Passage of Aryl-Tipped Alkyl Groups through Molecular Cavities: The Role of Flexibility

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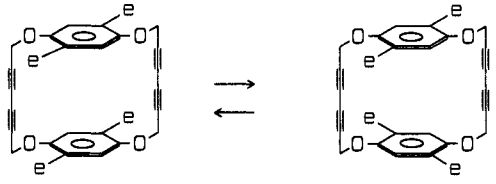
Abstract: A series of ω-phenylalkyl esters of cyclophane **2** were synthesized. Cyclophane **2** has a cavity ca. 4.5 Å by 6 Å through which the phenylalkyl groups may pass. The activation energy for passage of the phenylalkyl groups through the cyclophane's cavity varies with structure in a manner which suggests dominant importance of alkyl group flexibility. These conclusions are supported by molecular mechanics calculations.

Host–guest chemistry[1] centered around molecules having cavities of varying degrees of guest stickiness,[1f,2] hydrophobicity,[3] and size[4] is of some current interest as a basis for the construction of artificial enzymes.[5–7] The importance of the nature of a molecular cavity in this context has led us to investigate the syn–anti conformational interconversion of **2** (eq 1) as a probe cavity size in this class of molecule.[2,9a–d].

Since this series of compounds possesses rigid dioxacoctadiyne bridges ("spacers"), they may be viewed as boxed with rigid sides; syn–anti interconversion ("flipping"[10]) is of necessity a process involving passage of the ester ("e") appendage through the box.

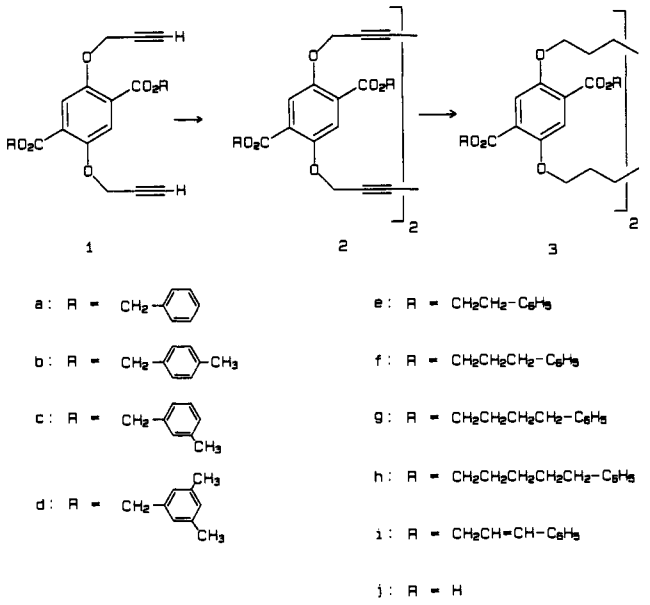


(1)

e = CO_2R

One may thus probe the size and rigidity of the interior of the box by examining the dependence of the syn ⇄ anti activation energy on the size of the alkyl part of the ester. Most simply defined, a molecular box is a molecule possessing a rigid cavity of fixed dimensions. In this sense all objects below a certain size should be accommodated equally well by the box. As the size of the object passing through the cavity of the box increases, there should be at some point a discontinuous increase in repulsive interaction between the box interior and the object: at this point the object is "too big".

Scheme I



This picture is appealing in its simplicity and, if correct, permits the design of molecules possessing cavities of well-defined size and functionality, using such mechanical design tools as molecular models and computationally simplified variants of molecular mechanics[11] programs. Our initial work[8] on the syn–anti interconversion of eq 1 supported some but not all features of this model. When e is large (i.e., neopentyl esters), flipping does not occur: the neopentyl group cannot pass through the box. When e is small (e.g., ethyl ester), flipping is rapid and the dynamics of this process may be studied by DNMR techniques. The discontinuity was found at the isobutyl ester. Here syn–anti interconversion is slow ($t_{1/2} \sim 5$ h at 25 °C) and is entropically controlled. The isobutyl ester just fits the box.

Contrary to the above model, however, is the observation[8] that as e ranges from free acid to methyl to ethyl to *n*-propyl to *n*-decyl esters, there is a monotonic increase in activation energy (enthalpy) for syn–anti interconversion of roughly 2 kcal/mol per methylene group. This observation raises some worrisome questions about the validity of the molecular box concept, in particular the idea that one can design a rigid box-shaped cavity that will just fit some predefined substrate geometry with no attendant steric repulsive effects. This strikes right at the heart of designing highly selective artificial enzymes. On the other hand, eq 1 is only an approximate probe of the rigid box concept, and these observations might be an artifact of the experimental probe employed. It was to study

(1) General references: (a) Tabushi, I.; Yamamura, K. *Top. Curr. Chem.* **1983**, *113*, 145–182. (b) Murakami, Y. *Top. Curr. Chem.* **1983**, *115*, 107–155. (c) *Top. Curr. Chem.* **1981**, *98*, 1–162. (d) *Top. Curr. Chem.* **1982**, *101*, 1–94. (e) Cram, D. J.; Cram J. M. *Acc. Chem. Res.* **1978**, *11*, 8. (f) Cram, D. J.; Trueblood, K. N. *Top. Curr. Chem.* **1981**, *98*, 43–106. (g) Vögtle, F.; Sieger, H.; Muller, W. M. *Top. Curr. Chem.* **1981**, *98*, 107–161.

