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Solid-State Photooligomerization of an Extended Chiral Bifunctional Monomer, (+)-2,4:3,5-Di-*O*-methylene-D-mannitol 1,6-Di-*trans*-cinnamate

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Abstract: Irradiation of crystalline (+)-2,4:3,5-di-*O*-methylene-D-mannitol 1,6-di-*trans*-cinnamate (**1**) induces intermolecular cyclobutane formation leading to chiral oligomers of increasing length. The dimer, trimer, tetramer, and pentamer have been isolated and characterized. The intramolecular distance between the olefinic residues within the molecules of **1** is larger than in any previous examples of solid-state photodimerization or oligomerization and, in spite of the large, bulky tetraoxa-*cis*-decalin group separating the reaction centers, the cinnamate groups of the monomer are properly aligned for intermolecular photocycloaddition. Crystals of **1** are monoclinic, a = 15.218 (6) Å, b = 13.217 (7) Å, c = 5.882 (3) Å, β = 76.95 (3)°; the space group is $P2_1$, with two molecules in the cell. The structure has been solved by direct methods and refined to an R factor of 0.043 on 2270 nonzero reflections. The crystal structure analysis establishes the correct molecular structure of the sugar alcohol derivative, previously in doubt, and elucidates the molecular packing which is responsible for the observed products. The chemical consequences of solid-state irradiation of compound **12**, a monothiophene analogue of **1**, have been considered; **12**, however, shows an unexpected reluctance to crystallize in the same structure as **1**.

Introduction

Solid state produced polymers are unique in their potential for specificity in directional properties compared to polymers prepared in fluid phases, and hence have been a subject of continuing interest.[2a-c] In recent developments it has been shown that optically active photodimer and photopolymers can be prepared in the medium of a chiral crystalline environment and that optical yields may approach 100%.[2d,e]

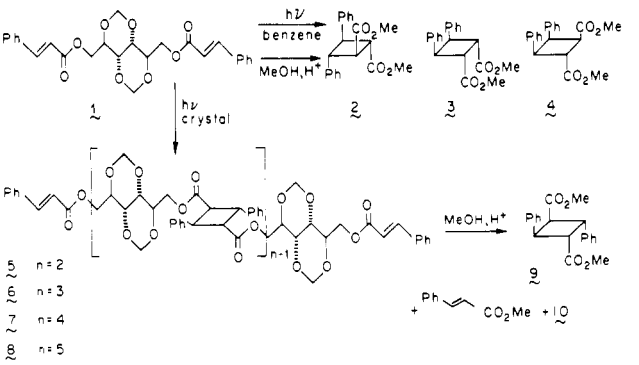
We describe here a solid-state photooligomerization reaction with several interesting features: an inexpensive, readily available starting material, D-mannitol, provides a source of chirality which is manifested by crystallization in a chiral crystallographic space group; the products contain alternating blocks of hydrophobic and hydrophilic regions (the latter may be accentuated by chemical modification); the low molecular weight oligomers can be isolated in pure form and provide potential starting materials for new syntheses; the two halves of the monomer are related by a molecular twofold axis which is very nearly retained in the crystal; finally it is the unique nature of the crystal structure which leads to the product specificity.

Results and Discussion

When the sugar alcohol dicinnamate derivative (+)-2,3:4,5-di-*O*-methylene-D-mannitol 1,6-di-*trans*-cinnamate (**1**) is irradiated in solution, photocycloaddition takes place to yield cyclobutane isomers, which, on ester exchange with methanol, yield the truxinic esters **2**, **3**, and traces of **4**. The optical yield in the synthesis of (−)-**2** is 48%.[3]

When the same D-mannitol dicinnamate **1** is irradiated in the *solid state* only intermolecular cycloaddition is observed and the products are the dimer, trimer, tetramer, pentamer, and higher oligomers of **1** where, in each case, the cyclobutane link has the α-truxillate (**9**) stereochemistry.

Prior to the work reported here solid-state photodimerization and oligomerization have been observed only in molecules where the two reacting olefins are separated by planar or nearly planar aromatic, ester, or amide groups, or short, unsubstituted aliphatic chains.[2b,e,4] Bulky groups such as the tetraoxa-*cis*-decalin have not been previously reported as "spacers" between the reaction centers in solid-state oligomerizations nor are there any examples where the two reacting groups are separated, as in **1**, by 11 covalent bonds. In addition, the molecular structure of **1** was open to question,[5] and it was therefore important to perform a crystal structure analysis in order to elucidate both the molecular structure of **1** and the nature of the intermolecular packing which leads to the formation of the observed photoproducts **5–8**.



