Medium-size cyclophanes, 71. Synthesis, structures and photo-induced cyclisation of 1,2-diphenyl[2.*n*]metacyclophan-1-enes

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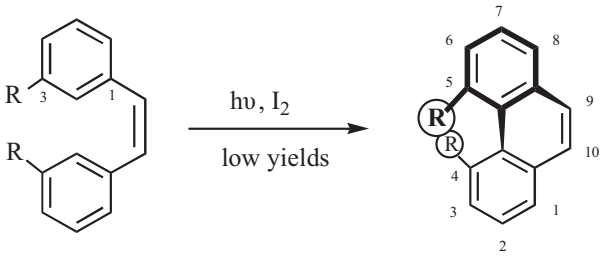
McMurry cyclisation of 1,*n*-bis(5-benzoyl-2-methoxyphenyl)alkanes **2** afforded 1,2-diphenyl[2.*n*]metacyclophan-1-enes **3**, which were converted into the corresponding [*n*](4,5)phenanthrenophanes **5** by photo-induced cyclisation in the presence of iodine as an oxidant.

Keywords: cyclophanes, metacyclophan-1-enes, McMurry reaction, conformation, photo-induced cyclisation

For many years various research groups have been attracted by the chemistry and spectroscopic properties of the 4,5-disubstituted phenanthrene skeleton.[2] Many attempts have been made to accomplish photo-induced cyclisations of 3,3'-disubstituted stilbenes to afford 4,5-disubstituted phenanthrenes, but these have failed because of the low yields due to the steric hindrance between the two substituents on the 4,5-positions of phenanthrene products (Scheme 1).[2–4]

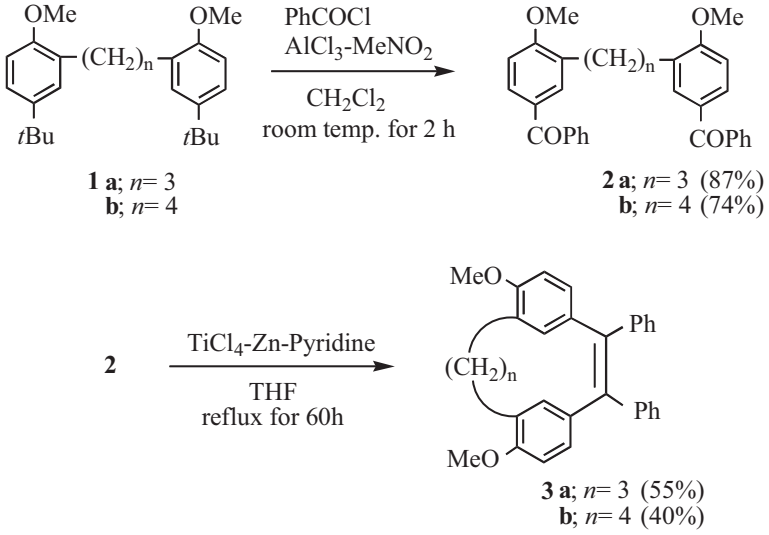
On the other hand, most investigations of the photoconversion of stilbene derivatives into 10b,10c-dihydrophenanthrenes have been for *anti*-[2.2]MCP-1-enes (MCP = metacyclophane)[5] and *anti*-[2.2]MCP-1,9-dienes.[6] Boekelheide and co-workers reported the photocyclisation of *anti*-[2.2]MCP-1-enes in the presence of oxidants to afford the corresponding phenanthrenes, but this was limited to the *anti*-conformation. Later, Mitchell *et al*. and others reported[7] the synthesis of *syn*-[2.2]MCP-1,9-diene, which valence isomerised to *cis*-dihydropyrene, but readily isomerised to *anti* cyclophane systems. These findings suggest that the extent of conformation fixing in the ground and transition states affect the photo-induced cyclisation reaction. Thus, there is substantial interest in investigating the photocyclisation of [2.*n*]MCP-enes which can adopt *syn*- and *anti*-conformations to form 4,5-disubstituted phenanthrenes. We now report on the syntheses of 1,2-diphenyl[2.*n*]MCP-1-enes using the low-valent titanium-induced McMurry reaction and the photo-induced cyclisation reactions to afford 9,10-diphenyl[*n*](4,5) phenanthrenophanes.