(2) Miller, S. P.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* **1984**, *106*, 1492–1494.

(3) Diederick, F.; Dick, K. *Tetrahedron Lett.* **1982**, *23*, 3167. Diederick, F.; Dick, K. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 715.

(4) Marshall, J. A. *Acct. Chem. Res.* **1980**, *13*, 213–218.

(5) Breslow, R.; Doherty, J. B.; Guillot, G.; Hersh, C. L. *J. Am. Chem. Soc.* **1978**, *100*, 3227.

(6) Breslow, R.; Gzarniecky, M. F.; Emert, J.; Hamaguchi, H. *J. Am. Chem. Soc.* **1980**, *102*, 762.

(7) Cram, D. J. *Tech. Org. Chem.* **1976**, *10*, 815–873.

(8) Whitlock, B. J.; Whitlock, H. W. *J. Am. Chem. Soc.* **1983**, *105*, 838–844.

(9) (a) Jarvi, E. T.; Whitlock, H. W. *J. Am. Chem. Soc.* **1980**, *102*, 657–663. (b) Whitlock, B. J.; Jarvi, E. T.; Whitlock, H. W. *J. Org. Chem.* **1981**, *46*, 1832–1836. (c) Adams, S. P.; Whitlock, H. W. *J. Am. Chem. Soc.* **1982**, *104*, 1602–1610. (d) Jarvi, E. T.; Whitlock, H. W. *J. Am. Chem. Soc.* **1982**, *104*, 7196.

(10) Terminology: For the purpose of this paper we refer to the conformational interconversion of eq 1 as a "flip". Cyclophanes **2a–l** are referred to as "rigid", **3a–l** as flexible. The term "box" for cyclophanes of structure **2** is not strictly accurate, as their depth (through-cavity) is not simply calculated and they are, unlike most boxes, conformationally mobile. However, there is no common term for this type of *macroscopic* object other than "bag" or "pipe", both terms of which suffer from other drawbacks. We plead author's license.

(11) Burkert, U.; Allinger, N. L. *ACS Monogr. Ser.* **1982**, *No. 177*.

0002-7863/85/1507-1325$01.50/0

Table I

ester	$\Delta\nu$(H)[a]	anti/syn[b]	$t_{1/2}$	temp, °C	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, kcal/mol	$\Delta G^{\ddagger}_{298}$,[c] kcal/mol
benzyl, **2a**	32, 64	1.32	49 h	20	20.2	−15.3	24.8
			106 min	50.2			
			48 min	58			
m-methylbenzyl, **2b**	42, 62	1.29	108 h	20	19.5	−19.3	25.3
			222 min	50.8			
			36 min	72.0			
p-methylbenzyl, **2c**	45, 65	1.24	109 h	20	22.3	−10.8	25.5
			256 min	50.0			
			35 min	71.0			
3,5-dimethylbenzyl, **2d**	38, 62	*d*					>35
phenethyl, **2e**	47, 81	0.89	328 min	10.3	20.4	−8.1	22.9
			75 min	21.6			
phenylpropyl, **2f**	45, 71	1.38	311 min	−15[e]	14.1	−24.9	21.5
			81 min	0			
			62 min	0			
			8 min	22.9			
phenylbutyl, **2g**	38, 58	1.34	32 min	13.0	19.5	−7.3	21.6
			9 min	24.1			
phenylpentyl, **2h**	36, 58	1.36	3 min	<−4			18.9 (−4 °C)
cinnamyl, **2i**	61, 61	*d*					>35
isobutyl[8]	64, 67	1.69	312 min	24	14.2	−30.4	23.6
			35 min	51			
			6 min	71			

[a] Chemical shift differences $\Delta\nu_{A,B}$ of the bridge methylene protons ($OCH_{A,B}C{\equiv}C$) of the anti and syn isomers of the rigid cyclophanes **2**. The anti isomer is arbitrarily assigned the lower value. J_{AB} = 17 Hz. Data are measured at 270 MHz ($CDCl_3$). [b] The equilibrium ratio of anti/syn isomers. [c] Activation parameters are for the kinetic scheme of eq 1. [d] These isomers did not interconvert after extended heating at 51 °C. [e] This is an average value. Range is −13 °C to −20 °C.

these questions that the present work was undertaken.

Results

Preparation and Structure. Cyclophane tetraesters **2a–i** (Scheme I, "rigid" cyclophanes) were prepared by cupric acetate–pyridine oxidative cyclodimerization of the corresponding 2,5-bis(propynyloxy)terephthalate esters. Hexadecahydro derivatives **3a–f** ("flexible" cyclophanes[10]) were prepared by catalytic hydrogenation of **2a** and **2f**, respectively. In all cases the rigid cyclophanes (**2**) were isolated as a syn–anti mixture from which the less soluble isomer (assigned as syn) could be isolated by low-temperature crystallization. Except for phenethyl ester **2e**, the less soluble isomer was also the less stable one as determined by direct equilibration. This was the basis for assigning it as the syn isomer. A similar correlation was noted previously.[8] Generally the major, more soluble, isomer could not be isolated free of the other isomer. Spectra subtraction and production of a similar isomer mixture by direct equilibration of the syn isomer left little doubt, however, as to the identity of the more stable anti.

