# Synthesis of Small-Sized Stilbenophanes and Their Transannular Delocalization

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Stilbenes are an important class of compounds with a wide range of applications for $\pi$-conjugated systems.[1] In particular, the optical and charge-conducting properties of stilbenoid compounds have been utilized in producing a variety of materials.[2] Their physical properties can be controlled by the conjugated length, stereochemistry, regiochemistry, and introduction of donor and/or acceptor groups. Although the transmission of the substituent effects from one benzene ring to another through a double bond in stilbenes has been well investigated,[3] to the best of our knowledge, the study of the transmission of electronic effects between stilbene units through a transannular interaction is very limited. Small-sized cyclophanes can be regarded as fascinating structures for the models to study the transannulary transmission between stilbene units, since the aromatic units can be fixed in a forced proximity and particular orientation. In particular, metacyclophanes (MCPs) and related compounds are characterized by a strong and unique transannular interaction between their two aromatic rings. We have already reported simple and efficient synthetic methods for the preparation of [2.2]MCPs and devoted our attention to their spectral properties and reactivities.[4] Although stilbenoid dimers based on the [2.2]paracyclophane skeleton have been recently reported,[5] knowledge of the conjugated state of stilbene chromophores fixed in close proximity in the MCP systems is very limited. We have also been very interested in the quantitative estimation of the transannular interaction in MCPs using optical properties. Therefore, we decided to synthesize and investigate the small-sized cyclophanes comprising stilbene units (stilbenophanes).

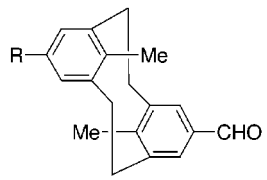
**Table 1. Preparation, Configuration, and $\lambda_{max}$ of Stilbenophanes**

| | | | $\lambda_{max}$[a] (nm) | |
|---|---|---|---|---|
| compd | yield(%) | *Z*/*E* ratio | Z | E |
| **4a** | 83 | 80/20 | 317 | 335 |
| **4b** | 74 | 54/46 | 309 | 334 |
| **4c** | 85 | 38/62 | 329 | 331 |
| **4d** | 71 | 68/32 | 321 | 337 |
| **4e** | 59 | 50/50 | | 339 |
| **4f** | 46 | 50/50 | 321 | 333 |
| **4g** | 66 | 46/54 | | 337 |
| **4h** | 100[b] | 36/64 | | 344 |
| **5a** | 78 | 74/26 | 304 | 327 |
| **5b** | 76 | 32/68 | 323 | 327 |
| **6** | 45[c] | 0/100 | 327 | 348 |
| **6** | 37[d] | 76/24 | | |
| **8** | 99 | 58/42 | 286 | 300 |

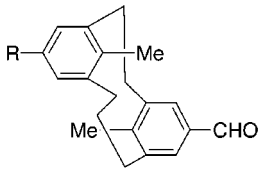
[a] In cyclohexane at 27 °C. [b] From 4c. [c] McMurry reaction. [d] Wittig reaction.

## Results and Discussion

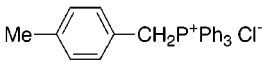
**Preparation of Stilbenophanes.** Formyl [2.2]MCPs **1a**−**f** were prepared according to the reported methods[6] and modified methods. Interestingly, formyl[2.2]MCP **1g** was obtained by ipso formylation of the corresponding di-*tert*-butyl[2.2]MCP in 36% yield. Formyl [2.3]MCPs **2a** and **2b** were synthesized using methods similar to those for the [2.2]MCPs.[7]




**1a**: R=H
**1b**: R=Br
**1c**: R=$NO_2$
**1d**: R=$CH_3$
**1e**: R=$OCH_3$
**1f**: R=CHO
**1g**: R=*t*-Bu




**2a**: R=H
**2b**: R=$NO_2$




**3**

The Wittig or the McMurry procedure[8] was employed to construct the stilbene moiety. The reaction of MCP **1a** and the phosphonium chloride **3** with *n*-butyllithium in THF gave the desired stilbenophane **4a**, whose *Z*/*E* ratio was 80:20 in 83% yield. The *Z*/*E* ratio of the product was determined by its NMR spectrum. The *Z* and *E* isomers were successfully separated by thin-layer chromatography. When MCP **1b**−**e** and **1g** were treated under similar conditions, the corresponding stilbenophane **4b**−**e** and **4g** were prepared. The yields and *Z*/*E* ratios of the products are summarized in Table 1. Using 1 equiv of **3** in the reaction of MCP **1f**, the stilbenophane **4f** was isolated in 46% yield. The reaction of **4c** with Raney Ni

