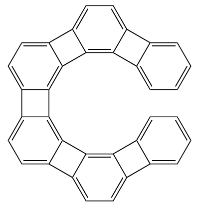
[18] T. E. M. van den Hark, P. T. Beurskens, *Acta Crystallogr. Sect. C* **1976**, *5*, 247; see also: P. T. Beurskens, G. Beurskens, T. E. M. van den Hark, *Acta Crystallogr. Sect. C* **1976**, *5*, 241.
[19] S. Grimme, J. Harren, A. Sobanski, F. Vögtle, *Eur. J. Org. Chem.* **1998**, 1491.
[20] R. H. Janke, G. Haufe, E.-U. Würthwein, J. H. Borken, *J. Am. Chem. Soc.* **1996**, *118*, 6031.
[21] While we cannot rule out accidental isochronism of the methylene hydrogens, its selective occurrence in two derivatives of differing symmetry would seem unlikely.
[22] S. Han, D. R. Andersen, A. D. Bond, H. V. Chu, R. L. Disch, D. Holmes, J. M. Schulman, S. J. Teat, K. P. C. Vollhardt, G. D. Whitener, *Angew. Chem.* **2002**, *114*, 3361–3364; *Angew. Chem. Int. Ed.* **2002**, *41*, 3227–3230.

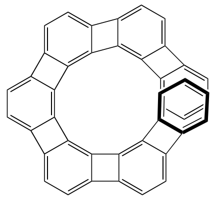
Total Syntheses of Angular [7]-, [8]-, and [9]Phenylene by Triple Cobalt-Catalyzed Cycloisomerization: Remarkably Flexible Heliphenes**

Sangdon Han, D. Ryan Anderson, Andrew D. Bond, Hiufung V. Chu, Raymond L. Disch, Daniel Holmes, Jerome M. Schulman, Simon J. Teat, K. Peter C. Vollhardt,* and Glenn D. Whitener

We have reported on the total syntheses of the first helical phenylenes (heliphenes), angular [6]- (**1**) and [7]phenylene (**2**), by a double cobalt-catalyzed cyclotrimerization strategy.[1] These hydrocarbons are the highest members of the, so far, five angular phenylene systems and, with **2**, match the current size limit of all phenylenes.[2] Their properties are intriguing, including unusual mass spectrometric fragmentations for **1**, a strongly attenuated bathochromic increment in the UV spectrum of **2**, shielding of the terminal rings in **2** as a result of spatial overlap, alternating ring current intensities along the angular frame, X-ray crystallographic data that detail the helical and σ-π distortive features, and, most surprisingly, an unusually low barrier for the enantiomerization of **2**, which decreases on introduction of terminal substituents. To better understand these results, the construction of even higher members of the series was deemed imperative.

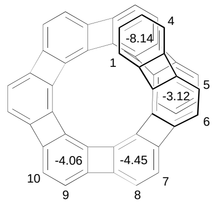


1

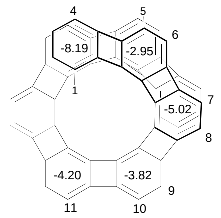


2

Here, we describe the total synthesis of angular [8]- (**3a**) and [9]phenylene (**4a**) [nucleus-independent chemical shift (NICS)(0) values are given inside the rings], together with another assembly of [7]phenylene (**2**), by an unprecedented triple cobalt-catalyzed cycloisomerization protocol, the X-ray structure of **3a**, and experiments addressing the conformational flexibility of the targets.



3a



4a

Retrosynthetic analysis of **3** and **4** along the lines used in the formation of the lower benzocyclobutadienologues **1** and **2**[1] proved problematic because of the absence of suitably functionalized angular [3]phenylene building blocks. As a result, a challenging disconnection of three inner benzene rings was contemplated. This approach would require the stitching together of the corresponding nonayne precursors and was first tested on a known final product, **2** (Scheme 1). For this purpose, the scaffold of the crucial intermediate **7** was put together by linking two units of **5**[1] with a C_2 bridge in a stepwise manner via **6**.[3] Gratifyingly, cobalt-catalyzed cyclization of **7** gave **2**. While the yield of this transformation is modest, it should be viewed within the context of what it accomplishes, namely the generation of the desired helical topology by forming nine rings in one step, including all six of the component cyclobutadienes with an associated estimated strain of about 300 kcal mol^{-1}![4]

Encouraged by these results, we employed the same strategy en route to **3** (Scheme 2) and **4** (Scheme 3). Triyne **8**[5] and the requisite biphenylene reagents **11**,[6] **12**,[1] and **16**[6] were known, allowing for the iterative Pd-catalyzed build-up of the target nonaynes **10** and **15**. Attempts to shorten the sequences depicted (in particular, exploiting the symmetry inherent in **7** and **15**) were less effective.

