Preparation and Diels–Alder Reactions of the [n](1,4)Naphthalenophanes. Isolation of a Paddlane Derivative Containing the Tricyclo[14.2.2.2^{1,6}]docosane Ring System

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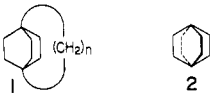
Abstract: The [n](1,4)naphthalenophanes (n = 8, 9, 10, and 14) were prepared and treated with dicyanoacetylene. The major product in all cases was the Diels–Alder adduct at the unsubstituted aromatic ring. The paddlane, 2,3-dicyano-1,4-ethano-1,4-dihydro-1,4-tetradecanonaphthalene (**28**), a derivative of the parent hydrocarbon, tricyclo[14.2.2.2^{1,6}]docosane, was isolated as a minor product from the reaction of [14](1,4)naphthalenophene with dicyanoacetylene. A minor product in the reaction of [8](1,4)naphthalenophane with dicyanoacetylene was a 1:1 adduct with rearranged structure. The nuclear magnetic resonance spectra of the [n](1,4)naphthalenophanes and their Diels–Alder adducts exhibit characteristic trends within the homologous series: as the value of n decreases, the molecule becomes more distorted and the bridging chain is held in closer proximity to the aromatic rings. In addition, when n = 8, 9, or 10, the molecule is frozen into one conformation at room temperature on the nuclear magnetic resonance (NMR) time scale, whereas, when n = 14, the molecule rapidly interconverts from one conformation to another at room temperature.

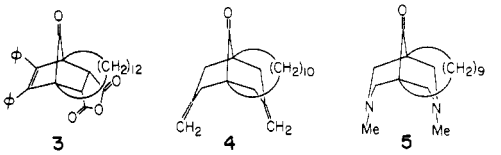
The effects of distorting the tetrahedral geometry about carbon have received considerable study, both experimentally and theoretically. Although distortion toward a square-planar or pyramidal geometry has been examined theoretically,[2] relatively little experimental work has appeared dealing with the potential function for such distortion. Compounds which have four nonzero bridges between a pair of bridgehead atoms, as in **1**, appear to have considerable potential for providing the needed experimental data. These compounds, termed "paddlanes",[3] will become progressively more distorted as the number of methylene groups, n, is decreased. A compound of particular interest is **2** in which a pyramidal geometry would



1 2

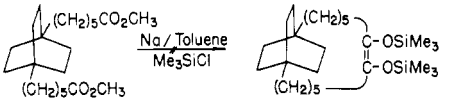
be expected for the bridgehead carbons. Even when n is as large as 4 or 5, it would be expected that the bicyclo[2.2.2]octane unit in **1** should be considerably distorted toward a square-planar geometry.

Some of the known simple compounds of this type are **3**,[4] **4**,[5] and **5**.[6] In addition, a related paddlane derivative in which



3 4 5

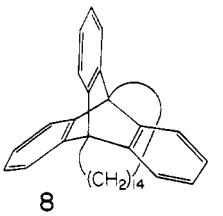
the methylene bridge has been replaced by an oxygen has been prepared.[7] These examples all contain a one-atom bridge and do not have the same potential for bond angle deformation as does **1**. In **1** the atoms attached to the bridge carbons should coincide with the threefold axis of symmetry, which is not the case with compounds containing the smaller bridge. Thus, for a given size of external bridge, the strain present in **1** should be significantly greater than that in **3–5**. Several attempts to prepare derivatives of **1** from the intramolecular and intermolecular condensation of bicyclo[2.2.2]octane systems have yielded only dimeric and polymeric reaction products.[3,8] For example, 1,4-bis(5-carbomethoxy-n-pentyl)bicyclo[2.2.2]-octane (**6**) was subjected to acyloin condensation conditions in the presence of trimethylsilyl chloride,[9] to yield, in addition to some unreacted starting material, a small amount of dimeric



6 7

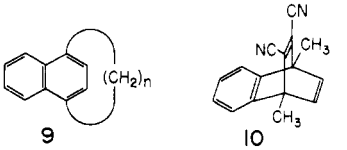
material. None of the desired intramolecular cyclization product (**7**) was formed in this reaction.[8] Finally, a number of compounds derived by intramolecular Diels–Alder reactions contain a paddlane structure,[10] although in these cases the additional bridges relieve some of the potential nonbonded strain present in **1**.

One possible synthetic approach to compounds containing the ring system in **1** is the Diels–Alder reaction of a bridged aromatic ring. The tribenzo paddlane derivative (**8**) has recently been prepared by such a route.[11] Diels–Alder reaction of a dithia(9,10)anthracenophane with benzyne (5% yield) followed by 450 °C pyrolysis of the bissulfone (in "low yield") gave **8**. Nuclear magnetic resonance studies indicated that **8**



8

is conformationally immobile up to 120 °C.[11] Aromatic systems are relatively unreactive when normal dienophiles are used, but the highly reactive dicyanoacetylene is known to add to aromatic systems such as benzene[12] and naphthalene[13] to give [4 + 2] adducts. In order to ensure that the addition of the dienophile would not occur ortho to the polymethylene bridge, as was the case in the addition of dicyanoacetylene to [2.2]-paracyclophane,[12] the [n](1,4)naphthalenophanes (**9**) were chosen as substrates. Compounds of structure **9** could potentially add a dienophile in either ring. The substituted ring, being more electron rich, should be favored on electronic



9 10

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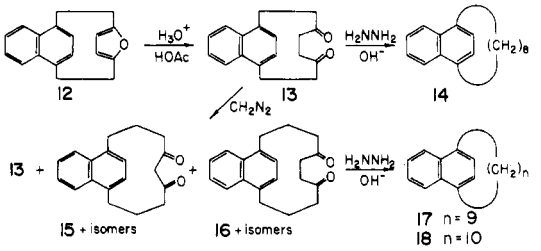
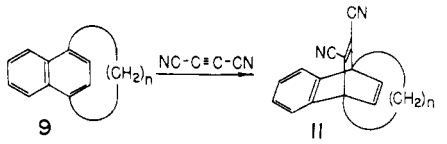
Scheme I



grounds. To test this prediction, 1,4-dimethylnaphthalene was treated with dicyanoacetylene to give the desired adduct, **10**, as the major product (54%) along with a small amount (4%) of the adduct derived from addition to the unsubstituted ring. It would be expected that if the value of n is sufficiently large, the resultant [n](1,4)naphthalenophane should show behavior similar to 1,4-dimethylnaphthalene and add a dienophile in the ring containing the bridge, thus resulting in the formation of the paddlane, **11**. The effect of reducing the value of n would



be manifest in an increase in the strain in the substituted diene as well as an increase in steric hindrance to approach of a dienophile from one side of the substituted diene in **9**.

