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CONDENSATION OF 1-ALKOXY-1,3-BUTADIENES WITH OPTICALLY ACTIVE GLYOXYLIC ACID ESTERS[1]

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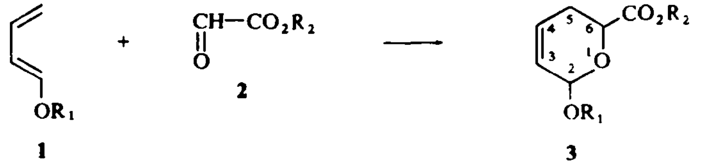
Abstract—The condensation of 1-alkoxy-1,3-butadienes with optically active esters of glyoxylic acid leading to esters of 2-alkoxy-5,6-dihydro-2H-pyran-6-carboxylic acids was studied and the dependence of asymmetric induction on the following parameters examined: alkoxy group in dienes, dissymetric group in glyoxylates, solvent and the temperature of condensation. The optical yield and absolute configuration of the adducts were determined by optical rotation measurements of methyl malate obtained by degradation. The data are rationalized by postulating parallel formation of four active complexes corresponding to a *transoid* and *cisoid* conformation of the glyoxylate ester in the transition state.

CONDENSATION of glyoxylic acid esters (2) with 1-alkoxy-1,3-butadienes (1) yields esters of 2-alkoxy-5,6-dihydro-2H-pyran-6-carboxylic acids (3).[2] Compounds of type 3 are suitable substrates for stereoselective syntheses of various monosaccharides, e.g. methyl 4-deoxy-hexopyranosides,[3] methyl 4,6-dideoxy-hexopyranosides,[4] 2,4-dideoxy-hexopyranoses,[5] etc. Sugars obtained by this method are racemic mixtures,

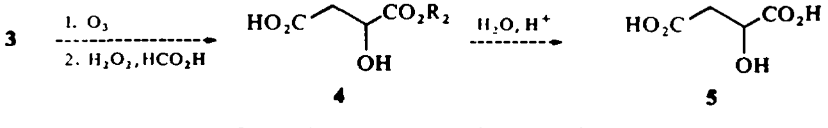


(1)

Studies of the title reaction were designed to obtain compounds of type 3 in the enantiomeric form, which eventually could be used for the syntheses of optically active monosaccharides.

In principle, asymmetric induction in reaction 1 may be realized by locating the chiral centre in R_1 or in R_2. From these two possibilities chiral R_2 was selected. since optically active glyoxylic acid esters are readily available.

In adduct 3, the chiral centres are at C-2 and C-6; after the transformation of compound 3 into monosaccharides, these atoms become C-1, i.e. the anomeric center, and C-5, i.e. carbon atom determining the configuration series. To ascertain the results of asymmetric induction, compound 3 was converted by ozonolysis to the semiester of malic acid (4); this ester contained atom C-6 of the starting adduct.



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Ester **4** was hydrolyzed in acid to give malic acid (**5**), which was then estrified with CH_2N_2 to dimethyl malate (**6**). The results of asymmetric induction, i.e. the optical yield of the reaction and the absolute configuration of C-6 were determined by optical rotation measurements of ester **6**.

The configuration at C-2 followed from the relationship between the substituents at C-2 and C-6 (*cis* or *trans*) in compound **3**. The condensation formulated in reaction 1 is not fully stereospecific.[6] Pure *trans* isomers of 1-alkoxy-1,3-butadienes always lead to mixtures of *cis-trans* adducts **3**. The isomeric composition of **3** can be determined by gas chromatography or—even more conveniently—by NMR spectra (*cf.* Experimental). We did not succeed in preparative separation of the isomers of **3** into pure components. Consequently, the results of asymmetric induction presented in this study refer to the *endo* and *exo* addition treated jointly.

RESULTS

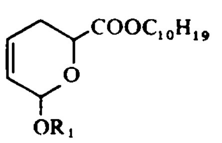
The following parameters were varied in the studies of the magnitude and direction of the optical induction in the examined condensation (eq. 1):

(a) alkyl group R_1 in diene **1**,
(b) dissymetric group R_2 in esters **2**,
(c) solvent,
(d) temperature of the reaction.

The results are presented in Tables 1–4, in which yields of adduct **3**, proportions of *cis* and *trans* isomers, optical yields and configuration of the induced centre at C-6 are given.

