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First Synthesis of Exomethylene Paracyclophanes and Their Structural Properties

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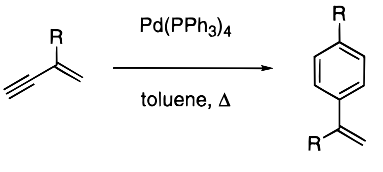
A series of novel exomethylene paracyclophanes was synthesized by the intramolecular benzannulation of conjugated enynes in the presence of tetrakis(triphenylphosphine)palladium(0). Detailed spectral studies revealed that the conformation of the exomethylene paracyclophanes depends on the size of the ring; the alkene moiety does not conjugate with the adjacent phenyl group in the smaller exomethylene paracyclophanes.

The study of macrocyclic compounds has expanded our view of chemistry. Many compounds such as cyclophanes, crown ethers, calixarenes, and metallacycles possess interesting properties in terms of molecular recognition, ion transportation, conformational analysis, and so on.[1] Paracyclophanes are among the first macrocyclic compounds investigated. Though paracyclophanes and their derivatives were first synthesized in 1950s[2] and since then several synthetic methods have been developed,[2−8] the preparation of these compounds is still not easy.

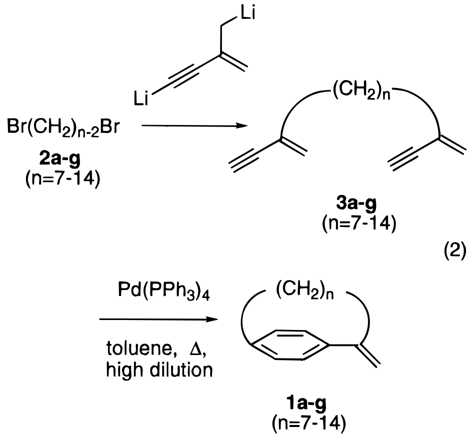
During our study of transition metal catalyzed reactions of enynes, we found that conjugated enynes cyclodimerize in the presence of Pd(0) catalysts (eq 1).[9] We applied this new reaction to the preparation of an exomethylene paracyclophane.[9] In this paper we report the first synthesis of a series of exomethylene paracyclophanes and their novel structural properties.



(1)

Results

Synthesis of New Exomethylene Paracyclophanes. We prepared new exomethylene paracyclophanes in two steps from commercially available compounds. Dibromoalkanes **2a**−**g** reacted with dilithiated 2-methyl-1-buten-3-yne to the corresponding bis-enynes **3a**−**g** in good yields.[10] The bis-enynes were converted, in the presence of $Pd(PPh_3)_4$ in dry toluene under highly diluted condition at 100 °C, to the corresponding exomethylene paracyclophanes **1a**−**g** (eq 2).



(2)

The yield of **1** depends on the concentration and the length of the carbon chain of **3** (Table 1). When the reaction of **3d** was carried out under concentrated condition (250 mM),[11] the product was mainly a mixture of dimers, trimers, and polymers. It was necessary to carry out the reaction of **3d** under a highly diluted condition to prevent the formation of cyclic dimers (entries 4−6). In the reaction of **3a**,**b** which have a shorter carbon chain, the formation of oligomeric compounds which were formed *via* intermolecular reactions could not be effectively avoided, and the yields of the monomeric compounds **1a**,**b** were low even under a highly diluted condition (2.5 mM, entries 1 and 2). On the other hand, the yields of paracyclophanes **1f**,**g**, which have longer carbon chains, were good (71%) even under a relatively

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(1) For a review, see *Cyclophane Chemistry*; Fögtle, J. P., Ed.; Wiley: Chichester, England, 1993.

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(11) This condition was originally used for the intermolecular cyclodimerization of conjugated enynes. See ref 9.

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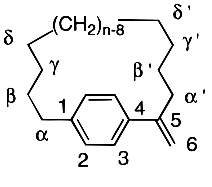
Table 1. Synthesis of Paracyclophanes 1a–g from 3a–g[a]

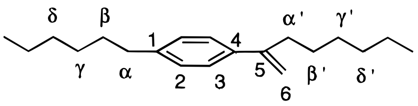
		reaction conditions				
entry	bis-enyne **3**	$Pd(PPh_3)_4$ (mmol)	toluene (mL)	time (min)	product **1**	isolated yield (%)
1	**3a** ($n = 7$)	0.2	200	20	**1a** ($n = 7$)	1.7
2	**3b** ($n = 8$)	0.2	200	30	**1b** ($n = 8$)	18
3	**3c** ($n = 9$)	0.2	200	15	**1c** ($n = 9$)	36
4	**3d** ($n = 10$)	0.2	200	15	**1d** ($n = 10$)	47
5		0.1	60	90		28[b,c]
6		0.1	20	60		7[b,d]
7	**3e** ($n = 11$)	0.2	200	15	**1e** ($n = 11$)	61
8		0.05	200	25		51
9	**3f** ($n = 12$)	0.2	100	15	**1f** ($n = 12$)	71
10		0.05	100	15		59
11	**3g** ($n = 14$)	0.2	100	10	**1g** ($n = 14$)	71
12		0.05	100	15		67

[a] A solution of bis-enyne **3** (0.5 mmol) and $Pd(PPh_3)_4$ in dry toluene was heated to 100 °C under Ar, unless otherwise noted. For detail, see Experimental Section. [b] The reaction was carried out at 80 °C. [c] An inseparable mixture of cyclic dimers ($M^+ = 484$) was obtained in 27% yield. [d] A mixture of cyclic dimers was obtained in 7% yield.

