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Synthesis of Cyclic Porphyrin Trimers through Alkyne Metathesis Cyclooligomerization and Their Host–Guest Binding Study

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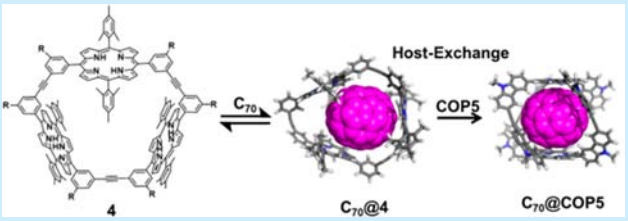
Supporting Information

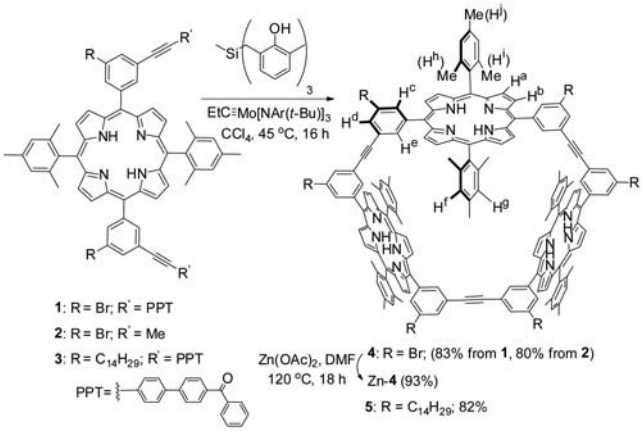
ABSTRACT: Cyclic porphyrin trimers were synthesized through one-step cyclooligomerization via alkyne metathesis from diyne monomers. These macrocycles show interesting host–guest binding interactions with fullerenes, selectively binding C_{70} (6×10^3 M^{-1}) over C_{60} and C_{84} (no binding observed). The fullerene-encapsulated host–guest complex can undergo guest or host exchange in the presence of another guest (2,4,6-tri(4-pyridyl)-1,3,5-triazine) or host (cage COP5) molecule with higher binding affinity.



Porphyrin-based compounds have been of great interest in molecular electronics,[1−3] host–guest chemistry,[4−6] catalysis,[7,8] solar energy conversion,[9] and molecular sieving.[10,11] Since the discovery of the light-harvesting antenna (LH2) with ring-like arrangement of porphyrinic chromophores in the purple bacterium *Rhodopseudomonas acidophila*,[12,13] oligomeric cyclic porphyrins have attracted tremendous research interest.[4,14,15] A cyclic array of porphyrins offers many attractive features, such as large internal voids, unprecedented electronic properties (e.g., migration of excitation energy and electronic coupling), and unusual coordination environment synergistically provided by multiple porphyrin centers. In addition to the unique physical properties, such cyclic structures alone, especially covalently linked stable multiporphyrin rings, are interesting and synthetically challenging. Two approaches have been explored so far: template-assisted preorganization followed by cyclization, and stepwise synthesis of linear oligomers and subsequent cyclization under high dilution conditions.[16] Elegant Vernier-templating syntheses of multiporphyrin nanorings reported by the Anderson group represent a milestone in the synthesis of porphyrinic macrocycles.[17−20] These previous synthetic approaches heavily rely on cross-coupling reactions, which have a high tolerance of functional groups and generally give high yields in individual steps, yet are irreversible and unable to correct undesired bond formation. Dynamic covalent chemistry is a conceptually distinctive approach that relies on reversible covalent reactions under thermodynamic control.[21−23] Herein, we report template-free, one-step synthesis of trimeric porphyrin macrocycles through alkyne metathesis cyclooligomerization in excellent yields. Provided a large internal cavity, these macrocycles show interesting host–guest binding interactions with fullerenes and pyridine derivatives.

