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10a-(4-Biphenyl)-10b-methyl-10a,10b-dihydropyrene: a conformational study and ring current effect

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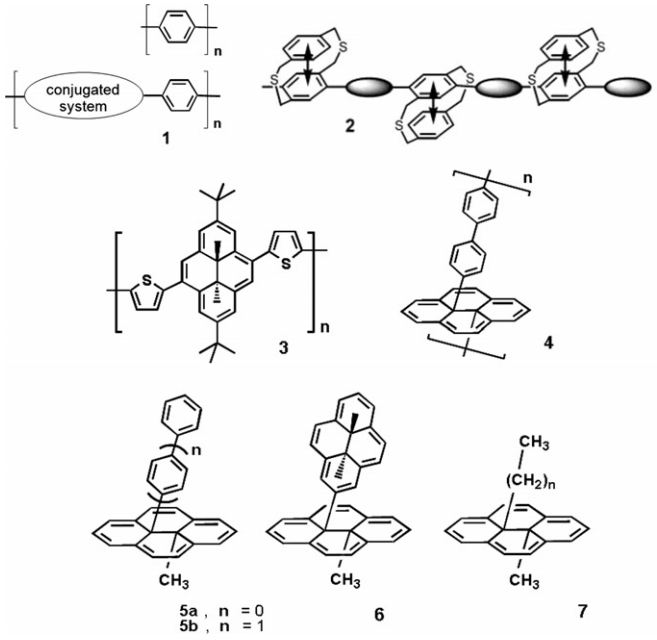
ABSTRACT

A dithiacyclophane was employed as a precursor to the title compound. A conformational study of the dithiacyclophane revealed a unique phenomenon in its terphenyl unit: one ring is rigidly held, the other terminal ring undergoes free rotation and the central ring exhibits restricted mobility. The aromatic protons of the biphenyl unit are all shielded by the dihydropyrene unit and well resolved in the ^{1}H NMR spectrum, consistent with a ring current effect extended to eight conjugated carbon atoms away from the molecular plane of dihydropyrene.

The first examples of doping poly(*p*-phenylene) (PPP) to establish its conducting properties were reported some 30 years ago.[1] Many PPP derivatives of type **1** copolymers have since been prepared for various applications based on their electrical, electronic, and/or optical properties.[2] They are collectively among the most comprehensively studied organic polymers today. The properties of copolymers **1** depend significantly on the linear conjugation in the polymer backbone. A series of copolymers **2** incorporating paracyclophanes into the polymer backbone showed that transannular π–π interactions could affect the optical properties of polymers significantly.[3] Thus an interesting area is to investigate whether homo-conjugation could also be employed to tune the properties of polymers. Compound **3**[4] is the only example where a carbocylic non-benzenoid has been introduced into a polymer backbone. It is a low molecular weight polymer, which shows interesting photochromic properties. A designer copolymer could be **4** where propagation of the properties of the polymer depends on homo-conjugation between the biphenyl and dihydropyrene segments. While relatively inconclusive in the study of **5a**,[5] homo-conjugation was evident in its naphthalene derivatives[6] and compound **6**.[7]

In this Letter, dihydropyrene **5b** was used as a model for **4** to investigate the conformational mobility of the biphenyl segment. Another interesting aspect is to examine whether adjacent dihydroypyrenes in **4** would be in sufficient proximity to interact. A study of **7**[8] showed that its ring current effect reached the protons on the C8 carbons but its methylene chain could be folded.



Monitoring the proton at C4″ (Scheme 1) in the rigid biphenyl unit in **5b** should provide a better indication of the extent of the ring current effect of the dihydropyrene.