Results and Discussion

Preparation of [n](1,4)Naphthalenophanes. The preparation of [8](1,4)naphthalenophane (**14**) was effected by the acid-catalyzed ring opening[14] of [2.2](1,4)naphthaleno(2,5)-furanophane (**12**)[15] to yield the diketone **13** which was converted via a Wolff-Kishner reduction to **14** (90% overall yield from **12** (Scheme I). Diazomethane homologation[16] of the diketone **13** was used to prepare [9](1,4)napthalenophane (Scheme I). Treatment of **13** with diazomethane gave a mixture of diketones: **13** (26%), **15** (63%), and **16** (11%) which was subjected directly to a Wolff-Kishner reduction. [9](1,4)-Naphthalenophane (**17**) was separated from [8]- and [10]-(1,4)naphthalenophane by high temperature gas chromatography. Preparation of **17** by an acyloin route (Scheme II) from methyl 5-[4-(3-carbomethoxypropyl)-(1-naphthyl)]valerate (**19**) was attempted without success.[17] Only unreacted starting material (97%) was recovered when **19** was subjected to acyloin condensation conditions.

The [10]- and [14](1,4)naphthalenophanes (**18** and **24**, respectively) were conveniently prepared by acyloin condensations followed by Clemmenson and Wolff-Kishner reductions (Scheme II). Thus, [10](1,4)naphthalenophane was prepared from dimethyl 1,4-naphthalenedivalerate (**20**) in 29% overall yield and [14](1,4)naphthalenophane was prepared from dimethyl 1,4-naphthalenediheptanoate (**22**) in 42% overall yield.[18]

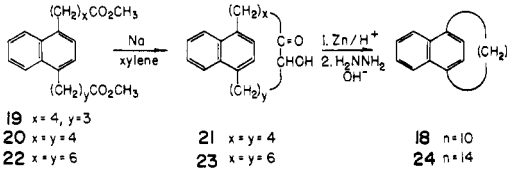
NMR Spectra of the [n](1,4)Naphthalenophanes. The NMR spectra of the [n](1,4)naphthalenophanes are summarized in Table I. The benzylic protons of the [8]-, [9]-, and [10]-(1,4)naphthalenophanes appear as two separate multiplets of two hydrogens each (δ 2.5 and 3.5), while those of [14](1,4)-naphthalenophane occur as a simple multiplet corresponding to four hydrogens (δ 3.0). These results can be accounted for by the increase in conformational mobility attended by an increase in the value of n. In the cases where n is relatively small (n = 8, 9, 10), the molecule is effectively frozen into either conformation **25** or **26**. In these cases the two benzylic protons H_a and H_b are considerably different and are seen as two separate peaks in the NMR spectrum. On the other hand, as the value of n increases (n = 14), the two conformers undergo

Table I. NMR Spectra of the [n](1,4)Naphthalenophanes[a,b]

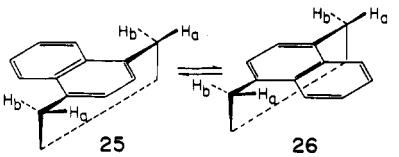
n			
8 (**14**)	9 (**17**)	10 (**18**)	14 (**24**)
−0.70 (2 H)	−0.36 (2 H)	−0.40 (2 H)	
0.30 (2 H)	0.32 (4 H)	0.60 (4 H)	
0.96 (4 H)	0.82 (4 H)	1.26 (8 H)	1.08 (20 H)
1.58 (4 H)	1.48 (4 H)	1.78 (2 H)	1.70 (4 H)
2.42 (2 H)	2.67 (2 H)	2.53 (2 H)	
3.50 (2 H)	3.46 (2 H)	3.52 (2 H)	3.02 (4 H)
7.01 (2 H)	7.02 (2 H)	7.03 (2 H)	7.04 (2 H)
7.26,	7.22,	7.30,	7.28,
7.82 (4 H)	7.82 (4 H)	7.87 (4 H)	7.90 (4 H)

[a] $CDCl_3$, δ (ppm). [b] For complete splitting information, see Experimental Section.

Scheme II



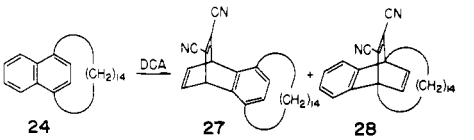
rapid interconversion on the NMR time scale and the four benzylic protons appear as an average of H_a and H_b.



Another interesting feature of the NMR spectra of these species is the drastic difference in the appearance of the various methylene protons. The smaller ring compounds show proton bands at relatively high field (δ −1 to +1), indicating, as expected, that some of the methylene groups are held over the aromatic ring and thereby subject to a diamagnetic shielding effect. In contrast, the methylene groups of [14](1,4)-naphthalenophane appear to be only slightly affected by the presence of the aromatic system.

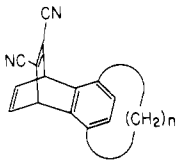
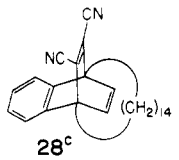
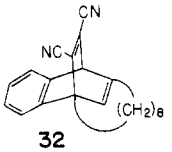
Finally, the aromatic region of the [n](1,4)naphthalenophanes is very characteristic. In all cases the four aromatic protons on the unsubstituted ring appear as an AA'BB' pattern (centered at δ 7.25 and 7.85), while the two aromatic protons on the substituted ring give a singlet (δ 7.0).

Diels-Alder Reactions of the [n](1,4)Naphthalenophanes with Dicyanoacetylene. The [n](1,4)naphthalenophanes were treated with an excess of dicyanoacetylene (DCA) at 100 °C for from 1 to 7 days. In the case of the [14](1,4)naphthalenophane, two 1:1 addition products were obtained which could be separated by high pressure liquid chromatography. The major product (54%) gave an NMR spectrum (Table II) which is consistent with adduct **27**, the product resulting from Diels-Alder addition to the unsubstituted ring. The NMR spectrum of this compound did not exhibit the AA'BB' pattern present in the starting material, but showed peaks corresponding to two bridgehead protons (δ 5.34), two olefinic protons (δ 6.82) and two aromatic protons (δ 6.64). The benzylic protons in **27** (δ 2.73, 4 H) imply that, as in the starting material (**24**), an average value of two conformations is being



observed. The second reaction product (7%) proved to be the desired paddlane (**28**), 2,3-dicyano-1,4-etheno-1,4-dihydro-

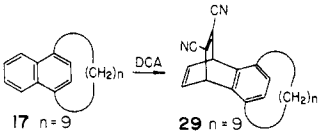
Table II. NMR Spectra of the Diels–Alder Adducts of the [*n*](1,4)Naphthalenophane and Dicyanoacetylene[a,b]

	n		
	8 (**31**)	10 (**30**)	14 (**27**)
(a) 	−0.40 (2 H)	−0.08 (2 H)	
	0.44 (2 H)		
	0.86 (4 H)	0.74 (4 H)	
	1.22 (2 H)	1.14 (8 H)	1.10 (20 H)
	1.70 (2 H)	1.80 (2 H)	1.60 (4 H)
	2.56 (2 H)	2.46 (2 H)	2.73 (4 H)
	3.08 (2 H)	3.09 (2 H)	
	5.36 (2 H)	5.33 (2 H)	5.34 (2 H)
	6.80 (2 H)	6.70 (2 H)	6.64 (2 H)
	6.94 (2 H)	6.88 (2 H)	6.82 (2 H)
(b)  **28**[c]	1.24 (20 H)		
	1.85 (4 H)		
	2.54 (4 H)		
	6.62 (2 H)		
	6.76, 6.97 (4 H)		
 **32**		1.46 (10 H)	
		2.30 (4 H)	
		2.69 (2 H)	
		4.79 (1 H)	
		6.56 (1 H)	
		7.02, 7.22 (4 H)	

[a] $CDCl_3$, δ (ppm). [b] For complete splitting information, see Experimental Section. [c] NMR of model system, the analogous Diels–Alder product from 1,4-dimethylnaphthalene and dicyanoacetylene (2,3-dicyano-1,4-etheno-1,4-dimethylnaphthalene (**10**)): δ 2.12 (6 H), 6.57 (2 H), 7.04, 7.24 (4 H). (See Experimental Section.)