Table 2. ^1H NMR Spectroscopic Data of Paracyclophanes 1a–g and 5[a]



1



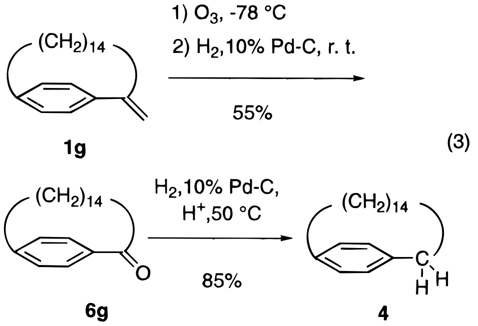
5

entry	compound	aromatic H	olefinic H	αCH_2	βCH_2	γCH_2	δCH_2	$\alpha' CH_2$	$\beta' CH_2$	$\gamma' CH_2$	$\delta' CH_2$	others
1	**1a** ($n = 7$)	7.24, 7.16	5.07, 4.94	2.65	1.32	0.84	−0.55	2.39	1.07	0.74	–	
2	**1b** ($n = 8$)	7.14[b]	4.97[b]	2.63	1.42	0.96	0.14	2.21	1.06	0.6[b]	0.6[b]	
3	**1c** ($n = 9$)	7.23, 7.16	5.21, 4.99	2.66	1.52	1.04	−0.14	2.55	1.28	0.91	0.7[b]	0.7[b]
4	**1d** ($n = 10$)	7.23, 7.15	5.07, 5.00	2.61	1.59	1.16	0.68[b]	2.47	1.40	0.90	0.82	0.66−0.71[b]
5	**1e** ($n = 11$)	7.25, 7.13	5.15, 5.00	2.62	1.56	*c*	*c*	2.56	1.32	*c*	*c*	0.7−1.2, 0.62
6	**1f** ($n = 12$)	7.26, 7.14	5.12, 4.99	2.64	1.68	*c*	*c*	2.56	1.33	*c*	*c*	0.9−1.2, 0.73
7	**1g** ($n = 14$)	7.29, 7.12	5.15, 4.99	2.65	1.66	*c*	*c*	2.53	1.32	*c*	*c*	1.0−1.2
8	**5**	7.32, 7.12	5.24, 5.00	2.59	1.61	*c*	*c*	2.47	1.44	*c*	*c*	1.0−1.2

[a] Assignments based on the decoupling experiments. [b] Overlapped signals. [c] Not assigned because of overlapping signals.

concentrated condition (5 mM, entries 9, 11).[12] The yield of **1g** did not decrease to a significant extent even in the presence of a smaller amount (10 mol %) of the catalyst (entry 12). As is the case in the intermolecular version of this reaction, no isomeric product (e.g. metacyclophane derivative) could be isolated in this reaction.

The structure of **1d** was confirmed by the chemical correlation to a known cyclophane. Thus, **1d** was converted to a known oxocyclophane (**6g**)[13] by ozonolysis. We also found that **6g** could be reduced to give [15]paracyclophane (eq 3).



^1H- and ^{13}C-NMR Spectra of 1a–g. The structure of the exomethylene paracyclophanes **1** was first investigated by means of NMR spectroscopy.

^1H NMR chemical shifts of **1a–g** and an acyclic compound (**5**)[9] are shown in Table 2.

Compared to the chemical shifts of the acyclic analog **5**, the signals of some methylene protons (βCH_2–δCH_2, $\beta' CH_2$–$\delta' CH_2$) of **1a–d** shifted to higher fields. The chemical shift of δCH_2 was especially sensitive to the size of the ring of **1**, and the difference of the chemical shift of δCH_2 was very large; the difference of the chemical shift between the δCH_2 of **1a** and that of **1g** was more than 1.5 ppm. The difference between the chemical shifts of methylene protons of **1e–1g** was small. The signals of δCH_2 methylenes shifted to the highest field in the spectra of **1a–d** (entries 1–4).[14] The chemical shifts of the methylene proton, appearing at the highest field, of each exomethylene paracyclophane are shown in Table 3.

The value of the chemical shifts increased in the following order; **1g** > **1f** > **1e** > **1d** > **1b** > **1c** > **1a**. This order correlated with the length of the carbon chain with the notable exception of **1c** ($n = 9$). The signals of **1** shifted to the higher fields compared to those of the corresponding [*n*]paracyclophanes.

The difference between ^{13}C NMR chemical shifts of **1a–g** was less distinct than that between the ^1H NMR

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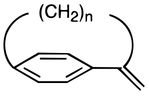
[12] A modified procedure slightly improved the yield of **1g**. Gevorgyan, V.; Tsuboya, N.; Saito, S.; Yamamoto, Y. Unpublished results.

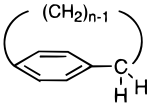
[13] Han, H.; Lei, X.; Turro, N. J. *J. Org. Chem.* **1991**, *56*, 2927–2930.

[14] This result is in accordance with the data of [*n*]paracyclophanes reported by Misumi *et al.* See ref 7c.

