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Liquid-Crystalline Solvents as Mechanistic Probes. 18. The Micromorphology of Crystalline and Liquid-Crystalline Phases of 5α-Cholestan-3β-yl trans-Cinnamate as Discerned from Photochemical Studies[1]

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Liquid-Crystalline Solvents as Mechanistic Probes. 18. The Micromorphology of Crystalline and Liquid-Crystalline Phases of 5α-Cholestan-3β-yl *trans*-Cinnamate as Discerned from Photochemical Studies[1]

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The photoreactions of 5α-cholestan-3β-yl *trans*-cinnamate in its crystalline and liquid-crystalline phases and in isotropic solutions (*n*-hexane and *n*-hexadecane) have been investigated. In hydrocarbon solutions, geometric isomerization of the ester and its cleavage to cholestene and cinnamic acid are the dominant processes; in the crystalline and liquid-crystalline phases, dimerization is the principal reaction mode. Only one photodimer, bis(5α-cholestan-3β-yl) α-truxillate (head-to-tail), could be detected from the crystalline and liquid-crystalline phase experiments. The photochemistry of the liquid-crystalline phase of cholesteryl *trans*-cinnamate was reexamined and shown to proceed quite differently from that of the cholestanyl ester.

INTRODUCTION

Topochemically controlled solid state photodimerizations of cinnamic acid, substituted cinnamic acids, and cinnamate esters have been investigated in detail.[2] In the crystalline state, the molecular packing arrangement influences photoreactivity, and the mutual orientation of molecules determines the stereochemistry of the cyclobutane di-

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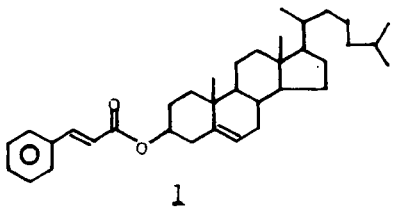
mers. Such topochemical control over photochemical reactions in organized systems can be useful not only to accomplish stereoselective syntheses but also to probe the micromorphology of molecular assemblies.

Recently, Reiser and co-workers[3,4] have demonstrated the usefulness of photodimerization of cinnamate esters to obtain information concerning the distribution of site geometries in ethyl cinnamate glasses and poly(vinyl cinnamate) matrices. Since the photodimerization of cinnamates is reasonably well understood, liquid-crystalline cinnamates are good candidates to investigate the micromorphology of mesophases. Here, we demonstrate that carefully conducted photoproduct analyses offer a complementary method to the spectroscopic techniques employed previously[5] to determine the orientations of cholesteric molecules in their mesophases.

Tanaka *et al.*[6,7] have studied qualitative aspects of the photoreaction of neat cholesteryl *trans*-cinnamate (*1*) in its solid, cholesteric, and isotropic phase (spanning a range from 25° to 225°C) suspensions in KBr matrices. They stated that α-truxillic acid, dicholesteryl α-truxillate, and cholesteryl *cis*-cinnamate could be detected by high performance liquid chromatography (hplc). Nuclear magnetic resonance (nmr) spectra of the reaction mixtures, however, indicated the major dimers to be other than the α-truxillates. The use of KBr as a surface support for the liquid-crystalline and isotropic films as well as the ambiguity of the dimeric products prompted us to reinvestigate the photochemistry of *1*.

Since we conjectured that the major photodimers from *1* might involve the 5,6 double bond of cholesterol, the photochemistry of the saturated analog of *1*, 5α-cholestan-3β-yl *trans*-cinnamate (*2*), was investigated in greater detail. Our results indicate that the reactive pathways available to *2* in its crystalline and liquid-crystalline phases are very similar. A discussion of the extent to which these results can be used to determine the orientations of nearest neighbors of *2* is presented.



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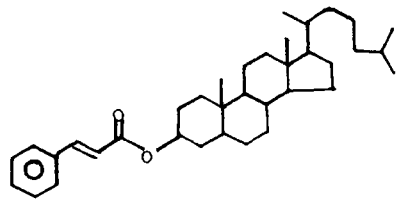

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EXPERIMENTAL

Proton magnetic resonance spectra were obtained with a 90 MHz Fourier Transform Bruker Model FHX-10 spectrometer. Infrared and ultraviolet spectra were recorded, respectively, on a Perkin-Elmer Model 457 grating spectrometer and a Perkin-Elmer 552 spectrometer. Melting points and transition temperatures were measured on a Kofler micro-hot stage microscope with polarizing lenses or a Gallenkamp melting point apparatus and are corrected.

