Catalytic asymmetric synthesis of polysubstituted cyclohexa-1,3-dienes from β-branched α,β-alkenals

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3-Methyl- and 3-phenylbut-2-enal in the presence of (*S*)-prolinol (0.1 eq.) in benzene or THF react with the acidic monoesters of alkenylidene-, arylmethylidene-, and alkylidenemalonic acids at −10 to +22 °C to give optically active esters of 4,6-disubstituted cyclohexa-1,3-diene-1-carboxylic acids in moderate (10—43 %) yields. The enantiomeric purity of the products formed from the first two types of acidic ylidenemalonates varies from 28 to 68 % and is higher than that observed in the case of related alkylidenemalonates. Under similar conditions cyclohexylideneacetaldehyde affords optically active derivatives of 1,5,6,7,8,8a-hexahydronaphthalene as mixtures of *cis* and *trans* isomers. The enantiomeric purity and absolute configuration of the cyclohexadienes thus obtained were determined using ^{1}H NMR spectroscopy in combination with chiral solvating agents.

Key words: (*S*)-prolinol; chiral 1-amino-1,3-dienes, generation and *in situ* transformation; chiral cyclohexa-1,3-dienes and hexahydronaphthalenes, synthesis; monoalkylidenemalonates; [4+2] cycloaddition, stereoselectivity.

Preparation of chiral carbocyclic and heterocyclic compounds by means of [4+2] cycloaddition reactions has been one of the main areas of modern asymmetric synthesis (for review, see Refs. 1—4). Typically, for a long period the research in this area was focused mainly on a quest for effective chiral catalysts of these reactions[2] and on designing and employing various chiral dienophiles. Much less attention was paid to the use of homochiral 1,3-dienes (such as certain cyclopentadienes,[4] 1-*O*-methylmandeloxy-1,3-dienes and their analogs,[5—7] 1-*O*-substituted dienes containing carbohydrate-derived moieties,[8] or 1-substituted and 2-substituted 1,3-dienes with allylic, functionally substituted asymmetric centers[9,10]), largely due to the difficulty of their preparation. Moreover, in contrast to dienophiles, acyclic dienes are conformationally more flexible. This conformational mobility makes it difficult to predict and explain the stereochemical outcome of reactions involving such chiral dienes (*cf.* Refs. 5 and 6).

It is only recently that a number of successful asymmetric syntheses employing homochiral 1,3-dienes with more predictable conformational behavior (arising from vicinal arrangement of the asymmetric center and diene moiety) were reported. They involve 1-sulfinyl- and 2-sulfinyl-1,3-dienes,[11,12] 1-aza-1-aminodienes,[13] and, particularly, 2-aminodienes with chiral pyrrolidine[14] or morpholine[15] moieties (partly reviewed in Ref. 16). Still, the synthesis of such dienes is tedious enough, and the regeneration of a chiral inductor from the cycloadduct is either impossible[11,12] or, at least, non-quantitative.

Surprisingly, homochiral 1-amino-1,3-dienes ("dienamines"), which can be prepared in one step from the readily accessible α,β-enals of the general type $RCH_2C(R^1)=C(R^2)CHO$ and lower chiral secondary amines (for review, see Ref. 17), found for a long time no use in the Diels—Alder reactions. The nearest analogy to this approach was the formation of chiral *N*-dienyllactams from α,β-enals of the above structural type and the esters of (*S*)-pyroglutamic acid.[18] However, the yields of these lactams were moderate (40—65 %), and regenerating the chiral inductor from the cycloadducts therefrom (*de* 34—88 %) was not always an easy task.

Recently we found that the optically active polysubstituted cyclohexa-1,3-dienes could be obtained upon contacting equimolar amounts of 3-methylbut-2-enal (**1a**) and monoalkyl prenylidene- or benzylidenemalonate with 0.1 molar equivalent of chiral secondary amine.[19] Although the intermediate chiral dienamine was not isolated or characterized, its transient formation and subsequent cycloaddition to the acidic dienophile leaves no doubt considering the mechanism of formation of polysubstituted cyclohexadienes from isoprenoidal α,β-enals and monoalkyl ylidenemalonates in the presence of achiral secondary amines. This mechanism, proven by us earlier (Scheme 1),[20] incorporates the formation of dienamines of the type **B** as reaction intermediates, and a spontaneous regeneration of a secondary amine at the final stage of the process (**D**→**E**).