Symmetric porphyrin monomers (**1**–**3**) bearing ethynylene groups were designed and synthesized as the building blocks for the cyclic trimers **4** and **5** (Scheme 1). Since alkyne metathesis is a reversible reaction, the equilibrium can be driven to the product side by removal of one alkyne product. Either (benzoyldiphenyl)acetylene (PPT) or propynyl substituents were attached to the phenyl groups on the 5- and 15-*meso* positions, in order to easily remove byproduct bis(benzoyldiphenyl)acetylene (PPT—≡—PPT) by precipitation or 2-butyne by trapping in 5 Å molecular sieves. Although the precipitation-driven alkyne metathesis approach is not atom economic, installation of polar PPT groups facilitates the purification of monomers (e.g., the purification of monomer **1** was much easier than monomer **2**). Tetradecyl chains were installed on monomer **3** to obtain the macrocyclic product with

Scheme 1. Synthesis of Cyclic Porphyrin Trimers



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better solubility. Alkyne metathesis[24−29] was then conducted at 45 °C for 16 h using an *in situ* generated molybdenum catalyst consisting of a multidentate triphenolsilane ligand.[30] The desired product **4** was obtained in good isolated yields either from monomer **1** (83%) or from monomer **2** (80%). Similarly, macrocycle **5** was obtained in good yield (82%) from monomer **3** through the precipitation-driven alkyne metathesis approach. The Zn-metalated analogue (Zn-**4**) was conveniently obtained from macrocycle **4** in high yield (93%).

As mentioned previously, one-step cyclooligomerization[31−37] through dynamic alkyne metathesis is conceptually different from the kinetically controlled cross-coupling approach. The former provides the most thermodynamically favored product at the equilibrium, whereas product distribution is kinetically determined in the latter approach. It has been reported that Glaser coupling of a similar porphyrin building block substituted with 3-ethynylphenyl groups at 5,15-positions yielded a mixture of a cyclic dimer (20%) and a cyclic trimer (18%) under high dilution conditions in the presence of large excess of Cu(I) catalyst (0.5 mM monomer solution, 120 equiv cat., 80 °C for 24 h).[38] This is in great contrast to the predominant formation of the thermodynamic product, cyclic trimer (**4**/**5**, >80%), under high concentration (120 mM monomer solution) and mild conditions (3 mol % cat., 45 °C for 16 h) presented herein, highlighting the power of the dynamic covalent assembly approach.

The cyclic porphyrin trimers **4** and **5** were fully characterized using gel permeation chromatography (GPC), matrix-assisted laser desorption/ionization-time-of-flight mass spectrometry (MALDI-TOF MS), and ^{1}H and ^{13}C NMR spectra. The GPC trace of macrocycle **4** showed a narrow peak (PDI = 1.04), indicating that a single species was formed (Figure S1). MALDI-TOF mass spectra of **4** and **5** showed molecular ion peaks ($[M + Li]^+$) at *m*/*z* 2642.07 and 3346.83, respectively, which are consistent with the calculated theoretical values (Figure S2). Both ^{1}H and ^{13}C NMR spectra displayed one set of signals for each aromatic proton on the backbone of the ring, confirming the high symmetry of the macrocycle. Two singlets were observed for aromatic protons (H^f and H^g) of the mesityl group, and three singlets were observed for the methyl protons (H^h, H^i, and H^j). This result indicates that the rotation of the mesityl ring is restricted within the NMR time scale, presumably due to the rigidity of the structure and the steric hindrance between the methyl group and porphyrin hydrogen. The structures of **4** and **5** were further confirmed by various 2D NMR spectra (gCOSY, gHSQC, gHMBC, and ROESY, Figures S20−S30).

Multiphorphyrinic structures have been reported to be excellent fullerene receptors.[4,6,39−41] Hydrogen-bonded or metal−ligand-bonded supramolecules containing porphyrin moieties are most commonly studied, while robust covalently linked multiporphyrin hosts are relatively less explored, primarily due to their laborious syntheses.[42] Cyclic porphyrin trimers (**4**, **5**, and Zn-**4**) were examined as possible hosts for fullerenes. ^{1}H NMR titration experiments of the macrocycles with fullerenes were conducted at room temperature in toluene-d_8. Interestingly, we did not observe any binding interactions of these macrocycles with C_{60} or C_{84}. On the contrary, all three macrocycles showed high affinity for C_{70}. Upon C_{70} binding, the resonance peaks of *endo* protons (H^e and H^i) showed significant downfield shifts, and those of *exo* protons (H^c and H^h) shifted slightly upfield (Figures S5, S9, and S13). Analysis of the Job plot (Figures S7, S11, and S14) showed that the binding interactions between C_{70} and these macrocycles are in 1:1 stoichiometry, with association constants (K_{assoc}) of 6.1×10^3, 6.9×10^3, and 6.2×10^3 M^{-1}, respectively, for **4**, **5**, and Zn-**4**. Such host−guest interactions between C_{70} and the macrocycles are further confirmed by MALDI-TOF MS of a mixture of C_{70} and each macrocycle, which showed the peaks corresponding to the pure macrocycle and the 1:1 complex (e.g., C_{70}@**4**). The selectivity toward C_{70} over C_{60} and C_{84} likely arises from the rigidity of these trimers, which provides a well-defined cavity of a certain size with preorganized functional groups (i.e., porphyrin) interacting with fullerenes. The internal cavity of the macrocycle (diameter ∼1.4 nm) is likely too small to accommodate C_{84} and too large for binding C_{60}. Our results show the great advantage of rigid ethynylene-linked macrocyclic structures, offering preorganization and size-based recognition and thus high guest-binding affinities and selectivity.

