H-13), 6.25 (s, 1 H, H-1), 6.63 (s, 1 H, H-4), 7.29 (d, J = 8.1 Hz, 1 H, H-12), 7.40 (d, J = 8.1 Hz, 1 H, H-11); mass spectrum m/e 427 (M^+, 24), 384 (28), 369 (12), 368 (44), 367 (56), 354 (57), 352 (100), 340 (28), 339 (30), 338 (43), 324 (37), 294 (22); CD $\Delta\epsilon_{nm}$ -6.53_{217}, $+3.86_{239}$, -2.75_{270}, -2.36_{292}, -3.38_{328}, $+1.49_{392}$; R_f 0.49.

23: $C_{25}H_{27}O_8N$; amorphous; λ_{max} 235 (sh), 292, and 372 nm (log ϵ 4.24, 3.69, and 3.27); ν_{max} 1740, 1730, and 1695 cm^{-1}; NMR δ 2.09 (s, 3 H, $COCH_3$), 2.15 (s, 3 H, $COCH_3$), 2.44 (s, 3 H, N-CH_3), 3.54 (s, 3 H, 9-OCH_3), 3.73 (s, 3 H, 2-OCH_3), 3.84 (s, 3 H, 3-OCH_3), 5.73 (s, 1 H, H-13), 6.12 (s, 1 H, H-1), 6.57 (s, 1 H, H-4), 6.55 (d, J = 10.0 Hz, 1 H, H-12), 7.22 (d, J = 10.0 Hz, 1 H, H-11); mass spectrum m/e 469 (M^+, 1.4), 442 (2), 425 (2), 383 (3), 367 (4), 352 (6), 308 (1), 278 (3), 221 (5), 150 (9); R_f 0.67.

2,3-(Methylenedioxy)-8-keto-9-methoxy-10-hydroxy-*syn*-13-hydroxyspirobenzylisoquinoline (24). Compound **20** (12 mg, 0.03 mmol) was dissolved in 5% aqueous hydrogen chloride (1 mL) and kept at room temperature overnight. Workup including TLC gave **24** (7.8 mg, 72%).

24: $C_{20}H_{19}O_6N$; amorphous; λ_{max} 227, 265, 293, and 335 nm (log ϵ 4.52, 3.98, 3.67, and 3.40); NMR δ 2.25 (s, 3 H, N-CH_3), 4.12 (s, 3 H, 9-OCH_3), 4.93 (s, 1 H, H-13), 5.88 and 5.89 (q, J_{gem} = 1.2 Hz, 2 H, OCH_2O), 6.13 (s, 1 H, H-1), 6.59 (s, 1 H, H-4), 7.38 (s, 2 H, H-11 and H-12); mass spectrum m/e 369 (M^+, 30), 354 (35), 336 (10), 324 (39), 308 (22), 204 (25), 190 (100), 149 (16); CD $\Delta\epsilon_{nm}$ -5.13_{267}, -5.26_{331}, $+2.10_{380}$; R_f 0.52.

2,3,9-Trimethoxy-8-keto-10-hydroxy-*syn*-13-hydroxyspirobenzylisoquinoline (25). Compound **21** (8.5 mg, 0.03 mmol) was dissolved in 5% aqueous hydrogen chloride (1 mL) and kept at room temperature overnight. Workup including TLC supplied **25** (5.9 mg, 77%).

25: $C_{21}H_{23}O_6N$; amorphous; λ_{max} 225 (sh), 265, 293, and 336 nm (log ϵ 4.49, 4.02, 3.51, and 3.42); ν_{max} 1700 and 3500 cm^{-1}; NMR δ 2.41 (s, 3 H, N-CH_3), 3.60 (s, 3 H, 2-OCH_3), 3.85 (s, 3 H, 3-OCH_3), 4.09 (s, 3 H, 9-OCH_3), 5.08 (s, 1 H, H-13), 6.07 (s, 1 H, H-1), 6.62 (s, 1 H, H-4), 7.41 (s, 2 H, H-11 + H-12); mass spectrum m/e 385 (M^+, 54), 370 (58), 354 (10), 342 (16), 340 (38), 324 (18), 310 (11), 220 (35), 206 (100), 190 (24); CD $\Delta\epsilon_{nm}$ $+1.79_{237}$, -5.22_{270}, -6.60_{332}, $+1.79_{385}$; R_f 0.40.

2,3,9-Trimethoxy-8-keto-10-hydroxy-*syn*-13-methoxyspirobenzylisoquinoline (26). Compound **21** (13 mg, 0.03 mmol) dissolved in dry methanol (6 mL) was refluxed in the presence of potassium *tert*-butoxide (10 mg, 0.09 mmol) for 8 h. The reaction mixture was cooled and neutralized with methanolic hydrogen chloride. The solvent was removed in vacuo and the residue extracted with chloroform. The organic layer was dried, evaporated, and purified by TLC to supply **26** (5.5 mg, 45%) and **28** (1.2 mg, 18%).

26: $C_{22}H_{25}O_6N$; amorphous; λ_{max} 225 (sh), 260, 291, and 334 nm (log ϵ 4.47, 4.00, 3.53, and 3.41); NMR δ 2.31 (s, 3 H, N-CH_3), 3.51 (s, 3 H, 13-OCH_3), 3.64 (s, 3 H, 2-OCH_3), 3.86 (s, 3 H, 3-OCH_3), 4.92 (s, 1 H, H-13), 6.09 (s, 1 H, H-1), 6.63 (s, 1 H, H-4), 7.32 (d, J = 8.0 Hz, 1 H, H-12), 7.35 (d, J = 8.0 Hz, 1 H, H-11); mass spectrum m/e 399 (M^+, 49), 384 (38), 367 (20), 353 (27), 352 (37), 340 (100), 325 (23), 310 (21), 294 (14), 265 (10), 220 (10), 206 (28); CD $\Delta\epsilon_{nm}$ $+2.59_{230}$, -3.11_{267}, -5.49_{330}, $+1.97_{395}$; R_f 0.52.

2,3-Dimethoxy-8-keto-9-ethoxy-10-hydroxy-*syn*-13-ethoxyspirobenzylisoquinoline (27). Compound **21** (17 mg, 0.4 mmol) dissolved in dry ethanol (8 mL) was refluxed in the presence of potassium *tert*-butoxide (13.5 mg, 0.12 mmol) for 8 h. After workup, including purification by TLC, **27** (3.6 mg, 21.2%) and **28** (3.2 mg, 36%) were obtained.

27: $C_{24}H_{29}O_6N$; amorphous; λ_{max} 221, 256, 295 (sh), and 330 nm (log ϵ 4.35, 3.96, and 3.41); NMR δ 1.21 (t, J = 7.0 Hz, 3 H, CH_3), 1.40 (t, J = 7.0 Hz, 3 H, CH_3), 2.35 (s, 3 H, N-CH_3), 3.62 (s, 3 H, 2-OCH_3), 3.86 (s, 3 H, 3-OCH_3), 4.28-4.39 (m, 4 H, 2 × CH_2), 5.00 (s, 1 H, H-13), 6.06 (s, 1 H, H-1), 6.63 (s, 1 H, H-4), 7.32 (d, J = 8.2 Hz, 1 H, H-12), 7.37 (d, J = 8.2 Hz, 1 H, H-11); mass spectrum m/e 427 (M^+, 6.4), 397 (9.4), 354 (17), 322 (3), 207 (29), 169 (60); CD $\Delta\epsilon_{nm}$ $+1.50_{228}$, -3.64_{269}, -6.26_{330}, $+1.01_{395}$; R_f 0.50.

28: $C_{12}H_{15}O_3N$; amorphous; NMR δ 3.14 (s, 3 H, N-CH_3), 3.92 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 6.64 (s, 1 H, H-5), 7.61 (s, 1 H, H-8); mass spectrum m/e 221 (M^+, 65), 219 (17), 178 (81), 150 (100), 135 (18), 107 (11); R_f 0.51.

Acknowledgment. This research was supported by grant No. NS 15437 awarded by The National Institute of Neurological and Communicative Disorders and Stroke, PHS, DHHS. G.B. is the recipient of an IREX fellowship.

Registry No. **1**, 20411-03-4; **2**, 31225-67-9; **3**, 28230-70-8; **6**, 80781-56-2; **7**, 80781-57-3; **8**, 80781-58-4; **9**, 80781-59-5; **10**, 80781-60-8; **12**, 80781-61-9; **13**, 80781-62-0; **14**, 80781-63-1; **15**, 80781-64-2; **16**, 80781-65-3; **20**, 80781-66-4; **21**, 80781-67-5; **22**, 80781-68-6; **23**, 80781-69-7; **24**, 80781-70-0; **25**, 80781-71-1; **26**, 80781-72-2; **27**, 80781-73-3; **28**, 6514-05-2.

Synthesis, Conformation, and Complexation Behavior of 2,9,18,25-Tetraoxa-33,34,35,36-tetrakis(acyloxymethyl)[8.8]-(1,4)naphthalenophanes[1]

Steven P. Adams and Howard W. Whitlock*

Contribution from the Samuel M. McElvain Laboratories of Organic Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received June 12, 1981*

Abstract: Title compounds with acetate, propionate, phenylacetate, *p*-bromophenylacetate, and *N,N*-dimethylglycyl acyl groups were synthesized with dioxaocta-3,5-diyne and with dioxaoctyl bridges (**7** and **8**), rigid molecules containing a hydrophobic pocket. Dynamic NMR spectroscopy revealed the presence of a conformational equilibrium between limiting syn and anti conformations. A water-soluble phane was observed by fluorescence and NMR spectroscopy to form inclusion complexes with 8-anilino-1-naphthalenesulfonic acid and with 2-naphthalenesulfonic acid having an association constant, in the case of 1,8-ANS, of 590 M^{-1}.

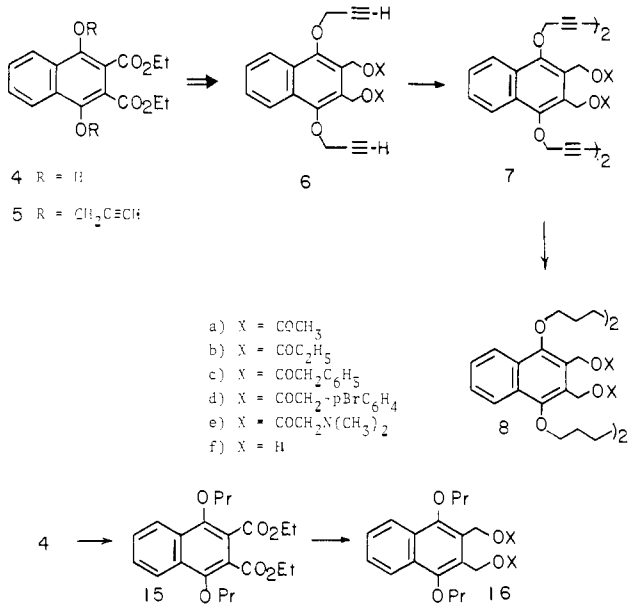
Introduction

Interest in water-soluble molecules containing a hydrophobic pocket as models of biological complexation has prompted us to prepare and study a number of [8.8](1,4)benzophanes[2] and [8.8](2,6)- and [8.8](1,4)naphthalenophanes.[3,4] Our results to date indicate that dioxaocta-3,5-diyne bridges as in **1** are effective in enforcing a rigid conformation in which the rings define a hydrophobic cavity ca. 3.6 Å (ring-ring distance of 7.2 Å) wide. When the diyne bridges are hydrogenated, NMR cyclization shifts (Δ_{cyc})[2,5] suggest that the rings collapse on each other with con-

(1) Abstracted in part from the Ph.D. Thesis of Steven Paul Adams, University of Wisconsin—Madison, 1980.
(2) E. T. Jarvi and H. W. Whitlock, *J. Am. Chem. Soc.*, **102**, 657 (1980).
(3) (a) B. J. Whitlock, E. T. Jarvi, and H. W. Whitlock, *J. Org. Chem.*, **46**, 1832 (1981); (b) E. T. Jarvi, H. W. Whitlock.
(4) S. P. Adams and H. W. Whitlock, *J. Org. Chem.*, in press.