Table 3. ^{1}H NMR Chemical Shift of Methylene Proton in the Highest Field



1a-g
(n=7-14)



[n]Paracyclophanes

compound	chemical shift (ppm)	compound	chemical shift (ppm)
	–	[7]paracyclophane	−0.3 to −0.9[a]
1a ($n = 7$)	−0.55	[8]faracyclophane	0.19[b]
1b ($n = 8$)	0.14	[9]paracyclophane	0.33[b]
1c ($n = 9$)	−0.14	[10]paracyclophane	0.48[b]
1d ($n = 10$)	0.68	[11]paracyclophane	0.68[b]
1e ($n = 11$)	0.62	[12]paracyclophane	0.78[b]
1f ($n = 12$)	0.73		c
1g ($n = 14$)	1.04	[15]paracyclophane (**4**)	1.1[d]

[a] Reference 4b. [b] Reference 7b. [c] No data. [d] This work.

chemical shifts (Table 4). However, there is a small difference between ^{13}C NMR chemical shifts of **1a**,**b** and **1c**−**g**; the chemical shifts of C-5 and C-6 of **1a**,**b** are different (1−3 ppm) from those of **1c**−**g**.

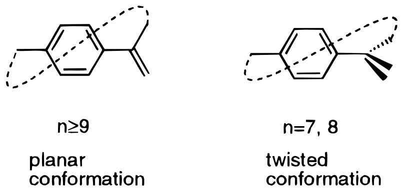
IR Spectra. The observation of the IR spectra gave us further information concerning the structure of these paracyclophanes. The olefin C=C stretching frequencies of **1a**−**g** are listed in Table 5. The $\upsilon_{C=C}$ of **1c**−**g** (1625−1629 cm^{-1}) were in accordance with the $\upsilon_{C=C}$ (1625 cm^{-1}) of alkenes conjugated with aromatic ring. This value is also in accordance with $\upsilon_{C=C}$ (1624 cm^{-1}) of an acyclic compound **5**. On the other hand, the $\upsilon_{C=C}$ of **1a**,**b** was different from the $\upsilon_{C=C}$ of **1c**−**g**. Especially the $\upsilon_{C=C}$ of **1b** (1643 cm^{-1}) was significantly different from other compounds, and the frequency was close to that of nonconjugated alkenes (1650 cm^{-1}).

UV-vis Spectra. UV-vis spectral data of **1a**−**g** and **5** are listed in Table 6. The spectral data of **6a**−**g** and **7**[7a,f] are also listed. The UV-vis spectra of the paracyclophanes **1a**,**b** were again different from that of **1c**−**g**. A hypochromic effect was observed in the UV-vis spectra of **1a**, and a hypsochromic shift and a hypochromic effect are observed in the UV-vis spectra of **1b**. The UV-vis spectra of other cyclophanes **1c**−**g** were similar to that of a 1,4-disubstituted benzene **5**.

Discussion

Though [*n*]paracyclophanes and the derivatives are attractive compounds for organic chemists, the preparation of them was not easy.[2−8] Multistep synthesis is usually required for the preparation of the compounds. We found that the benzannulation provided a new efficient method for the synthesis of paracyclophanes.[9] Paracyclophane skeleton was prepared only in two steps from commercially available compounds. It is noteworthy that the yield of the ring-forming reaction of **1b** (18%) was much higher compared to the yield (2.3%) of oxocyclophane **6b** which was synthesized by intramolecular Friedel−Crafts acylation.[7a] In contrast to the result that oxocyclophane **6a** could not be isolated by the intramolecular Friedel−Crafts acylation of the corresponding precursor,[7a] we succeeded in the synthesis of a cyclophane **1a** ($n = 7$) as a chemically stable compound, though the yield was 1.7%. The improved yields may be explained in terms of the extent of the strain in the transition state of the reaction: the rigid aromatic ring which is included in the precursors of **6a**,**b** would lead to the lower yields of **6a**,**b**, while such an unfavorable structure is not included in the precursors **3a**,**b** and the aromatization and cyclization take place at once. Though we expected that isomeric metacyclophane might be isolated in the reaction of bis-enynes which have a shorter carbon chain, we could not isolate any isomeric compound from the reaction mixture. This result indicates that the mode of addition is strictly controlled to give 1,4-disubstituted compounds exclusively.[9]

Further investigation revealed that exomethylene paracyclophanes have interesting properties. The comparison of IR and UV-vis spectra of **1a**−**g** indicates that the conformation of **1a**,**b** is different from that of other cyclophanes **1c**−**g** and an acyclic compound **5**. Different olefin C=C stretching frequencies in the IR spectrum, and a hypsochromic shift (blue shift) and hypochromic effect in the UV-vis spectrum of **1b** were best understood in terms of the *non*conjugated alkene moiety. Thus, the dihedral angle between the olefinic moiety and the benzene ring is close to 0° (coplanar) in cyclophanes **1c**−**g** and **5** in order to maximize the stabilization energy obtained by conjugation, while the dihedral angle is not 0° in paracyclophane **1b**; **1b** adopt a twisted conformation in order to minimize the strain energy caused by the shorter carbon chain at the expense of conjugation energy. The results are in accordance with the data reported by Huisgen *et al.*, who have also proposed a twisted conformation for an oxocyclophane **6b** based only on the UV-vis spectrum of the compound (Table 6).[7a]



While we successfully carried out the preparation of **1a** as the smallest cyclic compound in our study, the spectral behavior was rather confusing. Though the