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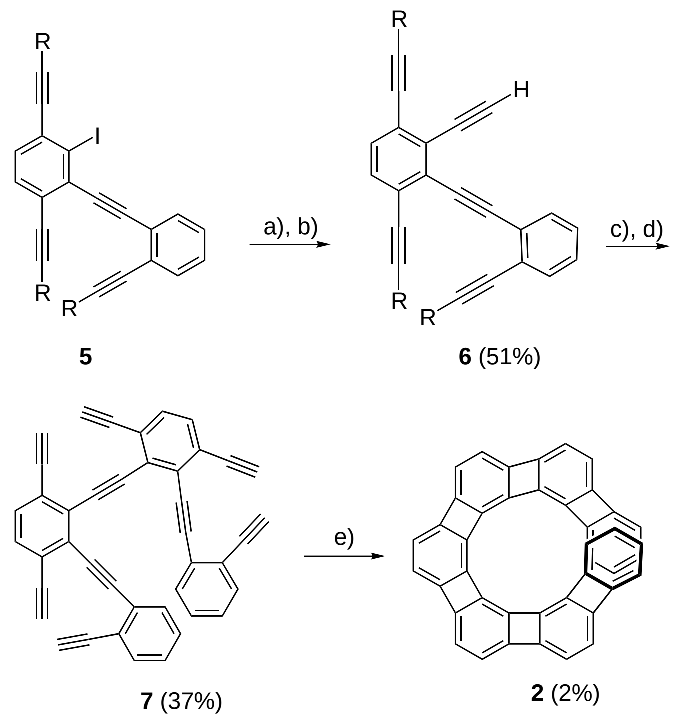
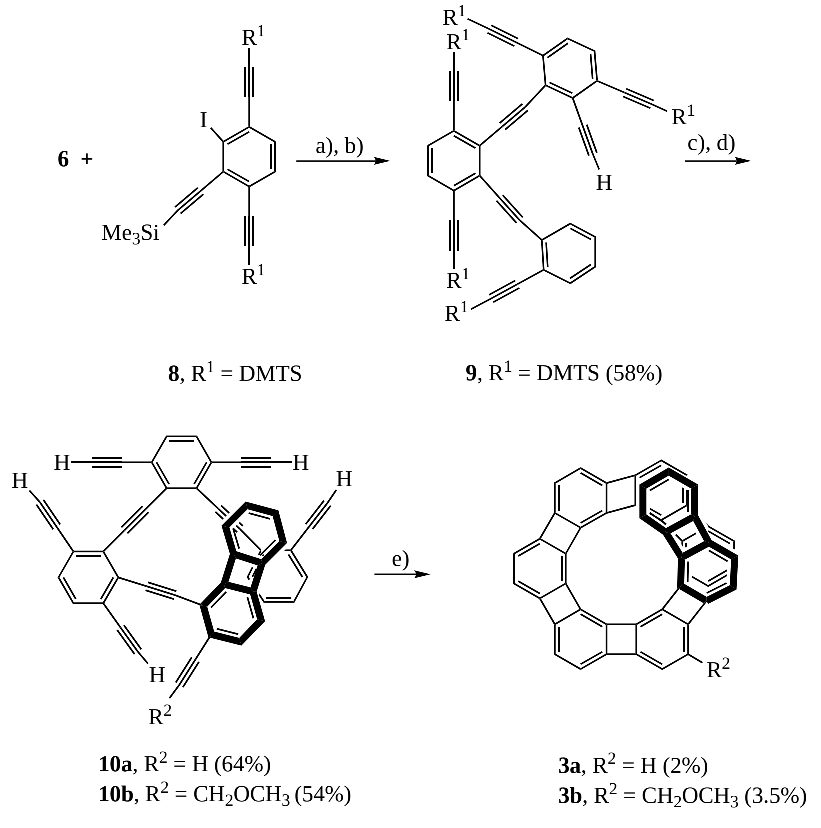