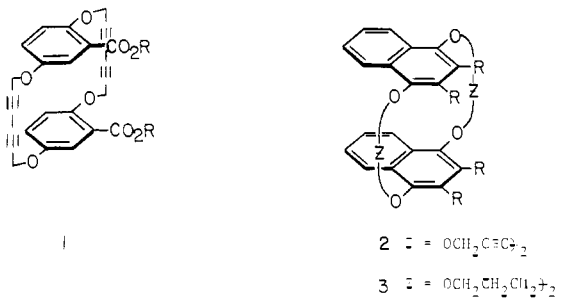
0002-7863/82/1504-1602$01.25/0

Scheme I



sequent shielding of the aromatic protons.

In organic solvents, the macrocyclic naphthalenophanes are observed to form charge-transfer complexes of the classical π-stacking variety.[4] In aqueous solution the simple benzophane **1**



preferred to flatten, forming a π-stacking rather than an inclusion complex with 2-naphthylmethyltriethylammonium chloride. This flattening is prevented in the [8.8](2,6)naphthalenophane series by steric requirements and complexation is of the inclusion type.[3] A second attempt at preventing the flat conformation was to fuse a benzo ring onto **1** giving **2** (R = H); however, the hydrogenated molecule **3** (R = H) exists in a "face-edge" conformation.[4] This work describes the preparation, conformation, and complexation behavior of substituted analogues of **2** and **3** (R = CH_2OCR).

Synthesis

As described in an earlier paper,[4] the stepwise synthesis of (1,4)naphthalenophanes substituted in the C_2 or $C_{2,3}$ positions, successful in our previous experience,[2,3] was foiled by the extreme lability of **2** (R = H) toward electrophilic and nucleophilic reagents; however, the direct cyclodimerization of appropriately substituted precursors has provided the desired products. Earlier we showed that 1,4-bis(propynyloxy)naphthalene[4] and 2,6-bis(propynyloxy)naphthalene[3a] cyclodimerized to afford the desired (but very insoluble) cyclodimers in 35–40% yield. Appropriate cyclodimerization substrates **6** (Scheme I) were prepared from **4**[4,24] by alkylation with propargyl bromide in the presence of potassium carbonate followed by careful reduction with lithium aluminum hydride and acylation with an appropriate anhydride or acid chloride. Cyclodimerization of **6a–d** using cupric acetate in pyridine at 45 °C afforded **7a–d** in ca. 1% yield. The products were isolated by chromatography and crystallization and characterized, along with their hydrogenation products **8**, by a combination of NMR and mass spectrometry, and elemental analysis. The low yields are attributed to increased steric encumbrance by the $C_{2,3}$ functionality and to the lability of the acyloxymethyl substituents. The potentially water-soluble phane **7e** could not be obtained by direct cyclodimerization but was available from the tetraacetate **7a** by methanolysis using potassium carbonate in 1:1 methanol/acetone followed by acylation of the resulting **7f** with *N,N*-dimethylglycine hydrochloride via Hassner's procedure.[6] Hydrogenation in the presence of platinum or palladium catalysts resulted in extensive hydrogenolysis, but Wilkinson's catalyst[7] gave acceptable results affording **8a–d** in fair yield. Again, **8e** was prepared from **8a** by methanolysis followed by acylation with *N,N*-dimethylglycine. Dipropyl ether models for the hydrogenated naphthalenophanes were prepared from **4** as shown in Scheme I.

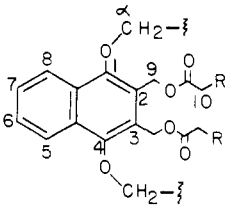
Table I. Cyclization Shifts (Δ_{cyc}) for Naked (2 and 3, R = H) and Acyloxymethyl-Substituted (7 and 8a-f) Cyclophanes[a]

phane	$H_{5,8}$	$H_{6,7}$	H_9	H_{10}	bridge[b]
2 (R = H)	0.05	0.01	0.09[c]	(H2,3)	r
3 (R = H)	0.10	0.04	0.83[c]	(H2,3)	f
7f (X = H)	0.03	−0.03	0.12		r
8f (X = H)	0.20	0.17	0.17		f
7a (X = $COCH_3$)	0.20	0.02	0.02	0.49	r
8a (X = $COCH_3$)	0.19	0.15	0.23	0.07	f
7b (X = COC_2H_5)	0.19	0	0	0.44	r
8b (X = COC_2H_5)	0.20	0.17	0.21	0.08	f
7c (X = $COCH_2C_6H_5$)	0.26	0.13	0	0.10	r
8c (X = $COCH_2C_6H_5$)	0.26	0.21	0.24	0.05	f
7d (X = $COCH_2C_6H_4Br$)	0.36	0.09	−0.08	0.50	r
8d (X = $COCH_2C_6H_4Br$)	0.26	0.23	0.22	0.05	f
7e (X = glycyl)	0.17	0.01	0.03	0.33	r
8e (X = glycyl)	0.21	0.16	0.21	0.04	f

[a] Positive Δ_{cyc} values correspond to upfield shifts on cyclization. [b] "r" indicates the rigid 2,4-hexadiynyl bridge; "f" the floppy 1,6-hexamethylene bridge. [c] For H_2 and H_3 protons.

Conformations

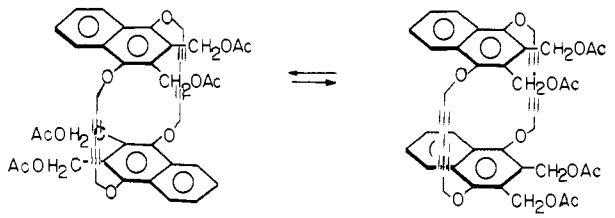
To facilitate discussion, the numbering convention depicted below will be followed throughout. As before, we define the



cyclization shift, Δ_{cyc}, of a proton as the chemical shift difference between its signal in the cyclophane and the corresponding proton in an uncyclized model. A positive Δ_{cyc} corresponds to movement upfield on cyclization. The Δ_{cyc} values for the rigid phanes **7** and for the flexible phanes **8** are compiled in Table I. As is apparent, the diyne bridges are effective in isolating the rings so that they do not interact. The aromatic Δ_{cyc}'s are very small while those for the appended functional groups at $C_{2,3}$ increase with distance from the aromatic ring to which they are bound, indicating that they span the distance imposed by the rigid bridges to "see" the opposing transannular ring. These same general trends, very small Δ_{cyc} values, are also noted for other rigid cyclophanes, namely, the analogous benzenophane[2] [8.8]naphthalenophanes in the (2,6) series[3] and in the (1,4) series[4] as well as for [12.12]paracyclophane-6,8,22,24-tetrayne.[8] The fused benzo ring gives rise to a possible conformational equilibrium between limiting syn and anti conformations. The fact that the functional groups in **7a–e** are strongly shielded suggests an anti conformation where the

(5) Δ_{cyc} is defined as the chemical shift of a proton in a given cyclophane minus the chemical shift of the corresponding proton in an appropriate "half molecule" model compound. Negative values are upfield shifts.

(6) A. Hassner and V. Alexanian, *Tetrahedron Lett.*, 4475 (1978).
(7) Tris(triphenylphosphine)rhodium(I) chloride: A. J. Birch and D. H. Williamson, *Org. React.*, **24**, 1 (1976).
(8) T. Matsuoka, T. Negi, T. Otsube, Y. Sakata, and S. Misumi, *Bull. Chem. Soc. Jpn.*, **45**, 1825 (1972).



transannular ring is favorably disposed for shielding. Additionally, dynamic NMR evidence, presented below, supports the presence of the anti conformation.

The flexibly bridged phanes **8a–e**, following previously established precedent,[2-4] have moderate Δ_{cyc} values for the aromatic hydrogens of 0.2 to 0.4 ppm resulting from collapse of the rings upon each other as the rigid constraint as the diyne bridge is removed.

Dynamic NMR Results

Rigid Naphthalenophanes. Variable-temperature proton NMR spectra of **7a–c** reveal that conformational interconversion occurs at a rate accessible by the DNMR technique. The room-temperature NMR of **7a** (Figure 1) in $CDCl_3$ had broad peaks for H_9 and H_α which sharpened upon warming, but more interestingly, upon cooling, each singlet went through its coalescence points (H_9 = +7 °C, H_α = +12 °C) and eventually split into a pair of AB doublets of equal intensity. The results for the propionate tetraester **7b** were essentially the same with coalescence points of H_9 = +6 °C and H_α = +17 °C. Because of poor solubility it was necessary to obtain the dynamic data for the phenylacetate cyclophane **7c** in pyridine solvent. That the results obtained could be correlated with **7a** and **7b** in chloroform followed from the dynamic results for **7a** obtained in pyridine. Though the distance $\Delta\delta$ between the "frozen" (−45 °C) AB doublets (H_9 = 40 Hz, H_α = 178 Hz) in **7a** (pyridine solvent) varied slightly from the results in chloroform (H_9 = 85 Hz, H_α = 130 Hz), the coalescence points and $\Delta G_c^\ddagger$ (12.3 kcal) were virtually the same in the two solvents.

Variable-temperature spectra of **7c** show striking similarities with those of **7a** and **7b**. The coalescence of the AB quartets of **7c** appears at about +10 °C. An interesting difference in the DNMR spectra of **7c** is notable at low temperature (Figure 2). The high-field doublet in the AB patterns for the H_α bridge protons and for the phenylacetate methylene protons broaden and collapse at ca. −65 °C (1:1 acetone/pyridine) while the downfield doublets remain sharp. The high-field signals are most logically assigned to those protons close to the rigid diyne bridge and/or the aromatic rings of the phenyl acetate groups, so the second dynamic process, reflected in their broadening, probably results from some, as yet unclarified, hindered motion involving the phenyl acetates and the transannular ring. The model compound **6c** does not exhibit any dynamic behavior to −80 °C, indicating that the transannular ring in **7c** as an integral component of the observed exchange.

