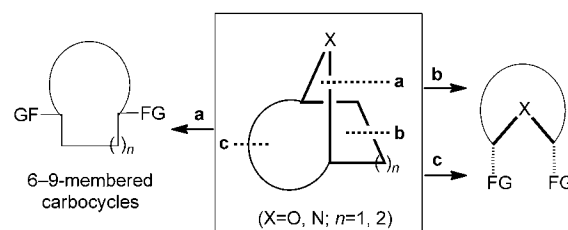


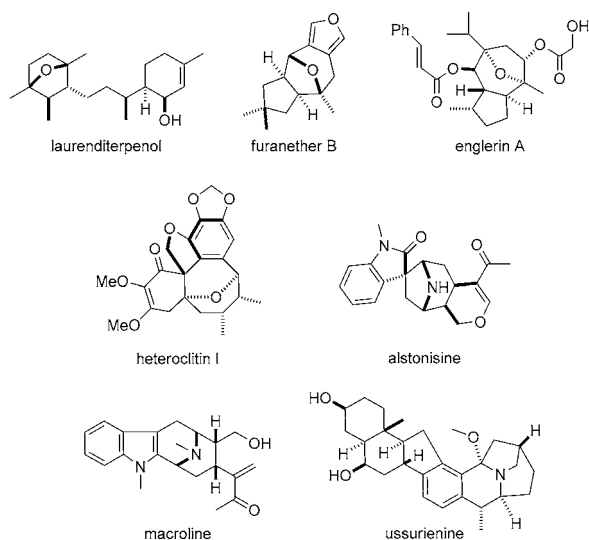
Lewis Acid Catalyzed Intramolecular [4+2] and [3+2] Cross-Cycloaddition of Alkynylcyclopropane Ketones with Carbonyl Compounds and Imines**

Yu Bai, Weijie Tao, Jun Ren, and Zhongwen Wang*

The structurally diverse and complex family of compounds that have bridged oxa/aza- $[n.2.1]$ and oxa/aza- $[n.3.1]$ skeletons ($n = 2, 3, 4$) widely occurs in nature and exhibits a broad range of biological activities (Scheme 1). Additionally, such bridged skeletons can also be used as key intermediates in organic synthesis because of their inherent stereochemistry and multiple functionalizable sites.^[1] A general strategy for the construction of medium-sized carbocycles may be provided by C–O or C–N bond cleavage in bridged skeletons (Scheme 2).^[2–5] As important substructures that are prevalent in natural products, *cis*-2,5-disubstituted tetrahydrofuran/



Scheme 2. Oxa-/aza- $[n.2.1]$ or oxa-/aza- $[n.3.1]$ skeletons used as key intermediates in organic synthesis. FG = functional group.



Scheme 1. Representative natural products containing oxa-/aza- $[n.2.1]$ or oxa-/aza- $[n.3.1]$ skeletons.

pyrrolidine and *cis*-2,6-disubstituted tetrahydropyran/piperidine may also be obtained by C–C bond cleavage (Scheme 2). The development of a general strategy to construct such differently bridged skeletons is important for both the synthesis of natural products and the construction of structurally diverse molecular libraries for chemical biology and the discovery of pharmaceutical and agrochemical leads.

Cycloaddition and domino reactions belong to the most efficient and direct transformations of cyclic skeletons. Although various cycloaddition and domino reactions have been developed for construction of such bridged skeletons,^[6,7] most of them focus on the synthesis of one type or one subclass of the big and structurally diverse family of $[n.2.1]$ and $[n.3.1]$ skeletons, and development of a more general, efficient, and conceptually new strategy still remains important and challenging.