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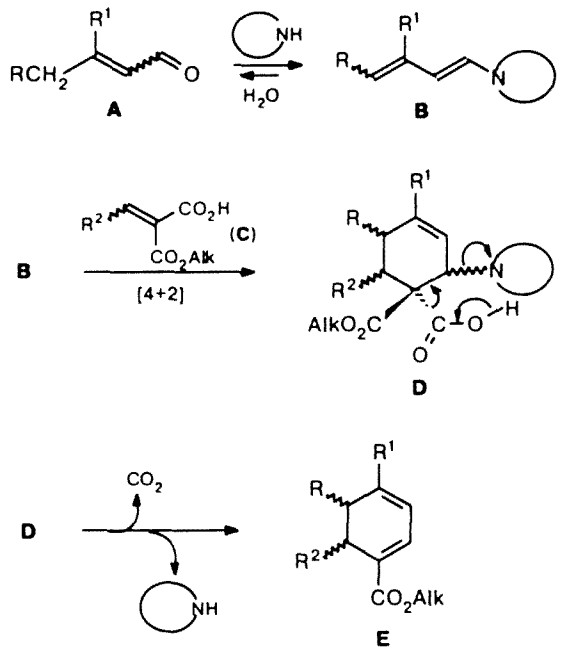
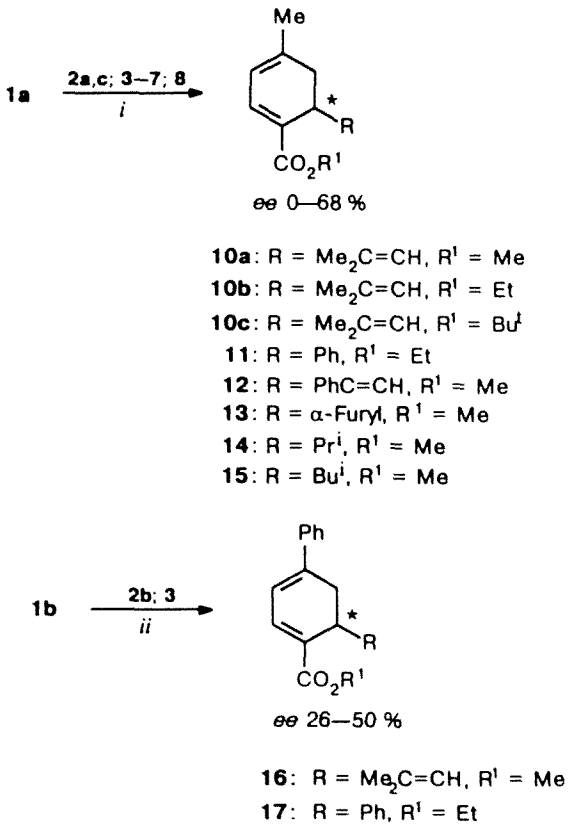
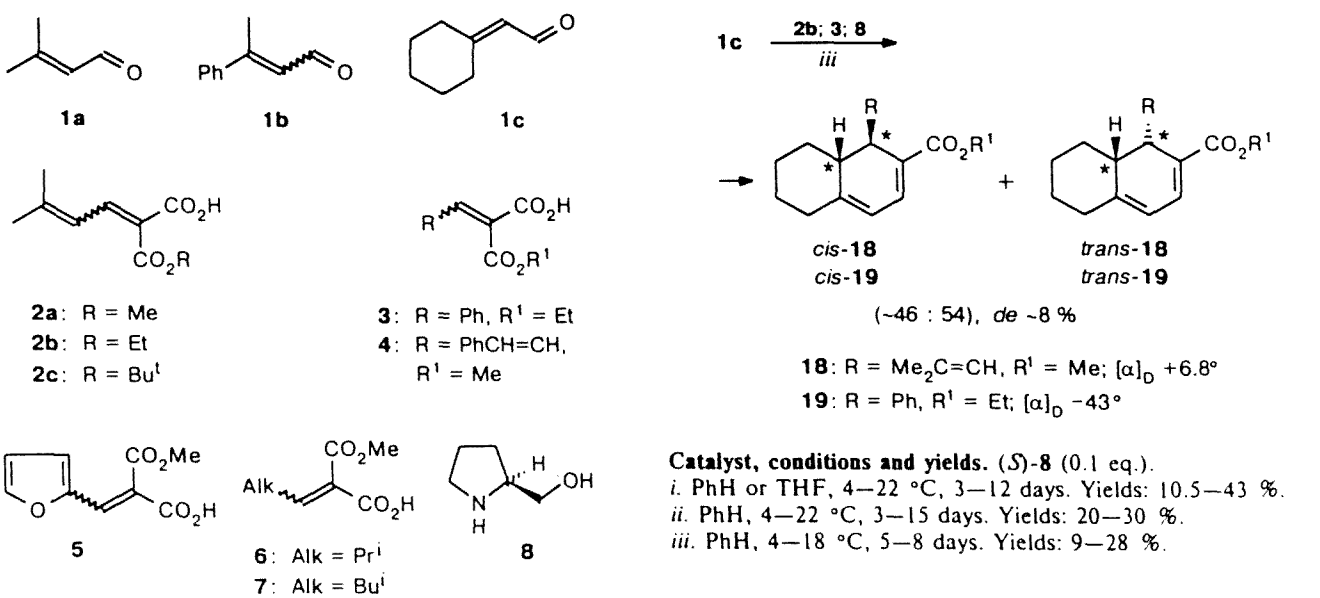
Scheme 1



