DOI: 10.1002/ejoc.200601046

Synthesis and Versatile Reactions of β-Azidotetraarylporphyrins

Dong-Mei Shen,[a] Chao Liu,[a] and Qing-Yun Chen*[a]

Keywords: Porphyrinoids / Azido / Thermal reactions / Cycloaddition

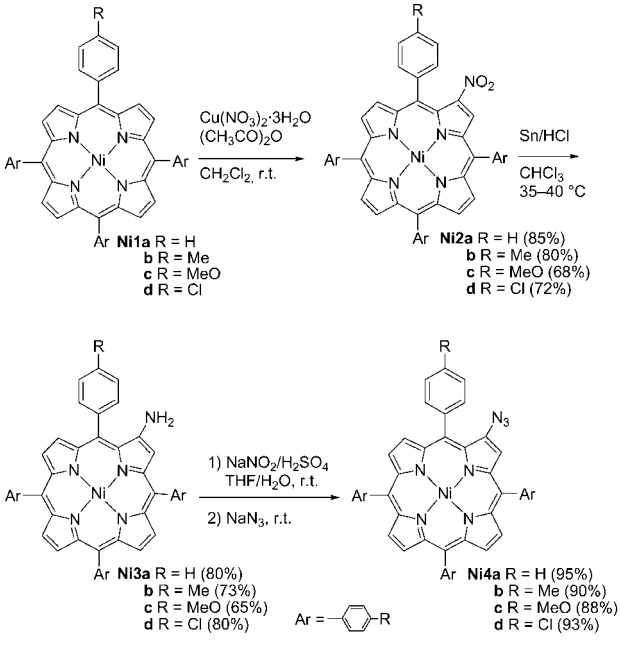
A variety of β-azidotetraarylporphyrins were conveniently synthesized by classical conversion of the amino groups of β-aminotetraarylporphyrins into azido groups through diazotization and subsequent treatment with sodium azide. Their thermal reaction and Cu^{I}-catalyzed 1,3-dipolar cycloaddition with various alkynes were also reported.

Introduction

Over the past decade, functionalization of porphyrins has aroused considerable interest because incorporation of functionality into the porphyrin core can systematically modulate the properties of the porphyrin macrocycle and also afford access to various porphyrin-based molecular architecture by providing a reactive site for further bond construction.[1] Significant efforts have been devoted to develop new and efficient methods to functionalize porphyrins. For example, bromoporphyrins are proven to be robust and efficient catalysts for various oxidation reactions because of the introduction of the electron-withdrawing bromine atoms into the porphyrin periphery.[2] Moreover, they have been intensively used in various cross-coupling reactions for facile and efficient synthesis of a large amount of novel and potentially useful porphyrins.[3] Introduction of azido groups at the periphery of the porphyrins remain sparse although organic azides are valuable intermediates and widely used in organic synthesis.[4] To continue our ongoing efforts on porphyrin functionalization,[3a–f,5] we herein present the synthesis and versatile reactions of β-azido-substituted tetraarylporphyrins.

Results and Discussion

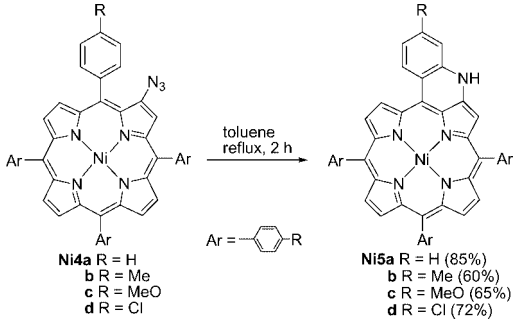
Our initial attempts to synthesize azido-substituted porphyrins were conducted with (2-bromo-5,10,15,20-tetraphenylporphyrinato)nickel(II)[3d,5a] and sodium azide under the conditions reported by Ma's group.[6] Unfortunately, the reaction resulted in complete recovery of the starting bromoporphyrin. The ready availability of β-aminotetraarylporphyrins and the well-known conversion of an amino group into an azido group by diazotization and subsequent treatment with sodium azide inspired our synthetic approach to the target azido porphyrins. As outlined in Scheme 1, nitro porphyrins **Ni2** are readily prepared by a literature chromatography-free procedure from porphyrin **Ni1** on gram-scale in good yields of 68–85%.[7] Reduction of nitro derivatives **Ni2** with an improved Sn/HCl procedure provides amino porphyrins **Ni3**.[7b] Diazotization by reaction with $H_2SO_4/NaNO_2$ in THF, followed by in situ reaction with NaN_3 led to the formation of β-azidotetraarylporphyrins **Ni4** in high yields up to 88–95%.[4] These azido porphyrins are unstable and decompose under laboratory illumination at room temperature, but can be preserved without decomposition in a refrigerator for a long time. To the best of our knowledge, this is the first reported isolation of azido-substituted porphyrins.