(1) For example, see: (a) Mallory, F. B.; Mallory, C. W. *Photocyclization of Stilbenes and Related Molecules*, John Wiley & Sons: New York, 1984, *Vol. 30*, p1. (b) Waldeck, D. H. *Chem. Rev.* **1991**, *91*, 415.
(2) Meier, H. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1399.
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(4) For example, see: (a) Tsuge, A.; Moriguchi, T.; Mataka, S.; Tashiro, M. *Chem. Lett.* **1992**, 579. (b) Tsuge, A.; Moriguchi, T.; Mataka, S.; Tashiro, M. *J. Chem. Soc., Perkin Trans 1* **1993**, 2211. (c) Tsuge, A.; Moriguchi, T.; Mataka, S.; Tashiro, M. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 27. (d) Tsuge, A.; Moriguchi, T.; Mataka, S.; Tashiro, M. *J. Org. Chem.* **1995**, *60*, 4930. (e) Tsuge, A.; Moriguchi, T.; Mataka, S.; Tashiro, M. *Liebigs Ann.* **1996**, 769.
(5) (a) Warren, W. J., Jr.; Miao, Y.-J.; Lachicotte, R. J.; Bazan, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 419. (b) Bazan, G. C.; Warren, W. J., Jr.; Lachicotte, R. J.; Tretiak, S.; Chernyak, V.; Mukamel, S. *J. Am. Chem. Soc.* **1998**, *120*, 9188.
(6) (a) Tashiro, M.; Yamato, T. *J. Org. Chem.* **1981**, *48*, 2313. (b) Tashiro, M.; Yamato, T. *J. Chem. Soc., Perkin Trans 1* **1984**, 2165. (c) Tsuge, A.; Ishii, T.; Sawada, T.; Mataka, S.; Tashiro, M. *Chem. Lett.* **1994**, 1529. (d) Tsuge, A.; Ishii, T.; Mataka, S.; Tashiro, M. *J. Chem. Res(S).*, **1992**, 312.
(7) Yamato, T.; Matsumoto, J.; Kabu, S.; Takezaki, Y.; Tashiro, M. *J. Chem. Res(S).*, **1993**, 44.
(8) McMurry, J. E. *Chem. Rev.* **1984**, *74*, 87.

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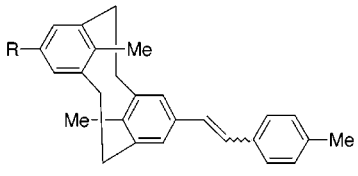
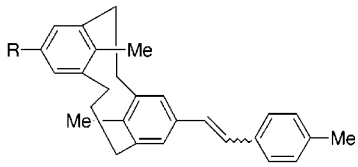
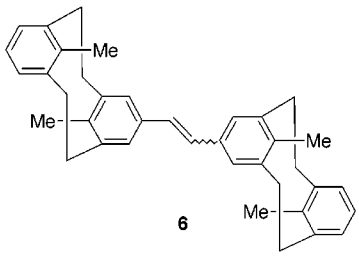
under hydrogen afforded the stilbenophane **4h** in quantitative yield without the reduction of the double bond. Except for **4e**, **4g**, and **4h**, both the *Z* and *E* isomers were identified. The stilbenophanes **5a** and **5b** were also prepared by the reaction of MCP **2a** and **2b** with **3** in 78% and 76% yields, respectively. The *Z*/*E* ratios of the isomers for **5a** and **5b** were 74:26 and 32:68, respectively.



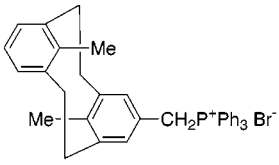

**4a**: R=H **4e**: R=$OCH_3$
**4b**: R=Br **4f**: R=CHO
**4c**: R=$NO_2$ **4g**: R=*t*-Bu
**4d**: R=$CH_3$ **4h**: R=$NH_2$



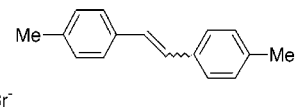

**5a**: R=H
**5b**: R=$NO_2$




**6**




**7**




**8**

MCP **1a** was subjected to the McMurry reaction with the $TiCl_3(DME)_{1.5}$ complex and Zn−Cu in DME to give the stilbenophane **6** in 45% yield, which was identified as the *E* isomer. We also tried the coupling of MCP **1a** and the phosphonium bromide **7** prepared from the corresponding bromomethyl compound to preferentially give the *Z* isomer of **6**. As the referential compound, *p*,*p*′-dimethylstilbene **8** was prepared from *p*-tolualdehyde and **3**.

