ENANTIOSELECTIVE DIELS–ALDER REACTION OF (*E*)-1-TRIMETHYLSILYLOXY-1,3-BUTADIENE WITH CHIRAL GLYOXYLATES*

Otakar ČERVINKA[a], Aleš SVATOŠ[b], Petr TRŠKA[a] and Pavel PECH[a]

[a] *Department of Organic Chemistry, Prague Institute of Chemical Technology, 166 28 Prague 6 and*
[b] *Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6*

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Dedicated to Professor Otto Exner on the occasion of his 65th birthday.

Enantioselective Diels–Alder reaction of (*E*)-1-trimethylsilyloxy-1,3-butadiene (*I*) with chiral (−)-menthyl (*II*) and (−)-8-phenylmenthyl (*III*) glyoxylates in various solvents without or with catalysts was studied. The reaction gave a mixture of *trans*- and *cis*-isomers of (−)-menthyl (*IV*) and (−)-8-phenylmenthyl (*V*) 2-trimethylsilyloxy-5,6-dihydro-2*H*-pyran-6-carboxylates. The regioselectivity of the reaction was explained by quantum-chemical calculations, the enantioselectivity was determined using ^{13}C NMR spectroscopy and the absolute configuration of the addition products was assigned on the basis of chemical correlation with (*S*)-(−)-dimethyl malate.

For its high selectivity[1] (enantioselectivity[2] in case of chiral components) the Diels–Alder addition represents a method suitable for synthesis of six-membered ring compounds. Reactions of carbonyl compounds with activated dienes have been thoroughly studied by Danishefsky[3]; Zamojski, Jurczak[4–7] and David[8] have used enantioselective additions of glyoxylates to 1-alkoxy-1,3-butadienes in the synthesis of some pyranose derivatives.

In the present paper we study the Diels–Alder reaction of (*E*)-1-trimethylsilyloxy-1,3-butadiene (*I*), available by addition of trimethylchlorosilane to crotonaldehyde[9], with (−)-menthyl (*II*) and (−)-8-phenylmenthyl (*III*) glyoxylates in various solvents and in some cases in the presence of catalysts. The reaction leads to a mixture of *cis*- and *trans*-esters *IVa*–*IVd* and *Va*–*Vd*.

The described preparation of (−)-menthyl[10] and (−)-8-phenylmenthyl[11] glyoxylates starts from esters of the alcohols with bromoacetic acid. The esters are converted into nitrates which are oxidized with dimethyl sulfoxide. The glyoxylates

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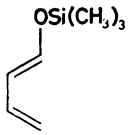
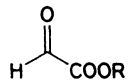
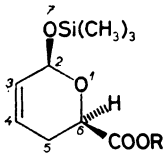
form very stable hydrates and the water was removed by distillation under diminished pressure immediately before the reaction.



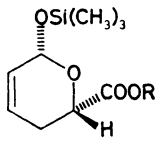
I



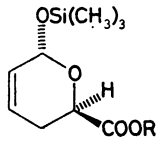
II, R = (−) − menthyl
III, R = (−) − 8 − phenylmenthyl



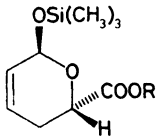
IVa, *Va*
(2*R*, 6*R*)



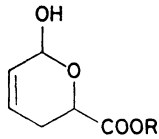
IVb, *Vb*
(2*S*, 6*S*)



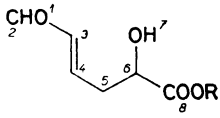
IVc, *Vc*
(2*S*, 6*R*)



IVd, *Vd*
(2*R*, 6*S*)



VIa, *VIb*



VIIa, *VIIb*

In formulae *IVa* − *IVd*, *VIa*, *VIIa*: R = (−) − menthyl
Va − *Vd*, *VIb*, *VIIb*: R = (−) − 8 − phenylmenthyl

As judged from the data of Jurczak, compound *I* is more reactive than the 1-alkoxy-1,3-butadienes used by this author. The reaction products are acid-labile, losing the trimethylsilyl group under formation of unstable hemiacetals *VIa*, *VIb*. After ring cleavage and isomerization of the double bond they were converted into stable aldehydes *VIIa* and *VIIb*. This behaviour made impossible the isolation of the addition products by column chromatography on silica gel. Only after deactivation of the silica gel with triethylamine flash chromatography was successful[12].

The relative configuration of the ester and trimethylsilyloxy groups in the stereoisomeric compounds *IV* was determined by the ^{1}H NMR spectra. On the basis of published data[13], the proton on C-2 (δ 5·48 ppm) in the more populated isomer

was assigned the pseudoequatorial position. The corresponding proton signal in the minor isomer was shifted downfield (δ 5·52 ppm) and was assigned the pseudoaxial position. (The measurements were carried out with a product mixture obtained in benzene and the expressions "more or less populated isomer" relate to this sample.)