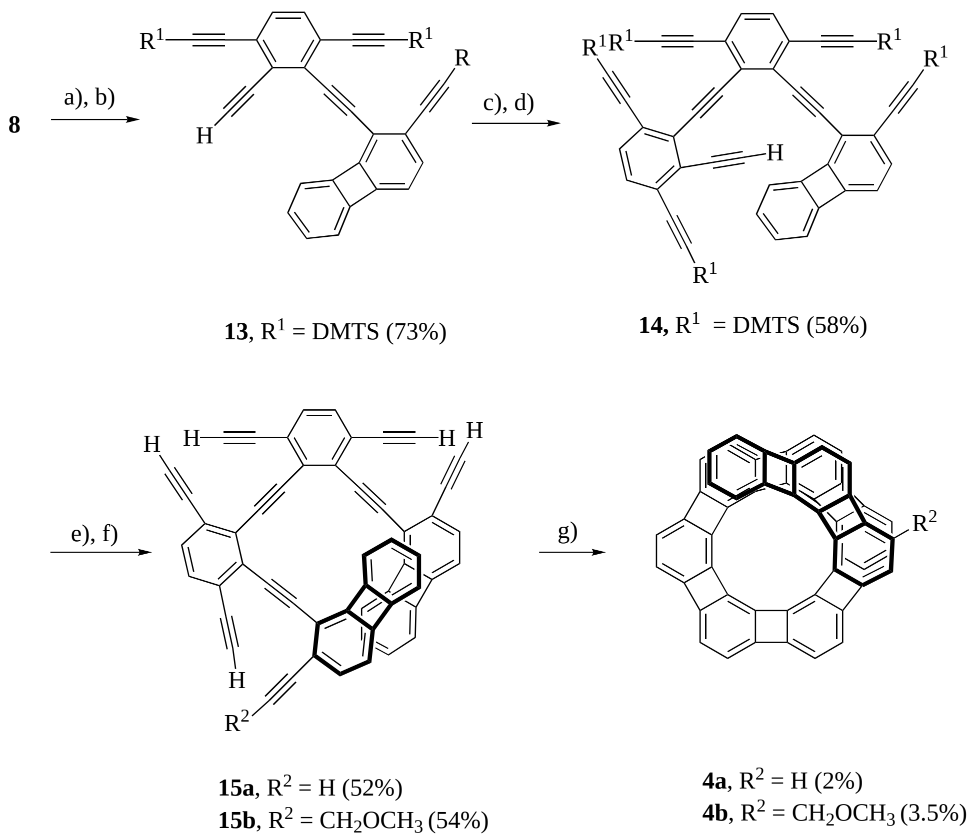
Scheme 1. a) Trimethylsilylethyne (2 equiv), 5% $[Pd(PPh_3)_2Cl_2]$, 6% CuI, Et_3N, 85°C, 14 h; b) K_2CO_3 (0.5 equiv), THF, MeOH, 30 min; c) **6** (1 equiv), 8% $[Pd(PPh_3)_2Cl_2]$, 8% CuI, Et_3N, 65°C, 17 h; d) $Bu_4N^+F^-$ (7 equiv), THF, 23°C, 1 h; e) $[CpCo(CO)_2]$ (5 equiv), *m*-xylene, *hν*, △, 1 h. R = DMTS = $SiMe_2(CMe_2CHMe_2)$ (dimethylthexylsilyl).

Systems **3** and **4**, the largest phenylenes known, are orange-red solids, stable to air for one to two days (in solution for several hours, requiring rapid column chromatography on silica with hexane/CH_2Cl_2 gradient), and moderately soluble in common solvents.[7] The spectral data (Table 1) reflect the novel topology and electronic features of the systems. Thus, the mass spectra show the molecular ion as the base peak, typical of polycyclic aromatic hydrocarbons,[8] but no discernible M^{2+} peaks or (for the parent compounds) significant fragmentations. The electronic spectra continue to show the typical patterns of the lower angular phenylenes, with a set of high-intensity peaks at lower wavelengths, followed by a corresponding group of weaker absorptions at higher wavelengths.[1,9] Significantly, in light of the attenuated (from a $\Delta\lambda = 20$–22 nm in the lower analogues) incremental bathochromic shift of the longest-wavelength band of **2** ($\Delta\lambda = 12$ nm), the corresponding data for **3** ($\Delta\lambda \sim 10$ nm) and **4** ($\Delta\lambda \sim 9$ nm) seem to confirm a trend to smaller values. Indeed, a plot of the corresponding λ_{max} values versus $1/(N+0.5)$[10] for $N = 2$–9, where N is the number of six-membered rings, provides a straight line ($R^2 = 0.9954$) that extrapolates to 578 nm (2.14 eV), a possible measure of the solution band gap for the hypothetical polyheliphene. A similar graph for the helicenes gives 505 nm (3.24 eV), a clear reflection of the relative electronic activation of the phenylenes.