1,4-tetradecanonaphthalene. The NMR spectrum (Table II) of this compound showed the AA′BB′ pattern intact. In addition, the two protons (δ 7.04) on the substituted aromatic ring in the starting material were shifted upfield (δ 6.62) in the product, consistent with the change in these protons from aromatic in **24** to olefinic in **28.**

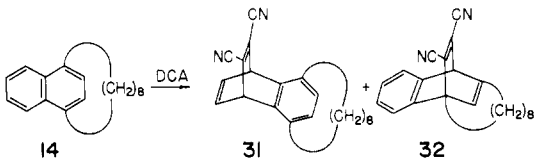
The [9]- and [10](1,4)naphthalenophanes gave none of the paddlane product, but rather dicyanoacetylene reacted exclusively at the unsubstituted ring. In both cases, the NMR spectrum (Table II) of the resultant 1:1 adduct confirms that addition occurred in the unsubstituted aromatic ring. The benzylic protons in **30** (δ 2.46 (2 H) and 3.09 (2 H) imply that



17 n = 9
18 n = 10
29 n = 9
30 n = 10

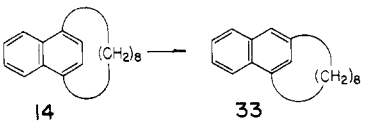
the conformers are frozen out on the NMR time scale, as in the case of the [8]-, [9]-, and [10](1,4)naphthalenophanes discussed previously.

The reaction of dicyanoacetylene with [8](1,4)naphthalenophane gave two 1:1 adducts. One product (**31**) (17%) resulted from addition to the unsubstituted ring and the second isomeric product (2%) had an NMR spectrum implying that rearrangement had occurred. The AA′BB′ pattern suggests that the unsubstituted ring had remained intact. The absence of upfield protons (δ −1 to +1) supports this argument since this



14 **31** **32**

implies that none of the aliphatic bridge protons are above an aromatic ring and therefore subject to diamagnetic shielding. This absence of upfield protons is in sharp contrast to the spectra of **14** and **31,** both of which contain an eight-membered polymethylene chain above an aromatic ring. The doublets at δ 4.79 (1 H, J = 2 Hz) and δ 6.56 (1 H, J = 2 Hz) in this minor product were shown by decoupling experiments to be coupled to one another. The chemical shifts of these doublets imply that one (δ 4.79) could be a bridgehead proton and the other (δ 6.56) an olefinic proton. Finally, the triplet at δ 2.69 (2 H, J = 7 Hz) indicates that two of the C_8 bridge hydrogens are attached to a carbon which bears no protons. Structure **32** accommodates all of the above spectral data. Such a product could result from a rearrangement of **14** to [8](1,3)naphthalenophane (**33**), a rearrangement known to occur in the paracyclophanes when a Friedel–Crafts catalyst or acid is present.[19] Since **33** has much less strain than **14,** it could easily react with dicyanoacetylene to yield the observed product.



14 **33**

Conclusions

The synthesis of a paddlane containing the general ring system in **1** has been accomplished. The conversion of the paddlane (**28**) into **1** would involve a series of straightforward transformations. This course, however, does not appear practical at this time because of the low yield obtained in the formation of **28.** In addition, the fact that **28** undergoes a rapid conformational change at room temperature implies that the compound is reasonably unstrained and therefore that the bicyclo[2.2.2]octane system is not distorted to any interesting extent. The Diels–Alder reaction of dicyanoacetylene with [12]naphthalenophane would, by analogy with the systems studied, be expected to give only a fraction of the low yield of desired adduct obtained in the case of [14]naphthalenophane. In contrast, the use of larger bridges would undoubtedly make the desired Diels–Alder addition more favorable. However, in such cases, the larger bridge would decrease the distortion in the paddlane to an even greater extent.

Experimental Section

Proton magnetic resonance spectra were recorded on a Jeolco MH-100 spectrometer. Deuteriochloroform containing 1% tetramethylsilane as internal standard was used as the solvent unless otherwise indicated. Infrared spectra were obtained on a Perkin-Elmer 237B spectrophotometer by using carbon tetrachloride as the solvent. Ultraviolet spectra were measured by using either a Shimadzu (Bausch and Lomb) spectronic 200 UV or a Beckman DB-G spectrophotometer with 95% ethanol as the solvent. The mass spectra were taken on a Hitachi Perkin-Elmer RMU-6 or an AEI Model MS-9 mass spectrometer. Vapor phase chromatography was accomplished by using a Varian Aerograph A-90-P gas chromatograph. The Waters' ALC/GPC-301 liquid chromatograph was used for the high pressure liquid chromatography separations. Melting points and boiling points are uncorrected.

[2.2](1,4)Naphthaleno(2,5)furanophane (12). Twelve liters of 2 N sodium hydroxide followed by 5 L of water was passed through a column containing 454 g of Amberlite IRA-400 anion-exchange resin. Then solutions of 150 g (0.51 mol) of (5-methyl-2-furfuryl)trimethylammonium iodide[20] in 450 mL of water and 150 g (0.56 mol) of (4-methyl-1-naphthylmethyl)trimethylammonium bromide[21] in 550 mL of water were passed through the column. The column was washed with 1500 mL of water and the combined salt solutions (about 2.5 L) were reduced in volume to 500 mL using a rotary evaporator and temperatures not exceeding 40 °C.

The aqueous solution of quaternary ammonium hydroxides was added dropwise with caution over 8 h to a stirred refluxing solution of 3 L of xylene and 1 g of phenothiazine. The reaction mixture was

heated to reflux an additional 12 h, cooled, and filtered. Xylene was removed from the mother liquor to give 71.0 g of crude product. To this product was added 200 mL of chloroform and 130 g of Celite and the chloroform was removed. The resulting powder was subjected to column chromatography (150 g of neutral alumina) by using hexane as the eluent to give 23.3 g (contained in the first 2 L of eluent) of product which consisted of 41% of [2.2](1,4)naphthaleno(2,5)furanophane (this corresponds to 9.8 g (87%) of the "cross" coupling product) and 59% of [2.2](2,5)furanophane.[22] This mixture of products was used directly in the next reaction.[23]

3,6-Diketo[8](1,4)naphthalenophane (13). The above mixture was heated to reflux with stirring for 18 h with 210 mL of glacial acetic acid, 100 mL of water, and 6 mL of 10% sulfuric acid. The reaction mixture was cooled, poured into 1 L of water, and extracted with chloroform. The combined chloroform extracts were washed with saturated sodium chloride, 5% sodium bicarbonate, and saturated sodium chloride and dried over magnesium sulfate. Removal of the solvent gave 24.8 g of crude product which was used directly in the next reaction.