In all of the dynamic spectra examined, no evidence has been seen for the syn isomer accumulating to any extent. If it were present to an extent greater than 5–10% one would expect the environments for the ester groups to be sufficiently different to be able to detect both syn and anti forms at low temperature. Upon closer examination of the spectra for cyclophane **7a** it was noted that the acetate methyl group broadened as the temperature was lowered, achieving a maximum width of 8.9 Hz at −13 °C after which continued cooling caused the signal to resharpen (see Figure 3). This phenomenon, "hidden partner exchange", is precisely that predicted for the exchange of two singlets between different environments where one environment is present to a lesser extent than the other. The theory of this exchange has been developed by Anet[9] and Sorensen[10] based on Gutowsky and Holm's treatment[11] of exchanging singlets. Representative examples are available in the work of Mislow[12] and Anet.[13]

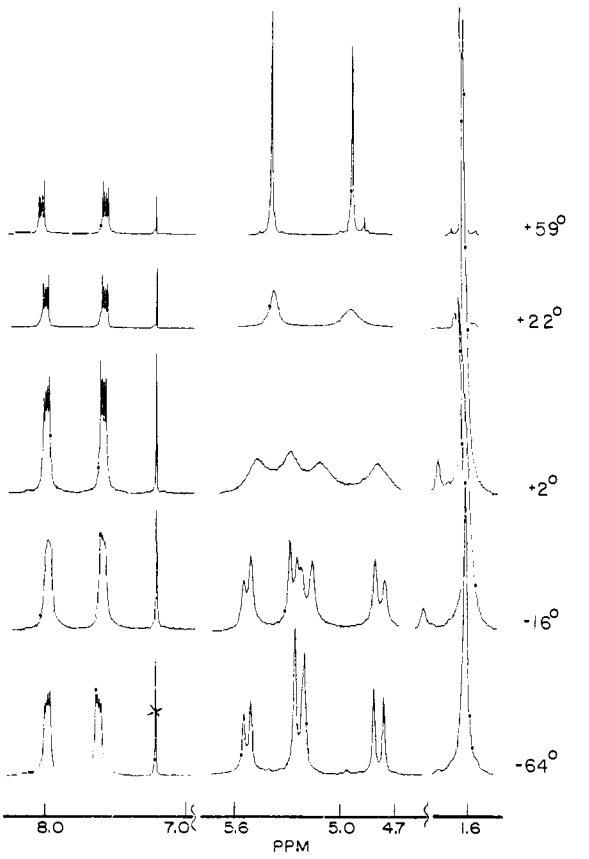


Figure 1. Variable-temperature proton spectra of acetoxymethyl derivative **7a** in $CDCl_3$.

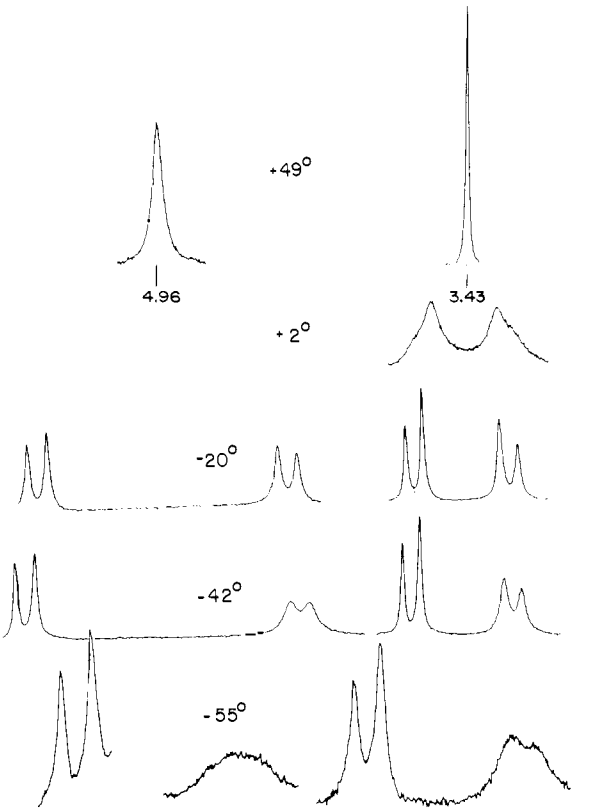


Figure 2. Variable-temperature proton NMR spectra of phenylacetate **7c** in pyridine-d_5, showing splitting of OCH_2 singlets into AB quartets at ~20 °C and dynamic behavior of these at lower temperature. The peak centered at δ 4.96 is H_α; that centered at δ 3.43 is H_{10}.

Using Anet's approximate treatment and assuming $\rho << 1$, the line width at maximum broadening is $\rho|(\nu_A - \nu_B)|$ and the

(9) F. A. L. Anet and V. J. Basus, *J. Magn. Reson.*, **32**, 339 (1978).
(10) N. Okazawa and T. S. Sorensen, *Can. J. Chem.*, **56**, 2737 (1978).
(11) H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, 1228 (1956).

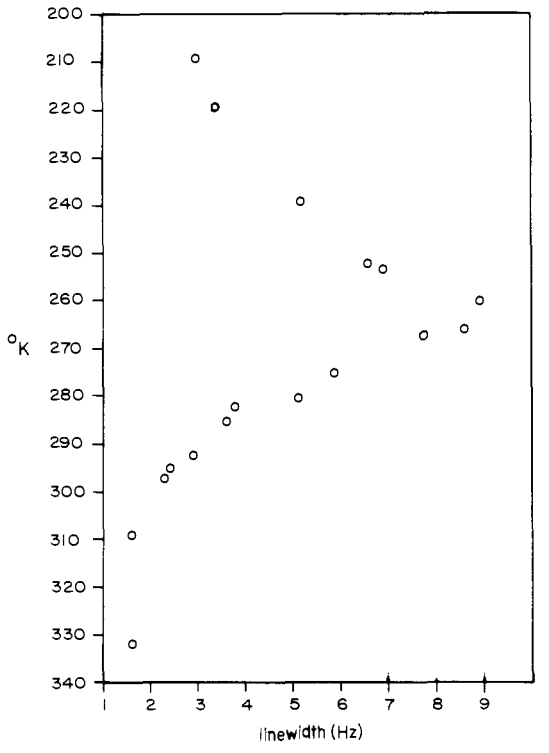


Figure 3. Plot of acetate **7a**'s methyl line width vs. temperature. Maximum line width due to exchange with the minor (presumed syn) component is at −13 °C.

corresponding rate constant is $2\pi|(\nu_A - \nu_B)|$ at the temperature of maximum broadening. Here $(\nu_A - \nu_B)$ is the chemical shift difference (in hertz) between the singlets at the slow exchange limit (the minor components shift must be estimated) and ρ is the proportion of the minor component present. For the present case with a 270-MHz resonance frequency, a maximum line width for **7a** of 8.9 Hz is achieved at −13 °C where the chemical shift of the major component is 1.58 ppm (425 Hz). A plausible estimate for the shift of the minor component, the acetate methyl in the syn conformation where very little shielding should occur, is 2.08 ppm (562 Hz), the shift of the acetate methyl in the model compound **6a**; therefore, $|(\nu_A - \nu_B)| = 137$ Hz. The equations indicate that the minor component is present to the extent of 6.5% at −13 °C and that the rate constant for anti to syn conversion is 860 s^{-1}. Using the expression

$$\Delta G^{\ddagger} = -RT[\ln (k/T) - 23.76]$$

one obtains a value of 11.7 ± 0.2 kcal/mol for the forward activation free energy which is in good agreement with a $\Delta G^{\ddagger}_{260}$ of 12.5 kcal determined from the anti → anti' exchange described below. The rate constant for the reverse exchange, k_r, was derived as follows:

$$\textit{anti}\text{-}\mathbf{7a} \underset{k_r}{\overset{k_f}{\rightleftharpoons}} \textit{syn}\text{-}\mathbf{7a}$$

$$K = k_f/k_r = [\text{syn}]/[\text{anti}]$$

$$k_r = k_f/K = k_f[\text{anti}]/[\text{syn}]$$

This gives $k_r = (861)(93.5)/6.5 = 12390$ s^{-1}, which in turn gives a free energy of activation at this temperature for the reverse reaction, syn → anti, of 10.2 ± 0.2 kcal/mol. ΔG°_{298} for the anti–syn equilibrium is +1.58 kcal/mol.

A total band-shape analysis was conducted for the dynamic spectra of **7a–c** using a computer program written for a Commodore PET that simulates an interconverting AB spectrum.[14] In the case of **7a** and **7b** exchange rate constants are obtained from simulations of the bridge H_α and of the H_9 protons, and agreement between the two is excellent (Tables II and III). For **7c** the bridge H_α and the phenylacetate methylene protons are used in the simulation, also resulting in internal consistency (Table IV). Simulated and experimental spectra for the exchange of H_α in **7a** are in Figure 4. Thermodynamic parameters were calculated using a computer least-squares fit of the experimental exchange

Table II. Exchange Rate Constants at Various Temperatures for the H_9 and H_α Protons in 7a ($CDCl_3$ Solvent)

	exchange rate constants, s^{-1}	
temp, K	H_9	H_α
234	1.3	2.5
238	2.0	15.4
253	14.7	21.3
256	20.8	21.3
266	40	38.5
275	114.9	114.9
280	200	188.7
282	250	232.6
284	277.8	250
285	317.5	303
292	666.7	666.7
295	1000	1000
309	3333	3333
Input Parameters (Hz)		
peak separation	89	135
coupling constant	12.1	17.3
line width	3	3

Table III. Exchange Rate Constants at Various Temperatures for the H_9 and H_α Protons in 7b ($CDCl_3$ Solvent)

	exchange rate constants, s^{-1}	
temp, K	H_9	H_α
237	3.3	3.3
251	10.5	11.1
264	25	27
275	102	90.9
279	178.6	153.8
285	333.3	250
287	384.6	277.8
289	465.1	416.7
291	526.3	526.3
297	952.4	970.9
315	5 000	5 000
333	25 000	25 000
Input Parameters (Hz)		
peak separation	75	147
coupling constant	11.8	17.3
line width	3	3

Table IV. Exchange Rate Constants at Various Temperatures for the H_{10} and H_α Protons in 7c (Pyridine-d_5 Solvent)

	exchange rate constants, s^{-1}	
temp, K	H_{10}	H_α
253	10.2	10.2
264	22.2	22.2
286	259.7	250
300.6	1 136	
311.7	3 846	3 846
322	10 000	10 000
Input Parameters (Hz)		
peak separation	90	247
coupling constant	15.8	17.3
line width	1.5	2

(12) S. G. Baxter, H. Fritz, G. Hellman, B. Kitsche, H. J. Lindner, K. Mislow, C. Ruchart, and S. Weiner, *J. Am. Chem. Soc.*, **101**, 4493 (1979).
(13) F. A. L. Anet, I. Yavari, I. J. Ferguson, A. R. Katritzky, M. Moreno-Manas, and M. J. T. Robinson, *J. Chem. Soc., Chem. Commun.*, 399 (1976).
(14) J. Heidberg, J. A. Weil, G. A. Jamusonis, and J. K. Anderson, *J. Chem. Phys.*, **41**, 1033 (1964).