Structure Description. The crystal structure analysis of **1** establishes the correct molecular structure of the diol, from

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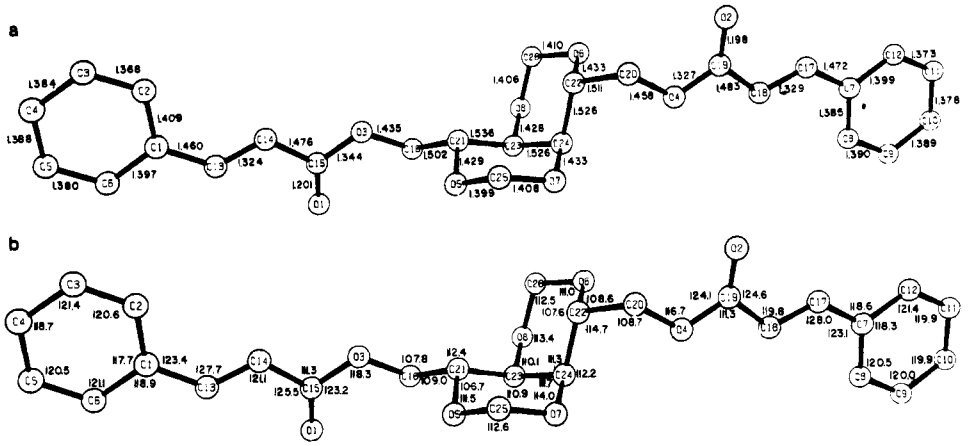


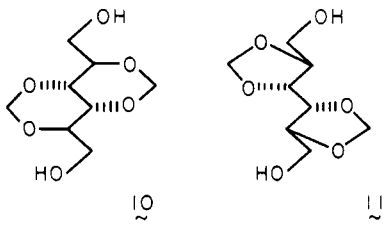
Figure 1. (a) Bond lengths for nonhydrogen atoms in **1** (average esd 0.004 Å; range 0.003–0.005 Å). (b) Bond angles for nonhydrogen atoms in **1** (average esd 0.2°; range 0.2–0.3°). C–H bonds are in the range 0.87–1.14 Å with average esd's of 0.04 Å.

Table I. Torsion Angles (deg) for **1**[a]

atoms	angle	atoms	angle
C6-C1-C13-C14	−179.1	C12-C7-C17-C18	178.2
C2-C1-C13-C14	3.0	C8-C7-C17-C18	−3.1
C13-C14-C15-O3	−175.8	C17-C18-C18-O4	179.6
C13-C14-C15-O1	4.8	C17-C18-C19-O2	0.3
C16-O3-C15-O1	0.1	C20-O4-C19-O2	−0.6
C14-C15-O3-C16	−179.3	C18-C19-O4-C28	−179.9
C15-O3-C16-C21	−136.6	C19-O4-C20-C22	133.4
O3-C16-C21-O5	74.3	O4-C20-C22-O6	−62.8
O3-C16-C21-C23	−167.6	O4-C20-C22-C24	57.6
C16-C21-O5-C25	−176.2	C20-C22-O6-C26	−175.5
C21-O5-C25-O7	−63.6	C22-O6-C26-O8	−63.0
C24-O7-C25-O5	55.2	C23-O8-C26-O6	58.1
C21-C23-O8-C26	74.6	C22-C24-O7-C25	77.8
C24-C23-O8-C26	−50.8	C23-C24-O7-C25	−47.6
C16-C21-C23-O8	60.9	C20-C22-C24-O7	59.9
C24-C23-C21-O5	−54.6	C23-C24-C22-O6	−53.8
C16-C21-C23-C24	−174.1	C20-C22-C24-C23	−174.8

[a] The torsion angle is for the combination 1-2-3-4, looking down the 2-3 bond, atom 2 toward the viewer, a positive angle being a clockwise rotation. Chemically equivalent torsion angles are given on the same line.

which **1** was synthesized, as **10** and not **11** as was previously suggested.[3,5]



10 **11**

Bond lengths and bond angles for **1** (Figure 1) are normal for the various chemical groups represented in the molecule. Chemically equivalent bonds in the two cinnamate groups have equal values to within 3 esd's (0.012 Å) except for the pairs C1–C2, C7–C8; C2–C3, C8–C9; C15–O3, C19–O4; O3–C15, O4–C25, for which the largest difference is 5 esd's. Chemically equivalent bond angles show a greater tendency toward differences which exceed 3 esd's but no special significance is attached to any of these differences.

Conformational differences in terms of torsion angles between the two "halves" of the molecule might play a discriminating role in terms of their chemical activity. The chemically equivalent torsion angles are given in Table I. For the cinnamate groups the conformations are nearly identical "mirror images" as indicated by the torsion angles of similar magnitude but opposite sign. The only exception is the pair of angles O3–C16–C21–C23 and O4–C20–C22–C24. The two rings of the bicyclic system have virtually identical chair conformations, and are fused to each other such that the oxygens adjacent to the common bond are in equatorial positions and the carbons are in axial positions.

The equations for the best planes for the benzene rings, the vinyl ester groups, and the bicyclic system are given in Table II. In the computation of each of these planes we obtain a Cartesian coordinate system based on the group's three principal moments of inertia, with the origin at the center of mass of the group and the two "in-plane" coordinate axes (L, M) corresponding to the smallest and second smallest moments of inertia. The remaining axis (N) is about the largest moment, and coordinates along this axis are a measure of the atoms' deviations from the best plane. Thus, relationships among the atomic coordinates in this axial system can yield information about approximate molecular symmetry which is not dictated by crystallographic symmetry requirements.