Sublimation (135 °C at 0.04 mm) of a small sample of the crude diketone gave pure 3,6-diketo[8](1,4)naphthalenophane, mp 162–163 °C: NMR ($CDCl_3$), δ (ppm) 0.94 (2 H, m), 1.74 (2 H, m), 2.48 (4 H, m), 3.10 (2 H, m), 3.70 (2 H, m) 7.08 (2 H, s), 7.48 and 7.96 (4 H, AA'BB'); IR 1706 cm^{-1}; mass spectrum, *m/e* 266, 168, 153. Anal. ($C_{18}H_{18}O_2$) C, H.

[8](1,4)Napthalenophane (14). The crude product from the previous reaction (24.8 g) was heated to reflux overnight with 71 mL (1.2 mol) of 85% hydrazine hydrate, 500 mL of triethylene glycol and 27.8 g (0.5 mol) of potassium hydroxide. The reaction mixture was then heated to 190–220 °C for 6 h, cooled, and added to 500 mL of water. The product was taken up in methylene chloride, dried over magnesium sulfate, and concentrated to give 11.8 g of crude product. Alumina column chromatography of this product gave 8.5 g (90% from [2.2](1,4)naphthaleno(2,5)furanophane) of [8](1,4)naphthalenophane. NMR ($CDCl_3$) δ (ppm) −0.70 (2 H, bm), 0.30 (2 H, bm), 0.96 (4 H, bm), 1.58 (4 H, bm), 2.42 (2 H, m), 3.50 (2 H, m), 7.01 (2 H, s), 7.26 and 7.82 (4 H, AA'BB'); UV, 234 nm (ϵ 38 600), 292 nm (5160); mass spectrum, *m/e* 238, 167, 154, 141.

An analytical sample of pure [8](1,4)naphthalenophane was prepared by gas chromatography (10 ft × 0.25 in. Dexsil 300 GC (15%) on 60–80 Chromosorb W; column temperature, 270 °C). Anal. ($C_{18}H_{22}$) C, H.

[9](1,4)Naphthalenophane (17). According to the procedure of De-Boer and Backer,[24] 21.5 g (100 mol) of Diazald[25] in 100 mL of diethyl ether was added dropwise to a solution at 65 °C of 5.0 g (90 mmol) of potassium hydroxide, 8 mL of water, and 28 mL of 95% ethanol. The diazomethane generated (about 3 g, 70 mmol) was distilled into a stirred, ice-cold solution of 2.0 g (7.5 mmol) of 3,6-diketo[8]-(1,4)naphthalenophane in 40 mL of chloroform and 50 mL of 95% ethanol. Stirring was stopped and the reaction mixture was allowed to come to room temperature slowly. After 5 days at room temperature, the mass spectrum of a small aliquot of the solution indicated 68% starting material (*m/e* 266) and 32% of the product ring expanded by one methylene group (*m/e* 280).[26] Diazomethane (3 g, 70 mmol) was again added to the reaction mixture as above. After 5 more days of reaction, the mass spectrum indicated 37% starting material and 56% *m/e* 280. Another addition of diazomethane (3 g, 70 mmol) and reaction at room temperature for 5 days indicated 26% starting material, 63% of *m/e* 280 and 11% of *m/e* 294 (corresponding to the addition of two methylene groups to the starting diketone). Excess diazomethane was destroyed by dropwise addition of glacial acetic acid. Water was added and the layers were separated. The aqueous layer was neutralized with 5% sodium bicarbonate and then extracted with chloroform. The combined organic layers were washed with 5% sodium bicarbonate and saturated sodium chloride and dried over magnesium sulfate. Removal of solvent gave 3.0 g of crude product, a mixture of the homologous diketones.

The mixture of diketones (3.0 g) was subjected to the Wolff-Kishner reduction procedure used previously to give 2.15 g of crude product, a mixture of [8]-, [9]-, and [10](1,4)naphthalenophanes. The mixture of hydrocarbons was separated by gas chromatography (10 ft × 0.25 in. Dexsil 300 GC (15%) on 60–80 Chromosorb W; column temperature, 270 °C). The following retention times were observed for the[*n*](1,4)naphthalenophanes: *n* = 8, 12–15 min; *n* = 9, 18–22 min; *n* = 10, 24–28 min. Pure [9](1,4)naphthalenophane (0.20 g) was obtained by using the above procedure: NMR ($CDCl_3$) δ (ppm) −0.36 (2 H, m), 0.32 (4 H, m), 0.82 (4 H, m), 1.48 (4 H, m), 2.67 (2 H, m), 3.46 (2 H, m), 7.02 (2 H, s), 7.22 and 7.82 (4 H, AA'BB'); UV, 234 nm (ϵ 46 400), 296 nm (6200); mass spectrum, *m/e* 252, 154. Anal. ($C_{19}H_{24}$) C, H.

Methyl 5-[4-(3-Carbomethoxypropyl)-(1-naphthyl)]valerate (19). Naphthalene (108 g, 0.84 mol), γ-carbomethoxybutyryl chloride[27] (150 g, 0.84 mol), and 340 mL of carbon disulfide were added to a 300-mL three-necked round-bottomed flask equipped with a mechanical stirrer and a thermometer. A 250-mL Erlenmeyer flask containing 225 g (1.7 mol) of aluminum chloride was connected to the reaction vessel with Tygon tubing. The reaction mixture was cooled with stirring to −10 °C by using an ice-salt bath. The aluminum chloride was then added in portions to the reaction mixture over a period of 1 h, while the temperature was kept below +5 °C. After an additional 15 min of stirring at 0 °C, the reaction mixture was poured into 1 L of ice with manual stirring. Cold, concentrated hydrochloric acid (300 mL) was added and the mixture was extracted three times with methylene chloride (total volume, 2 L). The organic layers were washed with saturated sodium chloride, 5% sodium bicarbonate, and saturated sodium chloride and dried over anhydrous magnesium sulfate. After the solvent had been removed, 10% aqueous ethanolic sodium hydroxide (90 g sodium hydroxide in 100 mL of water and 750 mL of 95% ethanol) was added to the crude reaction product and the resulting mixture was heated to reflux for 6 h. Water (500 mL) was added and ethanol was removed by distillation. The aqueous solution was poured into a 2-L beaker and was cooled in an ice-salt bath. The solution was acidified with cold, concentrated hydrochloric acid and stirred an additional 30 min at ice-bath temperature. The water was decanted from the crude product, a yellow gum, which was then transferred to a 2-L round-bottomed flask using methylene chloride. Removal of the methylene chloride gave crude γ-(1-naphthoyl)butyric acid[28] (128 g, 63%) which was used directly in the next step.