Each isomer, syn or anti, exhibited a single AB quartet (^{1}H NMR) for the bridging $OCH_2C{\equiv}C$ group. Geminal coupling constants and $\Delta\nu_{AB}$ are summarized in Table I, and are generally similar to those found for the aliphatic esters reported earlier. The more stable anti isomer consistently exhibit a smaller $\Delta\nu_{AB}$ than their syn counterparts (Table I). This apparently reflects some shielding by distal ester aryl groups. Cyclization shifts,[9a] the difference in chemical shift of the aromatic protons in **1** and **2**, were all quite small (ca. −0.07 ppm) as has been found[9a–d] to be characteristic of these rigid cyclophanes with their well-separated aromatic rings.

Flexible cyclophanes (**3**) were in each case isolated as a *single* isomer, presumably the more stable. No isomerization occurred on prolonged heating, suggesting that the syn–anti stability difference (presumably favoring the anti isomer) is magnified by the proximal relationship between the two aromatic rings. This, together with substantial upfield ArH cyclization shifts (ca. −0.4 ppm) and previous work,[9] is consistent with the flexible cyclophanes existing in a crowded collapsed conformation. Lack of highfield (>270 MHz) ^{1}H NMR capability precluded a complete unraveling of chemical shifts and coupling constants of the hexamethylene bridge of the flexible cyclophanes. It is clear, however, that these bridges enjoy well-defined conformations. For **3f** the bridge $ArOCH_2CH_2CH_2$ unit elaborated to $ArOCH_{AB}CH_{XX'}CH_2$, with J_{AB} = 8.8 Hz, $\Delta\nu_{AB}$ = 64 Hz, J_{AX} = 10 Hz, J_{BX} = 3 Hz, and others being zero. The more flexible ester side chain elaborated as $ArCOOCH_{AB}CH_{XX'}CH_2C_6H_5$ with J_{AB} = 10.7 Hz, J_{AX} = J_{BX} = 6.6 Hz, and $\Delta\nu_{AB}$ = 13 Hz.

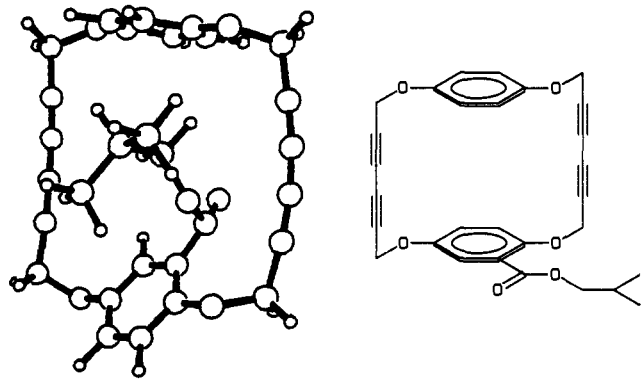
Dynamic Conformational Effects. The set of rigid cyclophanes **2a–i** permits the study of three effects of structure on the barrier to ester group flipping as defined in eq 1: the effect of chain length (benzyl (**2a**) to 5-phenylpentyl (**2h**)), the effect of methyl substitution on phenyl (**2a–d**), and the effect of conformational flexibility of the methylene chain (**2f** vs. **2i**). To summarize our results, increasing the chain length of the phenyl-tipped alkyl group leads to a monotonic *decrease* in activation energy (**2a,e–h**), the phenyl tip is remarkably tolerant of simple alkyl substitution (**2a–d**), and replacing a $(CH_2)_2$ group by a *trans*-ethenediyl group greatly increases the barrier.

None of the present series of compounds are sufficiently mobile conformationally to exhibit DNMR effects. As commented above, **2** was isolated as a ca. 60:40 mixture of anti and syn isomers from which the less stable syn could be isolated in pure form. Upon standing the syn isomer reverted to an equilibrium anti–syn mixture. This equilibrium ratio is typically ca. 60–40 and seems not to reflect transannular interaction between the ester alkyl groups. One may thus reasonably interpret equilibration rate differences in terms of differential activation rather than ground-state energies. Syn–anti flipping rates were determined by classical means, treating the system as a reversible first-order reaction. Changes of the bridge $OCH_2C{\equiv}C$ protons (from one AB quartet to two) were monitored by ^{1}H NMR, deconvoluting the overlapping Lorentzians as required. No attempt was made to apply the Forsen–Hoffman saturation-transfer[12] technique.

Kinetic data and results are summarized in Table I. Data in this table may be scrutinized with the following points in mind. Activation enthalpy and entropy values (and hence $\Delta G^{\ddagger}$ normalized to 25 °C) are not very accurate. Entropies of activation in particular can only be said to be modestly negative. Because of the experimental difficulties, we report half-lives for approach to equilibrium rather than rate constants. Anti–syn ratios were determined at >10 half-lives of equilibration and closely match those found for isolated mixtures of the two diastereomers. Neither the 3,5-dimethylbenzyl nor the cinnamyl esters underwent any

(12) Hoffman, R. A.; Forsén, S. *Prog. Nucl. Magn. Reson. Spectrosc.* **1966**, *1*, 15–204.

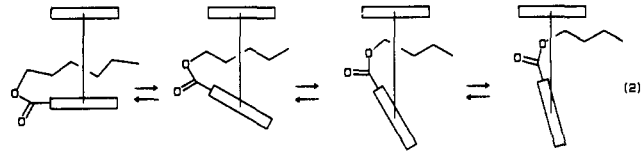
Scheme II



equilibration. The estimated $\Delta G^{\ddagger} > 35$ kcal/mol for these cyclophanes was calculated assuming less than 10% equilibration during the time periods used. Thus, the **2d** mixture isolated from the esterification of **2j** reflects kinetic rather than thermodynamic factors.