The bicyclic sugar system is obviously not planar, but a calculation of the "best plane" for this group is quite revealing in terms of the approximate molecular symmetry. Atoms C23, C24, O7, and O8 have very nearly the same N values (ca. −0.60 Å) while the remaining six atoms have positive deviations from the plane, which may be paired as follows: C25:C26 (0.42 Å); C21:C22 (0.47 Å); O5:O6 (0.31 Å). Furthermore, the L and M coordinates of the atoms in these pairs and the pairs C23, C24 and O7, O8 are essentially equal in magnitude but opposite in sign. These relationships suggest the presence of a pseudomolecular twofold axis parallel to the "out-of-plane" axis and passing through the center of mass which is the midpoint of bond C23–C24. With reference to the same plane and axial system, chemically equivalent atoms in the two cinnamate groups are related by the same axis, but the center of mass is displaced by about 0.37 Å from the center of mass of the bicyclic system, as determined by the difference between N coordinates in any pair. This shift of the center of mass for the two units of the molecule is the factor responsible for lack of a "true" twofold axis in the usual point group symmetry terms.

Packing and Environment for the Solid-State Photooligomerization. The packing is shown in Figure 2. The long axis of the molecule is very nearly parallel to the b crystallographic axis. However, an unusual feature of the structure is the fact that the length of the molecule in this direction (i.e., the difference between the fractional y coordinates of H4 and H10) is about 1.6 times greater than that axis. Thus the complete molecular chemical entity does not "fit" in the cell. In crys-

Table II. Equations of Some Best Planes in the Molecule[a]

plane	M_1	M_2	M_3	d
ring C1-C6	−9.647	−6.647	2.524	−3.069
ring C7-C12	−9.544	−6.654	2.572	0.0
vinyl ester C13, C14, C15, O6, O7, O3	−11.081	−6.449	1.791	−3.614
vinyl ester C17, C18, C19, C20, O2, O4	−10.387	−6.610	2.148	−0.478
sugar C21-C26, O5-O8	6.052	5.296	5.258	4.110

[a] Equations of planes ($M_1x + M_2y + M_3z - d = 0$). x, y, and z are fractional coordinates.

tallographic terms, this simply means that the asymmetric unit (which *must* fit in the cell) is comprised of two parts of the molecule which, within a single unit cell, are not chemically bonded together.

Photooligomerization can occur if the crystal packing is consistent with the topochemical rules; namely, the reactive double bonds should be nearly parallel, with a separation of about 4 Å.[8] In Figure 2b, it is seen that the two planar cinnamate groups on a single molecule are essentially parallel to each other and that a translation along the *b* axis brings one cinnamate group over the second one. The registry prior to reaction is shown in Figure 2c, wherein it is seen that the double bond C13=C14 is parallel to C17=C18 in the next molecule related by a *b*-axis translation, and the distance between the centers of the two bonds is 3.98 Å; thus the topochemical requirements for photoreaction are satisfied by the packing arrangement.[8]

Generally, in solid-state photocycloaddition reactions of olefins, the two reacting double bonds are related either by translation, such that mirror-symmetric cyclobutane derivatives result, or by centers of symmetry, such that centrosymmetric substituted cyclobutanes are produced.[8] The intermolecular reaction of a bifunctional molecule where the reactive centers of the two molecules are unrelated by any symmetry elements is much less common.[2e] The present case is unique, however, in the fact that the intramolecular olefinic functions are separated by a much larger distance, 13.6 Å (11 bonds), than in any other cases of intermolecular reaction of bifunctional molecules, and that this separation is accomplished by the large bulky tetraoxa-*cis*-decalin system.

The photoreactivity of **1** indicates that the solid-state photooligomerization reaction may yield products which link a larger variety of central groups than was heretofore considered possible. However, it must be emphasized that the structural requirements which bring the two double-bond functions into correct register for cycloaddition cannot, in general, be readily predicted. Of a group of six crystalline D-mannitol derivatives with appended cinnamate groups,[3] only **1** exhibits photoreactivity in the solid state.

The molecular packing of **1** only allows photooligomerization to take place along a stack of molecules related by a *b* translation. A second stack, related to the first by the twofold screw axis of the space group, also undergoes reaction by the same mechanism, but between stacks there are no contacts of the type which could lead to photoreaction. Hence the crystal structure restricts the oligomerization to linear products only.

Photoproducts. The products were separated by chromatography and their characterization is described in the Experimental Section. Although the dimer through pentamer were isolated in pure form, TLC indicated the presence of three additional compounds which, by extrapolation, were assigned the hexamer through octamer structures. The irradiation of larger quantities of monomer might have facilitated the isolation of these in pure form. The product distribution is controlled by irradiation time; short periods favor formation of dimer **5** and the shorter oligomers, while long irradiation periods afford highly insoluble material which, on the basis of TLC behavior, contains ≥ten monomer units.