(a) R(−)-menthyl glyoxylate was condensed with four homologous 1-alkoxy-1,

TABLE 1. CONDENSATION OF 1-ALKOXY-1,3-BUTADIENES WITH R(−)-MENTHYL GLOXYLATE AT 20°C



			Dimethyl malate				
			$[\alpha]_{546}^{20}$ in MeOH			Abs. conf.	Optical yield
R_1	Yield %	*cis:trans*	found	corr.[a]	c		%
in CH_2Cl_2							
Me	90	64:36	− 0·54	− 0·57	10·27	S	5·7
Et	90	61:39	− 0·51	− 0·55	10·34	S	5·5
n-Pr	86	63:37	− 0·58	− 0·60	7·05	S	6·0
n-Bu	85	64:36	− 0·47	− 0·51	10·04	S	5·1
in C_6H_6							
Me	66	53:47	+ 0·48	+ 0·52	10·30	R	5·2
Et	60	58:42	+ 0·24	+ 0·30	8·20	R	3·0
n-Pr	55	59:41	+ 0·30	+ 0·35	8·22	R	3·5
n-Bu	59	59:41	+ 0·25	+ 0·31	10·04	R	3·1

[a] Corrected according to the procedure described in Experimental.

3-butadienes (1, R_1 = Me, Et, n-Pr, n-Bu) in CH_2Cl_2 at room temperature for about 48 hours.

The yields of adduct 3 were high. *Cis* compounds were predominantly formed. In all four cases, configuration S was induced at C-6. The fact that the optical yields in this series remain within the range of 5–6% indicates that the alkoxy substituent present in dienes 1 has but little effect on the magnitude of the optical induction.

(b) Maintaining the same parameters as above (solvent, time and reaction temperature), we reacted *trans* 1-methoxy-1,3-butadiene with glyoxylates of four optically active alcohols. The yields of the adducts were good, and the predominance of *cis* isomers maintained. The optical yields of the reactions decline in the order: R(−)-menthyl > R(−)-bornyl > R(−)- and S(+)-2-octyl > R(−)- and (S+)-2,2-dimethyl-3-butyl. This result is conflicting with the assumption that in the above-mentioned group of alcohols the "inducing power" of the 2,2-dimethyl-3-butyl residue ought to be the highest (*cf.* Prelog[7]). Another noteworthy observation is the change in the direction of induction at C-6 in the condensations with R(−)- and S(+)-2,2-dimethyl-3-butyl glyoxylates.

(c) Solvent was studied for its effect on the results of asymmetric induction in the condensation of *trans* 1-methoxy-1,3-butadiene with R(−)-menthyl glyoxylate.

The yields of adduct 3 in the reactions performed in CH_2Cl_2, $CHCl_3$, CCl_4 and C_6H_6 were good, and the predominance of the *cis* isomer maintained. The optical yields varied within a fairly wide range: from 1·1% for CCl_4 to 13% for $CHCl_3$. The most significant observation involves the fact that in CH_2Cl_2 and $CHCl_3$ R(−)-menthyl

TABLE 2. CONDENSATION OF 1-METHOXY-1,3-BUTADIENE WITH GLYOXYLIC ACID ESTERS AT 20°C

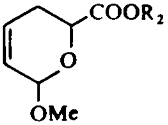
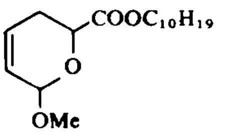
				Dimethyl malate				
				$[\alpha]^{20}_{546}$ in MeOH			Abs. conf.	Optical yield
R_2	Abs. conf.	Yield %	*cis:trans*	found	corr.	c		%
in CH_2Cl_2								
Menthyl	R	90	64:36	− 0·54	− 0·57	10·27	S	5·7
Bornyl	R	77	77:30	− 0·25	− 0·30	4·84	S	3·0
2-Octyl	R	71	60:40	− 0·12	− 0·15	10·58	S	1·5
	S	76	58:42	+ 0·14	+ 0·17	10·57	R	1·7
2,2-Dimethyl-	R	80	60:40	+ 0·03	+ 0·04	10·90	R	0·4
3-butyl	S	75	66:34	− 0·05	− 0·06	9·63	S	0·6
in C_6H_6								
Menthyl	R	66	53:47	+ 0·48	+ 0·52	10·30	R	5·2
Bornyl	R	61	56:44	+ 0·26	+ 0·31	3·05	R	3·1
2-Octyl	R	52	54:46	+ 0·12	+ 0·15	10·38	R	1·5
	S	54	54:46	− 0·11	− 0·14	10·25	S	1·4
2,2-Dimethyl-	R	60	60:40	+ 0·38	+ 0·43	10·33	R	4·3
3-butyl	S	58	61:39	− 0·64	− 0·66	9·84	S	6·6

Table 3. Condensation of 1-methoxy-1,3-butadiene with R(−)-menthyl glyoxylate in different solvents



Solvent			Dimethyl malate $[\alpha]^{20}_{546}$ in MeOH			Abs. conf.	Optical yield %
	Yield %	*cis*:*trans*	found	corr.	c		
C_6H_6	66	53:47	+ 0·48	+ 0·52	10·30	R	5·2
CCl_4	84	62:38	+ 0·09	+ 0·11	9·19	R	1·1
$CHCl_3$	89	64:36	− 1·30	− 1·30	10·07	S	13·0
CH_2Cl_2	90	64:36	− 0·54	− 0·57	10·27	S	5·7

induces S configuration at C-6, while in the two other solvents the configuration is opposite.