Discussion

We previously noted that in aliphatic esters of **2**, increasing the chain length of the alkyl group led to an increase in the rotational flipping barrier. We currently feel that several factors are involved here. Segmental motion of the alkyl group is probably important in barrier differences between *n*-propyl and *n*-decyl esters. A series of *n* metastable intermediates as in eq 2 should lead to an increase in the observed activation free energy of RT ln $(n + 1)$. This effect should, however, only come into play with

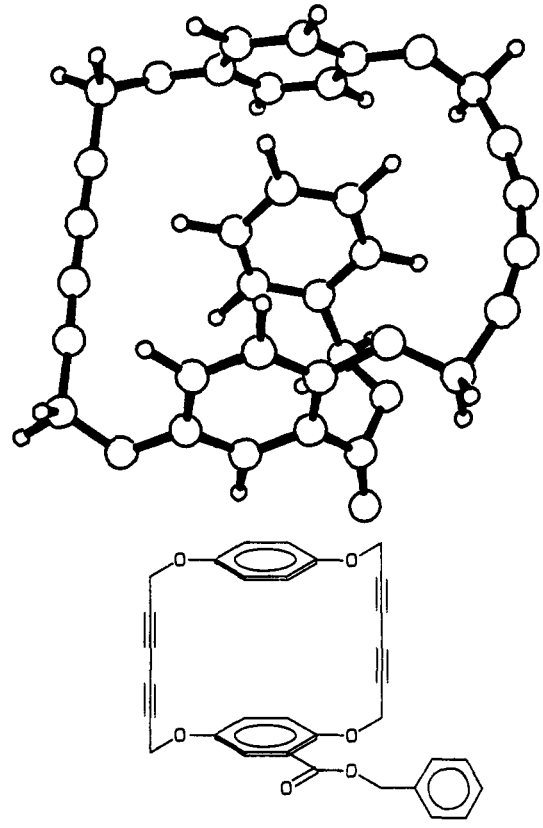


(2)

alkyl groups longer than *n*-propyl and should not account for the methyl–ethyl–propyl differences. We have carried out a series of molecular mechanics[13] simulations of these rotational processes in order to investigate these latter differences. Rather than use the dihedral angle driver contained in Allinger's MM2 program, we forced incremental conformational changes at the job control language level, using a locally generated structure editing routine.[14] Scheme II is a drawing of the simulated rotational transition state for the model isobutyl ester **4**. Molecular mechanics calculations (e.g., MM2) are "gas-phase" procedures and do not account for transient changes in solvent structure. These syn–anti interconversion barriers seem to be relatively insensitive to solvent changes,[8] so this was ignored. It should be noted, however, that solvent effects may be large for passage of *ionic* groups through these cavities (e.g., **2j** anion). This will be reported later. For the present work we use the term "transition conformation" for that one of highest energy[15] in a set of energy-minimized conformations varying in angle of rotation of one cyclophane aryl group. This can only be, of course, a crude approximation to the transition state of the flipping process.

The steric energy of the transition conformation relative to the starting conformation with coplanar aromatic rings is 18 kcal/mol for isobutyl ester **4**. This is to be compared with $\Delta H^{\ddagger} = 14.2$ kcal/mol found experimentally for the tetraisobutyl ester. As is

Scheme III



apparent from Scheme II, there are at least three interacting terms contributing to the energy of this transition conformations: (1) Steric repulsion between the cyclophane skeleton and the intracavity ester. (This is seen in the upward bowing of the top aromatic ring and the outward bowing of the proximal diyne bridge); (2) deviation of the $ArOCH_2$ from planarity, a resonance effect; and (3) substantial deformation of the benzoate ester appendage from an anti conformation coplanar with the aromatic ring. This involves both a steric and resonance component and varies with the alkyl group structure. It is this deformation that seems to account for differences between the various simple alkyl groups, an energy minimization of various conflicting structural demands. As Allinger[11] has so elegantly demonstrated, minimum energy conformations involve tradeoffs amongst a variety of factors. Here are anti alkyl group conformational, anti ester conformational, planar *o*-alkyloxybenzoate resonance, and steric ester–cyclophane repulsive interactions. These effects account for roughly one-half of the steric strain of **4**, and it is our feeling that this conceptually diffuse set of interactions accounts for most of the variation of rotational activation enthalpies in the simple alkyl esters. On the one hand, this is not very satisfying, since there is no one dominant interaction. On the other hand, though, it is consistent with the MM2 structural model and our basic box hypothesis, in that it arises from particular differences between the various alkyl ester appendages.

