Organic Letters
Letter
pubs.acs.org/OrgLett

Tetra- and Octapyrroles Synthesized from Confusion and Fusion Approaches

Jiahui Kong,[†] Qiong Zhang,[‡] Mathew Savage,[§] Minzhi Li,[∥] Xin Li,[⊥] Sihai Yang,[§] Xu Liang,[∥] Weihua Zhu,[∥] Hans Ågren,[⊥] and Yongshu Xie*,[†]

[†]Key Laboratory for Advanced Materials and Institute of Fine Chemicals, School of Chemistry and Molecular Engineering, East China University of Science and Technology, Shanghai 200237, China

[‡]School of Physical Science and Technology, ShanghaiTech University, Shanghai 200031, China

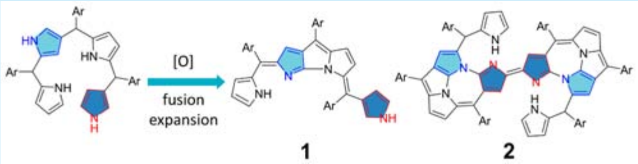
[§]School of Chemistry, University of Manchester, Manchester, M13 9PL, U.K.

[∥]School of Chemistry & Chemical Engineering, Jiangsu University, Zhenjiang 212013, China

[⊥]Department of Theoretical Chemistry and Biology, School of Biotechnology, KTH Royal Institute of Technology, Stockholm SE-10691, Sweden

Supporting Information

ABSTRACT: By oxidation of an alternately N-confused bilane in CH_2Cl_2, a C−N fused tetrapyrrin was synthesized that bears a 5.5.5-tricyclic ring generated from an intramolecular C−N linkage. When CH_3CN was used as the reaction medium, a multiply C−N-fused octapyrrolic dimer was also obtained that contained two 5.5.5.7.5-pentacyclic moieties and a bipyrrole unit generated from the intramolecular C−N linkage and intermolecular C−C linkage, respectively. This could be coordinated with $Ni(acac)_2$ to afford a mixed-ligand complex.



As a class of promising intermediates in synthetic porphyrin chemistry,[1] and coordinating ligands for constructing supramolecular assemblies[2] and sensing various ions,[3] linear oligopyrroles with pyrrole units interconnected at the α positions have attracted extensive attentions in recent years.[4] Tetrapyrrolic bilanes are unique members of linear oligopyrroles because they contain the same numbers of pyrrolic units as porphyrins and they have been used for the syntheses of porphyrins and their analogues, such as corroles, through acid-catalyzed condensation or oxidative cyclization.[5,6] In these cases, terminal pyrrole units are interconnected at the free α positions. Supplementary to the macrocyclic compounds, we have reported an example of synthesizing a linear octapyrrole by oxidative dimerization of a bilane with one of the terminal α positions blocked with an acyl substituent (Scheme.1).[7] To further enrich the structural diversity, N-confused pyrrole units, i.e., α,β′-linked pyrroles, may be employed.[8] Thus, a number of bilane isomers have been reported (Scheme 1, **a**−**e**).[9,10] Owing to the higher reactivity of N-confused pyrrole units, oxidation of these confused bilanes gives rise to a diversity of porphyrin analogues. For example, the singly N-confused bilanes **a** and **b** could be oxidized to afford confused corrole isomers.[9] If two confused pyrrole units are introduced, three doubly N-confused bilanes (Scheme.1, **c**−**e**) may be developed. The doubly terminal-confused bilane **c** and the doubly adjacent-confused bilane **d** could be oxidatively cyclized to afford corrorin and C-fused norrole, respectively.[8d,10]

In spite of the excellent examples of porphyrin analogues obtained from the singly and doubly confused bilanes, the oxidation of the alternately N-confused bilane (**e**) remains unexplored.[11] In this work, simply by oxidizing **e**, a C−N fused tetrapyrrin (**1**) and a multiply C−N fused octapyrrolic dimer (**2**) were obtained, and both an intramolecular C−N linkage and intermolecular C−C linkages were observed. Surprisingly, no porphyrin analogue was obtained at all. To check the possibility of metal coordination, a Ni(II) complex of **1** was also synthesized. Despite the abundant examples of intramolecular ring fusion in porphyrin analogues,[12] ring-fused linear oligopyrroles are still quite rare. This work demonstrates the possibility of combined confusion and fusion approaches for synthesizing novel linear oligopyrroles applicable in coordination chemistry and synthetic porphyrinoid chemistry.