This fact led us to repeat the reactions in C_6H_6, as described in Table 1 and 2.

The optical yields of adduct 3 resulting from condensations of four 1-alkoxy-1, 3-butadienes with R(−)-menthyl glyoxylate in C_6H_6 were lower than those observed for reactions performed in CH_2Cl_2. Just as previously (Table 1) there was no effect of the R_1 radical on the magnitude of asymmetric induction. In the entire series R configuration at C-6 was induced.

In the series of condensations of *trans* 1-methoxy-1,3-butadiene with glyoxylates of four optically active alcohols in C_6H_6, the opposite direction of induction at C-6 was observed relative to the reactions in CH_2Cl_2 (Table 2). In this series, the R(−)- and S(+)-2,2-dimethyl-3-butyl residues afforded relatively high optical yields.

(d) Reaction temperature was investigated for its effect on the optical yield. The results of five experiments carried out without solvents are recorded in Table 4 (entries 1 to 5). Up to 100°, the yield of the adduct increased. At 150°, some decomposition of product took place. In all experiments the optical yields were low. The change of the induced configuration at C-6 at higher temperatures was accompanied by a shift in the proportion of the geometric isomers towards the thermodynamically more stable *trans* isomer (*cf.* ref. [6]).

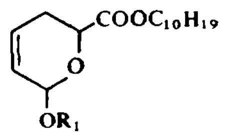
Analogous results were obtained for condensations of four 1-alkoxy-1,3-butadienes with R(−)-menthyl glyoxylate at 100° without solvents (Table 4, entries 4,6,7,8). The yields of adducts were quantitative and the *trans* isomers prevailed in the mixtures The optical yields remained within the range of 3·8–5·4% with the induced R-configuration of the C-6 centre.

DISCUSSION

The results presented in Tables 1–4 show that the reaction given in eq. 1 fails to yield ester 3 of satisfactory optical purity. Thus, the primary aim: synthesis of enantiomeric ester 3, was not attained. The examined condensation is undoubtedly a synthesis of Diels–Adler type. This follows from kinetic[6a] and stereochemical (preference of *endo* addition leading to *cis* isomers) data [6a,6b]. In this light, the value of the present results lies in the fact that they represent new data on asymmetric induction in Diels–Alder synthesis.

It is surprising, how little is known about asymmetric induction in Diels–Alder synthesis. Until now only five papers[8–12] on this subject were published, though the first appeared in 1948. In fact, these studies deal with only one type of synthesis, namely, condensation of achiral dienes with esters of acrylic or fumaric acids with optically active alcohols. The results may be summarized as follows:

TABLE 4. CONDENSATION OF 1-ALKOXY-1,3-BUTADIENES WITH R(−)-MENTHYL GLYOXYLATE IN DIFFERENT TEMPERATURES (WITHOUT SOLVENTS)

						Dimethyl malate				
						$[\alpha]^{20}_{546}$ in MeOH			Abs. conf.	Optical yield
N°	R_1	Temp.	Time hr.	Yield %	*cis:trans*	found	corr.	c		%
1	Me	− 20	120	53	70:30	− 0·13	− 0·16	6·00	S	1·6
2	Me	0	120	69	68:32	− 0·21	− 0·25	11·02	S	2·5
3	Me	20	120	85	67:33	− 0·15	− 0·18	10·96	S	1·8
4	Me	100	6	100	43:57	+ 0·38	+ 0·43	9·83	R	4·3
5	Me	150	6	91	32:68	+ 0·31	+ 0·35	10·03	R	3·5
6	Et	100	6	100	37:63	+ 0·33	+ 0·38	11·49	R	3·8
7	n-Pr	100	6	100	41:59	+ 0·42	+ 0·47	10·76	R	4·7
8	n-Bu	100	6	100	37:63	+ 0·50	+ 0·54	10·16	R	5·4