Scheme 1

Results and discussion

1,*n*-Bis(5-*tert*-butyl-2-methoxyphenyl)alkanes **1** have been prepared according our previous papers.[8] The $AlCl_3$–$MeNO_2$-catalysed acylation of compounds **1** with benzoyl chloride at 20°C led to an *ipso*-acylation reaction[9] affording the desired 1,*n*-bis(5-benzoyl-2-methoxyphenyl)alkanes (**2**) in good yield. 1,*n*-Bis(5-benzoyl-2-methoxyphenyl)alkanes **2** were subjected to reductive coupling by the McMurry reaction following Grützmacher's procedure[10,11] (Scheme 2). Thus, the reductive coupling reaction of **2a** carried out using $TiCl_4$–Zn in refluxing THF under high dilution conditions afforded the desired compound 6,13-dimethoxy-1,2-diphenyl[2.3]MCP-1-ene (**3a**) in 55% yield. Similarly, treatment of **2b** with $TiCl_4$–Zn in refluxing THF afforded 6,14-dimethoxy-1,2-diphenyl[2.4]MCP-1-ene (**3b**) in 40% yield. The structures of products **3** were determined on the basis of their elemental



Scheme 2

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analysis and spectroscopic data. The mass spectral data for **3a** and **3b** (M^+ (*m/z*) = 432 for **3a** and 446 for **3b**) strongly support the cyclic structure. [2.*n*]MCP-1-enes can adopt either a "staircase" *anti*-conformation or a *syn*-conformation with overlaying aromatic rings (Fig. 1).[12] Depending on the size of the bridges and on the presence of intraannular substituents, the interconversion between the *syn* and *anti* conformers occurs by ring flipping.[12]

The conformations of 1,2-diphenyl[2.3]MCP-1-enes **3** were readily apparent from their ^{1}H NMR spectra. Thus, the 300 MHz ^{1}H NMR spectrum of **3a** showed an upfield shift of the intraannular proton H_i at δ 6.10 ppm (broad singlet) due to the ring current of the opposite benzene ring[12] in addition to the resonances at δ 6.58 and 6.68 ppm for the other two protons of the aromatic rings. These observations suggested that the structure of **3a** corresponded exclusively to the *anti*-conformer. The protons of the phenyl groups attached to the etheno bridge were observed as a broad singlet at δ 7.11 ppm and the methoxy protons appeared at δ 3.77 ppm. The protons of the trimethylene bridge gave rise to a complicated signal pattern as expected for a rigid [2.3]MCP-1-ene. The diastereotopic protons of the benzylic CH_2 group were observed as two multiplets centred at δ 1.97 and 2.99 ppm which were further split by coupling with the protons of the central CH_2 group. The central CH_2 group was observed as a multiplet centred at δ 1.72 ppm. The peak pattern ascribed to the chemically distinct benzylic protons of the propano bridge proved the absence of a rapid *anti–anti* interconversion which would exchange H_A and H_B of each benzylic CH_2 group.

As the temperature of the solution of **3a** in $CDBr_3$ was increased, the individual peaks of the benzyl protons merged and eventually a broad single peak around δ 2.43 ppm was observed above 100°C. This observation indicated that the rate of conformational ring flipping of **3a** 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 17.0 kcal mol^{-1} higher value than that of *anti*-1,2-dimethyl[2.3]MCP-1-ene *anti*-**4** (T_C = 70°C, $\Delta G^{\neq}$ = 15.6 kcal mol^{-1}).[13] These observations suggested a much more rigid structure for **3a** than *anti*-**4** due to the introduction of two phenyl groups on the etheno bridge.

Similarly, the 300 MHz ^{1}H NMR spectrum of **3b** showed the resonances at δ 6.60 and 6.65 ppm for the two protons of the aromatic rings but the intra-annular proton H_i was observed at δ 7.12 ppm as a doublet (J = 2.0 Hz). These observations suggested that the structure of **3b** is exclusively as the *syn*-conformer. It was also found that the protons of the butano bridge were observed as two broad singlets centred at δ = 1.28 and 2.55 ppm, respectively, consistent with a fast interconversion of the two *syn* conformations of **3b** by ring flipping. However, as the temperature of the solution in $CDCl_3$–CS_2 (1: 3) is decreased, the single peak of the benzyl protons splits into a pair of broad singlets at

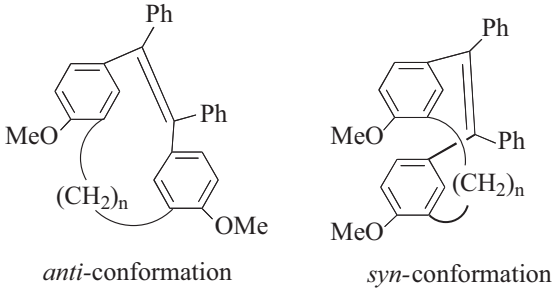
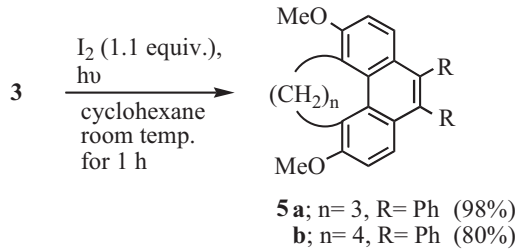


Fig. 1 Possible conformations of 1,2-diphenyl[2.*n*]MCP-enes 3.