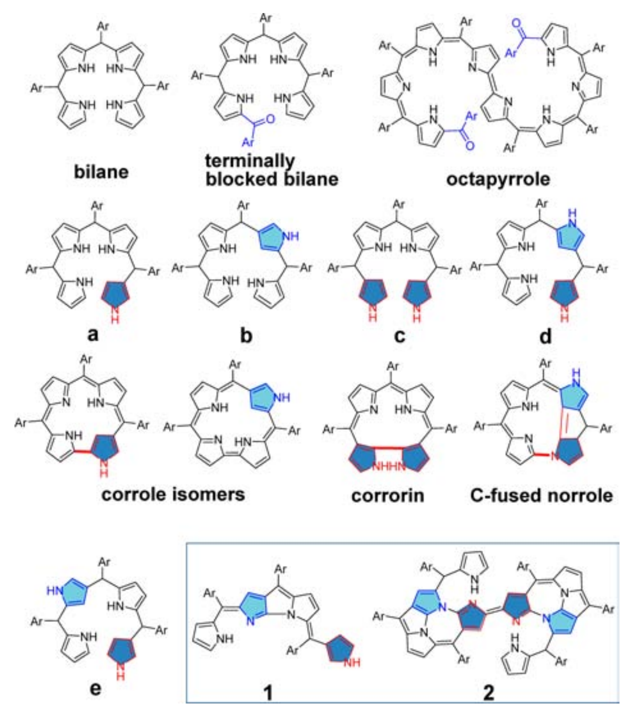
The reaction details are outlined in Scheme 2. Bilane **e** was first oxidized with 3.0 equiv of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in CH_2Cl_2 (route A), affording **1** in a 45% yield. When $FeCl_3$ or MnO_2 was used as the oxidant, no identifiable compound could be obtained.

Compound **1** was characterized using NMR spectroscopy and HRMS (Figures S1 and S4). The parent ion of **1** was observed at m/z of 797.0822, which was identical with that calculated from the corrolelike framework. However, the ^1H NMR spectrum of **1** in $CDCl_3$ at 298 K revealed nine pyrrolic CH signals in the range of 6.0−7.3 ppm and two NH signals at 8.46 and 10.60 ppm, totally different from those observed for aromatic corrole-like macrocycles that exhibit inner NH signals

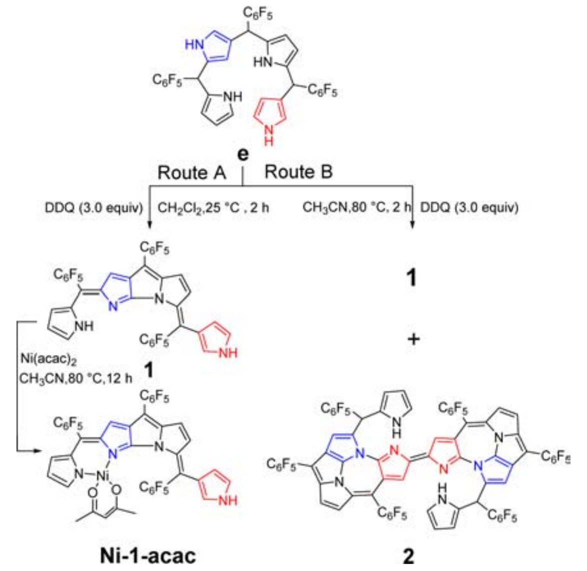
Received: August 20, 2016
Published: September 22, 2016

DOI: 10.1021/acs.orglett.6b02495
Org. Lett. 2016, 18, 5046−5049

Scheme 1. Examples of Bilanes, Confused Bilanes, and the Corresponding Oxidation Products (Ar = C_6F_5)



Scheme 2. Syntheses of 1 and 2 by Oxidation of Bilane e with DDQ in CH_2Cl_2 and CH_3CN, Respectively, and Coordination of 1 with Ni(II)



at higher fields and peripheral CH at lower fields. The characters observed for **1** in the NMR and HRMS were consistent with the intramolecular C−N fused structure (vide infra), generated from intramolecular oxidative coupling between the NH and α CH moieties. It is noteworthy that **1** still contains free α positions. In particular, the terminally confused pyrrole ring still contains two free α positions, which may undergo further fusion or expansion reactions. Thus, we attempted the further oxidation of **1** with various oxidants. Unfortunately, only some unidentified decomposed compounds were detected from the reactions.