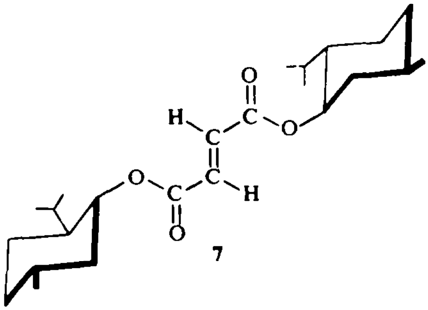
1. Optical purities of the adducts obtained in thermal reactions are low (1–11 %). These values—at least to some extent—are unexpected; on account of the rigid transition state of the Diels–Alder reaction, high induction could be anticipated.
2. Reactions performed in the presence of catalysts of Lewis acid type ($AlCl_3$, BF_3, $SnCl_4$) afforded adducts of high and even very high optical purity.
3. The direction of induction, *i.e.* the configuration of the chiral centres in the adducts are related to such factors as catalysts, temperature and even solvent.

The interpretation of these fairly complex results is incomplete. According to Walborsky,[9] the results of asymmetric induction in thermal condensation of butadiene with R(−)-menthyl fumarate may be explained by a "Prelog-like" conformation of the ester in the transition state (transoid arrangement of the ethylenic bond with both carbonyl groups, (7). On the other hand, for the same condensation carried out in the presence of $AlCl_3$ (yielding an adduct of markedly increased optical purity and changed absolute configuration) *cisoid* or twisted conformation of the ester should probably be assumed.

Before giving the interpretation of our results, we want to point out the following facts:

1. The optical purities of adduct 3 are low. Despite the change of the R_1 substituent

in diene 1 and the inducing centre R_2 in dienophile 2, as well as reaction parameters (solvent, temperature) these values remain in the range of 0·4–6%, in only one case reaching 13%. However, these values are close to those claimed for diene synthesis with chiral dienophiles, e.g. Walborsky *et al.*[9]: 1–3%, Sauer and Kredel[10]: 1·5–11%, Farmer and Hamer[11]: 3–8%.



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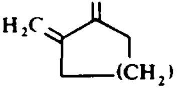
2. The optical yield of adduct 3 resulting from condensations of *trans* 1-methoxy-1, 3-butadiene with optically active glyoxylates are not directly related to the bulkiness of the substituents at the chiral centres, as was found in Prelog's atrolactic acid esters synthesis[7] (cf. Table 2).

3. With all other reaction parameters fixed, the configuration of the C-6 centre in adduct 3 depends on the solvent used as reaction medium (*cf.* Table 3).

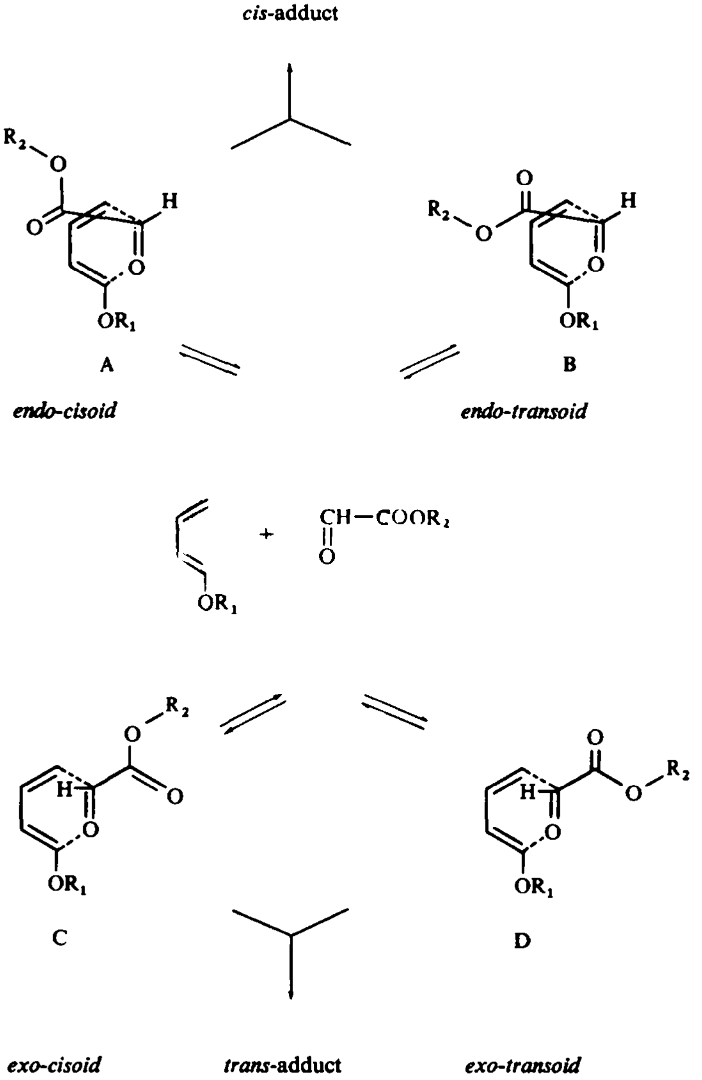
We assume, in accord with the accepted views,[13] that optical induction in the investigated diene reaction takes place owing to the different accessibility of two sides of the glyoxylate formyl group. Therefore, it is necessary to consider the conformation of glyoxylate ester at the stage of formation of the active complex with diene.