The assignments of the ^{1}H NMR spectra were consistent with those made for the lower angular phenylenes[1,9] and with calculated spectra,[11,12] and used the simplifying effects of substitution in the alkylated derivatives (Schemes 2 and 3). Nevertheless, the correlations of the close-lying signals for H5, H6, and H7 in **4a** are tentative. As is typical for the series,[1,9] the terminal rings are most diatropic (aromatic), the penultimate ones the least (most cyclohexatrienic). Interestingly, however, in comparing the spectrum of **3a** with that of **2**,[1] we note that the resonances for H1, H2, and H3 have moved slightly downfield, and those for H4, H5, and H6 upfield. A possible rationale for this behavior is found on inspection of the structure of **3a** (Figure 1), in which the former hydrogens are placed above the cyclohexatrienoid, and hence relatively less diatropic, penultimate ring of the opposite helical frame. Conversely, the latter hydrogens are now located above and relatively closer to the corresponding terminal ring, thus experiencing relatively increased shielding. Noteworthy is also the position of the peak for the internal hydrogens H9/H10 at higher field than those of their neighbors H7 and H8, in accord with the alternation of cyclohexatrienoid and aromatic character discussed previously, and nicely reproduced by the NICS(0) data (see structural drawing).[1] The spectrum of **4a** reveals similar trends, particularly in comparison to that of **3a**, notably pronounced relative shielding of H7 and H8,



Scheme 2. a) 12% $[Pd(PPh_3)_2Cl_2]$, 9% CuI, Et_3N, 80°C, 16 h; b) K_2CO_3 (3 equiv), Et_2O, MeOH, 23°C, 15 h; c) for **10a**: 2-(DMTS-ethynyl)-1-iodobiphenylene (**11**, 1 equiv), 25% $[Pd(PPh_3)_2Cl_2]$, 18% CuI, Et_3N, 85°C, 20 h; for **10b**: 1-iodo-2-(3-methoxy-1-propynyl)biphenylene (**12**, 1 equiv), 22% $[Pd(PPh_3)_2Cl_2]$, 17% CuI, Et_3N, 85°C, 16 h; d) $Bu_4N^+F^-$ (12–13 equiv), THF, 23°C, 1–2 h; e) $[CpCo(CO)_2]$ (8–10 equiv), *m*-xylene, *hν*, △, 30 min.



Scheme 3. a) 2-(DMTS-ethynyl)-1-ethynylbiphenylene (**16**) (1 equiv), 22% [Pd(PPh$_3$)$_2$Cl$_2$], 16% CuI, Et$_3$N, 75 °C, 17 h; b) K$_2$CO$_3$ (2 equiv), Et$_2$O, MeOH, 23 °C, 2 h; c) **8** (1 equiv), 25% [Pd(PPh$_3$)$_2$Cl$_2$], 19% CuI, Et$_3$N, 80 °C, 15 h; d) K$_2$CO$_3$ (3 equiv), Et$_2$O, MeOH, 23 °C, 18 h; e) for **15a**: **11** (1 equiv), 23% [Pd(PPh$_3$)$_2$Cl$_2$], 17% CuI, Et$_3$N, 85 °C, 1.5 d; for **15b**: **12** (1 equiv), 23% [Pd(PPh$_3$)$_2$Cl$_2$], 18% CuI, Et$_3$N, 85 °C, 1 d; f) Bu$_4$N$^+$F$^-$ (12–13 equiv), THF, 23 °C, 1–2 h; g) [CpCo(CO)$_2$] (8–10 equiv), *m*-xylene, *hν*, △, 25 min.

