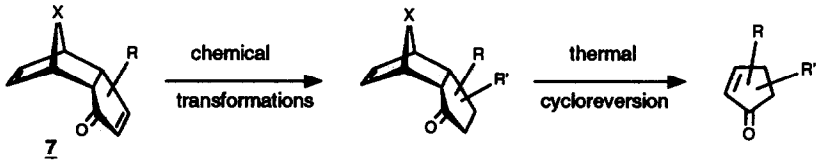
Scheme 1



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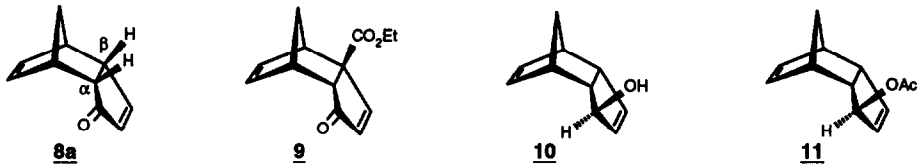
syntheses for these relatively small, but highly functionalized molecules[3-5]. We[4] and others[5] have attained access to this class of cyclopentenoids utilizing tricyclodecadienones 7 as synthetic equivalents of cyclopentadienone. The basic strategy underlying this approach, which is depicted in scheme 1, involves stereoselective nucleophilic addition to the enone moiety followed by chemical transformations to introduce the desired functionalities and thermal cycloreversion using the technique of flash vacuum thermolysis as the ultimate step to give functionalized cyclopentenones[6].

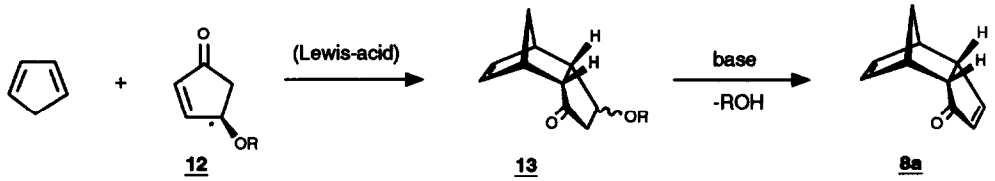
For the synthesis of enantiopure parent *endo*-tricyclodecadienone 8a, which is the pivotal starting material in this strategy, two practical methods have been reported so far. They are based on the enzymatic enantioselective hydrolysis or esterification of a suitable tricyclodecenyl precursor, *viz.* tricyclic ester 9, allylic alcohol 10 or allylic acetate 11[7].



8a 9 10 11

Both these routes suffer from the disadvantage of a kinetic enzymatic resolution, namely that of a particular enantiomer maximally 50% can be obtained enantiopure. Although interconversion of both enantiomers of 8a can be achieved by using Wharton's reaction sequence, the overall yield is generally poor[5b]. Therefore, an alternative route to this chiron was investigated.

Scheme 2



12 13 8a

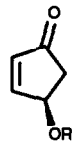
A most direct and general route to racemic *endo*-tricyclodecadienone 8a would be the crossed Diels-Alder reaction of cyclopentadienone and cyclopentadiene. However, due to the strong tendency of cyclopentadienone to dimerize[8], this approach is low yielding and has no synthetic value. In this paper readily available 4-oxycyclopent-2-en-1-ones 12 are considered as possible synthetic equivalents of cyclopentadienone in the Diels-Alder reaction[9]. The cycloaddition of dienophile 12 would lead to a 5-substituted tricyclodecadienone 13 which can undergo elimination, either spontaneously or base-induced, to

give tricyclodecadienone **8a** (Scheme 2). Enantiopure 4-substituted cyclopentenones **12** may have interesting prospects in an asymmetric Diels-Alder reaction to produce enantiomerically pure tricyclodecadienone **8a** as the ultimate product. This concept is particularly attractive because enantiopure (R)-(+)-4-acetoxycyclopent-2-en-1-one **12b** is readily available on multigram scale. In addition to acetate **12b**, (R)-(+)-4-substituted cyclopentenones **12a** and **12c-h** were synthesized to study possible substituent effects on their Diels-Alder reactions with dienes.

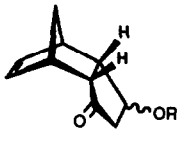
SYNTHESIS OF (R)-(+)-4-HYDROXYCYCLOPENT-2-EN-1-ONE DERIVATIVES AND THEIR DIELS-ALDER REACTIONS WITH CYCLOPENTADIENE

Synthesis

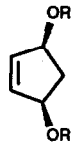
(R)-(+)-4-acetoxycyclopent-2-en-1-one **12b** can readily be prepared starting from cyclopentadiene[10-12]. Reductive singlet oxygen oxidation followed by acetylation gives *meso*-diacetate **14b** which is hydrolyzed enantioselectively by *Porcine Pancreatic Lipase* (PPL) to mono-acetate (+)-**15b** in excellent chemical and optical yield. Recrystallization of (+)-**15b** followed by Swern oxidation leads to enantiopure (+)-**12b** in an excellent overall yield. A chiral economical conversion of **14b** into enantiopure (+)-**12b** was accomplished by



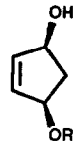
12a-h



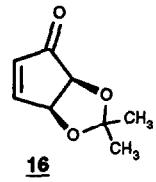
13a-h



14a-e



15b,d



16

a: R= H
b: R= $COCH_3$
c: R= $COCH_2CH_3$
d: R= $CO(CH_2)_2CH_3$
e: R= $COCH(CH_3)_2$
f: R= $COC(CH_3)_3$
g: R= COC_6H_5
h: R= $Si(CH_3)_2C(CH_3)_3$

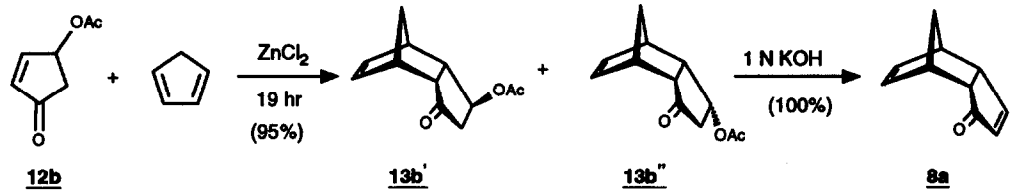
acetylation of the optically inferior mother liquor, obtained from the crystallization of mono-acetate (+)-**15b**, to give *meso*-diacetate **14b** again. Access to the opposite enantiomers of **15** is provided either by hydrolysis of *meso*-diacetate **14b** with *Pig Liver Esterase* (PLE) in a 0.1 M phosphate buffer (68%, *ee*>98%, after crystallization)[14] or by enantioselective transesterification of *meso*-diol **14a** using *Pancreatin*, triethylamine and 2,2,2-trichloroethyl acetate in THF (48%, *ee* 95%)[15]. Of the ester analogs **12c-g** only *n*-butyrate **12d** could be obtained enantiopure by PPL-catalyzed hydrolysis of *meso*-dibutyrate **14d**. Enzymatic hydrolysis of *meso*-diesters **14c** and **14e** either failed completely or lacked the desired selectivity.

Because of its propensity for racemization[16] under acidic and basic conditions, (R)-(+)-4-hydroxycyclopent-2-en-1-one **12a** was synthesized by careful enzymatic hydrolysis of acetate **12b** at pH=7.0 using *Wheat Germ Lipase*[17]. Under these conditions the optical integrity was completely retained. The esters **12c** and **e-g** and silyl-ether **12h** were prepared from alcohol **12a** using mild basic conditions (*cf.* experimental section) yielding all derivatives in the same optical purity as the starting alcohol **12a**. Enantiopure acetonide (+)-**16** (>98% *ee*) was obtained in 33% overall yield starting from mono-acetate (1R,4S)-(+)-**15b** following the three-step procedure of Deardorff *et al.*[18].

Diels-Alder reactions

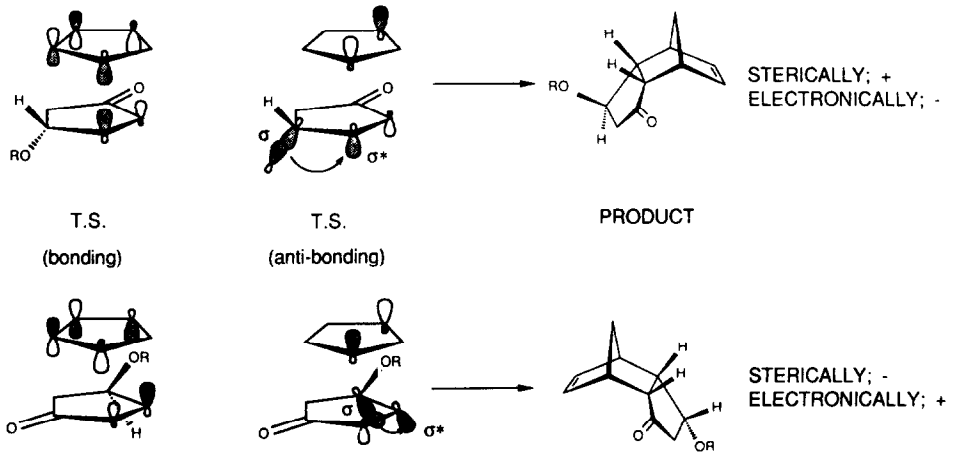
Wenkert and Taticchi and others[19] demonstrated that cyclopent-2-en-1-ones are poor dienophiles and require Lewis acid catalysis, *e.g.* aluminum chloride, and elevated temperatures in order to undergo a Diels-Alder reaction with either cyclic or acyclic dienes. 4-Acetoxycyclopentenone **12b** conforms to this general behavior of cyclopentenones and did not react at all with cyclopentadiene in organic solvents in the absence of a Lewis catalyst. However, when aluminum trichloride was added a rapid reaction took place to give *endo*-tricyclodecadienone **8a** as the main product in 41% yield. The expected initial cycloadducts, *viz.* 5-acetoxytricyclodecenones **13b'** and **13b''**, were not isolated, but product **8a** was obtained instead.

Scheme 3



Apparently, elimination of acetic acid readily takes place under these conditions. When the milder catalyst zinc chloride was used, the cycloaddition proceeded slower but gave an almost quantitative formation of a mixture of *endo*-tricyclic acetates **13b'** and **13b''** in a 3:1 ratio, while no tricyclodecadienone **8a** was formed at all (Scheme 3). Treatment of acetates **13b** with 1N KOH gave pure (+)-*endo*-tricyclodecadienone **8a** after

Scheme 4



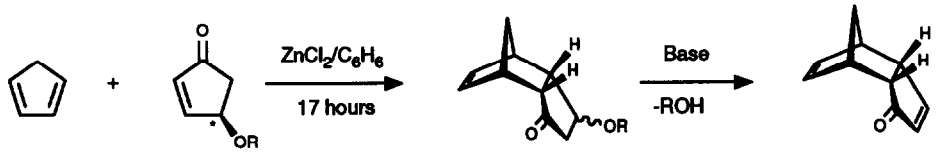
flash chromatography in an excellent overall yield of 95% and with an enantiomeric purity of 48%. This enantioselectivity is fully accord with the π-facial selectivity observed for the formation of **13b'** and **13b''** (ratio 3:1). With aluminum as well as zinc chloride only a small amount (approximately 2%) of *exo*-tricyclodecadienone was isolated, showing that this cycloaddition of **12b** with cyclopentadiene has a high

endo-stereoselectivity which is hardly affected by the nature of the catalyst.

The preferential formation of (+)-**8a** from (+)-**12b**, proves that, as may be expected, the sterically least hindered transition state is favored (Scheme 4). Nevertheless, the amount of contra-steric approach is unexpectedly high, as is indicated by the *ee* of only 48% for (+)-**8a**. In order to quantify the steric impact of the substituent at C_4 in cyclopentenones **12**, AM1-calculations[20] were carried out. These calculations show that in the most favored conformation for esters **12b-g**, the ester function points away from the cyclopentenone ring, with the consequence that steric interactions between the ester function and the diene moiety in the transition state of the cycloaddition are not very pronounced, thus resulting in a rather low diastereofacial selectivity. These calculations also indicate that by increasing the steric bulk of the acyl moiety of the ester function only a slight positive effect on the diastereoselectivity may be expected.

The Diels-Alder reactions of **12b-g** with cyclopentadiene indeed show that an increase in the steric volume of the C_4-substituent only slightly affects the π-facial selectivity. Surprisingly however, there is a decrease rather than an increase in the diastereofacial selectivity (Table 1). To shed light on this paradoxical

Table 1. Diels-Alder Reaction of Cyclopentadiene with (R)-(+)-**12a-h** in the presence of Zinc Chloride.