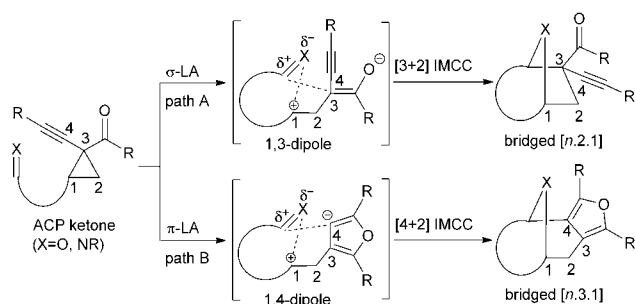
Alkynylcyclopropane (ACP) ketone has recently been introduced as a useful all-carbon 1,4-dipole. Zhang and Schmalz reported a Lewis acid (LA) catalyzed domino cycloisomerization/nucleophilic ring-opening process of ACP ketones.^[8] Subsequently Zhang and co-workers developed a gold-catalyzed intermolecular [4+2] cycloaddition of ACP ketones with alkenes, carbonyl compounds, and imines.^[9a] Some other types of cycloadditions have also been successfully developed by Zhang and co-workers, and by our research group.^[10] We have recently developed a general strategy for construction of bridged oxa- and aza- $[n.2.1]$ skeletons and have successfully applied it to the total synthesis of platensimycin and bruguierol.^[11,12] We also described a novel intramolecular cross-cycloaddition reaction (IMCC) on two types of functionalized cyclopropanes, which were used as all-carbon 1,3-dipoles. We hoped to apply this IMCC on ACP ketone to develop a [4+2] IMCC as a general strategy for construction of oxa- and aza- $[n.3.1]$ skeletons (Scheme 3). Moreover, the difference between π -electrophilic (π -LAs) and σ -electrophilic (σ -LAs) LAs was consid-

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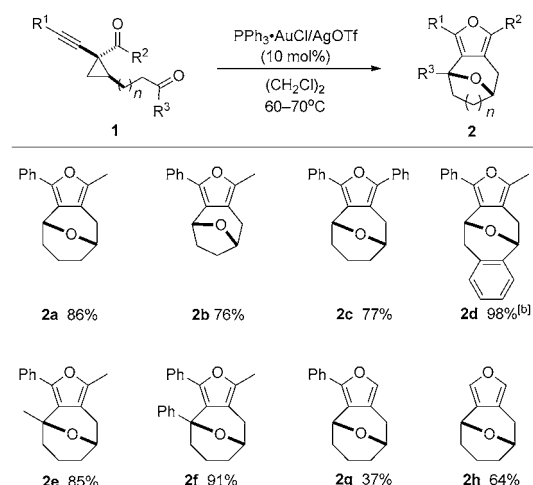
Scheme 3. Concept of LA-regulated [3+2] and [4+2] IMCC.

ered^[13], as demonstrated in the studies by Zhang and co-workers^[10b] and by our research group^[10c] on reactions of ACP ketones with nitrones. We therefore envisioned that by an appropriate selection of the LA, the cycloaddition mode of an ACP ketone with a carbonyl compound or imine might be switched between [3+2] IMCC (path A) and [4+2] IMCC (path B), and thus a more general strategy for construction of both [n.2.1] and [n.3.1] skeletons could be developed.

Compound **1a** was prepared as a model substrate to verify the concept, and various LAs were tested with 1,2-dichloroethane as solvent (Table 1). Most of the investigated LAs catalyzed the IMCC and gave [4+2] and/or [3+2] cycloadducts in various ratios. In most cases, the [4+2] or [3+2] cycloadduct was obtained as a major product by catalysis with π -LAs or σ -LAs, respectively. Some LAs showed excellent reaction selectivity between the [4+2] and [3+2] IMCC, for example, $\text{PPh}_3\cdot\text{AuCl}/\text{AgOTf}$ gave [4+2] cycloadduct **2a** (Table 1, entry 1) and $\text{Ni}(\text{ClO}_4)_2\cdot 6\text{H}_2\text{O}$ gave [3+2] cycloadduct **3a** (Table 1, entry 14), both as sole products in good yields. These conditions were used for the subsequent investigation. By selecting suitable LAs, bridged oxa-[3.2.1] or oxa-[3.3.1] skeletons could be constructed selectively. It should be noted that triflic acid (Brønsted acid) also gave [3+2] and [4+2] cycloadducts (Table 1, entry 20). To the best of our knowledge, this is the first intramolecular cycloaddition and also the first [3+2] cycloaddition of ACP ketone.

For construction of oxa-[n.3.1] skeletons, various ACP ketones **1** were prepared and subsequently subjected to [4+2] IMCC with carbonyl compounds (Scheme 4). Substrates with various substituents afforded oxa-[3.2.1] and oxa-[3.3.1] skeletons. The structure of **2d** was confirmed by NMR spectroscopy, HRMS analysis, and X-ray crystal structure analysis^[14] (Figure 1). Formation of the oxa-[4.3.1] skeleton failed, however we were delighted that construction of the aza-[4.3.1] skeleton was successful (see below).