Table V. Thermodynamic Properties for the Anti–Anti Exchange Process in 7a–c

	7a	7b	7c
E_a, kcal/mol	14.7 ± 0.3	14.8 ± 0.4	16.5 ± 0.5
log A	13.8	13.9	15.1
$\Delta G^{\ddagger}_{298}$, kcal/mol	12.3 ± 0.3	12.3 ± 0.4	12.3 ± 0.5
$\Delta H^{\ddagger}_{298}$, kcal/mol	14.1	14.2	15.9
$\Delta S^{\ddagger}_{298}$, eu	6.0	6.3	12.0

rates at various temperatures to the Eyring equation. The activation parameters obtained in this fashion are presented in Table V and confirm the impression that the anti → syn → anti′ equilibrium does not result from rotation of the acyloxymethyl groups through the cavity of the cyclophanes. The similar values of $\Delta H^{\ddagger}_{298}$ for all three cyclophanes, and especially the equivalence of $\Delta G^{\ddagger}_{298}$ (12.3 kcal), leads pretty much inescapably to the conclusion that syn–anti interconversion occurs by a process which is independent of the acyloxymethyl groups. Rotation of the fused benzo ring through the molecular interior is the most plausible process.

Very few values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are available for conformational exchange processes in cyclophanes with which to compare these results. However, the values of $\Delta S^{\ddagger}_{298}$ for **7a** (6.0 eu) and **7b** (6.3 eu) are reasonable when compared with those obtained for other unimolecular rearrangement reactions. Even though the systematic error in $\Delta S^{\ddagger}$ for **7a** and **7b** is probably 30%, it seems likely that $\Delta S^{\ddagger}$ is truly positive. This is consistent with the model for interconversion where the "face-edge" transition state, this time with the benzo ring in the interior, allows for increased rotational freedom of the functional groups that are hindered in the ground state by the transannular ring. The larger value of $\Delta S^{\ddagger}_{298}$ for **7c** (12.0 eu, log A = 15.1) at first glance begs to be interpreted as arising from the same effect, a consequence of its greater size. However, the number is simply too large to be reasonable. It is outside of the log A range observed for other unimolecular rearrangements and approaches the value observed for some dissociation reactions. This result must be attributed to some unclarified systematic error, as the precision of the data is quite good. The analysis at low temperature was conducted using the downfield portions of the AB spectra which did not appear to broaden in response to the second dynamic process reflected in the high-field AB signals, but this second process may still very well contribute to the systematic error. These differences with **7c** confirm the perceptive comment offered by Binsch[15] on the care that must be observed in interpreting entropies of activation obtained via the DNMR technique.

Conclusion

Anti → syn → anti′ equilibration of the rigid proceeds by rotation of the unsubstituted portion of the naphthalene rings through the molecular interior of the cyclophane. It should be noted, however, that this conclusion rests on the assumption that there is no complicated itinerary available for the acyloxymethylenes' snaking through the cavity. One can imagine processes that are entropy—but not enthalpy—controlled and independent of the size of the appended groups, but in the absence of further data we dismiss these by application of Occam's Razor.

Felxible Naphthalenophanes. The NMR spectra of the hydrogenated naphthalenophanes **8a–c** and **8e** are temperature independent to −60 °C and show no sign of diastereotopic methylene groups. All signals are sharp at room temperature, and, upon cooling, no coalescence points are observed until ca. −60 °C. Below −60 °C temperature-dependent changes in the spectra were observed for **8a–e** but these involved the aromatic protons, H_5–H_8, rather than the potentially diastereotopic side-chain methylene groups. At the lowest temperatures available, ca. −97 °C, the H_6–H_7 peak split into two. Assuming the two species observed to be the syn and anti isomers, the data permit calculation of equilibrium constants for the syn:anti equilibrium. These are

(15) G. Binsch, *Top. Stereochem.*, **3**, 97 (1968).

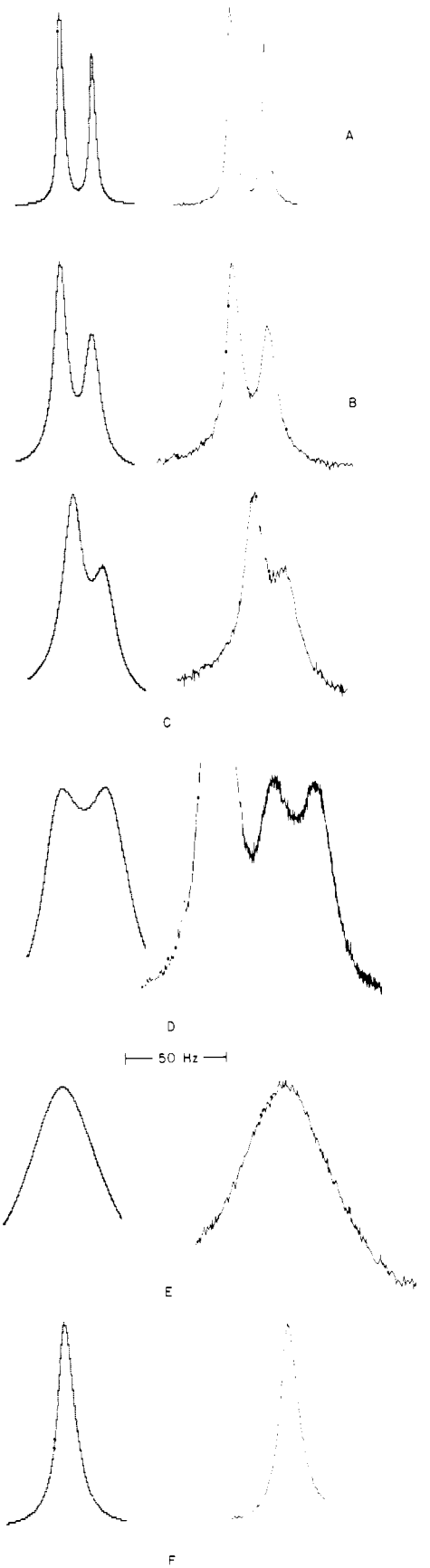


Figure 4. Experimental and simulated spectra of the H_α proton in **7a**. At slow exchange (spectra A–C), the high-field AB doublet is presented. Near coalescence (spectrum D) both components of the spectrum are plotted. Input parameters for the simulation were: J = 17.3 Hz, 2δ = 135 Hz, line width = 3 Hz, no. of points = 100 with the following lifetimes: (A) 0.4 s, (B) 0.047 s, (C) 0.026 s, (D) 0.004 s, (E) 0.0015 s, (F) 0.0003 s.

Table VI. Equilibrium and Thermodynamic Parameters for the Syn-Anti Equilibria of 8a-c,e[a]

	anti:syn	K_{eq}	$-\Delta G_{298}$, cal/mol
8a (−93°)	1.3:1	1.3	155
8b (−92°)	2.1:1	2.1	440
8c (−94°)	2.6:1	2.6	565
8e (−97°)	2.3:1	2.3	495

[a] Ratios are calculated from low-temperature peak ratios of spectra as in Figure 5.

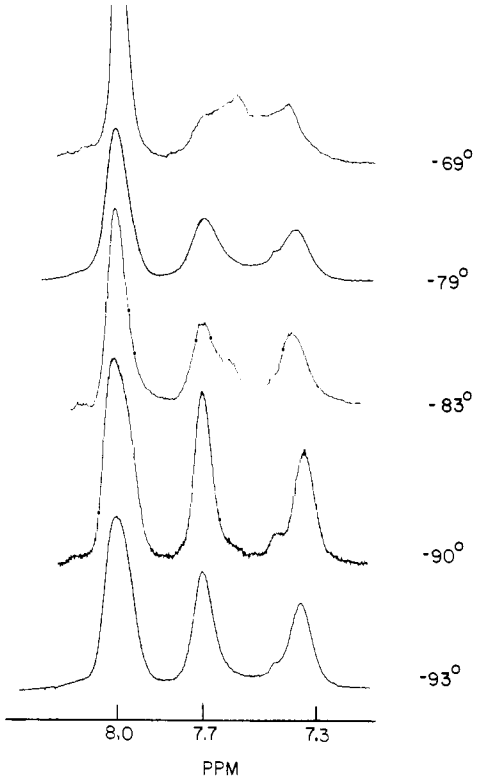


Figure 5. Variable-temperature spectra (in pyridine-d_5 of acetoxy phane **8a** showing splitting of the H_6–H_7 peak at δ 7.5 into two at ~−65 °C. The H_5–H_8 peak at δ 8.0 does not split.

presented in Table VI. It is seen that the anti–syn equilibrium constant increases as the bulk of the side chain increases, going from 1.3 for the acetate **8a** to 2.6 for the phenylacetate **8c**. It is the high-field H_6–H_7 peak that corresponds in all cases to the minor nsyn) isomer. This is expected from our work[3b] on [8.8](2,6)naphthalenophane; H_6 and H_7 of the syn isomer experience ring current shielding effects which are absent in the anti isomer.

An estimate of the rate of anti → syn interconversion of acetate **8a** may be based on the low-temperature behavior of its aromatic proton signals (Figure 5). Taking the syn:anti ratio as unity, application of the approximation[16] $\Delta G_c^{\ddagger} = RT_c(22.96 + \ln(T_c/\Delta\delta))$ with $\Delta\delta$ = 105 Hz and T_c = −60 °C (213 K) affords a free energy of activation of 10 kcal/mol as an upper limit for this process.

We have been unsuccessful, regardless of temperature or solvent, in observing the side-chain methylene groups of these hydrogenated phanes as AB quartets. This is in striking and uniform contrast to the situation in their progenitors **7a–e**. There are two limiting explanations for this fact. Firstly, it is possible that the syn–anti barrier in the hydrogenated phanes is comparable to that in the unsaturated ones, and that the very-low-temperature process observed ($\Delta G^{\ddagger}$ ~ 10 kcal) involves side-chain conformational changes of these 1,2,3,4-tetrasubstituted naphthalenes. If this were the case, however, we would have to ascribe the absence of diastereotopic AB patterns to chance equivalence. This is not an uncommon situation and, in fact, Vogtle has advanced such an argument to explain the apparent absence of dynamic behavior in a metacyclophane.[17]

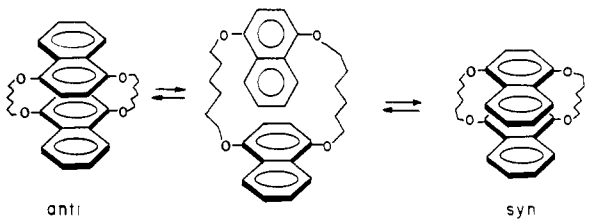


Figure 6. Proposed mechanism for syn:anti interconversion of [8.8]-(1,4)naphthalenophanes via invagination of the benzo appendage.

We have examined temperature dependence of the NMR spectra of the hydrogenated phanes in a variety of aromatic and nonaromatic solvents but in no cases observe the sought-for AB quartets. The second explanation, and the one we favor, is simply that the hydrogenated phanes are appreciably more mobile than their acetylenic counterparts, and that only at the low-temperature limit of our machinery are we observing dynamic behavior. This, coupled with diminished chemical shift differences of AB proton pairs, would account for our experimental results. We favor this as the simpler explanation and are led to the following conclusions.

