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Synthesis and Diels–Alder Reactions of 1,2-Dimethylene[2.*n*]metacyclophanes

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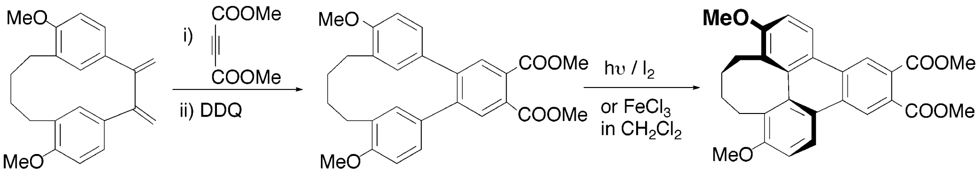
ABSTRACT



The Diels–Alder reaction of 1,2-dimethylene[2.*n*]MCPs (MCP = metacyclophane) with suitable dienophiles followed by aromatization and photoinduced or FeCl$_3$-induced transannular cyclization afforded phenanthrene-anellated polycyclic aromatic hydrocarbons, which were found to adopt helical chirality in the solid state.

Although well-established, the Diels−Alder reaction has been used for a new type of application in recent years. Thus, de Meijere et al. reported[1] that the Diels−Alder reaction of highly strained 1,2-dimethylene[2.*n*]paracyclophanes with dienophiles could be used to prepare arene-anellated [2.*n*]-paracyclophanes. 1,2-Dimethylene[2.*n*]MCPs lower the barriers of the Diels−Alder reactions by virtue of the dienes adopting a fixed *s*-cis conformation in the ground and transition states.[2,3]

It is also well-known that the photoinduced transannular cyclization reaction of stilbene derivatives affords phenanthrenes in the presence of an oxidant.[4] We reasoned that potentially, these two reactions could be combined to allow the preparation of phenanthrene-anellated polycyclic aromatic hydrocarbons provided that suitable substituted 1,2-dimethylene[2.*n*]MCPs were available. In this paper, we report on the first successful synthesis of 1,2-dimethylene-[2.*n*]MCPs and on their conversion to phenanthrene-anellated polycyclic aromatic hydrocarbons through Diels−Alder reaction and photoinduced, or Lewis acid-induced, transannular cyclization.

In cyclophane chemistry, the reductive coupling of carbonyl compounds, catalyzed by low-valent titanium,[5] has been used to synthesize cyclophanes with glycol units as bridges.[6] Grützmacher et al.[7] used this method in the cyclization of suitable dialdehydes to afford unsaturated cyclophanes. Given these past precedents we decided to examine the coupling reactions of 1,3-bis(5-acetyl-2-methoxy-phenyl)propane **1a** and 1,4-bis(5-acetyl-2-methoxyphe-

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(1) (a) König, B.; de Meijere, A. *Chem. Ber.* **1992**, *125*, 1895−1898. (b) de Meijere, A.; König, B. *Synthesis* **1997**, 1221−1232.

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(3) Grützmacher, H.-F.; Albrecht, K. *Chem. Ber.* **1989**, *122*, 2299−2302.

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(5) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513−1524.

(6) Mitchell, R. H.; Weerawana, S. A. *Tetrahedron Lett.* **1986**, *27*, 453−456.

(7) (a) Grützmacher, H.-F.; Neumann, E.; Ebmeyer, F.; Albrecht, K.; Schelenz, P. *Chem. Ber.*, **1989**, *122*, 2291−2297. (b) Grützmacher, H.-F.; Neumann, E. *Chem. Ber.* **1993**, *126*, 1495−1497. (c) Grützmacher, H.-F.; Nolte, G. *Chem. Ber.* **1994**, *127*, 1157−1162. (d) Grützmacher, H.-F.; Mehdizadeh, A.; Mülverstedt, A. *Chem. Ber.* **1994**, *127*, 1163−1166.