The synthetic route to **5b** is summarized in Scheme 1. A Ni(II)-catalyzed[9] coupling reaction between the Grignard reagent prepared from 4-bromobiphenyl and 1-bromo-2,6-dimethylbenzene

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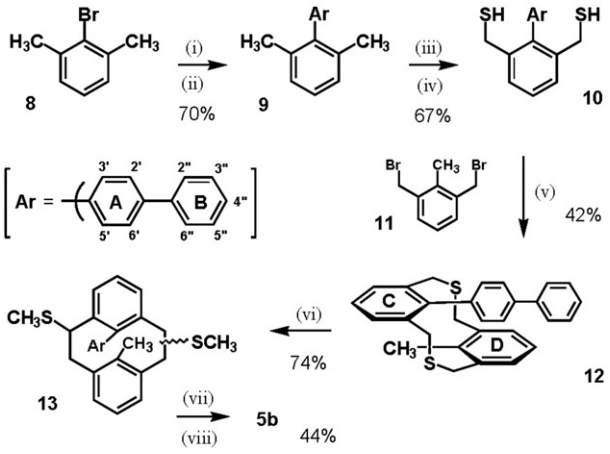
8 afforded the terphenyl **9**.[10] Free radical benzylic bromination[11] of **9** gave the desired dibromide which was converted to the dithiol **10**.[12] A cyclization reaction between **10** and the dibromide **11**[13] gave a mixture of *anti*-dithiacyclophane **12** and its *syn* isomer in an approximately 9:1 ratio based on ^{1}H NMR estimation.[14] The *anti* stereochemistry of **12** was clearly evident from a significantly shielded methyl signal at δ 1.55. Compound **12** was obtained in 42% yield after repeated recrystallizations. Its *syn* isomer, however, could not be isolated in pure form. A Witting rearrangement[15]–Hofmann elimination[16] sequence[13] on **12** afforded a 44% yield of the desired *trans*-dihydropyrene **5b** isolated as dark green crystals after chromatography and recrystallization. The trans stereochemistry was evident from a strongly shielded methyl signal at δ −4.28 in its ^{1}H NMR spectrum. In fact, a spectrum of the product mixture immediately after reaction indicated about 10% of the cis-isomer ($\delta CH_3 = -2.64$). This compound could not, however, be isolated due to its decomposition on chromatography.

The conformational behavior of *p*-terphenyl,[17] methyl-substituted *p*-terphenyls,[18] and oligo(*p*-phenylene)s[19] has been studied. *p*-Terphenyl was shown to exist as two stable rotational isomers around the inter-ring C–C bonds in solution.[17] In the terphenyl unit in **12**, ring C is conformationally rigid, it would be interesting to examine whether rings A and B would exhibit unrestricted rotation about the two C–C bonds independently. The ^{1}H NMR spectrum of dithiacyclophane **12** at or near room temperature (Fig. 1) showed well-resolved signals that could be assigned, through homo-decoupling and NOE experiments, to all the aromatic protons except those in ring A (Scheme 1). In fact the resolution of these signals remained relatively unchanged apart from marginal shifts when the sample was cooled from 308 to 213 K. This is a clear indication that there was unrestricted rotation about the bond joining ring A and ring B even at the low temperature limit. The aromatic protons at C2, C3, C5, and C6 in ring A were not observed at or below room temperature suggesting that there was a separate slow exchange process. At 213 K, these protons (H2′, H3′, H5′, and H6′) were observed as four separate sets of well-resolved double doublets (Fig. 1). This is a clear indication that there was restricted rotation about the C–C bond between ring A and ring C. Wobbling behavior, as shown in Figure 2, is believed to occur as was evident by the presence of only two well-resolved AB systems for the four pairs of bridging methylene protons.[14] As the temperature was raised,



Scheme 1. Synthetic route to dihydropyrene **5b**. Reagents and conditions: (i) 4-bromobiphenyl/Mg, THF, reflux, 3 h; (ii) Ni(acac)$_2$, THF, −78 °C, 5 min; reflux, 15 h; (iii) NBS, CCl_4, *hν*, reflux, 3 h; (iv) $(NH_2)_2CS$, 95% EtOH, reflux, 1 h; KOH, H_2O, reflux, 15 h; (v) KOH, 95% EtOH/benzene (4:1), 65 °C, 23 h; (vi) LDA, THF, rt, 10 min; MeI, THF, rt, 30 min; (vii) $(CH_3O)_2CHBF_4$, CH_2Cl_2, −30 °C, 15 min; rt, 20 h; (viii) *t*-BuOK, THF, reflux, 1 h.