Considering that **1** is already fully conjugated and the reactivity may have been decreased, we returned to check the oxidation conditions for the precursor **e**. Interestingly, when **e** was oxidized with 3.0 equiv of DDQ in CH_3CN (Scheme 2, route B), **2** was generated in addition to **1**. Although **2** was not fully conjugated (vide infra), further oxidation of **2** with DDQ only afforded some decomposed compounds, whereas **2** was not observed when the reaction was performed in CH_2Cl_2, toluene, or THF. The HRMS ($2 + Na^+$) of compound **2** (Figure S6) shows a molecular peak at m/z of 1611.1068, roughly double of that for **e**, implying that **2** might be a dimerized form of **e**. The ^1H NMR spectrum of **2** (Figure S3) exhibits a symmetrical structure, bearing only two NH protons at 8.27 ppm, consistent with the presence of multiple fused rings generated by forming interpyrrolic C−N bonds.

To further elucidate the chemical structures of **1** and **2**, we successfully obtained their single crystals.[13] X-ray crystallographic analysis reveals that **1** contains a linear fully conjugated tetrapyrrolic framework (Figure 1a). The α-carbon of the middle confused pyrrole ring B and the nitrogen atom of adjacent regular pyrrole ring C are oxidatively linked through a C−N bond, affording a 5.5.5-tricyclic fused ring, which is nearly coplanar with the terminal pyrrole ring A, and the terminally confused pyrrole D is titled from this plane with a dihedral angle of 36.4°, probably because of the steric hindrance associated with the β hydrogen atoms from these two pyrroles. Within the molecule, N2 is hydrogen bonded to H1 with N2···N1 distance of 2.770(7) Å. The molecular structure of compound **2** was also unambiguously elucidated by X-ray crystallographic analysis (Figure 1b). As expected, **2** has an octapyrrolic structure, generated by linking two tetrapyrrolic units of **e** at the α positions of the terminally confused pyrroles. Within each tetrapyrrolic unit, the two central pyrroles and the

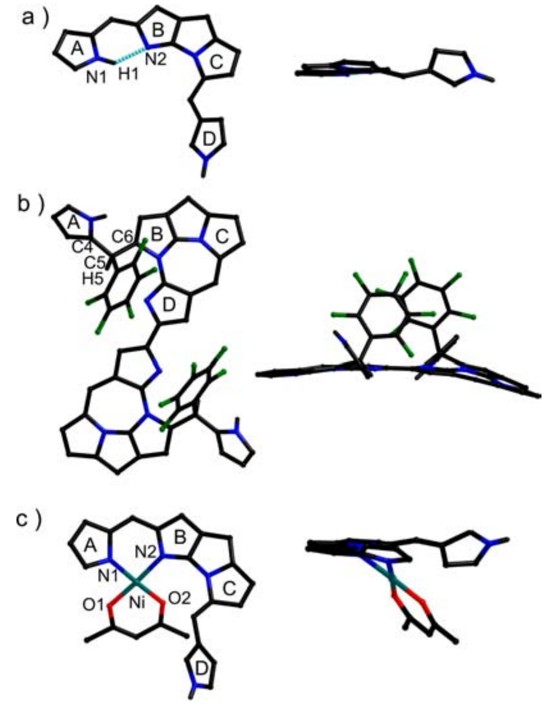


Figure 1. Complementary views of the crystal structures of compounds **1** (a), **2** (b), and **Ni-1-acac** (c). C_6F_5 groups and the hydrogens attached to sp^2 carbons are omitted for clarity.

terminally confused pyrrole are fully conjugated and fused by forming two interpyrrolic C−N bonds. Thus, fusion of pyrroles B−D affords a nearly planar 5.5.5.7.5-pentacyclic moiety. It is noteworthy that the two terminal regular pyrrole rings in **2** are linked with the pentacyclic moieties through sp^3 *meso*-carbon atoms, which can be clearly evidenced by the bond distances and angles around C5, lying within the ranges of 1.489−1.529 Å and 109.9−112.6°, respectively. As a result, pyrrole A is tilted from the pentacyclic moiety with a large dihedral angle of 55.4°, which also indicates that these two moieties are not fully conjugated.