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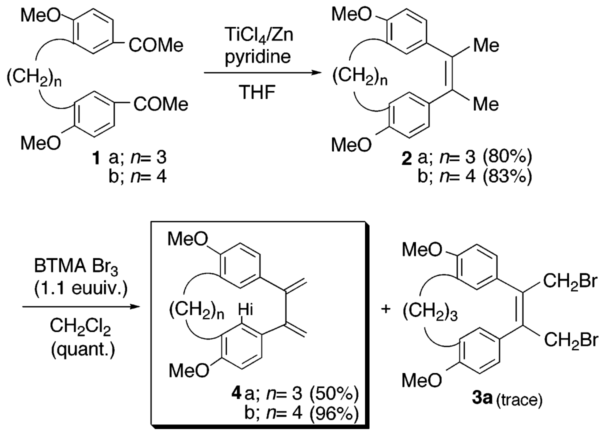
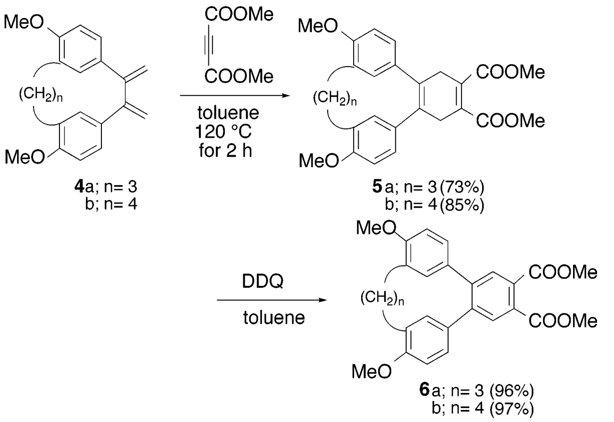
Scheme 1. Synthesis of 1,2-Dimethylene[2.*n*]MCPs **4**



Scheme 2. Synthesis of Areno-Bridged MCPs **6**



nyl)butane **1b**,[8] respectively, with low-valent titanium ($TiCl_4$/Zn) and obtained **2a** and **2b** in good yields. The structures of **2a** and **2b** were elucidated on the basis of their elemental analyses and spectral data. In particular, the mass spectral data for **2** ($M^+ = 308$ for **2a** and 322 for **2b**) strongly supported the cyclic structure.

Interestingly, bromination of 1,2-dimethyl[2.3]MCP-1-ene **2a** with 1 equiv of benzyltrimethylammonium tribromide ($BTMABr_3$)[9,10] at room temperature afforded the corresponding 1,2-dimethylene[2.3]MCP **4a** in 50% yield along with a trace amount of 1,2-bis(bromomethyl)[2.3]MCP-1-ene **3a**. This transformation probably occurred by addition of bromine to the double bond followed by a twofold dehydrobromination to give the diene **4a**. In fact, the same treatment of **2a** at -10 °C afforded a mixture of the trans adduct to the bridging double bond and **3a** in quantitative yield.[11] Similar results were obtained with **2b**, which provided **4b** in quantitative yield. The 270 MHz ^1H NMR spectrum of **4a** in $CDCl_3$ showed a doublet for the intra-annular proton H_i at δ 6.92 ppm ($J = 2.0$ Hz) in addition to the resonances at δ 6.26 and 6.47 ppm for the other two protons of the aromatic rings. The *exo*-methylene protons of the ethanobridge were observed as doublets at δ 5.16 and 5.62 ppm ($J = 2.0$ Hz), and the methoxy protons appeared at δ 3.60 ppm. The protons of the trimethylene bridge gave rise to a complicated signal pattern as expected for a rigid *syn*-[2.3]-MCP. The protons of the benzylic CH_2 group were observed as two multiplets centered at δ 2.28 and 3.14 ppm, which were further split by coupling with the protons of the central CH_2 group. This central CH_2 group was also observed as two multiplets centered at δ 1.32 and 1.83 ppm. The peak pattern ascribed to the six chemically distinct protons of the propanobridge proved the absence of a syn−syn interconversion, which would exchange H_A and H_B of each CH_2 group. In contrast, the internal aromatic proton of **2a** showed an upfield shift (δ 5.68 ppm) due to the ring current of the opposite benzene ring.[2b,9] The structure of **2a** corresponded exclusively to the anti conformer. These observations suggested that the introduction of two double bonds of the ethanobridge might control the syn and anti conformation of 1,2-dimethylene[2.3]MCP **4a**.

As the temperature of the solution of **4a** in $CDCl_3$ was increased, the individual peak of the benzyl protons merged and eventually a single peak was observed above 30 °C. This observation indicated that the rate of conformational ring flipping of **4a** was faster than the NMR time scale at this temperature. The energy barrier to the conformational ring flipping estimated from the coalescence temperature (T_C) was 14.0 kcal mol^{-1} lower value than that of *anti*-1,2-dimethyl-[2.3]MCP-1-ene **2a** ($T_C = 70$ °C, $\Delta G^\ddagger = 15.6$ kcal mol^{-1}).