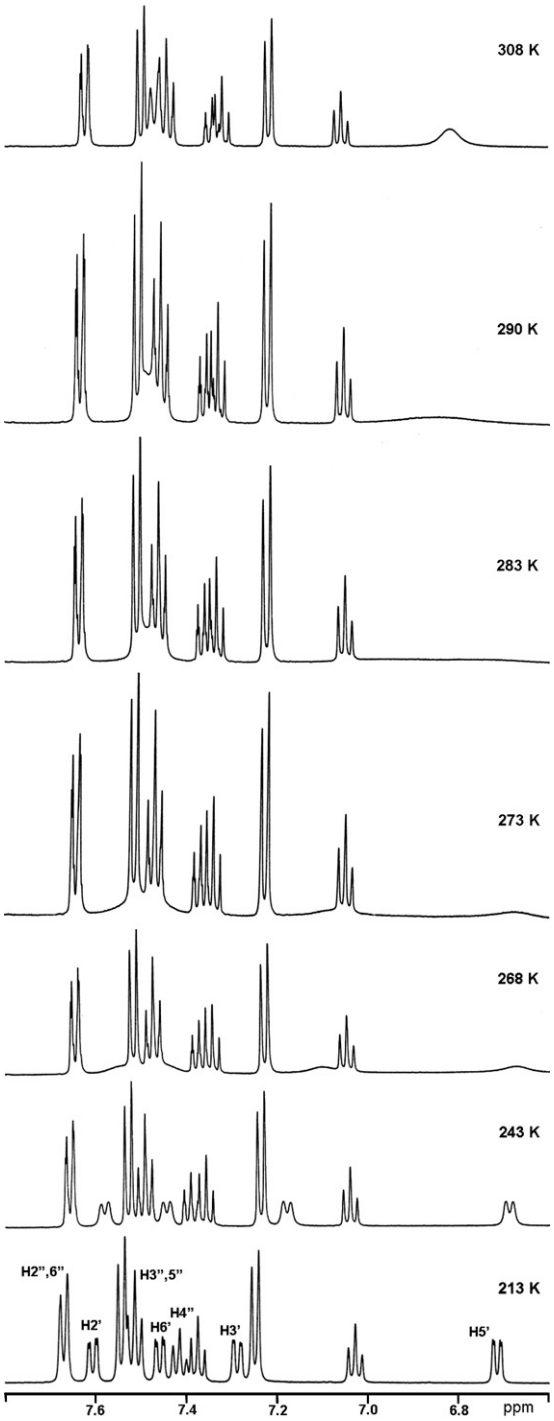


Figure 1. ^{1}H NMR spectra (500 MHz, $CDCl_3$) of the aromatic protons in dithiacyclophane **12** at different temperatures [proton numbering as in Scheme 1].

in addition to signal broadening, there were significant shifts of the four double doublets resulting in the appearance of only two singlets at the higher temperature limit (Fig. 1) consistent with a fast exchange process (unrestricted rotation of ring A). The two singlets [δ 7.48 (sharp, H2′,6′); δ 6.82 (broad, H3′,5′)], however, did not appear at the approximate centers of the corresponding pairs of double doublets [δ 7.61 (H2′), 7.47 (H6′); δ 7.29 (H3′), 6.71 (H5′)]. The significant signal shifts could be a result of the varying angle α (Fig. 2) at different temperatures (thus varying averaged chemical shifts) before free rotation occurred after a certain temperature.

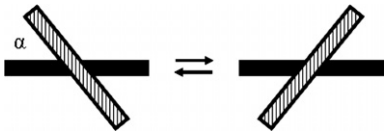


Figure 2. The wobbling process in dithiacyclophane **12** at low temperatures (■: Ring C; ▥: Ring A).