Analytical hplc was conducted on a Waters Model 6000A chromatograph connected to a Waters 440 UV-detector (254 nm) and a Varian (Model CDS 111) integrator. Separation between *2* and its irradiation products was achieved using a Waters Rad-Pak B silica column and 95/5 (v/v) chloroform/*n*-hexane as eluent. *Trans*- and *cis*-cinnamic acids and cholestene were detected on a Waters Rad-Pak C_{18} column using methanol or 60/40 (v/v) methanol/THF as eluent.

Materials. 3β-Cholesteryl *trans*-cinnamate (*1*) (Aldrich) was recrystallized from 2-butanone: 162 $\overset{C}{\longleftrightarrow}$ 214°C [lit.:[6] 163 $\overset{C}{\longleftrightarrow}$ 216°C]. 5-cholestene (Sigma), hexane (Fischer, hplc grade) and chloroform (Burdick and Jackson hplc grade) were used as received. *Cis*-cinnamic acid[8] was a gift from Dr. Joe Otruba.

5α-cholestan-3β-yl *trans*-cinnamate (*2*) was synthesized by converting *trans*-cinnamic acid (mp. 133–134°C) to its acid chloride and adding it to 5α-cholestan-3β-ol (mp. 139–140°C) in 99/1 dry ether/pyridine. After 4 recrystallizations from 95% ethanol, pure *2* was obtained in 55% yield. Its physical and spectral data are collected in Table I.

Bis(5α-cholestan-3β-yl) truxillates and truxinates (3–6). α-Truxillic acid (mp. 290–293°C [lit:[9] mp. 274–278°C (uncorrected)]), γ-truxillic acid (mp 233–242°C [lit.:[10] mp. 228°C (uncorrected)]), δ-truxinic acid (mp. 185–191°C [lit.:[11] mp. 175°C (uncorrected)]), and μ-truxinic acid (mp. 254–256°C [lit.:[12] mp. 252–254°C]) were synthesized by known procedures.[3,9–12] The corresponding bis(5α-cholestan-3β-yl) esters were synthesized by converting the acids to the acid chlorides and adding them to 5α-cholestan-3β-ol (Aldrich) in 1/99 pyridine/dry ether. The crude esters (*3–6*), obtained in 20–30% yields, were purified by preparative TLC (silica gel/chloroform) and/or recrystallization from 95% ethanol. Their physical and spectral data are collected in Table I. Dicholesteryl α-truxillate, mp. 218.5–219.5°C, was synthesized from α-truxillic acid in a manner similar to that employed for *3*.

TABLE I

Spectral and physical data for *2–6*.

Compound	Transition Temperature (°C)	UV(*n*-hexane) λ_{max}nm(ε)	IR (KBr or CCl_4) cm^{-1}	^{1}H-NMR ($CDCl_3$/TMS) δ
5α-cholestan-3β-yl *trans*-cinnamate (*2*)	K $\xleftrightarrow{159.5}$ C $\xleftrightarrow{194}$ I	271 (30500)	2850 2930 1710 1640 1580	0.654–2.0 (46H), 4.80 (1H,m) 6.41 and 7.66 (2H, d, J = 16.2 Hz) 7.34 (5H, m)
Bis(5α-cholestan-3β-yl) α-truxillate (*3*)	mp. 252–254	231 (8000)	2860 2930 1720	0.6–2.0 (cholestanyl methyl & methylenes) 3.85 and 4.35 (cyclobutane protons) 7.22 (aromatic)
Bis(5α-cholestan-3β-yl) γ-truxillate (*4*)	mp. 229–232	231 (8000)	2860 2930 1720	0.6–2.0 (cholestanyl-CH_3 and CH_2) 3.72 and 4.41 (cyclobutane protons) 7.24 (aromatic)
Bis(5α-cholestan-3β-yl) δ-truxinate (*5*)	mp. 106–108	231 (7320)	2860 2930 1720	0.6–2.0 (cholestanyl-CH_3 and CH_2) 3.55 and 4.18 (cyclobutane protons) 7.24 (aromatic)
Bis(5α-cholestan-3β-yl) μ-truxinate (*6*)	mp. 241–244	231 (7750)	2860 2930 1720	0.6–2.0 (cholestanyl-CH_3 and -CH_2) 3.84 and 4.57 (cyclobutane protons) 7.24 (aromatic)