It is noteworthy that in the discussion of the mechanism underlying the Diels–Alder reaction only the conformation of diene, the mutual orientation of diene and dienophile (*endo–exo*), the part played by the substituents in diene and dienophile, etc.,[14] have so far been dealt with, whereas little attention has been given to the conformation of open-chain dienophiles in the transition state (see however ref. 15 and 16). In fact, cyclic compounds with fixed *transoid* conformation (most typical examples: maleic anhydride, *p*-benzoquinone) very readily enter into reaction with dienes. However, dienophiles with fixed *cisoid* conformation of the C=C–C=O system (e.g. α-methylene-cyclopentanone (8) or α-methylene-cyclohexanone (9)[17,18] also react with dienes without difficulty. It can be thus concluded that in the Diels–Alder reaction both transition states, with *cisoid* and *transoid* conformation of dienophiles, are possible.



8 : n = 1
9 : n = 2

We assume that in the case of open-chain dienophiles reacting with dienes there is the possibility of parallel formation of active complexes with different conformations of dienophiles*. We also assume that the differences in free energy ($\Delta\Delta G\ddagger$) between these complexes are small. Thus, for the condensation of 1-alkoxy-1,3-butadienes with glyoxylic acid esters we postulate parallel formation of four complexes differing in geometry, which correspond to *exo* and *endo* additions of dienophiles in *cisoid* and *transoid* conformations. (Scheme 1).



SCHEME 1

The concept of parallel transition states has some important consequences:

1. *Cisoid* dienophile of configuration R induces a 6S centre in adduct 3 in both

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* Cisoid conformation of diene in the transition state of Diels–Alder reaction is well-founded.[14]

types of addition: *endo* and *exo*. The same dienophile of transoid conformation induces an opposite configuration at C-6[*].

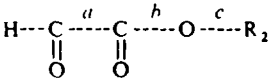
2. The magnitude of asymmetric induction should be related to the equilibrial A $\rightleftharpoons$ B and C $\rightleftharpoons$ D. Therefore, the differences in the bulkiness of groups S, M and L[13] at the chiral centre should not decide on the optical yield of condensations.

3. The configuration of the induced chiral centre in adduct **3** should be related to the equilibria: A $\rightleftharpoons$ B and C $\rightleftharpoons$ D. In turn, these equilibria should depend on the reaction parameters such as solvation, dipole moment of the solvent, temperature of the reaction etc.

The concept of parallel transition states satisfactorily accommodates the present results. Two *endo* (or two *exo*) transition states induce asymmetric centres with opposite configurations. Equilibria of active complexes A and B (or C and D) with only small excess of one of them cause low optical yield of condensations[†]. The results of condensation of 1-methoxy-1,3-butadiene with R(−)- and S(+)-2,2-dimethyl-3-butyl glyoxylates, which are at variance with predictions based on Prelog's model of asymmetric induction may be explained by postulating that optical yields do not directly depend on the differences in the effective bulkiness of substituents S, M and L. The observed dependence of the sign of the induced C-6 configuration with the reaction medium (Table 3) may be rationalized by the assumption that the position of equilibria A $\rightleftharpoons$ B and C $\rightleftharpoons$ D is related to the solvent type. Finally, the change in the direction of induction, observed in condensations carried out at elevated temperatures (Table 4), can be explained by thermal isomerisation of adducts *cis* to *trans* proceeding at atom C-6. It is known from earlier data[6] that an increase in the temperature enhances the isomerization of *cis* esters **3** to *trans* compounds showing higher thermodynamic stability.