Scheme 2



The scope of the reaction. In order to apprise the scope and limitations of the found asymmetric reaction in this work we studied the interaction of three β-branched α,β-enals with monoesters of prenylidenemalonic (**2a—c**), benzylidenemalonic (**3**), cinnamylidenemalonic (**4**), furfurylidenemalonic (**5**), isobutylidenemalonic (**6**), and 3-methylbutylidenemalonic acid (**7**) in the presence of (*S*)-(+)-prolinol (**8**).



The results of the study are summarized in Scheme 2 and Table 1.

When alkenals **1a—c** reacted with equimolar amounts of acidic monoalkyl ylidenemalonates in the presence of amine **8** (0.1 eq.) in benzene or THF at 4—22 °C, the resultant products coincided by their TLC data and

Table 1. Yields and chirality characteristics of the derivatives of cyclohexa-1,3-diene and 1,5,6,7,8,8a-hexahydronaphthalene derivatives prepared under standard conditions[a]

Entry	Reactants		Reaction temperature (°C)	Time (h)	Product	Yield (%)	$[\alpha]_D$ ($c \approx 1$; PhH)	*ee* (%)[c]
	Enal	Monoester[b]						
1	**1a**	**2a** (20 : 80)	+4	72	**10a**	34	+184°	68
2	**1a**	**2b** (45 : 55)	+4	72	**10b**	36	+111°	60
3	**1a**	**2c** (60 : 40)	+4	72	**10c**	15	+29°	≤10
4	**1a**	**3** (8 : 92)	+22	360	**11**	33	−52°	28
5	**1a**	**4** (<1 : 99)	+4[d]	96[d]	**12**	36[d]	+121°	32[d]
6	**1a**	**5** (40 : 60)	+4	120	**13**	14	+50°	66
7	**1a**	**5** (40 : 60)[d]	+4[d]	96[d]	**13**	41	+28°	37[d]
8	**1a**	**6** (50 : 50)	+4	120	**14**	10.5	+18°	20
9	**1a**	**7** (40 : 60)	+4	72	**15**	43	~0°	~0
10	**1a**	**7** (40 : 60)[e]	−10[e]	288[e]	**15**	3	+26°	20[e]
11	**1b**	**2b** (20 : 80)	+4	96	**16**	30	+103°	50
12	**1b**	**3** (8 : 92)	+22	360	**17**	20	−60°	26
13	**1c**	**2b** (20 : 80)	+4	120	**18** (*trans*>*cis*)	28	+6.8°	*f*
14	**1c**	**3** (8 : 92)	+18	192	**19** (*trans*>*cis*)	9	−43°	*f*

[a] Molar ratio enal/monoester = 1 : 1, (*S*)-prolinol **8** (0.1 eq.) as the catalyst, dry benzene as the solvent. [b] *E* : *Z* ratios, determined from ^{1}H NMR spectra of these monoalkyl malonates (see Ref. 21), are given in brackets. [c] Determined by using the integral intensity ratios of the signals from RC$\underline{H}$ and/or $CO_2CH_2R^2$ (R^2 = H or Me) in ^{1}H NMR spectra of the products in C_6D_6; the signals become split upon adding 1—3 eq. of (*S*)-(**9**) or (*R*)-**9**. [d] Dry THF was used as the solvent. [e] Dry toluene was used as the solvent. [f] Diastereomeric excess (*de*) is about 8 % in favor of the *trans*-steroisomer (determined from ^{1}H NMR spectra, *cf.* Ref. 21); the values of *ee* for the poorly separated components of products **18** and **19** could not be determined.