Compound **4a** is too labile a solid to purify. When in solution, or in air, compound **4a** slowly decomposes. However, the compound is easily trapped by the reaction with dimethyl acetylenedicarboxylate to afford **5a** in good yield. Diels−Alder adduct **5a** was converted to areno-bridged MCP **6a** by aromatization with dichlorodicyano-*p*-benzoquinone (DDQ). Similarly, **6b** was obtained from **4b** as described above. The present Diels−Alder reaction of **4** with dimethylacetylenedicarboxylate was completed within 2 h in toluene at reflux, which was much faster than that of 2,3-diphenyl-1,3-butadiene (12 h). Thus, the Diels−Alder reactivity of **4** exceeds that of 2,3-diphenyl-1,3-butadiene. This result suggests that the energy of the fixed *s*-cis conformation in **4** in the ground and transition state might lower the Diels−Alder barriers due to the inflexibility of the cyclophane ring.

The Diels−Alder reaction of **4** with suitable dienophiles followed by aromatization can be used to prepare a range of areno-bridged [2.*n*]MCPs. The Diels−Alder reactivities of **4a** were tested in reactions with *p*-benzoquinone and 1,4-naphthoquinone. Upon heating a mixture of **4a** and 0.5 equiv of *p*-benzoquinone in toluene at reflux, a Diels−Alder adduct was formed in 36% yield. Successively, treatment of the reaction mixture with DDQ led to dehydrogenation to afford

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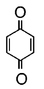
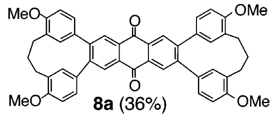
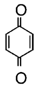
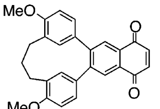
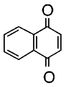
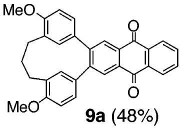
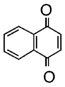
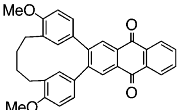
[9] (a) Tashiro, M.; Yamato, T. *J. Org. Chem.* **1981**, *46*, 4556−4562. (b) Tashiro, M.; Yamato, T. *J. Org. Chem.* **1983**, *48*, 1461−1468.

[10] Kajigaeshi, S.; Kakinami, T.; Tokiyama, H.; Hirakawa, T.; Okamoto, T. *Chem. Lett.* **1987**, 627−630.

[11] (a) Yamato, T.; Sato, M.; Noda, K.; Matsumoto, J.; Tashiro, M. *Chem. Ber.* **1993**, *126*, 447−451. (b) Yamato, T.; Matsumoto, J.; Ide, S.; Suehiro, K.; Tashiro, M. *J. Chem. Res., Synop.* **1993**, 394−395.

Table 1. Diels−Alder Reaction of **4a** and **4b** with Dienophiles in Toluene Followed by Aromatization with DDQ

Entry	Substrate	Dienophile	Dienophile (equiv.)	Products (yield, %)[a]
1	**4a**		0.5	 **8a** (36%)
2	**4a**		2.0	 **7a** (30%) + **8a** (28%)
3	**4a**		1.2	 **9a** (48%)
4	**4b**		1.2	 **9b** (74%)

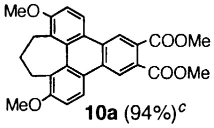
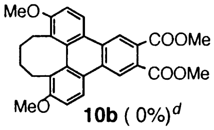
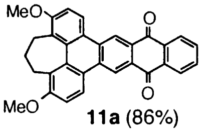
[a] Isolated yields are shown.

bis(1,2-naphthoquinono[2.3]MCP, "twin-phane" **8a**, in quantitative yield. Treatment of **4a** with 2.0 equiv of *p*-benzoquinone in toluene at reflux followed by dehydrogenation yielded a mixture of 1,2-(6,7)naphthoquinono[2.3]-MCP **7a** and bisadduct **8a** in 30 and 28% yields, respectively. Under similar conditions the addition of **4a** and **4b** to 1,4-naphthoquinone afforded the cycloadducts **9a** and **9b** in 48 and 74% yields, respectively.

Examination of molecular models led us to believe that the transformation of **6a** into phenanthrene **10a** would be straightforward, since the p orbitals in the conformationally rigid stilbene moiety of **6a**, which are involved in the photoinduced disrotatory cyclization leading to the phenanthrene **10a** eventually, are apparently very close in space.

Actually, when **6a** was irradiated by a 400 W high-pressure mercury lamp in the presence of an oxidant under standard conditions (I_2),[12] the desired phenanthrene **10a** was obtained in 94% yield. This result is quite different from the photoinduced transannular cyclizations of 3,3′-disubstituted stilbenes to afford 4,5-disubstituted phenanthrenes only in low yields due to the steric hindrance between the two substituents on the 3,3′-positions.[13] However, in the case of **10b** only the starting compound was recovered despite the prolonged reaction time. These findings suggest that the extent of fixing conformations in the ground and transition state affect the photoinduced transannular cyclization reaction.