The concept of parallel transition states in the Diels–Alder reaction is postulated for the first time and should be examined further. It is especially necessary to investi-

[*] In principle, we may consider conformers of glyoxylic acid ester due to rotation around bonds *a*, *b* and *c*:



$$\mathrm{H}\text{---}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\overset{a}{\text{-----}}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\overset{b}{\text{-----}}\mathrm{O}\overset{c}{\text{-----}}\mathrm{R}_2$$

We assume that only conformers resulting from rotation around bond *a* are of importance, whereas the remaining atoms occur in *cisoid* arrangement, with a hydrogen atom at C-3 (in menthyl residue) facing nearer carbonyl group. In the light of recent investigations[19] on the conformation of esters, this assumption seems to be well-founded. It should be added that the conformation of glyoxylic acid esters in the ground state has not yet been studied. However, there are some data regarding the conformation of ethyl phenylglyoxylate. From the dipole moment measurements, Oehme and Schellenberger[20] have concluded that this ester occurs in a conformation in which both carbonyl groups form a dihedral angle of 75°. For R(−)-menthyl p-bromophenyl-gloxylate, Parthasarathy, Horeau *et al.*[21] have determined (X-ray) a conformation, in which the carbonyl groups form a dihedral angle of about 104°, and the axial hydrogen atom (from C-3 atom of the menthyl residue) faces the neighbouring CO group.

[†] Since we have not determined separately optical purities of *cis* and *trans* isomers, the low optical yields can be explained in still another way. Namely, it may be assumed that condensations give rise to the *cis* and *trans* isomers of adduct **3** of high optical purity, but of opposite configurations at C-6. Although at present this possibility cannot be ruled out, it seems hardly probable, since then it will be difficult to explain the change of the configuration at C-6 under such a weak influence as change of reaction medium.

TABLE 5. B.PS, RI'S AND ANALYTICAL DATA OF 2-ALKOXY-5,6-DIHYDRO-2H-PYRAN-6-CARBOXYLIC ACID ESTERS (3)

R_1	R_2	B.p.	n_D^{20}	Formula	Analysis % Calc. C	H	Found C	H
Me	R(−)-menthyl	120–1/0·001 mm	1·4734	$C_{17}H_{28}O_4$	68·89	9·52	68·90	9·52
Et	R(−)-menthyl	132–3/0·05 mm	1·4708	$C_{18}H_{30}O_4$	69·64	9·74	69·51	10·01
n-Pr	R(−)-menthyl	137–9/0·03 mm	1·4705	$C_{19}H_{32}O_4$	70·33	9·94	69·90	10·13
n-Bu	R(−)-menthyl	140–1/0·005 mm	1·4702	$C_{20}H_{34}O_4$	70·97	10·13	71·12	10·35
Me	R(−)-bornyl	98–9/0·005 mm	1·4889	$C_{17}H_{26}O_4$	69·36	8·90	69·54	8·92
Me	R(−)-2-octyl	89–90/0·1 mm	1·4594	$C_{15}H_{26}O_4$	66·63	9·69	66·89	10·09
Me	S(+)-2-octyl	90–92/0·1 mm	1·4601					
Me	R(−)-2,2-dimethyl-3-butyl	100–2/1·5 mm	1·4549	$C_{13}H_{22}O_4$	64·44	9·15	64·34	9·35
Me	S(+)-2,2-dimethyl-3-butyl	101–2/1·5 mm	1·4548					

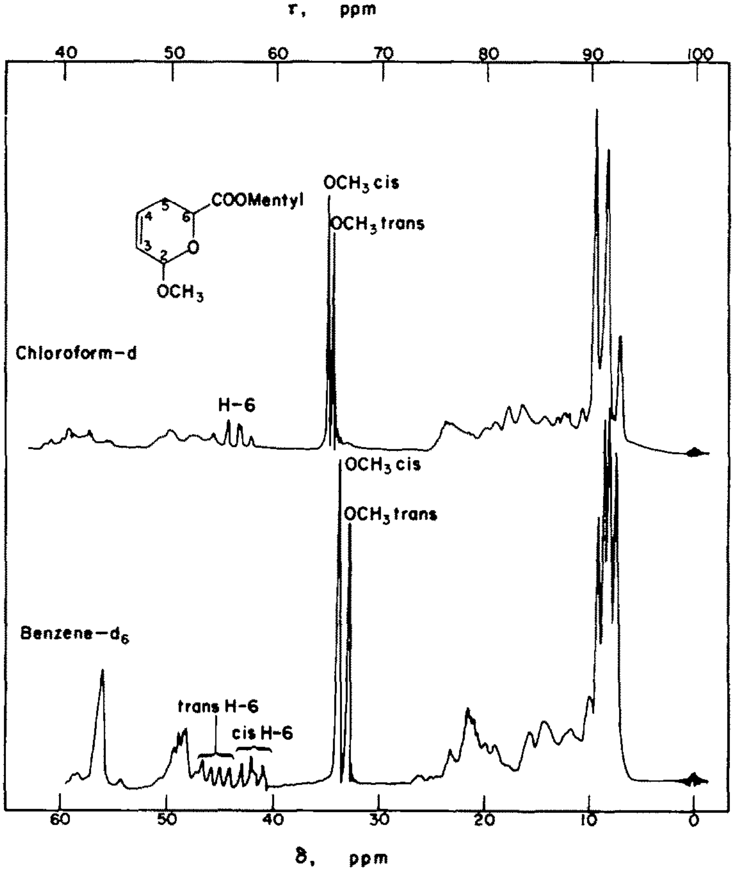


Fig. 1.