Theoretically, *cis*- and *trans*-isomers of compound *IV* may exist in two half-chair conformations ${}^6H_1$ and ${}^1H_6$. Using the Karplus equation[14] for the coupling constants of protons on C-6 and C-5 carbon atoms and for the ^{13}C NMR spectral data, and comparing the literature data on similar compounds[13,15], we concluded that both isomers of compound *IV* exist exclusively in the conformation ${}^1H_6$ with torsion angles H(5*a'*)—C(5)—C(6)—H(6) = 170° and H(5*e'*)—C(5)—C(6)—H(6) = 50°. In both isomers the ester group is pseudoequatorial; the trimethylsilyloxy group in the *trans*-isomer is thus pseudoaxial whereas in the *cis*-isomer pseudoequatorial (Fig. 1).

As follows from the above analysis, in nonpolar solvents the reaction predominantly affords that isomer of *IV* in which the relative configuration of the ester and trimethylsilyloxy group is *trans* (pseudoequatorial proton on C-2) whereas the *cis*-isomer arises in only minor amounts.

The relation between the trimethylsilyl and ester groups in compound *V* was determined analogously. Thus in the major isomer the relative configuration of these two groups is *trans* (Table I).

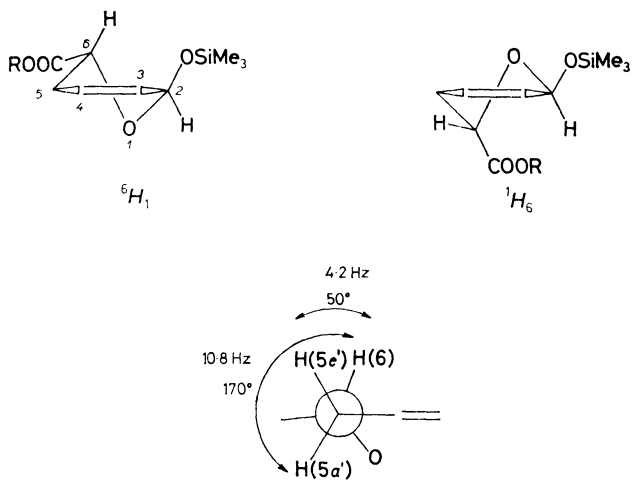
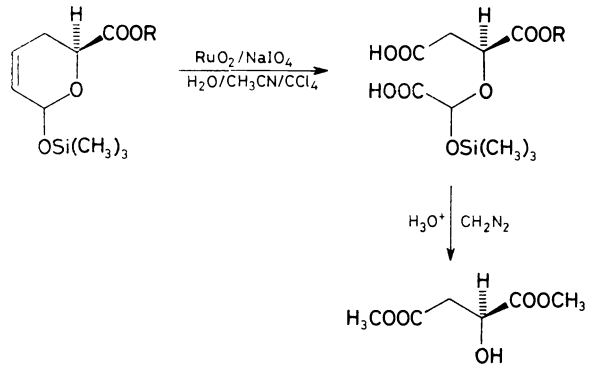


FIG. 1

Assumed conformations ${}^6H_1$ and ${}^1H_6$ for compounds *IV* and *V*

The ratio of the *cis*- and *trans*-isomers of compounds *IV* and *V* was also estimated from the ratio of the trimethylsilyl signals in the 400 MHz proton spectrum and from the HPLC analysis on silica gel (Tables III and IV).

The absolute configuration on the C-6 carbon atom was determined by chemical correlation[6,16] of compounds *IV* and *V* with optically active dimethyl malate of known absolute configuration (Scheme 1). From the obtained CD spectra we determined the enantiomeric purity of the reaction products (Table II).



SCHEME 1

For determination of enantiomeric excess by spectral methods we made use of the fact that the products contain not only two new chiral centers at C-2 and C-6 but also an auxiliary chiral component which is enantiomerically pure and together with the mentioned chiral centers forms four diastereoisomers of different physicochemical properties.

In the ^{1}H NMR spectrum of compound *IV* the signals of diastereoisomers *IVa*, *IVb* and *IVc*, *IVb* overlapped (small differences in chemical shifts of protons on C-2

TABLE I

Coupling constants (Hz) between protons on C-5 and C-6 in compounds *IV* and *V*

Protons	Compound *IV*		Compound *V*	
	trans (*IVc* + *IVd*)	*cis* (*IVa* + *IVb*)	*trans* (*Vc* + *Vd*)	*cis* (*Va* + *Vb*)
H(5*a*)—H(6)	10·8	10·5	11·5	11·5
H(5*e*′)—H(6)	4·2	4·0	3·9	3·7