$\text{Ni}(\text{ClO}_4)_2\cdot 6\text{H}_2\text{O}$ was selected as LA catalyst for [3+2] IMCC (Scheme 5). Oxa-[2.2.1] and oxa-[3.2.1] skeletons were constructed successfully, and products with a high diversity of substituents were obtained in most cases with moderate to excellent yields, and with excellent stereoselectivities. The



Scheme 4. Construction of oxa-[3.2.1] and oxa-[3.3.1] skeletons. Reaction conditions (0.3 mmol scale): $\text{PPh}_3\cdot\text{AuCl}/\text{AgOTf}$ (10 mol%), $(\text{CH}_2\text{Cl})_2$ (10.0 mL), 60–70 °C, 0.5–2 h, under Ar. All yields reported are those of isolated products. [a] AgNTf_2 was used instead of AgOTf .

structure of **3d** was unambiguously confirmed by NMR spectroscopy, HRMS analysis, and X-ray crystal structure analysis^[14] (Figure 1).

Table 1: [3+2] and/or [4+2] IMCC catalyzed by various Lewis acids.^[a]

1a

Lewis acid
(CH₂Cl)₂

2a oxa-[3.3.1]

and/or

3a oxa-[3.2.1]

Entry	Lewis acid	T [°C]	t	2a [%]	3a [%]	1a [%] ^[b]	Yield [%] ^[c]
1	PPh ₃ ·AuCl/AgOTf	60–70	2 h	93	0	0	93
2	Cu(OTf) ₂	60–70	2 h	85	3	1	88
3	AuCl ₃	60–70	3 h	82	3	5	85 (90)
4	CuOTf	60–70	3 h	60	0	0	60
5	Bi(OTf) ₃	60–70	2 h	59	41	0	100
6	Zn(OTf) ₂	60–70	4 h	54	0	8	54 (62)
7	Hg(OTf) ₂	60–70	1 h	45	0	0	45
8	PtCl ₂	60–70	4 h	31	0	15	31 (46)
9	Pd(OAc) ₂	60–70	4 h	10	0	30	10 (40)
10	FeCl ₃ ·6H ₂ O	60–70	1 h	9	15	0	24
11	In(OTf) ₃	60–70	3 h	6	27	0	33
12	Yb(OTf) ₃	60–70	4 h	4	42	54	46 (100)
13	Sn(OTf) ₂	60–70	3 h	3	28	0	31
14	Ni(ClO ₄) ₂ ·6H ₂ O	60–70	4 h	0	70	6	70 (76)
15	Sc(OTf) ₃	60–70	4 h	0	48	52	48 (100)
16	BF ₃ ·OEt ₂	RT	17 min	0	59	0	59
17	TMSOTf	60–70	22 min	0	19	0	19
18	TiCl ₄	RT	25 min	0	21	0	21
19	SnCl ₄	RT	30 min	0	11	0	11
20	triflic acid	55	35 min	15	37	0	52

[a] Reaction conditions: **1a** (10 mg, 0.039 mmol) in $(\text{CH}_2\text{Cl})_2$ (3 mL), Lewis acid (10 mol%), yields determined by ^1H NMR spectroscopy (internal standard: 1-chloro-2,4-dinitrobenzene). [b] Recovered starting material. [c] Yields based on recovered starting material are given in parentheses. Tf = trifluoromethanesulfonyl, TMS = trimethylsilyl.

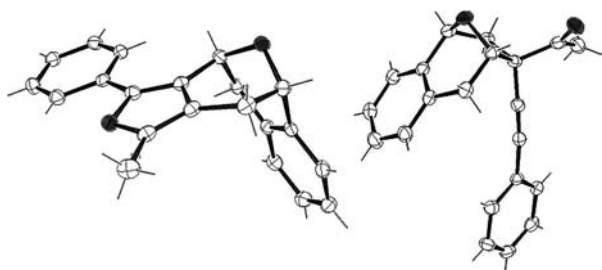
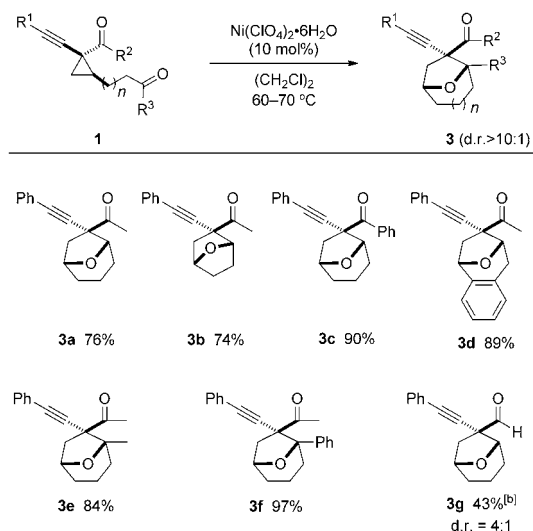


Figure 1. X-ray crystal structures of **2d** and **3d**. Thermal ellipsoids are set at 50% probability.