Irradiation Procedures. The light source was a Hanovia 450 W medium pressure mercury arc with Pyrex and water filters. In *n*-hexane and *n*-hexadecane, irradiations were conducted on nitrogen-saturated solutions of *1* and *2* in closed Pyrex tubes. During irradiation of dilute (5×10^{-4} M) *n*-hexane solutions of *2*, aliquots were analyzed periodically by hplc to follow the *trans* → *cis* isomerization. Samples in *n*-hexadecane and concentrated (1.54×10^{-2} M) *n*-hexane solutions of *2* were analyzed after irradiation.

The neat cholesteric phases of *1* and *2* were irradiated in flame-sealed Kimax cells (0.04 cm path length) under vacuum (3×10^{-4} Torr). Since *1* and *2* were observed to decompose when warmed to their isotropic phases, no heat was applied during degassing and sealing procedures. The cells were thermostated and irradiated in a preheated device[13] (166.5 ± 0.5°C). After irradiation (5 min), the cells were crushed in a beaker containing chloroform and an aliquot of the resulting solution was analyzed directly by hplc.

In the crystalline state, a weighed sample of *2* was carefully sandwiched between two Pyrex glass circular microslides and irradiated at room temperature (27–28°C). Then, the solid was dissolved in chloroform and analyzed by hplc.

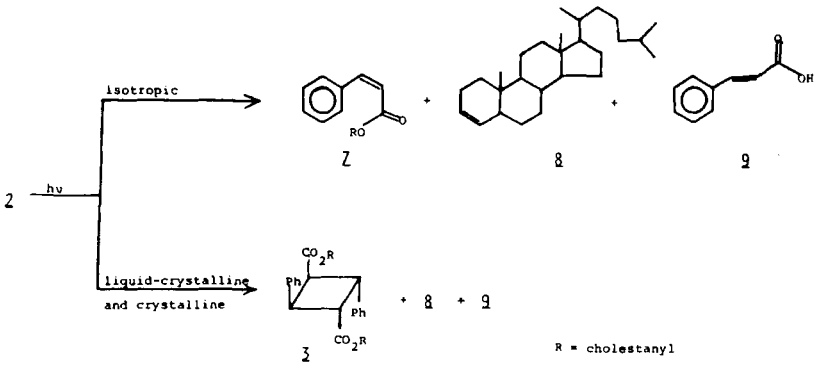
Photochemical and thermal stability of 3–6. Dimers *3–6*, in flame sealed Kimax cells under vacuum, were heated at 166.5°C and irradiated for 15 min and then analyzed by hplc. No decomposition products (stilbene, *2*, cholestene or cinnamic acid) could be detected and no appreciable change in the melting points of *3–6* were observed.

RESULTS AND DISCUSSION

Irradiation of 1. The uncertainty introduced by the work of Tanaka *et al.*[5,6] led us to examine the photochemistry of *1* in *n*-hexane (0.013 *M*) at room temperature and in its neat liquid-crystalline phase (166°C). At *ca.* 20% conversion, the major irradiation products from the hexane solutions were the expected *cis* isomer of *1* and a series of dimers which were neither truxillic nor truxinic in nature. Small amounts of dicholesteryl α-truxillate and *trans*-cinnamic acid were also detected.[14] The same products, albeit in slightly different relative yields, were identified from irradiations of the liquid-crystalline material to *ca.* 10% conversion.