^{1}H NMR, IR, an UV spectra with the racemic cyclic dienes obtained earlier[21] upon heating the same reactants in benzene (0.5—2 h) in the presence of piperidine. To the exclusion of the reaction between **1a** and **7**, all the reactions of enals **1a—c** with dienophiles **2a—c** and **3—6** within the above temperature range gave rise to the products with significant specific rotations (see Table 1). The optically active product from the reaction of **1a** with **7** was, however, obtained (albeit in very low yield) when the reaction was carried out at −10 °C in toluene. Enantiomeric purity of the products was determined from their ^{1}H NMR spectra according to a known procedure[22,23] by using the integral intensity ratios for the signals corresponding to the protons at the asymmetric center and for those of the protons of the ester grouping (both in the preponderant and minor enantiomer); These signals become splitted in the presence of a chiral solvating agent (CSA). In this work, (*S*)-(−)- and (*R*)-(+)-1,1′-bi-2-naphthol [(*S*)-**9** and (*R*)-**9**] were used as such agents.

From the data of Table 1 it appears that catalytic asymmetric synthesis of chiral 1,3-cyclohexadiene systems from β-branched enals of the type **A** and dienophiles like **2—7** may be of reasonably wide scope. Under comparable conditions (4 °C, 3—5 days) the highest asymmetric induction (32—68 % *ee*) was observed for the addition of the dienamines of **1a,b** to those of the monoalkyl ylidenemalonates which possess an additional, moderately delocalized double bond (**2a,b**, **4**, and **5**), while the lowest enantioselectivity (*ee* ≤ 20 %) was characteristic of the reactions involving alkylidenemalonates **6** and **7**; the addition of the same dienamines to the acidic benzylidenemalonate **3** gave the products with intermediate values of *ee*. Judging by the yields attained under identical conditions in comparable reaction spans, the reactivity of the enals towards dienophiles **2a,b** and **3** diminishes in the order **1a** > **1b** > **1c**. Among the ylidenemalonates **2—7**, monoester **3** shows the lowest reactivity toward the dienamines.

The synthesis of chiral cyclohexadienes described in this work appears to be the first example of employing chiral 1-amino-1,3-dienes in the Diels—Alder reaction (*cf.* Ref. 24).

Factors affecting the effeciency and stereoselectivity of the process. ***(a) The effect of temperature.*** With a view of selecting an optimal temperature range, the reaction of enal **1a** with monoester **2b** was carried out at 60, 4, and −10 °C, and that with monoester **2a** — at 4 and 22 °C (in benzene). Lowering the temperature from 60 to 4 °C greatly diminishes the yield of the product and the rate of its formation. However, these disadvantages are compensated by a considerably higher optical purity of the cyclic dienes **10a** and **10b** obtained at 4 °C. Further lowering of the temperature to −10 °C does not improve chemical and optical yield, but only slows down the process (Table 2).

The effect of temperature is also visible in the reaction of **1a** with monoester **7** (*cf.* entries 9 and 10 in Table 1). The reaction of **1a** with monoethyl benzylidenemalonate practically does not occur at 4 °C; after

Table 2. Temperature dependence of the rate and stereoselectivity

Reactants	Product	T/°C	Time/h	Yield (%)	$[\alpha]_D^{20}$	*ee* (%)
1a + **2b**	**10b**	60	0.33	68	+20°	11
		4	72	36	+111°	60
		−10*	144*	42	+109°	60*
1a + **2a**	**10a**	22	2	39	+54°	20
		4	72	34	+184°	68

* Reaction was carried out in toluene.

two weeks of exposure the yield of diene **11** was as low as 2.5 %.

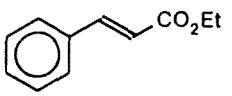
(b) The effect of the solvent. When more polar THF is substituted for benzene as the solvent, both the rate of the reaction and the yield are increased, whereas the optical purity of the product is markedly lowered (*cf.* entries 6 and 7 in Table 1).

(c) Stereoisomeric composition of the dienophile. The reaction of enal **1a** with two specimens of monoester **3** differing in the ratio of *E*- and *Z*-isomers,* catalyzed by amine **8** (0.2 eq.) in benzene (22 °C, 360 h), afforded two specimens of product **11** of identical optical purity; it was only their yield that depended on the ratio of stereoisomers in **3**:

E-**3** : *Z*-**3**	Yield of **11** (%)	$[\alpha]_D^{20}$	*ee* (%)
5.5 : 94.5	25	−45°	24
33.4 : 66.6	12	−45°	24

This result suggests that the cycloaddition of the dienamine formed from **1a** to *E*-**3** proceeds slower than its addition to *Z*-**3**. At the same time, the orientation of the dienophile with respect to the diene in the reaction complex (that is, whether the COOEt grouping is in the *pro*-endo- or in *pro*-exo position) is of little importance for the stereochemistry of the end product.