TABLE II

Values of $\Delta\varepsilon$ at 214 nm in CD spectra of dimethyl malate, isolated from chemical correlation of compound *IV*, obtained under various reaction conditions

Conditions of preparation of *IV*		$\Delta\varepsilon$ 214 nm (in methanol)[a]	Optical purity, %
Solvent	Catalyst		
Benzene	—	−0·07	8
$CHCl_3$	—	+0·04	5
Pyridine	—	+0·03	4
Benzene	Rh complex-(+)-DIOP	−0·00	0
Benzene	Rh complex-$P(C_6H_5)_3$	−0·03	4
Tetrahydrofuran	$ZnCl_2$	+0·05	6
CH_2Cl_2	$ZnCl_2$	+0·14	16
$CHCl_3$[b]	—	+0·08	9

[a] Optically pure (*S*)-(−)-dimethyl malate: $\Delta\varepsilon$ (214 nm) +0·90 (methanol); [b] *cis*-isomer.

TABLE III

HPLC, ^{1}H NMR and ^{13}C NMR analyses of compound *IV* (addition of *II* to *I*)

Conditions of addition			Compound *IV*			
Solvent	time, h	yield, %	*trans*/*cis*		e.e., %[a] (configuration)	
			HPLC	^{1}H NMR	*trans*	*cis*
CCl_4	24	50	82/18	81/19	14 (2*S*, 6*R*)	[b]
Benzene	41	98	65/35	64/36	12 (2*S*, 6*R*)	14 (2*R*, 6*R*)
THF	120	61	62/38	[c]	10 (2*S*, 6*R*)	6 (2*R*, 6*R*)
$CHCl_3$	24	68	56·5/43·5	57/43	6 (2*S*, 6*R*)	8 (2*S*, 6*S*)
THF[d]	14	14	—	85/15	9 (2*R*, 6*S*)	[b]

[a] From ^{13}C NMR spectra, mean value from data for C-2 and C-6; [b] bad resolution; [c] *trans*- and *cis*-isomers separated and measured separately; [d] catalyzed with $MgBr_2$.

and C-6) making their integration impossible. A more favourable situation was with compound *V*. The signals of protons on the C-6 carbon atom differed from those of the trimethylsilyloxy group, thus being possible to determine the ratio of diastereoisomers *Vc* and *Vd* and also the enantiomeric purity of the addition products. The large chemical shift differences in the spectra of compounds *V* (compared with *IV*) are probably caused by the phenyl group which shields differently the protons in the individual diastereoisomers. The population of all the four diastereoisomers of compounds *IV* as well as *V* was determined from the ^{13}C NMR spectra. Although some of the signals differed only by a tenth of ppm, they were well separated, enabling the integration (Tables III and IV).

Combination of chemical correlation data with those derived from ^{13}C NMR spectra for the same reaction mixtures allowed us to assign the chemical shifts of the C-2 and C-6 carbon atoms to all the diastereoisomers of *IV* (*a*–*d*). The assignment was confirmed by comparison of the ^{13}C NMR spectra of pure *cis*-isomer of *IV* (8% e.e., absolute configuration of the predominating diastereoisomer 2*S*,6*S*) with the results of chemical correlation (9% e.e., (6*S*)-configuration).

In the case of derivative *V* the reaction in chloroform gave predominantly the *trans*-isomer of (6*S*)-configuration (Table IV) as shown by chemical correlation. This means that the major diastereoisomer (^1H NMR chemical shift of the proton on C-6: 4·04 ppm, ^{13}C NMR chemical shift of the C-6 signal 65·7 ppm) is of (2*R*,6*S*)-configuration whereas the minor isomer (chemical shifts: ^1H NMR 4·20 ppm, ^{13}C NMR 66·5 ppm) has (2*S*,6*R*)-configuration (the configuration of the (−)-8-phenylmenthyl moiety being the same in both compounds).

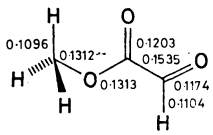
TABLE IV
HPLC, ^1H NMR and ^{13}C NMR analyses of compound *V* (addition of *III* to *I*)

Conditions of addition			Compound *V*		
			trans/*cis*		e.e., %[a]
Solvent	time, h	yield, %	HPLC	^1H NMR	*trans* (2*R*, 6*S*)
CCl_4	24	40	97/3	98/2	36
Benzene	80	52	80/20	76/24	20
$CHCl_3$	24	22	—	94/6	22
THF[b]	12	5	100/0	98/2	82

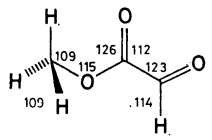
[a] From ^{13}C NMR spectra, mean value from data for C-2 and C-6, ^1H NMR spectra gave identical values; [b] catalyzed with $MgBr_2$.