Employing the coalescence temperature method[20] to estimate the free energy of activation ($\Delta G_c^{\ddagger} = 4.57\ T_c[9.97 + \log_{10}(T_c/\Delta\upsilon)]$),[21] there are two sets of data available for comparison. The coalescence temperatures (T_c) for the two pairs of double doublets ($\Delta\upsilon$ = 74 and 287 Hz) could be estimated at 270 and 283 K, respectively (Fig. 1). These correspond to $\Delta G_c^{\ddagger}$ values of 54.4 and 53.9 kJ mol^{-1}. It was surprising to note that this conformational barrier of about 54 kJ mol^{-1} observed for **12** was essentially identical to that estimated for its phenyl (in place of biphenyl) analog.[22] Clearly ring B in **12** does not inflict any undesirable buttressing/steric effect on ring A in hindering its rotation about the C–C bond between ring A and ring C.

All the aromatic protons of dihydropyrene **5b** were resolved in its ^{1}H NMR spectrum (Fig. 3). The spectrum remained essentially unchanged with only marginal broadening and shifts when a sample was cooled from 298 to 213 K. It is evident that the biphenyl unit in **5b** enjoyed unrestricted free rotation even at the low temperature limit. Protons H3′, 5′ were strongly shielded at δ 2.89. Although the shielding effect declined quickly for H2′, 6′ and H2″, 6″ (Fig. 3), H3″, 5″ and H4″ appeared at δ 7.10 and δ 7.05, respectively. These are, however, still at relatively higher field than the corresponding protons (δ 7.3–7.6) in 4-*t*-butylbiphenyl[23] as a reference. It is apparent that the ring current effect of the dihydropyrene extends to even H4″—eight conjugated carbon atoms away from the molecular plane of the dihydropyrene within **5b**. This supports an empirical correlation established in the study of **7** where the proton shielding was also extended to C8 of the methylene chain.[8] An interesting observation was that H4″ is slightly less shielded than H3″,5″ in **5b**. These three protons are near the limit of the ring current effect and thus in addition to the distance from the center of the dihydropyrene molecular plane, their actual coordinates may result in the marginal difference in their chemical shifts.

In conclusion, free rotation of the aromatic rings in **5b**, and **12** at above room temperature, suggests that free rotation of the biphenyl spacer in polymer **4** is expected to allow conformational flexibility in their alignment for optimal homoconjugation with the dihydropyrenes. Secondly, a ring current study may suggest that the adjacent dihydropyrenes in **4** could be held by the rigid spacer in sufficient proximity to interact magnetically or electronically to propagate their properties along the polymer backbone.

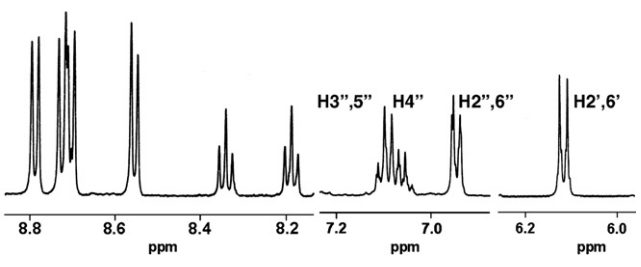


Figure 3. ^{1}H NMR spectrum (MH_2, CD_2Cl_2) of aromatic protons (excluding H3′, 5′ at δ 2.89) in dihydropyrene **5b**.