Conformational Conclusions

1. The anti conformation is the preferred one of these [8.8](1,4)naphthalenophanes. This tendency is accentuated as the C_2, C_3 substituents get larger.
2. Unlike the acetylenic phanes with their rigid hexadiyne spacers, the hydrogenated phanes exist in a time-averaged collapsed conformation. This has been observed in related phanes[3a] and implies that the hexamethylene spacer of **8a–e** adopts one or more gauche conformations.[21c]
3. The anti ⇌ anti interconversion of the acetylenic phanes proceeds primarily (but probably not exclusively) by rotation of the benzo- rather than acyloxymethylenes through the cavity.
4. Despite the more compact conformation of the hydrogenated phanes, they can accommodate the benzo group in their cavity more readily than can the acetylenic phanes. This implies that the hydrogenated phanes undergo an accordian-like breathing in the syn:anti conversion. While NMR data clearly indicate that they exist in a collapsed conformation in the ground state, the transition state must resemble the rather open, fully extended anti conformation of the hexamethylene chain. This process is pictured in Figure 6.

Complexation

In chloroform solution, **7a** and **8a** formed traditional charge-transfer spectra with trinitrobenzene (TNB), having association constants that were indistinguishable from complexes with appropriate "half-molecule" models.[18]

Naphthalenophane **7e**, functionalized with four *N,N*-dimethylglycycloxymethyl groups, was too insoluble in dilute aqueous acid under ambient conditions to study its complexation behavior in this solvent by NMR. However, it was possible to measure its effect upon the fluorescence intensity of 8-anilino-1-naphthalenesulfonic acid (1,8-ANS), and an association constant for the complex could be obtained. At 60 °C, **7e** was also sufficiently soluble in 5% DCl/D_2O to examine its NMR behavior in the presence of 2-naphthalenesulfonic acid.

Fluorescence Enhancement. A solution of **7e** and 1,8-ANS exhibited a significant fluorescence intensity enhancement of 1.7

(16) R. J. Abraham and P. Loftus, "Proton and Carbon-13 NMR Spectroscopy", Heyden, London, 1979, p 167.

(17) F. Vogtle, J. Grutze, R. Natscher, W. Wider, E. Weber, and R. Grun, *Chem. Ber.*, **108**, 1694 (1975).

(18) The association constants were determined by NMR using the Benesi–Hildebrand technique[19] with TNB in 20-fold excess. Least-squares fits to the equation $1/\Delta_{obsd} = (1/K\Delta_0)(1/[TNB]) + 1/\Delta_0$ gave association constants as follows: **6a**, 1.5–3.1 M^{-1}; **7a**, 1.6–2.1 M^{-1}; 2,3-bis(acetoxymethyl)-1,4-bis(1-propoxy)naphthalene, 2.2–3.3 M^{-1}; **8a**, 1.7–2.6 M^{-1}.

Table VII. Experimental and Computed Values of Fluorescence Intensity for 1,8-ANS in the Presence of 7e

[7e] × 10^4	exptl FI	calculated FI[a]		
		A	B	C
3.45	108	108.3	108.0	107.8
2.30	95	95.3	95.4	95.4
1.72	89	88.3	88.4	88.5
1.29	84	82.8	82.9	83.1
1.03	78	79.4	79.5	79.7
least-squares error		4.12	3.96	4.08

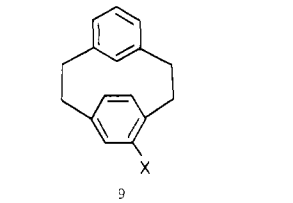
[a] (A) $K = 500$, $\epsilon_{AT} = 7.3 \times 10^6$; (B) $K = 590$, $\epsilon_{AT} = 6.5 \times 10^6$; (C) $K = 700$, $\epsilon_{AT} = 5.8 \times 10^6$.

compared with pure 1,8-ANS. Under the same conditions, the model compound **6e** had an enhancement of 1.1. These observations implicate the presence of an increasingly hydrophobic complexation site for 1,8-ANS.[20]

To obtain an association constant for the complex, the solution of **7e** was diluted successively with 1,8-ANS solution, observing the fluorescence intensity at each new concentration of **7e**. The results are compiled in Table VII. The experimental parameters were fit to the equation

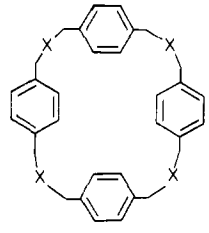
$$FI = \epsilon_A[A] + \epsilon_{AT}[AT]$$

where FI is fluorescence intensity, [A] and [AT] are the concentrations of 1,8-ANS and complex, respectively, and ϵ_A and ϵ_{AT} are proportionality constants analogous to the extinction coefficient of absorption spectroscopy. The technique is detailed in Appendix I. The best fit of the data gave an association constant of 590 M^{-1} which is comparable with association constants of 300–7000 M^{-1} for inclusion complexes between 1,8-ANS and several heterocyclophanes (**10–12**) prepared by Tabushi et al.[21] In a case where guest and host are more optimally fitted (**13**), an association constant of 16000 M^{-1} has been observed.[22] The association constant for the model compound **6e** was estimated from its fluorescence intensity (see Appendix I) to be about 67 M^{-1}, so clearly **7e** is forming a "special" complex with 1,8-ANS.



9

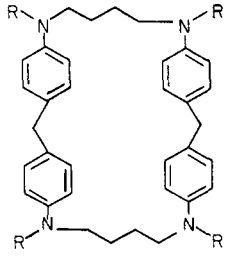
X = CO_2CH_3, $COCH_3$, CH_3, CH_2OH, CHO, H



10 X = CH_3N

11 X = $(CH_3)_2N^+$ BF_4^-

12 X = CH_2S^+ BF_4^-



13

(19) R. Foster, "Organic Charge Transfer Complexes", Academic Press, New York, 1969.

(20) D. C. Turner and L. Brand, *Biochemistry*, **7**, 3381 (1968).

(21) (a) I. Tabushi, Y. Kuroda, and Y. Kimura, *Tetrahedron Lett.*, 3327 (1976); (b) I. Tabushi, H. Sasaki, and Y. Kuroda, *ibid.*, 5727 (1976). (c) The role of conformation about the hydroquinone oxygens is problematical; see G. R. Newkome, S. J. Garbis, V. K. Majestic, F. R. Fronczek, and G. Chiari, *J. Org. Chem.*, **46**, 833 (1981).

(22) K. Odashima, A. Itai, Y. Iitaka, and K. Koga, *J. Am. Chem. Soc.*, **102**, 2504 (1980).

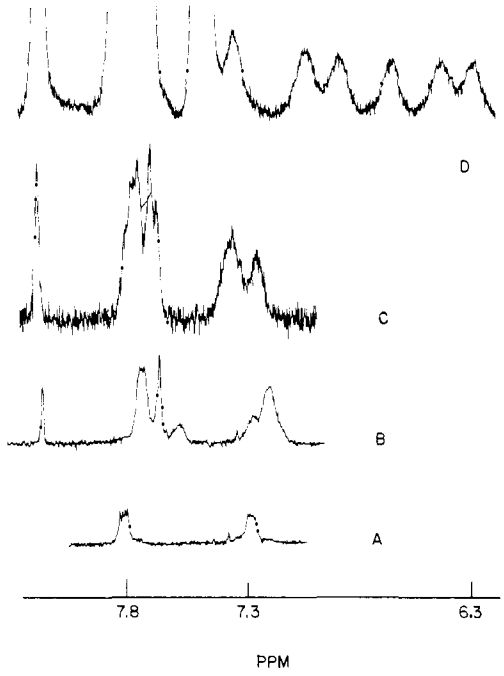


Figure 7. NMR spectra of 12.7 mM rigid dimethylglycyloxy phane **7e** in 5% DCl/D_O in the presence of various ratios of 2-naphthalenesulfonic acid (2-NSA): (A) no 2-NSA, (B) 1:1 **7e**:2-NSA, (C) 1.3 **7e**:2-NSA, (D) 1:40 **7e**:2-NSA. A little precipitate was present in experiment C.

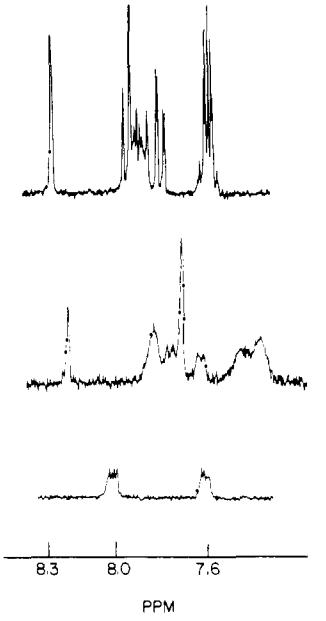


Figure 8. NMR spectra (12.7 mM in 5% DCl/D_2O) of (A) 2-naphthalenesulfonic acid, (B) 1:1 **6e**:2-NSA, and (C) **6e**.

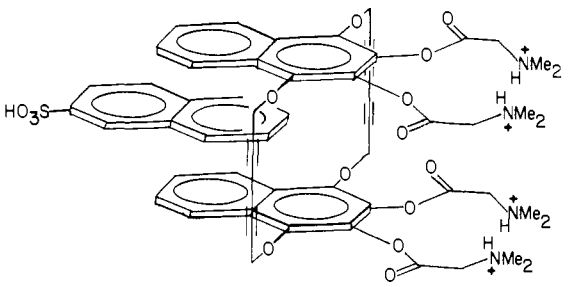
NMR Complexation with 2-Naphthalenesulfonic Acid. When a 1:1 solution of model **6e** and 2-naphthalenesulfonic acid (2-NSA) was examined by NMR at room temperature, a general upfield shift of ca. 0.2 ppm was noted (Figure 8) for all aromatic protons in the two molecules and the association constant was estimated[23] to be ca. 25 M^{-1}, entirely consistent with a simple π-stacking picture.

Of greater interest was the NMR spectrum of **7e** in the presence of 2-NSA, when compared with the results for **6e**. As can be seen in Figure 7, at 60 °C with a 1:1 ratio at the same concentration

(23) A Benesi–Hildebrand treatment by NMR at 50 °C gave an association constant of 7 M^{-1} and upfield complexation shifts for **6e** in pure complex of ca. 1.2 ppm. At room temperature, assuming the complexation shifts are the same, a shift of 0.2 ppm implies about 20% complexation and an association constant of 25 M^{-1} for 0.0127 M **6e** and 2-NSA.

as **6e**, upfield shifts of 0.23 ppm for $H_{5,8}$ and 0.02 ppm for $H_{6,7}$ in **7e** and 0.41 ppm for H_{5-8} in 2-NSA were observed. These results are inconsistent with a simple π-stacking picture. First, the association seems to be much greater; the NMR shifts for **7e** are larger at 60 °C than those observed for **6e** at 22 °C; and secondly, the shifts in **7e**, rather than being about the same for all the aromatic protons, are much larger for the unsubstituted ring of 2-NSA with $H_{6,7}$ in **7e** experiencing no net shielding. When additional 2-NSA was added to give a threefold excess, the $H_{6,7}$ protons in **7e** moved upfield slightly and the 2-NSA aromatics moved back downfield. In both cases the peaks were broadened. The spectrum with a 40-fold excess of 2-NSA gave striking results. As is apparent in Figure 7, some very large upfield shifts are observed for aromatic protons which appear to be undergoing some type of dynamic exchange. When integrated and compared with that of the *N*-methyl peak, it was determined that the aromatic signals account for 20–24 protons, or on the order of three 2-NSA molecules.[25,26] Further investigation of this behavior was not possible. When the temperature was lowered, precipitation occurred, and when increased, the sample decomposed. However, it appears that some type of higher order aggregation of 2-NSA occurs in the presence of cyclophane.

