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cis-Stereoselective nickel-catalyzed cyclization/alkylation and arylation reactions of allenyl-aldehydes and -ketones with organozinc reagents†

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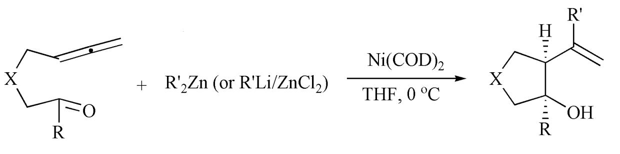
Highly stereoselective alkylative and arylative cyclization reactions of allenyl-aldehydes and -ketones with organozinc reagents occur efficiently in the presence of catalytic Ni(COD)$_2$ to afford *cis*-fused homoallylic cyclopentanols.

The transition metal-catalyzed cyclization reactions of unsaturated substrates is undoubtedly one of the most useful synthetic procedures for the preparation of cyclic compounds. The transition metal-catalyzed cyclization reactions of dienes, enynes, and diynes[1–4] have been described. The titanium-catalyzed reductive cyclization reactions of enals and enones to form cyclopentanols *via* oxametallacycles were investigated by Buchwald[5] and Crowe.[6] Recently Montgomery[7a] developed a chemoselective, nickel-catalyzed cyclization/alkylation reaction of ynals with organozinc reagents, which produces exo-methylene-containing allylic-cyclopentanols, together with his extensive nickel-catalyzed three component processes.[7b]

To the best of our knowledge cyclization reactions of allenyl-aldehydes and -ketones with organozinc reagents have not been described previously. We recently probed[8] cyclization reactions of tethered allenyl-aldehydes and allenyl-ketones as precursors of 2-alkenyl substituted cyclopentanols. Here we wish to describe *cis*-stereoselective, alkenylcyclopentanol forming, nickel-catalyzed alkylative and arylative cyclization reactions of allenyl-aldehydes and -ketones with organozinc reagents (Scheme 1).[9,10]

Reaction of **1a** with Ni(acac)$_2$ and Et$_3$B in THF at 0–25 °C did not yield any cyclized product. When Et$_2$Zn is used in place of Et$_3$B, nickel-catalyzed reaction of **1a** in THF at 0 °C gives rise to the cyclized product **3b** in 68% yield. Importantly, **3b** is formed as a sole product (90%) when Ni(COD)$_2$ is employed as the catalyst for the reaction of **1a** with Et$_2$Zn in THF at 0 °C.

We next explored the scope of this cyclization reaction. We observed that the allenyl-aldehyde **1a** reacts with Me$_2$Zn in THF in the presence of Ni(COD)$_2$ (10 mol%) at 0 °C for 10 min to afford the *cis*-fused cyclopentanol **3a** in 77% isolated yield (entry 1, Table 1). The *cis*-stereochemistry of **3a** was assigned by using the 2D NOESY technique, coupled with molecular mechanics calculations (see ESI†). Nickel-catalyzed reaction of allenyl-aldehyde **1a** with BuLi and ZnCl$_2$ affords the butyl adduct **3c** (entry 3). In addition, the phenyl substituted homoallylic cyclopentanol **3d** is generated in 83% yield (entry 4) by reaction of **1a** with PhLi/ZnCl$_2$ and Ni(COD)$_2$ at 0 °C in THF for 30 min. The stereochemistry of **3d** was unambiguously assigned by using X-ray crystallographic methods (see ESI†).



1 **2** **3**

X = NTs, C(CO$_2$Et)$_2$, CH$_2$

R = H, CH$_3$, Et R' = Me, Et, *n*Bu, Ph

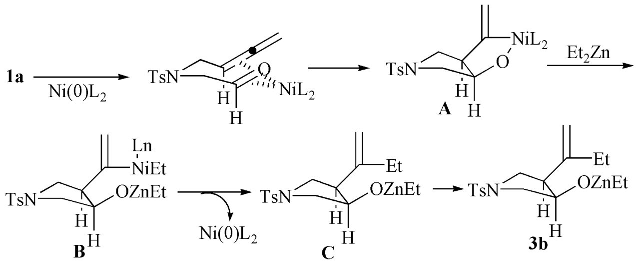
Scheme 1

This method was extended to allenyl-ketones to introduce quaternary homoallylic centers. Allenyl-ketone **1b** reacts with Me$_2$Zn to produce the tertiary-cyclopentanol **3e** in 58% yield (entry 5). A strong NOE in the NMR between the methyl and ring junction protons suggests that **3e** has *cis*-stereochemistry. Likewise, Et$_2$Zn and PhLi/ZnCl$_2$ are used to promote cyclization of **1b** to furnish the respective cyclization products **3f** (66%) and **3g** (69%) (entries 6 and 7). The structure and stereochemistry of **3g** were assigned by X-ray data (ESI†). It is notable that the higher branched ethyl ketone **1c**, bigger than the methyl ketone, tolerated Et$_2$Zn to give **3h** (entry 8).