The formation of **2** may be attributed to the effect of the more polar solvent, which favors the proton-transfer related oxidation reactions.[14] The successful synthesis of compounds **1** and **2** indicates that novel linear oligopyrroles may be developed by combining the confusion and oxidative fusion and coupling approaches.

Considering that compound **1** contains a dipyrrin unit composed of pyrroles A and B, it may be employed as a bidentate ligand to coordinate with metal ions. Consistent with this expectation, when **1** was treated with $Ni(acac)_2 \cdot 2H_2O$ for 10 h in CH_3CN at reflux, the color of the solution gradually changed from light brown to dark brown. Thus, a mixed-ligand nickel complex **Ni−1-acac** was obtained in a 88% yield (Scheme 2). In the ^{1}H NMR spectrum of **Ni−1-acac**, the NH peak observed for **1** at 10.60 ppm has disappeared (Figure S2), indicative of the coordination of the dipyrrin moiety. The signals at 5.32 and 1.77 ppm could be assigned to the coordinated acetylacetonate ligand. Consistently, the crystal structure of **Ni−1-acac** (Figure 1c) reveals that the Ni(II) atom is coordinated with two N atoms from **1** and two O atoms from acac, thus affording a square planar coordination environment, with Ni−N and Ni−O distances of 1.869, 1.929, 1.866, and 1.834 Å, respectively.

The absorption spectra of **1**, **Ni−1-acac**, and **2** are shown in Figure 2. Compound **1** exhibits a strong absorption at 452 nm and a weak peak at 653 nm, assignable to HOMO→LUMO+1 and HOMO→LUMO, respectively (Table S3). **Ni−1-acac** shows split peaks at 446 and 553 nm, consistent with HOMO→LUMO+1 and HOMO−1→LUMO, respectively. In addition, shoulder peaks appear at 632 and 682 nm. In contrast to the singly fused tetrapyrrin **1**, the absorption of the more conjugated dimer **2** is obviously red-shifted, exhibiting a relatively strong and broad peak at 719 nm corresponding to HOMO→LUMO, which may be related to its larger π-conjugation structure as well as the multiply fused structure.

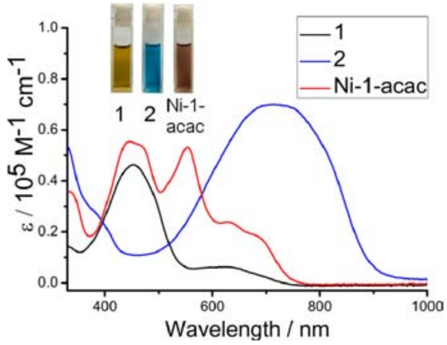


Figure 2. UV−vis−NIR spectra of **1**, **2**, and **Ni−1-acac** in CH_2Cl_2. Inset: photographs of these compounds in CH_2Cl_2.

Moreover, the absorption spectra measurements revealed that all of the compounds are quite stable under diverse conditions except that **Ni−1-acac** was demetalated upon addition of TFA (Figures S10−S18).

In order to investigate the redox behavior of compounds **1**, **2**, and **Ni−1-acac**, their electrochemical properties were analyzed with cyclic voltammetry in CH_2Cl_2 containing 0.1 M tetra-*n*-butylammonium perchlorate (TBAP). Compound **1** displays one reduction and two oxidation processes (Figure S8). Similar behavior was observed for compounds **2** and **Ni−1-acac**. The electrochemically obtained HOMO−LUMO gaps were found to be 1.88, 1.41, and 2.23 eV for **1**, **2**, and **Ni−1-acac**, respectively, under the given experimental conditions.

To gain further insight into the distribution of the energy levels, density functional theory (DFT) calculations were carried out using the Gaussian 09 program package.[15] The optimized structures were obtained, and the HOMO−LUMO gaps of **1**, **2**, and **Ni−1-acac** were calculated to be 2.23, 1.56, and 2.24 eV, respectively (Tables S1 and S2). Relative to compound **1**, the octapyrrolic **2** has a larger π-conjugation framework, resulting in the smaller energy gaps and absorption bands at longer wavelengths.

According to previous reports,[6,9,10] the oxidation of bilanes may generate various macrocyclic products. Accordingly, **1** has some possible linear and macrocyclic isomers (Figure S9). DFT calculations[15] indicate that the energy of the linear isomer **1a** is 25.6 kJ/mol higher than that of **1** (Figure 3). Moreover, the energies of the representative macrocyclic isomers (**1b−d**) are also higher than **1**. These results may well rationalize the fact that the linear fused tetrapyrrin **1** is the main product of the oxidation reaction and no macrocyclic product could be obtained.