**Absorption Spectra of Stilbenophanes.** One apparent way to investigate the conjugation system in the stilbenophanes is to know the influence of the conjugation on the wavelength in their UV spectra; thus, their $\lambda_{max}$ values are listed in Table 1 together with those of stilbene **8**.

All stilbenophanes prepared here exhibit a bathochromic shift as compared to the referential compound **8** in both the *Z* and *E* forms, which can probably be ascribed to the effect of the cyclophane skeleton, since the cyclophane unit could work as an electron-releasing group toward the stilbene chromophore resulting in the extent of conjugation. This trend also indicates that the electronic state of the stilbenophanes is delocalized to a large extent over the entire molecule. Alternation in the configuration from the *E* isomer to the *Z* isomer leads a hypsochromic shift in the cyclophane systems as well as the stilbene **8** because the *Z* isomers are supposed to be the less elongated form. Although the stilbene **8-*E*** shows an absorption peak at 300 nm, it shifts to 335 and 348 nm in stilbenophanes **4a-*E*** and **6-*E***, respectively. Compound **6**, which holds two cyclophane structures, exhibits a further bathochromic shift. Apparently, such a bathochromic shift can be ascribed to the more effective delocalization which is enhanced by the transannular interaction in two cyclophane skeletons. [2.3]Stilbenophanes **5a** and **5b** show a hypsochromic shift against the corresponding [2.2]stilbenophanes **4a** and **4c**. In general, the extent of conjugation in the $\pi$-electron system results in a bathochromic shift; therefore, it can be speculated that there exists a less extended conjugation in the [2.3]-MCP system than in the [2.2]MCP system. Such a different mode of conjugation in the [2.*n*]MCP systems can be correlated to the transannular interaction, in other words, distance or orientation of the two aromatic rings. In a previous X-ray study,[9] it was found that the distance between the two aromatic rings of [2.3]MCPs (2.96 Å) is somewhat grater than the corresponding distance of [2.2]-MCPs (2.82 Å). Accordingly, the transannular interaction is reduced in the [2.3]MCP systems resulting in a decrease of through-space delocalization.

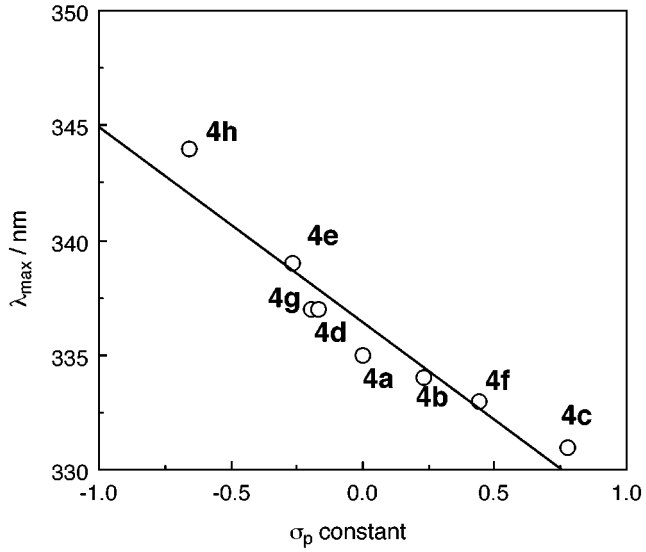



**Figure 1.** Correlation between $\lambda_{max}$ of *E* forms of stilbenophanes **4** and the $\rho_p$ constant of the substituent.

The effect of the functional group on the electronic state is also interesting. The nitro group on the aromatic ring affects the $\lambda_{max}$ values of *Z* isomers in both the [2.2] and [2.3]stilbenophanes resulting in 12 and 19 nm bathochromic shifts, respectively. The Hammett substituent constants are widely used to express the electronic effects of substituents.[10] Thus, when the $\lambda_{max}$ values for **4** are plotted against $\sigma_p$ of the substituent introduced into the [2.2]MCP skeleton, a straight line is obtained for the *E* isomers as shown in Figure 1. However, a clear relationship was not observed for the *Z* isomers.

