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Incorporation of a Flexible, Pyridine-Functionalized Diaza-Crown Ether into Discrete Supramolecules via Coordination-Driven Self-Assembly

Ki-Whan Chi,*,† Chris Addicott, and Peter J. Stang*

Department of Chemistry, University of Utah,
315 S. 1400 E. Salt Lake City, Utah 84112

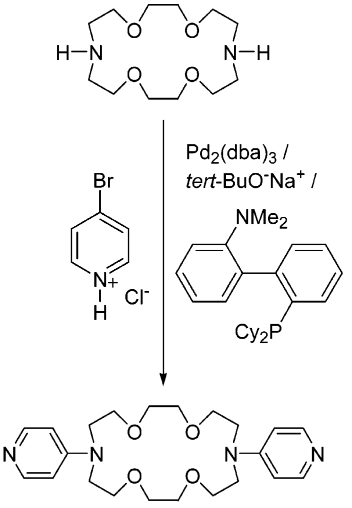
stang@chem.utah.edu

Received January 20, 2004

Abstract: A flexible, pyridine-functionalized diaza-crown ether was self-assembled into discrete supramolecules of differing stoichiometries upon combination with various organoplatinum molecules. They are characterized by electrospray ionization mass spectrometry and $^{31}P\{^1H\}$ and ^1H NMR. In one case, $^1H-^1H$ NOE enhancements of a [1 + 1] assembled structure demonstrate the puckered shape of the macrocyclic ring. Despite its inherent flexibility, the dipyridyl-substituted 18-membered diaza-crown ligand prefers to self-assemble into closed systems when reacted with platinum-containing acceptors.

Coordination-driven transition-metal-mediated self-assembly has been used to prepare a wide variety of two- and three-dimensional discrete supramolecules in recent years.[1-10] The strategy frequently employed for their preparation involves the combination of rigid starting materials of well-defined shape and bonding directionality.[11,12] This generally allows a reasonably accurate prediction of the assembled product structure. In contrast, the successful use of flexible building blocks in self-assembling discrete structures is less documented due to the increased chance of numerous reaction pathways and products. When they are used, a template molecule or ion is often necessary to control the self-assembly outcome.[13-17] One exception is the preparation of a discrete metallamacrocycle from a dipyridyl-substituted nine-membered 1,4-diazacycloalkane ring and $Pd(en)(NO_3)_2$.[18]

SCHEME 1. Synthesis of Di-4-pyridyl-Substituted Diaza-Crown Ether 1



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Since their discovery[19] in 1967, macrocyclic crown ether compounds and derivatives, as well as their properties and applications, have been extensively examined.[20-23] More recent studies[24-28] focused on diaza-crown ethers with functionalized heteroaromatic sidearms. Relative to conventional crown ethers, these species showed enhanced complex stability with, and transport ability of, numerous alkali, alkaline earth, and transition metal cations.[27,28]

To date, there are no reports of platinum- or palladium-mediated self-assembly of pyridyl-substituted diaza-crown ethers into supramolecular species. Herein, we report the preparation of di-(4-pyridyl)-substituted 18-membered diaza-crown ether **1** (Scheme 1) and then describe the nontemplated self-assembly of this flexible ligand into discrete supramolecules **2**−**4** upon reaction with platinum-containing acceptors **5**−**7** of differing geometries (Scheme 2). They are characterized by elec-