The above discussion affords a framework for understanding the behavior of the ω-phenylalkyl series. Here, in contrast to the simple alkyl esters, increasing the chain length leads to a smooth *decrease* in the rotational barrier. The phenylalkyl esters **2a**,**e**–**h** are all slower than the simple alkyl esters. It is passage of the phenyl group through the cavity rather than the alkyl chain that determines the overall barrier. Schemes III and IV show the simulated transition conformation of model benzyl (**5**) and phenethyl (**6**) esters, respectively. The calculated benzyl barrier shown, $\Delta H^{\ddagger} = 23$ kcal/mol, and 2-phenethyl barrier, 32 kcal/mol, are only in modest agreement with the experimental barriers of ca. 20 kcal/mol. The high barrier calculated for **6** is an artifact of the conformational driving technique used and probably can't be improved on. The importance of the chain's flexibility is

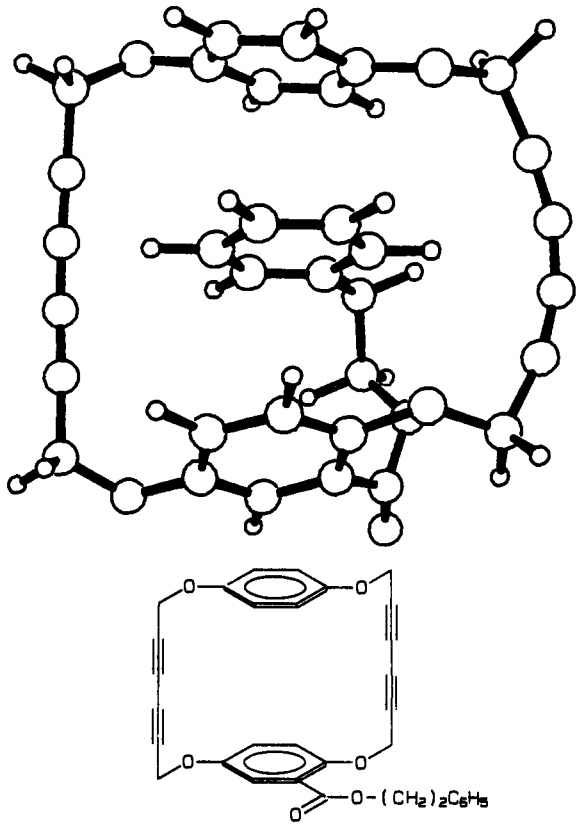
(13) A version of Allinger's MM2 program (QCPE no. 395) segmented to run on a local Harris/7 minicomputer was used.

(14) This was necessitated by slow energy minimization of these molecules together with local restrictions on job execution time.

(15) This assumes numerous random shakings and reminimization runs in order to avoid dead-end conformations. With this caveat, these simulations produce only a single (occasionally broad) maximum energy conformation.

(16) Support of this work by the National Science Foundation is gratefully acknowledged. Structural diagrams were drawn by "WIMP" (Wisconsin Interactive Molecule Processor).

Scheme IV



apparent from Scheme III. The geometrical constraints of the three-atom $COOCH_2$ connector results in a pushing of the phenyl group into the proximal diyne bridge and a leverlike movement of it into the top cyclophane phenyl group by the rotation of the bottom phenyl ring. Both of these are relieved as the chain becomes longer. It is surprising that the chain-lengthening effect is still operative at the 5-phenylpentyl ester **2h**. Meaningful simulation of this ring inversion case is beyond our computational resources. It seems clear though that passage of the phenyl group through the cavity is a surprisingly unhindered but quite constrained process. By this we mean that when the alkyl chain is sufficiently long that the phenyl group has a "fair crack" at the cavity, the barrier to its passage is minimal. This was not predicted from initial CPK molecular model studies.

The *m*- and *p*-methylbenzyl and the 3,5-dimethylbenzyl esters **2c,d** were examined in order to probe the above questions. While the *m*- and *p*-methylbenzyl esters are "larger" than benzyl, the effect is small. We interpret this as the transition conformation having enough lateral flexibility to accommodate the additional methyl group. The 3,5-dimethylbenzyl ester does not undergo this flipping process at all. The barrier here is at least 15 kcal/mol higher than for the analogous monomethylbenzyl esters. Scheme V is an idealized view of the effect of methyl substitution on the passage of a benzyl ester. While one methyl can be accommodated, two *m*-methyl groups act as horns, snagging on the diyne bridge and preventing passage of the dimethylbenzyl group through the cyclophane cavity.

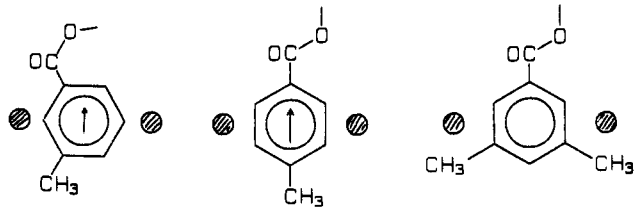
The cinnamyl ester **2i** is surprisingly resistant to conformational flipping, being similar to **2d** in this respect. Again, we see the importance of chain flexibility.

Experimental Section

Preparation of Acetylenic Esters 1a–i. Saponification (5% NaOH in methanol) of diethyl 2,5-bis(propargyloxy)terephthalate (**1**, R = Et),[8] afforded acid **1j**, mp 245 °C dec, in 83% yield. This acid could be converted to the various desired esters by the following representative procedure given for ester **1d**.

To a suspension of 1.23 g (4.5 mM) of acid **1j**, 2.4 g (9.2 mM) of triphenylphosphine, and 1.5 g (10.7 mM) of 3,5-dimethylbenzyl alcohol in 6 mL of THF was added dropwise 1.6 g (9.1 mM) of diethyl azodicarboxylate in 2 mL of THF. After stirring overnight, the ester **1d**, mp 137.5–139.5 °C (EtOAc), was obtained in 56% yield, after crystallization of the product obtained by chromatography of the reaction mixture.