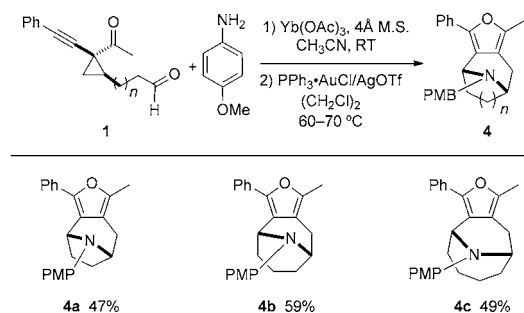


Scheme 5. Construction of oxa-[2.2.1] and oxa-[3.2.1] skeletons. Reaction conditions (0.3 mmol scale): $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (10 mol%), $(\text{CH}_2\text{Cl})_2$ (10.0 mL), 60–70 °C, 0.5–2 h, under Ar. All yields reported are those of isolated products. [a] $\text{Sc}(\text{OTf})_3$ was used instead of $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$.

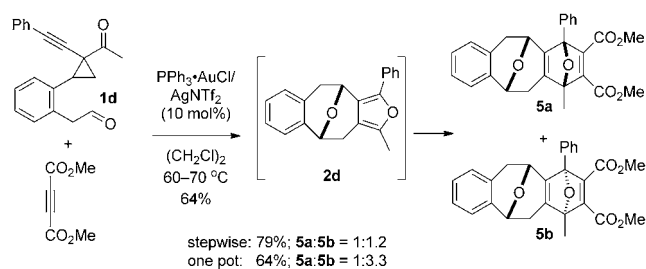
An attempt to achieve a [3+2] IMCC of ACP ketones with imines failed under catalysis with $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$, because of the quick decomposition of the substrates. However, after formation of the imine,^[15] the [4+2] IMCC was successful under catalysis with $\text{PPh}_3 \cdot \text{AuCl}/\text{AgOTf}$, and aza-[3.2.1], aza-[3.3.1], and even aza-[4.3.1] skeletons were successfully constructed (Scheme 6).

Polycyclic skeletons with fused six-membered carbocycles are prevalent in natural and synthetic products (e.g., Kagan's ether^[16]). A Diels–Alder cycloaddition of **2d** with dimethyl acetylenedicarboxylate (DMAD) was carried out under heating in toluene and gave a 6-8-6 carbocyclic core skeleton (**5a:5b** = 1:1.2; Scheme 7). Under catalysis by $\text{PPh}_3 \cdot \text{AuCl}/\text{AgNTf}_2$, an efficient one-pot domino variant of this reaction has also been developed successfully.

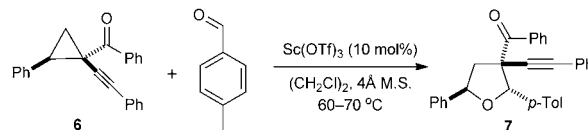
An intermolecular [3+2] cycloaddition of ACP ketone **6** with 4-methylbenzaldehyde was also carried out (Scheme 8). This is the first intermolecular [3+2] cycloaddition of an ACP ketone. The method afforded 2,5-*trans*-disubstituted tetrahydrofuran **7** as a sole isomer, the high diastereoselectivity of which was quite different from that of cyclopropane 1,1-



Scheme 6. Construction of aza-[*n*.3.1] skeletons. Reaction conditions (0.4 mmol scale): $\text{Yb}(\text{OAc})_3$ (1.05 equiv), 4 Å M.S., CH_3CN (30 mL), 2 h, RT; after filtration and evaporation: $\text{PPh}_3 \cdot \text{AuCl}/\text{AgOTf}$ (10 mol%), $(\text{CH}_2\text{Cl})_2$ (20 mL), 60–70 °C, 0.5–2 h, under Ar. All yields reported are those of isolated products. M.S. = molecular sieves.



Scheme 7. Domino and stepwise [4+2] IMCC and [4+2] Diels–Alder reaction.