Table 2. Photoinduced and $FeCl_3$-Induced Transannular Cyclization Reaction of Areno-Bridged MCPs **6** and **9** to Afford Phenanthrene-anellated Polycyclic Aromatic Hydrocarbons

Entry	Substrate	Conditions[b]	Products (yield, %)[a]
1	**6a**	**A**	 **10a** (94%)[c]
2	**6b**	**A**	 **10b** (0%)[d]
3	**9a**	**A**	 **11a** (86%)
4	**6a**	**B**	**10a** (97%)
5	**6b**	**B**	**10b** (96%)
6	**9a**	**B**	**11a** (92%)

[a] Isolated yields are shown. [b] Conditions: (A) I_2, $h\nu$ in benzene for 40 h; (B) $FeCl_3$ in CH_2Cl_2 at room temperature for 3 h. [c] Reaction time was 12 h. [d] Starting compound **6b** was recovered in quantitative yield.

The presently developed method was further applied to bridge-anellated [2.3]MCP **8a** and **9a**. Similarly, photoinduced transannular cyclization of areno-bridged MCP **9a** afforded phenanthrene-anellated polycyclic aromatic hydrocarbons **11a** in 86% yield. No photoinduced reaction in the benzoquinone moiety was observed under the conditions used. However, several attempted photoinduced transannular cyclizations of "twin-phane" **8a** under the various conditions failed due to low solubility in benzene. Only the recovery of the starting compound **8a** resulted. Several attempts at using Lewis acids ($AlCl_3$, $TiCl_4$, $SnCl_4$) to catalyze the transannular cyclization of areno-bridged MCP **6a** failed. Only recovery of the starting compound or the formation of the intractable mixture of products resulted. Fortunately, we have found that when the transannular cyclization of **6a** is carried out in CH_2Cl_2 at room temperature in the presence of the $FeCl_3$[14] (10 equiv), the desired phenanthrene-anellated polycyclic aromatic hydrocarbon **10a** is formed in 97% yield within 3 h. Similarly, $FeCl_3$-induced transannular cyclizations of **6b** and **9a** afforded **10b** and **11a** in 96 and 92% yields, respectively. Although currently the detailed mechanism has yet to be clarified, the presently developed method provides good yields and easily isolated products.

Interestingly, X-ray analysis revealed that triphenylene **10b** adopts helical chirality, yet surprisingly, the dihedral angle of arylenes connected by the phenyl unit is 33.98°. As a consequence, the compound is chiral and the (*M*)- and (*P*)-isomers are packed alternatively in the crystal as depicted schematically in Figure 2.[15]

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(12) Mallory, F. B.; Mallory, C. W. *Org. React.* **1984**, *30*, 1−456.

(13) (a) Ben, I.; Castedo, L.; Saá, J. M.; Seijas, J. A.; Suau, R.; Tojo, G.*J. Org. Chem.* **1985**, *50*, 2236−2240. (b) Cosmo, R.; Hambley, T. W.; Sternhell, S. *J. Org. Chem.* **1987**, *52*, 3119−3123. (c) Armstrong, R. N.; Ammon, H. L.; Darnow, J. N. *J. Am. Chem. Soc.* **1987**, *109*, 2077−2082. (d) Grimme, S.; Pischel, I.; Nieger, M.; Vögtle, *F. J. Chem. Soc., Perkin Trans. 2* **1996**, 2771−2774.

(14) Borner, R. R. C.; Jackson, R. F. W. *J. Chem. Soc., Chem. Commun.* **1994**, 845−846.

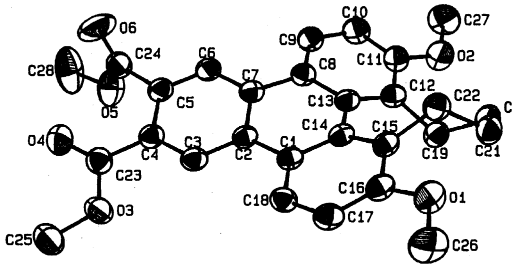

Figure 1. ORTEP view of (*P*)-**10b** (thermal ellipsoids for 50% probability). Hydrogens are omitted for clarify.