Scheme V



Similarly prepared diesters **1** (R, melting point, yield given) were as follows: **1b**, *m*-methylbenzyl, 137–138.5 °C (EtOAc), 77%; **1c**, *p*-methylbenzyl, 109.5–112 °C (EtOAc–hexane), 63%; **1f**, 3-phenylpropyl, 72–73 °C (EtOAc–hexane), 68%; **1g**, 4-phenylbutyl, 85–87 °C (EtOAc–hexane), 49%; **1h**, 5-phenylpentyl, 66–68 °C (EtOAc–hexane), 81% **1i**, cinnamyl, 106–107 °C (EtOAc–hexane) (melted and resolidified at temperature <100 °C), 55%.

Bis(2-Phenylethyl) ester 1e, mp 112.5–114.5 °C (EtOAc–hexane), was obtained in 70% yield by direct esterification of acid **1j** (5% H_2SO_4 in 2-phenylethanol).

Dibenzyl ester 1a, mp 99–101 °C ($CHCl_3$–hexane), was prepared in 85% yield by refluxing a solution in benzene of the acid chloride (prepared from the potassium salt of acid **1j** and oxalyl chloride) for 20 h with benzyl alcohol.

Preparation of Cyclic Dimer 2. The acetylenic ethers **1a–i** were cyclized in 5–10% yield to the corresponding dimers **2a–i** by the cupric acetate–pyridine procedure described[8] previously. Both syn and anti isomers were identified in the purified product by their distinctive NMR spectra. Low-temperature crystallization afforded samples enriched in the less soluble isomer, generally in a high degree of purity. With the exception of the tetraphenethyl ester **2e**, the less soluble isomer corresponded to the minor isomer observed in the equilibrated product.

Tetrabenzyl ester 2a, mp 182–183.5 °C (EtOAc–hexane), the minor component of the mixture derived from **1a**, had δ 7.515 (1 H, s, Ar′*H*), 7.3–7.4 (5 H, m, Ar*H*), 5.315 (1 H, d, J = 12.5 Hz, $COOCH_A$), 5.209 (1 H, d, J = 12.5 Hz, $COOCH_B$), 4.937 (1 H, d, J = 17 Hz, $CH_AC{\equiv}C$), and 4.699 (1 H, d, J = 17 Hz, $CH_BC{\equiv}C$). The more soluble isomer of **2a** had absorptions at δ 7.532 (1 H, s, Ar*H*), 5.266 (1 H, d, J = 12 Hz, $COOCH_A$), 5.163 (1 H, d, J = 12 Hz, $COOCH_B$), 4.911 (1 H, d, J = 17 Hz, $CH_AC{\equiv}C$), and 4.771 (1 H, d, J = 17 Hz, $CH_BC{\equiv}C$).

Tetrakis(*m*-methylbenzyl) ester 2b, mp 197 °C dec (EtOAc), obtained as a mixture enriched in the less soluble isomer had δ 7.515 and 7.527 (0.7 H, 0.3 H, s, Ar′H), 7.1–7.5 (5 H, m, Ar*H*), 5.277 and 5.290 (0.7 H, 0.3 H, d, J = 12.5 Hz, $COOCH_A$), 5.166 and 5.197 (0.7 H, 0.3 H, d, J = 12.5 Hz, $COOCH_B$), 4.943 and 4.915 (0.7 H, 0.3 H, d, J = 17 Hz, $CH_AC{\equiv}C$), 4.711 and 4.757 (0.7 H, 0.3 H, d, J = 17 Hz, $CH_BC{\equiv}C$), 2.357 (3 H, s, $ArCH_3$).

Tetrakis(*p*-methylbenzyl) ester 2c, mp 216 °C dec (EtOAc), the minor component of the mixture, had δ 7.493 (1 H, s, Ar′*H*), 7.279 (2 H, d, J = 8 Hz, ArH_A), 7.158 (2 H, d, J = 8 Hz, ArH_B), 5.279 (1 H, d, J = 12.5 Hz, $COOCH_A$), 5.151 (1 H, d, J = 12.5 Hz, $COOCH_B$), 4.926 (1 H, d, J = 17 Hz, $CH_AC{\equiv}C$), 4.687 (1 H, d, J = 17 Hz, $CH_BC{\equiv}C$), 2.348 (3 H, s, CH_3). The more soluble isomer of **2c** had δ 7.508 (1 H, s, Ar′*H*), 7.293 (2 H, d, J = 8 Hz, ArH_A), 7.167 (2 H, d, J = 8 Hz, ArH_B), 5.275 (1 H, d, J = 12 Hz, $COOCH_A$), 5.174 (1 H, d, J = 12 Hz, $COOCH_B$), 4.909 (1 H, d, J = 17 Hz, $CH_AC{\equiv}C$), 4.747 (1 H, d, J = 17 Hz, $CH_BC{\equiv}C$), 2.348 (3 H, s, CH_3).

Tetrakis(3,5-dimethylbenzyl) ester 2d, mp 228 °C dec, obtained as a mixture of isomers, had δ 7.532 and 7.515 (0.6 H, 0.4 H, s, Ar′*H*), 7.029 (1 H, s, Ar*H*), 7.001 (1 H, s, Ar*H*), 6.951 (1 H, s, Ar*H*), 5.266 and 5.232 (0.6 H, 0.4 H, d, J = 12 Hz, $COOCH_A$), 5.163 and 5.120 (0.6 H, 0.4 H, d, J = 12 Hz, $COOCH_B$), 4.911 and 4.945 (0.6 H, 0.4 H, d, J = 17 Hz, $CH_AC{\equiv}C$), 4.711 and 4.716 (0.6 H, 0.4 H, d, J = 17 Hz, $CH_BC{\equiv}C$), 2.315 (6 H, s, $ArCH_3$).