5 a; n= 3, R= Ph (98%)
b; n= 4, R= Ph (80%)

Scheme 3

δ 2.24 and 2.90 ppm below –40°C. The energy barrier to the conformational ring flipping estimated from the coalescence temperature (T_c) is 11.7 kcal mol^{-1}. This finding indicates more a flexible structure for **3b** than for **3a** attributable to the larger cyclophane ring size. The solution conformation of 1,2-diphenyl[2.*n*]MCP-1-enes **3** is sensitive to the chain length of the bridges. The ring-inversion barriers determined by variable temperature ^{1}H NMR decrease with the increasing length of the bridges.

Examination of molecular models led us to believe that the transformation of 1,2-diphenyl[2.3]MCP-1-ene into 9,10-diphenyl[3](4,5)phenanthrenophane would be straightforward, since the *p* orbitals in the conformationally rigid stilbene moiety of [2.3]MCP-1-ene, which are involved in the photo-induced conrotatory cyclisation leading to the 4,5-propanophenanthrene eventually, are apparently very close in space.

Actually, when 1,2-diphenyl[2.3]MCP-1-ene *anti*-**3a** was irradiated by a 400-W high-pressure mercury lamp in the presence of an oxidant under standard conditions (I_2),[2] the desired phenanthrene **5a** was obtained in quantitative yield. Similarly, irradiation of *syn*-**3b** in the presence of I_2 afforded **5b** in 80% yield along with recovery of the starting compound. The rate of the photocyclisation of *anti*-**3a** was found to be much faster than that of *syn*-**3b** and reaction was almost completed within 1 h. Different reactivities for the irradiation of *anti*-**3a** and *syn*-**3b** were observed. In the present photocyclisation reaction of *syn*-**3b**, the photo-induced *syn*-*anti*-isomerisation might afford the corresponding *anti*-conformer *anti*-**3b**, which is cyclised to the product **5b**, but the space between the two benzene rings slightly increases. This is consistent with the result from the variable temperature ^{1}H NMR spectroscopy of *syn*-**3b** in which *syn*-*anti*-isomerisation can easily occur at room temperature.

These results are quite different from the photo-induced cyclisations 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 4,5-positions of phenanthrene products.[3] No photo-induced reaction in the 1,2-diphenyl moiety was observed under the conditions used. These findings suggest that the extent of conformation fixing in the ground and transition states affect the photo-induced cyclisation reaction. The reason for the present preference for the formation of *trans*-dihydrophenanthrene rather *cis*-dihydrophenanthrene as the intermediate might be attributable to the chair-form transition state being more stable than the boat one and conformational fixation to the chair form in the ground and transition states is possible in the *anti*-conformer.

Conclusions

A new synthesis of *anti*-1,2-diphenyl[2.*n*]MCP-1-enes **3** by a McMurry cyclisation has been developed and applied to the formation of 9,10-diphenylphenanthrenes connected by an alkyl chain at positions 4 and 5 by a photo-induced cyclisation

reaction. Further studies on the spectroscopic and chemical properties of the present novel 9,10-diphenyl[*n*](4,5)phenanthrenophanes are now in progress.

Experimental

All melting points are uncorrected. ^{1}H NMR spectra were recorded at 300 MHz on a Nippon Denshi JEOL FT-300 NMR spectrometer in deuteriochloroform with Me_4Si as an internal reference. IR spectra were measured as KBr pellets on a Nippon Denshi JIR-AQ2OM spectrometer. Mass spectra were obtained on a Nippon Denshi JMS-HX110A Ultrahigh Performance Mass Spectrometer at 75 eV using a direct-inlet system. Elemental analyses were performed by Yanaco MT-5.