Scheme 8. An intermolecular [3+2] cycloaddition.

diesters in which a 2,5-*cis*-disubstituted tetrahydrofuran was obtained.^[17]

In summary, we have successfully developed a general strategy for construction of structurally diverse bridged oxa-/aza-[*n*.3.1] and oxa-/aza-[*n*.2.1] skeletons by a novel [4+2] and [3+2] IMCC of ACP ketones with carbonyl compounds and imines. This method also supplied a potential general strategy for construction of medium-sized carbocyclic skeletons. Features of this strategy include good structural diversity, LA-regulated selective formation of [*n*.3.1] and [*n*.2.1] skeletons from common starting materials, excellent stereoselectivity, and mild conditions. To the best of our knowledge, this is the first intramolecular cycloaddition and the first intermolecular [3+2] cycloaddition of ACP ketones. These results indicated the potential use of ACP ketones as multifunctional building blocks in organic synthesis. Future studies will include investigation of the [4+2] or [3+2] IMCC strategy and development of the intermolecular [3+2] cycloaddition, including potential applications on natural products synthesis.

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- [1] For general reviews, see: a) C. S. Schindler, E. M. Carreira, *Chem. Soc. Rev.* **2009**, 38, 3222; b) I. V. Hartung, H. M. R. Hoffmann, *Angew. Chem.* **2004**, 116, 1968; *Angew. Chem. Int. Ed.* **2004**, 43, 1934; c) M. Lautens, K. Fagnou, S. Hiebert, *Acc. Chem. Res.* **2003**, 36, 48; d) O. Arjona, J. Plumet, *Curr. Org. Chem.* **2002**, 6, 571; e) A. M. Misske, H. M. R. Hoffmann, *Chem. Eur. J.* **2000**, 6, 3313; f) P. Vogel, J. Cossy, J. Plumet, O. Arjona, *Tetrahedron* **1999**, 55, 13521; g) P. Chiu, M. Lautens, *Top. Curr. Chem.* **1997**, 190, 1; h) S. Woo, B. A. Keay, *Synthesis* **1996**, 669; i) M. Lautens, *Synlett* **1993**, 177; j) M. Lautens, *Pure Appl. Chem.* **1992**, 64, 1873.
- [2] For general reviews on construction of medium-sized carbocyclic rings, see: a) S. K. Chattopadhyay, S. Karmakar, T. Biswas, K. C. Majumdar, H. Rahaman, B. Roy, *Tetrahedron* **2007**, 63, 3919; b) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, 104, 2127; c) M. D. McReynolds, J. M. Dougherty, P. R. Hanson, *Chem. Rev.* **2004**, 104, 2239; d) P. A. Wender, J. L. Baryza, S. E. Brenner, M. O. Clarke, G. G. Gamber, J. C. Horan, T. C. Jessop, C. Kan, K. Pattabiraman, T. J. Williams, *Pure Appl. Chem.* **2003**, 75, 143; e) M. E. Maier, *Angew. Chem.* **2000**, 112, 2153; *Angew. Chem. Int. Ed.* **2000**, 39, 2073; f) M. Harmata, *Acc. Chem. Res.* **2001**, 34, 595; g) B. R. Bear, S. M. Sparks, K. J. Shea, *Angew. Chem.* **2001**, 113, 864; *Angew. Chem. Int. Ed.* **2001**, 40, 820; h) L. Yet, *Chem. Rev.* **2000**, 100, 2963; i) L. Yet, *Tetrahedron* **1999**, 55, 9349; j) G. Mehta, V. Singh, *Chem. Rev.* **1999**, 99, 881; k) G. A. Molander, *Acc. Chem. Res.* **1998**, 31, 603; l) I. Ojima, M. Tzamarioudaki, Z. Li, R. J. Donovan, *Chem. Rev.* **1996**, 96, 635; m) S. M. Sieburth, N. T. Cunard, *Tetrahedron* **1996**, 52, 6251; n) B. B. Snider, *Chem. Rev.* **1996**, 96, 339; o) G. Rousseau, *Tetrahedron* **1995**, 51, 2777; p) C. J. Roxburgh, *Tetrahedron* **1993**, 49, 10749; q) P. A. Evans, A. B. Holmes, *Tetrahedron* **1991**, 47, 9131; r) G. Illuminati, L. Mandolini, *Acc. Chem. Res.* **1981**, 14, 95.
