Chiral Solvent-induced Asymmetric Synthesis. Part 2.[1] Photosynthesis of Optically Enriched Hexahelicenes

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Irradiation of 2-styrylbenzo[*c*]phenanthrene (1) in eleven different, chiral solvents gave rise to the formation of non-racemic hexahelicene with optical yields of 0.2—2.0%. The role of the chiral solvents is ascribed to their influence on the equilibrium between enantiomeric conformations of *cis*- (1), which leads to an excess of one of them. The magnitude and sign of the effect can be related to the size and position of large apolar residues at the chiral centre in the solvent molecules. Similar experiments were done with some other precursors of hexahelicene and some of its derivatives. It is concluded that the solvent behaves as a matrix, in which the photoreaction takes place.

UNTIL now two procedures have been applied to obtain optically active helicenes by induced, asymmetric photosynthesis. Chemically induced, asymmetric photosyntheses were used by Martin *et al.* to obtain an optically pure hexahelicene derivative from a precursor containing a chiral paracyclophane residue [2] and in the diastereoselective photosynthesis of menthyloxycarbonylhexahelicene.[3] Induced, asymmetric syntheses in the preparation of helicenes by irradiation of optically inactive diarylethylenes with left- or right-handed circularly polarized light have been reported by two other groups.[4,5] The optical yield reported for hexahelicene is 0.05%.

In this paper we describe a third procedure for

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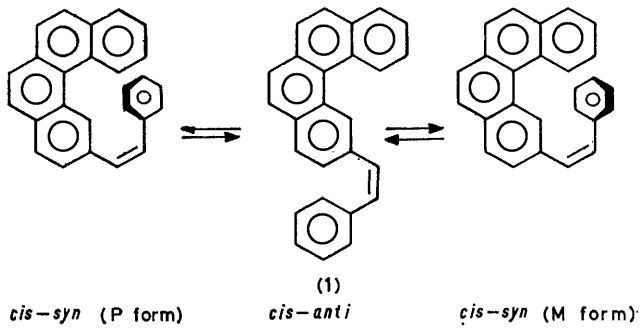
obtaining optically active helicenes which is based on the application of chiral solvents. Some years ago [6,7] it was shown that the usual parent compound for the photosynthesis of hexahelicene, *cis*-2-styrylbenzo[*c*]phenanthrene [1] (1), has a preference for the *cis-syn*-conformation over the *cis-anti*-conformation. The conformational equilibrium depends on the solvent used. As the *cis-syn* conformation exists in two enantiomeric forms (P and M) [8] it was anticipated that the equilibria between the *cis-anti*-form and the P and M conformations of the *cis-syn*-form should be influenced differently by a chiral solvent, leading to a higher equilibrium concentration for one of the enantiomeric forms. On this basis we reasoned that this would be a promising starting situation for the formation of hexahelicene enriched in one of its enantiomers, provided that irradiation does not lead to levelling of the concentrations of the *cis-syn*-P and *cis-syn*-M conformers. This might be the case when the establishment of the conformational equilibria in the ground state is slow in comparison with the radiationless reversal of excited molecules from the S_1 state to the ground state. This seems, however, improbable.



(1)

RESULTS

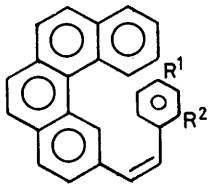
2-Styrylbenzo[*c*]phenanthrene (1) was irradiated in several chiral solvents in the presence of iodine as an oxidant. It was not necessary to use the pure *cis*-isomer of the starting compound as it is known that *trans–cis*-isomerization of (1) is a much more efficient process than its photodehydrocyclization. Some solutions were irradiated at various temperatures. In several cases irradiations were also done in the chiral solvent diluted with benzene to various degrees. Addition of benzene provided the possibility of including some chiral ' solvents ' which are not liquids at room temperature. Specific optical rotations of the hexahelicene formed in the experiments are given in Table 1.