gate asymmetric induction in condensation with the participation of chiral, conformationally rigid dienophile. It is stressed, however, that the results of asymmetric induction in other so far studied Diels–Alder condensations[8–12] can be explained on the basis of the postulated model. The low optical yields in thermal reactions should be related to the parallel formation of two active complexes (in one type of addition: *endo* or *exo*) and explained as above. We think that the actions of catalysts in these syntheses consist in the formation of a more stable complex with one transition state than with another, and thus shifting the equilibria of A $\rightleftharpoons$ B and C $\rightleftharpoons$ D type on one side. This results in high optical yields of the catalyzed condensations.

TABLE 6. CHEMICAL SHIFT (δ SCALE) OF RING HYDROGEN ATOMS IN THE NMR SPECTRA ($CDCl_3$ AND C_6H_6) OF 2-ALKOXY-5,6-DIHYDRO-2H-PYRAN-6-CARBOXYLIC ACID ESTERS (3)

		H-2		H-3,H-4		H-5		*cis* H-6		*trans* H-6		*cis* OMe		*trans* OMe	
R₁	R₂	a	b	a	b	a	b	a	b	a	b	a	b	a	b
Me	R(−)-menthyl	4·99	4·85	5·50–6·20	5·63	2·31	1·60–2·60	4·33	4·20	4·45	4·55	3·50	3·39	3·45	3·29
Et	R(−)-menthyl	5·10	4·98	5·50–6·20	5·66	2·30	1·60–2·60	4·32	4·20	4·49	4·59	—	—	—	—
n-Pr	R(−)-menthyl	5·08	4·98	5·50–6·20	5·63	2·30	1·60–2·60	4·31	4·20	4·48	4·64	—	—	—	—
n-Bu	R(−)-menthyl	5·08	4·99	5·50–6·20	5·63	2·29	1·60–2·60	4·30	4·20	4·48	4·60	—	—	—	—
Me	R(−)-bornyl	5·00	4·87	5·50–6·20	5·62	2·33	1·60–2·60	4·38	4·17	4·48	4·55	3·49	3·39	3·45	3·28
Me	S(+)-2-octyl	5·00	4·87	5·50–6·20	5·60	2·32	1·60–2·60	4·33	4·17	4·43	4·57	3·48	3·38	3·45	3·27
Me	S(+)-2,2-dimethyl-3-butyl	4·99	4·87	5·50–6·20	5·61	2·30	1·60–2·60	4·36	4·17	4·47	4·54	3·48	3·38	3·45	3·28

[a] $CDCl_3$; [b] C_6H_6;

EXPERIMENTAL

B.ps and m.ps are uncorrected. The compounds were chromatographed over silicagel (ø < 0·08 mm, Merck and 200-300 mesh, Schuchardt). The purity of the products was examined by TLC (Silicagel G, Merck) and GLC (W. Giede's Gaschromatograph 18·3 with flame ionization detector. Column: 10% Reoplex 400 on Chromosorb W, carrier gas: nitrogen).

The NMR spectra were recorded on a Varian HR-60/IL spectrometer. Rotations were measured using a Perkin–Elmer PE-141 spectropolarimeter (sensitivity: 0·002°, accuracy 0·001°). Elemental analyses were performed on a micro scale. All spectral and analytical measurements were performed in the Physicochemical Department of this Institute (Head: Prof. J. Dabrowski).

Trans 1-alkoxy-1,3-butadienes were obtained from 1,1,3-trialkoxybutanes by dealcoholation with H_3PO_4.[22] Using the previously developed analytical methods (GC, IR),[23] these compounds were found to be virtually pure *trans* isomers.