We tried to explain the marked regioselectivity of the studied reaction by quantum-chemical calculations, using methods[17] CNDO/2 and INDO. The starting geometries were taken from the microwave spectral data for glyoxylic acid[18] and (*E*)-1-methoxy-1,3-butadiene[19] and were complemented by other tabulated values[20] (Fig. 2). For simplicity, glyoxylates *IV* and *V* were substituted by methyl glyoxylate.

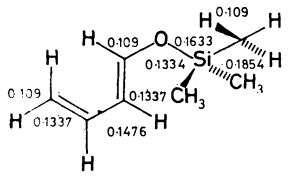
It is known[21] that regioselectivity of reactions is connected with the magnitude of expansion coefficients in the frontier orbitals of the reacting components. Using the CNDO/2 method we found that the greatest bond overlap exists between the HOMO of the diene and the LUMO of the glyoxylate. However, the aldehyde carbonyl expansion coefficients in the LUMO of glyoxylate are of almost the same magnitude (C: −0·516 and O: 0·521) and thus the frontier molecular orbital approach cannot explain the observed regioselectivity. Besides the concerted mechanism, we also may consider an ionic mechanism, which has been experimentally proven for similar systems[22]. The calculated charge distribution in diene *I* (corresponds to *ab initio* calculations for analogous compounds[23]) and the dienophile is given in Scheme 2. We assume that the calculated charge distribution indicates



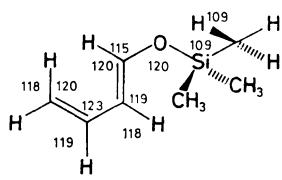
r_x (nm)



valence angle (°)



r (nm)

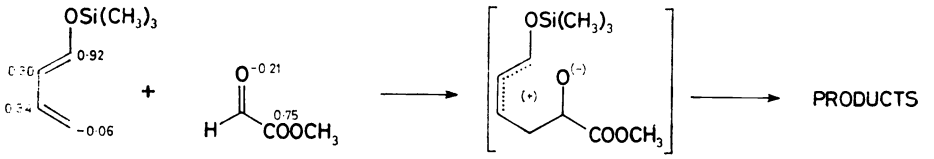


valence angle (°)

FIG. 2

Internuclear distances (r_x) and valence angles used in quantum-chemical calculation of frontier orbitals for methyl glyoxylate and diene *I* (CNDO/2 and INDO methods)

a charge-controlled reaction which manifests itself most in the presence of Lewis acids.



SCHEME 2

Investigating the reaction stereoselectivity we have found that the *trans*/*cis* ratio of isomers of *IV* depends on the solvent polarity, ranging from 82/18 in tetrachloromethane as the least polar solvent to 57/43 in chloroform (Table III).

Excepting the reaction in benzene, the addition of glyoxylate *III* to diene *I* was almost completely *trans*-stereoselective, the *trans*/*cis* ratio being 94–100/6–0%. In benzene the selectivity was lower: the product contained 80% of *trans*-isomers of *V*. The higher *trans*-selectivity in the reaction of *III* may be explained by a greater steric hindrance in the *endo*-approach of the glyoxylate to diene *I* due to the steric repulsion between the phenyl group and the diene. The complete *trans*-selectivity in the reaction of *III* in the presence of magnesium bromide in tetrahydrofuran, as well as the marked *trans*-selectivity (85%) in the reaction of *II* under the same conditions, is due to formation of a chelate (**B**, Fig. 3) which reacts *exo*-selectively. Danishefsky[24] observed complete *exo*-selectivity (leading exclusively to *trans*-isomer) in reaction of α-alkoxyaldehydes with activated dienes, performed under the same conditions.