The γ-(1-naphthoyl)butyric acid (128 g, 0.53 mol) was heated to reflux overnight with 380 mL (6.5 mol) of 85% hydrazine hydrate, 1300 mL of triethylene glycol, and 150 g (2.7 mol) of potassium hydroxide. The condenser was replaced with a distillation head and the reaction solution was heated to 190–220 °C for 6 h. After cooling, the mixture was poured into a separatory funnel containing 2 L of water. Extraction with methylene chloride followed by acidification of the aqueous layer gave a dark-brown oil which was dissolved in methylene chloride. The solution was dried over magnesium sulfate and the solvent was removed to give crude δ-(1-naphthyl)valeric acid (104 g, 86%).[28]

Esterification of the acid was accomplished by heating to reflux with 121 mL (98 g, 2.1 mol) of absolute ethanol, 400 mL of benzene, and 6.5 mL of concentrated sulfuric acid. A Dean-Stark trap was used to azeotrope water from the reaction. After 3 days of refluxing, the mixture was cooled, a mixture of 13 g of sodium carbonate in 200 mL of water was added and the organic solvents were removed by vacuum distillation. The aqueous solution was extracted with chloroform and the chloroform extracts were washed with saturated sodium chloride solution and dried over magnesium sulfate. Removal of the solvent and vacuum distillation of the crude product gave 88.1 g (41% from naphthalene) of pure ethyl δ-(1-naphthyl)valerate, bp 150–153 °C at 0.04 mm: NMR ($CDCl_3$) δ (ppm) 1.15 (3 H, t, J = 7 Hz), 1.68 (4 H, m), 2.24 (2 H, m), 2.96 (2 H, m), 4.02 (2 H, q, J = 7 Hz), 7.14–7.96 (7 H, m); IR, 1735 cm^{-1}; mass spectrum, *m/e* 256, 210, 141. Anal. ($C_{17}H_{20}O_2$) C, H.

Aluminum chloride (65.0 g, 0.49 mol) was added portionwise to 40.0 g (0.16 mol) of ethyl δ-(1-naphthyl)valerate, 17.2 g (0.17 mol) of succinic anhydride in 230 mL of 1,1,2,2-tetrachloroethane. After stirring for 3 days at room temperature, the reaction mixture was worked up as in the preparation of δ-oxo-1,4-naphthalenedivaleric acid to give crude keto diacid which was subjected to Wolff-Kishner reduction conditions to give crude 5-[4-(3-carboxypropyl)-(1-naphthyl)]valeric acid.

Esterification of the above diacid was accomplished by heating to reflux overnight with 41 mL of methanol, 54 mL of 1,2-dichloroethane, and 1 mL of concentrated sulfuric acid. Workup as before followed by column chromatography (150 g of neutral alumina) using benzene (2 L) as the eluent gave 36.4 g (68% yield from ethyl δ-(1-naphthyl)valerate) of pure methyl 5-[4-(3-carbomethoxypropyl)-(1-naphthyl)]valerate: NMR ($CDCl_3$), δ (ppm) 1.72 (6 H, m), 2.32 (4 H, m), 3.00 (4 H, m), 3.58 (6 H, s), 7.10 (2 H, s), 7.38 and 7.92 (4 H, AA'BB'); IR 1740 cm^{-1}; mass spectrum *m/e* 342.

An analytical sample of the dimethyl ester was prepared by gas

chromatography (2 ft × 0.25 in. Dexsil 300 GC (15%) on 60–80 Chromosorb W; column temperature, 245 °C). Anal. ($C_{21}H_{26}O_4$) C, H.

Attempted Preparation of [9](1,4)Naphthalenophane (17) via an Acyloin Condensation. Following the acyloin procedure used by Cram and Steinberg,[29] 25.0 g (73 mmol) of methyl 5-[4-(3-carbomethoxypropyl)-(1-naphthyl)]valerate in 250 mL of xylene was added over 48 h to 7.60 g (330 mmol) of sodium stirred at 8000 rpm in 700 mL of refluxing xylene. Workup of the reaction mixture gave 24.3 g of starting material. A second attempt was made, but again only starting material was recovered.

Dimethyl 1,4-Naphthalenedivalerate (20). Aluminum chloride (96.5 g, 0.72 mol) was added portionwise with stirring over 3 h to an ice-cold solution of 59.5 g (0.23 mol) of ethyl δ-(1-naphthyl)valerate, 41.4 g (0.23 mol) of γ-carbomethoxybutyryl chloride, and 175 mL of 1,1,2,2-tetrachloroethane. The mixture was stirred overnight at room temperature and then poured into ice containing 70 mL of cold, concentrated hydrochloric acid. The layers were separated and the aqueous layer was washed three times with methylene chloride. The combined organic layers were washed with saturated sodium chloride, 5% aqueous sodium bicarbonate, and saturated sodium chloride and dried over magnesium sulfate. Removal of the solvent gave an oil which was heated to reflux for 6 h with 100 mL of 10% sodium hydroxide in aqueous ethanol. Additional water was added and ethanol was distilled from the reaction solution. Acidification of the resulting aqueous solution gave crude δ-oxo-1,4-naphthalenedivaleric acid (68 g, 87%) which was used directly in the next step.

Recrystallization (three times from ethyl acetate) of a small sample of the crude keto diacid gave pure δ-oxo-1,4-naphthalenedivaleric acid, mp 152–153 °C. Anal. ($C_{20}H_{22}O_5$) C, H.

The δ-oxo-1,4-naphthalenedivaleric acid was heated to reflux overnight with 137 mL (2.3 mol) of 85% hydrazine hydrate, 67.2 g (1.2 mol) of potassium hydroxide, and 900 mL of triethylene glycol. The reaction temperature was then held at 190–220 °C for 6 h and worked up as in previous Wolff–Kishner reductions to give crude 1,4-naphthalenedivaleric acid (58.5 g, 89%).

A small sample of crude diacid was recrystallized four times from ethyl acetate to give pure 1,4-naphthalenedivaleric acid, mp 158–159 °C. Anal. ($C_{20}H_{24}O_4$) C, H.

The 1,4-naphthalenedivaleric acid (58.5 g, 0.18 mol) was heated to reflux overnight with 75 mL (59 g, 1.8 mol) of methanol, 100 mL of 1,2-dichloroethane, and 2 mL of concentrated sulfuric acid. Workup as before followed by column chromatography (300 g silica gel) of the crude dimethyl ester using benzene (2 L) as the eluent gave 54.3 g (66% from ethyl δ-(1-naphthyl)valerate) of pure dimethyl 1,4-naphthalenedivalerate: NMR ($CDCl_3$) δ (ppm) 1.72 (8 H, m), 2.32 (4 H, m), 3.04 (4 H, m), 3.64 (6 H, s), 7.06 (2 H, s), 7.32 and 7.94 (4 H, AA′BB′); IR 1745 cm^{-1}; mass spectrum, *m/e* 356.

An analytical sample of the dimethyl ester was prepared by gas chromatography (2 ft × 0.5 in. Dexsil 300 GC (15%) on 60–80 Chromosorb W; column temperature, 260 °C). Anal. ($C_{22}H_{28}O_4$) C, H.