- [3] For reviews on construction of seven-membered carbocycles and heterocycles, see: a) H. Pellissiera, *Adv. Synth. Catal.* **2011**, 353, 189; b) H. Butenschön, *Angew. Chem.* **2008**, 120, 5367; *Angew. Chem. Int. Ed.* **2008**, 47, 5287; c) M. A. Battiste, P. M. Pelphrey, D. L. Wright, *Chem. Eur. J.* **2006**, 12, 3438; d) N. L. Snyder, H. M. Haines, M. W. Pecuh, *Tetrahedron* **2006**, 62, 9301; e) L. A. Byrne, D. G. Gilheany, *Synlett* **2004**, 933; f) E. J. Kantowski, M. J. Kurth, *Tetrahedron* **2000**, 56, 4317; g) M. Filipini, J. Rodriguez, *Chem. Rev.* **1999**, 99, 27; h) J. O. Hoberg, *Tetrahedron* **1998**, 54, 12631.
- [4] For selected reviews on construction of eight-membered carbocycles and heterocycles, see: a) I. Shiina, *Chem. Rev.* **2007**, 107, 239; b) A. Michaut, J. Rodriguez, *Angew. Chem.* **2006**, 118, 5870; *Angew. Chem. Int. Ed.* **2006**, 45, 5740; c) J. Chang, J. Reiner, J. Xie, *Chem. Rev.* **2005**, 105, 4581; d) M. Murakami, *Angew. Chem.* **2003**, 115, 742; *Angew. Chem. Int. Ed.* **2003**, 42, 718; e) see Ref. [2]; f) N. A. Petasis, M. A. Patane, *Tetrahedron* **1992**, 48, 5757.
- [5] Because of the involved inherent unfavorable enthalpic and entropic factors and transannular interactions, the direct construction of medium-sized rings is more difficult than that of five- and six-membered rings: G. Illuminati, L. Mandolini, *Acc. Chem. Res.* **1981**, 14, 95.
- [6] For selected reviews, see: a) A. G. Lohse, R. P. Hsung, *Chem. Eur. J.* **2011**, 17, 3812; b) W. Zhao, *Chem. Rev.* **2010**, 110, 1706; c) M. Harmata, *Chem. Commun.* **2010**, 46, 8886; d) V. Singh, U. M. Krishna Vikrant, G. K. Trivedi, *Tetrahedron* **2008**, 64, 3405; e) V. Nair, T. D. Suja, *Tetrahedron* **2007**, 63, 12247; f) F. López, J. L. Mascarenas, *Chem. Eur. J.* **2007**, 13, 2172; g) M. Harmata, P. Rashatasakhon, *Tetrahedron* **2003**, 59, 2371; h) G. Mehta, S. Muthusamy, *Tetrahedron* **2002**, 58, 9477; i) P. A. Wender, J. A. Love in *Advances in Cycloaddition*, Vol. 5 (Ed.: M. Harmata), JAI, Stamford, CT, **1999**, p. 1; j) J. L. Mascarenas in *Advances in Cycloaddition*, Vol. 6 (Ed.: M. Harmata), JAI, Stamford, CT, **1999**, p. 1; k) H. M. L. Davies in *Advances in Cycloaddition*, Vol. 5 (Ed.: M. Harmata), JAI, Stamford, CT, **1999**, p. 119; l) J. H. Rigby, *Tetrahedron* **1999**, 55, 4521; m) M. Harmata, *Tetrahedron* **1997**, 53, 6235; n) C. O. Kappe, S. S. Murphree, A. Padwa, *Tetrahedron* **1997**, 53, 14179; o) F. G. West in *Advances in Cycloaddition*, Vol. 4 (Ed.: M. Lautens), JAI, Stamford, CT, **1997**, p. 1; p) J. H. Rigby, F. C. Pigge, *Org. React.* **1997**, 51, 351; q) G. A. Molander, C. R. Harris, *Chem. Rev.* **1996**, 96, 307; r) A. Padwa, M. D. Weingarten, *Chem. Rev.* **1996**, 96, 223; s) J. H. Rigby, *Acc. Chem. Res.* **1993**, 26, 579; t) H. M. L. Davies, *Tetrahedron* **1993**, 49, 5203; u) A. Padwa, *Acc. Chem. Res.* **1991**, 24, 22; v) B. H. Lipshutz, *Chem. Rev.* **1986**, 86, 795; w) A. R. Katritzky, N. Dennis, *Chem. Rev.* **1989**, 89, 827; x) J. Mann, *Tetrahedron* **1986**, 42, 4611; y) H. M. R. Hoffmann, *Angew. Chem.* **1984**, 96, 29; *Angew. Chem. Int. Ed. Engl.* **1984**, 23, 1; z) R. Noyori, *Acc. Chem. Res.* **1979**, 12, 61; aa) H. M. R. Hoffmann, *Angew. Chem.* **1973**, 85, 877; *Angew. Chem. Int. Ed. Engl.* **1973**, 12, 819.