(d) The effect of the catalyst concentration. Comparing the above yields and *ee* values for the product of the reaction **1a** + **3** → **11** with the respective data of entry 4 in Table 1 one observes that a twofold increase in the concentration of amine **8** brings about a certain decrease of both the yield and optical purity of diene **11**. Moreover, an attempt to accelerate the reaction **1a** + **3** → **11** and increase the yield of **11** by using about an equimolar amount of amine **8** (1.1 eq.; in benzene, 22 °C) resulted, contrary to our expectations, in formation of ethyl cinnamate (**20**), that is, in decarboxylation of monoester **3**. The yield of **20** after 48 h was 39 %. An additional crop of cinnamate **20** (yield 32 %) was obtained from a tarry residue, left after the extraction of **20** from the reaction mass with hexane, upon extracting this residue with boiling benzene for 1 h.



20

Apparently, an increase in the concentration of **8** in the reaction mixture results in enhancing the rate of its Michael addition to the double bond of monoester **3**. Then the resultant betaine-like adduct (an acyclic analog of the intermediate **D** in Scheme 1) undergoes a spontaneous fragmentation which gives rise to CO_2 and compounds **20** and **8**. This process, well-known for the β′-amino-β-dicarbonyl compounds,[25] is an inherent competitor of that presented by Scheme 1, and was already observed in our previous work.[21]

On the other hand, amine **8** does not apparently induce decomposition or racemization of the resulting chiral cyclohexadienes. Thus, a specimen of ester **10b** with $[\alpha]_D^{20}$ +111° was quantitatively recovered after ten days of exposure to amine **8** (0.4 eq.) in benzene at 4 °C without any alteration of its spectral characteristics, R_f, and $[\alpha]_D$. This result points to the chemical and configurational stability of the chiral cyclohexadienes under the selected conditions of their catalytic synthesis.

(e) Steric effect of the ester group in the dienophile. Comparison of the results obtained upon reacting **1a** with acidic prenylidenemalonates **2a**—**c** (entries 1, 2, and 3 in Table 1) reveals that the larger the volume of the ester grouping, the lower is the optical purity of the respective cyclohexadiene. On passage from CO_2Me to CO_2Et the size of the ester grouping changes only slightly, and, correspondingly, the *ee* values of products **10a** and **10b** are not much different. On the other hand, substituting CO_2Bu^t for CO_2Et brings about a sharp increase in the size of the ester group, which is accompanied by a sharp fall of both the *ee* value and the yield of compound **10c**. Such a decrease of the yield and *ee* cannot be attributed to the effect of the stereoisomeric composition of the dienophile, since the *E* : *Z* ratios in the parent monoesters **2b** and **2c** are fairly similar.

Absolute configuration of the products and stereoselectivity of the cycloaddition. Configuration of the optically active cyclohexadienes **10a**—**c**, **11**—**15** and **16**, **17** were elucidated by employing the procedure of Toda *et al.*,[22] which had originally been developed for determining the absolute configuration of chiral sulfoxides and amines. Considering the structural and chemical analogy between sulfoxides and carbonyl compounds, we thought that the topology of the binding between the CSA and esters might be depicted by a model postulated earlier[22] to account for the changes induced in the ^1H NMR spectra of chiral sulfoxides by the addition of (*S*)-**9** and (*R*)-**9**.

By analogy with the binding topology discussed in Ref. 22, it can be assumed that the planes of the naph-

* Specimens of compound **3** with stereoisomeric composition indicated below were obtained earlier[21] by fractional crystallization of native **3** from heptane—cyclohexane.