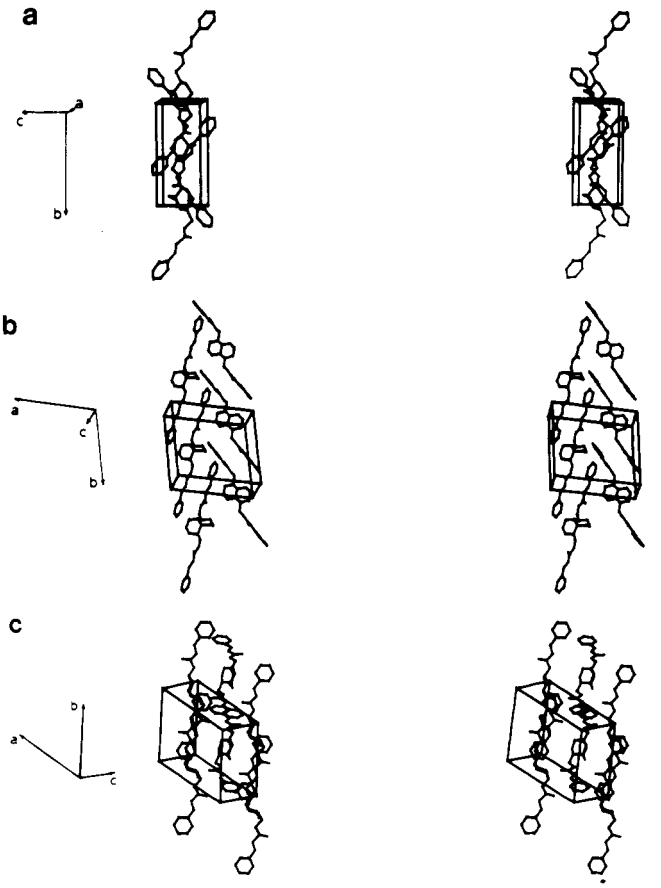


Figure 2. Stereoviews of the structure of **1**. (a) View down the *a* axis; molecules in one stack nearly parallel to *b* axis are related to second stack by the twofold screw axis parallel to *b*. (b) View on the "best plane" of the bicyclic system. The reference molecule, whose coordinates are given in Table III, is the middle one in the right-hand stack. (c) View on best plane of ring C1-C6 showing registry of double bonds which is suitable for photooligomerization.

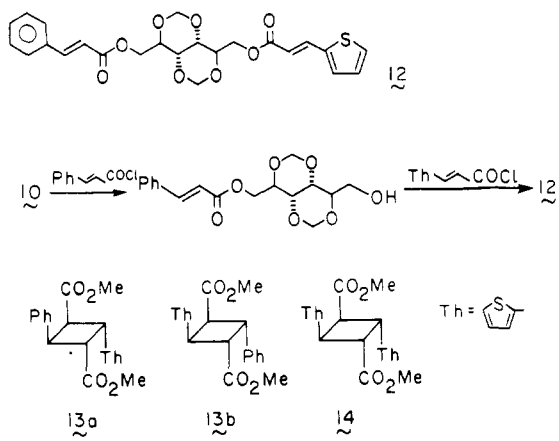
As the oligomeric chain lengthens, reactivity toward ester exchange in refluxing methanolic HCl is sharply decreased: dimer **5** is completely reacted in less than 12 h, while the tetramer **7** requires nearly 5 days for complete reaction. The oligomeric products containing five or more monomer units may also be considered for further *intra*molecular photocycloaddition reactions in solution.[3,9]

Symmetry Aspects of Crystalline 1. On passing from fluid phases into the crystalline phase, the time-averaged molecular symmetry is invariably lowered.[10] The chemical consequences of this have been exploited infrequently; for example, asymmetric synthesis has proceeded in crystals comprising molecules that are asymmetric in the solid, although they have time-averaged planar, symmetric conformations in solution.[2d,11]

In solution, compound **1** has a time-averaged twofold axis and the two cinnamate groups are thus chemically equivalent. On crystallization, the ideal twofold symmetry is broken. Although the two cinnamate groups are no longer equivalent, the crystal structure analysis indicates that **1** maintains a pseudo-twofold axis in the solid. The *chemical* differences between the two ends of the molecule **1** in the crystalline assembly are emphasized by the photoproducts **5–7**. Although solutions of **1** display NMR signals for only one kind of cinnamoyl group, as expected for a C_2 molecule, the NMR spectra

of **5–7**, which are asymmetric molecules (C_1), each show two different cinnamoyl group signals. Thus, interaction of the crystalline pseudo-twofold molecule **1** with neighboring molecules enhances the C_1 rather than the C_2 "character" of **1**.

We have considered the chemical consequences of this "approximate" symmetry and have posed the question of how an unsymmetrical molecule closely similar to **1** but containing two different end groups would crystallize. On the basis of considerable previous experience where thiophene and benzene analogues were found to be isomorphous,[2d,12] compound **12** appeared to be a good candidate to provide an answer to this question and hence this material was synthesized. If, indeed, this modification of the cinnamate group represents a minor perturbation of the molecular structure, the unsymmetrical molecule might be expected to crystallize in the same crystal structure as **1**.[2d] It would then be possible to inquire into the relative orientation of the intrinsically unsymmetrical molecule **12**: is there total disorder (i.e., the crystal "sites" do not distinguish between the phenyl and thienyl groups) or perfect order (i.e., molecules **12** all point in the same direction), or an intermediate situation? In addition to the intrinsic interest in the degree of subtle molecular discrimination that the crystal may exhibit, the order or disorder of **12** would result respectively in high optical yield or racemic product **13**. Perfect order would afford a pure enantiomeric product, either **13a** or **13b** depending on the orientation of **12**, while a completely random orientation of **12** would afford racemic **13**, and the achiral products **9** and **14** in the ratio 2:1:1.