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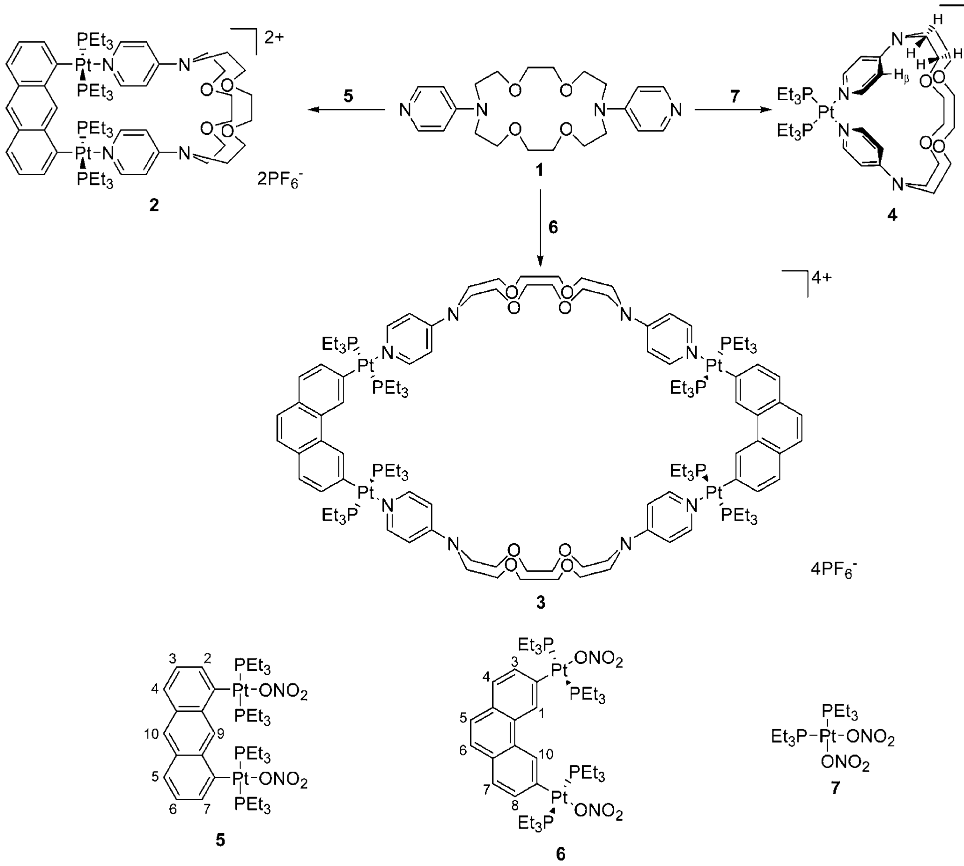
[†] Visiting Professor from the Department of Chemistry, University of Ulsan, Ulsan 680-749, Republic of Korea.

(1) Seidel, S. R.; Stang, P. J. *Acc. Chem. Res.* **2002**, *35*, 972.
(2) Swiegers, G. F.; Malefetse, T. J. *Coord. Chem. Rev.* **2002**, *225*, 91.
(3) Fujita, M.; Umemoto, K.; Yoshizawa, M.; Fujita, N.; Kusukawa, T.; Biradha, K. *Chem. Commun.* **2001**, 509.
(4) Cotton, F. A.; Lin, C.; Murillo, C. A. *Acc. Chem. Res.* **2001**, *34*, 759.
(5) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853.
(6) Swiegers, G. F.; Malefetse, T. J. *Chem. Rev.* **2000**, *100*, 3483.
(7) Baxter, P. N. W.; Lehn, J.-M.; Baum, G.; Fenske, D. *Chem. Eur. J.* **1999**, *5*, 102.
(8) Caulder, D. L.; Raymond, K. N. *Acc. Chem. Res.* **1999**, *32*, 975.
(9) Caulder, D. L.; Raymond, K. N. *J. Chem. Soc., Dalton Trans.* **1999**, 1185.
(10) Fujita, M. *Chem. Soc. Rev.* **1998**, *6*, 417.
(11) Holliday, B. J.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 2022.
(12) Stang, P. J.; Olenyuk, B. *Acc. Chem. Res.* **1997**, *30*, 502.
(13) Ikeda, A.; Udzu, H.; Zhong, Z.; Shinkai, S.; Sakamoto, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **2001**, *123*, 3872.
(14) Liu, H.-K.; Sun, W.-Y.; Ma, D.-J.; Yu, K.-B.; Tang, W.-X. *Chem. Commun.* **2000**, 591.
(15) Hiraoka, S.; Kubota, Y.; Fujita, M. *Chem. Commun.* **2000**, 1509.
(16) Hiraoka, S.; Fujita, M. *J. Am. Chem. Soc.* **1999**, *121*, 10239.
(17) Fujita, M.; Nagao, S.; Ogura, K. *J. Am. Chem. Soc.* **1995**, *117*, 1649.
(18) Schneider, R.; Hosseini, M. W.; Planeix, J.-M.; De Cian, A.; Fischer, J. *Chem. Commun.* **1998**, 1625.
(19) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 2495.
(20) Bradshaw, J. S.; Izatt, R. M.; Bordunov, A. V.; Zhu, C. Y.; Hathaway, J. K. In *Comprehensive Supramolecular Chemistry*; Gokel, G. W., Ed.; Elsevier: Oxford, UK, 1996; Vol. 1, pp 35−95.
(21) *Crown Compounds: Toward Future Applications*; Cooper, S. R., Ed.; VCH: New York, 1992.
(22) Hiraoka, M., Ed. *Crown Ethers and Analogous Compounds*; Elsevier: Amsterdam, 1992.
(23) Gokel, G. W., Ed. *Crown Ethers and Cryptands*; The Royal Society of Chemistry: Cambridge, 1991; Vol. 3.
(24) Hu, J.; Barbour, L. J.; Gokel, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 10940.
(25) Prodi, L.; Bargossi, C.; Montalti, M.; Zaccheroni, N.; Su, N.; Bradshaw, J. S.; Izatt, R. M.; Savage, P. B. *J. Am. Chem. Soc.* **2000**, *122*, 6769.
(26) Prodi, L.; Bolletta, F.; Montalti, M.; Zaccheroni, N.; Savage, P. B.; Bradshaw, J. S.; Izatt, R. M. *Tetrahedron Lett.* **1998**, *39*, 5451.
(27) Bradshaw, J. S.; Izatt, R. M. *Acc. Chem. Res.* **1997**, *30*, 338.
(28) Tsukube, H. *Coord. Chem. Rev.* **1996**, *148*, 1.