12a-h **13a-h** **8a**

a: R= H **c**: R= COEt **e**: R= CO-i-Pr **g**: R= COPh

b: R= COMe **d**: R= CO-n-Pr **f**: R= CO-t-Bu **h**: R= Si-t-Bu(Me)$_2$

entry	1	2	3	4	5	6	7	8
dienophile	**12a**	**12b**	**12c**	**12d**	**12e**	**12f**	**12g**	**12h**
yield	54% [a]	95%	quant.	90%	quant.	81%	88%	38% [b]
ee	56%	48%	42%	40%	35%	27%	35%	61%
enantiomer	+	+	+	+	+	+	+	- ! [c]

[a] after 28 hours [b] $AlCl_3$/toluene/2.5 hours, after treatment with TBAF [c] sterically most hindered transition state prevailing !

observation the two *endo*-transition states (*i.e. endo-syn* and *endo-anti*) for each of these cycloadditions were analyzed by semi-empirical AM1 calculations[20] (Table 2). The calculated transition state bond distances between the interacting atoms α, α^* and β, β^* confirm the anticipated concerted character of the cycloadditions in all cases, the β-β^* bond being somewhat stronger than the α-α^* due to a more effective orbital overlap. Although in each case the differences between the calculated heats of activation for *syn*- and *anti*-addition predict a larger diastereofacial selectivity than was observed experimentally, the calculations *grosso modo* agree with the experimental observation of a decrease in facial selectivity with increasing size of

Table 2. AM1 Calculated Heats of Reaction and Activation of the *endo*-TS-Structures for the Diels-Alder reaction of **12b-g** with cyclopentadiene.

entry	dienophile	ΔH_f [a] in kcal/mol	transition state	$\Delta H_{rct.}$ [b] in kcal/mol	$\Delta H_{act.}$ [c] in kcal/mol	$\Delta(\Delta H_{act.})$ [d] in kcal/mol
1	**12b**	- 101.34	*syn*	- 20.23	+ 34.08	
2	**12b**	- 101.34	*anti*	- 18.40 [e]	+ 31.38	]------- + 2.70
3	**12c**	- 107.38	*syn*	- 20.25	+ 33.95	
4	**12c**	- 107.38	*anti*	- 23.74	+ 31.33	]------- + 2.62
5	**12d**	- 114.30	*syn*	- 20.26	+ 33.98	
6	**12d**	- 114.30	*anti*	- 23.74	+ 31.41	]------- + 2.57
7	**12e**	- 111.74	*syn*	- 19.86	+ 34.03	
8	**12e**	- 111.74	*anti*	- 23.73	+ 31.44	]------- + 2.59
9	**12f**	- 113.67	*syn*	- 20.28	+ 33.89	
10	**12f**	- 113.67	*anti*	- 23.49	+ 31.45	]------- + 2.44
11	**12g**	- 66.08	*syn*	- 20.31	+ 33.95	
12	**12g**	- 66.08	*anti*	- 23.72	+ 31.36	]------- + 2.59

[a] Heat of formation of dienophile, ΔH_f(cyclopentadiene)= + 37.06 kcal/mol [b] Heat of reaction [c] Heat of activation
[d] $\Delta(\Delta H_{act.}) = \Delta H_{act.,syn} - \Delta H_{act.,anti}$ [e] not reliable as minimization of **13b'** converged to a local instead of a global minimum.

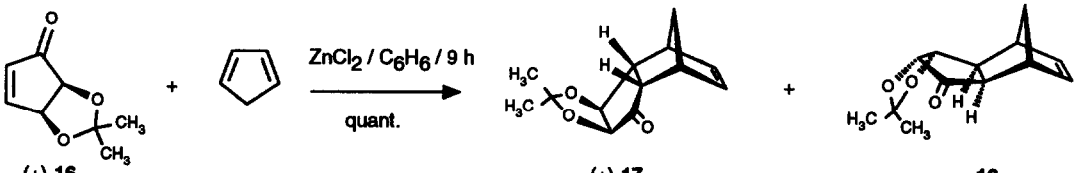
the ester group in **12b-g**. These calculations also confirm that in the transition state the ester function lies at the periphery of the actual reaction center and therefore will not have a decisive steric effect on the diastereoselectivity of the cycloadditions.

The appreciable amount of *endo-syn*-addition in the Diels-Alder reactions of **12a-g** can best be rationalized by invoking stereoelectronic effects in terms of the Cieplak-theory[21,22]. The stabilizing interaction of the emerging σ^*-orbital of the incipient bond at C_β with a suitably aligned σ-bond at C_γ favors *syn*-addition due to the larger electron donating ability of the σ_{CH}-bond in comparison with the σ_{CO}-bond at C_γ (Scheme 4), which can counterbalance the steric constraints of this *endo-syn*-addition. Recently, Danishefsky *et al.*[21d] observed a strong preference for *syn*-addition in the Diels-Alder reaction of butadiene with 4-(*tert*-butyldimethylsilyloxy)cyclopent-2-en-1-one **12h** notwithstanding the steric bulk of the silyloxy group. This result has also been explained in terms of the Cieplak theory. In order to establish the effect of a 4-silyloxy group in **12** the cycloaddition of **12h** with cyclopentadiene was studied. The silyl ether **12h** turned out to be less reactive than the related alcohol **12a** and the esters **12b-g**. As an appreciable reaction could only be accomplished by using aluminum trichloride as the Lewis catalyst, considerable decomposition of starting material and product(s) occurred. Tricyclodecadienone (-)-**8a** was obtained in only 37% yield with an *ee* of 61%. The striking fact is that now the opposite antipode of **8a** is formed by preference, which clearly

demonstrates the electronic effect of the silyloxy group on this Diels-Alder reaction. It also shows that in the transition state the bulky *tert*-butyldimethylsilyloxy group can, like the esters functions, position itself outside the actual reaction site, which limits its net steric effect. The preferred reaction of **12h** with cyclopentadiene via the sterically most hindered *endo-syn*-transition state is in line with the findings of Danishefsky *et al.*[21d], mentioned above and with those of Burnell *et al.*[21a], who observed exclusive *syn*-addition when reacting *cis*-5,6-bis(trimethylsilyloxy)-1,3-cyclohexadiene with *N*-phenylmaleimide.

It may be expected that for 4-substituted cyclopentenones in which the 4-substituent cannot escape the

Scheme 5



(+)-**16** 100% ee

(+)-**17** 100% ee

18 100% ee

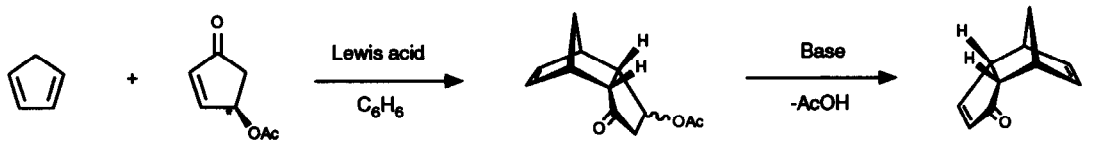
8 : 1

severe steric interaction with the incoming diene system, will show higher if not complete diastereofacial selectivity in the Diels-Alder reaction with cyclopentadiene. For this purpose, we studied the cycloaddition of the rigid cyclopentenone acetonide (+)-**16** with cyclopentadiene (Scheme 5). With zinc chloride in benzene a quantitative formation of *endo*-(+)-**17** and *exo*-**18** (*endo*/*exo* 8:1) was observed. Enantiopure tricyclic acetonide (+)-**17**, was obtained after chromatographic removal of *exo*-isomer **18**. This result convincingly demonstrates that for such rigid cyclopentenones as **16** product formation is solely determined by steric factors which now prevail over the opposing electronic effects.

Effect of Lewis-acids

As outlined in the preceding section the electron-donating ability of the σ_{CO}-bond at C_4 in dienophile **12** is responsible for a considerable electronic effect in controlling the diastereoselectivity of the Diels-Alder reaction with cyclopentadiene. Lewis acids may also influence the electron donating features of this particular σ_{CO}-bond, *e.g.* by complexation with the carbonyl oxygen of the C_4 acetoxy group whereby a more effective complex will induce a larger electron deficiency at the carbonyl carbon atom, hence diminishing the electron-donating effect of the σ_{CO} bond and as a consequence a lower diastereoselectivity would result. Various Lewis acids were tested as catalysts in the Diels-Alder reaction of **12b** and cyclopentadiene. The results, collected in table 3, clearly demonstrate the predicted trend, namely that the stronger the Lewis acid[23], the lower the observed *ee*. The highest *ee* was observed for the relatively weak catalyst $CdCl_2$. It was ascertained that this Lewis acid effect is not due to a racemization of **12b** under the conditions of the reactions. Treatment of **12b** with $ZnCl_2$ or $AlCl_3$ for 4 and 1 hour, respectively, led to recovered starting materials without loss of optical purity. The decrease in chemical yield of cycloadduct (+)-**8a** associated with the use of strong Lewis acids is caused by the formation of bis-adducts **19a** and **19b**[24] as by-products. Strong Lewis acids facilitate elimination of the acetate group from the initial adducts **13b** and accordingly,

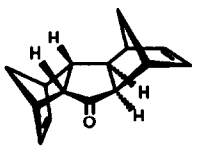
Table 3. Influence of the Lewis-acid on the Diels-Alder Reaction between (R)-(+)-4-acetoxycyclopent-2-en-1-one **12b** and Cyclopentadiene.



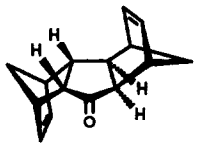
(R)-(+)-**12b** **13b** (+)-**8a**

entry	1	2	3	4	5	6	7	8	9	10	11
Lewis acid [a]	$AlCl_3$	$FeCl_3$	$SnCl_4$	$TiCl_4$	$BF_3.(OEt)_2$	$Ti(OR)_2Cl_2$ [b]	$ZnCl_2$	ZnI_2	$Ti(OR)_3Cl$ [b]	$CdCl_2$	HgI_2
time [c]	0.5	0.8	0.8	0.8	0.8	2 days	19	5	3 days	7 days	------- [d]
yield	41%	60%	77%	81%	69%	65%	95%	78%	72%	41% [e]	-------
ee	16%	23%	28%	33%	35%	47%	48%	49%	50%	65%	-------

[a] 0.2 equiv., except for entries 7,9 and 10 (1.0 equiv.) and entries 6 and 8 (0.15 equi.) [b] R=$CH(CH_3)_2$ [c] in hours, unless stated otherwise [d] no reaction observed
[e] 30% **12b** recovered.



19a

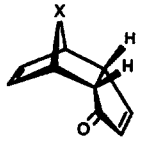


19b

by-product formation will be promoted by a further reaction of **8a** with cyclopentadiene, which requires catalysis by strong Lewis acids[24b].

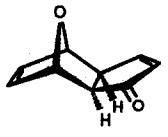
DIELS-ALDER REACTION OF (R)-(+)-4-ACETOXYCYCLOPENTENONE WITH OTHER DIENES

To establish the scope of the Diels-Alder reaction of 4-oxycyclopentenones **12**, various other dienes were investigated. Under the conditions used for cycloaddition with cyclopentadiene in the presence of $ZnCl_2$ at ambient temperatures, less reactive dienes failed to react. However, cyclohexadiene, furan, isoprene and 2,3-dimethyl-1,3-butadiene did react with **12b**. At 12 kbar and employing zinc chloride as catalyst the corresponding cycloadducts were obtained in reasonable to good chemical yields (Table 4). At a pressure of 15 kbar cyclohexadiene and 2,3-dimethyl-1,3-butadiene reacted even without added Lewis acid catalyst. In contrast, cycloheptadiene failed to react at all in the presence of a variety of Lewis acids, even at 15 kbar (Table 4). The cycloadditions of cyclohexadiene and 2,3-dimethyl-1,3-butadiene led to a mixture of the corresponding acetates, which on treatment with 1N of KOH gave *endo*-tricyclo[5.2.2.$0^{2,6}$]undecadienone **8b** and tetrahydroindenone **21c** in yields of 72% and 60-65%, respectively. The Diels-Alder reaction of cyclohexadiene with **12b** was also attempted at atmospheric pressure and room temperature using other Lewis-acids. Cycloaddition could be accomplished when $FeCl_3$ or $AlCl_3$ was used, however, $SnCl_4$ failed to promote this reaction. The first-mentioned reaction proceeded only sluggishly (± 60% conversion after 8 days), while the second one gave a large amount of by-products, among which bis-adducts similar to **19a** and **19b**. As may be expected for the reaction of isoprene with **12b**, a mixture of regio-isomers **21a** and **21b** was produced (ratio of 1:2). Consideration of the HOMO-coefficients at both C-termini of the diene in isoprene (0.60 at C_1 and 0.51 at C_4 by semi-empirical AM1-calculations)[20] led to the assignment of structure **21b** as the major product. The reduced regioselectivity observed for this cycloaddition of isoprene with 4-acetoxycyclopentenone **12b** as compared with the reaction of isoprene with cyclopent-2-en-1-one[19a] which proceeds completely regioselectively to give the *para*-adduct only, can be attributed to the difference between the LUMO-coefficients at C_α and C_β in the respective dienophiles (0.17 for cyclopent-2-en-1-one and 0.14 for **12b**). The potential of 4-acetoxycyclopentenone **12b** as a dienophile, albeit under high pressure conditions, is convincingly demonstrated by its successful cycloaddition with furan, which generally is considered a relatively poor diene in Diels-Alder reactions. Although at a rate considerably lower than that observed for the other dienes, cycloadduct **20** was eventually isolated in a yield of 35% at 12 kbar after treatment of the crude reaction mixture with base. Both the structure and the *exo*-configuration of oxatricyclodecadienone **20** were unequivocally established by comparison of its spectral data with an authentic sample[25]. The reaction of **12b** with anthracene was best performed at room temperature and