The binding selectivity of these macrocycles toward C_{70} over C_{60} and C_{84} is attractive, which could have potential applications in fullerene purification. We envisioned that the fullerenes encapsulated inside the cavity can be released by the addition of a proper guest with a higher binding affinity. We chose tritopic Zn-**4** consisting of three metalated porphyrin moieties as the model system and tridentate 2,4,6-tri(4-pyridyl)-1,3,5-triazine (Py_3T) as the replacing ligand, which has good shape complementarity with the cavity of the host. Sanders and co-workers previously reported that a butadiyne-linked cyclic porphyrin trimer has an affinity of ca. 10^{10} M^{-1} for Py_3T.[43,44] Similarly, ethynylene-linked Zn-**4** shows a high binding affinity toward Py_3T. We performed ^{1}H NMR and UV−vis titration experiments in order to evaluate the binding affinity of Py_3T to Zn-**4**. In the NMR titration experiment (Figure S16), the addition of Py_3T to the solution of Zn-**4** resulted in the decreasing signals of free Zn-**4** with the appearance of a new set of peaks in the more downfield region. The presence of two distinct sets of NMR signals corresponding to free Zn-**4** and the ligand-encapsulated complex Py_3T@Zn-**4** indicates that the ligand dissociation/association is slow on the NMR time scale at room temperature. When 1.0 equiv of Py_3T was added, the proton peaks of the free host almost completely disappear and the signals corresponding to the complex Py_3T@Zn-**4** increase to the full intensity. In the UV−vis titration experiment (Figure S17), we observed decreasing absorption of the free host and increasing absorption of the complex. UV−vis titration data further support the formation of a 1:1 inclusion host−guest complex. The binding constant for Py_3T@Zn-**4** was estimated to be around 4×10^9 M^{-1}.

Given the high binding affinity of Zn-**4** toward Py_3T, we performed a guest exchange experiment (i.e., releasing of C_{70} from the host−guest complex C_{70}@Zn-**4** and re-encapsulation of Py_3T) (Figure 1). Since the guest molecules are bound to the hosts through supramolecular interactions, their release and rebinding are under equilibrium. The introduction of a second guest would cause the competition between the two guest molecules to complex with Zn-**4**. To demonstrate the release of C_{70} and re-encapsulation of Py_3T, we titrated the mixture of Zn-**4** and C_{70} (1:1 molar ratio) with Py_3T. On addition of Py_3T to the mixture, we observed a decrease of the original peaks of C_{70}@Zn-**4** and emergence of a new set of peaks corresponding to Py_3T@Zn-**4** (Figure S18). When ∼1.0 equiv of Py_3T was added, clean formation of Py_3T@Zn-**4** was observed, indicating