Table 1. Selected physical data for **3a** and **4a**.[7][a]

3a: orange-red solid; MS (70eV): *m*/*z* (%): 596 ([*M*$^+$], 100); ^{1}H NMR (400 MHz, CD$_2$Cl$_2$): $\delta = 6.92$ (d, $J = 6$ Hz, 2H, H1), 6.69 (t, $J = 6.8$ Hz, 4H, H2, H3), 6.54 (d, $J = 6.4$ Hz, 2H, H4), 6.49 (d, $J = 6.8$ Hz, 2H, H7), 6.47 (d, $J = 6.8$ Hz, 2H, H8), 6.44 (s, 4H, H9, H10), 6.13 (d, $J = 6.4$ Hz, 2H, H6), 5.98 ppm (d, $J = 7.2$ Hz, 2H, H5); UV/Vis (CH$_2$Cl$_2$): λ_{max} (lgε) = 235 (4.81), 264 (4.81), 320 (4.83), 387 (4.10), 416 (4.01), 465 (3.64), 498 (3.42), 515 nm (sh, 2.79). High-resolution MS calcd for C$_{48}$H$_{20}$: 596.1565; found: 596.1559.

4a: orange-red solid; MS (70eV): *m*/*z* (%): 670 ([*M*$^+$], 100); ^{1}H NMR (400 MHz, CD$_2$Cl$_2$): $\delta = 6.95$ (d, $J = 6.4$ Hz, 2H, H1), 6.61 (m, 4H, H2, H3), 6.59 (m, 2H, H4), 6.43 (s, 2H, H11), 6.39 (AB m, 4H, H9, H10), 6.23 (d, $J = 6.8$ Hz, 2H, H8), 6.06 (d, $J = 6.4$ Hz, 2H, H7), 6.04 (d, $J = 6.4$ Hz, 2H, H6), 5.99 ppm (d, $J = 6.4$ Hz, 2H, H5); UV/Vis (CH$_2$Cl$_2$): λ_{max} (lgε) = 240 (4.45), 273 (4.50), 315 (4.33), 408 (sh, 3.69), 460 (sh, 3.36), 507 (sh, 3.04), 524 nm (sh, 2.72). High-resolution MS calcd for C$_{54}$H$_{22}$: 670.1721; found: 670.1715.

[a] For the labeling of the protons see the structural formulae.

and the occurrence of the peak for the internal hydrogens H11/H12 at lower field than that of their neighbors H9/H10.

The X-ray crystal structure of **3a**·[CH$_2$Cl$_2$]$_{0.5}$ is depicted in Figure 1.[13] The molecule is unsymmetrical (because of the cocrystallizing CH$_2$Cl$_2$) and crystallizes as alternating enantiomers. The bond parameters are in excellent agreement with calculations.[11,12] Unlike the lower analogues and not reflecting the NMR data, the percent bond fixation[1] does not alternate on proceeding from the least bond-alternated terminal to the internal benzene rings, but remains essentially constant [averaged for twofold symmetry: 29%, 54%, 52%, 54%; shortest bond 1.344(6) Å, longest bond 1.459(6) Å], perhaps reflecting the limiting value for polyheliphene. The closest intramolecular contact is between C37 and H5 [2.888 Å (calculated[12] 3.043 Å), numbering in Figure 1]. The terminal ring centroids are separated by 4.41 Å (5.49 Å), and the corresponding interplanar angle is 23.6° (41.1°). The interplanar angles between consecutive six- and four-membered rings starting from the terminus defined by C1-C2-C3-C4-C5-C6 are 1.51, 1.60, 2.93, 6.02, 6.94, 5.99, 4.83, 4.76, 5.01, 5.15, 2.64, 2.98, 3.60, and 3.61°, describing an uneven and unsymmetrical helical turn, presumably affected by the presence of the solvating CH$_2$Cl$_2$. Taking the central four-membered ring as a reference, the inner helix climbs 3.35 Å (4.24 Å) and turns in plane by 393.0° (389.1°). Unfortunately, crystals suitable for X-ray analysis could not be obtained for **4a** (or **4b**). However, the calculated structure[12] gives an impression of its molecular topology. As in **3a**, the inner six-membered rings maintain