[10](1,4)Naphthalenophane (18). Following the acyloin procedure used by Cram and Steinberg,[29] 25.4 g (70 mmol) of dimethyl 1,4-naphthalenedivalerate in 250 mL of pure dry xylene was added over 27 h to 7.20 g (310 mmol) of sodium stirred at 8000 rpm in 700 mL of refluxing xylene. The crude acyloin (13.3 g, 64%) was used without purification in the next step.

A stirred solution of 13.3 g (45 mmol) of the above crude acyloin in 18 mL of glacial acetic acid, 18 mL of concentrated hydrochloric acid, and 23.4 g of 80 mesh zinc was heated to reflux. Four 18-mL portions of hydrochloric acid were then added over 45-min intervals to the reaction mixture. After an additional hour of stirring, the reaction mixture was cooled, diluted with water, and extracted with ether. The ether extracts were washed with saturated sodium chloride, 5% sodium bicarbonate, and saturated sodium chloride and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave 10.6 g of crude product, a mixture of monoketone and hydrocarbon. This mixture was used directly in the following reaction.

The product (10.6 g) from the Clemmenson reduction was heated to reflux overnight in 10.6 mL (0.18 mol) of 85% hydrazine hydrate, 10.6 g (0.19 mol) of potassium hydroxide, and 106 mL of triethylene glycol. The reaction temperature was then maintained at 190–220 °C for 6 h. Workup as before gave 8.6 g of crude hydrocarbon which was subjected to column chromatography (100 g of alumina) using hexane (1 L) as the eluent to give 5.3 g (29% from the dimethyl ester) of pure [10](1,4)naphthalenophane: NMR ($CDCl_3$) δ (ppm) −0.40 (2 H, bm), 0.60 (4 H, m), 1.26 (8 H, bm), 1.78 (2 H, bm), 2.53 (2 H, m), 3.52 (2 H, m), 7.03 (2 H, s), 7.30 and 7.87 (4 H, AA′BB′); UV, 229.5 (ε 43 500), 282 (4650), 291 (4800), 300 nm (3250); mass spectrum, *m/e* 266, 167, 154, 141.

An analytical sample of [10](1,4)naphthalenophane was prepared by gas chromatography (2 ft × 0.25 in. Dexsil 300 GC (15%) on 60–80 Chromosorb W; column temperature, 250 °C).

Dimethyl 1,4-Naphthalenediheptanoate (22). 1,4-Naphthalenedivaleric acid (37.7 g, 0.12 mol) was added over 3 days by using a Soxhlet extractor to a stirred, refluxing mixture of 26.4 g (0.7 mol) of lithium aluminum hydride in 4 L of anhydrous diethyl ether. After heating to reflux an additional 2 days, excess lithium aluminum hydride was destroyed according to the procedure of Fieser and Fieser[30] by successive dropwise addition of 27 mL of water, 27 mL of 15% sodium hydroxide solution, and 81 mL of water. The granular precipitate was filtered and ether was evaporated from the resulting filtrate to give 26.4 g (75%) of crude 1,4-bis(5-hydroxypentyl)naphthalene, which was used directly in the next reaction.

Sulfuric acid (19.1 g, 11.5 mL, 0.2 mol) was added dropwise to a stirred solution of 1,4-bis(5-hydroxybutyl)naphthalene (26.4 g, 0.09 mol) in 60.8 g (41 mL, 0.36 mol) of 48% hydrobromic acid. After stirring overnight at room temperature, an additional 9 mL of sulfuric acid was added and the reaction mixture was heated to reflux for 10 h. The mixture was cooled, diluted with water, and extracted with ether. The ether extracts were washed with saturated ammonium chloride solution, 5% sodium bicarbonate and water, and dried over magnesium sulfate. Removal of the solvent gave 32.3 g of a viscous black oil to which was added 200 mL of methylene chloride and 45 g of Celite. Removal of the solvent gave a dark powder which was added to a column containing 60 g of Celite.[31] Elution with hexane (500 mL) gave 17.8 g (47%) of 1,4-bis(5-bromopentyl)naphthalene which was used directly in the next step.

Following the malonic ester reaction procedure of Cram and coworkers,[18] a mixture of 1,4-bis(5-bromopentyl)naphthalene (11.4 g, 27 mmol) and 5 mL of diethyl malonate was added dropwise over 30 min to a stirred refluxing solution containing 27.0 g (170 mmol) of diethyl malonate in 460 mL of absolute ethanol and 2.06 g (90 mmol) of sodium. After heating to reflux for 18 h, excess ethanol was removed by distillation and the resulting crude tetraester was heated to reflux for 3 h with 36.0 g (640 mmol) of potassium hydroxide in 180 mL of water. The mixture was cooled, acidified with 6 N sulfuric acid, extracted with ether and the ether solution was reextracted with 5% aqueous potassium hydroxide. The aqueous solution was acidified with 6 N sulfuric acid and extracted with ether. The ether extracts were washed with saturated aqueous sodium chloride and dried over magnesium sulfate. Ether was removed and the crude tetraacid was decarboxylated by heating to 180–200 °C for 3 h. The product was dissolved in ether; the ether extracts were washed with saturated sodium chloride and dried over magnesium sulfate. Removal of the solvent gave 10.4 g (100%) of crude 1,4-naphthalenediheptanoic acid.

The 1,4-naphthalenediheptanoic acid (10.4 g, 27 mmol) was heated to reflux overnight with 26 mL (20.5 g, 640 mmol) of methanol, 38 mL of 1,2-dichloroethane, and 1 mL of sulfuric acid. Workup as in previous esterifications gave 9.2 g of crude dimethyl ester which was subjected to column chromatography on alumina. Elution with benzene gave 6.1 g (55% yield from the dibromide) of pure dimethyl 1,4-naphthalenediheptanoate: NMR ($CDCl_3$) δ (ppm) 1.58 (16 H, bm), 2.28 (4 H, m), 2.98 (4 H, m), 3.60 (6 H, s), 7.12 (2 H, s) 7.38 and 7.92 (4 H, AA′BB′); IR 1745 cm^{-1}; mass spectrum, *m/e* 412.

An analytical sample of dimethyl 1,4-naphthalenediheptanoate was prepared by gas chromatography (2 ft × 0.25 in. Dexsil 300 GC (15%) on 60–80 Chromosorb W; column temperature, 280 °C). Anal. ($C_{26}H_{36}O_4$) C, H.

[14](1,4)Naphthalenophane (24). Following the procedure used to make [10](1,4)naphthalenophane, 6.1 g (14.8 mmol) of dimethyl 1,4-naphthalenediheptanoate in 250 mL of xylene was added dropwise over 43 h to a refluxing mixture of 700 mL of xylene and 2.25 g (98 mmol) of sodium stirred at 8000 rpm. The crude acyloin (6.1 g) was reduced by using Clemmenson and then Wolff–Kishner reduction conditions described before to give 6.1 g of crude hydrocarbon. Column chromatography (100 g alumina) of this crude product with hexane (1 L) gave 2.0 g (42% from the dimethyl ester) of pure [14](1,4)naphthalenophane: NMR ($CDCl_3$) δ (ppm) 1.08 (20 H, bm), 1.70 (4 H, bm), 3.02 (4 H, m), 7.04 (2 H, s), 7.28 and 7.90 (4 H,

AA'BB'); UV 229 (ε 46 000), 282 (4650), 290 (5450), 301 nm (3720); mass spectrum, *m/e* 322.