The synthesis of **12** was straightforward. However, despite repeated attempts at crystallization using various solvents and different techniques, good single crystals of **12** did not result. Furthermore, X-ray powder diffraction spectra of **12** show that **12** and **1** are *not* isomorphous. Even when solutions of **12** were seeded with crystalline **1**, the desired $P2_1$ structure was not obtained. Although crystalline **12** also displays solid-state photoreactivity, the structures of the products, not yet fully characterized, differ from those obtained from **1**.

In view of the isomorphous structures in many systems where thiophene and benzene groups are interchanged,[2d,12] it is surprising that in **1** and **12**, where the net difference appears to be so small, the two nevertheless adopt different structures. Apparently, in the particular crystal structure of **1** the environment about the phenyl group prevents a thienyl group from replacing it. Further investigation of this point using substitutional solid solutions containing increasing amounts of **12** in **1** is now called for.

Experimental Section

X-ray Structure Determination of the Monomer. Crystal data follow: $C_{26}H_{26}O_8$, mol wt 466.21, monoclinic, a = 15.218 (6) Å, b = 13.217 (7) Å, c = 5.882 (3) Å, β = 76.95 (3)°, V = 1152.6 × 10^{-24} cm^3, $F(000)$ = 246, μ = 3.69 cm^{-1} (Cu Kα), ρ_{calcd} = 1.34 g cm^{-3}, ρ_{obsd} = 1.347 g cm^{-3}, Z = 2, systematic absences, $0k0$, $k = 2n + 1$, leads to space group $P2_1$ (no. 4) (Cu Kα, λ = 1.5418 Å).

Collection and Reduction of Diffractometer Data. Intensity data were collected on a crystal of approximately 0.3 mm on an edge which was cut from crystals grown from methanol–methylene chloride. Unique reflections to a 2θ limit of 142° were measured on a Syntex $P\bar{1}$ diffractometer with a moving crystal–moving counter technique and a scan rate which varied between 2 and 24°/min and was determined by a rapid prescan of each reflection. A total of 2270 unique reflections were measured; of these 37 were less than 2σ and were considered unobserved. The structure was solved by direct methods and refined using the SHELX program.[13] The only unusual feature of the solution was the necessity to include a reflection (*1101*) of relatively low $|E|$ value (1.22) among the origin determining reflections owing to a paucity of strong reflections in this parity group. Thirty-one of the 34 atoms in the asymmetric unit appeared in the first E map. The remainder were found in a subsequent Fourier map. Least-squares refinement proceeded as follows. Three cycles (full matrix) on all heavy atoms with isotropic temperature factors and $\sin\theta/\lambda < 0.65$ led to an R of 0.129. The molecule was then divided into five blocks, corresponding to the two benzene rings, the bicyclic system, and the two vinyl ester groups. Two cycles with all reflections and heavy atoms anisotropic yielded an R of 0.106 at which point ten hydrogen atoms appeared in the difference map. Six additional cycles, with difference maps after each pair, located the remaining hydrogen atoms, which were refined isotropically. A final two cycles led to conventional R of 0.043 and a weighted R_w of 0.052.[14] Final values of atomic coordinates are given in Table III.[15]

Solid-State Irradiation of (+)-2,4:3,5-Di-*O*-methylene-D-mannitol 1,6-Di-*trans*-cinnamate (1). Powdered 1-g samples of **1**[3] were spread between pairs of 20 × 20 cm glass plates and irradiated with Westinghouse sunlamps at 30–35 °C. After 18 days the material was no longer completely soluble in chloroform; the solubility further decreased with increasing irradiation.

TLC analysis (20% ethyl acetate in benzene, two developments) showed a series of spots, all less mobile than the starting material, which gradually become more poorly resolved with decreasing R_f values: R_f 0.61 (starting material, **1**), 0.48 (dimer, **5**), 0.35 (trimer, **6**), 0.25 (tetramer, **7**), 0.17 (pentamer, **8**), and three barely resolved spots at 0.12, 0.09, and 0.06, as well as a strong spot at R_f 0. With increasing irradiation the proportion of starting material decreased and, finally, the mobile spots became weak and the R_f 0 spot was the sole dominant one.

A 2.0-g sample of **15** was irradiated for 30 days and chromatographed on silica gel (80 g). Elution with 25% ethyl acetate in *n*-hexane (2 L) afforded unreacted starting material, **1** (0.19 g).

Elution with 30% ethyl acetate in *n*-hexane (4 L) afforded the dimer **5** (0.20 g). NMR data: 7.83 and 7.80 (d, d, J = 16 Hz, 2 H, PhCH=C), 7.80–7.25 (m, 20 H, Ph), 6.56 and 6.51 (d, d, J = 16 Hz, 2 H, -C=CHCO), and 5.00–3.35 ppm (broad m, 28 H, CH_2O-, CHO-, and cyclobutane hydrogens). After crystallization from MeOH-CH_2Cl_2 the dimer had mp 83–86 °C.