Materials

Preparation of 1,*n*-bis(5-*tert*-butyl-2-methoxylphenyl)alkanes (**1**) has been described previously.[8]

Preparation of 1,3-bis(5-benzoyl-2-methoxyphenyl)propane (**2a**)

To a solution of 1,3-bis(5-*t*-butyl-2-methoxyphenyl)propane (**1a**) (3.68 g, 10 mmol) and benzoyl chloride (4.22 g, 30 mmol) in methylene dichloride (80 cm^3) was added a solution of aluminum chloride (5.94 g, 45 mmol) in nitromethane (10 cm^3) at 0°C. After the reaction mixture had been stirred at room temperature for 2 h, it was poured into ice-water (100 cm^3). The organic layer was extracted with CH_2Cl_2 (50 cm^3 × 2). The extract was washed with water (50 cm^3 × 2), dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel (Wako C-300, 300 g) with $CHCl_3$ as eluent to give crude 1,3-bis(5-benzoyl-2-methoxyphenyl)propane (**2a**) (4.04 g, 87%) as a pale yellow oil; ν_{max}(NaCl)/cm^{-1}: 1656 (C=O); δ_H ($CDCl_3$): 1.92 (2H, m, *CH*$_2$), 2.34 (4H, m, *CH*$_2$), 3.86 (6H, s, O*Me*), 6.86 (2H, d, *J* = 8.8 Hz, Ar–*H*), 7.76–7.92 (14H, m, Ar–*H*); *m*/*z*: 239 (100), 464 (M$^+$, 6). Anal. calcd. for $C_{31}H_{28}O_4$ (464.57): C, 80.15; H, 6.1. Found: C, 79.9; H, 6.2.

Compound **2b** was synthesised from **1b** in the same manner as described above for **2a** in 74% yield.

1,4-Bis(5-benzoyl-2-methoxyphenyl)butane (**2b**) was obtained as colourless prisms (AcOEt), m.p. 207–209°C; ν_{max}(KBr)/cm^{-1}: 1584 (C=O); δ_H ($CDCl_3$): 1.62–1.68 (4H, m, *CH*$_2$), 2.53–2.72 (4H, m, *CH*$_2$), 3.88 (6H, s, O*Me*), 6.87 (2H, d, *J* = 8.7 Hz, Ar–*H*), 7.41–7.78 (14H, m, *Ar-H*); *m*/*z*: 105 (100), 478 (M$^+$, 14). Anal. calcd. for $C_{32}H_{30}O_4$ (478.59): C, 80.3; H, 6.3. Found: C, 80.25; H, 6.2.

McMurry coupling reaction of **2**. *Typical procedure*

The McMurry reagent was prepared from $TiCl_4$ [23.8 g (13.8 cm^3), 125 mmol] and 18 g (275 mmol) of Zn powder in 500 cm^3 of dry THF, under nitrogen. A solution of **2a** (1.39 g, 3 mmol) and pyridine (22.5 cm^3, 200 mmol) in dry THF (250 cm^3) was added within 60 h from two Hershberg funnels to the black mixture of the McMurry reagent by using a high-dilution technique with continuous refluxing and stirring. The reaction mixture was refluxed for additional 8 h, cooled to room temp., and treated with aqueous 10% K_2CO_3 (200 cm^3) at 0°C. The reaction mixture was extracted with CH_2Cl_2 (200 cm^3 × 3). The combined extracts were washed with water, dried with Na_2SO_4 and concentrated. The residue was chromatographed over silica gel (Wako C-300, 300 g) with benzene as eluent to give crude **3a** as a colourless solid. Recrystallisation from ethyl acetate gave *anti*-6,13-dimethoxy-1,2-diphenyl[2.3]MCP-1-ene (**3a**) (713 mg, 55%) as colourless prisms, m.p. 270–272°C; ν_{max}(KBr)/cm^{-1}: 2999, 2937, 2833, 1597, 1498, 1439, 1270, 1245, 1129, 1029, 805; δ_H ($CDCl_3$, 27°C): 1.65–1.80 (2H, m, *CH*$_2$), 1.90–2.04 (2H, m, *CH*$_2$), 2.92–3.07 (2H, m, *CH*$_2$), 3.77 (6H, s, O*Me*), 6.10 (2H, broad s, Ar–*H*), 6.58 (2H, broad s, Ar–*H*), 6.68 (2H, broad s, Ar-*H*), 7.11 (10H, broad s, Ar–*H*); δ_H ($CDBr_3$, 120°C): 1.9–2.0 (2H, m, *CH*$_2$), 2.43 (4H, broad s, *CH*$_2$), 3.80 (6H, s, O*Me*), 6.30 (2H, broad s, Ar–*H*), 6.55 (4H, broad s, Ar–*H*), 7.0–7.2 (10 H, broad s, Ar–*H*); *m*/*z*: 432 (M$^+$, 100). Anal. calcd. for $C_{31}H_{28}O_2$ (432.57): C, 86.1; H, 6.5. Found: C, 86.0; H, 6.65.