10.1021/jo049883t CCC: $27.50

SCHEME 2. Self-Assembly of 1 with Organoplatinum Reagents 5−7 into Discrete Assemblies 2−4



trospray ionization mass spectrometry (ESIMS) and $^{31}P\{^1H\}$ and ^1H NMR.

The synthesis of **1** (Scheme 1) was achieved by palladium-mediated coupling of commercially available 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane with an excess of 4-bromopyridine hydrochloride using the reported conditions.[29] A modest yield (53%) was obtained. The self-assembly of supramolecules **2**−**4** was performed in the same general manner. An acetone-d_6/D_2O solution of **1** and a particular organoplatinum acceptor **5**−**7** was heated at 60 °C for up to 16 h. Anion exchange with KPF_6 facilitated straightforward isolation of the assemblies as hexafluorophosphate salts in high yield.

Unexpectedly, the $^{31}P\{^1H\}$ NMR spectrum of the [1 + 1] assembly **2** displayed two singlets of approximately equal intensity near 9.40 ppm (assigned to PCH_2CH_3) with concomitant ^{195}Pt satellites (Figure S1, Supporting Information). Their upfield shift relative to **5** (15.33 ppm) is consistent with back-donation from the platinum atoms upon pyridine coordination. When the sample was heated to 80 °C, coalescence of these signals was observed. Changes were also observed in the ^1H spectrum (Figure S2, Supporting Information). At room temperature, there was a single, well-defined set of anthracene/pyridyl hydrogens, while complex signals for the ethyl phosphine and methylene groups of the diazacrown ring were observed. At 80 °C, the ethyl signals simplified dramatically, the methylenes became sharper and more resolved, while the pyridine hydrogens broadened significantly. The spectra returned to their original appearance when the sample was cooled back to room temperature. We believe the nonequivalent phosphine groups in **2** are distorted from their ideal position perpendicular to the anthracene plane at room temperature. At 80 °C, increased rotation makes them indistinguishable by NMR. Partial rotation of the pyridine rings also occurs at elevated temperature, as the two distinct sets of α- and β-hydrogens at room-temperature broaden upon heating. In the mass spectrum (Figure S3, Supporting Information), peaks assignable to $[\mathbf{2} - PF_6^-]^+$ ($m/z = 1600$) and $[\mathbf{2} - 2PF_6^-]^{2+}$ ($m/z = 727$) added support for the structure of **2**. The former was isotopically resolved and is in excellent agreement with the theoretical distribution. No evidence for any larger assemblies was found.