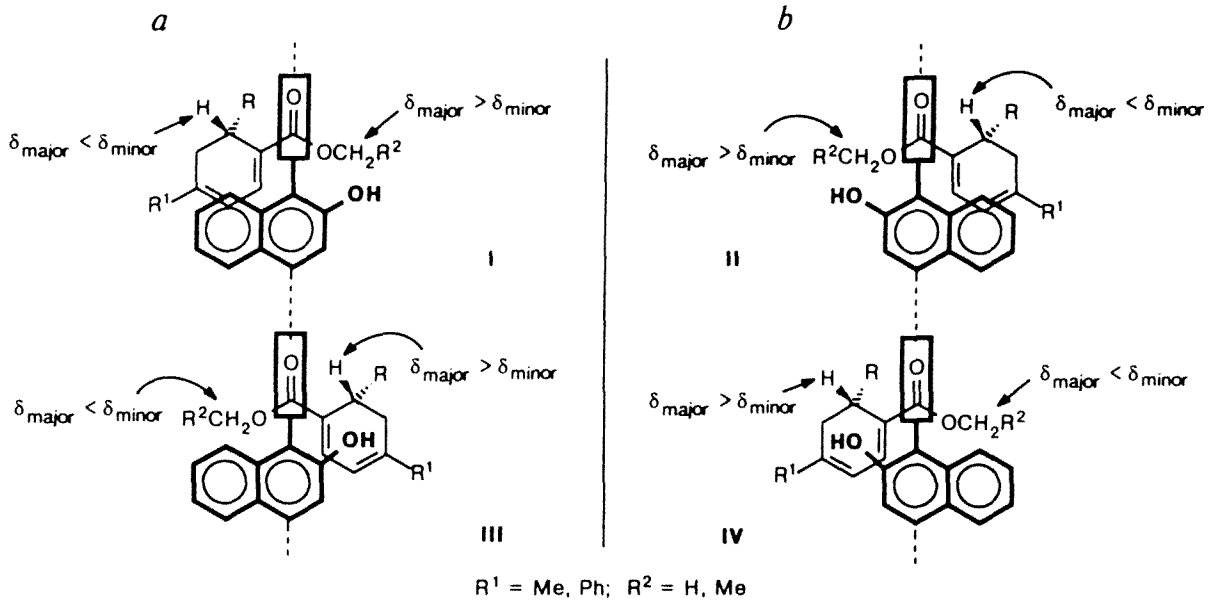


Fig. 1. Hypothetical topology of the bonding of CSA with enantiomeric cyclohexadienes **10**—**17** and the resultant alterations in the ^{1}H NMR spectra of their nonracemic mixtures (δ_{major} and δ_{minor} are the signals from the preponderant and minor component): *a*) CSA = (*S*)-(−)-**9**; *b*) CSA = (*R*)-(+)-**9**.

thalene rings in enantiomeric binaphthols **9** would be forming a right dihedral angle along the C(1)—C(1′) axis, while the coordination of a molecule of **9** with an ester molecule would be mediated by a hydrogen bond between one of the phenolic hydroxy groups and the oxygen atom of the carbonyl group. Moreover, in a complex thus formed the ester molecule would be turned to the molecule of CSA by its sterically less hindered face. If these provisions hold good, then four topological situations (I—IV), corresponding to the interaction of (*S*)-**9** and (*R*)-**9** with enatiomeric esters of 4,6-disubstituted cyclohexa-1,3-diene-1-carboxylic acids, can be visualized (Figure 1).

If one and the same enantiomer of a cyclohexadiene ester forms complexes with (*S*)-**9** or (*R*)-**9** (*cf.* the pairs I, IV and II, III), the zone of diamagnetic shielding, created by the "lower" naphthalenic moiety, can be occupied either by the nearest atom H-6 at the asymmetric center of the diene ester (situations I, II) or by the nearest alkoxy group (situations III, IV). Thus, absolute configurations of the preponderant and minor component in an analyzed specimen can be deduced from the changes of the respective δ_H in the spectrum.

In the ^{1}H NMR spectra of ester **10a** (in benzene-d_6, 250 MHz, measurement accuracy ±0.002 p.p.m.; see Table 3, entries 1a and 1b) the CSA-induced displacements of the chemical shifts attributable to the major (δ_{major}) and minor component (δ_{minor}) corresponded to topological situations II and III. On this basis the prevailing enantiomer in specimen **10a** (R = Me_2C=CH) was characterized as the (*S*)-enantiomer. The spectrum of **10b** in the presence of (*S*)-**9**, and the spectrum of **10c** in the presence of (*R*)-**9** undergo the same changes as those induced by these two CSAs in the spectrum of **10a**. Displacements, observed in the spectrum of ester **13** upon the addition of (*S*)-**9**, and those occurring in the spectra of compounds **12** and **14**—**16** upon the addition of (*R*)-**9**, are compatible with mutual orientations of the type III and II, respectively. Therefore, preponderant enantiomers in esters **12**—**16** have the same absolute configuration as in the esters **10a**—**c**. According to the priority rules of the *RS*-designation system this corresponds to the *S*-configuration for compounds **12**, **14** and **16** and to *R*-configuration for **13**, **15**. All of the above cyclohexadienes are dextrorotatory (*cf.* Table 1 and Table 3).