The preparation and properties of optically active glyoxylic acid esters have been reported in an earlier paper.[24]

Condensations of trans *1-alkoxy-1,3-butadienes with optically active glyoxylic acid esters*

The reations between *trans* 1-alkoxy-1,3-butadienes and optically active glyoxylates were carried out at various temperatures without solvents or at room temperature in various solvents (*cf.* Tables 1–4). As examples, the conditions of reactions performed without solvent at 100° (A) and in CH_2Cl_2 at room temperature (B) will be given. (A) A mixture of 2·12 g (0·01 mole) R(−)-menthyl glyoxylate, 1·0 g (0·012 mole) *trans*-1-methoxy-1,3-butadiene and 0·01 g hydroquinone was heated under reflux at 100°, for 6 hr. R(−)-menthyl ester of *cis*, *trans*-2-methoxy-5,6-dihydro-2H-pyran-6-carboxylic acid was obtained in a quantitative yield. (B) To a solution of 2·12 g R(−)-menthyl gloxylate in 20 ml of CH_2Cl_2 1·0 g *trans* 1-methoxy-1, 3-butadiene was added, the mixture was left at room temperature for 48 hr. Subsequently, solvent was removed by evaporation under reduced pressure, and the product (90% yield) was directly subjected to ozonolysis (see below).

Analytical samples of R(−)-menthyl ester of 2-methoxy-5,6-dihydro-2H-pyran-6-carboxylic acid were purified on a column with silicagel and then distilled *in vacuo*.

Physical properties and analyses of the adducts are shown in Table 5, and the assignment of ring hydrogen signals in the NMR spectra (solvents: $CDCl_3$ and C_6H_6) is presented in Table 6.

Determination of the isomeric composition of adducts 3

All adducts of type 3 exhibited on GC two signals corresponding to *cis* (longer retention time) and *trans* isomers. However, on account of the isomerisation of *cis* compounds to *trans*, occurring in the course of chromatography, this method could not be directly applied to the determination of the proportions of the isomers. The comparison of the NMR spectra of adducts of type 3 performed in $CDCl_3$ and C_6H_6 is presented in Table 6 and Fig. 1.

It is clearly visible that the differences in the chemical shift of both—OMe groups and protons at C-6—are larger in the spectra taken in C_6H_6. Signals due to H-6 protons were integrated, from which this *cis*, *trans* isomer composition was calculated. Proportions of the isomers determined in this way were consistent (± 5%) with the values obtained by integration of the OMe group signals.

Ozonolytic degradation of optically active esters of 2-*alkoxy*-5,6-*dihydro*-2H-*pyran*-6-*carboxylic acids* (3)

Ozonolysis of 2·4 g of R(−)-menthyl ester of 2-methoxy-5,6-dihydro-2H-pyran-6-carboxylic acid in 75 ml CH_2Cl_2 was performed at − 70°. The solvent was then evaporated under reduced pressure. To the gelatinous ozonide 10 ml of 90% HCOOH and 10 ml of 30% H_2O_2 were added; the mixture was heated at 100° for 30 min, whereupon H_2O_2 and HCOOH were removed under reduced pressure. The residual semi-crystalline mass containing R(−)-menthyl monoester of malic acid was hydrolysed with 50 ml 3% HCl (100°, 30 min.); menthol was removed by careful steam distillation. Water and HCl were evaporated under reduced pressure (< 50°). The product consist of nearly colourless crystalline mass of malic acid. The sample to be analysed was crystallized from acetone and dried under reduced pressure, m.p. 121–122°. This material showed chemical and spectral properties identical with those of commercial, laevorotatory malic acid.

Crude malic acid from the degradation was dissolved in 20 ml MeOH, whereupon an etheral solution of CH_2N_2 was added till completion. After removal of ether and MeOH under reduced pressure, the residual yellow oil was chromatographed on a silicagel column. Dimethyl malate was distilled at 83–85°C/0·8 mm (air bath temp.). The yield was 0·83 g (64%). The sample showed full chemical and spectral identity with the ester obtained from commercial malic acid and CH_2N_2.

Rotation measurements were performed in MeOH at 546 nm. Mixtures of 1% to 15% of laevorotatory, optically pure dimethyl malate with racemic ester were prepared, and for these mixtures the specific rotations were calculated and compared with the results of the polarimetric measurements.[25] On this basis the rotation values of samples of dimethyl malate obtained from degradation were corrected. The degradation to malic acid was repeated at least twice for each adduct 3.

In order to determine whether the conditions of treatment of the degradation product (hydrolysis, methylation, column chromatography, distillation) did not induce racemization, optically pure malic acid was esterified with CH_2N_2; the resulting ester was hydrolysed with diluted HCl and treated in an exactly identical way, as described for the degradation product. Resulting malic acid was re-esterified with CH_2N_2, the product was chromatographed and distilled. Thus, obtained dimethyl malate showed no change in specific rotation $[\alpha]^{20}_{546}$ − 9·90 ± 0·03°), as compared with starting ester $[\alpha]^{20}_{546}$ − 9·94 ± 0·03°).

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