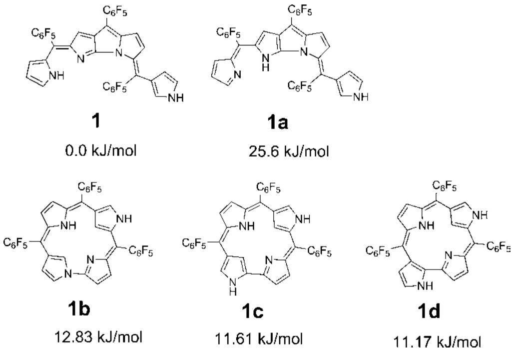


Figure 3. Relative energies (kJ/mol) for **1**, its possible linear isomer **1a**, and three possible macrocyclic isomers **1b−d**.

In conclusion, we have reported the syntheses of a C−N-fused tetrapyrrin (**1**) and a multiply C−N-fused octapyrrolic dimer (**2**) by oxidizing an alternately N-confused bilane in CH_2Cl_2 and CH_3CN, respectively. Thus, **1** and **2** contain 5.5.5-tricyclic and 5.5.5.7.5-pentacyclic moieties, respectively. In addition, **1** was used to coordinate with $Ni(acac)_2$ to afford a mixed-ligand complex of **Ni−1-acac**. These results demonstrate the effectiveness of the combined confusion and fusion approaches for synthesizing novel oligopyrroles, which may provide possibilities for developing unique porphyrinoids.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b02495.

X-ray data for **1** (CIF)
X-ray data for **Ni−1-acac** (CIF)
X-ray data for **2** (CIF)
Complete experimental details; spectroscopic and analytical data; details on DFT calculations (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: yshxie@ecust.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was financially supported by NSFC (21472047, 91227201), the Program for Professor of Special Appointment (Eastern Scholar, GZ2016006) at Shanghai Institutions of Higher Learning, and the Fundamental Research Funds for the Central Universities (WK1616004).

■ REFERENCES

(1) (a) Sessler, J. L.; Seidel, D. *Angew. Chem., Int. Ed.* **2003**, *42*, 5134. (b) Tsuda, A.; Osuka, A. *Science* **2001**, *293*, 79. (c) 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. (d) Wang, Y. Q.; Chen, B.; Wu, W. J.; Li, X.; Zhu, W. H.; Tian, H.; Xie, Y. S. *Angew. Chem., Int. Ed.* **2014**, *53*, 10779. (e) Xie, Y. S.; Yamaguchi, K.; Toganoh, M.; Uno, H.; Suzuki, M.; Mori, S.; Saito, S.; Osuka, A.; Furuta, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 5496. (f) Stepien, M.; Sprutta, N.; Latos-Grażyński, L. *Angew. Chem., Int. Ed.* **2011**, *50*, 4288. (g) Wojaczynski, J.; Latos-Grażyński, L. *Chem. - Eur. J.* **2010**, *16*, 2679. (h) Lash, T. D.; Lammer, A. D.; Ferrence, G. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 9718. (i) Ito, T.; Hayashi, Y.; Shimizu, S.; Shin, J. Y.; Kobayashi, N.; Shinokubo, H. *Angew. Chem., Int. Ed.* **2012**, *51*, 8542. (j) KC, C. B.; Lim, N. G.; D'Souza, F. *Angew. Chem., Int. Ed.* **2015**, *54*, 5088.

(2) (a) Haketa, Y.; Sakamoto, S.; Chigusa, K.; Nakanishi, T.; Maeda, H. *J. Org. Chem.* **2011**, *76*, 5177. (b) Maeda, H.; Chigusa, K.; Sakurai, T.; Ohta, K.; Uemura, S.; Seki, S. *Chem. - Eur. J.* **2013**, *19*, 9224.