- [7] For some recently reported strategies on the synthesis of oxa-/aza-[n.2.1] or oxa-/aza-[n.3.1] skeletons, see: a) G. Song, D. Chen, Y. Su, K. Han, C. L. Pan, A. Jia, X. Li, *Angew. Chem.* **2011**, 123, 7937; *Angew. Chem. Int. Ed.* **2011**, 50, 7791; b) D. M. Jaber, R. N. Burgin, M. Hepler, P. Zavalij, M. P. Doyle, *Chem. Commun.* **2011**, 47, 7623; c) M. Iqbal, R. J. G. Black, J. Winn, A. T. Reeder, A. J. Blake, P. A. Clarke, *Org. Biomol. Chem.* **2011**, 9, 5062; d) K. Ishida, H. Kusama, N. Iwasawa, *J. Am. Chem. Soc.* **2010**, 132, 8842; e) T. M. Teng, A. Das, D. B. Huple, R.-S. Liu, *J. Am. Chem. Soc.* **2010**, 132, 12565; f) A. Mendoza, P. Pardo, F. Rodriguez, F. J. Fananas, *Chem. Eur. J.* **2010**, 16, 9758; g) W. K. Chung, S. K. Lam, B. Lo, L. L. Liu, W. T. Wong, P. Chiu, *J. Am. Chem. Soc.* **2009**, 131, 4556; h) H. S. Yeom, J. E. Lee, S. Shin, *Angew. Chem.* **2008**, 120, 7148; *Angew. Chem. Int. Ed.* **2008**, 47, 7040; i) C. H. Oh, J. H. Lee, S. J. Lee, J. I. Kim, C. S. Hong, *Angew. Chem.* **2008**, 120, 7615; *Angew. Chem. Int. Ed.* **2008**, 47, 7505; j) E. C. Garnier, L. S. Liebeskind, *J. Am. Chem. Soc.* **2008**, 130, 7449; k) H. Kusama, K. Ishida, H. Funami, N. Iwasawa, *Angew. Chem.* **2008**, 120, 4981; *Angew. Chem. Int. Ed.* **2008**, 47, 4903; l) B. Trillo, F. Lopez, M. Gulias, L. Castedo, J. L. Mascarenas, *Angew. Chem.* **2008**, 120, 965; *Angew. Chem. Int. Ed.* **2008**, 47, 951; m) S. Bhunia, K. C. Wang, R.-S. Liu, *Angew. Chem.* **2008**, 120, 5141; *Angew. Chem. Int. Ed.* **2008**, 47, 5063; n) R. P. Reddy, H. M. L. Davies, *J. Am. Chem. Soc.* **2007**, 129, 10312; o) E. Jiménez-Núñez, C. K. Claverie, C. Nieto-Oberhuber, A. M. Echavarren, *Angew. Chem.* **2006**, 118, 5578; *Angew. Chem. Int. Ed.* **2006**, 45, 5452; p) J. Barluenga, A. Dieguez, A. Fernandez, F. Rodriguez, F. J. Fananas, *Angew. Chem.* **2006**, 118, 2145; *Angew. Chem. Int. Ed.* **2006**, 45, 2091; q) K. M. Peese, D. Y. Gin, *J. Am. Chem. Soc.* **2006**, 128, 8734; r) H. Kusama, H. Funami, M. Shido, Y. Hara, J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* **2005**, 127, 2709; s) J. Barluenga, A. Dieguez, F. Rodriguez, F. J. Fananas, *Angew. Chem.* **2005**, 117, 128; *Angew. Chem. Int. Ed.* **2005**, 44, 126; t) J. Barluenga, P. Garcia-Garcia, M. A. Fernandez-Rodriguez, E. Aguilar, I. Merino, *Angew. Chem.* **2005**, 117, 6025; *Angew. Chem. Int. Ed.* **2005**, 44, 5875; u) J. Huang, R. P. Hsung, *J. Am. Chem. Soc.* **2005**, 127, 50; v) C. Rameshkumar, R. P. Hsung, *Angew. Chem.* **2004**, 116, 625; *Angew. Chem. Int. Ed.* **2004**, 43, 615; w) G. A. Molander, D. J. St. Jean, Jr., J. Haas, *J. Am. Chem. Soc.* **2004**, 126, 1642; x) M. Harmata, S. K. Ghosh, X. Hong, S. Wachar-