The $^{31}P\{^1H\}$ NMR spectrum of the [2 + 2] product **3** exhibited a single peak at 15.97 ppm (PCH_2CH_3), which was flanked by minor impurities (Figure S4, Supporting Information). A septet for the PF_6^- counterions was centered at −143.1 ppm. The restricted rotation of the pyridine rings was evident in the ^1H spectrum by two sets of α-hydrogens (Figure S5, Supporting Information). An unidentified byproduct was also present (7.01 ppm). In contrast to **2** (and **4**), the appearance of the diazacrown ring methylene signals in **3** resembled those of **1**. Clearly, the conformation of the 18-membered ring in **3** is more similar to that of **1** rather than in assemblies **2** and **4**. This has marked effects on the ^1H line shape. The structure was confirmed using ESIMS (Figure S6, Supporting Information). Peaks corresponding to the succes-

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[29] Zhang, X.-X.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 8027.

sive loss of PF_6^- ions were observed: $[\mathbf{3} - PF_6^-]^+$ (m/z = 3344), $[\mathbf{3} - 2PF_6^-]^{2+}$ (m/z = 1600) and $[\mathbf{3} - 3PF_6^-]^{3+}$ (m/z = 1018). The theoretical and experimental isotope distributions of $[\mathbf{3} - PF_6^-]^+$ correlate well.

The [1 + 1] assembly **4** was formed with little or no byproducts. In the $^{31}P\{^1H\}$ NMR spectrum, the phosphines gave rise to a single peak at 2.75 ppm (Figure S7, Supporting Information). The chemical shifts of the pyridyl hydrogen nuclei ($H_{\alpha-Py}$ 7.92 ppm, $H_{\beta-Py}$ 6.76 ppm) were almost unchanged relative to **1** (in CD_3NO_2: $H_{\alpha-Py}$ 8.07 ppm, $H_{\beta-Py}$ 6.64 ppm). This is in contrast to the downfield shift these hydrogens normally exhibit in pyridine−Pt-based assemblies.[30,31] Electron donation from the nitrogen atoms of the diaza-ring must offset the loss of electron density that occurs upon coordination. We have observed similar behavior in a model study with 4-(dimethylamino)pyridine and *cis*-$(PMe_3)_2Pt(OTf)_2$. The appearance of the diaza-crown methylene signals resembles that of **2** and is characteristic of the highly folded conformation the macrocycle adopts in **4**. An interesting feature is the chemical shifts of the hydrogens in the $N-CH_2$ group. These inequivalent nuclei give rise to peaks at 3.93 and 3.31 ppm and lie on either side of the large multiplet assigned to $-CH_2OCH_2CH_2OCH_2-$ (3.65 ppm). When the $H_{\beta-Py}$ signal (6.76 ppm) was irradiated, positive NOE enhancements were observed at 7.92 ($H_{\alpha-Py}$), 3.93 ($-N-CHH-$) and 3.65 ppm ($-CHHOCH_2CH_2OCH_2-$) (Figure S9, Supporting Information). These enhancements illustrate the close proximity of these nuclei. Isotopically resolved ESIMS peaks $[\mathbf{4} - PF_6^-]^+$ (m/z = 993) and $[\mathbf{4} - 2PF_6^-]^{2+}$ (m/z = 424) reinforced the structure of **4** (Figure S10, Supporting Information). Evidence for higher assemblies was not found.

The formation of the [1 + 1] products **2** and **4** is entropically favorable over larger supramolecules. This is apparently the dominant factor in their formation despite the introduced ring strain of these two assemblies. In the reaction of **1** and platinum acceptor **6**, a [1 + 1] product is geometrically impossible, thus the formation of the [2 + 2] species **3**.

In conclusion, the coordination-driven self-assembly of supramolecules **2**−**4** from a dipyridyl-substituted diaza-crown ring **1** and varying platinum acceptors **5**−**7** has been described. This work shows for the first time that a conformationally flexible, dipyridyl-substituted 18-membered diaza-crown ring can be incorporated effectively into discrete species of varying size and shape.

Experimental Section

Methods and Materials. Organoplatinum compounds **5**,[32] **6**,[33] and **7**[34] were prepared as reported.