Scheme 1. Synthesis of β-azidotetraarylporphyrins.

[a] Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China
E-mail: chenqy@mail.sioc.ac.cn
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

With these β-azidotetraarylporphyrins (Scheme 2) in hand, we first investigated their thermal reaction. When a toluene solution of **Ni4a** was heated at reflux under a nitrogen atmosphere for 2 h, the color of the solution changed from red to green. TLC revealed the complete consumption of the starting porphyrin and the formation of a green main product. We were delighted to find, according to spectral analysis, that it was an interesting fused six-membered porphyrin, **Ni5a**. Porphyrin **Ni5a** might be produced by in situ insertion of the nitrene into a C–H bond of a phenyl ring at the adjacent *meso* position. The X-ray structure of **Ni5a**[8] evidently demonstrated a Ni^{II} porphyrin skeleton that displays strongly typical ruffle distortion.[9] (Figure 1) Because of the C–N bond formation that locks the *meso*-phenyl group into the plane of the newly formed six-membered ring, the UV/Vis spectrum of **Ni5** demonstrates a large bathochromic shift and broadening of the Soret band. Depending on the nature of the substituents, the yields for various β-azidotetraarylporphyrins varied from 60 to 85%.



Scheme 2. Thermal reaction of various β-azidotetraarylporphyrins.

Recently, by making use of some selective reactions, "click chemistry" has emerged as a convenient and effective approach for the preparation of a large amount of novel compounds with desired functionalities through simple workup and purification procedures under benign reaction conditions.[10] The Cu^{I}-catalyzed Huisgen 1,3-dipolar cycloaddition of azides and alkynes, which results in 1,2,3-triazoles, is one of the most important and powerful click reactions.[11] Introduction of 1,2,3-triazole into the porphyrin macrocycle should impose interesting and different properties to the porphyrin ring. Subsequently, we tried to subject the azido porphyrins to the click reaction. By using **Ni4a** and phenylacetylene **6a** as model substrates, we studied various reaction conditions to obtain optimal conditions. As summarized in Table 1, the reaction with either CuI or CuCl as the catalyst resulted in an inseparable complex mixture (Entries 1 and 2, Table 1). When $CuBr(PPh_3)_3$ was utilized, **Ni7** instead of desired **Ni8a** was obtained as the sole product in quantitative yield (Entry 3, Table 1). Sharpless et al.[10a] recently found that the catalyst for Huisgen 1,3-dipolar cycloaddition is better prepared in situ by the reduction of Cu^{II} salts with ascorbic acid; this method gave good yields of desired **Ni8a** (Entry 4, Table 1). Reaction temperatures were also found to influence the yield of the product and the reaction speed. High temperatures markedly accelerated the reaction (Entry 5, Table 1), but too high of a temperature may be harmful, which leads to partial decomposition of the starting azido porphyrin and lower yield of the product (Entry 6, Table 1). Among various solvents screened, DMF stood out (Entries 7–10, Table 1). The optimal reaction conditions include the use of DMF as the solvent heated at 50 °C in the presence of $CuSO_4 \cdot 5H_2O$/ascorbic acid.