Table 4. ^{13}C NMR Spectroscopic Data of Paracyclophanes 1a−g and 5[a]

entry	compound	C-1, C-4	C-2, C-3	C-5	C-6	others
1	**1a** ($n = 7$)	141.1, 140.7	129.4, 129.3	152.6	108.8	40.8, 36.0, 31.6, 30.7, 29.7, 28.3, 26.6
2	**1b** ($n = 8$)	140.7, 140.4	129.4, 129.0	152.7	109.0	37.3, 35.6, 30.0, 28.1, 28.0, 26.4, 25.3, 24.1
3	**1c** ($n = 9$)	140.7, 138.8	128.9, 128.3	149.8	111.3	36.2, 34.9, 29.5, 27.8, 27.3, 27.1, 26.8, 25.1, 24.2
4	**1d** ($n = 10$)	141.2, 141.0	129.1, 127.5	151.8	111.7	35.8, 34.9, 29.3, 29.2, 28.8, 27.8, 27.1, 26.9, 26.7, 25.3
5	**1e** ($n = 11$)	141.7, 139.2	128.9, 127.1	150.2	111.9	35.5, 35.4, 29.3, 28.1, 27.3, 27.24, 27.17, 27.1, 26.6, 26.1, 25.1
6	**1f** ($n = 12$)	141.5, 138.9	128.7, 126.7	149.9	112.1	35.5, 29.4, 28.7, 28.0, 27.72, 27.67, 27.1, 26.7, 26.5, 26.3[b]
7	**1g** ($n = 14$)	141.1, 138.5	128.6, 126.2	149.4	112.0	35.9, 34.7, 29.7, 29.3, 28.3, 28.1, 27.8, 27.7, 27.58, 27.55, 27.3, 26.3[b]
8	**5**	142.0, 138.7	128.2, 125.9	148.5	111.1	35.6, 35.3, 31.73, 31.66, 31.4, 29.1, 29.0, 28.3, 22.62, 22.60, 14.09, 14.07

[a] Assignments are based on proton decoupling and C−H COSY experiments. [b] Overlapped signals.

Table 5. IR Spectral Data for the Paracyclophanes 1a−g and 5

entry	compound	$\nu_{C=C}$ (cm^{-1})
1	**1a** (*n* = 7)	1636
2	**1b** (*n* = 8)	1643
3	**1c** (*n* = 9)	1626
4	**1d** (*n* = 10)	1629
5	**1e** (*n* = 11)	1626
6	**1f** (*n* = 12)	1625
7	**1g** (*n* = 14)	1626
8	**5**	1624

spectral difference between **1a** and **1c**−**g** was less distinct than that between **1b** and **1c**−**g**, we assume that the conformation of **1a** is similar to that of **1b**, because **1a** should be more strained. This assumption is supported by the similarity between the ^{13}C NMR spectra of **1a** and **1b**. In the case of **1a**, the strain energy may be partially released by the deformation of the benzene ring which makes the dihedral angle between olefin and benzene ring closer to 0° compared to that of **1b**. The hypsochromic effect which should be observed in the UV-vis spectra of **1a** will be partially canceled out by the bathochromic shift (red shift) which is caused by the deformation of the benzene ring.[15]

The conformational difference is also reflected in the ^{1}H NMR spectra of **1**. Except for the chemical shifts of **1c**, the signals of the methylene protons moved to the higher field when the number of methylene group was smaller. This phenomena could easily be interpreted in terms of the deshielding effect of the aromatic ring, which becomes stronger when the distance between the methylene group and the benzene ring becomes shorter. Comparison of the chemical shifts of **1** with that of [*n*]-paracyclophanes indicates that the distance between the methylene group and the benzene ring is somewhat shorter than that of the corresponding unsubstituted paracyclophane (Table 3). The difference of the chemical shifts could be explained in terms of the different conformation caused by conjugation. Thus, the alkene moiety and the benzene ring are coplanar in case of substituted paracyclophanes **1c**−**g**, which makes the distance between the methylene group and the benzene ring shorter. The exceptional *low field shift* (compared to **1c**) of the signals of the methylene proton of **1b** could be explained in terms of the conformational difference which resulted in the longer distance between the methylene group and the benzene ring of **1b** compared to that of **1c**; unlike conjugated paracyclophanes, nonconjugated paracyclophanes will definitely adopt a conformation which have a longer distance between the two groups. However, the distance between the methylene group and the benzene ring will still be shorter compared to the corresponding [*n*]paracyclophanes, since the bond angle of an sp^2 carbon is larger than that of an sp^3 carbon; the larger bond angle will "pull" the carbon chain to the benzene ring and make the distance between the two groups shorter. Therefore the high field shifts (compared to [*n*]paracyclophanes) of the signals of the methylene protons of **1a**,**b** were observed. The chemical shift of **1a** (−0.55 ppm) is comparable to that of [7]paracyclophane (−0.3 to −0.9 ppm),[7b] indicating the short distance between the methylene group and the benzene ring; cyclophane **1a** will be as strained as [7]paracyclophane.

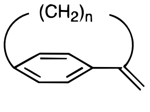
Conclusion

We efficiently prepared a series of exomethylene paracyclophanes by the intramolecular benzannulation of conjugated enynes. We examined the spectral data of the exomethylene paracyclophanes and found that the conformation of the paracyclophanes depends on the size of the ring; the alkene moiety does not conjugate with the adjacent phenyl group in the smaller exomethylene paracyclophanes.