The spectrum of compound **11**, recorded in the presence of (*S*)-**9**, and that of compound **17**, taken upon the addition of (*R*)-**9**, correspond to topological situations I and IV, respectively. Hence, the configuration of major enantiomers in both **11** and **17** is opposite (*R*) to that assigned to cyclohexadienes **10a**—**c** and **12**—**16**. Symptomatically, both **11b** and **17** are levorotatory.

The derivatives of 1,5,6,7,8,8a-hexahydronaphthalene (**18**, **19**), resulted from the reactions of enal **1c** with monoesters **2a** and **3**, were obtained as poorly separable mixtures of 1,8a-*trans*- and 1,8a-*cis*-isomers, both of which can be present in two enantiomeric forms. For that reason, no attempt was made to establish the absolute configuration of the preponderant stereoisomer by combined ^{1}H NMR—CSA technique. Previously we found[21] that the reactions of **1a** with **2a** and **1c** with **3** in the presence of piperidine gave rise to racemic mixtures of respective hexahydronaphthalenes which contained mainly 1,8a-*trans*-isomers (~67 % in the case of **2a** and ~90 % in the case of **3**). However, when the same

Table 3. Displacements of chemical shifts of diagnostic signals in ^{1}H NMR spectra of cyclohexadienes **10—17** induced by chiral solvating agents (*R*)-**9** and (*S*)-**9** (in C_6D_6 at 20—22 °C; [substrate] ≈ 0.1 *M*; molar ratio substrate : CSA = 1 : 3)

Entry	Substrate[a]	CSA	δ (p.p.m.) in absence of CSA			δ (p.p.m.) in presence of CSA[b]			Tentative absolute configuration[c]
			6-H	OMe	OCH_2Me	6-H	OMe	OCH_2Me	
1a	**10a**	(*S*)-(−)-**9**	3.825	3.480	—	3.837 3.810	3.452 3.480	—	(*S*)-(+)
1б	**10a**	(*R*)-(+)-**9**				3.775 3.798	3.443 3.426	—	
2	**10b**	(*S*)-(−)-**9**	3.875	4.11	1.040	3.910 3.885	—	4.01 and 1.00 4.04 1.01	(*S*)-(+)
3	**10c**	(*R*)-(+)-**9**	3.873	—	—	3.850 3.861	—	—	(*S*)-(+)
4	**11**	(*S*)-(−)-**9**	4.223	4.02	0.984	4.130 4.150	—	4.04 and 0.98 3.97 0.96	(*R*)-(−)
5	**12**	(*R*)-(+)-**9**		не опр.		3.700 3.720	3.480 3.464	—	(*S*)-(+)
6	**13**[d]	(*S*)-(−)-**9**	4.125[d]	3.720[d]	—	4.333[d] 4.320	3.451[d] 3.461	—	(*R*)-(+)
7	**14**	(*R*)-(+)-**9**	2.605	3.740	—	2.805[e]	3.505 3.494	—	(*S*)-(+)
8	**15**	(*R*)-(+)-**9**	3.051	3.567	—	~3.0—2.9[e]	3.540 3.530	—	(*R*)-(+)
9	**16**	(*R*)-(+)-**9**	3.988	3.524	—	~4.0—3.9[e]	3.502 3.485	—	(*S*)-(+)
10	**17**	(*R*)-(+)-**9**	4.380	3.96	1.01	4.315 4.280	—	3.96 and 0.96 3.99 0.97	(*R*)-(−)

[a] Enantiomeric composition of specimens is the same as indicated in Table 1. [b] The values of δ in the upper line relate to the major enantiomer, and those in the lower line relate to the minor enantiomer. [c] The signs of the absolute configuration relate to the major enantiomer; the configurations are determined by analogy with the model of Toda *et al.*[22] depicting the interaction of enantiomeric CSAs with the enantiomers of the substrate. [d] In $CDCl_3$. [e]Broad, poorly resolved multiplet.

reactions were catalyzed by (*S*)-prolinol, the resultant diene esters **18** and **19** had another diastereomeric composition. As follows from their ^{1}H NMR spectra, in both of them the sum of *trans*-isomers (1*S*,8a*R* and 1*R*,8a*S*) and the sum of *cis*-isomers (1*R*,8a*R* and 1*S*,8a*S*) are in a ratio of about 54 : 46, thence *de* ≈8 %. Such a composition of the product mixtures makes it difficult to infer the configuration of the major component judging by the $[\alpha]_D$ alone (+6.8° for **18** and −43° for **19**).