On the other hand, NMR spectra of **10b** show totally systematic patterns at room temperature. Upon lowering the temperature, the signals experience broadening to some extent, although no splitting is observed even at −80 °C. This phenomenon may possibly be explained in terms of a rapid fluxional conformational change in solution between the enantiomeric species that innately should give rise to unsymmetrical patterns.[16]

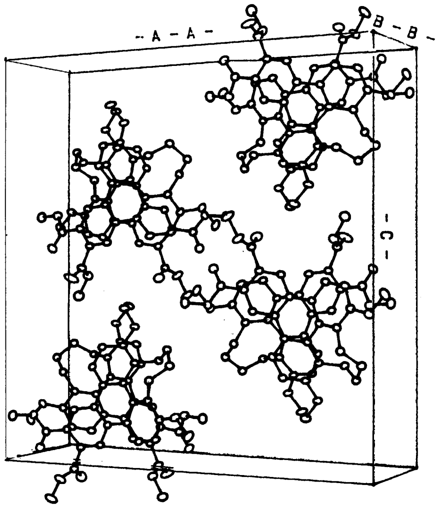

Figure 2. Partial view of **10b** in the crystal.

In conclusion, a new synthesis of areno-bridged [2.*n*]-MCPs by the Diels−Alder reaction of **4** with suitable dienophiles has been developed and applied to the synthesis of phenanthrene-anellated polycyclic aromatic hydrocarbons by the successive photoinduced or $FeCl_3$-induced transannular cyclization reaction.[17] Further investigations are in progress to widen the range of this new pathway to phenanthrene-anellated polycyclic aromatic hydrocarbons for advanced materials.

Supporting Information Available: Experimental procedure of preparation of compounds **1**−**11**, physical data, spectral data for all new compounds, and crystallographic data of **10b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[15] Crystal data for **10b**: $C_{28}H_{26}O_6$, $M = 482.52$, orthorhombic, *Pbca* (No. 61), $a = 24.505(3)$, $b = 7.3151(8)$, $c = 25.162(2)$ Å, $V = 4510.5(8)$ Å^3, $Z = 8$, $D_c = 1.350$ g cm^{-3}, μ(Cu Kα) = 1.54184 Å, $T = 291$ K, colorless prisms; 5256 independent observed reflections $F^2 > 3\sigma$, 2856 parameters. CCDC 246144.

[16] Müllen, K.; Heinz, W.; Klärner, F. G.; Roth, W. R.; Kindermann, I.; Adamczak, O.; Wette M.; Lex, J. *Chem. Ber.* **1990**, *123*, 2349−2371.

[17] All new compounds have been fully characterized by ^{1}H NMR, IR, and mass spectroscopy and elemental analyses. Some physical properties and spectral data of the compounds obtained in the present work were shown. Spectral data of **2a**: colorless prisms (MeOH), mp 122−125 °C; ^{1}H NMR ($CDCl_3$, −40 °C) δ 1.59−1.77 (2H, m), 1.90−2.05 (2H, m), 2.20 (6H, s), 2.86−2.98 (2H, m), 3.85 (6H, s), 5.68 (2H, d, *J* 2.4), 6.73 (2H, d, *J* 8.3), 7.08 (2H, dd, *J* 8.3, 2.4); MS (EI) *m/z* 308 (M$^+$). Spectral data of **4a**: colorless prisms (MeOH), mp 78−79 °C; ^{1}H NMR ($CDCl_3$, −60 °C) δ 1.19−1.45 (1H, m), 1.74−1.92 (1H, m), 2.20−2.37 (2H, m), 3.07−3.21 (2H, m), 3.60 (6H, s), 5.16 (2H, d, *J* 2.0), 5.62 (2H, d, *J* 2.0), 6.26 (2H, d, *J* 8.3), 6.47 (2H, dd, *J* 2.0, 8.3), 6.92 (2H, d, *J* 2.0); MS (EI) *m/z* 306 (M$^+$). Spectral data of **6a**: colorless needles (EtOH/benzene 2:1), mp 273−275 °C; IR (KBr) 1722 cm^{-1}; ^{1}H NMR ($CDCl_3$, 27 °C) δ 1.63−1.87 (2H, m), 1.96−2.11 (2H, m), 2.90−3.14 (2H, m), 3.88 (6H, s), 5.78 (2H, broad s), 6.83 (2H, broad s), 7.08 (2H, broad s), 7.93 (2H, broad s); MS (EI) *m/z* 446 (M$^+$). Spectral data of **10a**: yellow prisms (EtOH), mp 183−184 °C; IR (KBr) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$, 27 °C) δ 2.46−2.53 (2H, m), 2.79 (4H, t, *J* 6.8), 3.99 (12H, s), 7.29 (2H, d, *J* 8.3), 8.42 (2H, d, *J* 8.3), 8.77 (2H, s); MS (EI) *m/z* 444 (M$^+$).