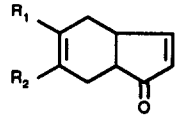


8a-c

a: X= -CH_2-
b: X= -$(CH_2)_2$-
c: X= -$(CH_2)_3$-

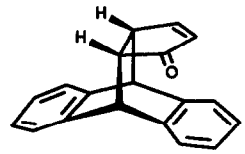


20



21a-c

a: R_1= H, R_2= CH_3
b: R_1= CH_3, R_2= H
c: R_1= R_2= CH_3



22

Table 4. Diels-Alder Reaction of Various Dienes with (R)-(+)-4-acetoxycyclopent-2-en-1-one **12b**.

diene	catalyst/solvent /pressure/time	yield/product [a]	*ee*
X = -CH_2-	$ZnCl_2$/C_6H_6/1 atm./19 h	95% **8a** [b]	48%
X = -$(CH_2)_2$-	$ZnCl_2$/MeCN/12 kbar/18 h	68% **8b** [b]	63%
	--------/C_6H_6/15 kbar/18 h	51% **8b** [b,c]	59%
X = -$(CH_2)_3$-	$ZnCl_2$/MeCN/15 kbar/17 h	0% **8c**	-----
X = -O-	$ZnCl_2$/MeCN/12 kbar/3 d	35% **20** [d]	53%
isoprene	$ZnCl_2$/MeCN/12 kbar/16 h	25% **21a**, 50% **21b**	[e]
2,3-dimethylbutadiene	$ZnCl_2$/MeCN/12 kbar/18 h	60% **21c**	52%
	--------/C_6H_6/15 kbar/20 h	65% **21c** [f]	52%
anthracene	$AlCl_3$/C_6H_6/atm./0.5 h	83% **22**	94%

[a] not optimized [b] 97-99% endo and 1-3% exo [c] ca. 60% conversion (cap. GC) [d] 98-99% *exo* and 1-2% *endo* [e] mixture of **21a** and **21b** inseparable [f] ca. 90% conversion (cap. GC).

atmospheric pressure using aluminum trichloride as Lewis catalyst. In this case the initial adduct rapidly loses acetic acid to yield the enone **22**. This acetic acid deactivates aluminum trichloride and therefore an excess of 1.1 equivalents of Lewis catalyst is required to complete the cycloaddition.

The *ee* values for the dienes entered in table 4 are in the same range as those observed for cyclopentadiene, meaning that the balance of steric and electronic (Cieplak) effects are of the same order. Anthracene is an exception as the cycloaddition proceeds with a high diastereofacial selectivity (94% *ee* for **22**). Semi-empirical TS-calculations[20] show that in this cycloaddition, **12b** cannot adopt a conformation in which the acetoxy group can escape strong steric interaction with the diene component in the transition state (Table 5, entries 7 and 8). For other dienes, the experimental findings are also in line with these semi-empirical transition state calculations (Table 5, entries 1-6).

Table 5. AM1 Calculated Transition State Prameters for the Diels-Alder Reaction of **12b** with Various Dienes.

entry	diene	ΔH_f [a] in kcal/mol	transition state	$\Delta H_{rct.}$ [b] in kcal/mol	$\Delta H_{act.}$ [c] in kcal/mol	$\Delta(\Delta H_{act.})$ [d] in kcal/mol
1	cyclopentadiene	+ 37.06	*endo-syn*	- 20.23	+ 34.08	]------ + 2.70
2	cyclopentadiene	+ 37.06	*endo-anti*	- 18.40	+ 31.38	
3	furan	+ 2.96	*exo-syn*	- 12.88	[e]	
3	furan	+ 2.96	*exo-anti*	- 15.57	+ 29.14	
4	cyclohexa-1,3-diene	+ 17.49	*endo-syn*	- 30.38	+ 35.13	]------ + 2.92
4	cyclohexa-1,3-diene	+ 17.49	*endo-anti*	- 33.91	+ 32.21	
5	2,3-dimethyl-1,3-butadiene	+ 16.88	*syn*	- 49.41	+ 28.69	]------ + 3.60
6	2,3-dimethyl-1,3-butadiene	+ 16.88	*anti*	- 53.46	+ 25.09	
7	anthracene	+ 62.92	*syn*	- 23.33	+ 37.19	]------ + 4.85
8	anthracene	+ 62.92	*anti*	- 27.69	+ 32.34	

[a] Heat of formation of diene, ΔH_f(**12b**)= - 101.34 kcal/mol [b] Heat of reaction [c] Heat of activation [d] $\Delta(\Delta H_{act.}) = \Delta H_{act.,syn} - \Delta H_{act.,anti}$. [e] calculation failed.

EFFECTS OF SOLVENT AND PRESSURE

Pressure

For the effect of pressure on the Diels-Alder reaction of (R)-(+)-4-acetoxycyclopentenone **12b** and cyclopentadiene a considerable increase in rate may be expected[26]. Less obvious is the effect of pressure on the diastereoselectivity of the Diels-Alder reaction. Some literature reports suggest that an increase of pressure leads to an enhancement of the facial selectivity of the asymmetric Diels-Alder reaction[27]. However, this is certainly not a general rule. The effect of pressure on the Diels-Alder reaction of **12b** and cyclopentadiene in benzene in the presence of zinc chloride is marginal, in acetonitrile there is an appreciable rate enhancement, however with a lower chemical yield due to decomposition of the dienophile under pressure (Table 6, entries 1 and 5-7). In both solvents the effect of pressure on the diastereoselectivity was marginal.

The reaction of 4-substituted cyclopentenones **12a,b** was also investigated without any added catalyst and only using high pressure (entries 8 and 9). In both cases an acceptable optical yield was obtained, slightly higher than in the case where zinc chloride was used (entry 6). Hence, these results suggest a beneficial effect of pressure on the π-facial selectivity.

Table 6. Diels-Alder reactions of **12a,b** and **g** under various conditions.

dienophile	entry	solvent	special cond.	temperature [a]	time [b]	yield [c]	*ee* [d]
12b	1	benzene	1 eq. $ZnCl_2$	RT	19	95%	48%
12b	2	*o*-xylene	1 eq. $ZnCl_2$	RT	43	78%	44%
12b	3	*m*-xylene	1 eq. $ZnCl_2$	RT	120	71%	45%
12b	4	*p*-xylene	1 eq. $ZnCl_2$	RT	120	80%	45%
12b	5	acetonitrile	1 eq. $ZnCl_2$	RT	90	86%	46%
12b	6	benzene	1 eq. $ZnCl_2$/15 kbar	RT	19	90%	47%
12b	7	acetonitrile	1 eq. $ZnCl_2$/15 kbar	RT	18	64%	41%
12a	8	benzene	15 kbar	RT	16	54%	59%
12b	9	benzene	15 kbar	RT	16	77%	63%
12a	10	water	ultrasound	45	22	82%	82%
12b	11	water	ultrasound	45	54	75%	63%
12g	12	water	ultrasound	45	48	quant.	67%
12b	13	buffer [e]	Baker's yeast [f]	37	24	72%	64%

[a] in °C [b] in hours [c] not optimized [d] of isolated (+)-**8a** [e] 2:1 mixture of 30% ethanol in water and a phosphate buffer (pH 7.0)
[f] Baker's yeast (*Saccharomyces Cerevisiae*) was purchased from Sigma Chemical Co., USA.

Organic solvents

The effect of various organic solvents was studied for the Diels-Alder reaction of (R)-(+)-4-acetoxy-cyclopentenone **12b** and cyclopentadiene, using zinc chloride as the catalyst (Table 6, entries 1-5). The results show that the chemical and optical yield of cycloadduct **8a** are not significantly affected by the polarity of the solvent (entries 1 and 5). As the best results were obtained in benzene donor-acceptor interactions[28] between solvent and reagents (*e.g.* π-stacking)[29] may play a role in this cycloaddition[30]. The results with the xylenes (entries 2-4), however, indicate that the cycloaddition of **12b** is not sensitive to such π-π interactions.

Aqueous solvents

The use of water as reaction medium for these Diels-Alder reactions with cyclopentadiene, applying ultrasound agitation, resulted in relatively high chemical and optical yields (entries 10-12). The positive effect of water on Diels-Alder reactions has several precedents in the literature and has been attributed to enforced hydrophobic association[31a-c], micellar catalysis[31d], hydrogen bonding[31e] or solvent polarity[31f]. The use of ultrasound is essential for the success of this reaction. In spite of the positive effect of water on the Diels-Alder reaction with cyclopentadiene, other dienes such as cyclohexadiene, 2,3-dimethylbutadiene and furan, failed to react with **12b** under these conditions.

The high optical yield in the case of **12a** is remarkable in comparison with other conditions, which is probably the result of a hydrogen bond between water and the hydroxyl function at C_4 in **12a**. In order to obtain the electronically more favorable *endo-syn* transition state which eventually would lead to (-)-**8a**, this hydrogen bonding has to be disrupted. No hydrogen bond disruption is necessary to reach the sterically more favorable *endo-anti* transition state which ultimately leads to (+)-**8a**. The optical yield for the cycloaddition in water corresponds to an energy difference of ca. 1.4 kcal/mol between the *endo-syn* and *endo-anti* transition state, which is 0.6 kcal/mol higher than that for the high pressure catalyzed cycloaddition in benzene. This increase in the energy difference for both transition states is well within the limit of the average OH--O-hydrogen bond. Evidently, the lower diastereoselectivity observed for the esters **12b** and **g** as compared with **12a** is the result of the weaker OH--O= hydrogen bonding between water and the ester functions in the former compounds. No precedent of this effect of hydrogen bonding on the facial selectivity in Diels-Alder cyclizations in water was found in the literature. It may have interesting synthetic consequences as water can now be applied not only to accelerate a Diels-Alder reaction but also to promote the diastereoselectivity in asymmetric cycloadditions.

Inspired by the report of Rao *et al.*[32] who used *Baker's yeast* in aqueous medium to enhance the *exo/endo* selectivity in Diels-Alder reactions of cyclopentadiene with maleic, fumaric, crotonic and *trans*-cinnamic acid derivatives, the present case was also studied under these rather unusual conditions (*i.e.* stirring a suspension of **12b**, cyclopentadiene and *Baker's yeast* in a 2:1 mixture of 30% of ethanol in water and a phosphate buffer (pH= 7.0) at 37 °C). The result was rather rewarding, namely 72% chemical yield and 64% optical yield (entry 13), however there is no evidence for any special contribution of the yeast because the result is practically the same as without yeast (entry 11).

CONCLUDING REMARKS

The above results clearly demonstrate, that *endo*-tricyclodecadienone **8a** and related annelated cyclopentenones **8b** and **20-22** can conveniently be synthesized in good overall chemical yields by a Diels-Alder reaction of 4-hydroxycyclopent-2-en-1-one **12a** and its derivatives **12b-h** with an appropriate diene. Due to opposing steric and electronic effects (Cieplak theory), the diastereofacial selectivity of the asymmetric version of this reaction is moderate, in most cases. However, by carefully selecting substrates and reaction conditions this π-facial selectivity can be improved significantly. The most rewarding results were obtained from the reaction of **12b** with anthracene (Table 4, *de* 94%) and the cycloaddition of **12a** with cyclopentadiene in aqueous medium (Table 6, *de* 82%).

It is of mechanistic interest that stereoelectronic effects play a decisive role in determining the facial stereoselectivity in the Diels-Alder reaction of cyclopentenones **12** with various dienes. In particular, the preferential formation of (-)-**8a** in the reaction of *tert*-butyldimethylsilyl ether **12h** with cyclopentadiene is remarkable, because this bulky substituent at C_4 the *endo-syn*-transition state is considerably favored. The results presented above form convincing evidence for the validity of Cieplak's theory in explaining the stereoelectronic effects of substituents on the stereochemistry of bond forming reactions.

Finally, it was shown that water can be applied as reaction medium to accelerate the cycloaddition of cyclopentenones **12** with cyclopentadiene and also to enhance the diastereoselectivity of these cycloadditions. Hydrogen bonding of water with the 4-oxysubstituent in **12a-g** which leads to a distinct hydrophilic and a

lipophilic face of the dienophile is most likely responsible for this effect.

EXPERIMENTAL SECTION

General remarks

Melting points were measured with a Reichert Thermopan microscope and are uncorrected. IR spectra were taken on a Perkin Elmer 298 infrared spectrophotometer. ^{1}H-NMR spectra were recorded on a Bruker AM-400, using TMS as an internal standard. For mass spectra a double focussing VG 7070E mass spectrometer was used. Flash chromatography was carried out at a pressure of *ca.* 1.5 bar, a column length of 15-25 cm and a column diameter of 1-4 cm, using Merck Kieselgel 60H, unless stated otherwise. Elemental analyses were performed on a Carlo Erba Instruments CHNS-O 1108 Elemental Analyzer. All solvents used were dried and distilled according to standard procedures.