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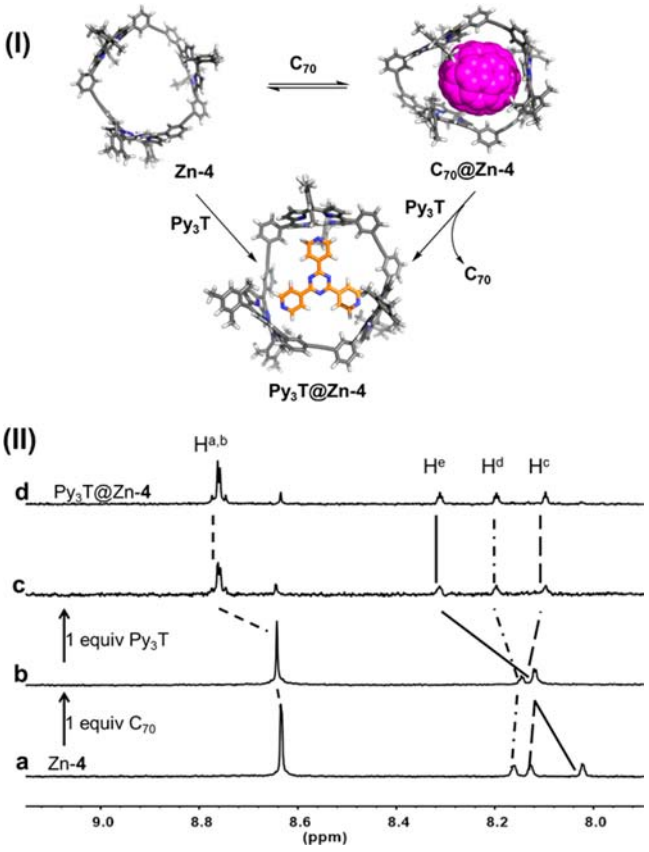

Figure 1. (I) Schematic representation of the guest exchange experiment; (II) ^{1}H NMR spectra of free Zn-**4** (a), a complex obtained after the addition of 1 equiv of C_{70} to Zn-**4** (b), a complex obtained after the addition of Py_3T to the solution in b (c), and a complex obtained from a 1:1 molar ratio of Zn-**4** and Py_3T (d).

nearly complete release of C_{70} and replacement by Py_3T (Figure 1).

Previously, our group reported the free base bis-porphyrinic cage COP5 (Figure 2b), which can reversibly bind with fullerenes upon acid/base stimuli.[35] With a binding constant of 1.5×10^8 M^{-1} toward C_{70} and 1.4×10^5 M^{-1} toward C_{60} in toluene, COP5 is one of the most C_{70}-selective hosts reported and has shown great promise for purification of fullerenes. Given the ~10^5 times higher binding affinity of COP5 toward C_{70} compared to that of macrocycle **4**, we were interested in competitive C_{70} binding between host molecules. We thus conducted a host exchange experiment (Figure 2a) by titrating the solution of C_{70}@**4** obtained from a mixture of macrocycle **4** and 3 equiv of C_{70} with an increasing amount of COP5. As shown in Figure 2c, we observed the emergence of a new set of peaks corresponding to C_{70}@COP5, which indicates the encapsulation of C_{70} in COP5. On the contrary, the original host–guest complex C_{70}@**4** releases C_{70}, which was evidenced by the significant upfield shifts of the *endo* protons (H^e and H^i) and downfield shifts of the *exo* protons (H^c and H^h) of macrocycle **4**. Such reversible guest binding illustrated by guest exchange and host exchange experiments provides a nice platform for investigating self-sorting (i.e., binding specificity) behavior of host–guest complexes. To the best of our knowledge, although guest exchange experiments have been reported,[45,46] this is the first report of a host exchange study for fullerenes.

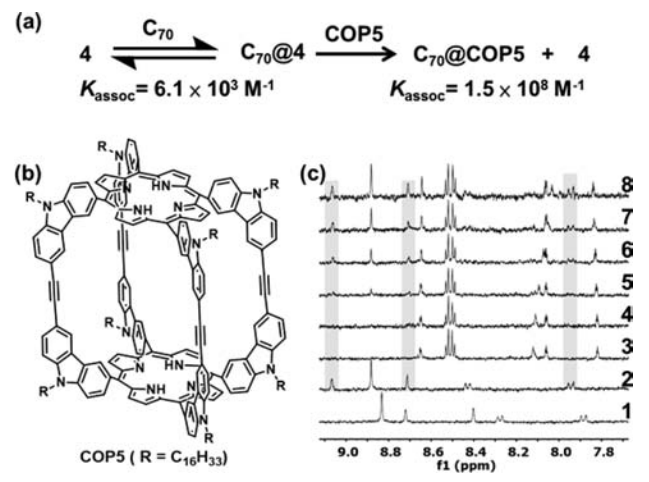

Figure 2. (a) Host exchange experiment: In the presence of COP5, C_{70} is released from macrocycle **4** and re-encapsulated by COP5; (b) the structure of COP5; (c) ^{1}H NMR spectra of COP5 (1), C_{70}@COP5 (2), a mixture of **4** and C_{70} in 1:3 molar ratio (3), and the mixtures after addition of 0.2, 0.4, 0.8, 1.2, and 1.6 equiv of COP5 (4–8, respectively).