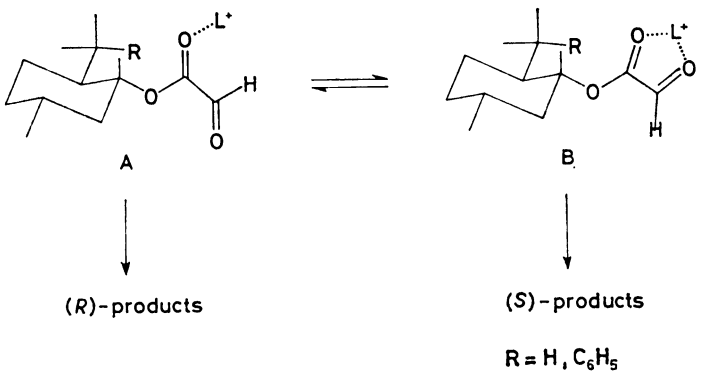


FIG. 3
Chelation of Lewis acids (L^+) with glyoxylates

Our results are at variance with observations of Polish authors[6] who studied the reaction of glyoxylate *II* with 1-methoxy-1,3-butadiene. They obtained the *cis*-isomer as the predominant product and the *trans*/*cis* ratio did not depend on the solvent polarity. The *trans*/*cis* ratio may reflect either a kinetic or thermodynamic control of the reaction. In a concerted process, the *trans*-isomer arises by an *exo*-attack of the diene *I*. Although in Diels–Alder reactions the *endo*-attack[1] is preferred, in our case the steric repulsion between the diene and dienophile probably markedly influences the direction of the attack. This is also evident from the composition of products formed from glyoxylates *II* and *III* with diene *I*. The reaction of the sterically more bulky glyoxylate *III* affords substantially more *trans*-isomers of compound *V*. Considering the conformational equilibrium in glyoxylates[6], we see on the Dreiding models that, for steric reasons, the transoid form of glyoxylate *II* in the transition state prefers the *exo*-approach, giving the *trans*-isomer of absolute configuration *R*, in accord with the Prelog's rule. With the cisoid form, the *exo*-attack is not unequivocally more favourable than the *endo*-attack, leading to the *cis*-isomer (Fig. 4). With increasing polarity of the medium (and thus with increasing population of the cisoid conformer) the reaction should give more *cis*-isomer.

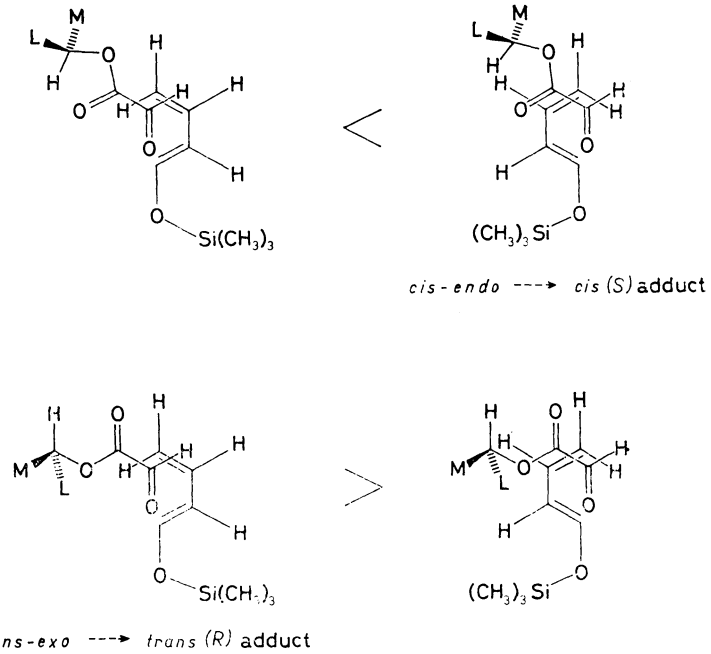


FIG. 4
Transition states for reaction of glyoxylates *II* and *III* with diene *I*

An alternative explanation, i.e. that the studied addition is not influenced by the polarity of the medium but that this medium to a different extent isomerizes the anomeric center C-2 in the originally formed products, has been excluded by the observation that the *trans*/*cis* ratio does not change during the reaction. Also no interconversion of the pure isomers has been observed.

The reaction of glyoxylate *II* with diene *I* was only little enantioselective (maximum 14% e.e. in tetrachloromethane). Also in this case we observed that the enantiomeric purity of the reaction products depends markedly on solvent polarity. We interpret this fact as the consequence of conformational equilibrium of the glyoxylate group[6] which we have proven by infrared spectroscopy[25].

Also the absolute configuration of products depends on the polarity of the medium. In less polar solvents (tetrachloromethane, benzene, tetrahydrofuran) in which the glyoxylate *II* exists predominantly in the transoid conformer, the reaction leads predominantly to products of (*R*)-configuration on the C-6 carbon atom (in accord with the Prelog's rule). In more polar solvents (chloroform, pyridine), in which the conformational equilibrium is shifted more to the *cis*-conformer side, products of (6*S*)-configuration are formed.

When using catalysts of the Lewis acids type we observed that the reaction gave products of opposite configuration than when it was performed in pure solvents. We assume that the Lewis acid coordinates either with both glyoxylate carbonyl groups under formation of a chelate or only with the more charged carbonyl (Fig. 3). The diene attacks then the chelate to give a product of opposite configuration than in the uncatalyzed reaction.

With rhodium complexes in benzene the reaction was less enantioselective than in benzene alone. In the case of rhodium complex with (+)-DIOP* as a chiral ligand, the optical purity of products substantially dropped. This can be explained by the presence of two chiral groups ((−)-menthol in glyoxylate *II* and (+)-DIOP as ligand in the complex) which probably induce the formation of products of opposite absolute configuration.