Semi-empirical transition state calculations

All semi-empirical calculations were performed using the VAMP 4.3[33] and MOPAC 6.0[34] programs on the CONVEX C120 computer of the CAOS/CAMM Center[20] and the AM1 Hamiltonian[35]. The geometries of starting materials and products were optimized using the Eigenvector Following (EF) routine implemented in MOPAC 6.0. Starting from the geometries of the products, preliminary transition state geometries were calculated using the saddle-point method of McIver and Komornicki[36] implemented in VAMP 4.3. The Diels-Alder reactions were simulated by simultaneously elongating both bonds formed during cycloaddition, in steps of 0.1 Å from their initial length (around 1.55 Å in the products) up to 2.55 Å using the SYMMETRY routine in combination with a path calculation. Subsequently, two structures (mostly those at 1.95 and 2.35 Å) close to the approximate transition state (near 2.15 Å) were used to determine preliminary transition state geometries using the SADDLE routine[37], which is also implemented in VAMP 4.3. Refinement of these preliminary transition state geometries, using the TS routine implemented in MOPAC 6.0 provided final transition state geometries and their heats of formation. Most geometries obtained in this way, were found to have either a single imaginary vibrational frequency as required for a genuine transition state or a relatively small second imaginary vibrational frequency.

General procedures

A: Synthesis of diesters **14c-e**

To a solution of **14a** and triethylamine in 150 ml dry dichloromethane, a solution of the acid chloride in 30 ml dry dichloromethane is added dropwise at 0 °C. After the addition is completed, the mixture is allowed to warm to room temperature and stirred for another 3 h. The resulting mixture is cooled, the precipitated $Et_3N.HCl$ filtered off and the filtrate washed with 200 ml saturated sodium bicarbonate and 200 ml brine, successively. The aqueous fractions are extracted once with 100 ml dichloromethane and the combined organic phases are dried with $MgSO_4$. Filtration, evaporation of the solvent at reduced pressure and finally vacuum distillation affords the diesters **14c-e**.

B: Synthesis of esters **12c** *and* **12e-g**

To a solution of **12a** and triethylamine in 20 ml dry dichloromethane, a solution of 1.2 equiv. of the acid chloride in 10 ml dry dichloromethane is added dropwise at 0 °C. After all acid chloride is added, the resulting mixture is stirred overnight at room temperature, filtered and the residue is washed successively with 3% HCl, saturated sodium bicarbonate and brine. The aqueous phases are extracted once with 30 ml dichloromethane and the combined organic fractions dried ($MgSO_4$), filtered and concentrated at reduced pressure. The crude products are purified by flash chromatography.

C: Diels-Alder reactions in organic solvents at atmospheric pressure

In a flask equipped with a $CaCl_2$-tube a mixture of dienophile and Lewis acid in the organic solvent was stirred for 15 minutes at room temperature to allow for complexation. Next the diene was added and the resulting mixture was stirred at room temperature until the reaction was judged complete by cap. GC. In the case of ester substituents at C_5 in the products **13'** and **13''**, ether and 2% $NaOH/H_2O$ were added and the mixture was vigorously stirred for half an hour. After separation of organic and aqueous phases, the organic phase was washed successively with saturated sodium bicarbonate and brine and the aqueous fractions were extracted twice with ether. The combined organic fractions were dried ($MgSO_4$), filtered and concentrated at reduced pressure. Finally, the crude products thus obtained were purified by flash

chromatography and/or crystallization.

D: Lewis catalyzed Diels-Alder reactions in organic solvents at high pressure
A mixture of diene, dienophile, Lewis acid and *p*-benzoquinone in the organic solvent was poured into a teflon cylinder and the top was screwed on tightly. The mixture was then allowed to react at the indicated temperature and pressure. See general procedure C for work-up and purification.

E: Uncatalyzed Diels-Alder reactions in organic solvents at high pressure
A mixture of diene, dienophile and *p*-benzoquinone in the organic solvent was poured into a teflon cylinder and the top was screwed on tightly. The mixture was then allowed to react at the indicated temperature and pressure. See general procedure C for work-up and purification.

F: Diels-Alder reactions in water at atmospheric pressure
In a flask the diene was added to a mixture of the dienophile and water. The flask was stoppered and the mixture was subjected to ultrasonic agitation until the reaction was complete according to cap. GC. See general procedure C for work-up and purification.

cis-*Cyclopent*-4-*ene*-1,3-*diol* **14a**[10a]
In an irradiation flask, Rose Bengal (1.5 g) and thiourea (83 g, 1.1 mol) were dissolved in methanol (2.5 l). The mixture was cooled to -40 °C and flushed continuously with oxygen. Next, cyclopentadiene (108 g, 1.6 mol) was added. The resulting mixture was stirred vigorously and irradiated for 8 h at -32 °C with a 500 W tungsten halogen lamp (Philips 7785 R). Finally, the mixture was shielded from light and stirred overnight at room temperature. After work-up[10a], the dark-red residue was purified by vacuum distillation to give 81.7 g (51%) **14a** as a slightly yellow solid.
14a: m.p.: ± 20 °C. b.p.: 96-97 °C/1.0 mmHg [Lit[10a] b.p.: 100-102 °C/1.3 mmHg]. ^{1}H-NMR (100 MHz, $CDCl_3$)[10a]: δ 5.96 (s, 2H, H_4 and H_5), 4.84 (bs, 2H, OH), 4.66-4.54 (m, 2H, H_1 and H_3), 2.71 A of AB (dt, $J_{2a,2s}$=14.4 Hz, $J_{1,2s}\approx J_{2s,3}\approx$7.2 Hz, 1H, H_{2s}), 1.50 B of AB (dt, $J_{1,2a}\approx J_{2a,3}\approx$3.4 Hz, 1H, H_{2a}).

cis-3,5-*Diacetoxycyclopent*-1-*ene* **14b**[10a]
To a solution of **14a** (101 g, 1.0 mol) and triethylamine (258 g, 2.6 mol) in dry dichloromethane (600 ml), a solution of acetic anhydride (257 g, 2.5 mol) in dry dichloromethane (100 ml) was gradually added at 0 °C. After addition of the anhydride the mixture was allowed to warm to room temperature and stirred overnight. The resulting mixture was washed successively with 3% hydrochloric acid (1 l), saturated aqueous sodium bicarbonate (1 l) and brine (1 l). The aqueous fractions were extracted twice with dichloromethane (500 ml) and the combined organic phases were dried ($MgSO_4$). Filtration, evaporation of the solvent at reduced pressure and finally vacuum distillation gave 181 g (97%) **14b** as a colorless oil.
14b: b.p.: 78-79 °C/0.1 mmHg [Lit[10a] b.p.: 110-112 °C/8 Torr]. ^{1}H-NMR (90 MHz, $CDCl_3$): in accordance with Lit[10a]. IR (CH_2Cl_2): υ 2980-2890 (C-H, sat.), 1730 (C=O), 1365 ($OCOCH_3$), 1230 (C-O) cm^{-1}. CI/MS: *m/e* (%) 185 (1,M^++1), 141 (1,M^+-CH_3CO), 125 (100,-CH_3CO_2H), 82 (33,-CH_3CO,-CH_3CO_2H), 43 (81,CH_3CO^+).

cis-3,5-*Dipropionyloxycyclopent*-1-*ene* **14c**
Following general procedure A [triethylamine (12.6 g, 0.13 mol), propionyl chloride (11.6 g, 0.13 mol)], **14a** (5.0 g, 50 mmol), gave, after work-up, 8.9 g (84%) **14c** as a slightly yellow oil.
14c: b.p.: 107-108 °C/6.1 mmHg. ^{1}H-NMR (90 MHz, $CDCl_3$): δ 6.02 (s, 2H, H_1 and H_2), 5.50 (dd, $J_{3,4s}=J_{4s,5}\approx$7.5 Hz, $J_{3,4a}=J_{4a,5}\approx$3 Hz, 2H, H_3 and H_5), 2.83 (dt, $J_{4a,4s}\approx$14 Hz, 1H, H_{4s}), 2.27 (q, $J_{CH_2CH_3}\approx$7.5 Hz, 4H, -CH_2CH_3 (2x)), 1.66 (dt, 1H, H_{4a}), 1.13 (t, 6H, -CH_2CH_3 (2x)). IR (CCl_4): υ 3070 (C-H, unsat.), 3020-2840 (C-H, sat.), 1735 (C=O), 1175 (C-O) cm^{-1}. CI/MS: *m/e* (%) 213 (0.3,M^++1), 155 (1,M^+-C_2H_5CO), 139 (100,-$C_2H_5CO_2H$), 82 (54,-C_2H_5CO,-$C_2H_5CO_2H$), 57 (100,$C_2H_5CO^+$).

cis-3,5-*Di*-n-*butyryloxycyclopent*-1-*ene* **14d**
Following general procedure A [triethylamine (12.7 g, 0.13 mol), *n*-butyryl chloride (13.4 g, 0.13 mol)], **14a** (5.0 g, 50 mmol), gave, after work-up, 11.1 g (92%) **14d** as a slightly yellow oil.
14d: b.p.: 111-112 °C/3.8 mmHg. ^{1}H-NMR (90 MHz, $CDCl_3$): δ 6.02 (s, 2H, H_1 and H_2), 5.52 (dd, $J_{3,4s}=J_{4s,5}\approx$7.5 Hz, $J_{3,4a}=J_{4a,5}\approx$3.5 Hz, 2H, H_3 and H_5), 2.85 (dt, $J_{4a,4s}\approx$15 Hz, 1H, H_{4s}), 2.25 (t, $J_{CH_2CH_2}\approx$7 Hz, 4H, -$CH_2CH_2CH_3$ (2x)), 1.83-1.52 (m, 5H, H_{4a} and -$CH_2CH_2CH_3$ (2x)), 0.93 (t, $J_{CH_2CH_3}\approx$7 Hz, 6H, -$CH_2CH_2CH_3$ (2x)). IR (CCl_4): υ 3070 (C-H, unsat.), 3040-2760 (C-H, sat.), 1735 (C=O), 1175 (C-O) cm^{-1}. CI/MS: *m/e* (%) 153 (66,M^+-$C_3H_7CO_2$), 82 (28,M^+-C_3H_7CO, -$C_3H_7CO_2$), 71 (100,$C_3H_7CO^+$), 43 (60,$C_3H_7^+$).

cis-3,5-*Di*-iso-*butyryloxycyclopent*-1-*ene* **14e**
Following general procedure A [triethylamine (12.6 g, 0.13 mol), *iso*-butyryl chloride (13.4 g, 0.13 mol)], **14a** (5.0 g, 50 mmol), gave, after work-up, 10.5 g (87%) **14e** as a slightly yellow oil.
14e: b.p.: 107-108 °C/6.1 mmHg. ^{1}H-NMR (90 MHz, $CDCl_3$): δ 6.07 (s, 2H, H_1 and H_2), 5.53 (dd, $J_{3,4s}=J_{4s,5}\approx6$ Hz, $J_{3,4a}=J_{4a,5}\approx3$ Hz, 2H, H_3 and H_5), 2.83 (dt, $J_{4a,4s}\approx13.5$ Hz, 1H, H_{4a}), 2.51 (sept, $J_{CH,CH3}\approx7$ Hz, 2H, -CH(CH_3)$_2$ (2x)), 1.65 (dt, 1H, H_{4a}), 1.16 (d, 12H, -CH(CH_3)$_2$ (2x)). IR (CCl_4): υ 3070 (C-H, unsat.), 3040-2820 (C-H, sat.), 1730 (C=O) cm^{-1}. CI/MS: *m/e* (%) 153 (77,M^+-$C_3H_7CO_2$), 82 (7,M^+-C_3H_7CO,-$C_3H_7CO_2$), 71 (100,$C_3H_7CO^+$), 43 (75,$C_3H_7^+$).