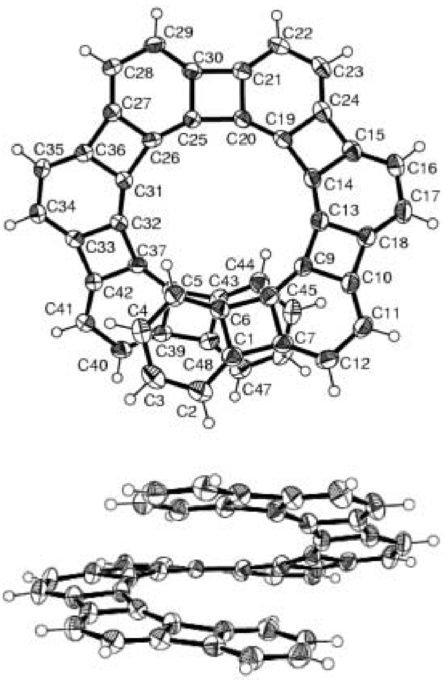


Figure 1. Structure of **3a**·[CH$_2$Cl$_2$]$_{0.5}$ (from CH$_2$Cl$_2$) in the crystal: views from above (top) and the side (bottom). Solvent of crystallization has been omitted for clarity.

approximately the same level of bond fixation (23%, 53%, 48%, 48%, 49%, shortest bond 1.358 Å, longest bond 1.456 Å). The interplanar angles between consecutive six- and four-membered rings starting from the terminus are 1.31, 2.98, 3.61, 4.67, 3.84, 5.47, 4.50, and 4.99°, a smoother progression than that of **3a**, likely due to the absence of crystal lattice forces.[14] The closest contact is between H1 and C22f (2.99 Å), the terminal ring centroids are separated by 7.48 Å, with an interplanar angle of 33.2°. Taking the central six-membered ring as a reference, the inner helix climbs 5.07 Å and turns in plane by 415.7°.

Are heliphenes **3** and **4** sufficiently extended to render their enantiomers amenable to resolution? The answer is provided by variable-temperature NMR experiments carried out on derivatives **3b** and **4b**. Remarkably, decoalescence of the potentially diastereotopic methylene hydrogens of the substituent in **3b** occurred only on cooling, providing $\Delta G^{\ddagger}_{-4.5\,^{\circ}\mathrm{C}} = 13.4 \pm 0.4\ \mathrm{kcal\,mol^{-1}}$ (400 MHz, $\Delta\nu_{\max} = 12.6$ Hz, [D$_8$]toluene). This value is less than 1 kcal mol^{-1} higher than that of the corresponding [7]heliphene **2**.[1] To our further surprise, [9]heliphene **4b** did not show any change in the shape of the corresponding methylene singlet signal down to the (solubility) limiting temperature of −45 °C (400 MHz, [D$_8$]toluene), suggesting a lower barrier to enantiomerization, less than around 12 kcal mol^{-1}. As proposed previously,[1,15] it appears that steric activation of the helical ground state toward unwinding the helix is responsible for the observed dynamic behavior. Structural elements, such as additional stereocenters biasing the helix or steric blockers locking it, will have to be introduced to render the heliphene frame configurationally robust. Finally, it is evident that extensions of the "stitching" procedures outlined in Schemes 1–3 should provide access to even higher members of the heliphene series. Such is the focus of future research.

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[1] S. Han, A. D. Bond, R. L. Disch, D. Holmes, J. M. Schulman, S. J. Teat, K. P. C. Vollhardt, G. D. Whitener, *Angew. Chem.* **2002**, *114*, 3357–3361; *Angew. Chem. Int. Ed.* **2002**, *41*, 3223–3227

[2] R. Boese, A. J. Matzger, D. L. Mohler, K. P. C. Vollhardt, *Angew. Chem.* **1995**, *107*, 1630; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1478.

[3] Attempted direct Pd-catalyzed installation of the C_2 bridge with ethyne failed, although it is successful in related couplings, see: a) R. Boese, A. J. Matzger, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1997**, *119*, 2052; b) M. Iyoda, A. Vorasingha, Y. Kuwatani, M. Yoshida, *Tetrahedron Lett.* **1998**, *39*, 4701; c) K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, 4467.

[4] H.-D. Beckhaus, R. Faust, A. J. Matzger, D. L. Mohler, D. W. Rogers, C. Rüchardt, A. K. Sawhney, S. P. Verevkin, K. P. C. Vollhardt, S. Wolff, *J. Am. Chem. Soc.* **2000**, *122*, 7819.