All of the observations associated with the fluorescence and NMR experiments lead to the conclusion that **7e** forms an inclusion complex with aromatic guest molecules of the form depicted below with 2-NSA. This contention is strongly supported



by the following considerations. (1) The fluorescence intensity enhancement of 1,8-ANS in the presence of **7e** indicates that the cyclophane provides a complexation site that is much more hydrophobic than model compounds. The enforced contamination of **7e** provides 1,8-ANS only two possibilities for complexation, either a classical π-stacking complex no different from **6e**, or an inclusion complex with the syn conformation. The latter would be expected to offer a more hydrophobic environment. (2) The 10-fold increase in association constant for the **7e**·1,8-ANS complex relative to **6e** is inconsistent with a classical complex where van der Waals attractive forces and the hydrophobic effect should not be much different for the two cases. The inclusion complex, on the other hand, offers a second ring for association and makes a more compact complex, less disruptive of water structure. (3) The enhanced shielding in the NMR of the unsubstituted ring protons H_{5-8} of 2-NSA is consistent with its intercalation between two naphthalene rings. Further, the deshielding influence of the sulfonic acid functionality in 2-NSA may be the origin of the net absence of shielding of the $H_{6,7}$ protons in **7e**.

The complexation behavior of the water-soluble naphthalenophane **7e** represents another addition to the repertoire of cyclophane inclusion complexes; and with further refinement, this class of compounds may very well provide for increased association and catalytic activity.

Experimental Section

Fluorescence intensity measurements in this work were made on 3.45 × 10^{-4} M solutions of **6e** or **7e** in pH 1.5 HCl/KCl buffer that was 5 × 10^{-5} M in 1,8-ANS using a Farrand MK-2 spectrofluorimeter. The excitation wavelength was 375 nm and observation was made at 510 nm.

(24) A. H. Homeyer and V. H. Wallingford, *J. Am. Chem. Soc.*, **64**, 798 (1942).

(25) This observation was absent in the NMR spectra of pure 2-NSA, pure **7e**, and **6e** containing excess 2-NSA.

(26) The $H_{6,7}$ protons were obscured by solvent peaks.

NMR spectra were obtained on 0.0127 M solutions of **6e** or **7e** by weighing each directly into an NMR tube and adding the appropriate amount of 2-NSA followed by 0.5 mL of 5% DCl/D_2O and an external TSP reference. The instrument employed was a Bruker WH-270.

Diethyl 1,4-Bis(propynyloxy)naphthalene-2,3-dicarboxylate (5). To a solution of 77 g (0.253 mol) of **4**[4,24] in 350 mL of anhydrous acetone are added 100 g (0.85 mol) of propargyl bromide and 190 g of anhydrous potassium carbonate. The reaction was stirred mechanically and refluxed for 8 h after which it was cooled and worked up to afford, after recrystallization from methanol, 68.7 g (71%) of **5**, mp 78–80 °C (methanol); NMR δ ($CDCl_3$) 8.36 (dd, J = 3, 6 Hz, 2 H), 7.72 (dd, J = 3,6 Hz, 2 H), 4.87 (d, J = 3 Hz, 4 H), 4.45 (q, J = 8 Hz, 4 H), 2.62 (t, J = 3 Hz, 2 H), 1.42 (t, J = 8 Hz, 6 H); MS 380 (20), 342 (11), 307 (18), 267 (14), 257 (14), 240 (14), 239 (49), 229 (100).

Anal. Calcd for $C_{22}H_{20}O_6$: C, 69.46; H, 5.30; *m/e* 380.1259. Found: C, 69.77; H, 5.33; *m/e* 380.1256.

1,4-Bis(propynyloxy)-2,3-bis(hydroxymethyl)naphthalene (6f). To a mechanically stirred suspension of 7.5 g (0.197 mol) of lithium aluminum hydride in 200 mL of anhydrous ether maintained below −50 °C, was added over 30–45 min 25.0 g (0.0658 mol) of **5** dissolved in 200 mL of anhydrous ether. The cooling bath was removed after the last addition and the reaction mixture was stirred for exactly 15 min at which time the internal temperature had risen to 7 °C. The cooling bath was removed and the reaction was quenched by the dropwise addition of 50 mL of absolute ethanol followed by 200 mL of ethyl acetate, 8 mL of water, 8 mL of 10% sodium hydroxide, and 24 mL of water, in that order. Dilution with warm ethyl acetate followed by vacuum filtration through a cake of filter cell and evaporation afforded 15.0 g (77%) of **6f**, mp 146.5–147 °C (dichloroethane): NMR δ (acetone-d_6) 8.21 (dd, J = 3.3, 6.6 Hz, 2 H), 7.60 (dd, J = 3.3, 6.6 Hz, 2 H), 5.02 (s, 4 H), 4.83 (d, J = 2.6 Hz, 4 H), 3.15 (t, J = 2.6 Hz, 2 H), 2.87 (bs, 2 H); MS 296 (4), 211 (7), 43 (100).

Anal. Calcd for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44; *m/e* 296.1048. Found: C, 72.55; H, 5.47; *m/e* 296.1044.

1,4-Bis(propynyloxy)-2,3-bis(acetoxymethyl)naphthalene (6a). A solution of 26.5 g (0.09 mol) of **6f** and 45 g (0.44 mol) of acetic anhydride in 175 mL of pyridine was allowed to stir at room temperature for 5 h after which it was poured onto concentrated HCl/ice, filtered, and rinsed. Drying afforded 32.5 g (96%) of **6a**, mp 143–143.5 °C (methanol); UV λ_{max} ($CHCl_3$) 330 (2500), 294 (7400); NMR δ ($CDCl_3$) 8.18 (dd, J = 3.3, 6.4 Hz, 2 H), 7.61 (dd, J = 3.3, 6.4 Hz, 2 H), 5.45 (s, 4 H), 4.74 (d, J = 2.4 Hz, 4 H), 2.61 (t, J = 2.4 Hz, 2 H), 2.08 (s, 6 H).

Anal. Calcd for $C_{22}H_{20}O_6$: C, 69.46; H, 5.30; *m/e* 380.1259. Found: C, 69.74; H, 5.45; *m/e* 380.1263.

1,4-Bis(propynyloxy)-2,3-bis(propanoyloxymethyl)naphthalene (6b). A solution of 4.8 g (16.2 mmol) of **6f** and 10.5 g (81 mmol) of propionic anhydride in 40 mL of pyridine was stirred at room temperature for 12 h. The reaction mixture was worked up as for **6a** to provide 5.8 g (88%) of **6b**, mp 122–122.5 °C (methanol): NMR δ ($CDCl_3$) 8.18 (dd, J = 3.4, 6.6 Hz, 2 H), 7.60 (dd, J = 3.4, 6.6 Hz, 2 H), 5.46 (s, 4 H), 4.73 (d, J = 2.2 Hz, 4 H), 2.60 (t, J = 2.2 Hz, 2 H), 2.35 (q, J = 7.3, 4 H), 1.15 (t, J = 7.3 Hz, 6 H).

Anal. Calcd for $C_{24}H_{24}O_6$: C, 70.58; H, 5.92; *m/e* 408.1566. Found: C, 70.45; H, 5.99; *m/e* 408.1559.

1,4-Bis(propynyloxy)-2,3-bis(phenylacetyloxymethyl)naphthalene (6c). A suspension of 5.0 g (16.9 mmol) of **6f** and 7.8 g (50 mmol) of phenylacetyl chloride in 50 mL of benzene was heated on a steam bath until solution was achieved after which the reaction was allowed to stir at room temperature for 1 h. The reaction mixture was diluted with 8% sodium bicarbonate solution and stirred vigorously for 30 min. Extraction and evaporation gave, after recrystallization, 7.7 g (85%) of **6c**, mp 112–113 °C (1:2 benzene/hexane): NMR δ ($CDCl_3$) 8.15 (dd, J = 3.3, 6.6 Hz, 2 H), 7.58 (dd, J = 3.3, 6.6 Hz, 2 H), 7.25 (m, 10 H), 5.41 (s, 4 H), 4.59 (d, J = 2.6 Hz, 4 H), 3.60 (s, 4 H), 2.49 (t, J = 2.6 Hz, 2 H).

Anal. Calcd for $C_{34}H_{28}O_6$: C, 76.68; H, 5.30; *m/e* 532.1884. Found: C, 76.57; H, 5.42; *m/e* 532.1875.

1,4-Bis(propynyloxy)-2,3-bis(4-bromophenylacetyoxymethyl)naphthalene (6d). A suspension of 3.08 g (10.4 mmol) of **6f** and 6.12 g (26.2 mmol) of *p*-bromophenylacetyl chloride in 30 mL of benzene was heated on a steam bath until solution was achieved; the reaction was allowed to stir at room temperature for 2 h after which the reaction was worked up as for **6c** to afford 6.2 g (86%) of **6d**, mp 153–154 C (1:1 benzene/hexane): NMR δ ($CDCl_3$) 8.15 (dd, J = 3.3, 6.6 Hz, 2 H), 7.60 (dd, J = 3.3, 6.6 Hz, 2 H), 7.40 (A of AB, J = 8.5 Hz, 4 H), 7.10 (B of AB, J = 8.5 Hz, 4 H), 5.43 (s, 4 H), 4.62 (d, J = 2.6 Hz, 4 H), 3.55 (s, 4 H), 2.54 (t, J = 2.6 Hz, 2 H).

Anal. Calcd for $C_{34}H_{26}O_6Br_2$: C, 59.15; H, 3.80; *m/e* 688.0096. Found: C, 59.46; H, 3.79; *m/e* 688.0087.

1,4-Bis(propynyloxy)-2,3-bis(*N*,*N*-dimethylglycyloxymethyl)naphthalene (6e). A solution of 1.93 g (6.52 mmol) of **6f**, 3.24 g (15.7

mmol) of dicyclohexylcarbodiimide, 2.19 g (15.7 mmol) of *N,N*-dimethylglycine hydrochloride, and 0.19 g (1.57 mmol) of 4-(*N,N*-dimethylamino)pyridine in 25 mL of dichloromethane was allowed to stir at room temperature for 5 h. The solvent was evaporated and the residue was taken up in 5% hydrochloric acid, filtered, and extracted with chloroform. The aqueous layer was made basic with solid potassium carbonate, extracted with chloroform, and evaporated. Recrystallization from 1:2 benzene/hexane afforded 2.15 g (76%) of **6e**, mp 95–97.5 °C (1:2 CCl_4/hexane): NMR δ 8.17 (dd, J = 3.3, 6.6 Hz, 2 H), 7.61 (dd, J = 3.3, 6.6 Hz, 2 H), 5.51 (s, 4 H), 4.74 (d, J = 2.6 Hz, 4 H), 3.19 (s, 4 H), 2.35 (s, 12 H); δ (5% DCl/D_2O, 64 °C) 8.14 (dd, J = 3.3, 6.6 Hz, 2 H), 7.70 (dd, J = 3.3, 6.6 Hz, 2 H), 5.71 (s, 4 H), 4.85 (d, J = 2.6 Hz, 4 H), 4.24 (s, 4 H), 3.05 (s, 12 H).

Anal. Calcd for $C_{26}H_{30}O_6N_2$: C, 66.94; H, 6.48; *m/e* 466.2102. Found: C, 66.83; H, 6.55; *m/e* 466.2102.