Preparation of 7,16-(Di-4-pyridyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane 1.[29] 1,4,10,13-Tetraoxa-7,16-diazacyclooctadecane (131 mg, 0.50 mmol), 4-bromopyridine hydrochloride (311 mg, 1.6 mmol), tris(dibenzylideneacetone)dipalladium (13.7 mg, 0.015 mmol), 2-dicyclohexylphosphino-2′-(*N*,*N*-dimethylamino)biphenyl (35.4 mg, 0.09 mmol), and sodium *tert*-butoxide (259 mg, 2.70 mmol) were placed in an oven-dried Schlenk flask. The flask was evacuated and backfilled with N_2. Freshly distilled toluene (2 mL) was added, and the mixture was heated in an oil bath at 100 °C for 36 h. The reaction was diluted with CH_2Cl_2 (50 mL) and filtered through Celite. The filtrate was evaporated, and the residue chromatographed on SiO_2 using 1% triethylamine/20% CH_3OH/CH_2Cl_2 as an eluent. Further purification was achieved by precipitation from a CH_2Cl_2 solution using hexane. Yield 53%. Mp = 220−222 °C. ^1H NMR (CD_3OD, 300 MHz) δ 8.12 (d, ^3J = 7.5 Hz, 4H, $H_{\alpha-Py}$), 7.05 (d, ^3J = 7.5 Hz, 4H, $H_{\beta-Py}$), 3.80 (m, 16H, $-CH_2OCH_2CH_2OCH_2-$), 3.68 (s, 8H, $-NCH_2-$). ^{13}C NMR (CD_3OD, 75 MHz) δ 158.3 ($C_{\gamma-Py}$), 141.8 ($C_{\alpha-Py}$), 108.9 ($C_{\beta-Py}$), 72.1 ($-NCH_2CH_2O-$ or $-CH_2OCH_2CH_2O-$), 69.5 ($-CH_2OCH_2CH_2O-$ or $-NCH_2CH_2O-$), 53.0 ($-NCH_2-$). HRMS $C_{22}H_{32}N_4O_4$ requires M^+ 416.2424; found, M^+ 416.2401.

General Procedure for the Preparation of Assemblies 2−4. Diaza-crown **1** (4 μmol) and platinum acceptor **5**−**7** (4 μmol) were placed in a 1 dram vial. Acetone-d_6 (0.7 mL) and D_2O (0.4 mL) were added. The vial was sealed with Teflon tape, and the reaction stirred and heated in an oil bath at 60 °C for 4 h (**4**) or 16 h (**2**, **3**). Excess KPF_6 was added to precipitate the product, which was collected and washed with water and then dried in vacuo.

2: Yellow solid. Yield 92%. Mp = 186−191 °C dec. ^1H NMR (CD_3NO_2, 300 MHz) δ 9.88 (s, 1H, H_9), 8.51 (d, ^3J = 6.6 Hz, 2H, $H_{\alpha-Py}$), 8.41 (s, 1H, H_{10}), 8.30 (d, ^3J = 6.7 Hz, 2H, $H_{\alpha'-Py}$), 7.77 (d, ^3J = 8.5 Hz, 2H, $H_{2,7}$ or $H_{4,5}$), 7.66 (d, ^3J = 6.8 Hz, 2H, $H_{4,5}$ or $H_{2,7}$), 7.20 (dd, ^3J = 8.1 Hz, ^3J = 6.9 Hz, 2H, $H_{3,6}$), 7.08 (dd, ^3J = 6.6 Hz, ^4J = 2.8 Hz, 2H, $H_{\beta-Py}$), 6.63 (dd, ^3J = 6.9 Hz, ^4J = 3.0 Hz, 2H, $H_{\beta'-Py}$), 3.85−3.56 (m, 24H, $-NCH_2CH_2O-$), 1.87−1.52 (m, 24H, PCH_2), 1.32−0.80 (m, 36H, PCH_2CH_3). $^{31}P\{^1H\}$ NMR (CD_3NO_2, 121 MHz) δ 9.43 (^{195}Pt satellites, $^1J_{Pt-P}$ = 2688 Hz, PCH_2CH_3), 9.40 (^{195}Pt satellites, $^1J_{Pt-P}$ = 2688 Hz, PCH_2CH_3), −143.1 (septet, $^1J_{P-F}$ = 707 Hz, PF_6^-). Anal. Calcd for $C_{60}H_{100}F_{12}N_4O_4P_6Pt_2$: C, 41.29; H, 5.77; N, 3.21. Found: C, 41.44; H, 5.87; N, 3.01.