TABLE 1

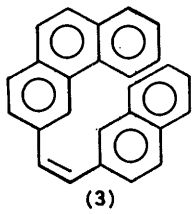
Optical rotations $[\alpha]_D$ and optical yields of hexahelicene obtained by irradiation of 2-styrylbenzo[*c*]phenanthrene (1) in chiral solvents

	Solvent	$[\alpha]_D$ (°)	$[\alpha]_D$ neat (°)	Optical yield (%)
a	(+)-α-Pinene		−7	0.21
b	(*S*)-(−)-Ethyl lactate (20 °C)		+15	0.42
c	(*S*)-(−)-Ethyl lactate (100 °C)		+6	0.18
d	(*S*)-(+)-Ethyl mandelate		+71	2.1
e	(*S*)-(+)-Ethyl mandelate–benzene (1 : 1)	+36.3	+72	
f	(*S*)-(+)-Ethyl mandelate–benzene (1 : 4)	+14.6	+73	
g	(*S*)-(+)-Ethyl *O*-benzoylmandelate		+2	0.04
h	(±)-Ethyl mandelate		0	0.0
i	(*RR*)-(+)-Diethyl tartrate		−40	1.1
j	(*RR*)-(+)-Diethyl *OO'*-dibenzoyltartrate–benzene (1 : 3)	+28.2	+113	
k	(*RR*)-(+)-Diethyl *OO'*-dibenzoyltartrate–benzene (1 : 5)	+18.5	+111	
l	(*S*)-(+)-Ethyl *O*-benzoyl-lactate		−30	0.84
m	(*S*)-(+)-Ethyl *O*-benzoyl-lactate–benzene (1 : 1)	−14.3	−29	
n	(*S*)-(+)-Ethyl *O*-(α-naphthoyl)-lactate		−57	1.6
o	(*S*)-(+)-Ethyl *O*-(α-naphthoyl)-lactate–benzene (1 : 4)	−13.5	−67	
p	(*S*)-(+)-Ethyl *O*-(β-naphthoyl)-lactate–benzene (1 : 1)	−30.6	−60	
q	(*S*)-(+)-Ethyl *O*-(β-naphthoyl)-lactate–benzene (1 : 2)	−21.1	−63	
r	(*S*)-(+)-Ethyl *O*-(4-phenylbenzoyl)-lactate–benzene (1 : 5)	−17	−102	
s	(*S*)-(+)-Ethyl *O*-(2-phenylbenzoyl)-lactate		−30	0.84
t	(*S*)-(+)-Ethyl *O*-(2-phenylbenzoyl)-lactate–benzene (1 : 1)	−14.7	−29	

Optical yield = [α] of product/[α] of pure enantiomer of hexahelicene.



(2)
a; $R^1=CH_3$, $R^2=H$
b; $R^1=H$, $R^2=CH_3$



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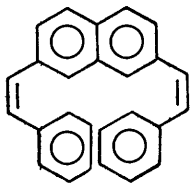

(4)

A small number of similar experiments have been done with 2-(*p*-methylstyryl)- and 2-(*o*-methylstyryl)-benzo[*c*]-phenanthrene (2a and b), which give rise to 2- and 4-methylhexahelicene, respectively, on irradiation. Furthermore, some experiments have been done with other compounds which yield hexahelicene by photodehydrocyclisation, *viz.* 1-(β-naphthyl)-2-(3-phenanthryl)ethylene (3) and 2,7-distyrylnaphthalene (4). From the latter com-

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pound hexahelicene arises *via* two photodehydrocyclizations.[4d] Results from these experiments are given in Table 2.

DISCUSSION

All irradiations of (1) in chiral solvents led to optically active hexahelicene, and a control experiment with a racemic solvent (Table 1, h) affirms that the enrichment in one of the enantiomers of the product must be due to the presence of a chiral solvent. Experiments with chiral solvents at different dilutions (Table 1, d—f; j, k; l, m; p, q) showed that dilution leads to a proportional decrease of the specific rotation of the isolated product. Apparently the viscosity of the solvent does not influence the results very much. This allowed us to calculate theoretical $[\alpha]_D$ values and optical yields for solvents which could not be used neat at room temperature (Table 1, j, k; p, q; r). Experiments at higher temperatures (Table 1, c) revealed that the optical yield under these circumstances is lower than at room temperature. This can be explained by the lower preference of *cis*- (1) at higher temperatures for the *cis-syn* conformation,[7] which results in diminished stereospecific interaction of the substrate with the solvent molecules.