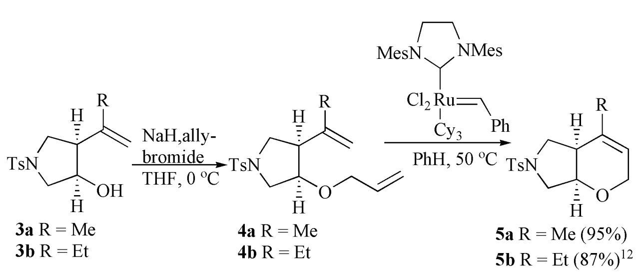
Information about the functional group compatibility of the process is gained from the reaction of malonate branched allenyl-aldehyde **1d** with PhLi/ZnCl$_2$, which yields cyclized product **3i** (60%) (entry 9). When allenyl-ketone **1e** is utilized as substrate, cyclizations with Me$_2$Zn and PhLi/ZnCl$_2$ unexpectedly generate the bicyclic lactones **3k** and **3l**, respectively, as sole products (entries 11 and 12). In these cases, the initially formed adducts undergo intramolecular lactonization between the tertiary alcohol and carboethoxy groups.

As a plausible mechanism, oxidative cyclization of the Ni(0) allenyl-aldehyde complex occurs to form the oxametallacycle **A**. Transmetallation between the organozinc reagent and oxametallacycle, involving nickel–oxygen bond cleavage, then gives the intermediate **B**, which upon reductive elimination affords the zinc alkoxide precursor of the cyclopentanol **C** (Scheme 2).

To elaborate the cyclized 2-alkenyl substituted cyclopentanols **3a** and **3b**, *O*-allylation followed by ring-closing metathesis using Grubbs' carbene metathesis catalyst[11] generated the bicyclic heterocycles **5a** and **5b**, respectively (Scheme 3).



Scheme 2



Scheme 3

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† Electronic supplementary information (ESI) available: typical procedures, NMR-data, and X-ray data. See http://www.rsc.org/suppdata/cc/b2/b207620a/

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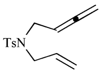
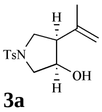
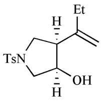
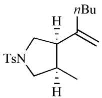
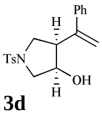
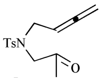
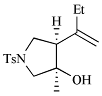
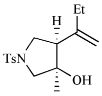
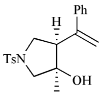
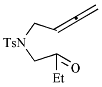
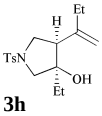
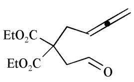
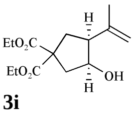
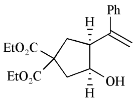
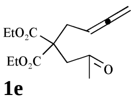
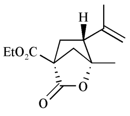
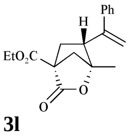
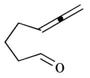
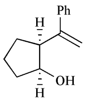
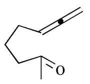
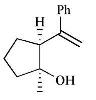
Table 1 *cis*-Stereoselective nickel-catalyzed alkylative cyclization of allenyl-aldehydes and -ketones with organozincs

Entry	Substrate	Reagent	Time	Product	Isolated yield (%)
1	 **1a**	Me_2Zb **2a**	10 min	 **3a**	77
2	**1a**	Et_2Zn **2b**	10 min	 **3b**	90
3	**1a**	*n*BuLi/$ZnCl_2$ **2c**	1 h	 **3c**	61
4	**1a**	PhLi/$ZnCl_2$ **2d**	30 min	 **3d**	83
5	 **1b**	**2a**	30 min	 **3e**	58
6	**1b**	**2b**	10 min	 **3f**	66
7	**1b**	**2d**	10 min	 **3g**	60
8	 **1c**	**2b**	2 h	 **3h**	83
9	 **1d**	**2a**	30 min	 **3i**	72
10	**1d**	**2d**	2 h	 **3j**	60
11	 **1e**	**2a**	30 min	 **3k**	77
12	**1e**	**2a**	3 h	 **3l**	67
13	 **1f**	**2d**	30 min	 **3m**	73
14	 **1g**	**2d**	1 h	 **3n**	75

In summary, a new procedure has been developed to promote efficient, $Ni(COD)_2$-catalyzed, alkylative and arylative cyclization of allenyl-aldehydes and allenyl-ketones with organozinc reagents to form *cis*-fused homoallylic cyclopentanols.