Experimental

The reaction masses were monitored, and the purity of isolated products was controlled by TLC using Silufol® plates. Silica gel L (Czech Republic, 40—100 mm) was used for column chromatography. ^{1}H NMR spectra were recorded in C_6D_6 at 20—22 °C on a Bruker WM-250 spectrometer (250 MHz); optical purity of the products was measured in NMR tubes filled with solutions containing a specimen to be analyzed together with a CSA [(*S*)-**9** or (*R*)-**9**] in concentrations of 0.1 *M* and 0.3 *M*, respectively. Specific rotations of the products were determined in benzene (*c* = 1.0) at 20—22 °C by using a Jasco—DIP 360 polarimeter. Structural identification of cyclohexadienes **10a,b** and **11—19** was carried out by comparing their ^{1}H NMR, IR, and UV spectra with those recorded previously[21] for the respective racemic products.

The reactions were performed with the same specimens of enals **1a—c** and acidic ylidenemalonates (**2a,b**, **3—7**) as before.[21] Monoester **2c** was prepared according to an earlier procedure.[20] (*S*)-(+)-Prolinol (**8**) with b.p. 74—75 °C (2 Torr) and $[\alpha]_D^{20}$ +31.2° (*c* = 1.0, C_6H_6) was prepared from L-proline (Reanal, Hungary) according to the procedure of Enders *et al.*[26] (*S*)-(−)- and (*R*)-(+)-1,1′-bi-2-naphthol [(*S*)-**9** and (*R*)-**9**] were obtained by resolving racemic binaphthol **9** *via* diastereomeric derivatives according to a known procedure.[27]

Optically active cyclohexadienes 10—19. General procedure. To a vigorously stirred mixture of a monoalkyl ylidenemalonate (**2—7**; 1.0 mmol) and amine **8** (0.01 mL, ~0.1 mmol) in dry benzene (2 mL) at 20—22 °C an aldehyde (**1a—c**; 1.0 mmol) was added. After additional five minutes of stirring, the reaction vessel was either transferred onto the lower shelf of the refrigerator (+4 °C) or left at room temperature (18—22 °C)for a period indicated in Table 1. Periodically, aliquots of the reaction mass were taken to follow the progress of the reaction until the reactants had been consumed. Then the reaction mass was concentrated under re-

duced pressure, and the residue was dissolved in a minimal volume of hexane or hexane—Et_2O (4 : 1, v/v), deposited onto a pad of silica gel, and chromatographed on a column of SiO_2 (7—12 g; adsorbent/adsorbate ratio ≈ 30 : 1, w/w) using a hexane—Et_2O gradient as the eluent.

With the exception of compounds **16** (m.p. 64—65 °C) and **17** (m.p. 107—108 °C) all the cyclohexadienes thus obtained are viscous, colorless oils. All of them display characteristic UV absorption at 300—310 nm (**10a—c**, **11—15** and **18**, **19**) or at 342—346 nm (**16**, **17**). Their ^1H NMR, IR, and UV spectra are the same as those of the respective racemates (see Ref. 21).

***tert*-Butyl (*S*)-(+)-4-methyl-6-(2-methylpropen-1-yl)cyclohexa-1,3-diene-1-carboxylate (10c)** was obtained as an oil. ^1H NMR (δ, p.p.m.; *J*/Hz): 1.51 (s, 9 H, *t*-Bu); 1.60 (s, 3 H, 2′-Me); 1.67 (s, 3 H, 3′-H_3); 1.90 (s, 3 H, 4-Me); 1.96 (dd, 1 H, 5-H_a, J_{gem} = 17, $J_{5,6}$ = 8); 2.48 (bdd, 1 H, 5-H_e, J_{gem} = 17, $J_{5,6}$ = 10.5); 3.87 (m, 1 H, 6-H); 5.53 (m, 1 H, 1′-H); 5.72 (m, 1 H, 2-H); 6.98 (d, 1 H, J_{vic} = 6.5). UV, λ_{max}: 307 (ε 8500, in EtOH). IR (ν/cm^{-1}): 1708 (s), 1650, 1590, 1245 (film).

Methyl (*S*)-(+)-4-methyl-6-(2-methylprop-1-yl)cyclohexa-1,3-diene-1-carboxylate (15) was obtained according to the above general procedure, but using toluene instead of benzene and keeping the reaction mixture in the upper section of the refrigerator (−10 °C).

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