In summary, ethynylene-linked cyclic porphyrin trimers were synthesized through template-free one-step alkyne metathesis cyclooligomerization in good isolated yields, and their host–guest chemistry was explored. Fullerene binding studies show that these macrocycles selectively bind C_{70} over C_{60} and C_{84}, with binding constants of around 6×10^3 M^{-1} in toluene at room temperature. The trapped C_{70} in the host–guest complex C_{70}@Zn-**4** can be released from the macrocycle through a guest exchange experiment upon the addition of 2,4,6-tri(4-pyridyl)-1,3,5-triazine. Host exchange behavior of C_{70} was also observed when COP5 with a higher binding affinity was added to the solution of C_{70}@**4**. The ready accessibility and interesting properties of these multiporphyrin macrocycles will advance further exploration of their various applications in chemistry, biology, and materials science.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01293.

Materials and general synthetic methods, synthetic procedures, proton assignments, host–guest chemistry, computer modeling, and NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Jurow, M.; Schuckman, A. E.; Batteas, J. D.; Drain, C. M. *Coord. Chem. Rev.* **2010**, *254*, 2297.
(2) Burrell, A. K.; Wasielewski, M. R. *J. Porphyrins Phthalocyanines* **2000**, *4*, 401.
(3) Boyle, N. M.; Rochford, J.; Pryce, M. T. *Coord. Chem. Rev.* **2010**, *254*, 77.
(4) Tashiro, K.; Aida, T. *Chem. Soc. Rev.* **2007**, *36*, 189.
(5) Sakaguchi, K.-i.; Kamimura, T.; Uno, H.; Mori, S.; Ozako, S.; Nobukuni, H.; Ishida, M.; Tani, F. *J. Org. Chem.* **2014**, *79*, 2980.
(6) Garcia-Simon, C.; Costas, M.; Ribas, X. *Chem. Soc. Rev.* **2016**, *45*, 40.
(7) Oliveri, C. G.; Gianneschi, N. C.; Nguyen, S. T.; Mirkin, C. A.; Stern, C. L.; Wawrzak, Z.; Pink, M. *J. Am. Chem. Soc.* **2006**, *128*, 16286.
(8) Kang, B.; Kurutz, J. W.; Youm, K.-T.; Totten, R. K.; Hupp, J. T.; Nguyen, S. T. *Chem. Sci.* **2012**, *3*, 1938.
(9) Walter, M. G.; Rudine, A. B.; Wamser, C. C. *J. Porphyrins Phthalocyanines* **2010**, *14*, 759.
(10) Ema, T.; Ura, N.; Eguchi, K.; Ise, Y.; Sakai, T. *Chem. Commun.* **2011**, *47*, 6090.
(11) García-Simón, C.; Garcia-Borràs, M.; Gómez, L.; Parella, T.; Osuna, S.; Juanhuix, J.; Imaz, I.; Maspoch, D.; Costas, M.; Ribas, X. *Nat. Commun.* **2014**, *5*, 5557.
(12) Mcdermott, G.; Prince, S. M.; Freer, A. A.; Hawthornthwaitelawless, A. M.; Papiz, M. Z.; Cogdell, R. J.; Isaacs, N. W. *Nature* **1995**, *374*, 517.
(13) Koepke, J.; Hu, X. C.; Muenke, C.; Schulten, K.; Michel, H. *Structure* **1996**, *4*, 581.
(14) Beletskaya, I.; Tyurin, V. S.; Tsivadze, A. Y.; Guilard, R.; Stern, C. *Chem. Rev.* **2009**, *109*, 1659.
(15) Canevet, D.; Perez, E. M.; Martin, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 9248.
(16) Burrell, A. K.; Officer, D. L.; Plieger, P. G.; Reid, D. C. W. *Chem. Rev.* **2001**, *101*, 2751.
(17) Hoffmann, M.; Wilson, C. J.; Odell, B.; Anderson, H. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 3122.