As with glyoxylate *II*, the enantiomeric purity of products from glyoxylate *III* also depends markedly on the solvent polarity. The reaction of glyoxylate *III* is 2−2·5 times more enantioselective. The phenyl group strongly directs the attack by the diene from one of the prochiral sides of the aldehyde group. Product of the highest enantiomeric purity was obtained in tetrahydrofuran in the presence of magnesium bromide. We obtained pure *trans*-isomer of compound *V* in 82% enantiomeric purity and the predominating diastereoisomer had absolute configuration 2*R*,6*S* on the dihydropyran ring.

* (+)-DIOP denotes (2*S*,3*S*)-(+)-2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane.

EXPERIMENTAL

The boiling points are uncorrected. The reaction course and product purity were monitored by thin-layer chromatography (TLC) on silica gel G according to Stahl (Merck). Column chromatography was performed on silica gel (Herrmann), flash chromatography on silica gel H 60 Art No. 7736 (Merck) under nitrogen pressure 1·0—1·5 . 10^5 Pa. Gas-liquid chromatography was carried out on Chrom 4 and Chrom 5 instruments (Laboratorní přístroje, Prague), using 3·5 × × 0·003 m glass column packed with 5% Carbowax 20M + 1% KOH on Inerton 0·125—0·160; carrier gas nitrogen.

Infrared spectra were taken in tetrachloromethane on a UR-20 (Carl Zeiss, Jena) and on a Perkin–Elmer 580 spectrometers. CD spectra were measured in methanol on a Roussel–Jouan instrument, mass spectra on an AEI MS-702 spectrometer at 70 eV. Proton NMR spectra were obtained with a Tesla BS-467 (60 MHz), a Varian XL-100A (100 MHz) (both in CW mode) and a Varian XL-200 (FT-mode; 200 MHz) instruments. The enantiomeric purity was determined by ^{1}H and ^{13}C NMR spectra (Bruker AM 400) at 400 MHz for ^{1}H and 100·6 MHz for ^{13}C (FT-mode).

Unless stated otherwise, the compounds were measured in deuterochloroform with tetramethylsilane as internal standard; chemical shifts are given in ppm. The ^{13}C NMR chemical shift values relate to the center of the deuterochloroform signal (chemical shift 77·00 ppm). The ^{1}H and ^{13}C NMR data of compounds *IVa*—*IVd*, *Va*—*Vd*, *VIIa* and *VIIb* are given in Tables V—VII.

The high performance liquid chromatography of isomeric mixtures of compounds *IV* and *V* was carried out using a set of a high-pressure LDC pump, a six-way valve (Knauer), a thermostated 250 × 8 mm column packed with Separon SIX (particle size 10 μm), a refractometric differential detector RIDK-10, a UT-10 thermostat and a 4003 recorder. Chromatographic conditions: mobile phase light petroleum–ethyl acetate 19 : 1 and 35 : 1 for compound *IV* and *V*, respectively, flow rate 2 ml/min, injection 2 μl of 50% (v/v) solution of the compound in the mobile phase (Table VIII).

Since the glyoxylates were hygroscopic, we worked under argon, pre-dried over potassium hydroxide and activated molecular sieve Potasit 3A.

(—)-Menthyl 2-Trimethylsilyloxy-5,6-dihydro-2*H*-pyran-6-carboxylate (*IV*)

A) *Diels–Alder reaction without catalyst.* A mixture of glyoxylate *II* (5·3 g, 25 mmol), (*E*)-1--trimethylsilyloxy-1,3-butadiene (*I*; 5·3 g, 40 mmol) and anhydrous benzene (20 ml) was allowed to stand at room temperature for 41 h. Evaporation of the solvent gave 8·7 g (98%) of the product, b.p. 122—123°C/9 Pa. For $C_{19}H_{34}O_4Si$ (382·6) calculated: 64·36% C, 9·66% H; found: 64·58% C, 9·73% H. The ^{1}H and ^{13}C NMR spectra of the four isomers *IVa*—*IVd* are given in Tables V—VII.

The addition was performed analogously in tetrahydrofuran, tetrachloromethane and chloroform. The stereoisomers were isolated by flash chromatography in light petroleum, containing 5% of ether and 0·1% of triethylamine. Composition of the reaction mixtures is given in Tables III and IV. On prolonged standing, compound *IV* decomposed to give aldehyde *VIIa* (Tables V—VII).

B) *Zinc chloride-catalyzed addition in dichloromethane.* A solution of glyoxylate *II* (1·05 g, 4·95 mmol) in dichloromethane (10 ml), followed by diene *I* (1·6 g, 8·8 mmol), was added under argon to a suspension of freshly fused zinc chloride (0·90 g, 4·95 mmol) in dichloromethane (20 ml). After 2·5 h at 0°C the reaction mixture was decomposed with saturated solution of sodium hydrogen carbonate under ice-cooling, the organic phase was separated and dried over magne-

sium sulfate. Evaporation of the solvent and distillation afforded 2·05 g of the product. The predominating stereoisomer (16% e.e.) had the (6*S*)-configuration. An analogously performed reaction in tetrahydrofuran afforded a mixture of stereoisomers. The major stereoisomer (6% e.e.) had the (6*S*)-configuration.