(9) Tsuge, A.; Yasutake, M.; Moriguchi, T.; Sakata, K.; Yamato, T.; Mataka, S.; Tashiro, M. *Chem. Lett.* **1997**, 413.
(10) Hammett, L. P. *J. Am. Chem. Soc.* **1937**, *59*, 96.

Such a linear relationship implies that the electronic effect of the substituent on the aromatic ring could be transferred to the stilbene chromophore and promote delocalization over the entire molecule through a transannular interaction. These observations suggest that such a through-space delocalization across the transannular gap leads to a more stable excited state than the isolated stilbene.

It is also indicated that the [2.*n*]MCPs are a nonplanar molecule with one conjugated system due to a strong transannular interaction between the two aromatic rings.

## Conclusion

The results obtained in this study reveal that the delocalization of the $\pi$-conjugated state in the stilbenophanes is strongly enhanced by the transannular interaction in the MCP skeleton. A straight line is obtained for the plot of the Hammett constant ($\sigma$p) of the substituent on one aromatic ring and $\lambda_{max}$ of the stilbene moiety on the other side, indicating that the electronic effects of the outer substituents transfer to the stilbene unit through the transannular interaction.

We also clarified a slight difference in the transannular interaction between [2.2]MCP and [2.3]MCP systems for the first time by examination of the spectral properties of the stilbenophanes. The cyclophane compounds in which stilbene units can be fixed in an appropriate position may offer a model for studying the interaction between chromophores and for developing a new material based on the transannular $\pi$-electron interaction. Investigation of the photoisomerization of these [2.*n*]stilbenophanes is now under progress in our laboratory.

## Experimental Section

**General Methods.** All melting points are uncorrected. $^1$H NMR spectra were recorded at 500 MHz in $CDCl_3$ with $Me_4Si$ as internal reference. *J* values are given in Hz. Mass spectra were obtained at 75 eV using a direct-inlet system. Column chromatography was carried out on silica gel (Wako gel, C-300). The amount of silica gel used was 5−100 g.

**Typical Procedure for Wittig Reaction of Formyl[2.*n*]-MCP and 3.** To a solution of **3** (274 mg, 0.68 mmol) in THF (10 mL) was added *n*-BuLi (1.6 M solution in hexanes) (0.46 mL, 0.68 mmol). After the solution was stirred for 10 min, the solution of **1a** (90 mg, 0.34 mmol) in THF (20 mL) was added. The reaction mixture was stirred at room temperature for 2 h, and then it was poured into a large amount of ice−water and extracted with ether. The extract was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The resultant residue was chromatographed using hexane as an eluent to afford the mixture of **4a-*Z*** and **4a-*E*** (99 mg, 83%), which was separated by thin-layer chromatography using hexane and chloroform to give **4a-*Z*** as a white powder (hexane): mp 172−175 °C; $^1$H NMR $\delta$ 0.56 (3H, s), 0.68 (3H, s), 2.32 (3H, s), 2.64−2.96 (8H, m), 6.43 (2H, s), 6.84 (1H, t, *J* 7.3), 7.04 (2H, s), 7.06 (2H, d, *J* 7.8), 7.08 (2H, d, *J* 7.3), 7.23 (2H, d, *J* 7.8); MS *m*/*z* 352 ($M^+$). Anal. Calcd for $C_{27}H_{28}$: C, 91.99; H, 8.01. Found: C, 91.77; H, 8.14.

**4a-*E*:** colorless prisms (hexane); mp 190−193 °C; $^1$H NMR $\delta$ 0.61 (3H, s), 0.69 (3H, s), 2.35 (3H, s), 2.74−2.99 (8H, m), 6.87 (1H, t, *J* 7.4), 6.99 (2H, s), 7.12 (2H, d, *J* 7.4), 7.15 (2H, d, *J* 8.0), 7.27 (2H, s), 7.39 (2H, d, *J* 8.0); MS *m*/*z* 352 ($M^+$). Anal. Calcd for $C_{27}H_{28}$: C, 91.99; H, 8.01. Found: C, 91.90; H, 8.06.