(1S,4R)-(+)-cis-4-*Acetoxycyclopent*-2-*en*-1-*ol*, (1S,4R)-(+)-**15b**[10b,c]
To a mixture of **14b** (81.8 g, 0.44 mol) and a K_2HPO_4/KH_2PO_4-buffer (pH=7.0, 400 ml), *Porcine Pancreatic Lipase*[38] (40.0 g) was added at 37 °C. The resulting mixture was stirred vigorously at this temperature, while the pH was maintained at 7.0 by an auto-burette, filled with 2 N KOH. The conversion was monitored by cap. GC and the consumption of base. After 3, 5 and 8 h extra enzyme (10 g) was added to the mixture. After 28 h the mixture was saturated with sodium chloride and subjected to a continuous extraction with ether. After 6 days the ether was dried ($MgSO_4$), filtered and evaporated to give 60.9 g (98%) white, crystalline (+)-**15b** (94% *ee*). One crystallization from a mixture of *n*-pentane and ether gave 34.9 g (57%) enantiopure (+)-**15b** as white needles.
(+)-**15b**: white needles (100 ml *n*-pentane:ether = 1:2 for ± 6.5 g **15b**). m.p.: 49.0-49.5 °C. $[\alpha]_D^{25}$= +66.9° (c=1.066, $CHCl_3$), >98% *ee* by ^{1}H-NMR using 0.8 equiv. Eu(hfc)$_3$. [Lit.[10b] $[\alpha]_D^{20}$= +65.6° (c=2.3, $CHCl_3$+1% EtOH); Lit.[10c,11] m.p.: 47.5-48 °C, $[\alpha]_D^{22}$= +75.0° (c=1.16, $CHCl_3$); Lit[13] m.p.: 46-48.5 °C, $[\alpha]_D$= +66.3° (c=1.53, $CHCl_3$); Lit.[15] m.p.: 49-50 °C, $[\alpha]_D^{20}$= -66° (enant., c=0.63, $CHCl_3$); Lit.[16] m.p.: 46-48 °C, $[\alpha]_D$= -66.3° (enant., c=1, $CHCl_3$)]. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.12 A of AB (d, $J_{2,3}$=5.5 Hz, 1H, H_2 or H_3), 5.99 B of AB (d, 1H, H_2 or H_3), 5.50 (m, 1H, H_4), 4.72 (bs, 1H, H_1), 2.81 A of AB (dt, $J_{5a,5s}$=14.7 Hz, $J_{1,5s}\approx J_{4,5s}\approx$7.3 Hz, 1H, H_{5s}), 2.06 (s, 3H, -OCOCH$_3$), 1.88 (bs, 1H, OH), 1.66 B of AB (dt, $J_{1,5a}\approx J_{4,5a}\approx$3.8 Hz, 1H, H_{5a}). IR (CH_2Cl_2): υ 3700-3100 (H-bonded OH), 3580 (free OH), 3060 (C-H, unsat.), 2990-2830 (C-H, sat.), 1725 (C=O), 1370 (OCOCH_3), 1235 (C-O, ester) cm^{-1}. CI/MS: *m/e* (%) 143 (31,M^++1), 125 (100,-H_2O), 99 (10,M^+-CH_3CO), 83 (100,-CH_3CO_2H), 71 (4,$C_3H_7CO^+$), 43 (100,CH_3CO^+).

(1S,4R)-(+)-cis-4-*Butyryloxycyclopent*-2-*en*-1-*ol*, (1S,4R)-(+)-**15d**[39]
To a mixture of **14d** (10.5 g, 44 mmol) and a KH_2PO_4/K_2HPO_4-buffer (pH=7.0, 50 ml), *Porcine Pancreatic Lipase*[38] (5.0 g) was added at 37 °C. The resulting mixture was stirred vigorously at this temperature, while the pH was maintained at 7.0 by an auto-burette, filled with 1 N KOH. The conversion was monitored by cap. GC and the consumption of base. After 3 h extra enzyme (3.0 g) was added. After 5½ h the mixture was saturated with sodium chloride and extracted with ethyl acetate (100 ml), until only butyric acid and *meso*-diol **14a** were isolated (7x). The organic fractions containing (+)-**15d** were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification of the crude product by vacuum distillation gave 4.6 g (62%) enantiopure (+)-**15d** as a slightly yellow oil.
(+)-**15d**: b.p.: 88-90 °C/0.5 mmHg. $[\alpha]_D^{26}$= +58.6° (c=1.110, $CHCl_3$), >95% *ee* by ^{1}H-NMR using 0.7 equiv. Eu(hfc)$_3$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.11 A of AB (dd, $J_{2,3}$=5.6 Hz, $J_{1,2}$ resp. $J_{3,4}$=1.2 Hz, 1H, H_2 or H_3), 5.98 B of AB (dd, $J_{1,2}$ resp. $J_{3,4}$=1.1 Hz, 1H, H_2 or H_3), 5.53-5.50 (m, 1H, H_4), 4.72 (bs, 1H, H_1), 2.81 A of AB (dt, $J_{5a,5s}$=14.6 Hz, $J_{1,5s}\approx J_{4,5s}\approx$7.3 Hz, 1H, H_{5s}), 2.28 (t, $J_{CH2,CH2}$=7.4 Hz, 2H, -OCOCH_2CH_2CH_3), 1.90 (bs, 1H, OH), 1.68-1.62 (m, 3H, -OCOCH_2CH_2CH_3 and H_{5a}), 0.95 (t, $J_{CH2,CH3}$=7.4 Hz, 3H, -OCOCH_2CH_2CH_3). IR (CH_2Cl_2): υ 3700-3100 (H-bonded OH), 3590 (free OH), 3060 (C-H, unsat.), 3010-2800 (C-H, sat.), 1725 (C=O), 1185 (C-O, ester) cm^{-1}. CI/MS: *m/e* (%) 171 (21,M^++1), 153 (100,-H_2O), 83 (70,-$C_3H_7CO_2H$), 71 (76,$C_3H_7CO^+$), 43 (21,$C_3H_7^+$). EI/HRMS *m/e*: 153.0915 (calc. for $C_9H_{13}O_2$ (M^+-OH): 153.0915).

R-(+)-4-*Hydroxycyclopent*-2-*en*-1-*one* **12a**[17]
To a mixture of enantiopure (R)-(+)-**12b** (8.0 g, 57 mmol, $[\alpha]_D$= +100.2° (c=0.927, CH_3OH)) and a K_2HPO_4/KH_2PO_4-buffer (pH=7.0, 200 ml), Wheat Germ Lipase[38] (4.0 g) was added at 32 °C. The resulting mixture was stirred vigorously at this temperature, while the pH was maintained at 7.0 by an auto-burette, filled with 1 N KOH. The conversion was monitored by cap. GC and the consumption of base. After 6.5 h the mixture was saturated with sodium chloride an subjected to a continuous extraction with ether. After 2 and 14 days the ether was dried ($MgSO_4$), filtered and evaporated to give after 2 days 1.2 g (21%) impure **12a** and after 14 days 3.2 g (57%) pure (R)-(+)-**12a**, both as a slightly yellow oil. If ether was used in the continuous extraction minimal racemization of (R)-(+)-**12a** was observed. The reaction was also performed on a 60 g scale, using ethyl acetate in the continuous extraction (yield: 29.4 g, 70%)). During this process isolated (R)-(+)-**12a** had racemized partially ($[\alpha]_D^{27}$= +51.0° (c=1.085, CH_3OH)), probably due to extraction of acetic acid together with desired (R)-(+)-**12a**.
(R)-(+)-**12a**: b.p.: 79-81 °C/1.3-1.4 mmHg. $[\alpha]_D$= +83.9° (c=0.132, CH_3OH), 94% *ee* by conversion to

(R)-(+)-**12h**. [Lit[40] $[\alpha]_D^{24}$= +83.1° (94% *ee* by ^{1}H-NMR, c=1.70, CH_3OH); Lit[17] $[\alpha]_D^{20}$= +59° (c=0.065, CH_3OH)]. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 7.63 A of AB (dd, $J_{2,3}$=5.7 Hz, $J_{3,4}$=2.3 Hz, 1H, H_3), 6.20 B of AB (dd, $J_{2,4}$=1.1 Hz, 1H, H_2), 5.01 (bs, 1H, H_4), 4.52 (bs, 1H, OH), 2.77 A of AB (dd, $J_{5a,5s}$=18.5 Hz, $J_{4,5s}$=5.9 Hz, 1H, H_{5s}), 2.25 B of AB (dd, $J_{4,5a}$=2.2 Hz, 1H, H_{5a}).

R-(+)-4-*Acetoxycyclopent-2-en-1-one* **12b**[10b,c]
Swern-oxidation[41] of enantiopure (1S,4R)-(+)-**15b** (68.5 g, 0.48 mol, $[\alpha]_D$= +66.9° (c=1.066, $CHCl_3$) in dry dichloromethane (500 ml), using a solution of oxalyl chloride (73.7 g, 0.58 mol) in dry dichloromethane (1.25 l), a solution of dry DMSO (84.6 g, 1.1 mol) in dry dichloromethane (250 ml) and finally triethylamine (248 g, 2.5 mol). After standard work-up and vacuum distillation of the crude product, 63.2 g (94%) (R)-(+)-**12b** was obtained as a clear, colorless oil.
(R)-(+)-**12b**: m.p.: ± 15 °C. b.p.: 107-108 °C/15 mmHg. $[\alpha]_D$= +100.2° (c=0.927, CH_3OH) [Lit[10b] $[\alpha]_D^{20}$= +101° (c=1.17, CH_3OH); Lit[42] b.p.: 45 °C/0.05 mmHg, $[\alpha]_D^{22}$= +97° (c=0.103, CH_3OH)]. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 7.59 A of AB (dd, $J_{2,3}$=5.7 Hz, $J_{3,4}$=2.3 Hz, 1H, H_3), 6.34 B of AB (bd, 1H, H_2), 5.89-5.83 (m, 1H, H_4), 2.84 A of AB (ddd, $J_{5a,5s}$=18.8 Hz, $J_{4,5s}$=6.3 Hz, $J_{2,5s}$=1.3 Hz, 1H, H_{5s}), 2.32 B of AB (dt, $J_{2,5a}\approx J_{4,5a}\approx$2.1 Hz, 1H, H_{5a}), 2.10 (s, 3H, -$OCOCH_3$).

R-(+)-4-*Propionyloxycyclopent-2-en-1-one* **12c**
Following general procedure B [triethylamine (720 mg, 7.1 mmol), 4-(*N*,*N*-dimethylamino)pyridine (10 mg), propionyl chloride (0.67 g, 7.3 mmol)], (R)-(+)-**12a** (504 mg, 5.1 mmol, ±52% *ee*), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 3:1), 0.59 g (74%) (R)-(+)-**12c** as a slightly yellow oil.
(R)-(+)-**12c**: $[\alpha]_D$= +55.4° (c=0.132, CH_3OH), 50±2% *ee* by ^{1}H-NMR using 0.5 equiv. Eu(Hfc)$_3$. [Lit[43] $[\alpha]_D$= +86.8° (c=0.16, CH_3OH)]. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 7.58 A of AB (dd, $J_{2,3}$=5.7 Hz, $J_{3,4}$=2.4 Hz, 1H, H_3), 6.31 B of AB (dd, $J_{2,4}$=1.3 Hz, 1H, H_2), 5.91-5.79 (m, 1H, H_4), 2.86 A of AB (dd, $J_{5a,5s}$=18.7 Hz, $J_{4,5s}$=6.3 Hz, 1H, H_{5s}), 2.35 (q, $J_{CH2,CH3}$=7.5 Hz, 2H, -$OCOC\underline{H_2}CH_3$), 2.27 B of AB (dd, $J_{4,5a}$=2.3 Hz, 1H, H_{5a}), 1.12 (t, 3H, -$OCOCH_2C\underline{H_3}$).

R-(+)-4-n-*Butyryloxycyclopent-2-en-1-one* **12d**
To a solution of enantiopure (1S,4R)-(+)-**15d** (2.0 g, 11.8 mmol, $[\alpha]_D$= +58.6° (c=1.110, $CHCl_3$)) in dry dichloromethane (20 ml), dry sodium acetate (0.98 g, 12.0 mmol) and PCC (3.8 g, 17.8 mmol) were added. The resulting mixture was cooled in a water-bath and stirred vigorously. After 3.5 h the reaction was complete according to TLC (Al_2O_3-Type E, *n*-hexane:ethyl acetate = 1:1, R_f(**15d**)=0.64 and R_f(**12d**)=0.85). After work-up[44], 1.2 g (61%) enantiopure (R)-(+)-**12d** was isolated as a colorless oil.
(R)-(+)-**12d**: ^{1}H-NMR (100 MHz, $CDCl_3$): δ 7.58 A of AB (dd, $J_{2,3}$=5.7 Hz, $J_{3,4}$=2.4 Hz, 1H, H_3), 6.34 B of AB (dd, $J_{2,4}$=1.1 Hz, 1H, H_2), 5.93-5.81 (m, 1H, H_4), 2.86 A of AB (dd, $J_{5a,5s}$=18.7 Hz, $J_{4,5s}$=6.2 Hz, 1H, H_{5s}), 2.41-2.20 (m, 3H, H_{5a} and -$OCOC\underline{H_2}CH_2CH_3$), 1.68 (sext, $J_{CH2,CH2}\approx J_{CH2,CH3}$=7.1 Hz, 2H, -$OCOCH_2C\underline{H_2}CH_3$), 0.96 (t, 3H, -$OCOCH_2CH_2C\underline{H_3}$). IR ($CH_2Cl_2$): υ 3000-2800 (C-H, sat.), 1720 (C=O,2x), 1590 (C=C, conj.), 1175 (C-O, ester) cm^{-1}. CI/MS: *m/e* (%) 169 (62,M^++1), 140 (11,M^+-CO), 81 (81,-$C_3H_7CO_2H$), 71 (100,$C_3H_7CO^+$), 43 (56,$C_3H_7^+$). EI/HRMS *m/e*: 168.0782 (calc. for $C_9H_{12}O_3$: 168.0786).