TABLE V
Chemical shifts (δ, ppm) of selected protons from ^{1}H NMR spectra of compounds *IVa*–*IVd*, *Vc*, *Vd*, *VIIa* and *VIIb*

Proton	*IVa*	*VIb*	*IVc*	*IVd*	*Vc*[a]	*Vd*[a]	*VIIa*[b]	*VIIb*[c,d]
6	4·33	4·34	4·52	4·53	4·20	4·04	4·36	3·24
5*a*	2·42	2·42	2·30	2·30	1·85	1·85	2·70	2·44
5*e*	2·42	2·42	2·30	2·30	2·01	2·01	2·87	2·67
4	5·93	5·93	5·98	5·98	6·05	5·84	6·87	6·61
3	5·69	5·69	5·78	5·78	5·65	5·69	6·21	6·02
2	5·52	5·52	5·48	5·48	5·50	5·41	9·52	9·44
7	0·19	0·19	0·20	0·20	0·18	0·22	3·40	3·50

[a] Aromatic protons 7·11–7·35 m, 5 H; [b] absolute configuration 5*R*; [c] absolute configuration 5*S*; [d] aromatic protons 7·04–7·40 m, 5 H.

TABLE VI
Coupling constants (*J*, Hz) between selected protons for compounds *IVa*, *IVc*, *Vc*, *Vd*, *VIIa* and *VIIb*

Protons	*IVa*	*IVc*	*Vc*	*Vd*	*VIIa*	*VIIb*
6, 5*a*′	10·8	10·5	11·5	11·5	6·7	7·0
6, 5*e*′	4·2	4·0	3·7	3·9	4·6	4·5
6, 4	0·2	0·2	0·2	0·2		
6·3	0·2	0·2	0·2	0·2		
6, 2	0·2	0·2	0·2	0·2		
5*a*′, 5*e*′	16·3	16·3	16·3	16·3	18·5	18·0
5*a*′, 4	2·8	2·8	1·0	1·0	1·2	1·2
5*a*′, 3	0·2	0·2	1·5	1·5		
5*a*′, 2	0·4	0·4	0·5	0·5		
5*e*′, 4	3·6	3·6	5·8	5·8	7·2	6·0
5*e*′, 3	0·6	0·6	1·5	1·5		
5*e*′, 2	0·4	0·4	0·3	0·3		
4, 3	10·3	10·3	9·9	9·9	15·7	16·0
4, 2	0·7	0·7	1·5	1·5	2·4	
3, 2	2·7	2·7	3·0	3·0	7·9	8·0

C) Magnesium bromide-catalyzed addition in tetrahydrofuran. A solution of magnesium bromide in ether (5 ml of 1M solution), followed by diene *I* (1·2 g, 8·5 mmol), was added to a solution of glyoxylate *II* (1·06 g, 5 mmol) in tetrahydrofuran (24 ml). After standing at 0°C for 3 h and at room temperature for 13 h, the reaction was quenched by addition of dry triethylamine (2·5 ml). The catalyst was removed by passing through a column of triethylamine-deactivated silica gel and the mixture was chromatographed to give 0·246 g (13%) of the product. An analogously executed experiment in benzene gave only 1% of the product.

D) $RhCl(P(C_6H_5)_3)_2(C_2H_4)_2$ *complex-catalyzed addition.* Glyoxalate *II* (1·06 g, 5 mmol) and diene *I* (1·07 g, 7·5 mmol) were added to a catalyst prepared by mixing $Rh_2Cl_2(C_2H_4)$ complex (19 mg, 50 mmol) and triphenylphosphine (52 mg, 200 mmol) in benzene (10 ml). After standing for 24 h the product was isolated; yield 1·2 g (63%), b.p. 125°C/20 Pa. The major stereoisomer (6% e.e.) had the (6*R*)-configuration.

E) $RhCl(+)$-DIOP$(C_2H_4)_2$ *complex-catalyzed addition.* Glyoxalate *II* (0·70 g, 3·3 mmol) and diene *I* (1 g, 7 mmol) were added to a catalyst obtained from $Rh_2Cl_2(C_2H_4)_2$ complex (32·6 mg, 84 μmol) and (+)-DIOP (82·9 mg) in benzene (5 ml). After standing for 67 h at room temperature, the isolated product was optically inactive.