An analytical sample of [14](1,4)naphthalenophane was prepared by gas chromatography (2 ft × 0.25 in. Dexsil 300 GC (15%) on Chromosorb W; column temperature, 250 °C). Anal. Calcd for $C_{24}H_{34}$: *m/e* 322.2662. Found: 322.2619.

Standard Diels-Alder Reaction Conditions. The substrate (1-3 g) was placed in a 13 × 18 mm glass tube and an approximately equal volume of dicyanoacetylene[32] was bulb-to-bulb distilled into the glass tube at 0.03 mm. The contents of the glass tube were then allowed to slowly come to room temperature and the two reactants were mixed by gently agitating the tube. The tube was cooled in dry ice-acetone and then liquid nitrogen, removed from the vacuum line, and sealed while still evacuated. It was slowly warmed to room temperature and was then placed in a water bath which was heated to reflux. After the reaction was completed the tube was broken open and washed onto a short alumina column (50 g) with methylene chloride. Elution of the column with methylene chloride removed black polymeric material and gave relatively clean reaction product(s). Further purification of the reaction product(s) is described in the following paragraphs.

Diels-Alder Reaction of 1,4-Dimethylnaphthalene and Dicyanoacetylene. 1,4-Dimethylnaphthalene (1.5 g, 9.6 mmol) was treated with excess dicyanoacetylene at 100 °C for 24 h. Workup of the reaction product as described above gave 1.5 g of crude product which was subjected to column chromatography (100 g silica gel) by using benzene as the eluent (500 mL) to give 1.2 g (54%) of 2,3-dicyano-1,4-etheno-1,4-dimethylnaphthalene and then with 1 L of benzene, to give 0.30 g of a mixture of two parts of 2,3-dicyano-1,4-etheno-1,4-dimethylnaphthalene and one part of 6,7-dicyano-5,8-etheno-5,8-dihydro-1,4-dimethylnaphthalene. Further column chromatography and attempts at fractional recrystallization failed to separate this mixture to give pure 6,7-dicyano-5,8-etheno-5,8-dihydro-1,4-dimethylnaphthalene (4% yield by NMR).

The major chromatography fraction (1.2 g) was recrystallized from methanol to give pure 2,3-dicyano-1,4-etheno-1,4-dimethylnaphthalene, mp 163-164 °C: NMR ($CDCl_3$) δ (ppm) 2.12 (6 H, s), 6.57 (2 H, s), 7.04 and 7.24 (4 H, AA'BB'); UV 210 (ε 22 400), 236 (6600), 245 (sh) (5800), 282 (990), 312 nm (900); mass spectrum, *m/e* 232, 217, 190. Anal. ($C_{16}H_{12}N_2$) C, H.

Diels-Alder Reaction of [14](1,4)Naphthalenophane (24) and Dicyanoacetylene. [14](1,4)Naphthalenophane (0.6 g, 1.86 mmol) was treated with excess dicyanoacetylene for 7 days at 100 °C. Column chromatography (100 g neutral alumina) of the crude reaction product (1.1 g) with methylene chloride (2 L) gave 0.10 g of a mixture of the two possible 1:1 adducts. Further elution of the column (3 L of methylene chloride) gave 0.40 g of pure 6,7-dicyano-5,8-etheno-5,8-dihydro-1,4-tetradecanonaphthalene (**27**), mp 165-167 °C: NMR ($CDCl_3$) δ (ppm) 1.10 (20 H, m), 1.60 (4 H, m), 2.73 (4 H, m), 5.34 (2 H, m), 6.64 (2 H, s), 6.82 (2 H, m); UV, 212 (ε 18 800), 233 (sh) (5050), 244 (sh) (3900), 270 (sh) (750), 315 nm (700). Anal. Calcd for $C_{28}H_{34}N_2$: *m/e* 398.2724. Found: *m/e* 398.2736.

The mixture of 1:1 adducts (100 mg) was subjected to high-pressure liquid chromatography (2 ft × 1/8 in. neutral alumina column, 1% tetrahydrofuran in hexane) to give 26 mg of (**27**) and 53 mg (7%) of 17,18-dicyano-19,20-benzotricyclo[14.2.2.2^{1,16}]docosa-17,19,21-triene (**28**), mp 189-192 °C: NMR ($CDCl_3$) δ (ppm) 1.24 (20 H, m), 1.85 (4 H, sm), 2.54 (4 H, sm), 6.62 (2 H, s), 6.76 and 6.97 (4 H, AA'BB'); UV 205.5 (ε 28 300), 238 (8300), 248 (sh) (7600), 293 (1100), 320 (750). Anal. Calcd for $C_{28}H_{34}N_2$: *m/e* 398.2724. Found: *m/e* 398.2744.

Diels-Alder Reaction of [10](1,4)Naphthalenophane (18) and Dicyanoacetylene. [10](1,4)Naphthalenophane (2.0 g, 7.5 mmol) was treated with excess dicyanoacetylene for 96 h at 100 °C. Workup of the reaction product gave 3.25 g of crude product which was subjected to column chromatography (150 g neutral alumina). Elution with hexane (2 L) gave 0.5 g of [10](1,4)naphthalenophane. The column was then eluted with methylene chloride (3 L) to give 0.9 g (41% based on starting material consumed) of 1:1 adduct which was recrystallized from methanol to give pure 6,7-dicyano-5,8-etheno-5,8-dihydro-1,4-decanonaphthalene (**30**), mp 164-166 °C: NMR ($CDCl_3$) δ (ppm) −0.08 (2 H, m), 0.74 (4 H, m), 1.14 (8 H, bm), 1.80 (2 H, m), 2.46 (2 H, m), 3.09 (2 H, m), 5.33 (2 H, m), 6.70 (2 H, s), 6.88 (2 H, m); UV, 216.5 (ε 19 500), 235 (sh, 6200), 245 (sh, 4750), 270 (sh, 900), 320 nm (750); mass spectrum *m/e* 342, 227. Anal. ($C_{24}H_{26}N_2$) C, H.

Diels-Alder Reaction of [9](1,4)Naphthalenophane (17) and Dicyanoacetylene. [9](1,4)Naphthalenophane (163 mg, 0.64 mmol) was treated with excess dicyanoacetylene for 24 h at 100 °C. Workup gave 120 mg of a mixture of approximately equal parts of starting material and 6,7-dicyano-5,8-etheno-5,8-dihydro-1,4-nonanonaphthalene. The highest peak in the mass spectrum of this mixture, *m/e* 328, corresponds to a 1:1 adduct of [9](1,4)naphthalenophane and dicyanoacetylene. The NMR spectrum of the mixture showed, in addition to other peaks, two symmetrical multiplets of approximately equal intensity centered at δ 5.34 and 6.90. These peaks are characteristic of the 6,7-dicyano-5,8-ethano-5,8-dihydro-1,4-[*n*]methylene-bridged naphthalenes (see cases in this section where *n* = 8, 10, and 14). No further separation of this mixture was attempted.

