

View Article Online View Journal

ChemComm

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: Y. Hayashi, Y. Hoshimoto, R. Kumar, M. Ohashi and S. Ogoshi, *Chem. Commun.*, 2016, DOI: 10.1039/C6CC01915C.



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about *Accepted Manuscripts* in the **Information for Authors**.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard <u>Terms & Conditions</u> and the <u>Ethical guidelines</u> still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.



www.rsc.org/chemcomm

Journal Name



Manuscrip

mm AC

Nickel(0)-Catalyzed Intramolecular Reductive Coupling of Alkenes and Aldehydes or Ketones with Hydrosilanes

Received 00th January 20xx, Accepted 00th January 20xx

Yukari Hayashi,^a Yoichi Hoshimoto,^{ab} Ravindra Kumar,^a Masato Ohashi^a and Sensuke Ogoshi^{*a}

DOI: 10.1039/x0xx00000x

www.rsc.org/

A nickel(0)-catalyzed reductive coupling of aldehydes and simple alkenes with hydrosilanes has been developed. A variety of silyl-protected 1-indanol derivatives were prepared in a highly diastereoselective manner (up to >99:1 dr) by employing a combination of nickel(0)/*N*-heterocyclic carbene and triethylsilane. The present system was also applied to a reductive coupling with ketones. Preliminary results of a nickel(0)-catalyzed asymmetric three-component coupling reaction of an aldehyde, an alkene, and triethylsilane are also shown.

A high level of efficiency and wide applicability would make the oxidative cyclization of two π components with nickel(0) a key process in a variety of catalytic molecular transformations proceeding through carbon-carbon bond formations. Indeed, much progress has been realized in nickel(0)-catalyzed molecular transformations, which were proposed to take place through hetero-nickelacycle intermediates generated by oxidative cyclization.^{1,2} We have also contributed to these developments^{1a,b} by the direct observation of the formation of oxanickelacycles from $(\eta^2$ -aldehyde: η^2 -alkene)nickel complexes through oxidative cyclization,^{3a} and by the expansion of this stoichiometric process to a catalytic hydroacylation yielding five- and six-membered benzocyclic ketones (Scheme 1a).^{3b} This hydroacylation was proposed to proceed through β hydride elimination from the oxanickelacycle intermediate, which was supported by the results of stoichiometric experiments. Oxanickelacycles could efficiently react with a reductant such as silanes, organoboranes, and organozincs, and these have been the key process for many nickel(0)-

catalyzed reductive coupling reactions.² Among them, the



reactions of alkynes and aldehydes have been welldeveloped.^{4,5} The use of 1,3-dienes⁶ or allenes⁷ instead of alkynes was also reported. Nevertheless, the use of alkenes has been rare, which probably is due to the difficulty of both the simultaneous coordination of these two components to nickel(0) and the following oxidative cyclization.^{2e} Thus far, the use of alkenes has been limited to the highly reactive ones methylenecyclopropane,⁸ norbornene⁹ as and such tetrafluoroethylene.¹⁰ Herein, we report an intramolecular reductive coupling reaction of simple alkenes and aldehydes with hydrosilanes catalyzed by nickel(0)/N-heterocyclic carbene (NHC), yielding a variety of silyl-protected 1-indanol derivatives in a diastereoselective manner (Scheme 1b). We also demonstrate a corresponding reductive coupling reaction with ketones instead of aldehydes.¹¹

Published on 04 April 2016. Downloaded by George Washington University on 04/04/2016 15:58:32.

^a Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan.

E-mail: ogoshi@chem.eng.osaka-u.ac.jp

^{b.} Frontier Research Base for Global Young Researchers, Graduate School of Engineering, Osaka University, Suita, Osaka 565-0871, Japan.