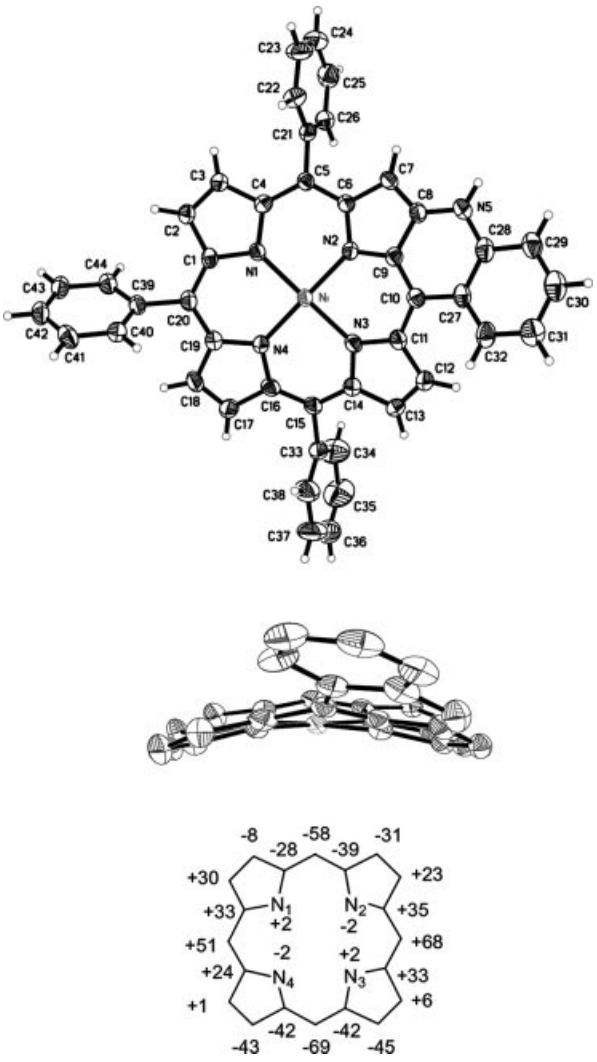
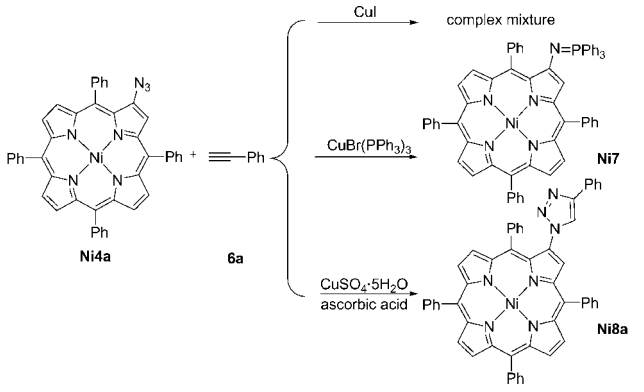


Figure 1. X-ray crystal structure (top), side view (middle), and displacements (in 0.01 Å) of the porphyrin core atoms from their least-squares plane of the nitrogen atoms (bottom) of **Ni5a**. The solvated molecules and hydrogen atoms were omitted for clarity. Representative bond lengths [Å] and angles [°] are as follows: Ni–N1 1.920(4), Ni–N2 1.909(4), Ni–N3 1.936(4), Ni–N4 1.914(4), C3–C2 1.326(7), C2–C1 1.431(7), C1–C20 1.387(7), C20–C39 1.485(7), C39–C44 1.395(7), C7–C8 1.364(7), C8–C9 1.418(7), C9–C10 1.353(7), C10–C27 1.467(7), C27–C28 1.432(7), C28–N5 1.416(7), N5–C8 1.346(7), N1–Ni–N3 178.65(17), N2–Ni–N4 178.09(16), N1–Ni–N2 90.39(16), N2–Ni–N3 88.50(17), C8–N5–C28 120.0(5), C8–C9–C10 122.0(5), C10–C11–C27 125.9(5), C2–C1–C20 126.1(5), C18–C19–C20 123.9(5).

Under the optimal reaction conditions, several representative alkynes were smoothly subjected to the cycloaddition reaction. As shown in Scheme 3, an alkyne with an electron-withdrawing group was more reactive than an electron-donating group, which is in line with the literature.[11]