A portion (0.14 g) of **5** was treated overnight with boiling methanol (50 mL) containing thionyl chloride (0.5 mL). The residue, after evaporation of the methanol, was dissolved in CH_2Cl_2 and the solution was washed with water, dried, and evaporated to dryness. The NMR spectrum of the residue (0.11 g) indicated the presence of methyl *trans*-cinnamate and dimethyl α-truxillate (**9**) and the ratio of integration of the corresponding -CO_2Me signals, ca. 1:1, was that anticipated from the dimer structure.

Elution with 35% ethyl acetate in *n*-hexane (1 L) gave 0.076 g of material comprising mainly dimer **5** and trimer **6** (TLC). Elution with 40% ethyl acetate in *n*-hexane (2.5 L) afforded 0.086 g of material containing almost pure trimer **6** (R_f 0.35). Crystallization of a portion (0.058 g) from EtOH-$CHCl_3$ afforded the pure trimer (0.043 g), mp 103–105 °C. NMR data: 7.81 and 7.76 (d, d, J = 16 Hz, 2 H, PhC*H*=C-), 7.62–7.17 (m, 30 H, Ph), 6.56 and 6.51 (d, d, J = 16 Hz, 2 H, CCHCO), and 5.0–3.33 ppm (broad m, 44 H, CH_2O-, CHO-, and cyclobutane hydrogens).

The trimer **6** (0.14 g) was treated with boiling methanol (50 mL) and thionyl chloride (0.5 mL) for 3 days. Workup, as described for the dimer, afforded a mixture of methyl cinnamate and dimethyl α-truxillate (**9**) in a ratio of 1:2 (integration of the corresponding -CO_2Me signals in the NMR spectrum).

Further elution with the same mixture of solvents afforded material (0.159 g) whose TLC chromatogram showed mainly two spots cor-

Table III. Atomic Coordinates in Fractional Crystal Coordinates[a,b]

atom	x	y	z
C(1)	0824(1)	6652	8522(3)
C(2)	1278(2)	6697(2)	10359(4)
C(3)	1137(2)	7489(2)	11895(4)
C(4)	0547(2)	8265(2)	11708(4)
C(5)	0098(2)	8235(2)	9899(5)
C(6)	0236(2)	7743(2)	8329(4)
C(7)	4127(1)	−5342(2)	1485(4)
C(8)	3670(2)	−5380(2)	−0301(4)
C(9)	3803(2)	−6183(2)	−1868(5)
C(10)	4401(2)	−6954(3)	−1658(5)
C(11)	4859(2)	−6922(2)	0111(5)
C(12)	4719(2)	−6132(2)	1699(4)
C(13)	0961(2)	5845(2)	6784(4)
C(14)	1477(2)	5033(2)	6687(4)
C(15)	1568(2)	4301(2)	4753(4)
C(16)	2236(2)	2723(2)	3333(5)
C(17)	4006(2)	−4521(2)	3220(4)
C(18)	3498(2)	−3697(2)	3320(4)
C(19)	3439(2)	−2973(2)	5247(4)
C(20)	2795(2)	−1426(2)	6896(5)
C(21)	2123(2)	1721(2)	4567(4)
C(22)	2909(2)	−0396(2)	5753(4)
C(23)	2478(2)	0836(2)	2921(4)
C(24)	2262(2)	−0175(2)	4174(4)
C(25)	1041(2)	0643(3)	6776(5)
C(26)	3975(2)	0662(3)	3395(7)
O(1)	1247(2)	4392(2)	3079(3)
O(2)	3825(2)	−3069(2)	6825(4)
O(3)	2073(1)	3502(1)	5077(3)
O(4)	2909(1)	−2196(1)	5077(3)
O(5)	1184(1)	1539(2)	5478(3)
O(6)	3810(1)	−0315(2)	4361(4)
O(7)	1337(1)	−0219(2)	5411(3)
O(8)	3418(1)	0896(2)	1859(3)
H(2)	174(3)	612(4)	1035(7)
H(3)	145(2)	750(4)	1314(6)
H(4)	048(2)	885(4)	1286(7)
H(5)	−034(2)	879(3)	995(6)
H(6)	−017(2)	734(4)	732(7)
H(8)	329(2)	−490(2)	−039(4)
H(9)	343(2)	−624(2)	−311(4)
H(10)	443(2)	−756(3)	−264(5)
H(11)	524(2)	−752(3)	039(6)
H(12)	500(2)	−619(3)	309(5)
H(13)	062(2)	582(3)	565(5)
H(14)	179(2)	480(3)	803(5)
H(16a)	180(2)	270(2)	238(5)
H(16b)	294(2)	281(3)	218(6)
H(17)	428(2)	−464(3)	440(5)
H(18)	313(2)	−356(2)	218(4)
H(20a)	220(2)	−150(3)	763(5)
H(20b)	321(2)	−156(3)	790(6)
H(21)	239(2)	171(2)	579(5)
H(22)	282(2)	007(2)	700(4)
H(23)	215(2)	083(3)	164(5)
H(24)	233(2)	−069(2)	312(5)
H(25a)	042(2)	057(3)	636(6)
H(25b)	139(2)	078(2)	808(4)
H(26a)	459(2)	069(3)	246(6)
H(26b)	384(2)	114(3)	469(5)