TABLE VII

Chemical shifts (δ, ppm) of selected carbon atom signals in ^{13}C NMR spectra of compounds *IVa—IVd*, *Vb*, *Vd*, *VIIa* and *VIIb*

Atom	*IVa*	*IVb*	*IVc*	*IVd*	*Vb*	*Vd*	*VIIa*[a]	*VIIb*[b]
6	71·2	71·4	66·1	66·2	71·7	65·7	69·2	68·9
5	27·2	27·1	27·7	27·7	27·6	27·7	37·2	37·1
4	126·2	126·1	125·7	125·8	126·4	125·7	151·6	151·6
3	130·1	130·1	127·9	127·9	130·0	127·8	135·4	135·5
2	93·0	93·3	89·4	89·5	93·2	89·5	193·3	193·3
7	0·26	0·26	0·14	0·14	0·46	0·12	—	—
8	170·0	169·5	170·5	170·5	169·1	170·0	173·3	173·3

[a] Absolute configuration 5*R*; [b] absolute configuration 5*S*.

TABLE VIII

HPLC retention times of isomers of compounds *IV* and *V*

t_r, min	*cis*[a] (*IVa* + *IVb*)	*trans*[a] (*IVc* + *IVd*)	*cis*[b] (*Va* + *Vb*)	*trans*[b] (*Vc* + *Vd*)
IV	4·0	4·5	7·2	8·3
V			8·5	11·3

[a] Light petroleum–ethyl acetate 19 : 1; [b] same solvents, 35 : 1.

(−)-8-Phenylmenthyl 2-Trimethylsilyloxy-5,6-dihydro-2*H*-pyran-6-carboxylate (*V*)

A) Diels–Alder reaction without catalyst. Glyoxalate *III* (0·585 g, 2·07 mmol) was mixed with diene *I* (0·56 g, 3·93 mmol) in dry benzene (10 ml). After standing at room temperature for 80 h the mixture was worked up; yield 0·452 g (52%) of compound *V*, containing (HPLC) 80% of *trans*-isomer and 20% of *cis*-isomer. For $C_{25}H_{38}O_4Si$ (458·7) calculated: 65·46% C, 8·35% H; found: 65·61% C, 8·42% H. The results, together with the outcome of analogous experiments in tetrachloromethane and chloroform, are given in Table III. The ^1H and ^{13}C NMR spectra are given in Tables V–VII.

B) Magnesium bromide-catalyzed addition in tetrahydrofuran. A solution of glyoxylate *III* (0·492 g, 1·71 mmol) in tetrahydrofuran (20 ml) was mixed in an inert atmosphere with ice-cold 1M ethereal magnesium bromide solution (1·7 ml) and after 10 min with diene *I* (0·57 g, 4·0 mmol). After standing at room temperature for 11 h, the reaction was quenched by addition of dry triethylamine (2·5 ml). The usual isolation procedure afforded 0·040 g (5%) of adduct *V*, together with 0·040 g (6·5%) of the desilylated product and 0·095 g (15·5%) of *trans*-aldehyde *VIIb*.

Chemical Correlation of Compound *IVa–IVc* with (*R*)-(+)-Dimethyl Malate

Ester *IV* (0·38 g, 1 mmol) was dissolved in a mixture of tetrachloromethane (12 ml) and acetonitrile (12 ml) and the obtained solution was added to a solution of sodium periodate (1·75 g, 8·2 mmol) in water (18 ml). The heterogeneous mixture was vigorously stirred and ruthenium (*IV*) oxide (5·4 mg) was added. After 4 h (complete reaction) dichloromethane (10 ml) was added the organic layer was separated and the aqueous one was washed with dichloromethane (3 × × 20 ml). The combined organic phases were dried over magnesium sulfate and the separated ruthenium was removed by filtration through a column of Celite. The solvent was evaporated and the residue was hydrolyzed by treatment with 0·7M-HCl (25 ml) at 100°C for 6 h. The liberated (−)-menthol was removed by steam-distillation and the hydrochloric acid was distilled off. The residue was dried, dissolved in methanol (15 ml) and mixed with an ethereal solution of diazomethane. Distillation afforded 100 mg (66%) of the methyl ester, b.p. 38–40°C/16 Pa, $\Delta\varepsilon$ (214 nm) −0·07 (methanol). The product was enantiomeric with the compound prepared by alkylation of (−)-malic acid with diazomethane; b.p. 43°C/30 Pa, $\Delta\varepsilon$ (214 nm) +0·90 (methanol). Correlations of other addition products are given in Table II.

Chemical Correlation of Compounds *Va– Vd* with (*S*)-(−)-Dimethyl Malate

Analogously as in the preceding experiment, the adduct *V* (0·10 g, 0·23 mmol) was converted into dimethyl malate (17·3 mg, 43%), $\Delta\varepsilon$ (214 nm) +0·18 (methanol). Optical purity 20%, absolute configuration *S*.

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