Conspicuously absent from both sets of experiments was any trace of α-truxillic acid, reported by Tanaka *et al.*[7] to be a product. Their

apparently larger percentage conversion and the use of KBr as a supporting matrix *may* explain the appearance of α-truxillic acid in their studies. If greater amounts of cinnamic acid are formed on the top surface, its subsequent dimerization in a net two-photon process would seem reasonable. The conditionality of this argument is necessitated by the disconcerting lack of peaks from the major products (non-truxillic and non-truxinic cyclobutane esters) in the hplc analyses published by Tanaka *et al.* Infrared and ^{1}H nmr analyses[15] of our major photoproducts (isolated by preparative hplc) indicated them to be intermolecular cycloadducts formed between the double bonds of cinnamate and cholesterol (Δ)[5,6]. Consistent with this interpretation, alkaline hydrolysis of each of the major photoproducts yielded cinnamic acid but no truxillic or truxinic acid.



Irradiations of 2 *in isotropic solutions (Table II).* The complications attendant to the photochemistry of *1* led us to investigate its partially saturated analog, 5α-cholestan-3β-yl *trans*-cinnamate (*2*). As expected, the photochemistry of *2* was less complex than that of *1*. To avoid secondary processes, all photoreactions were kept to low percent conversions.

Irradiation of 5×10^{-4} *M* 2 in *n*-hexane at room temperature resulted in *trans* to *cis* isomerization[16] (in accord with the known photochemistry of simple cinnamate esters)[17] and ester cleavage, a previously unreported photoprocess whose products are cholestene (*8*)[18-20] and *cis*- and *trans*-cinnamic acid (*9*). Since solutions of *2* are stable in the dark at room temperature, the ester cleavage is photochemically induced. Either homolysis of the carboxy-cholestane linkage (analogous to a Norrish I process) or γ-hydrogen abstraction, either followed by or concerted with carboxy-cholestane bond cleav-

TABLE II

Irradiation of *2* in isotropic, liquid-crystalline and crystalline phases.

Solvent/Phase	Irradiation[a] Temperature (°C)	% Conversion (±1%)	Relative Product Ratios[b] *3*	*7*	*8*
n-hexane (5×10^{-4} *M*)	25–26	31	c	28	72
n-hexane (1.54×10^{-2} *M*)	25–26	41	c	24	76
n-hexadecane (1.2×10^{-2} *M*)	25–26	27	c	29	71
n-hexadecane (2.5×10^{-2} *M*)	166.5	19	c	29	71
cholesteric liquid crystal (neat)[d]	166.5	4–6	86	c	14
crystal (neat)[d]	27–29	6	77	c	23

[a] ±0.5°C.

[b] Cinnamic acid was not analyzed for in these experiments. Its yield is presumed to be that of *8*.

[c] None detected.

[d] Average of at least 5 different experiments.

age,[21] may explain the formation of the elimination products. Were the former pathway being followed, expulsion of carbon dioxide might be expected, also.[22] We have not detected styrene as a product although it could have escaped our hplc detection. Even prolonged irradiation of a 0.015 *M* hexane solution of *2* at room temperature yielded no detectable photodimers. Apparently, even at the higher concentration of *2*, ester cleavage and geometric isomerization (unimolecular processes) remain much more efficient than dimerization.

The photochemical behavior of ca. 10^{-2} *M* *2* in *n*-hexadecane ($\eta^{25°C}$ = 2.8 cp) at room temperature and at 166°C is very similar to that in *n*-hexane ($\eta^{20°C}$ = 0.313 cp). From this, we infer that neither viscosity nor temperature exert a pronounced influence upon the photochemistry of *2* in isotropic solutions.

Irradiation of 2 in crystalline and liquid-crystalline phases (Table II). The necessity of allowing irradiation of *2* to proceed to no more than a few percent conversion is especially important in the neat ordered phases. In addition to creating the likelihood of secondary processes, high percentage conversions change drastically the original morphology of *2*. For these reasons, all irradiations of *2* in crystalline and liquid-crystalline phases were carried to no more than 6% conversion. No changes in the macroscopic nature of the phases could be detected by optical microscopy under these conditions. Surprisingly, the sole photoproducts detected were the dimer *3* and a rela-

tively small amount of ester cleavage product, cholestene; conspicuously absent was *7*, the *cis* isomer of *2*.