The overall picture of the results in Table 1 suggests that hydrocarbon residues, especially aromatic groups, in the solvents are responsible for the interaction with (1), as might be expected. The position of the largest hydrocarbon residue apparently determines if P- or M-hexahelicene will be formed in excess. Replacement of the methyl group in (*S*)-ethyl lactate by a phenyl group, giving (*S*)-ethyl mandelate, leads to a five-fold enrichment in the same (dextrorotatory) enantiomer of (1) (see Table 1, b and d). Introduction of a benzoyl residue in the polar hydroxy-function of (*S*)-ethyl lactate (Table 1, l) gives, however, hexahelicene in which the antipodal, laevorotatory enantiomer predominates. As expected, (*S*)-ethyl *O*-benzoylmandelate (Table 1, g) which differs from (*S*)-ethyl lactate by the replacement of the methyl by a phenyl group and the simultaneous benzoylation of the hydroxy-group gives hexahelicene of very low optical yield. Apparently, the solvent now provides two rather equivalent modes for interaction with (1), which are of opposite chirality.

The use of (*RR*)-diethyl tartrate (Table 1, i) which lacks aromatic residues still causes a rather high optical yield.

Finally, enlargement of the aromatic residue in (*S*)-ethyl *O*-benzoyl-lactate by annelation with a benzo-group (Table 1, n—q) or substitution by a phenyl group (Table 1, r) leads generally to a significant increase of the optical yield. In the latter case, however, *ortho*-substitution has a negligible effect in comparison with *para*-substitution, which may be ascribed to the non-planar structure of an *ortho*-substituted biphenyl system.

Summarizing, it can be concluded that the optical yield and the sign of the optical rotation of hexahelicene formed from (1) in chiral solvents, are determined by the size and the position at the asymmetric centre, respectively, of the largest apolar, hydrocarbon residue in the solvent molecules.

TABLE 2

Optical rotations $[\alpha]_D$ and optical yields of hexahelicenes obtained by irradiation of the precursors (2a and b), 3, and 4

Starting material	Solvent	$[\alpha]_D$ (°)	$[\alpha]_D$ neat (°)	Optical yield (%)
(2a)	(*S*)-(+)-Ethyl *O*-benzoyl-lactate		−32	0.84
(2b)	(*S*)-(+)-Ethyl *O*-benzoyl-lactate		−12	0.36
(3)	(*S*)-(+)-Ethyl *O*-benzoyl-lactate		0	0.0
(4)	(*S*)-(+)-Ethyl *O*-benzoyl-lactate–benzene (1 : 1)	−35.8	−72	
(4)	(*S*)-(+)-Ethyl *O*-benzoyl-lactate–benzene (1 : 2)	−24	−72	
(4)	(*S*)-(+)-Ethyl *O*-(β)-naphthoyl)-lactate–benzene (1 : 4)	15.6	−78	
(4)	(*S*)-(+)-Ethyl *O*-(β-naphthoyl)-lactate–benzene (1 : 5)	14	−84	

In the asymmetric synthesis of helicenes by irradiation of precursors with circularly polarized light the optical yield of the product from (2a) is five times higher than from (1). The different results have been ascribed to bond rotation of the phenyl residue in the parent compound in the excited state which reduces the imbalance of P and M excited forms.[5c]

In the asymmetric syntheses induced by a chiral solvent the optical yields from (1) and from (2a) are the same. This result leads to the idea that in the chiral solvent the rotation of the phenyl group in the excited state is diminished, which means that the solvent has an influence on the conformation of the helicene precursors in the excited state too. It behaves as a matrix, in which the photoreaction takes place.

The lower optical yield found for the *ortho*-substituted compound (2b) in the same solvent points to a lower selectivity of the chiral solvent towards the enantiomeric conformations of the photoprecursor.

A similar effect may explain that irradiation of 1-(2-naphthyl)-2-(3-phenanthryl)ethylene (3) in a chiral solvent does not give rise to the formation of non-racemic hexahelicene. It may be noted that for this compound as contrasted with (1) no preference for the *cis-syn*-conformation is observed.[7]

The results with 2,7-distyrylnaphthalene (4) give strong support to the idea, that the chiral solvents behave as stabilizing matrices in these photoreactions. The optical yield in several solvents is always higher than from (1), which is an intermediate in the photocyclization of (4). [In induced asymmetric synthesis with polarized light (1) and (4) give the same result.[4d]] This larger stereoselectivity must be achieved in the first cyclization step and the result of this must be largely retained until the second ring-closure takes place.