Acknowledgment

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10. 4-Bromobiphenyl (0.98 g, 4.2 mmol) in dry THF (20 ml) was added dropwise to Mg (11 mg, 4.5 mmol) in gently refluxing dry THF under Ar for 3 h. The resulting Grignard reagent was cooled to −78 °C, and 1-bromo-2,6-dimethylbenzene (0.77 g, 4.2 mmol) in dry THF (15 ml) was added dropwise (5 min) followed by Ni(acac)$_2$ (12 mg, 0.3 mmol). The mixture was warmed to rt and further maintained at refluxing temperature for 15 h. Water was added and the product was extracted into CH_2Cl_2, washed with 10% aqueous HCl and water, and dried. Chromatography on silica gel using hexane as eluent followed by recrystallization from cyclohexane gave **9** as a white solid (0.58 g, 70%), mp = 94–96 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (dd, J = 8.0, 1.7 Hz, 4H), 7.46 (t, J = 7.5 Hz, 2H), 7.35 (t, J = 7.4 Hz, 1H), 7.11–7.25 (m, 5H), 2.08 (s, 6H). EIMS m/z 258 (M$^+$, 100), 243 (30), 181 (26). CHN Calcd for $C_{20}H_{18}$: C, 92.98; H, 7.02. Found: C, 92.63; H, 7.36.
11. NBS (0.78 g, 4.4 mmol) and **9** (0.53 g, 2 mmol) in CCl_4 (200 ml) were heated at refluxing temperature by irradiation with visible light. When all the NBS had reacted (ca. 3 h), the mixture was cooled and filtered. The filtrate was washed with water and dried. Recrystallization from cyclohexane gave 2,6-bis-(bromomethyl)terphenyl as a white solid (0.82 g, 76%), mp = 146–147 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.73 (m, 4H), 7.36–7.51 (m, 8H), 4.27 (s, 4H). EIMS m/z 414 (M$^+$, 16; correct isotope pattern for Br_2), 255 (100). CHN Calcd for $C_{20}H_{16}Br_2$: C, 57.72; H, 3.88. Found: C, 57.58; H, 4.12.
12. 2,6-Bis(bromomethyl)terphenyl (0.473 g, 1.1 mmol) and thiourea (0.258 g, 3.3 mmol) in 95% EtOH were heated at refluxing temperature for 1 h. The resulting bis(thiouronium) salt precipitate was filtered and added to an aqueous solution of KOH (0.94 mg, 20 mmol). The mixture was heated at refluxing temperature for 15 h, cooled and acidified with 1 M aqueous HCl. The product was extracted into ether and dried. Chromatography of the product mixture on silica gel using hexane/CH_2Cl_2 (3:2) as eluent gave **10** (0.311 g, 88%) as a thick oil. Slow evaporation of a solution of **10** in cyclohexane kept at 0 °C gave pure **10**, mp = 62–65 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67–7.72 (m, 4H), 7.49 (br t, J = 7.6 Hz, 2H), 7.35–7.41 (m, 6H), 3.50 (d, J = 7.7 Hz, 4H), 1.64 (t, J = 7.7 Hz, 2H). EIMS m/z 322 (M$^+$, 69), 255 (100). CHN Calcd for $C_{20}H_{18}S_2$: C, 74.49; H, 5.63. Found: C, 74.85; H, 5.66.
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14. A solution of **10** (0.259 g, 0.8 mmol) and **11** (0.222 g, 0.8 mmol) in benzene (150 ml) was added dropwise with vigorous stirring over 8 h to KOH (0.75 g, 16 mmol) in 95% EtOH/benzene (4:1, 600 ml) at ca. 65 °C. The mixture was stirred at ca. 65 °C for another 15 h. The bulk of the solvent was removed under reduced pressure and the product was extracted into CH_2Cl_2 (150 ml). The ^{1}H NMR spectrum of the product mixture indicated a 9:1 ratio of *anti* (δCH_3 = 1.56): *syn* (δCH_3 = 2.35) isomers. Chromatography on silica gel using hexane/CH_2Cl_2 (1:1) as eluent followed by repeated recrystallizations from cyclohexane gave colorless crystals of **12** (0.148 g, 42%), mp = 180–181 °C. ^{1}H NMR (500 MHz, CD_2Cl_2, −60 °C) δ 7.67 (d, J = 7.4 Hz, 2H), 7.61 (dd, J = 8.1, 1.8 Hz, 1H), 7.54 (d, J = 7.6 Hz, 2H), 7.51 (t, J = 7.6 Hz, 2H), δ 7.47 (dd, J = 8.0, 1.9 Hz, 1H), 7.42 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.29 (dd, J = 8.1, 1.6 Hz, 1H), 7.25 (d, J = 7.6 Hz, 2H), 7.03 (t, J = 7.5 Hz, 1H), 6.71 (dd, J = 8.0, 1.7 Hz, 1H), 3.86 (d, J = 13.6 Hz, 2H), δ 3.81 (d, J = 14.3 Hz, 2H), 3.72 (d, J = 14.3 Hz, 2H), 3.49 (d, J = 13.6 Hz, 2H), 1.55 (s, 3H). EIMS m/z 438 (M$^+$, 62), 287 (30), 255 (100), 253 (46). Calcd for $C_{29}H_{26}S_2$: C, 79.41; H, 5.97. Found: C, 79.08; H, 6.11.
15. LDA prepared from *n*-BuLi (1.6 M in hexane; 0.4 ml) and diisopropylamine (61 mg, 0.6 mmol) in dry THF (5 ml) was added dropwise to **12** (109 mg, 0.25 mmol) in dry THF (10 ml) under N_2 at rt. After 10 min, excess MeI