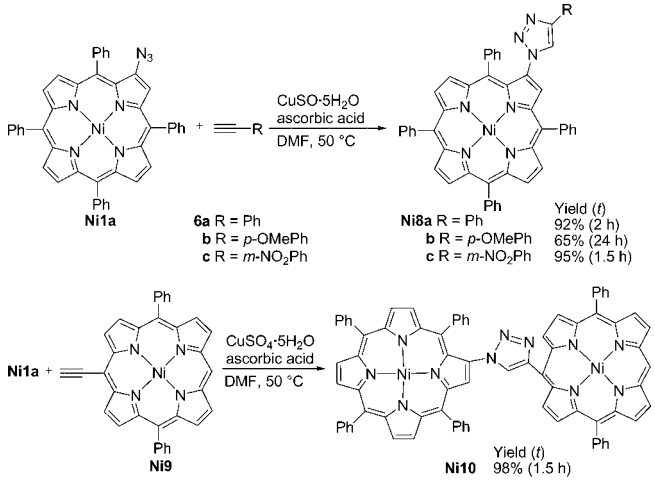
Table 1. The Huisgen 1,3-dipolar cycloaddition reaction of azidoporphyrin **Ni4a** and alkyne **6a** under various conditions.[a]



Entry	Cu^I	Solvent	T [°C]	t [h]	Product Yield [%][b]
1	CuI	DMF	25	24	–[c]
2	CuCl	DMF	25	24	–[c]
3	$CuBr(PPh_3)_3$	DMF	25	24	**Ni7** 98[d]
4	$CuSO_4·5H_2O$[e]	DMF	25	24	**Ni8a** 92
5	$CuSO_4·5H_2O$[e]	DMF	50	3	**Ni8a** 92
6	$CuSO_4·5H_2O$[e]	DMF	100	2	**Ni8a** 70
7	$CuSO_4·5H_2O$[e]	DMF/CH_2Cl_2	50	24	**Ni8a** 30[f]
8	$CuSO_4·5H_2O$[e]	CH_2Cl_2	50	24	–[g]
9	$CuSO_4·5H_2O$[e]	THF	50	24	–[g]
10	$CuSO_4·5H_2O$[e]	CH_2Cl_2/MeOH	50	24	–[h]

[a] Reactions were conducted under a N_2 atmosphere with **Ni4a** (30 mg, 1.0 equiv.) and **5a** (1.5 equiv.) in the presence of catalyst (10 mol-%). [b] Isolated yields. [c] The reaction resulted in an inseparable complex mixture. [d] Based on the catalyst used. [e] Ascorbic acid (0.5 equiv.) was used as a cocatalyst. [f] Recovery of **Ni4a**: 65%. [g] No reactions occurred. [h] Only a trace of desired product **Ni8a** was obtained. Recovery of **Ni4a**: 92%.

Noteworthy is that novel β,*meso*-1,2,3-triazole-linked bisporphyrin array **Ni10** was obtained in excellent yield when *meso*-ethynyldiphenylporphyrin (**Ni9**) was used as a substrate. This new connection might provide interesting and different electronic communication and bestow upon these products unusual electrooptical and nonlinear optical behaviors. However, in the case of (2-ethynyl-5,10,15,20-tetraphenylporphyrinato)nickel(II), no reaction occurred under similar conditions, which might be due to bulky steric hindrance between the two substrates.



Scheme 3. 1,3-Dipolar cycloaddition reactions of **Ni1a** and various alkynes.

Conclusions

In conclusion, we have conveniently synthesized versatile β-azidotetraarylporphyrins from readily available β-aminotetraarylporphyrins. Thermal reaction of these compounds yields interesting N-containing fused six-membered products. Furthermore, they can be utilized in Cu^I-catalyzed 1,3-dipolar cycloaddition reactions with various alkynes to effectively introduce the useful triazolyl group into the porphyrin periphery. Further studies on the properties of these new and potentially valuable porphyrins are currently under investigation.

Supporting Information (see footnote on the first page of this article): Detailed experimental procedures and full characterization data for all compounds synthesized.

Acknowledgments

Financial support from the Natural Science Foundation of China (Nos.20272026, D20032010, and 20532040) is gratefully acknowledged.

[1] *The Porphyrin Handbook* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Academic Press, San Diego, **2000**–**2003**, vols. 1–20.

[2] D. Dolphin, T. G. Traylor, L. Y. Xie, *Acc. Chem. Res.* **1997**, *30*, 251–259.