(3) (a) Ding, Y. B.; Tang, Y. Y. *Chem. Soc. Rev.* **2015**, *44*, 1101. (b) Ding, Y. B.; Zhu, W. H.; Xie, Y. S. *Chem. Rev.* **2017**, DOI: 10.1021/acs.chemrev.6b00021. (c) Ding, Y. B.; Li, T.; Zhu, W. H.; Xie, Y. S. *Org. Biomol. Chem.* **2012**, *10*, 4201. (d) Ding, Y. B.; Xie, Y. S.; Li, X.; Hill, J. P.; Zhang, W. B.; Zhu, W. H. *Chem. Commun.* **2011**, *47*, 5431. (e) Wang, Q. G.; Xie, Y. S.; Ding, Y. B.; Li, X.; Zhu, W. H. *Chem. Commun.* **2010**, *46*, 3669.

(4) (a) Saito, S.; Osuka, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 4342. (b) Stepien, M.; Sprutta, N.; Latos-Grażyński, L. *Angew. Chem., Int. Ed.* **2011**, *50*, 4288. (c) Roznyatovskiy, V. V.; Lee, C. H.; Sessler, J. L. *Chem. Soc. Rev.* **2013**, *42*, 1921.

(5) (a) Gryko, D. T.; Jadach, K. *J. Org. Chem.* **2001**, *66*, 4267. (b) Kalita, H.; Kalita, D.; Lee, W. Z.; Bellare, J.; Ravikanth, M. *Chem. - Eur. J.* **2014**, *20*, 10404. (c) Kumar, R.; Misra, R.; PrabhuRaja, V.; Chandrashekar, T. K. *Chem. - Eur. J.* **2005**, *11*, 5695.

(6) (a) Rambo, B. M.; Sessler, J. L. *Chem. - Eur. J.* **2011**, *17*, 4946. (b) Dogutan, D. K.; Lindsey, J. S. *J. Org. Chem.* **2008**, *73*, 6728. (c) Fang, Y. Y.; Koszelewski, D.; Kadish, K. M.; Gryko, D. T. *Chem. Commun.* **2014**, *50*, 8864.

(7) Zhang, K.; Savage, M.; Li, X.; Jiang, Y.; Ishida, M.; Mitsuno, K.; Karasawa, S.; Kato, T.; Zhu, W. H.; Yang, S. H.; Furuta, H.; Xie, Y. S. *Chem. Commun.* **2016**, *52*, 5148.

(8) (a) Xie, Y. S.; Wei, P. C.; Li, X.; Hong, T.; Zhang, K.; Furuta, H. *J. Am. Chem. Soc.* **2013**, *135*, 19119. (b) Wei, P. C.; Zhang, K.; Li, X.; Meng, D. Y.; Ågren, H.; Ou, Z. P.; Ng, S.; Furuta, H.; Xie, Y. S. *Angew. Chem., Int. Ed.* **2014**, *53*, 14069. (c) Zhang, K.; Zhang, J. D.; Li, X.; Guo, R.; Ågren, H.; Ou, Z. P.; Ishida, M.; Furuta, H.; Xie, Y. S. *Org. Lett.* **2015**, *17*, 4806. (d) Furuta, H.; Maeda, H.; Osuka, A. *J. Am. Chem. Soc.* **2001**, *123*, 6435−6436.

(9) Fujino, K.; Hirata, Y.; Kawabe, Y.; Morimoto, T.; Srinivasan, A.; Toganoh, M.; Miseki, Y.; Kudo, A.; Furuta, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 6855.

(10) Toganoh, M.; Kawabe, Y.; Furuta, H. *J. Org. Chem.* **2011**, *76*, 7618.

(11) Toganoh, M.; Gokulnath, S.; Kawabe, Y.; Furuta, H. *Chem. - Eur. J.* **2012**, *18*, 4380.

(12) (a) Furuta, H.; Ishizuka, T.; Osuka, A.; Ogawa, T. *J. Am. Chem. Soc.* **2000**, *122*, 5748. (b) Toganoh, M.; Kimura, T.; Uno, H.; Furuta, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 8913. (c) Toganoh, M.; Sato, A.; Furuta, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 2752.

(13) CCDC 1499916 (**1**), 1499917 (**Ni−1-acac**), and 1499918 (**2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(14) (a) Sakai, K. I.; Ishikawa, T.; Akutagawa, T. *J. Mater. Chem. C* **2013**, *1*, 7866. (b) McRae, R. P.; Schenter, G. K.; Garrett, B. C.; Svetlicic, Z.; Truhlar, D. G. *J. Chem. Phys.* **2001**, *115*, 8460.

(15) All of the calculations were achieved with Gaussian09 program package. See the Supporting Information for more details.