[a] C, O ×10⁴; H ×10³. Standard deviation in terms of last digit given in parentheses. [b] Atom numbering given in Figure 1.

responding to the trimer **6** and the tetramer **7**. Ethyl acetate in *n*-hexane (45%, 2.0 L) eluted 0.040 g of nearly pure tetramer **7** (R_f 0.25). Crystallization from EtOH–$CHCl_3$ afforded **7**, mp 105–108 °C. NMR data: 7.71 and 7.68 (d, d, J = 16 Hz, 2 H, PhC*H*=C-), 7.55–6.85 (m, 40 H, Ph), 6.43 and 6.40 (d, d, J = 16 Hz, 2 H, -C=CHCO), and 5.10–3.18 ppm (broad m, 60 H, $-CH_2O$, -CHO, and cyclobutane protons).

Ester exchange of **7** with methanol, as described for the dimer and trimer (reflux for 5 days), afforded a mixture of methyl cinnamate and dimethyl α-truxillate (**9**) in the ratio 2:3.

Further elution with the same mixture of solvents afforded 0.054 g of material whose TLC chromatogram showed several spots corresponding to tetramer **7**, pentamer **8** (R_f 0.17), and less mobile spots.

Elution with *n*-hexane–ethyl acetate (1:1, 0.5 L) afforded 0.087 g of pentamer **8**, which, after several crystallizations from ethanol–methylene chloride, had mp 112–115 °C. NMR ($CDCl_3$): δ 7.67 and 7.62 (d, d, J = 16 Hz, 2 H, PhC*H*=C-), 7.62–7.48 (m, 50 H, Ph), 6.42 and 6.38 (d, d, J = 16 Hz, 2 H, -C=CHCO), and 4.73–3.31 (broad m, 76 H, $-CH_2$, $-CH_2O$, -CHO, and cyclobutane protons).

2,4:3,5-Dimethylene-D-mannitol 1-*trans*-Cinnamate. To a solution of 2,4:3,5-dimethylene-D-mannitol[5] (4.9 g) in dry pyridine (50 mL) a solution of cinnamoyl chloride (4.3 g) in dry benzene (30 mL) was added dropwise while cooling (ice–water) and stirring. The mixture was stirred for 2 h in the cold and then at room temperature for 40 h.

After evaporation of the benzene, the pyridine solution was poured into ice–water (~200 mL) and the oil which separated was dissolved in $CHCl_3$. The solution was washed successively with HCl 1:4, 5% aqueous sodium hydrogen carbonate, and water, and then dried and concentrated. The residue (8.0 g) was eluted from silica gel (320 g) with 25% ethyl acetate in *n*-hexane and 70% ethyl acetate in *n*-hexane; the former afforded the dicinnamate **1** (2.57 g) and the latter afforded the monocinnamate as a colorless oil (2.77 g). NMR ($CDCl_3$): δ 7.81 (d, J = 16 Hz, 1 H, PhC*H*=C), 7.8–7.15 (m, 5 H, Ph), 6.50 (d, J = 16 Hz, 1 H, C=CHCO), 4.93 (broad singlet, 4 H, $-CH_2$), 5.25–3.45 (m, series of peaks, 8 H, $-CH_2O$, -CHO), and 2.90–2.15 (broad m, 1 H, -OH).

2,4:3,5-Dimethylene-D-mannitol 1-*trans*-Cinnamate 6-(β-2-*trans*-Thienylacrylate) (12). To a solution of the monocinnamate (2.7 g) in dry pyridine (30 mL), a solution of thienylacryloyl chloride (1.8 g) in dry benzene was added dropwise while cooling and stirring. The mixture was stirred in the cold for 2 h and at room temperature for 20 h. Workup as in the previous procedure afforded 3.2 g of material. Elution from silica gel (100 g) with 25% ethyl acetate in *n*-hexane (2 L) afforded **12** (0.76 g). Elution with 70% ethyl acetate in *n*-hexane afforded unreacted monocinnamate (1.0 g). Crystallization of **12** from ethanol afforded crystals (0.63 g), mp 110–112 °C. Anal. Calcd for $C_{24}H_{24}SO_8$: C, 61.0; H, 5.12. Found: C, 60.9; H, 5.19. NMR data: 7.80 (d, J = 16 Hz, 1 H, PhCH=C-), 7.71 (d, J = 16 Hz, 1 H, ThCH=C-), 7.78–6.85 (m, 9 H, Ph and Th), 6.53 (d, J = 16 Hz, 1 H, PhC=CHCO), 6.33 (d, J = 16 Hz, 1 H, ThC=CHCO-), 5.00 (s, 4 H, $-CH_2$), 5.3–3.8 ppm (m, 8 H, -OCH). *m/e* 473 (M^+); $[\alpha]_D$ +42.5° (*c* 2.23, acetone). Debye–Sherrer powder photographs of **12** grown from several solvents were identical and differed completely from that of **1**.