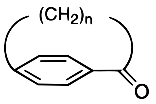
Experimental Section

2-Methyl-1-buten-3-yne was commercially available (Aldrich or Farchan) and purified by distillation prior to use. Tetrakis(triphenylphosphine)palladium(0) was prepared by the reduction of PdCl$_2$ with hydrazine hydrate in DMSO in the presence of triphenylphosphine under N$_2$[16] and stored under N$_2$ in sealed ampules at 4 °C. Commercially available n-BuLi in hexane, dry THF, dry toluene (Kanto Chemical Co., Japan), and tBuOK in dry THF (Aldrich) were used as the solvents and reagents. Bis-enynes **3a**−**g** were synthesized by the reaction of dilithiated 2-methyl-1-buten-3-yne with the corresponding dibromoalkanes.[10] All other reagents are commercially available and were used without further purification.

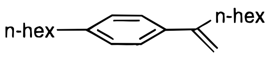
Table 6. UV-vis Spectral Data for 1a−g, 5, 6b−f, and 7[a]



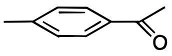
1a-g
(n=7-14)



6a-g
(n=7-14)



5



7

entry	compound	λ_{max} (nm)	ϵ	compound	λ_{max} (nm)	ϵ
1	**1a** (*n* = 7)	243	10000	**6a** (*n* = 7)	*b*	*b*
2	**1b** (*n* = 8)	232	9920	**6b** (*n* = 8)	250[c]	6600
3	**1c** (*n* = 9)	245	12600	**6c** (*n* = 9)	255[c]	11800
4	**1d** (*n* = 10)	240	11800	**6d** (*n* = 10)	255[c]	12400
5	**1e** (*n* = 11)	243	13000	**6e** (*n* = 11)	255[c]	13200
6	**1f** (*n* = 12)	243	12900	**6f** (*n* = 12)	256[c]	13900
7	**1g** (*n* = 14)	244	12800	**6g** (*n* = 14)	251[d]	15000
8	**5**	246	12800	**7**	253[c]	14700

[a] *n*-Hexane was used as the solvent, unless otherwise noted. [b] No data. [c] Reference 7a (solvent EtOH). [d] Reference 7f .

Synthesis of 3a−g. Representative Procedure. To a mixture of 2-methyl-1-buten-3-yne (3.8 mL, 40 mmol) and dry THF (5 mL) were successively added 1.57 M n-BuLi in hexane (57 mL, 90 mmol) and 1.0 M tBuOK (90 mL, 90 mmol) in THF at −80 °C under the flow of N_2. After an additional 30 min at −80 °C, the temperature was allowed fo rise to 5 °C, and the mixture was stirred at this temperature for 10 min. To the mixture was added a solution of anhydrous LiBr (7.82 g, 90 mmol) in dry THF (30 mL) at −20 °C, and the mixture was stirred for 10 min at −20 °C. The mixture was cooled to −70 °C, followed by the addition of 1,8-dibromooctane (18 mmol, 4.90 g) in dry THF (5 mL). The temperature of the mixture was kept at −70 °C for 15 min, and it was allowed to rise to 10 °C. The work up was carried out by adding 50 mL of saturated aqueous NH_4Cl to the mixture at −40 °C. The mixture was extracted with 200 mL of hexane, and the organic layer was separated, washed with brine, dried over $MgSO_4$, and evaporated to give the crude product **3d** as a yellow oil. The preparation of other bis-enynes **3** was also based on this procedure, and the products were purified by distillation or column chromatography. The yields were in range of 50−90%.

3,11-Bis(methylene)-1,12-tridecadiyne (3a): colorless oil; bp 70 °C/0.25 mmHg (Kugelrohr distillation); IR (neat) 3296(s), 3095(m), 2930(s), 2856(s), 2098(w), 1611(s), 1466(m), 1437(m), 1271(m), 905(s), 721(w), 638(m), 613(m) cm^{-1}; ^{1}H NMR (270 MHz) δ 5.40 (m, 2H), 5.28 (d, 2H, 1.9 Hz), 2.87 (s, 2H), 2.15 (t, 4H, 7.5 Hz), 1.53 (m, 4H), 1.31 (m, 6H). Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 90.19; H, 9.94.

3,12-Bis(methylene)-1,13-tetradecadiyne (3b): colorless oil; bp 88 °C/0.45 mmHg; IR (neat) 3297(s), 3096(m), 2929(s), 2856(s), 2099(w), 1610(m), 1466(m), 1437(m), 1272(m), 903(s), 721(w), 638(s), 613(s) cm^{-1}; ^{1}H NMR (270 MHz) δ 5.41 (d, 2H, 1.8 Hz), 5.28 (d, 2H, 1.5 Hz), 2.87 (s, 2H), 2.15 (t, 4H, 7.5 Hz), 1.52 (m, 4H), 1.30 (brs, 8H); HRMS (EI) calcd for $C_{16}H_{22}$ 214.1722, found 214.1722.

3,13-Bis(methylene)-1,14-pentadecadiyne (3c): colorless oil; IR (neat) 3297(s), 3096(w), 2928(s), 2855(s), 2098(w), 1813(w), 1611(m), 1466(m), 1439(m), 1394(w), 1269(m), 1090(w), 903(s), 721(w), 637(m), 611(m) cm^{-1}; ^{1}H NMR (270 MHz) δ 5.40 (s, 2H), 5.28 (s, 2H), 2.87 (s, 2H), 2.15 (t, 4H, 7.3 Hz), 1.52 (m, 4H), 1.29 (brs, 10H). Anal. Calcd for $C_{17}H_{24}$: C, 89.41; H, 10.59. Found: C, 89.21; H, 10.78. HRMS (EI) calcd for $C_{17}H_{24}$ 228.1876, found 228.1886.