3: Off-white solid. Yield 95%. Mp = 216−220 °C dec. ^1H NMR (CD_3NO_2, 300 MHz) δ 8.70 (s, 4H, $H_{1,10}$), 8.30 (d, ^3J = 6.6 Hz, 4H, $H_{\alpha-Py}$), 8.26 (d, ^3J = 6.6 Hz, 4H, $H_{\alpha'-Py}$), 7.76 (d, ^3J = 8.2 Hz, 4H, $H_{3,8}$), 7.58 (m, 8H, $H_{4,7}$ and $H_{5,6}$), 6.92 (m, 8H, $H_{\beta-Py}$), 3.82−3.70 (m, 48H, $-NCH_2CH_2O-$), 1.45 (m, 48H, PCH_2), 1.19 (m, 72H, PCH_2CH_3). $^{31}P\{^1H\}$ NMR (CD_3NO_2, 121 MHz) δ 15.97 (^{195}Pt satellites, $^1J_{Pt-P}$ = 2694 Hz, PCH_2CH_3), −143.1 (septet, $^1J_{P-F}$ = 707 Hz, PF_6^-). Anal. Calcd for $C_{120}H_{200}F_{24}N_8O_8P_{12}Pt_4$: C, 41.29; H, 5.77; N, 3.21. Found: C, 41.40; H, 5.87; N, 2.86.

4: Off-white solid. Yield 92%. Mp = 249−251 °C dec. ^1H NMR (CD_3NO_2, 300 MHz) δ 7.92 (d, ^3J = 7.1 Hz, 4H, $H_{\alpha-Py}$), 6.76 (d, ^3J = 7.1 Hz, 4H, $H_{\beta-Py}$), 3.93 (dt, ^2J = 15.5 Hz, 2 × ^3J = 5.5 Hz, 4H, $-N-CHH-$), 3.65 (m, 16H, $-CH_2OCH_2CH_2OCH_2-$), 3.31 (dt, ^2J = 15.4 Hz, 2 × ^3J = 5.6 Hz, 4H, $-N-CHH-$), 2.02 (m, 12H, PCH_2), 1.32 (m, 18H, PCH_2CH_3). $^{31}P\{^1H\}$ NMR (CD_3NO_2, 121 MHz) δ 2.75 (^{195}Pt satellites, $^1J_{Pt-P}$ = 3062 Hz, PCH_2CH_3), −143.1 (septet, $^1J_{P-F}$ = 707 Hz, PF_6^-). Anal. Calcd for $C_{34}H_{62}F_{12}N_4O_4P_4Pt$: C, 35.89; H, 5.49; N, 4.92. Found: C, 36.23; H, 5.46; N, 4.74.

Acknowledgment. Financial support from the National Science Foundation (CHE-0306720) and the National Institutes of Health (5R01GM57052) is gratefully acknowledged. We thank Dr. Yury K. Kryschenko for providing platinum acceptor **6** and Mr. Takuya Yamamoto for *cis*-$(PMe_3)_2Pt(OTf)_2$.

Supporting Information Available: NMR and mass spectral data for assemblies **2**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO049883T

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[30] Chi, K.-W.; Addicott, C.; Kryschenko, Y. K.; Stang, P. J. *J. Org. Chem.* **2004**, *69*, 964.

[31] Chi, K.-W.; Addicott, C.; Arif, A. M.; Das, N.; Stang, P. J. *J. Org. Chem.* **2003**, *68*, 9798.

[32] Kuehl, C. J.; Huang, S. D.; Stang, P. J. *J. Am. Chem. Soc.* **2001**, *123*, 9634.

[33] Kryschenko, Y. K.; Seidel, S. R.; Arif, A. M.; Stang, P. J. *J. Am. Chem. Soc.* **2003**, *125*, 5193.

[34] Kuehl, C. J.; Tabellion, F. M.; Arif, A. M.; Stang, P. J. *Organometallics* **2001**, *20*, 1956.