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Notes and references

1 For reviews see: (*a*) I. Ojima, M. Tzamarioudaki, Z. Li and R. J. Dobovan, *Chem. Rev.*, 1996, **96**, 635–662; (*b*) M. Lautens, W. Klute and W. Tam, *Chem. Rev.*, 1996, **96**, 49–92.

2 For recent studies of late transition metal-catalyzed cyclization of dienes: (*a*) Y. Yamamoto, N. Ohkoshi, M. Kameda and K. Itoh, *J. Org. Chem.*, 1996, **64**, 2178–2179; (*b*) N. S. Perch and R. A. Widenhoefer, *J. Am. Chem. Soc.*, 1999, **121**, 6960–6961; (*c*) R. A. Widenhoefer and M. A. Decal, *J. Am. Chem. Soc.*, 1998, **120**, 6960–6961; (*d*) B. Radetich and T. V. RajanBabu, *J. Am. Chem. Soc.*, 1998, **120**, 8007–8008.

3 For recent studies of late transition metal-catalyzed cyclization of enynes: (*a*) I. Ojima, J. Zhu, E. S. Vidal and D. F. Kass, *J. Am. Chem. Soc.*, 1998, **120**, 6690–6697; (*b*) B. M. Trost, C. D. Haffner, D. J. Jebaratnam and F. Rise, *J. Am. Chem. Soc.*, 1999, **121**, 4268–4278; (*c*) B. M. Trost and F. D. Toste, *J. Am. Chem. Soc.*, 2000, **122**, 714–715; (*d*) J. LePaih, D. C. Rodrigues, S. Derien and P. H. Dixneuf, *Synlett*, 2000, 95–97; (*e*) M. Mori, Y. Kozawa, M. Nishida, M. Kanamaru, K. Onozuka and M. Takimoto, *Org. Lett.*, 2000, **2**, 3245–3247; (*f*) S. Shin and T. V. RajanBabu, *J. Am. Chem. Soc.*, 2001, **123**, 8416–8417.

4 For recent studies of late transition metal-catalyzed cyclization of diynes: (*a*) T. Muraoka, I. Matsuda and K. Itoh, *Tetrahedron Lett.*, 1998, **39**, 7325–7328; (*b*) I. Ojima and S.-Y. Lee, *J. Am. Chem. Soc*, 2000, **122**, 2385; (*c*) M. Lautens, N. D. Smith and D. Ostrovsky, *J. Org. Chem.*, 1997, **62**, 8970–8971; (*d*) S. Onozawa, Y. Hatanaka and M. Tanaka, *Chem. Commun.*, 1997, 1229–1230; (*e*) S. Greau, B. Radetich and T. V. RajanBabu, *J. Am. Chem. Soc.*, 2000, **122**, 8579–8580.

5 N. M. Kablaoui and S. L. Buchwald, *J. Am. Chem. Soc.*, 1995, **117**, 6785–6786.

6 W. E. Crowe and M. J. Rachita, *J. Am. Chem. Soc.*, 1995, **117**, 6787–6788.

7 (*a*) E. Oblinger and J. Montgomery, *J. Am. Chem. Soc.*, 1997, **119**, 9065–9066; (*b*) J. Montgomery, *Acc. Chem. Res.*, 2000, **33**, 467–473.

8 S.-K. Kang, Y.-H. Ha, B.-S. Ko, Y. Lim and J. Jung, *Angew. Chem., Int. Ed.*, 2002, **41**, 343–345.

9 The nickel-catalyzed intramolecular reductive cyclization of 1,3-dienes and carbonyls has been reported by Mori *et al.* See: (*a*) Y. Sato, M. Takimoto, K. Hayashi, T. Katsuhara, K. Takagi and M. Mori, *J. Am. Chem. Soc.*, 1994, **116**, 9771–9772; (*b*) Y. Sato, M. Takimoto and M. Mori, *Tetrahedron Lett.*, 1996, **37**, 887–890.

10 The nickel-catalyzed intramolecular reductive homoallylic cyclization of ω-dienyl aldehydes in the presence of Et_3B or Et_2Zn was developed by Tamaru *et al.* See: (*a*) K. Shibata, M. Kimura, M. Shimizu and Y. Tamaru, *Org. Lett.*, 2001, **3**, 2181–2183and reference therein (*b*) A. Ezoe, M. Kimura, T. Inoue, M. Mori and Y. Tamaru, *Angew. Chem., Int. Ed.*, 2002, **41**, 2784–2786; (*c*) Recent Ni-catalyzed homoallylation: T.-P. Loh, H.-Y. Song and Y. Zhou, *Org. Lett.*, 2002, 2715–2717.

11 M. Scholl, S. Ding, C. W. Lee and R. H. Grubbs, *Org. Lett.*, 1999, 953–956.

12 The yield based on the recovered starting material (80% conversion).