[3] For recent and selective reports on porphyrin synthesis with the use of bromoporphyrins as convenient precursors, see: a) C. Liu, D. M. Shen, Q. Y. Chen, *J. Org. Chem.* **2006**, *71*, 9772–9783; b) D. M. Shen, C. Liu, Q. Y. Chen, *J. Org. Chem.* **2006**, *71*, 6508–6511; c) C. Liu, D. M. Shen, Q. Y. Chen, *Eur. J. Org. Chem.* **2006**, 2703–2706; d) D. M. Shen, C. Liu, Q. Y. Chen, *Chem. Commun.* **2005**, 4982–4984; e) C. Liu, Q. Y. Chen, *Synlett* **2005**, *8*, 1306–1310; f) C. Liu, Q. Y. Chen, *Eur. J. Org. Chem.* **2005**, 3680–3686; g) G. Y. Gao, A. J. Colvin, Y. Chen, X. P. Zhang, *J. Org. Chem.* **2004**, *69*, 8886–8892; h) G. Y. Gao, Y. Chen, X. P. Zhang, *Org. Lett.* **2004**, *6*, 1837–1840; i) G. Y. Gao, A. J. Colvin, Y. Chen, X. P. Zhang, *Org. Lett.* **2003**, *5*, 3261–3264; j) G. Y. Gao, Y. Chen, X. P. Zhang, *J. Org. Chem.* **2003**, *68*, 6215–6221; k) Y. Chen, X. P. Zhang, *J. Org. Chem.* **2003**, *68*, 4432–4438; l) T. Takanami, M. Hayashi, F. Hino, K. Suda, *Tetrahedron Lett.* **2003**, *44*, 7353–7357; m) M. M. Khan, H. Ali, J. E. van Lier, *Tetrahedron Lett.* **2001**, *42*, 1615–1617; n) L. L. Cheng, C. J. Chang, D. G. Nocera, *J. Org. Chem.* **2003**, *68*, 4075–4078; o) B. Vas, R. Alvarez, M. Nieto, A. I. Paniello, A. R. de Lera, *Tetrahedron Lett.* **2001**, *42*, 7409–7412; p) Y. Deng, C. K. Chang, D. G. Nocera, *Angew. Chem. Int. Ed.* **2000**, *39*, 1066–1068; q) P. M. Iovine, M. A. Kellett, N. P. Redmore, M. J. Therien, *J. Am. Chem. Soc.* **2000**, *122*, 8717–8727; r) S. Shanmugathasan, C. K. Johnson, C. Edwards, E. K. Matthews, D. Dolphin, R. W. Boyle, *J. Porphyrins Phthalocyanines* **2000**, *4*, 228–232; s) X. Shi, R. Amin, L. S. Liebeskind, *J. Org. Chem.* **2000**, *65*, 1650–1664; t) W. M. Sharman, J. E. van Lier, *J. Porphyrins Phthalocyanines* **2000**, *4*, 441–453 and references cited therein.

[4] For leading reviews, see: a) S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.* **2005**, *44*, 5188–5240; b) E. F. V. Scriven, K. Turnbull, *Chem. Rev.* **1988**, *88*, 297–368.

[5] a) C. Liu, D. M. Shen, Q. Y. Chen, *Chem. Commun.* **2006**, 770–772; b) Z. Zeng, C. Liu, L. M. Jin, C. C. Guo, Q. Y. Chen, *Eur. J. Org. Chem.* **2005**, 306–316; c) Z. Zeng, L. M. Jin, C. C. Guo, Q. Y. Chen, *Acta Chim. Sin.* **2004**, *62*, 288–294; d) L. Chen, L. M. Jin, C. C. Guo, Q. Y. Chen, *Synlett* **2005**, *6*, 963–970; e) L. M. Jin, L. Chen, C. C. Guo, Q. Y. Chen, *J. Porphyrins Phthalocyanines* **2005**, *9*, 109–120; f) L. M. Jin, L. Chen, J. J. Yin, C. C. Guo, Q. Y. Chen, *J. Fluorine Chem.* **2005**, *126*, 1321–1326; g) L. M. Jin, Z. Zeng, C. C. Guo, Q. Y. Chen, *J. Org. Chem.* **2003**, *68*, 3912–3917; h) L. M. Jin, L. Chen, J. J. Yin, J. M. Zhou, C. C. Guo, Q. Y. Chen, *J. Org. Chem.* **2006**, *71*, 527–536.

[6] W. Zhu, D. Ma, *Chem. Commun.* **2004**, 888–889.