General Cyclization Procedure for the Preparation of Tetraesters of 2,9,18,25-Tetraoxa-33,34,35,36-tetrakis(hydroxymethyl)[8.8](1,4)-naphthalenophane-4,6,20,22-tetrayne (7a–d). To a solution of 2.4 g (11.6 mmol) of cupric acetate monohydrate in 40 mL of pyridine stirring in a 43 °C oil bath was added dropwise, over 30 min, 5.3 mmol of the appropriate diyne precursor **6a–d** in 20 mL of pyridine. The reaction was stirred for 4 h, after which it was poured into 600 mL of concentrated hydrochloric acid/ice, extracted with chloroform, and evaporated.

Isolation of 7a. The black residue obtained above was chromatographed on a silica gel column (3 × 25 cm) eluting with 500 mL of 5% acetone/dichloromethane.

After evaporation, the glassy product was taken up in a few milliliters of hot benzene, transferred to a 3-mL centrifuge tube and reduced in volume to ca. 0.5 mL at which point product crystallized. Resuspension several times in 3:1 benzene/chloroform with centrifugation and removal of supernatant effected gross purification. The product at this point consisted of a 6:1 mixture of dimer **7a** and a second cyclic presumably trimeric product (**14**) which was separated by preparative TLC to afford 37 mg (1.8%) of **7a** and 5 mg (0.3%) of **14**.

7a: mp >250 °C (chloroform/acetone); UV λ_{max} ($CHCl_3$) 330 (1600), 292 (4800); NMR δ ($CDCl_3$) 7.97 (dd, J = 3, 6 Hz, 4 H), 7.59 (dd, J = 3, 6 Hz, 4 H), 5.44 (bs, 8 H), 4.94 (bs, 8 H), 1.59 (s, 12 H). Anal. Calcd for $C_{44}H_{36}O_{12}$: C, 69.84; H, 4.79. Found: C, 69.64; H, 4.90. **14**: mp >250 °C; NMR δ ($CDCl_3$) 8.10 (dd, J = 3.3, 6.2 Hz, 2 H), 7.58 (dd, J = 3.3, 6.2 Hz, 2 H), 5.41 (s, 4 H), 4.87 (s, 4 H), 1.97 (s, 6 H).

Isolation of 7b. Crude cyclization product was chromatographed and triturated as described for **7a** to afford 28 mg (1.4%) of **7b**, mp >250 °C: NMR δ ($CDCl_3$) 7.98 (dd, J = 3.3, 6.2 Hz, 4 H), 7.60 (dd, J = 3.3, 6.2 Hz, 4 H), 5.46 (bs, 8 H), 4.93 (bs, 8 H), 1.91 (bq, J = 7.3 Hz, 8 H), 0.63 (t, J = 7.3 Hz, 12 H).

Isolation of 7c. Crude cyclization product was chromatographed on a silica gel column (3 × 25 cm). Elution with chloroform was continued until a dark brown band just started to come off. Evaporation and workup as described for **7a** afforded 26 mg (1.0%) of **7c**, mp >250 °C: NMR δ (pyridine-d_5) 7.92 (dd, J = 3, 6.3 Hz, 4 H), 7.53 (dd, J = 3, 6.3 Hz, 4 H), 7.16 (m, 12 H), 7.00 (m, 8 H), 5.94 (bs, 8 H), 5.01 (bs, 8 H), 3.38 (bs, 8 H).

Isolation of 7d. Crude cyclization product was chromatographed on a silica gel column (3 × 25 cm); elution with chloroform was continued until a dark brown band just started to come off. Evaporation and workup as described for **7a** provided 16 mg (0.7%) of **7d**, mp >250 °C: NMR δ ($CDCl_3$) 7.79 (dd, J = 3.3, 6.4 Hz, 4 H), 7.51 (dd, J = 3.3, 6.4 Hz, 4 H), 7.21 (A of AB, J = 8.5 Hz, 8 H), 6.66 (B of AB, J = 8.5 Hz, 8 H), 5.51 (bs, 8 H), ca. 4.8 (hump, 8 H), 3.04 (bs, 8 H).

1,8,17,24-Tetraoxa-33,34,35,36-tetrakis(hydroxymethyl)-[8.8](1,4)-naphthalenophane-3,5,19,21-tetrayne (7f). A suspension of 64 mg (0.085 mmol) of **7a** in 3 mL of 1:1 methanol/acetone containing 100 mg of anhydrous potassium carbonate was stirred at room temperature under nitrogen for 6 h, after which it was diluted with 5 mL of water. The white, flocculant product was isolated by centrifugation and weighed 50 mg (100%). The product, **7f**, was pure as determined by its 270-MHz NMR: δ (Me_2SO-d_6) 8.08 (dd, J = 3.3, 6.2 Hz, 4 H), 7.63 (dd, J = 3.3, 6.2 Hz, 4 H), 5.07 (s, 8 H), 4.76 (bs, 8 H).

1,8,17,24-Tetraoxa-33,34,35,36-tetrakis(*N,N*-dimethylglycyloxymethyl)[8.8](1,4)naphthalenophane-3,5,19,21-tetrayne (7e). A mixture of 50 mg (0.085 mmol) of **7f** from above, 206 mg (1.0 mmol) of dicyclohexylcarbodiimide, 140 mg (1.0 mmol) of *N,N*-dimethylglycine hydrochloride, and 12 mg (0.1 mmol) of 4-(*N,N*-dimethylamino)pyridine in 1.5 mL of anhydrous pyridine was allowed to stir at room temperature for 4 h under a nitrogen atmosphere. The reaction was then diluted with 5% hydrochloric acid, filtered, and extracted with chloroform. The aqueous layer was made basic with solid potassium carbonate and extracted with dichloromethane which was evaporated to afford, after trituration with benzene, 65 mg (82%) of **7e**, mp 220 °C dec (benzene): NMR δ ($CDCl_3$) 8.00 (dd, J = 3.3, 6.6 Hz, 4 H), 7.59 (dd, J = 3.3, 6.6 Hz, 4 H), 5.47 (bs, 8 H), 4.98 (bs, 8 H), 2.86 (s, 8 H), 2.10 (s, 24 H); δ (5% DCl/D_2O; 69 °C) 7.95 (dd, J = 3.3, 6.3 Hz, 4 H), 7.41 (dd, J = 3.3, 6.3 Hz, 4 H), 5.64 (s, 8 H), 5.00 (s, 8 H), 4.11 (s, 8 H), 2.98 (s, 24 H).

General Procedure for the Preparation of Tetraesters of 2,9,18,25-Tetraoxa-33,34,35,36-tetrakis(hydroxymethyl)[8.8](1,4)naphthalenophane (8a–d). A suspension of 0.02–0.03 mmol of the appropriate tetrayne **7a–d** and an equal molar amount of Wilkinson's catalyst in 2–3 mL of benzene was hydrogenated under 1 atm of hydrogen. After 4–6 h the orange suspension occasionally turned pale yellow in which case another equivalent amount of catalyst was added and hydrogenation was continued until a clear homogeneous reaction mixture resulted.

Isolation of 8a. The reaction took 20–24 h, after which the reaction mixture was passed through a silica gel column and evaporated to dryness. The resulting product was purified by preparative TLC to afford a 35% yield of **8a**, mp 146–148 °C (2:1 benzene/hexane): NMR δ ($CDCl_3$) 7.92 (dd, J = 3, 6 Hz, 4 H), 7.39 (dd, J = 3, 6 Hz, 4 H), 5.19 (s, 8 H), 3.87 (t, J = 6.6 Hz, 8 H), 2.01 (s, 12 H), 1.74 (m, 8 H), 1.27 (m, 8 H).

Anal. Calcd for $C_{44}H_{52}O_{12}$: *m/e* 772.3458. Found: *m/e* 772.3475.

Isolation of 8b. The reaction took 10 h, after which it was worked up as described for **8a** to afford a 55% yield of product, mp 140–142 °C (benzene/hexane): NMR δ ($CDCl_3$) 7.92 (dd, J = 3, 6.2 Hz, 4 H), 7.38 (dd, J = 3, 6.2 Hz, 4 H), 5.20 (s, 8 H), 3.85 (t, J = 6.2 Hz, 8 H), 2.27 (q, J = 7 Hz, 8 H), 1.73 (m, 8 H), 1.26 (m, 8 H), 1.12 (t, J = 7 Hz, 12 H).

Anal. Calcd for $C_{48}H_{60}O_{12}$: *m/e* 828.4081. Found: *m/e* 828.4089.

Isolation of 8c. After 32 h the reaction was still not complete; the mixture was not homogeneous. The reaction mixture was evaporated and eluted through a silica gel column with chloroform. After evaporation the oily residue was taken up in warm chloroform and starting material (ca. 50%) crystallized. The chloroform supernatant was chromatographed by preparative TLC to afford a 30% yield of **8c**, mp 125–126 °C (benzene/hexane): NMR δ ($CDCl_3$) 7.84 (dd, J = 3.3, 6.6 Hz, 4 H), 7.32 (dd, J = 3.3 6.6 Hz, 4 H), 7.25 (m, 20 H), 5.13 (s, 8 H), 3.70 (t, J = 6.6 Hz, 8 H), 3.55 (s, 8 H), 1.60 (m, 8 H), 1.16 (m, 8 H).

Anal. Calcd for $C_{68}H_{68}O_{12}$: *m/e* 1076.4707. Found: *m/e* 1076.4691.

Isolation of 8d. The reaction required 20 h. Following chromatography on a silica gel column using chloroform and evaporation of the eluent, the residue was purified by preparative TLC to afford a 50% yield of **8d**, mp 176–177 °C (acetone): NMR δ ($CDCl_3$) 7.84 (dd, J = 3.2, 6.4 Hz, 4 H), 7.33 (dd, J = 3.2, 6.4 Hz, 4 H), 7.38 (A of AB, J = 8.5 Hz, 8 H), 7.07 (B of AB, J = 8.5 Hz, 8 H), 5.15 (s, 8 H), 3.73 (t, J = 6.7 Hz, 8 H), 3.49 (s, 8 H), 1.63 (m, 8 H), 1.19 (m, 8 H).

2,9,18,25-Tetraoxa-33,34,35,36-tetrakis(hydroxymethyl)[8.8](1,4)-naphthalenophane (8f) and 2,9,18,25-Tetraoxa-33,34,35,36-tetrakis-(*N,N*-dimethylglycyloxymethyl)-[8.8](1,4)naphthalenophane (8e). A solution of 20 mg (0.026 mmol) of **8a** in 2 mL of 1:1 methanol/acetone containing 50 mg of anhydrous potassium carbonate was stirred at room temperature for 6 h, after which it was diluted with water and centrifuged. The solid product was resuspended once in acetone, centrifuged again, and evaporated to dryness: NMR δ (Me_2SO-d_6) 7.85 (dd, J = 3, 6.2 Hz, 4 H), 7.40 (dd, J = 3, 6.2 Hz, 4 H), 4.66 (s, 8 H), 3.81 (t, J = 6.6 Hz, 8 H), 1.65 (m, 8 H), 1.17 (m, 8 H).