[5] C. Eickmeier, H. Junga, A. J. Matzger, F. Scherhag, M. Shim, K. P. C. Vollhardt, *Angew. Chem.* **1997**, *109*, 2194; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2103.

[6] R. H. Schmidt-Radde, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1992**, *114*, 9713.

[7] All new isolated compounds gave satisfactory analytical and/or spectral data (see Table 1).

[8] R. A. Hites in *Chemical Analysis of Polycyclic Aromatic Compounds* (Ed.: T. Vo-Dinh), Wiley, New York, **1989**, p. 219.

[9] D. L. Mohler, K. P. C. Vollhardt in *Advances in Strain in Organic Chemistry, Vol. 5* (Ed.: B. Halton), JAI, London, **1996**, p. 121.

[10] In analogy to: a) G. Wenz, M. A. Müller, M. Schmidt, G. Wegner, *Macromolecules* **1984**, *17*, 837; see also: b) R. E. Martin, F. Diederich, *Angew. Chem.* **1999**, *111*, 1441; *Angew. Chem. Int. Ed.* **1999**, *38*, 1350; c) Y. Geerts, G. Klärner, K. Müllen in *Electronic Materials: The Oligomer Approach* (Eds.: K. Müllen, G. Wegner), Wiley-VCH, Weinheim, **1998**, p. 1; for a caveat in applying this simple correlation, see d) H. Meier, U. Stalmach, H. Kolshorn, *Acta Polymer.* **1997**, *48*, 379.

[11] a) J. M. Schulman, R. L. Disch, *J. Phys. Chem. A* **1997**, *101*, 5596; b) J. M. Schulman, R. L. Disch, H. Jiao, P. von R. Schleyer, *J. Phys. Chem. A* **1998**, *102*, 8051.

[12] At the B3LYP/6-31G* level; the maximum and (in parentheses) average deviations of the calculated from the experimental bond lengths are 0.023 (0.0037) Å.

[13] X-ray structure analysis: **3a**·[CH$_2$Cl$_2$]$_{0.5}$ (synchrotron radiation, Station 9.8, SRS Daresbury): crystal size $0.08 \times 0.06 \times 0.01$ mm^3, space group $P2_1/c$ (no. 14), scan range $4.80 < 2\theta < 47.7°$, $a = 8.2710(6)$, $b = 23.1799(18)$, $c = 16.2279(13)$ Å, $V = 3090.5(4)$ Å^3, $Z = 4$, $\rho_{\mathrm{calcd}} = 1.374$ g cm^{-3}, $\mu(\lambda = 0.6880$ Å$) = 0.78$ cm^{-1}, 15619 total reflections, 5266 unique reflections ($R_{\mathrm{int}} = 0.0411$) at −53 °C, of which 4062 were taken as observed [$F^2 > 2.00\sigma(F^2)$], conventional $R_1 = 0.0878$, $R_w = 0.2369$ (on all 5266 F^2 data). CCDC-183203 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit @ccdc.cam.ac.uk).

[14] D. Holmes, S. Kumaraswamy, A. J. Matzger, K. P. C. Vollhardt, *Chem. Eur. J.* **1999**, *5*, 3399.

[15] While we cannot rule out accidental isochronism of the methylene hydrogens, its selective occurrence in **4b**, but not **3b** or the corresponding derivative of **2** in ref. [1], would seem unlikely.

A New Pd^0–Cu$^{\mathrm{I}}$ Bimetallic Catalyst for the Synthesis of Indoles from Isocyanates and Allyl Carbonates**

Shin Kamijo and Yoshinori Yamamoto*

In the research field of transition-metal-catalyzed organic synthesis, one of the modern trends is to use a bimetallic catalyst system to explore not only more efficient but also entirely new transformations. Representative examples of such bimetallic catalysis in palladium-catalyzed reactions[1] are the following: 1) cat.Pd^0/Cu$^{\mathrm{I}}$ in the Sonogashira coupling reaction, in which a catalytic amount of Cu salts activate terminal acetylenes to form copper–acetylide species;[2] 2) cat Pd^0/Cu$^{\mathrm{I}}$ in the Stille coupling reaction, in which organostannanes are transmetalated to give organocoppers which

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