3,14-Bis(methylene)-1,15-hexadecadiyne (3d): colorless oil; bp 118−119 °C/0.9 mmHg (partial polymerization); IR (neat) 3297(s), 3096(m), 2926(s), 2855(s), 2099(w), 1812(m), 1611(s), 1466(s), 1434(s), 1394(m), 1270(s), 904(s), 721(s), 637(s), 612(s), 549(m) cm^{-1}; ^{1}H NMR (270 MHz) δ 5.40 (s, 2H), 5.28 (s, 2H), 2.87 (s, 2H), 2.15 (t, 4H, 7.5 Hz), 1.5 (m, 4H), 1.3 (brs, 12H); HRMS (EI) calcd for $C_{18}H_{26}$ 242.2035, found 242.2047.

3,15-Bis(methylene)-1,16-heptadecadiyne (3e): colorless oil; IR (neat) 3298(s), 3096(w), 2926(s), 2855(s), 2098(w), 1610(m), 1466(m), 1437(w), 1394(w), 1271(w), 903(s), 721(w), 665(m), 637(s), 611(s) cm^{-1}; ^{1}H NMR (270 MHz) δ 5.40 (d, 2H, 1.8 Hz), 5.28 (d, 2H, 1.8 Hz), 2.87 (s, 2H), 2.15 (t, 4H, 7.5 Hz), 1.52 (m, 4H), 1.27 (bs, 14H). Anal. Calcd for $C_{19}H_{28}$: C, 88.99; H, 11.01. Found: C, 89.13; H, 11.22. HRMS (EI) calcd for $C_{19}H_{28}$ 256.2188, found 256.2183.

3,16-Bis(methylene)-1,17-octadecadiyne (3f): colorless oil; IR (neat) 3298(s), 3095(w), 2925(s), 2854(s), 2100(w), 1654(w), 1610(m), 1465(m), 1394(m), 1369(w), 1269(w), 902(s), 721(w), 638(m), 611(m) cm^{-1}; ^{1}H NMR (270 MHz) δ 5.40 (s, 2H), 5.28 (s, 2H), 2.86 (s, 2H), 2.15 (t, 4H, 7.5 Hz), 1.53 (m, 4H), 1.27 (m, 16H). Anal. Calcd for $C_{20}H_{30}$: C, 88.82; H, 11.18. Found: C, 88.61; H, 11.18. HRMS (EI) calcd for $C_{20}H_{30}$ 270.2347, found 270.2339.

3,18-Bis(methylene)-1,19-icosadiyne (3g): colorless oil; IR (neat) 3283(s), 3273(s), 2918(s), 2893(s), 2848(s), 2098(w), 1842(w), 1611(m), 1474(m), 1464(m), 1421(m), 1396(w), 1329(w), 1207(w), 916(s), 908(m), 817(w), 729(w), 719(w), 665(m), 646(m) cm^{-1}; ^{1}H NMR (270 MHz) δ 5.40 (d, 2H, 1.5 Hz), 5.28 (d, 2H, 1.1 Hz), 2.87 (s, 2H), 2.15 (t, 4H, 7.5 Hz), 1.49 (m, 4H), 1.26 (m, 20H). HRMS (EI) calcd for $C_{22}H_{34}$ 298.2658, found 298.2647.

Intramolecular Benzannulation of Bis-Enyne 3a−g. Representative Procedure. To a solution of $Pd(PPh_3)_4$ (231 mg, 0.2 mmol) in dry toluene (190 mL) was added **3d** (121 mg, 0.5 mmol) in dry toluene (10 mL) at room temperature under Ar. The yellow solution was heated to 100 °C for 15 min. The solvent was removed under reduced pressure, and the residue was passed through a short column of aluminum oxide using hexane as an eluent to remove the catalyst. The resulting solution was condensed, and the residue was purified by silica gel column chromatography with hexane to give **1d** (57 mg, 47%) as a colorless oil. The product was further purified by distillation. The procedure for the preparation of other cyclophanes (**1a−g**) was similar to the procedure decribed above, except for the amounts of the cataylst, solvent, and/or the temperature (see Table 1).

2-Methylenebicyclo[8.2.2]tetradeca-10,12,13-triene (1a): colorless oil; bp 60 °C/1.5 mmHg (molecular distillation); UV-vis see Table 6; IR (neat) 3074(w), 2926(s), 2855(s), 1636(m), 1508(m), 1462(m), 1438(m), 1115(s), 941(w), 891(m), 868(w), 818(m), 743(w), 617(w), 556(w) cm^{-1}; ^{1}H NMR (600 MHz) δ 7.24 (d, 2H, 8.2 Hz), 7.16 (d, 2H, 8.1 Hz), 5.07 (d, 1H, 2.2 Hz), 4.94 (m, 1H), 2.65 (t, 2H, 6.4 Hz), 2.39 (m, 2H), 1.32 (m, 2H), 1.07 (m, 2H), 0.84 (m, 2H), 0.74 (m, 4H), −0.55 (m, 2H). ^{13}C NMR (150.9 MHz) see Table 4. Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.91; H, 10.27. HRMS (EI) calcd for $C_{15}H_{20}$ 200.1564, found 200.1563.