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Supplementary Material Available: Thermal parameters of the atoms (Table IV) and a listing of observed and calculated structure factors (15 pages). Ordering information is given on any current masthead page.

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(15) The thermal parameters of the atoms (Table IV) and observed and calculated structure factors are available as supplementary material; see paragraph at end of paper.

Kinetic Applications of Electron Paramagnetic Resonance Spectroscopy. 35. The Search for a Dialkylaminyl Rearrangement. Ring Opening of *N*-Cyclobutyl-*N*-*n*-propylaminyl[1]

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Abstract: A search for a dialkylaminyl radical which rearranges at a rate suitable for study by kinetic EPR spectroscopy has shown that cyclobutyl-*n*-propylaminyl is such a species. This radical undergoes ring opening, and the rate constant for this process can be represented by $\log (k_r/s^{-1}) = (12.8 \pm 1.5) - (10.5 \pm 1.5)/\theta$, where $\theta = 2.3RT$ kcal/mol.

The most generally useful method for determining the rate at which a substrate reacts with a particular class of free radicals is to utilize a radical from this class which can undergo a competitive, irreversible rearrangement or scission. The kinetic scheme can be represented as

$$\begin{array}{l} R_A^{\cdot} + \text{substrate} \xrightarrow{k_A} \text{product A} \\ \quad \downarrow k_r \\ R_B^{\cdot} + \text{substrate} \longrightarrow \text{product B} \end{array}$$

Provided that the rate constant for the rearrangement, k_r, and the concentration of the substrate are both known, then the desired rate constant, k_A, can be calculated from the product ratio, i.e.

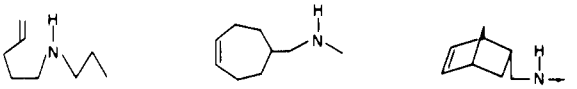
$$k_A = k_r \frac{[\text{product A}]}{[\text{product B}][\text{substrate}]}$$

There is now a well-filled stable[3] of primary alkyls for which rearrangement rates have been measured over a range of temperature by kinetic EPR spectroscopy.[4-10] There are also a few specific carbon-centered radicals from other classes for which the rearrangement rates have been measured by EPR (e.g., secondary alkyl,[11] acyl,[7,12] and alkoxycarbonyl[13]). Comparable data on heteroatom-centered radicals are almost nonexistent.[14] For example, no absolute rate constant has been measured for *any* unimolecular reaction of a dialkylaminyl radical. This is not to say that dialkylaminyl rearrangements are unknown. Indeed, a number of alkenylalkylaminyls have been shown to undergo intramolecular additions under neutral conditions[15] to form monocyclic,[16,17] bicyclic,[18,19] and even tricyclic[20] products. However, these results are of qualitative significance only. Cyclization rates were not measured and the experiments were such[15] that not even a rough estimate of rate can be made.

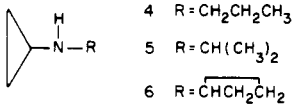
In this paper we report on our search by EPR for a suitably "paced" dialkylaminyl rearrangement. Naturally, this search began among the known rearrangements, but all were found to proceed much too slowly for study by EPR. Our investigation of other potential dialkylaminyl rearrangements uncovered several that were too fast and one that was too slow, but eventually the ring opening of cyclobutyl-*n*-propylaminyl proved to be "just right".

Experimental Section

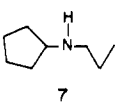
Materials. Amines. *N*-4-Pentenyl-*N*-*n*-propylamine, **1**, was prepared from bromopent-4-ene (0.05 mol) and *n*-propylamine (0.5 mol) by using the procedure described by Surzur et al.[21] We are also indebted to Professor C. J. Michejda for a sample of this amine and the derived tetrazene. Amines **2** and **3** were gifts from Dr. O. E. Edwards



1 **2** **3**



4 R = $CH_2CH_2CH_3$
5 R = $CH(CH_3)_2$
6 R = $\overline{CHCH_2CH_2}$



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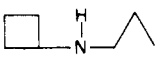
and from Professor B. Waegell and Dr. R. Furstoss, respectively. The cyclopropylamines **4**, **5**, and **6** were prepared by heating cyclopropylamine (0.5 mol) with the appropriate alkyl bromide (0.05 mol) in sealed tubes at 70 °C for 20 h. The amine, **7**, was prepared by the same general procedure as **1**.

N-Cyclobutyl-*N*-*n*-propylamine, **8**, was prepared from cyclobutanecarboxylic acid (which was itself prepared from trimethylene dibromide and diethyl malonate)[22] via the Schmidt reaction.[23] To 25



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g (0.25 mol) of cyclobutanecarboxylic acid in a 1-L distillation flask were added 200 mL of $CHCl_3$, 50 mL of concentrated H_2SO_4, and 16.9 g (0.26 mol) of solid NaN_3 in such portions as to maintain the well-stirred mixture at 45 °C. After standing for 48 h at room temperature, the solution was rendered alkaline with 150 g of KOH in 300 mL of water and the cyclobutylamine was distilled into 50 mL of

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