R-(+)-4-Iso-*butyryloxycyclopent-2-en-1-one* **12e**
Following general procedure B [triethylamine (740 mg, 7.3 mmol), 4-(*N*,*N*-dimethylamino)pyridine (12 mg), *iso*-butyryl chloride (0.78 g, 7.3 mmol)], (R)-(+)-**12a** (490 mg, 5.1 mmol, ±52% *ee*), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 4:1), 0.60 g (70%) (R)-(+)-**12e** as a slightly yellow oil.
(R)-(+)-**12e**: $[\alpha]_D$= +58.1° (c=1.294, CH_3OH), ±52% *ee* based on **12a**. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 7.60 A of AB (dd, $J_{2,3}$=5.7 Hz, $J_{3,4}$=2.4 Hz, 1H, H_3), 6.34 B of AB (dd, $J_{2,4}$=1.3 Hz, 1H, H_2), 5.92-5.81 (m, 1H, H_4), 2.86 A of AB (dd, $J_{5a,5s}$=18.7 Hz, $J_{4,5s}$=6.3 Hz, 1H, H_{5s}), 2.59 (sept, $J_{CH,CH3}$=7.0 Hz, 1H, -$OCOC\underline{H}(CH_3)_2$), 2.29 B of AB (dd, $J_{4,5a}$=2.3 Hz, 1H, H_{5a}), 1.19 (d, 6H, -$OCOCH(C\underline{H_3})_2$).

R-(+)-4-(2,2-*Dimethylpropionyloxy*)*cyclopent-2-en-1-one* **12f**
Following general procedure B [triethylamine (750 mg, 7.4 mmol), 4-(*N*,*N*-dimethylamino)pyridine (15 mg), pivaloyl chloride (0.87 g, 7.3 mmol)], (R)-(+)-**12a** (500 mg, 5.1 mmol, ±52% *ee*), gave after work-up and flash chromatography (*n*-hexane:ethyl acetate = 4:1), 0.59 g (63%) (R)-(+)-**12f** as a slightly yellow oil.
(R)-(+)-**12f**: $[\alpha]_D$= +61.6° (c=1.192, CH_3OH), ±52% *ee* based on **12a**. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.56 A of AB (dd, $J_{2,3}$=5.7 Hz, $J_{3,4}$=2.4 Hz, 1H, H_3), 6.34 B of AB (dd, $J_{2,4}$=1.3 Hz, 1H, H_2), 5.85-5.83 (m, 1H, H_4), 2.84 A of AB (dd, $J_{5a,5s}$=18.7 Hz, $J_{4,5s}$=6.4 Hz, 1H, H_{5s}), 2.28 B of AB (dd, $J_{4,5a}$=2.1 Hz, 1H, H_{5a}), 1.21 (s, 9H, -$OCOC(C\underline{H_3})_3$). IR (CH_2Cl_2): υ 3050-2840 (C-H, unsat. and sat.), 1715 (C=O,2x),

1590 (C=C, conj.), 1145 (C-O, ester) cm^{-1}. EI/MS: *m/e* (%) 182 (10,M^+), 98 (7,M^++1-$(CH_3)_3CCO$), 85 (12,$(CH_3)_3CCO^+$), 81 (17,-$(CH_3)_3CCO_2$), 57 (100, *t*-Bu^+). EI/HRMS *m/e*: 182.0939 (calc. for $C_{10}H_{14}O_3$ (M^+): 182.0943).

R-(+)-4-*Benzoyloxycyclopent-2-en-1-one* **12g**
Following general procedure B [triethylamine (1.3 g, 12.7 mmol), 4-(*N,N*-dimethylamino)pyridine (10 mg), benzoyl chloride (1.7 g, 12.2 mmol)], (R)-(+)-**12a** (1.0 g, 10.2 mmol, ±52% *ee*), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 2:1), 1.5 g (74%) (R)-(+)-**12g** as a white solid.
(R)-(+)-**12g**: m.p.: 89.5-90.0 °C. $[\alpha]_D$= +55.4° (c=0.132, CH_3OH), 53±2% *ee* by ^{1}H-NMR using 1.0 equiv. Eu(Hfc)$_3$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.04 (m, 2H, H_{ortho}), 7.71 (dd, $J_{2,3}$=5.7 Hz, $J_{3,4}$=2.4 Hz, 1H, H_3), 7.62-7.58 (m, 1H, H_{para}), 7.48-7.44 (m, 2H, H_{meta}), 6.41 (dd, $J_{2,4}$=1.3 Hz, 1H, H_2), 6.14-6.10 (m, 1H, H_4), 2.96 A of AB (dd, $J_{5a,5s}$=18.8 Hz, $J_{4,5s}$=6.4 Hz, 1H, H_{5s}), 2.50 B of AB (dd, $J_{4,5a}$=2.2 Hz, 1H, H_{5a}). IR (CH_2Cl_2): υ 3050-2990 (C-H, unsat.), 2990-2900 (C-H, sat.), 1725 (C=O,2x), 1600 (C=C, conj.), 1180 (C-O, ester) cm^{-1}. EI/MS: *m/e* (%) 202 (51,M^+), 174 (4,-CO), 122 (5,$C_6H_5CO_2H^+$), 105 (100,$C_6H_5CO^+$), 97 (3,-C_6H_5CO), 80 (38,-$C_6H_5CO_2H$), 77 (85,$C_6H_5^+$).

R-(+)-4-(tert-*Butyldimethylsilyloxy)cyclopent-2-en-1-one* **12h**[45]
To a solution of (R)-(+)-**12a** (1.5 g, 15.4 mmol, $[\alpha]_D$= +83.9° (c=0.132, CH_3OH), 94% *ee*) in dry dichloromethane (10 ml), 4-(*N,N*-dimethylamino)pyridine (189 mg) and triethylamine (1.7 g, 16.7 mmol) were added. The mixture was cooled to 0 °C and a solution of *tert*-butyldimethylsilyl chloride (2.7 g, 17.9 mmol) in dry dichloromethane (5 ml) was gradually added. After addition of the silyl chloride the mixture was stirred at room temperature. After 2.5 h the reaction was complete according to cap. GC. Evaporation of the solvent at reduced pressure and purification by flash chromatography (*n*-hexane:ethyl acetate = 3:1) gave 2.9 g (89%) (R)-(+)-**12h** of 94% ee as a colorless oil.
(R)-(+)-**12h**: $[\alpha]_D$= +62.3° (c=0.113, CH_3OH) [Lit[45] $[\alpha]_D$= +66.6° (c=1.0, CH_3OH)]. ^{1}H-NMR (100 MHz, $CDCl_3$): δ 7.45 A of AB (dd, $J_{2,3}$=5.7 Hz, $J_{3,4}$=2.1 Hz, 1H, H_3), 6.18 B of AB (bd, 1H, H_2), 4.98 (m, 1H, H_4), 2.72 A of AB (dd, $J_{5a,5s}$=18.1 Hz, $J_{4,5s}$=5.8 Hz, 1H, H_{5s}), 2.33 B of AB (dd, $J_{4,5a}$=2.3 Hz, 1H, H_{5a}), 0.91 (s, 9H, -C(CH_3)$_3$), 0.13 (s, 6H, -Si(CH_3)$_2$-). IR (CH_2Cl_2): υ 2980-2780 (C-H, sat.), 1715 (C=O, conj.), 1590 (C=C, conj.), 1390 and 1355 (C-H,C(CH_3)$_3$) cm^{-1}. EI/MS: *m/e* (%) 212 (1,M^+), 197 (4,-CH_3), 155 (100,-*t*-Bu), 81 (82,-$C_6H_{15}SiO$), 75 (59,$C_2H_7SiO^+$). EI/HRMS *m/e*: 212.1233 (calc. for $C_{11}H_{20}SiO_2$ (M^+): 212.1233).

(+)-4,5-(*Isopropylidenedioxy)cyclopent-2-en-1-one* **16**[18]
To a solution of enantiopure (1S,4R)-(+)-**15b** (8.3 g, 58.4 mmol, $[\alpha]_D$= +66.9° (c=1.066, $CHCl_3$)) in a 8:1 mixture of acetone/water (3.5 ml), *N*-methylmorpholine-*N*-oxide (18.4 g, 0.16 mol) and 4% aqueous OsO_4 (8.3 g) were added. The resulting mixture was stirred at room temperature until the reaction was complete according to cap. GC after 1.5 h. After evaporation of the solvent at reduced pressure and purification by flash chromatography (ethyl acetate:methanol = 9:1), 10.9 g (quant.) hydroxylated product was obtained as a brown oil, which was dissolved immediately in dry acetone (300 ml). To this solution 2,2-dimethoxypropane (15.9 g, 0.15 mol) and a crystal of *p*-toluenesulfonic acid were added and the mixture was stirred overnight at room temperature. Work-up[18], evaporation of the solvent at reduced pressure and purification of the crude product by flash chromatography (*n*-hexane:ethyl acetate = 1:1) gave 10.8 g (86%) enantiopure acetal as a colorless oil. Treatment of a solution of this acetal in acetone (590 ml), according to a literature procedure[46] with Jones reagent (26.6 ml of a 1.34 M solution), sodium bicarbonate (1.2 g) and $NaHSO_3$ (1.2 g) gave, after work-up, 2.9 g (38%) **16** as a white solid. The yield contrasts sharply with that of 95%, reported in the literature, probably due to hydrolysis of the ketal under the acidic conditions of the oxidation. The resulting hydroxylated compounds are lost during work-up.
(+)-**16**: $[\alpha]_D^{24}$= +68.9° (c=0.926, $CHCl_3$). [Lit[46] $[\alpha]_D^{25}$= +70.5° (c=0.90, $CHCl_3$, 98% *ee*); Lit[47] $[\alpha]_D^{24}$= +71.6° (c=1.01, $CHCl_3$); Lit[18] $[\alpha]_D^{26}$= +70.0° (c=0.92, $CHCl_3$)]. ^{1}H-NMR (100 MHz, $CDCl_3$)[18]: δ 7.62 A of AB (dd, $J_{2,3}$=5.9 Hz, $J_{3,4}$=2.2 Hz, 1H, H_3), 6.19 (d, 1H, H_2), 5.28 (dd, $J_{4,5}$=5.5 Hz, 1H, H_4), 4.45 (d, 1H, H_5), 1.39 (s, 6H, -C(CH_3)$_2$-).

endo-*Tricyclo*[5.2.1.$0^{2,6}$]*deca-4,8-dien-3-one* **8a**
Following general procedure C [dry benzene (10 ml), dry $ZnCl_2$ (454 mg, 3.3 mmol), cyclopentadiene (0.12 g, 3.3 mmol), room temperature, 17 h], enantiopure (R)-(+)-**12b** (0.15 g, 1.1 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 3:1), 0.15 g (95%) (+)-**8a** (48% *ee*) as a white solid. The same procedure was used for the reaction of (R)-(+)-**12a** and (R)-(+)-**12c-g** with cyclopentadiene to give (+)-**8a** (reaction times, yields and *ee*'s are listed in table 1).
Following general procedure D [dry benzene, cyclopentadiene (0.34 g, 5.1 mmol), $ZnCl_2$ (0.16 g, 1.2 mmol), hydroquinone, 15 kbar, room temperature, 19 h], enantiopure (R)-(+)-**12b** (0.15 g, 1.1 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up and flash chromatography (*n*-hexane:ethyl

acetate = 3:1), 0.14 g (89%) (+)-**8a** (47% *ee*) as a white solid.
Following general procedure D [dry acetonitrile, cyclopentadiene (0.56 g, 8.5 mmol), $ZnCl_2$ (10 drops of a saturated solution in acetonitrile), hydroquinone, 15 kbar, room temperature, 18 h], enantiopure (R)-(+)-**12b** (0.20 g, 1.4 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 3:1), 0.13 g (64%) (+)-**8a** (41% *ee*) as a white solid.
Following general procedure E [dry benzene, cyclopentadiene (0.38 g, 5.7 mmol), hydroquinone, 15 kbar, room temperature, 16 h], enantiopure (R)-(+)-**12b** (0.20 g, 1.4 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 3:1), 0.16 g (77%) (+)-**8a** (63% *ee*) as a white solid. The same procedure was used for the reaction of (R)-(+)-**12a** with cyclopentadiene to give (+)-**8a** (reaction time, yield and *ee* are listed in table 6).
Following general procedure F [water (20 ml), cyclopentadiene (0.40 mg, 6.1 mmol), 45 °C, 25 h], enantiopure (R)-(+)-**12b** (0.30 g, 2.2 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 3:1), 0.24 g (75%) (+)-**8a** (63% *ee*) as a white solid. The same procedure was used for the reaction of (R)-(+)-**12a** and **g** with cyclopentadiene to give (+)-**8a** (reaction times, yields and *ee's* are listed in table 6). The *ee's* were determined by correlation of the measured optical rotation with that of the known enantiopure compound ($[\alpha]_D$= 140.3° (c=0.548, MeOH)[7a]).
(+)-**8a**: white powder (*n*-pentane). m.p. dependent on *ee* of the sample; 59.0-59.5 °C for racemic compound and 76.0-77.0 °C for enantiopure compound. ^{1}H-NMR (400 MHz, $CDCl_3$)[48]: δ 7.38 (dd, $J_{4,5}$=5.7 Hz, $J_{5,6}$=2.6 Hz, 1H, H_5), 5.96 (dd, $J_{4,6}$=1.5 Hz, 1H, H_4), 5.95 A of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$=2.9 Hz, 1H, H_9), 5.78 B of AB (dd, $J_{7,8}$=3.0 Hz, 1H, H_8), 3.44-3.40 (m, 1H, H_6), 3.23 (bs, 1H, H_1), 2.98-2.96 (m, 1H, H_7), 2.80 B of AB (t, $J_{1,2}\approx J_{2,6}\approx$5.1 Hz, 1H, H_2), 1.76 A of AB (dt, $J_{10a,10s}$=8.4 Hz, J=1.7 Hz, 1H, H_{10a} or H_{10s}), 1.63 B of AB (d, 1H, H_{10a} or H_{10s}). IR ($CHCl_3$): υ 3100-2830 (C-H, unsat. and sat.), 1710 (C=O, conj.), 1580 (C=C, conj.) cm^{-1}.