The crude product from above, less 4 mg, which was 95% pure by NMR analysis, was dissolved with 206 mg (1 mmol) of dicyclohexylcarbodiimide, 140 mg (1 mm) of *N,N*-dimethylglycine hydrochloride, and 10 mg of dimethylaminopyridine in 0.75 mL of anhydrous pyridine and stirred at room temperature for 2 h. The mixture was diluted with 5% hydrochloric acid and filtered. The filtrate was extracted with chloroform and was then basified with solid potassium carbonate. Extraction with chloroform and evaporation afforded ca. 12 mg of product **8e** contaminated with dimethylaminopyridine: NMR δ (acetone-d_6) 7.96 (dd, J = 3.3, 6.6 Hz, 4 H), 7.48 (dd, J = 3.3, 6.6 Hz, 4 H), 5.24 (s, 8 H), 3.90 (t, J = 6.6 Hz, 8 H), 3.17 (s, 8 H), 2.30 (s, 24 H), 1.76 (m, 8 H), 1.31 (m, 8 H).

Diethyl 1,4-Bis(1-propyloxy)naphthalene-2,3-dicarboxylate (15). A solution of 10.0 g (0.033 mol) of **4**[4,24] and 20 g (0.164 mol) of 1-bromopropane in 25 mL of anhydrous acetone containing 25 g of anhydrous potassium carbonate was refluxed for 5 h, after which it was worked up to afford 12.1 g (95%) of **15** as a viscous oil, ca. 95% pure by TLC and NMR analysis and of sufficient purity for further manipulation: NMR δ ($CDCl_3$) 8.17 (dd, J = 3.3, 6.6 Hz, 2 H), 7.60 (dd, J = 3.3, 6.6 Hz, 2 H), 4.40 (q, J = 7.0 Hz, 4 H), 4.07 (t, J = 7.0 Hz, 4 H), 1.92 (sextet, J = 7.4 Hz, 4 H), 1.40 (t, J = 7.0 Hz, 6 H), 1.10 (t, J = 7.4 Hz, 6 H).

Preparation of 1,4-Bis(1-propyloxy)-2,3-bis(hydroxymethyl)-naphthalene (16f). To a suspension of 1.0 g (26.3 mmol) of lithium aluminum hydride in 50 mL of anhydrous ether, stirring in an ice bath,

was added dropwise over 15 min, 9.0 g (23.3 mmol) of **15** in 50 mL of anhydrous ether. The ice bath was removed and stirring was continued for 30 min; then the ice bath was replaced and the reaction was quenched by the careful dropwise addition of absolute ethanol. Acidic workup afforded 6.2 g (88%) of **16f**, mp 104–105 °C (1:3 benzene/hexane): NMR δ ($CDCl_3$) 8.09 (dd, J = 3.3, 6.3 Hz, 2 H), 7.51 (dd, J = 3.3, 6.3 Hz, 2 H), 4.97 (s, 4 H), 3.96 (t, J = 7.0 Hz, 4 H), 3.11 (bs, 2 H), 1.95 (sextet, J = 7.3 Hz, 4 H), 1.14 (t, J = 7.3 Hz, 6 H).

Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95; m/e 304.1637. Found: C, 71.18; H, 7.75; m/e 304.1667.

Procedure for the Preparation of Diesters of 1,4-Bis(1-propyloxy)-2,3-bis(hydroxymethyl)naphthalene (16a–e). The desired products were obtained by reaction and workup as described for the propargyl ethers **6a–e**; they had the following properties.

16a: mp 98–99 °C (hexane); NMR δ ($CDCl_3$) 8.11 (dd, J = 3.3, 6.3 Hz, 2 H), 7.54 (dd, J = 3.3, 6.3 Hz, 2 H), 5.42 (s, 4 H), 3.96 (t, J = 6.8 Hz, 4 H), 2.08 (s, 6 H), 1.96 (sextet, J = 7.3 Hz, 4 H), 1.14 (t, J = 7.3 Hz, 6 H). Anal. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.27; m/e 388.1884. Found: C, 68.27; H, 7.48; m/e 388.1887.

16b: mp 40–42 °C (hexane, 30 °C); NMR δ ($CDCl_3$) 8.12 (dd, J = 3.3, 6.3 Hz, 2 H), 7.55 (dd, J = 3.3, 6.3 Hz, 2 H), 5.41 (s, 4 H), 3.95 (t, J = 7.0 Hz, 4 H), 2.35 (q, J = 7.3 Hz, 4 H), 1.96 (sextet, J = 7.3 Hz, 6 H), 1.15 (t, J = 7.3 Hz, 6 H), 1.13 (t, J = 7.4 Hz, 6 H); irradiation of δ 2.35 (q) collapses δ 1.16 nt) to a singlet. Anal. Calcd for $C_{24}H_{32}O_6$: C, 69.21; H, 7.74; m/e 416.2197. Found: C, 69.36; H, 7.87; m/e 416.2190.

16c: mp 74–75 °C (hexane): NMR δ ($CDCl_3$) 8.09 (dd, J = 3.3, 6.3 Hz, 2 H), 7.53 (dd, J = 3.3, 6.3 Hz, 2 H), 7.24 (m, 10 H), 5.37 (s, 4 H), 3.82 (t, J = 7.0 Hz, 4 H), 3.59 (s, 4 H), 1.85 (sextet, J = 7.0 Hz, 4 H), 1.05 (t, J = 7.0 Hz, 6 H). Anal. Calcd for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71; m/e 540.2510. Found: C, 75.72; H, 6.65; m/e 540.2504.

16d: mp 93–94 °C (3:1 hexane/benzene); TLC (dichloromethane) R_f 0.43; NMR δ ($CDCl_3$) 8.10 (dd, J = 3.3, 6.6 Hz, 2 H), 7.56 (dd, J = 3.3, 6.6 Hz, 2 H), 7.41 (A of AB, J = 8.1 Hz, 4 H), 7.11 (B of AB, J = 8.1 Hz, 4 H), 5.36 (s, 4 H), 3.84 (t, J = 6.6 Hz, 4 H), 3.55 (s, 4 H), 1.88 (sextet, J = 7.0 Hz, 4 H), 1.07 (t, J = 7.7 Hz). Anal. Calcd for $C_{34}H_{34}O_6Br_2$: C, 58.47; H, 4.91; m/e 696.0721. Found: C, 58.64; H, 5.05; m/e 696.0745.

16e (oil): NMR δ (acetone-d_6) 8.17 (dd, J = 3.3, 6.6 Hz, 2 H), 7.64 (dd, J = 3.3, 6.6 Hz, 2 H), 5.45 (s, 4 H), 3.99 (t, J = 6.6 Hz, 4 H), 3.21 (s, 4 H), 2.31 (s, 12 H), 1.95 (sextet, J = 7.3 Hz, 4 H), 1.14 (t, J = 7.3 Hz, 6 H).

Appendix I

The mathematical formula relating fluorescence intensity (FI) to the **7e** (T) concentration takes the form of the well-known Beer's law equation at low concentrations of fluorescer:

$$FI = \epsilon[T] \tag{1}$$

For the case at hand, two fluorescent species are present for the equilibrium between **7e** (T) and 1,8-ANS (A):

$$T + A \rightleftharpoons TA \tag{2}$$

so the equation takes the form

$$FI = \epsilon_A[A] + \epsilon_{AT}[AT] \tag{3}$$

where ϵ_A and ϵ_{AT} are proportionality constants analogous to the familiar extinction coefficients in absorption spectroscopy. The concentration terms [A] and [AT] are related to the equilibrium constant:

$$K = [AT]/[A][T] \tag{4}$$

Now, because **7e** was quite insoluble, it was not possible to conduct the experiment with a large excess of **7e**, allowing a simple, linear Benesi–Hildebrand treatment. Rather the observed fluorescence intensities and **7e** concentrations were fit to eq 3. The concentration terms AT, A, and T are related to the equilibrium constant K as follows. From the mass balance relationships

$$A_0 = A + AT \qquad AT = A_0 - A \tag{5}$$

$$T_0 = T + AT \qquad T = T_0 - AT = T_0 - A_0 + A \tag{6}$$

and eq 4, one may derive and solve the quadratic equation

$$KA^2 + A(1 + K(T_0 - A_0)) - A_0 = 0 \tag{7}$$

for the positive root to obtain

$$A = \frac{(K(A_0 - T_0) - 1) + [(K(T_0 - A_0) + 1)^2 + 4KA_0]^{1/2}}{2K} \tag{8}$$

Operationally, a computer program written in BASIC for a Commodore PET machine was used which interatively selected values of K and calculated the concentration of A from eq 8. A, along with ϵ_A, available from the fluorescence of pure 1,8-ANS, and ϵ_{AT}, which was the second iteratively determined parameter, were substituted into the equation

$$FI = \epsilon_A A + \epsilon_{AT}(A_0 - A) \tag{9}$$

The fluorescence intensity thus calculated for each data point from a given K and ϵ_{AT} was compared with the experimental value, and the square of the difference was summed for each point. By examining a large number of values for K and ϵ_{AT}, and by searching for the least-squared error, a best fit of the data to eq 9 was obtained. In this fashion, an association constant of 590 M^{-1} and a value of 6.5×10^6 M^{-1} for ϵ_{AT} were obtained from the data in Table VII. The least-squared error for these values was 3.96. The fluorescence intensities calculated using the best K and ϵ_{AT} were in excellent agreement with the experimental values as can be seen in Table VII.

As is frequently the case with this technique, the error minimum was quite broad and changes of 50–100 in association constant, when compensated for by a change in ϵ_{AT}, gave values that were still quite close to the observed values (Table VII). Nevertheless, by being careful to accept only reasonable numbers, one can make firm conclusions about the association behavior. In this case, K is clearly not 100 nor is it 1000.

If one assumes that the model compound **6e** has an ϵ_{AT} that is the same as for **7e** (a conservative estimate; it is probably lower), it is possible to estimate an association constant of 67 for the **6e** complex from its fluorescence intensity (1.1 enhancement), assumed stoichiometry, and eq 9. This is a likely estimate, in line with Tabushi's findings in his model compounds.[21]

Registry No. **2** (R = H), 77060-67-4; **3** (R = H), 77060-68-5; **4**, 59883-07-7; **5**, 80593-92-6; **6a**, 80593-93-7; **6b**, 80593-94-8; **6c**, 80593-95-9; **6d**, 80612-09-5; **6e**, 80593-96-0; **6f**, 80593-97-1; **7a**, 80593-98-2; **7b**, 80593-99-3; **7c**, 80594-00-9; **7d**, 80594-01-0; **7e**, 80594-02-1; **7f**, 80594-03-2; **8a**, 80594-04-3; **8b**, 80594-05-4; **8c**, 80594-06-5; **8d**, 80594-07-6; **8e**, 80612-10-8; **8f**, 80594-08-7; **14**, 80594-09-8; **15**, 80594-10-1; **16a**, 80594-11-2; **16b**, 80594-12-3; **16c**, 80594-13-4; **16d**, 80594-14-5; **16e**, 80594-15-6; **16f**, 80594-16-7; 1,8-ANS, 82-76-8; 2-NSA, 120-18-3; propargyl bromide, 106-96-7; phenylacetyl chloride, 103-80-0; *p*-bromophenylacetyl chloride, 37859-24-8; *N,N*-dimethylglycine HCl, 2491-06-7; 1-bromopropane, 106-94-5.