The probability of interaction of excited states of *2* with ground state *2* increases dramatically in a neat phase. The excited state lifetimes of ethyl cinnamate are known, for example, to be about 2×10^{-9}s and 3×10^{-6}s for the singlet and triplet, respectively, in ethanol.[23] Dimerization can occur from either excited state. Taking $k_{diff} = 3.3 \times 10^{10}\ M^{-1}s^{-1}$ in *n*-hexane at room temperature and the excited lifetimes of *2* to be near those of ethyl cinnamate, 99% of the longer lived triplets and ca. 50% of the singlets would encounter a ground state molecule of *2* in a 0.015 *M* solution. Empirically, others have noted that isotropic solution-phase dimerizations of cinnamates occur very inefficiently. We find that the inefficiency is exacerbated by the bulkiness of *2*. Apparently, only a very small fraction of the collisions during each encounter in isotropic solutions have orientations appropriate for dimer formation.

Since all nearest neighbors of excited *2* in crystalline and liquid-crystalline phases are ground-state *2*, the rate of inter-molecular reaction is limited by spatial considerations (i.e., initial orientations and rates of reorganization from non-reactive to reactive alignments). Ester cleavage, the major unimolecular cleavage pathway of *2* in hydrocarbon solutions, provides an internal clock by which the rate of bimolecular reactions can be measured. Geometric isomerization, the other unimolecular process, is suppressed probably for steric reasons in the crystalline and liquid-crystalline phases of *2*.

In both ordered phases, we find that the bimolecular processes of *2* are more important than isomerization and ester cleavage. However, only one dimer, bis(5α-cholestan-3β-yl) α-truxillate (*3*), was detected although several others (*4–6*) have been shown to be sufficiently stable to survive the reaction conditions at 166°C.

Micromorphology of the crystalline and liquid-crystalline phases of 2. Given the exceedingly high viscosities[24] and very low diffusional rates[25] of cholesteric and crystalline phases (*i.e.*, the very long times for substantial reorganization between molecules of *2*), the absence of the *cis* isomer *7* after irradiation, and the short lifetime of the excited states of *2*,[26] we believe the formation of *3* as the sole photodimer provides strong evidence that a large fraction of *2* exists in head-to-tail orientations compatible with facile photodimerization. Such arrangements are not unreasonable since they would be favored by the individual dipoles of the cinnamate groups. In fact, in several other crystalline and liquid-crystalline phases, similar antiparallel arrangements have been demonstrated by x-ray diffraction studies.[27]

Alternatively, it may be argued that the probability of dimer formation from other orientations is so low that their products are not seen. The fact that we can synthesize such dimers (*N.B.*, *5* and *6*) from their respective acids indicates that, were such orientations present in reasonable amounts, their photodimers would have been formed. Fortunately, the basic interpretation of our work does not depend upon this admittedly weak argument. Were we to assume that isomerization and cleavage occur when pairs of *2* are initially aligned head-to-head and dimerization occurs when the initial alignment is head-to-tail, we would still conclude that a large fraction of the molecules of *2* are oriented in their crystalline and liquid-crystalline phases in a head-to-tail arrangement.

While the use of product regiochemistry to determine the arrangement of constituent molecules in ordered phases is not always straightforward, we have shown that it can be a successful tool when employed judiciously. Our observation that molecules within cholesteric and crystalline *2* are aligned preferentially in an antiparallel arrangement provides further insights into the micromorphology of these phases. Using a similar approach, we have demonstrated recently that a smectic phase whose constituent molecules include cinnamate groups is interdigitated.[28]

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15. Infrared spectra of the two hplc isolated products showed absorptions at 1720 cm^{-1} and 1640 cm^{-1}, indicative of at least partial retention of the cinnamate moiety. ^{1}H-nmr spectra of the products were similar to those reported by Tanaka *et al.*[7]
16. *7*, the *cis* isomer of *2*, was synthesized from *2* by an adaptation of a described method.[8,17] The UV spectrum of *7* was very similar to those reported for methyl[17(a)] and ethyl cinnamate:[17(b)] λ_{max}(benzene) 267 nm.
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