endo-*Tricyclo*[5.2.2.$0^{2,6}$]*undeca*-4,8-*dien*-3-*one* **8b**
Following general procedure D [dry acetonitrile, cyclohexadiene (0.36 g, 4.5 mmol), $ZnCl_2$ (10 drops of a saturated solution in acetonitrile), hydroquinone, 12 kbar, room temperature, 18 h], enantiopure (R)-(+)-**12b** (0.31 g, 2.2 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 3:1), 0.23 g (68%) (+)-**8b** (63% *ee*) as a white solid.
Following general procedure E [dry benzene, cyclohexadiene (0.23 g, 4.3 mmol), hydroquinone, 15 kbar, room temperature, 20 h], enantiopure (R)-(+)-**12b** (0.30 g, 2.1 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 3:1), 0.17 g (51%) (+)-**8b** (59% *ee*) as a white solid.
(+)-**8b**: white powder (*n*-pentane). m.p.: 60.5-61.5 °C. $[\alpha]_D^{22}$= +102.8° (c=0.993, CH_2Cl_2), 63±2% *ee* by ^{1}H-NMR using 0.8 equiv. of $Eu(hfc)_3$. ^{1}H-NMR (400 MHz, $CDCl_3$)[48]: δ 7.43 (dd, $J_{4,5}$=5.7 Hz, $J_{5,6}$=2.5 Hz, 1H, H_5), 6.16 (dd, $J_{4,6}$=1.8 Hz, 1H, H_4), 6.04-6.00 A of AB (m, 1H, H_8 or H_9), 5.90-5.86 B of AB (m, 1H, H_8 or H_9), 3.00 (bs, 1H, H_1 or H_7), 2.96 A of AB (m, $J_{2,6}\approx$5.8 Hz, $J_{6,7}\approx$2.1 Hz, 1H, H_6), 2.74 (bs, 1H, H_1 or H_7), 2.36 B of AB (dd, $J_{1,2}$=3.3 Hz, 1H, H_2), 1.67-1.58 and 1.46-1.33 (2m, 2H and 2H, H_{10a}, H_{10s}, H_{11a} and H_{11s}). IR ($CHCl_3$): υ 3100-2830 (C-H, unsat. and sat.), 1690 (C=O, conj.), 1585 (C=C, conj.) cm^{-1}. EI/MS: *m/e* (%) 160 (17,M^+), 131 (15,-C_2H_5), 82 (100,$C_6H_{10}^+$), 80 (61,$C_5H_4O^+$). EI/HRMS *m/e*: 160.0888 (calc. for $C_{11}H_{12}O$ (M^+): 160.0888).

endo-5-tert-*Butyldimethylsilyloxy*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*dec*-8-*en*-3-*one* **13h**''[21d]
Following general procedure C [dry toluene (30 ml), cyclopentadiene (1.0 g, 15 mmol), $AlCl_3$ (0.49 g, 3.7 mmol), N_2, room temperature, 2½ h], (+)-**12h** (1.0 g, 4.7 mmol, $[\alpha]_D$= +62.3° (c=0.1134, CH_3OH), 94% *ee*), gave, after work-up, a crude mixture, which was separated into two halves of equal weight. Flash chromatography (*n*-hexane:ethyl acetate = 19:1) of one half gave 0.14 g (11%) **13h**'' as a colorless oil, whereas its exo-analog **13h'** could not be isolated, due to decomposition during chromatography and strong trailing. The second half of the crude mixture was dissolved in dry THF (20 ml), cooled to 0 °C and treated with 1 M TBAF/THF (3.8 ml, 3.8 mmol). The resulting mixture was stirred for 1 h at room temperature and treated with 1N KOH (25 ml) for 15 minutes. After standard work-up, flash chromatography gave 126 mg (19%) (-)-**8a** (57% *ee*) as a white solid. On the basis of isolated (-)-**8a** the yield of the Diels-Alder reaction amounted to 38% and its diastereofacial selectivity to 61% *de* (corrected for 94% *ee* of starting material), in favor of **13h**''.
13h'': ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.34 A of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=2.6 Hz, 1H, H_8 or H_9), 5.97 B of AB (dd, $J_{1,9}$ resp. $J_{7,8}$=3.0 Hz, 1H, H_8 or H_9), 4.51 (q, $J_{4n,5}\approx J_{4x,5}\approx J_{5,6}\approx$8.9 Hz, 1H, H_5), 3.20 (bs, 1H, H_1 or H_7), 3.13-3.08 (m, 2H, H_6 and H_1 or H_7), 2.91 (dd, $J_{2,6}$=8.4 Hz, $J_{1,2}$=5.0 Hz, 1H, H_2), 2.35 A of AB (ddd, $J_{4n,4x}$=18.8 Hz, J=1.3 Hz, 1H, H_{4n} or H_{4x}), 2.07 B of AB (dd, 1H, H_{4n} or H_{4x}), 1.49 A of AB (d, $J_{10a,10s}$=8.2 Hz, 1H, H_{10a} or H_{10s}), 1.36 B of AB (d, 1H, H_{10a} or H_{10s}), 0.92 (s, 9H, -$C(CH_3)_3$), 0.09 and 0.03 (2s, 3H and 3H, -$Si(CH_3)_2$-). IR (CH_2Cl_2): υ 3040-2780 (C-H, unsat. and sat.), 1730 (C=O), 1105 (C-O) cm^{-1}. EI/MS: *m/e* (%) 263 (1,M^+-CH_3), 221 (19,-*t*-Bu), 197 (3,-C_5H_6,-CH_3), 155

(100,-C_5H_6,-*t*-Bu), 75 (49,C_2H_7SiO), 66 (26,$C_5H_6^+$). EI/HRMS *m/e*: 263.1461 (calc. for $C_{15}H_{23}SiO_2$ (M^+-CH_3): 263.1467).

(+)-exo-4,5-(*Isopropylidenedioxy*)-endo-*tricyclo*[5.2.1.$0^{2,6}$]*dec*-8-*en*-3-*one* **17** *and* (+)-exo-4,5-(*isopropylidenedioxy*)-exo-*tricyclo*[5.2.1.$0^{2,6}$]*dec*-8-*en*-3-*one* **18**

Following general procedure C [dry benzene (20 ml), dry $ZnCl_2$ (0.60 g, 4.4 mmol), cyclopentadiene (0.74 g, 11.2 mmol), room temperature, 9 h], enantiopure (+)-**16** (0.56 g, 3.7 mmol, $[\alpha]_D^{24}$= +68.9° (c=0.926, $CHCl_3$), 98% *ee*), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 3:1) of the isolated 8:1 mixture (cap. GC) of **17** and **18**, 0.39 g (49%) enantiopure (+)-**17** as a white solid, 36 mg (5%) **18** as a colorless oil and 0.33 g (42%) of a mixture of (+)-**17** and **18**.

(+)-**17**: white needles (*n*-pentane). m.p.: 95-96 °C. $[\alpha]_D$= +282.0° (c=0.370, $CHCl_3$). [Lit[47] $[\alpha]_D^{24}$= +266.8° (c=0.68, $CHCl_3$)]. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.22 A of AB (dd, $J_{8,9}$=5.7 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.0 Hz, 1H, H_8 or H_9), 6.15 B of AB (dd, $J_{1,9}$ resp. $J_{7,8}$=2.9 Hz, 1H, H_8 or H_9), 4.30 A of AB (d, $J_{4,5}$=5.6 Hz, 1H, H_4 or H_5), 3.94 (bd, 1H, H_4 or H_5), 3.25 (bs, 1H, H_1 or H_7), 3.21 (bs, 1H, H_1 or H_7), 3.12-3.06 A and B of AB (m, 2H, H_2 and H_6), 1.58 A of AB (d, $J_{10a,10s}$=8.3 Hz, 1H, H_{10a} or H_{10s}), 1.47 B of AB (d, 1H, H_{10a} or H_{10s}), 1.36 and 1.28 (2s, 3H and 3H, -$C(CH_3)_2$-). IR ($CHCl_3$): υ 3080-2800 (C-H, unsat. and sat.), 1740 (C=O), 1080 (C-O) cm^{-1}. EI/MS: *m/e* (%) 220 (7,M^+), 205 (27,-CH_3), 177 (5,-C_3H_7), 162 (3,-C_3H_6O), 145 (10,-$C_3H_7O_2$), 139 (1,-C_5H_6,-CH_3), 97 (21,-C_5H_6,-C_3H_5O), 79 (22,-C_5H_6,-$C_3H_7O_2$), 66 (100,$C_5H_6^+$), 43 (22,$C_3H_7^+$). Found: C 70.83, H 7.19 (calc. for $C_{13}H_{16}O_3$: C 70.89, H 7.32).

18: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.26 A of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.1 Hz, 1H, H_8 or H_9), 6.18 B of AB (dd, $J_{1,9}$ resp. $J_{7,8}$=3.0 Hz, 1H, H_8 or H_9), 4.49 A of AB (d, $J_{4,5}$=5.8 Hz, 1H, H_4), 4.44 (dd, $J_{5,6}$=1.3 Hz, 1H, H_5), 3.07 (bs, 1H, H_1 or H_7), 3.01 (bs, 1H, H_1 or H_7), 2.53 A of AB (dd, $J_{2,6}$=7.8 Hz, J=1.3 Hz, 1H, H_2 or H_6), 2.42 B of AB (dd, J=0.9 Hz, 1H, H_2 or H_6), 1.46 A of AB (dt, $J_{10a,10s}$=9.6 Hz, $J_{2,10a}$≈$J_{6,10a}$=1.6 Hz, 1H, H_{10a}), 1.41 and 1.34 (2s, 3H and 3H, -$C(CH_3)_2$-), 1.01 B of AB (d, 1H, H_{10s}). EI/MS: *m/e* (%) 220 (8,M^+), 205 (17,-CH_3), 177 (1,-C_3H_7), 145 (7,-$C_3H_7O_2$), 97 (29,-C_5H_6,-C_3H_5O), 79 (10,-C_5H_6,-$C_3H_7O_2$), 66 (100,$C_5H_6^+$), 43 (17,$C_3H_7^+$).

exo-10-*Oxatricyclo*[5.2.1.$0^{2,6}$]*deca*-4,8-*dien*-3-*one* **20**

Following general procedure D [dry acetonitrile, furan (2.2 g, 32.5 mmol), $ZnCl_2$ (10 drops of a saturated solution in acetonitrile), hydroquinone, 12 kbar, room temperature, 3 d], enantiopure (R)-(+)-**12b** (1.5 g, 11.0 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 1:1), 0.56 g (35%) (+)-**20** (53±2% *ee*, *vide infra*; synthesis of (R)-(+)-**24**) as a white solid.

(+)-**20**: $[\alpha]_D^{22}$= +87.0° (c=0.1128, CH_3OH), 53±2% *ee* by transformation to known (R)-(+)-**24** (*vide infra*). ^{1}H-NMR (400 MHz, $CDCl_3$)[25]: δ 7.60 (dd, $J_{4,5}$=5.7 Hz, $J_{5,6}$=2.6 Hz, 1H, H_5), 6.54-6.51 A of AB (m, 1H, H_8 or H_9), 6.45-6.43 (m, 1H, H_4), 6.24-6.22 B of AB (m, 1H, H_8 or H_9), 5.00 (s, 1H, H_1 or H_7), 4.76 (s, 1H, H_1 or H_7), 3.03-3.01 (m, 1H, H_6), 2.40 (dd, $J_{2,6}$=4.9 Hz, $J_{1,2}$=1.5 Hz, 1H, H_2).