(18) O'Sullivan, M. C.; Sprafke, J. K.; Kondratuk, D. V.; Rinfray, C.; Claridge, T. D. W.; Saywell, A.; Blunt, M. O.; O'Shea, J. N.; Beton, P. H.; Malfois, M.; Anderson, H. L. *Nature* **2011**, *469*, 72.
(19) Kondratuk, D. V.; Perdigao, L. M. A.; Sullivan, M. C. O.; Svatek, S.; Smith, G.; Shea, J. N. O.; Beton, P. H.; Anderson, H. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 6696.
(20) Kondratuk, D. V.; Sprafke, J. K.; O'Sullivan, M. C.; Perdigao, L. M. A.; Saywell, A.; Malfois, M.; O'Shea, J. N.; Beton, P. H.; Thompson, A. L.; Anderson, H. L. *Chem. - Eur. J.* **2014**, *20*, 12826.
(21) Rowan, S. J.; Cantrill, S. J.; Cousins, G. R. L.; Sanders, J. K. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2002**, *41*, 898.
(22) Corbett, P. T.; Leclaire, J.; Vial, L.; West, K. R.; Wietor, J. L.; Sanders, J. K. M.; Otto, S. *Chem. Rev.* **2006**, *106*, 3652.
(23) Jin, Y.; Yu, C.; Denman, R. J.; Zhang, W. *Chem. Soc. Rev.* **2013**, *42*, 6634.
(24) Jyothish, K.; Zhang, W. *Angew. Chem., Int. Ed.* **2011**, *50*, 8478.
(25) Mortreux, A.; Blanchard, M. *J. Chem. Soc., Chem. Commun.* **1974**, 786.
(26) Zhang, W.; Moore, J. S. *Adv. Synth. Catal.* **2007**, *349*, 93.
(27) Schrock, R. R.; Czekelius, C. *Adv. Synth. Catal.* **2007**, *349*, 55.
(28) Wu, X.; Tamm, M. *Beilstein J. Org. Chem.* **2011**, *7*, 82.
(29) Fürstner, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 2794.
(30) Yang, H.; Liu, Z.; Zhang, W. *Adv. Synth. Catal.* **2013**, *355*, 885.
(31) Lee, S.; Yang, A.; Moneypenny, T. P.; Moore, J. S. *J. Am. Chem. Soc.* **2016**, *138*, 2182.
(32) Wang, Q.; Yu, C.; Zhang, C.; Long, H.; Azarnoush, S.; Jin, Y.; Zhang, W. *Chem. Sci.* **2016**, *7*, 3370.
(33) Zhang, W.; Moore, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 12796.
(34) Zhang, W.; Moore, J. S. *J. Am. Chem. Soc.* **2005**, *127*, 11863.
(35) Zhang, C.; Wang, Q.; Long, H.; Zhang, W. *J. Am. Chem. Soc.* **2011**, *133*, 20995.
(36) Wang, Q.; Zhang, C.; Noll, B. C.; Long, H.; Jin, Y.; Zhang, W. *Angew. Chem., Int. Ed.* **2014**, *53*, 10663.
(37) Wang, Q.; Yu, C.; Long, H.; Du, Y.; Jin, Y. H.; Zhang, W. *Angew. Chem., Int. Ed.* **2015**, *54*, 7550.
(38) Nobukuni, H.; Shimazaki, Y.; Uno, H.; Naruta, Y.; Ohkubo, K.; Kojima, T.; Fukuzumi, S.; Seki, S.; Sakai, H.; Hasobe, T.; Tani, F. *Chem. - Eur. J.* **2010**, *16*, 11611.
(39) Durot, S.; Taesch, J.; Heitz, V. *Chem. Rev.* **2014**, *114*, 8542.
(40) Zhang, C.; Long, H.; Zhang, W. *Chem. Commun.* **2012**, *48*, 6172.
(41) Yu, C.; Jin, Y.; Zhang, W. *Chem. Rec.* **2015**, *15*, 97.
(42) Gil-Ramírez, G. n.; Karlen, S. D.; Shundo, A.; Porfyrakis, K.; Ito, Y.; Briggs, G. A. D.; Morton, J. J. L.; Anderson, H. L. *Org. Lett.* **2010**, *12*, 3544.
(43) Vidal-Ferran, A.; Clyde-Watson, Z.; Bampos, N.; Sanders, J. K. M. *J. Org. Chem.* **1997**, *62*, 240.
(44) Anderson, H. L.; Anderson, S.; Sanders, J. K. M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2231.
(45) Shoji, Y.; Tashiro, K.; Aida, T. *J. Am. Chem. Soc.* **2004**, *126*, 6570.
(46) Meng, W.; Breiner, B.; Rissanen, K.; Thoburn, J. D.; Clegg, J. K.; Nitschke, J. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 3479.

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