Compound **3b** was synthesised from **2b** in the same manner as described above for **3a** in 40% yield.

6,14-Dimethoxy-1,2-diphenyl[2.4]MCP-1-ene (**3b**) was obtained as colourless prisms (MeOH), m.p. 267–269°C; ν_{max}(KBr)/cm^{-1}: 2973, 2938, 2833, 1634, 1603, 1490, 1265, 1242, 1114, 1038, 805, 702; δ_H ($CDCl_3$, 27°C): 1.20–1.35 (4H, broad s, *CH*$_2$), 2.48–2.61 (4H, broad s, *CH*$_2$), 3.76 (6H, s, O*Me*), 6.60 (2 H, dd, *J* = 8.8, 2.0 Hz, Ar–*H*), 6.65 (2H, d, *J* = 8.8 Hz, Ar–*H*), 7.03–7.12 (10H, m, Ar–*H*), 7.12 (2H, d, *J* = 2.0 Hz, Ar–*H*); δ_H ($CDCl_3$–CS_2 (1: 3), -40°C): 0.98 (2H, broad s, *CH*$_2$), 1.58 (2H, broad s, *CH*$_2$), 2.24 (2H, broad s, *CH*$_2$), 2.90 (2H, broad s, *CH*$_2$), 3.78 (6H, s, O*Me*), 6.62 (2 H, dd, *J* = 8.8, 2.0 Hz, Ar–*H*), 6.67 (2H, d, *J* = 8.8 Hz, Ar–*H*), 7.03–7.16 (10H, m, Ar–*H*), 7.18 (2H, d, *J* = 2.0 Hz, Ar–*H*); *m*/*z*: 446 (M$^+$, 100). Anal. calcd. for $C_{32}H_{30}O_2$ (446.59): C, 86.1; H, 6.8. Found: C, 85.8; H, 6.8.

Photoinduced cyclisation of **3** *in the presence of iodine. Typical procedure*

The mixture of **3a** (54 mg, 0.125 mmol) and iodine (35.0 mg, 0.137 mmol) was dissolved in cyclohexane (200 cm^3) in a Pyrex flask and then irradiated by a 400-W high-pressure mercury lamp while being monitored by GLC. Irradiation was continued until the disappearance of the reactant **3a** (1 h). The reaction mixture was washed with 10% sodium thiosulfate and water, dried with Na_2SO_4 and concentrated. The residue was chromatographed over silica gel (Wako C-300, 100 g) with hexane: benzene (1 : 1) as eluent to give **5a** (53 mg, 98%) as a colourless solid. Recrystallisation from ethyl acetate gave 9,10-diphenyl[3](4,5)phenanthrenophane (**5a**) as colourless prisms, m.p. 275–277°C; ν_{max}(KBr)/cm^{-1}: 2941, 1496, 1426, 1265, 1130, 1031, 805, 701; δ_H ($CDCl_3$): 2.51–2.64 (2H, m, *CH*$_2$), 2.89–2.92 (4H, m, *CH*$_2$), 3.95 (6H, s, O*Me*), 7.09–7.29 (14 H, m); *m*/*z*: 430 (M$^+$, 100). Anal. calcd. for $C_{31}H_{26}O_2$ (430.55): C, 86.5; H, 6.1. Found: C, 86.5; H, 6.0.

Compound **5b** was synthesised from **3b** in the same manner as described above for **3a** in 80% yield along with recovery of the starting compound **5b** in 20% yield.

9,10-Diphenyl[4](4,5)phenanthrenophane (**5b**) was obtained as colourless prisms (AcOEt), m.p. 276–278°C; ν_{max}(KBr)/cm^{-1}: 2931, 1523, 1488, 1421, 1253, 1174, 1164, 1103, 1025, 810, 727, 698; δ_H ($CDCl_3$): 1.93–2.22 (4H, m, *CH*$_2$), 2.12–2.41 (2H, m, *CH*$_2$), 3.09–3.27 (2H, m, *CH*$_2$), 3.95 (6H, s, O*Me*), 6.94–7.33 (14H, m, Ar–*H*); *m*/*z*: 444 (M$^+$, 100). Anal. calcd. for $C_{32}H_{28}O_2$ (444.58): C, 86.45; H, 6.35. Found: C, 86.6; H, 6.4.

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