4-*Methylbicylo*[4.3.0]*nona*-3,8-*dien*-7-*one* **21a** *and* 3-*methylbicylo*[4.3.0]*nona*-3,8-*dien*-7-*one* **21b**

Following general procedure D [acetonitrile, isoprene (0.27 g, 3.9 mmol), $ZnCl_2$ (10 drops of a saturated solution in acetonitrile), hydroquinone, 12 kbar, room temperature, 16 h], enantiopure (R)-(+)-**12b** (0.18 g, 1.3 mmol), $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up and flash chromatography (Al_2O_3, type E, *n*-hexane:ethyl acetate = 9:1), 0.14 g (74%) of an inseparable 1:2 mixture of **21a** and **21b** as a colorless oil.

1:2 mixture of **21a** and **21b**: colorless oil. m.p.: ±10 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.48 (dd, $J_{8,9}$=5.7 Hz, $J_{1,9}$=2.6 Hz, 2H, H_9 of **21a** and **b**), 6.18 (dd, $J_{1,8}$=1.9 Hz, 2H, H_8 of **21a** and **b**), 5.51-5.49 (m, 1H, H_4 of **21b**), 5.39-5.37 (m, 1H, H_3 of **21a**), 3.29-3.20 (m, 2H, H_1 of **21a** and **b**), 2.52-1.92 (m, 10H, H_{2n}, H_{2x}, H_{5n}, H_{5x} and H_6 of **21a** and **b**), 1.69 (s, 3H, -$C(CH_3)$=CH- of **21a**), 1.66 (s, 3H, -$C(CH_3)$=CH- of **21b**). IR (CH_2Cl_2): υ 3030 (C-H, unsat.), 3000-2800 (C-H, sat.), 1705 (C=O, conj.), 1590 (C=C, conj.) cm^{-1}. EI/GC-MS: *m/e* (%) **21a**: 148 (100,M^+), 133 (80,-CH_3), 105 (53,$C_6H_5CO^+$), 91 (46,$C_7H_7^+$), 77 (42,$C_6H_5^+$), 68 (27,$C_5H_8^+$), 55 (34,$C_3H_3O^+$). **21b**: 148 (100,M^+), 133 (85,-CH_3), 105 (63,$C_6H_5CO^+$), 91 (53,$C_7H_7^+$), 77 (50,$C_6H_5^+$), 68 (13,$C_5H_8^+$), 55 (45,$C_3H_3O^+$).

3,4-*Dimethylbicylo*[4.3.0]*nona*-3,8-*dien*-7-*one* **21c**

Following general procedure D [dry acetonitrile, 2,3-dimethyl-1,3-butadiene (0.38 g, 4.6 mmol), $ZnCl_2$ (10 drops of a saturated solution in acetonitrile), hydroquinone, 12 kbar, room temperature, 18 h], enantiopure (R)-(+)-**12b** (0.31 g, 2.2 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 3:1), 0.22 g (60%) (+)-**21c** (52% *ee*) as a colorless oil.

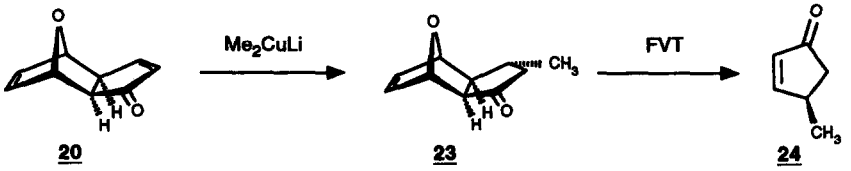
Following general procedure E [benzene, 2,3-dimethyl-1,3-butadiene (0.45 g, 5.4 mmol), hydroquinone, 15 kbar, room temperature, 20 h], enantiopure (R)-(+)-**12b** (0.30 g, 2.1 mmol, $[\alpha]_D$= +100.3° (c=0.991,

CH_3OH)), gave, after work-up and flash chromatography (*n*-hexane:ethyl acetate = 3:1), 0.23 g (65%) (+)-**21c** (52% *ee*) as a colorless oil.
(+)-**21c**: colorless oil. m.p.: ±10 °C. $[\alpha]_D^{22}$= +90.2° (c=1.019, CH_3OH), 52±2% *ee* by ^{1}H-NMR, using 0.3 equiv. of Eu(hfc)$_3$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.46 (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$=2.6 Hz, 1H, H_9), 6.16 (dd, $J_{1,8}$=1.9 Hz, 1H, H_8), 3.23-3.20 (m, 1H, H_1), 2.48 (dt, $J_{5n,6}$ resp. $J_{5x,6}$≈$J_{1,6}$≈6.7 Hz, $J_{5n,6}$ resp. $J_{5x,6}$=3.8 Hz, 1H, H_6), 2.33 A of AB (bdd, $J_{2n,2x}$=14.8 Hz, $J_{1,2n}$ resp. $J_{1,2x}$≈7.3 Hz, 1H, H_{2n} or H_{2x}), 2.26 A of AB (dd, $J_{5n,5x}$=14.6 Hz, 1H, H_{5n} or H_{5x}), 2.18 B of AB (bdd, 1H, H_{5n} or H_{5x}), 1.92 B of AB (dd, $J_{1,2n}$ resp. $J_{1,2x}$≈3.4 Hz, 1H, H_{2n} or H_{2x}), 1.64 and 1.60 (2s, 3H and 3H, -C(CH_3)=C(CH_3)-). IR (CH_2Cl_2): υ 3050-2800 (C-H, unsat. and sat.), 1700 (C=O, conj.), 1590 (C=C, conj.) cm^{-1}. EI/MS: *m/e* (%) 162 (100,M^+), 147 (94,-CH_3), 119 (30,-CH_3,-CO), 91 (29,$C_7H_7^+$), 77 (14,$C_6H_5^+$), 55 (31,$C_3H_3O^+$). EI/HRMS *m/e*: 162.1046 (calc. for $C_{11}H_{14}O$ (M^+): 162.1045).

8,10-*Dibenzotricyclo*[5.2.2.0^{2,6}]*undeca*-4,8,10-*trien*-3-*one* **22**
To a solution of enantiopure (R)-(+)-**12b** (0.30 g, 2.2 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)) in dry benzene (15 ml), $AlCl_3$ (0.54 g, 4.1 mmol) was added and the mixture was stirred for 15 minutes at room temperature to allow complexation. Next, anthracene (0.46 g, 2.6 mmol) was added and the resulting mixture was stirred for another 30 minutes at room temperature. The anthracene did not dissolve, but as the reaction proceeded it was replaced by a dark green solid, presumably a complex of the cyclo-adduct with $AlCl_3$. An excess well over 1 equiv. of the Lewis acid is required to achieve complete conversion. The resulting mixture was quenched with ice/water and washed successively with saturated aqueous sodium bicarbonate and brine. The aqueous fractions were extracted once with benzene (30 ml). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated at reduced pressure. Separation of excess anthracene and (+)-**22** by flash chromatography (*n*-hexane:ethyl acetate = 3:1) gave 0.46 g (83%) (+)-**22** (94% *ee*) as a white solid. One crystallization from acetone gave enantiopure (+)-**22**.
On a larger scale [dry benzene (1 l), $AlCl_3$ (24.6 g, 0.19 mol), anthracene (16.5 g, 92.6 mmol)], enantiopure (R)-(+)-**12b** (13.0 g, 92.8 mmol, $[\alpha]_D$= +100.3° (c=0.991, CH_3OH)), gave, after work-up, 23.4 g (98%) impure (+)-**22** (±90% *ee*), containing approximately 4% (R)-(+)-**12b** and 4% anthracene. Several crystallizations from acetone gave enantiopure (+)-**22**.
(+)-**22**: white powder (acetone). m.p.: 225.5-227 °C (± 175 °C, sublim.) [Lit[49] m.p.: 218-219.5 °C (racemic)]. $[\alpha]_D$= +194.0° (c=0.380, $CHCl_3$), 100% *ee* by ^{1}H-NMR using 1.5 equiv. of Eu(hfc)$_3$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.39 (dd, $J_{4,5}$=5.7 Hz, $J_{5,6}$=2.4 Hz, 1H, H_5), 7.35-7.32, 7.23-7.17, 7.14-7.12 and 7.08-7.05 (4m, 2H, 1H, 3H and 2H, $H_{arom.}$), 5.79 (dd, $J_{4,6}$=1.8 Hz, 1H, H_4), 4.63 (d, $J_{1,2}$=3.5 Hz, 1H, H_1), 4.45 (d, $J_{6,7}$=3.1 Hz, 1H, H_7), 3.39-3.36 (ddd, 1H, H_6), 2.76 (dd, $J_{2,6}$=6.2 Hz, 1H, H_2). IR ($CHCl_3$): υ 3100-2970 (C-H, unsat.), 2970-2880 (C-H, sat.), 1700 (C=O, conj.), 1585 (C=C, conj.) cm^{-1}. EI/MS: *m/e* (%) 258 (0.4,M^+), 178 (100,$C_{14}H_{10}^+$). Found: C 87.88, H 5.38 (calc. for $C_{19}H_{14}O$: C 88.34, H 5.46) [Lit[49] Found: C 88.0, H 5.2].

Determination of the ee *of* (+)-**20**
The furan-adduct (+)-**20**, isolated from the Diels-Alder reaction between enantiopure (R)-(+)-**12b** and

Scheme 6



20 **23** **24**

furan (*vide supra*) was reacted with dimethylcopperlithium to yield the 1,4-adduct **23**, which was subjected to flash vacuum thermolysis (FVT) to give the known[4c] (R)-(+)-4-methylcyclopent-2-en-1-one **24** (*vide infra*).

exo-5-*Methyl*-exo-10-*oxatricyclo*[5.2.1.0^{2,6}]*dec*-8-*en*-3-*one* **23**
To a suspension of CuI (1.1 g, 5.7 mmol) in dry ether (100 ml), 6.4 ml of a 1.6 M solution of methyllithium (10.2 mmol) in hexane was added at 0 °C under a nitrogen atmosphere. After addition was complete, the initially turbid, yellow mixture turned clear and colorless and was stirred for another 15 minutes at 0 °C. Next, a solution of (+)-**20** (0.54 g, 3.7 mmol, isolated from Diels-Alder reaction, *vide supra*) in ether (20 ml) and THF (20 ml) was gradually added. The mixture turned turbid and yellow once

more. After 0.5 h the reaction was complete according to TLC (SiO_2, *n*-hexane:ethyl acetate = 1:1). The resulting mixture was quenched with saturated aqueous ammonium chloride (120 ml) and the organic and aqueous phases were separated. The organic phase was washed twice with brine and the aqueous phase extracted twice with ether (75 ml). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated at reduced pressure. Flash chromatography (*n*-hexane:ethyl acetate = 3:1) gave 1,4-adduct (+)-**23** as a colorless oil in quantitative yield.
(+)-**23**: $[\alpha]_D$= +145.6° (c=1.354, CH_3OH), 53±2% *ee* by conversion to (R)-(+)-**24** (*vide infra*). ^{1}H-NMR (100 MHz, $CDCl_3$): δ 6.45 A of AB (dd, $J_{8,9}$=5.8 Hz, $J_{1,9}$ resp. $J_{7,8}$=1.5 Hz, 1H, H_8 or H_9), 6.35 B of AB (dd, $J_{1,9}$ resp. $J_{7,8}$=1.5 Hz, 1H, H_8 or H_9), 5.05 (bs, 1H, H_1 or H_7), 4.92 (bs, 1H, H_1 or H_7), 2.71 A of AB (dd, $J_{4n,4x}$=16.3 Hz, $J_{4n,5}$ resp. $J_{4x,5}$=7.1 Hz, 1H, H_{4n} or H_{4x}), 2.44-1.90 (m, 4H, H_2, H_5, H_6 and H_{4n} or H_{4x}), 1.13 (d, $J_{5,CH3}$=6.7 Hz, 3H, $-CH_3$). IR (CH_2Cl_2): υ 3040-2820 (C-H, unsat. and sat.), 1730 (C=O) cm^{-1}. EI/MS: *m/e* (%) 149 (11,M^+-CH_3), 68 (26,$C_4H_4O^+$), 28 (100,CO^+).

(R)-(+)-4-*Methylcyclopent-2-en-1-one* **24**
Flash vacuum thermolysis (pre-heating: 80 °C, oven-temperature: 500 °C, pressure: 0.03 mmHg, 1.5 h) of (+)-**23** (67 mg, 0.41 mmol, *vide supra*) gave (R)-(+)-**24** as a solution in approximately 5 ml ethanol. Yield (32 mg, 81%) and *ee* (53±2%) were determined by measuring the UV-spectrum of a 1,000-fold diluted sample[4c].
(+)-**24**: $[\alpha]_D^{25}$= +100.3° (c=0.745, EtOH).

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exhibits a much higher optical rotation (*i.e.* $[\alpha]_D$= +229° (c=0.04, MeOH)). The correct value was reported earlier by Laumen and Schneider[10b] (*i.e.* $[\alpha]_D$= +66° (c=0.63, $CHCl_3$)).
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