Tetrakis(2-phenylethyl) ester 2e, mp 202–204.5 °C (EtOAc), the major component of the mixture, had δ 7.2–7.4 (6 H, m, Ar*H* and Ar′*H*), 4.907 (1 H, d, J = 17 Hz, $CH_AC{\equiv}C$), 4.603 (1 H, d, J = 17 Hz, $CH_BC{\equiv}C$), 4.4 (2 H, m, OCH_2), 2.9 (2 H, m, CH_2Ar). The more soluble isomer of **2e** displayed an AB quartet ($CH_{A,B}C{\equiv}C$) centered at δ 4.76 (J_{AB} = 17 Hz, $\Delta\nu_{AB}$ = 47 Hz).

Tetrakis(3-phenylpropyl) ester 2f, mp 136–139.5 °C (EtOAc–hexane), the minor component, had δ 7.478 (1 H, s, Ar′*H*), 7.1–7.3 (5 H, m, Ar*H*), 4.933 (1 H, d, J = 17 Hz, $CH_AC{\equiv}C$), 4.670 (1 H, d, J = 17 Hz, $CH_BC{\equiv}C$), 4.3 (2 H, m, OCH_2), 2.76 (2 H, m, CH_2Ar), 2.05 (2 H, m, $CH_2CH_2CH_2$). The more soluble isomer showed an AB quartet ($CH_{A,B}C{\equiv}C$) centered at δ 4.82 (J_{AB} = 17 Hz, $\Delta\nu_{AB}$ = 48 Hz).

Tetrakis(4-phenylbutyl) ester 2g, mp 152.5–155 °C, (EtOAc), the minor component, had δ 7.463 (1 H, s, Ar′*H*), 7.18–7.31 (5 H, m, Ar*H*), 4.876 (1 H, d, *J* = 17 Hz, CH_AC≡C), 4.662 (1 H, d, *J* = 17 Hz, CH_BC≡C), 4.3 (2 H, m, COOCH_2), 2.66 (2 H, m, CH_2Ar), 1.76 (4 H, m, CH_2). The more soluble isomer of **2g** displayed an AB quartet (C$H_{A,B}$C≡C) centered at δ 4.79 (J_{AB} = 17 Hz, $\Delta\nu_{AB}$ = 38 Hz).

The less soluble isomer of tetrakis(5-phenylpentyl) ester **2h**, mp 138.5–9.5 °C (acetone), equilibrated very rapidly to a mixture of syn and anti isomers at 25 °C with distinctive aromatic singlet absorptions at δ 7.441 and 7.449 and two AB quartets (C$H_{A,B}$C≡C, J_{AB} = 17 Hz) centered at δ 4.708 ($\Delta\nu_{AB}$ = 58 Hz), and δ 4.730 ($\Delta\nu_{AB}$ = 36 Hz). When dissolved at a temperature lower than −14 °C, the spectrum appeared to be primarily that of a single compound corresponding to the minor component of the mixture, with δ 7.446 (1 H, s, Ar*H*′), 7.19–7933 (5 H, m, Ar*H*), 4.821 (1 H, d, *J* = 17 Hz, CH_AC≡C), 4.607 (1 H, d, *J* = 16.9 Hz, CH_BC≡C), 4.29 (2 H, m, COOCH_2), 2.64 (2 H, t, *J* = 7.7 Hz, CH_2Ar), 1.46–1.74 (6 H, m, CH_2).

Both isomers of tetracinnamyl ester **2i**, could be isolated by fractional crystallization. The less soluble isomer, mp 166.5–170 °C (EtOAc–hexane), had δ 7.498 (1 H, s, Ar′*H*), 7.2–7.5 (5 H, m, Ar*H*), 6.756 (1 H, d, *J* = 16 Hz, CH=C*H*Ar), 6.400 (1 H, dt, *J* = 16, 6.3 Hz, CH_2CH=CH), 4.991 (1 H, ddt, *J* = 13, 6.3, 1.2 Hz, COOCH_ACH=CH), 4.931 (1 H, ddt, *J* = 13,6.3, 1.2 Hz, COOCH_BCH=CH), 4.876 (1 H, d, *J* = 17 Hz, CH_AC≡C), 4.650 (1 H, d, *J* = 17 Hz, CH_BC≡C). The more soluble isomer of **2i**, decomposition without melting above 200 °C, had δ 7.527 (1 H, s, Ar′*H*), 7.2–7.5 (5 H, m, Ar*H*), 6.738 (1 H, d, *J* = 16 Hz, CH=C*H*Ar), 6.371 (1 H, dt, *J* = 16, 6.3 Hz, CH_2CH=CH), 4.991 (1 H, ddt, *J* = 12.5, 6.3, 1.2 Hz, CH_ACH=CH), 4.888 (1 H, ddt, *J* = 12.5, 6.3, 1.2 Hz, CH_BCH=CH), 4.913 (1 H, d, *J* = 17 Hz, CH_AC≡C), 4.689 (1 H, d, *J* = 17 Hz, CH_BC≡C).