2-Methylenebicyclo[9.2.2]pentadeca-11,13,14-triene (1b): colorless oil; bp 35−40 °C/0.5 mmHg (molecular distillation); UV-vis see Table 6; IR (neat) 3074(w), 2979(w), 2927(s), 2856(s), 1643(m), 1502(m), 1460(m), 1109(w), 893(m), 860(w), 840(w), 817(m), 750(w), 709(w), 615(w), 561(w) cm^{-1}; ^{1}H NMR (600 MHz) δ 7.14 (m, 4H), 4.97 (m, 2H), 2.63 (t, 2H, 6.3 Hz), 2.21 (t, 2H, 5.8 Hz), 1.42 (quint, 2H, 6.0 Hz), 1.06 (m, 2H), 0.96 (m, 2H), 0.59−0.67 (m, 4H), 0.14 (quint, 2H, 7.2 Hz); ^{13}C NMR (150.9 MHz) see Table 4. Anal. Calcd for $C_{16}H_{22}$: C, 89.66; H, 10.35. Found: C, 89.76; H, 10.64. HRMS (EI) calcd for $C_{16}H_{22}$ 214.1720, found 214.1713.

2-Methylenebicyclo[10.2.2]hexadeca-12,14,15-triene (1c): colorless oil; bp 45 °C/0.3 mmHg (molecular distillation); UV-vis see Table 6; IR (neat) 3076(w), 2924(s), 2855(s), 1626(m), 1560(m), 1508(m), 1456(m), 1016(w), 893(m), 831(m), 785(w), 750(w), 694(w), 605(w) cm^{-1}; ^{1}H NMR (600 MHz) δ 7.23 (d, 2H, 8.1 Hz), 7.16 (d, 2H, 8.1 Hz), 5.206(m, 2H), 4.996 (m, 2H), 2.66 (t, 2H, 6.3 Hz), 2.55 (t, 2H, 6.2 Hz), 1.52 (m, 2H), 1.25 (m, 2H), 1.04 (m, 2H), 0.91 (quint, 2H, 6.2 Hz), 0.71−0.78 (m, 4H), −0.14 (m, 2H); ^{13}C NMR (150.9 MHz) see Table 4. Anal. Calcd for $C_{17}H_{24}$: C, 89.41; H, 10.59. Found: C, 89.23; H, 10.72. HRMS (EI) calcd for $C_{17}H_{24}$ 228.1877, found 228.1880.

2-Methylenebicyclo[11.2.2]heptadeca-13,15,16-triene (1d): colorless oil; bp 95 °C/0.3 mmHg (molecular distillation); UV-vis see Table 6; IR (neat) 3076(w), 3020(w), 2928(s), 2855(s), 1628(m), 1510(m), 1460(m), 1444(m), 893(m), 829(m), 665(m) cm^{-1}; ^{1}H NMR (600 MHz) δ 7.23 (d, 2H, 8.2 Hz), 7.15 (d, 2H, 8.1 Hz), 5.07 (d, 1H, 2.1 Hz), 5.00 (dt, 1H, 0.9, 2.1 Hz), 2.61 (t, 2H, 6.1 Hz), 2.47 (dt, 2H, 0.9, 6.2 Hz), 1.59 (quint, 2H, 6.2 Hz), 1.40 (quint, $J = 6.5$ Hz, 2H), 1.16 (quint, $J = 6.3$ Hz, 2H), 0.9 (m, 4H), 0.7 (brs, 6H); ^{13}C NMR (150.9 MHz) see Table 4. Anal. Calcd for $C_{18}H_{26}$: C, 89.19; H, 10.81. Found: C, 88.99; H, 10.94. MS (EI) m/z 242 (M, 43%), 143 (100%), 131 (86%).

2-Methylenebicyclo[12.2.2]octadeca-14,16,17-triene (1e): colorless oil; bp 100−125 °C/0.55 mmHg (Kugelrohr distillation); UV-vis see Table 6; IR (neat) 3078(m), 2926(s), 2855(s), 1906(w), 1792(w), 1626(m), 1560(w), 1510(s), 1458(s), 1445(s), 1408(w), 1348(w), 1119(w), 1018(w), 891(s), 851(m), 826(m), 721(w), 712(w), 665(w), 619(w) cm^{-1}; ^{1}H NMR (270 MHz) δ 7.25 (d, 2H, 8.1 Hz), 7.13 (d, 2H, 8.1 Hz), 5.15 (d, 1H, 2.2 Hz), 5.00 (m, 1H), 2.65-2.53 (m, 4H), 1.60−1.50 (m, 2H), 1.37−1.27 (m, 2H), 1.16−0.74 (m, 12H), 0.62 (m, 2H); ^{13}C NMR (67.9 MHz) see Table 4. Anal. Calcd for $C_{19}H_{28}$: C, 88.99; H, 11.01.

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(15) Allinger *et al.* reported the bathochromic effect, which is caused by the deformation of the benzene ring, in the UV-vis spectra of [*n*]paracyclophanes as the size of the ring becomes smaller. See, Allinger, N. L.; Freiberg, L. A.; Hermann, R. B.; Miller, M. A. *J. Am. Chem. Soc.* **1963**, *85*, 1171−1177.

(16) *Palladium Reagents in Organic Synthesis*; Heck, R. F., Ed.; Acadimic Press: London, 1985.

Found: C, 89.03; H, 11.23. HRMS (EI) calcd for $C_{19}H_{28}$ 256.2189, found 256.2195.