[7] a) A. Giraudeau, H. J. Callot, J. Jordan, I. Ezhar, M. Gross, *J. Am. Chem. Soc.* **1979**, *101*, 3857–3862; b) H. K. Hombrecher, V. M. Gherdan, J. A. S. Cavaleiro, M. G. P. M. S. Neves, M. F. Condesso, *Tetrahedron* **1993**, *49*, 8569–8578.

[8] The crystals were grown by slow diffusion of petroleum ether into a methyl chloride solution. X-ray crystallographic data: crystal system, triclinic, space group, $P\bar{1}$, unit cell dimensions, a = 10.3157(12) Å, b = 10.7241(8) Å, c = 16.586(3) Å, α = 101.105(2)°, β = 92.682(2)°, γ = 98.685(2)°; Z = 2, F(000)= 760, $R1$ = 0.0637, $wR2$ = 0.1435. CCDC-622364 contains 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.

[9] a) M. O. Senge, *Chem. Commun.* **2006**, 243–256; b) M. O. Senge in *The Porphyrin Handbook* (Eds.: K. M. Kadishi, K. M. Smith, R. Guilard), Academic Press, San Diego, **2000**, vol. 1, ch. 6; c) W. R. Scheidt in *The Porphyrin Handbook* (Eds.: K. M. Kadishi, K. M. Smith, R. Guilard), Academic Press, San Diego, **2000**, vol. 3, ch. 16; d) C. J. Medforth, M. O. Senge, K. M. Smith, L. D. Sparks, J. A. Shelnutt, *J. Am. Chem. Soc.* **1992**, *114*, 9859–9869; e) W. R. Scheidt, Y. J. Lee, *Struct. Bonding (Berlin)* **1987**, *64*, 1–70.

[10] a) H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2001**, *40*, 2004–2021; b) H. C. Kolb, K. B. Sharpless, *Drug Discovery Today* **2003**, *8*, 1128–1137.

[11] For recent and selective reports, see: a) V. V. L. G. Rostovtsev Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2596–2599; b) C. W. Tornøe, C. Christensen, M. Meldal, *J. Org. Chem.* **2002**, *67*, 3057–3064; c) Q. Wang, T. R. Chan, R. Hilgraf, V. V. Fokin, K. B. Sharpless, M. G. Finn, *J. Am. Chem. Soc.* **2003**, *125*, 3192–3193; d) S. Löber, P. Rodriguez-Loaiza, P. Gmeiner, *Org. Lett.* **2003**, *5*, 1753–1755; e) F. Pérez-Balderas, M. Ortega-Muñoz, J. Morales-Sanfrutos, F. Hernández-Mateo, F. G. Calvo-Flores, J. A. Calvo-Asín, J. Isac-García, F. Santoyo-González, *Org. Lett.* **2003**, *5*, 1951–1954; f) A. Krasiński, V. V. Fokin, K. B. Sharpless, *Org. Lett.* **2004**, *6*, 1237–1240; g) S. Kamijo, T. Jin, Z. Huo, Y. Yamamoto, *J. Am. Chem. Soc.* **2003**, *125*, 7786–7787; h) S. Kamijo, T. Jin, Z. Huo, Y. Yamamoto, *J. Org. Chem.* **2004**, *69*, 2386–2393; i) P. Appukkuttan, V. V. Dehaen, F. Wim, E. Van der Eycken, *Org. Lett.* **2004**, *6*, 4223–4225; j) Y. M. Wu, J. Deng, X. Fang, Q. Y. Chen, *J. Fluorine Chem.* **2004**, *125*, 1415–1423; k) Y. M. Wu, J. Deng, Y. Li, Q. Y. Chen, *Synthesis* **2005**, *8*, 1314–1318; l) Y. M. Wu, J. Deng, Q. Y. Chen, *Synlett* **2006**, *4*, 645–647; m) V. D. Bock, R. Perciaccante, T. P. Jansen, H. Hiemstra, J. H. van Maarseveen, *Org. Lett.* **2006**, *8*, 919–922; n) S. Díez-González, A. Correa, L. Cavallo, S. P. Nolan, *Chem. Eur. J.* **2006**, *12*, 7558–7564; o) V. D. Bock, H. Hiemstra, J. H. van Maarseveen, *Eur. J. Org. Chem.* **2006**, *1*, 51–68.

Received: December 1, 2006
Published Online: February 2, 2007