EXPERIMENTAL

Irradiation of 2-styrylbenzo[*c*]phenanthrene (1) dissolved in a chiral solvent (c 5×10^{-3}) with some iodine added as an oxidant was performed in Pyrex tubes (10 ml) with the light of fluorescent lamps with a wavelength of maximum emission at 360 nm. After completion of the photoconversion, assessed by u.v. spectroscopy, the solvent was removed to isolate the product. Several methods were used. Sometimes distillation of the solvent (α-pinene) followed by column chromatography of the residue or, alternatively, only column chromatography was used. The ethyl lactate solution was poured into water and extracted with toluene. The aroylated solvents were hydrolysed by stirring the irradiated solution in an aqueous sodium hydroxide solution at room temperature for some hours and extracting the helicene with toluene. Use of different separation techniques applied to one solvent system (ethyl mandelate) had no effect on the results. For final purification the helicene-containing fraction was subjected to t.l.c. using silica gel plates and benzene as eluant. The isolated helicene was taken up in chloroform and diluted to 2 ml in a volumetric flask. The optical rotation of this solution was measured with a Perkin-Elmer 241 polarimeter. The accuracy of the value measured was estimated to be 0.002°. The solution was then diluted with chloroform to determine its concentration by u.v. spectroscopy using the ε values given in ref. 5*c*. The accuracy of the $[\alpha]_D$ values depends on the accuracy of ε, but all $[\alpha]_D$ values were better than $\pm 0.5\%$. Data in the Tables are mean values of at least two measurements which differ by $<5\%$.

The aroylated solvents which have not previously been described, were made by mixing ethyl lactate in pyridine with the appropriate acid chloride in pyridine. After stirring for 2 h the pyridine hydrochloride was filtered off, the filtrate poured into water, and the organic layer separated and purified in the usual way. (*S*)-(−)-Ethyl lactate (Fluka) had $[\alpha]_D$ −12.4° (neat); (*S*)-(−)-ethyl mandelate $[\alpha]_D$ 123.5° (c 5.64 $CHCl_3$) (lit.,[9] *R*-isomer $[\alpha]_{589.3}$ −126.2°); (*S*)-(+)-ethyl *O*-benzoylmandelate $[\alpha]_D$ 103.2° (c 5.12 $CHCl_3$) {lit.,[10] *R*-isomer $[\alpha]_D$ −142.2° (neat)}; (*R*,*R*)-(−)-diethyl tartrate $[\alpha]_D$ −2.16° (c 2.33, $CHCl_3$) {lit.,[11] $[\alpha]_D^0$ −6.75; $[\alpha]_D^{50}$ 1.26° (c 16, $CHCl_3$)}; (*RR*)-(−)-diethyl *OO'*-dibenzoyltartrate $[\alpha]_D$ −74.1° (c 3.90, $CHCl_3$) {(lit.,[12] $[\alpha]_D$ −90.14° (c 2.15 pyridine)}; (*S*)-(+)-ethyl *O*-benzoyl-lactate $[\alpha]_D$ 13.6° (c 3.48 $CHCl_3$) {lit.,[13] $[\alpha]_D$ −7.1° (C_2Cl_4)}; (*S*)-(−)-ethyl *O*-(α-naphthoyl)-lactate m.p. 57°, $[\alpha]_D$ −26.1° (c 11.56 $CHCl_3$); (*S*)-(+)-ethyl *O*-(β-naphthoyl)-lactate, m.p. 64—65°, $[\alpha]_D$ 42.4° (c 3.26 ($CHCl_3$); (*S*)-(+)-ethyl *O*-(4-phenylbenzoyl)-lactate, m.p. 88—89°, $[\alpha]_D$ 28.15° (c 1.78 $CHCl_3$); (*S*)-(+)-ethyl *O*-(2-phenylbenzoyl)-lactate $[\alpha]_D$ 13.54° (c 2.4 $CHCl_3$).

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[8] P. and M. correspond with the right- and left-handed conformations, respectively, according to the nomenclature of R. S. Cahn, C. K. Ingold, and V. Prelog, *Angew. Chem., Internat. Edn.*, 1966, **5**, 385.

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