(284 mg, 2 mmol) was added and the mixture stirred at rt for 30 min. Water and CH_2Cl_2 were then added, and the organic phase was separated and dried. Chromatography on silica gel using hexane/CH_2Cl_2 (3:1) gave a mixture of **13** as a white solid (86 mg, 74%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 6.2 Hz), 7.78 (d, J = 6.4 Hz), 7.5–7.7 (m), 7.53 (d, J = 7.1 Hz), 7.4–7.5 (m), 7.41 (t, J = 7.7 Hz), 7.2–7.3 (m), 7.15 (t, J = 7.4 Hz), 6.7–7.0 (m), 6.50 (d, J = 8.4 Hz), 4.28 (dd, J = 11.4, 7.1 Hz), 4.15–4.20 (m), 3.97 (dd, J = 11.3, 4.2 Hz), 2.65–2.95 (several sets of multiplets), 2.15, 2.19, 2.25 (s), 0.83, 0.85, 0.87 (s). EIMS m/z 466 (M^+, 21), 403 (29), 370 (24), 301 (100), 255 (65). Calcd for $C_{31}H_{30}S_2$ (MS): 466.6999. Found: 466.6986. This was used directly for subsequent reaction.

16. A mixture of **13** (0.140 g, 0.3 mmol) in CH_2Cl_2 (5 ml) was added to $(MeO)_2CHBF_4$ (162 mg, 1 mmol) suspended in CH_2Cl_2 (5 ml) at −30 °C under N_2. The mixture was then stirred at rt for 5 h. EtOAc (4 ml) was added and the mixture stirred for 15 h. The resulting bis(sulfonium) salt was filtered and dried. *t*-BuOK (103 mg, 1 mmol) was added to a suspension of the bis(sulfonium) salt in dry THF (15 ml) at rt under N_2. The mixture was heated at refluxing temperature for 1 h, cooled, and extracted with CH_2Cl_2. The organic layer was washed with water and dried. The ^{1}H NMR spectrum of the product mixture indicated a 10:1 ratio of trans (δCH_3 = −4.28): cis (δCH_3 = −2.64) isomers. Chromatography on silica gel using hexane as eluent followed by recrystallization from cyclohexane gave green crystals of *trans*-**5b** (49 mg, 44%), mp = 143–145 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, J = 7.8 Hz, 2H), 8.72 (d, J = 7.7 Hz, 2H), 8.70 (d, J = 7.7 Hz, 2H), 8.46 (d, J = 7.7 Hz, 2H), 8.34 (t, J = 7.7 Hz, 1H), 8.18 (d, J = 7.8 Hz, 1H), 7.10 (t, J = 7.2 Hz, 2H), 7.05 (t, J = 7.0 Hz, 1H), 6.94 (dd, J = 7.7, 1.6 Hz, 2H), 6.11 (d, J = 8.6 Hz, 2H), 2.89 (d, J = 8.6 Hz, 2H), −4.28 (s, 3H). EIMS m/z 370 (M^+, 26), 355 (43), 217 (36), 202 (100). Calcd for $C_{29}H_{22}$: C, 94.01; H, 5.99. Found: C, 93.82; H, 6.17.
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