2-Methylenebicyclo[13.2.2]nonadeca-15,17,18-triene (1f): colorless oil; bp 80−120 °C/0.6 mmHg (Kugelrohr distillation); UV-vis see Table 6; IR (neat) 3078(m), 2928(s), 2855(s), 1625(m), 1560(w), 1512(s), 1458(m), 1408(w), 1121(w), 1018(w), 891(m), 827(m) cm^{-1}; ^{1}H NMR (270 MHz) δ 7.26 (d, 2H, 8.2 Hz), 7.12 (d, 2H, 8.4 Hz), 5.12 (d, 1H, 2.2 Hz), 4.99 (m, 1H), 2.64 (m, 2H), 2.56 (m, 2H), 1.73−1.63 (m, 2H), 1.38−1.28 (m, 2H), 1.22−0.88 (m, 14H), 0.78−0.69 (m, 2H); ^{13}C NMR (67.9 MHz) see Table 4. Anal. Calcd for $C_{20}H_{30}$: C, 88.82; H, 11.18. Found: C, 88.70; H, 11.11. HRMS (EI) calcd for $C_{20}H_{30}$ 270.2345, found 270.2332.

2-Methylenebicyclo[15.2.2]heneicosa-17,19,20-triene (1g): colorless oil; bp 85−130 °C/0.4 mmHg (Kugelrohr distillation); UV-vis see Table 6; IR (neat) 3080(w), 3022(w), 2926(s), 2855(s), 1904(w), 1788(w), 1626(m), 1560(w), 1512(s), 1460(s), 1408(w), 1350(w), 1302(w), 1121(w), 1018(s), 891(m), 849(w), 824(w), 665(m) cm^{-1}; ^{1}H NMR (270 MHz) δ 7.29 (d, 2H, 8.4 Hz), 7.12 (d, 2H, 8.1 Hz), 5.15 (d, 1H, 1.8 Hz), 4.99 (s, 1H), 2.65 (t, 2H, 6.2 Hz), 2.53 (t, 2H, 6.4 Hz), 1.66 (quint, 2H, 6.7 Hz), 1.32 (quint, 2H, 7.0 Hz), 1.21−1.04 (m, 20H); ^{13}C NMR (67.9 MHz) see Table 4. Anal. Calcd for $C_{22}H_{34}$: C, 88.52; H, 11.48. Found: C, 88.37; H, 11.76. HRMS (EI) calcd for $C_{22}H_{34}$ 298.2658, found 298.2640.

Preparation of Bicyclo[15.2.2]heneicosa-17,19,20-trien-2-one (6g). A stream of ozone was passed through a solution of **1g** (119 mg, 0.4 mmol) in ethyl acetate (5 mL) at −78 °C until a light blue coloration persisted. Nitrogen was then passed through the solution for 15 min to remove excess ozone, and to the solution of the ozonide was added 11 mg of 10% Pd−C in 2 mL of ethyl acetate. The mixture was reduced with hydrogen (1 atm) at rt for 2 h. The mixture was filtered, and the solvent was evaporated. The crude product was purified by column chromatography (hexane:AcOEt = 20:1) to give **6g**[16] (67 mg, 55%) as a colorless powder. **6g**: mp 42.5 °C. IR (neat) 3026(w), 2926(s), 2855(s), 1674(s), 1601(s), 1570(w), 1460(m), 1412(m), 1369(w), 1325(w), 1267(m), 1252(w), 1182(w), 1119(w), 1015(w), 862(w), 856(w), 715(w), 577(w), 542(w) cm^{-1}; ^{1}H NMR (270 MHz) δ 7.87 (d, 2H, 8.4 Hz), 7.26 (d, 2H, 8.4 Hz), 2.90 (t, 2H, 6.8 Hz), 2.72 (t, 2H, 6.0 Hz), 1.77−1.62 (m, 4H), 1.25−0.96 (m, 20H). ^{13}C NMR (150.9 MHz) δ 202.3, 148.2, 135.1, 129.1, 128.4, 37.7, 35.2, 29.3, 29.2, 28.3, 28.2, 28.1, 27.8, 27.5, 27.4, 27.3, 26.4, 25.8, 25.6. Anal. Calcd for $C_{21}H_{32}O$: C, 83.94; H, 10.73. Found: C, 83.72; H, 10.75. HRMS (EI) calcd for $C_{21}H_{32}O$ 300.2450, found 300.2448.

Preparation of [15]Paracyclophane (Bicyclo[15.2.2]heneicosa-17,19,20-triene, 4). A mixture of **6g** (176 mg, 0.59 mmol), EtOH (8 mL), 10% Pd−C (30 mg in 4.7 mL EtOH), water (1.2 mL), and concd aqueous HCl (0.3 mL) was hydrogenated at atmosphere pressure at 50 °C for 22 h. After filtering off the catalyst, the solution was evaporated to give the crude product. The product was further purified by column chromatography (hexane) to give **4** as colorless powder (144 mg, 85%). **4**: mp 45.5−47 °C. IR (neat) 3049(w), 2926(s), 2853(s), 1898(w), 1510(m), 1460(m), 1445(m), 1418(w), 1367(w), 1350(w), 1118(w), 1022(w), 858(w), 796(w), 723(w), 582(m) cm^{-1}; ^{1}H NMR (270 MHz) δ 7.06 (s, 4H), 2.61 (m, 4H), 1.61 (m, 4H), 1.20−1.08 (m, 22H). ^{13}C NMR (67.9 MHz) δ 139.4, 128.5, 34.9, 30.3, 29.2, 28.4, 28.0, 27.6, 26.7. Anal. Calcd for $C_{21}H_{34}$: C, 88.04; H, 11.96. Found: C, 87.91; H, 11.87. HRMS (EI) calcd for $C_{21}H_{34}$ 286.2659, found 286.2672.

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