- asindhu, P. Kirchhoefer, *J. Am. Chem. Soc.* **2003**, *125*, 2058; y) F. P. Marmasäter, G. K. Murphy, F. G. West, *J. Am. Chem. Soc.* **2003**, *125*, 14724; z) C. M. Yu, J. Y. Lee, B. So, J. Hong, *Angew. Chem.* **2002**, *114*, 169; *Angew. Chem. Int. Ed.* **2002**, *41*, 161; aa) T. Graening, W. Friedrichsen, J. Lex, H. G. Schmalz, *Angew. Chem.* **2002**, *114*, 1594; *Angew. Chem. Int. Ed.* **2002**, *41*, 1524; ab) J. Barluenga, A. Dieguez, F. Rodriguez, J. Florez, F. J. Fananas, *J. Am. Chem. Soc.* **2002**, *124*, 9056; ac) F. López, L. Castedo, J. L. Mascarenas, *J. Am. Chem. Soc.* **2002**, *124*, 4218; ad) A. Delgado, L. Castedo, J. L. Mascarenas, *Org. Lett.* **2002**, *4*, 3091; ae) Y. S. Cho, H. Y. Kim, J. H. Cha, A. N. Pae, H. Y. Koh, J. H. Choi, M. H. Chang, *Org. Lett.* **2002**, *4*, 2025; af) N. Iwasawa, M. Shido, H. Kusama, *J. Am. Chem. Soc.* **2001**, *123*, 5814.
- [8] J. Zhang, H.-G. Schmalz, *Angew. Chem.* **2006**, *118*, 6856; *Angew. Chem. Int. Ed.* **2006**, *45*, 6704.
- [9] a) G. Zhang, X. Huang, G. Li, L. Zhang, *J. Am. Chem. Soc.* **2008**, *130*, 1814; b) G. Li, X. Huang, L. Zhang, *J. Am. Chem. Soc.* **2008**, *130*, 6944.
- [10] a) H. Gao, X. Zhao, Y. Yu, J. Zhang, *Chem. Eur. J.* **2010**, *16*, 456; b) Y. Zhang, F. Liu, J. Zhang, *Chem. Eur. J.* **2010**, *16*, 6146; c) Y. Bai, J. Fang, J. Ren, Z. Wang, *Chem. Eur. J.* **2009**, *15*, 8975; d) Y. Zhang, Z. Chen, Y. Xiao, J. Zhang, *Chem. Eur. J.* **2009**, *15*, 5208; for a DFT study, see: e) R. Fang, C. Su, C. Zhao, D. L. Phillips, *Organometallics* **2009**, *28*, 741.
- [11] a) S. Xing, Y. Li, Z. Li, C. Liu, J. Ren, Z. Wang, *Angew. Chem.* **2011**, *123*, 12813; *Angew. Chem. Int. Ed.* **2011**, *50*, 12605; b) S. Xing, W. Pan, C. Liu, J. Ren, Z. Wang, *Angew. Chem.* **2010**, *122*, 3283; *Angew. Chem. Int. Ed.* **2010**, *49*, 3215.
- [12] B. Hu, S. Xing, J. Ren, Z. Wang, *Tetrahedron* **2010**, *66*, 5671.
- [13] Y. Yamamoto, *J. Org. Chem.* **2007**, *72*, 7817.
- [14] CCDC 815284 (**2d**) and 815283 (**3d**) 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.
- [15] T. C. Nugent, M. El-Shazly, V. N. Wakchaure, *J. Org. Chem.* **1998**, *63*, 1297.
- [16] a) M. Harmata, T. Murray, *J. Org. Chem.* **1989**, *54*, 3761; b) M. E. Jung, A. B. Mossman, M. A. Lyster, *J. Org. Chem.* **1978**, *43*, 3698; c) J. Kagan, S.-Y. Chen, D. A. Agdeppa, Jr., W. H. Watson, V. Zabel, *Tetrahedron Lett.* **1977**, *18*, 4469.
- [17] a) P. D. Pohlhaus, J. S. Johnson, *J. Am. Chem. Soc.* **2005**, *127*, 16014; b) P. D. Pohlhaus, J. S. Johnson, *J. Org. Chem.* **2005**, *70*, 1057.