**Reduction of 4c.** To a suspension of W-2 Raney Ni in benzene (15 mL) was added the solution of **4c** (the mixture of *Z* and *E* isomers) (25 mg, 0.063 mmol) in benzene (5 mL). Hydrogen gas was bubbled into the suspension for 2 h at room temperature. After filtration, the reaction mixture was concentrated under reduced pressure to give the crude **4h** (23 mg, 100%), which was chromatographed using hexane and chloroform as eluents to afford **4h-*Z*** as yellow powder (hexane): mp 190−193 °C; $^1$H NMR $\delta$ 0.60 (3H, s), 0.82 (3H, s), 2.32 (3H, s), 2.62−2.96 (8H, m), 3.00−3.40 (2H, brs, exchanged by $D_2O$), 6.41 (2H, s), 6.48 (2H, s), 7.02 (2H, s), 7.03 (2H, d, *J* 8.2), 7.23 (2H, d, *J* 8.2); MS *m*/*z* 367 ($M^+$). Elemental analysis gave no satisfactory result.

**4h-*E*:** yellow powder (hexane); mp 227−229 °C; $^1$H NMR $\delta$ 0.60 (3H, s), 0.86 (3H, s), 2.35 (3H, s), 2.72−2.97 (8H, m), 3.00−3.40 (2H, brs, exchanged by $D_2O$), 6.53 (2H, s), 6.97 (2H, s), 7.15 (2H, d, *J* 8.0), 7.26 (2H, s), 7.39 (2H, d, *J* 8.0); MS *m*/*z* 367 ($M^+$). Anal. Calcd for $C_{27}H_{29}N$: C, 88.24; H, 8.03; N, 3.81. Found: C, 88.12; H, 8.03; N, 3.60.

**McMurry Reaction of 1a.** To the suspension of with $TiCl_3(DME)_{1.5}$ complex (1.16 g, 4.0 mmol) in dried DME (20 mL) was added Zn−Cu (1.08 g, 4.0 mmol), and then the suspension was refluxed for 2 h. After the mixture was cooled to room temperature, **1a** (264 mg, 1.0 mmol) was added to the suspension. The reaction mixture was filtered and washed with ether and dichloromethane. The filtrate was chromatographed using hexane and chloroform as eluents to give **6-*E*** (113 mg, 45%) as yellow prisms (toluene): mp 225−229 °C; $^1$H NMR $\delta$ 0.61 (3H, s), 0.71 (3H, s), 2.75−2.98 (16H, m), 6.87 (2H, t, *J* 7.3), 6.95 (2H, s), 7.13 (4H, d, *J* 7.3), 7.27 (4H, s); MS *m*/*z* 496 ($M^+$). Anal. Calcd for $C_{38}H_{40}$: C, 91.88; H, 8.12. Found: C, 91.70; H, 8.21.

**Wittig Reaction of 1a and 7.** To a solution of **7** (prepared from the corresponding bromomethyl compound and $PPh_3$, 63 mg, 0.11 mmol) in THF (10 mL) was added *n*-BuLi (15% solution in hexanes) (0.2 mL). After the solution was stirred for 10 min, the solution of **1a** (26 mg, 0.098 mmol) in THF (20 mL) was added. The reaction mixture was stirred at room temperature for 2 h, and then it was poured into a large amount of ice−water and extracted with ether. The extract was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The resultant residue was chromatographed using hexane as an eluent to afford the mixture of **6-*Z*** and **6-*E*** (18 mg, 37%), which was separated by thin-layer chromatography using hexane and chloroform to give **6-*Z*** as a yellow powder (hexane): mp 150−154 °C; $^1$H NMR $\delta$ 0.59 (3H, s), 0.74 (3H, s), 2.67−2.99 (16H, m), 6.37 (2H, s), 6.85 (2H, t, *J* 7.3), 7.09 (4H, d, *J* 7.3), 7.12 (4H, s); MS *m*/*z* 496 ($M^+$). Anal. Calcd for $C_{38}H_{40}$: C, 91.88; H, 8.12. Found: C, 91.61; H, 8.29.

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**Supporting Information Available:** Compound characterization data for **4b-*Z***, **4b-*E***, **4c-*Z***, **4c-*E***, **4d-*Z***, **4d-*E***, **4e-*Z***, **4e-*E***, **4f-*Z***, **4f-*E***, **4g-*Z***, **4g-*E***, **5a-*Z***, **5a-*E***, **5b-*Z***, and **5b-*E***. This material is available free of charge via the Internet at http://pubs.acs.org.

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