Diels-Alder Reaction of [8](1,4)Naphthalenophane (14) and Dicyanoacetylene. [8](1,4)Naphthalenophane (4.0 g, 16.9 mmol) was treated with excess dicyanoacetylene for 72 h at 100 °C and worked up as before to give 1.25 g of crude product. Column chromatography (100 g neutral alumina) of this material using hexane (2 L) as the eluent gave 0.5 g of unreacted starting material. Elution with methylene chloride (2 L) gave 0.75 g (19% based on reacted hydrocarbon) of a mixture of two 1:1 adducts of hydrocarbon and dicyanoacetylene. This mixture was separated by using high pressure liquid chromatography (LC) (2 ft × 1/8 in. neutral column, 2.5% tetrahydrofuran in hexane) to give 0.15 g (2%) of a compound with spectral characteristics consistent with structure **32**: NMR ($CDCl_3$) δ (ppm) 1.46 (10 H, m), 2.30 (4 H, m), 2.69 (2 H, t, J = 7 Hz), 4.79 (1 H, d, J = 2 Hz), 6.56 (1 H, d, J = 2 Hz), 7.02 and 7.22 (4 H, AA'BB'). Decoupling demonstrated the doublets at δ 4.79 and 6.56 are coupled to each other: UV, 213 (ε 19 000), 241 (6200), 252 (sh, 5700), 285 (sh, 740), 331 nm (400); mass spectrum, *m/e* 314, 216. Anal. Calcd for $C_{22}H_{22}N_2$: *m/e* 314.1784. Found: *m/e* 314.1770.

In addition to the compound described above, LC of the crude reaction products (0.75 g) gave pure 6,7-dicyano-5,8-etheno-5,8-dihydro-1,4-octanonaphthalene (**31**) (0.60 g, 17%), mp 238-240 °C: NMR ($CDCl_3$) δ (ppm) −0.40 (2 H, m), 0.44 (2 H, m), 0.86 (4 H, m, 1.22 (2 H, m), 1.70 (2 H, m), 2.56 (2 H, m), 3.08 (2 H, m), 5.36 (2 H, sm), 6.80 (2 H, s), 6.94 (2 H, m); UV, 208 (sh, ε 29 200), 222 (24 400), 248 (sh, 5700), 270 (sh, 1150), 323 nm (308); mass spectrum, *m/e* 314, 230, 215, 203, 190. Anal. Calcd for $C_{22}H_{22}N_2$: *m/e* 314.1784. Found: *m/e* 314.1754.

References and Notes

(1) Taken in part from the Ph.D. thesis of M.J.O., 1973. Present address: Department of Chemistry, Indiana University-Purdue University at Indianapolis, Indianapolis, Ind. 46205.
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Stereochemistry of Electrophilic Attack on the Putative Carbanion Intermediate in the Base-Catalyzed Ketonization of 3,7-Dimethyltricyclo[3.3.0.0^{3,7}]octan-1-ol. Evidence against an S_E1 Mechanism for Ketonization

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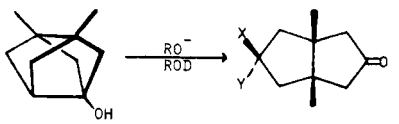
Abstract: The putative carbanion intermediate (**7**) in the base-catalyzed ketonization of 3,7-dimethyltricyclo[3.3.0.0^{3,7}]octan-1-ol (**1**) has been generated by oxidation of the epimeric hydrazines (**6**) in the presence of base. The hydrazines were synthesized by a five-step sequence starting from 1,5-dimethylbicyclo[3.3.0]octane-3,7-dione (**3**). From either epimer of **6** deuterium capture in D_2O and in $(CH_2OD)_2$ by the carbanion **7** is nearly stereorandom, and ketalization of the carbonyl group in **7** has little effect on this result. The nearly stereorandom electrophilic attack on **7** contrasts with the essentially stereospecific incorporation of deuterium in the base-catalyzed ketonization of **1** to **2a.** The retention of configuration observed in the ketonization of **1** and the contrasting stereorandom deuterium capture by **7** are both most economically accommodated by an S_E2 mechanism for the transformation of **1** to **2a,** although an S_E1 process is not totally excluded.

Several years ago we reported that the base-catalyzed ketonization of the tricyclic alcohol **1** gives only **2a** and that this



1 **2a**, X = H, Y = D; **b**, X = D, Y = H

stereochemical outcome is independent of the solvent in which the reaction is run.[1] Subsequent studies[2] have shown that retention of configuration is apparently a general result for the base-catalyzed ketonization of polycyclic alcohols that do not contain cyclopropanol rings.[3]

The stereochemical course of the ketonization of polycyclic alcohols like **1** stands in marked contrast to the results obtained by Cram and co-workers[4] with acyclic alcohols. They observed retention only in solvents of low dielectric constant (e.g., *tert*-butyl alcohol), while inversion predominated in solvents of high dielectric constant and with good proton-donating ability (e.g., ethylene glycol). An S_E1 mechanism, involving the formation of a carbanion intermediate, nicely rationalizes the dependence of stereochemistry on solvent found in Cram's studies.[4]

There are two alternative explanations for the stereochemistry observed in the base-catalyzed ketonization of **1.** (a) The mechanism is S_E1, but for some reason electrophilic attack on the putative carbanion intermediate (**7**) proceeds with retention of configuration, independent of solvent.[5] (b) The mechanism is S_E2 with retention being a consequence of the cyclic transition state that is expected to be favored for a concerted reaction of this type.[6] In order to differentiate between these two possibilities, we have generated the putative S_E1 intermediate by an independent route and determined the stereochemistry of deuterium capture by **7.**

Results

Cram and co-workers have shown that oxidation of 2-phenyl-2-butylhydrazine in the presence of base generates the 2-phenyl-2-butyl carbanion and that the stereochemistry of protonation roughly parallels that observed when the same carbanion is formed from an alcohol by base-catalyzed ketonization.[7] Stille and co-workers have used hydrazine oxidation in base to generate several bicyclic carbanions.[8] Therefore, we chose to synthesize the epimeric hydrazines **6** as the precursors of the carbanion **7.**

The hydrazines **6** were prepared from 1,5-dimethylbicyclo[3.3.0]octane-3,7-dione (**3**)[9] by the route shown in Scheme I. The diketone **3** was refluxed in benzene with 1.5 equiv of ethylene glycol and a catalytic amount of *p*-toluenesulfonic acid to give a mixture of **3** (7%), the desired monoketal (54%), and diketal (39%). Reduction of this mixture, followed by column chromatography on activity III basic alumina,[11] permitted the isolation of the epimeric hydroxyketals **4.** Partial separation of the slower moving **4a** from its *exo* isomer **4b** could be achieved, but only with inefficiency sufficient to render more practical the use of enriched mixtures in lieu of the pure epimers. With L-Selectride as the reducing agent, 88% epimerically pure **4a** could be obtained from **3** in 43% yield. Use of aluminum isopropoxide provided 73% epimerically pure **4b** in 27% yield. Since the diketal was recovered unchanged from these reductions and hydrolyzed back to **3** for recycling, the

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