Hexadecahydro Derivatives 3. Tetraacid **3j** was obtained by hydrolysis of the tetraethyl ester (**3**, R = Et),[8] using excess lithium hydroxide in 50% aqueous THF. A suspension of 104 mg (0.19 mM) of **3j**, 197 mg (0.75 mM) of triphenylphosphine, and 111 mg (1.0 mM) of benzyl alcohol in THF was treated with 129 mg (0.74 mM) of diethyl azodicarboxylate. Crystallization of the crude product obtained after chromatography afforded 59 mg of tetrabenzyl ester **3a**, mp 159.5–162 °C (EtOAc-hexane), in 54% yield: H NMR δ 7.3–7.5 (5 H, m, Ar*H*), 6.852 (1 H, s, Ar′*H*), 5.407 (1 H, d, *J* = 12 Hz, CH_AAr), 5.139 (1 H, d, *J* = 12 Hz, CH_BAr), 3.4–3.5 (2 H, m, OCH_2CH_2), 1.7 and 1.3 (2 H, m, OCH$_2$CH_2CH$_2$), 1.0 (2 H, m, OCH$_2$CH$_2$CH_2).

Tetraphenylpropyl ester 3f, was obtained in low yield as a colorless oil by a similar procedure: H NMR δ 7.1–7.3 (5 H, m, Ar*H*), 7.038 (1 H, s, Ar′*H*), 4.291 (1 H, dt, *J* = 11, 7 Hz, COOCH_A), 4.242 (1 H, dt. *J* = 11, 7 Hz, COOCH_B), 4.1 and 3.9 (2 H, m, Ar′OCH_2), 2.731 (2 H, t, *J* = 8 Hz, CH_2Ar), 2.0–2.1 (2 H, m, CH$_2$CH_2CH$_2$Ar), 1.4–2.0 (4 H, unassigned).

Interconversion of Syn–Anti Isomers. Except for 2-phenethyl ester **2e**, the less soluble isomer isolated from the cupric acetate cyclizations was the less stable isomer as determined by direct equilibration. The rate of equilibration was determined by observing changes in its proton spectra. For those interconversions that were inconveniently rapid at room temperature (**2e–h**), rates were determined at lower temperatures in a Bruker WH-270 spectrometer equipped with a liquid nitrogen cooled variable temperature probe. The probe temperature was determined (calibrated thermocouple) before and after a series of spectra. The temperature deviation during the time of a kinetic run was generally less than 0.5 °C. Rates of those interconversions that were slow at room temperature (**2a–d**, **i**) were determined by immersing a sealed NMR tube in a constant temperature bath and removing the sample periodically for proton spectra at 22 °C. Peak areas were determined by digital integration with the aid of an overlapping Lorentzian deconvolution program as appropriate. Peak areas were insensitive to variations in the spectrometer's pulse delay. Rate constants and the corresponding half-lives were extracted by treating the interconversions as reversible first-order processes (Table I).

Photochemistry of 1-Azatriptycene

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Abstract: 1-Azatriptycene (**1**) underwent photorearrangement in basic methanol with a quantum efficiency of 0.57 to give 4*H*-azepine derivative (**4**) as the main product. In the presence of TCNE, the Diels–Alder adduct (**5**) of the 1*H*-azepine intermediate was obtained. In acetic acid, a further photoreaction of the initially formed indenoacridine (**9**) gave the dihydromethyl derivative (**10**). The structures were established by spectral data. The 4*H*-azepine **4** was converted to the azepinium salt (**6**) by hydride abstraction. The observed photochemistry is interpreted in terms of the formation of 2-(9-fluorenyl)phenylnitrene (**3**). When 2-(9-fluorenyl)phenyl azide (**2**) was photolyzed with the purpose of generating **3** independently, the yields of **4**, **5**, and **9** were lower and some additional products were obtained. The difference in reactivity was more evident in the reactions of **1** and **2** in low-temperature matrices as monitored by UV absorptions and is interpreted in terms of the different conformation of **3**: the ap conformation of the initially formed **3a** from **1** and the sp form from **2**. The crossover of the photoproducts is presumably due to conformational interconversion from **3b** to **3a** through intermediate **17** formed by insertion of the phenylnitrenic center into its own ring. Irradiation of **1** and **2** at 4.2 K in methylcyclohexane glass in an ESR cavity showed a strong signal due to the *X*, *Y* transition of triplet **3**. The resonance field was again slightly different, corroborating the different conformations **3a** and **3b** from **1** and **2**, respectively. The ESR spectrum obtained by irradiation of **1** did not contain any signal due to a phenylcarbene but a set of signals due to a triplet species with the smaller D parameter. The latter was assigned to diradical **18** formed by the C–N bond cleavage as a side reaction. Diversion from a typical di-π-methane rearrangement route and the bridging regioselectivity are discussed. Lastly, the fluorescence and $S_n \leftarrow S_1$ absorption spectra of triptycenes were scrutinized to show that the fluorescent state is different from the Franck–Condon state and more like the excimer of xylenes.

Intramolecular interaction between benzene moieties plays an important role in the photophysics of aromatic polychromophoric systems in the photoexcited state.[1] One very well explored case is [2.2]paracyclophane, in which two benzene rings have a parallel orientation with a maximum overlap of the p orbitals and where an intramolecular charge-transfer band is observed in its absorption spectrum.[1c] The photolysis of the cyclophane in alcohols gives photosolvolytic products through the singlet state with a charge-transfer character, together with 1,2-diphenylethane derivatives through the triplet excited state.[2a] The reactivity can

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