[†] Electronic Supplementary Information (ESI) available: Experimental procedures and characterization data. See DOI: 10.1039/x0xx00000x

Table 1 Optimization of reaction conditions										
	+ H 1a +	catalys Et ₃ SiH	t (5 mol ^e	%)	OSiEt ₃					
			P	F						
entry	catalyst	solvent	temp. (°C)	time (h)	yield ^b (%)	dr ^b				
1 ^a	Ni(cod) ₂ /PCy ₃	toluene	rt	24	<1	-				
2 ^a	Ni(cod) ₂ /PPh ₃	toluene	rt	24	<1	-				
3	Ni(cod) ₂ /IPr	toluene	rt	24	14	86:14				
4	Ni(cod) ₂ /IMes	toluene	rt	24	5	70:30				
5	Ni(cod) ₂ /SIPr	toluene	rt	24	69	94:6				
6	Ni(cod) ₂ /SIMes	toluene	rt	24	20	69:31				
7	TNSI	toluene	rt	24	69	93:7				
8	TNSI	toluene	40	12	94 (99) ^c	>99:1				
9	TNSI	THF	40	12	83	>99:1				
10	TNSI	1,4-dioxane	40	12	92	>99:1				
11	TNSI	cyclohexane	40	12	80	92:8				

^a Employment of 5 mol% of Ni(cod)₂ and 10 mol% of phosphine ligands. ^b Determined by GC using *n*-pentadecane as an internal standard.

Published on 04 April 2016. Downloaded by George Washington University on 04/04/2016 15:58:32.

The reaction conditions were optimized through the use of o-allylbenzaldehyde (1a) and triethylsilane (Table 1). The 1-triethylsiloxy-2-methylindan (2a) formation of was confirmed when NHC ligands were employed, whereas PPh₃ and PCy₃ were not effective (entries 1–6). Among the NHCs we examined, SIPr gave 2a in a better yield at room temperature (69%, entry 5). In this reaction system, (η^6 -toluene)Ni(SIPr) (TNSI) was generated as a precursor for an active nickel(0)/SIPr catalyst.¹² Indeed, the reaction conducted with TNSI provided 2a without a loss of the yield compared with the system

Table 2 Scope of hydrosilanes									
5	H 1a	+ R ₃ SiH	TNSI (5 mol%) toluene, 40 °C, 12 h	rac-2a					
	entry	R₃SiH	yield ^a (%)	dr ^a					
	1	Et ₃ SiH	94 (99) ^b	>99:1					
	2	([/] Pr)₃SiH	98	96:4					
	3	^t BuMe ₂ S	iH 86	>99:1					
	4	PhMe ₂ S	iH 90	96:4					
	5	Ph ₂ MeS	iH 86	>99:1					
	6	Ph ₃ SiH	98	>99:1					
	7	(EtO) ₃ Si	H 49	96:4					
" Determined by GC using <i>n</i> -pentadecane as an internal standard.									

^b Isolated yield.



comprising Ni(cod)₂ and SIPr (entry 7 vs. 5). We thus used TNSI for a further optimization since TNSI can be prepared through a single-step, one-pot, and gram-scale method,¹² and it readily dissolves in a variety of solvents including alkane mediums, unlike Ni(cod)₂. In addition, the experimental manipulations were simplified and made more accurate by using the prepared nickel(0) complex. The reaction at 40 °C resulted in improvements in both yield and diastereoselectivity giving 2a in 99% isolated yield (entry 8). Among the various solvents we examined, toluene gave the highest vield and diastereoselectivity (entries 8-11). The syn-conformation between the silvl ether and the methyl groups in 2a was confirmed by comparison with reports in the literature after desilylation with TBAF (94% isolated yield).^{13,14}

The impact of the steric and electronic nature of silanes on both the yield and diastereoselectivity was not significant (Table 2). Good to excellent yields and diastereoselectivities were obtained across a broad range of silanes, with the exception of (EtO)₃SiH (entry 7). Other reducing reagents such as diethylzinc or triethylborane were less effective in this reaction.14

^c Isolated yield.

Published on 04 April 2016. Downloaded by George Washington University on 04/04/2016 15:58:32.

Journal Name

The scope of the reaction was investigated with respect to o-allylbenzaldehyde derivatives (1a-j) (Table 3). When electron-donating groups were bonded to the benzene ring (1b-c), the reaction proceeded well to give the corresponding silyl-protected 1-indanol derivatives in >97% isolated yields. The fluorine substituted products (2d-f) were obtained in >89% isolated yields; however, a trace amount of chlorinesubstituted product 2g was obtained. Both products with the o-benzyl group (2h) and the naphthyl structure (2i) were obtained in >99% isolated yields. In all of these reactions, the syn-isomer was obtained with >99:1 dr. The substituted allyl group was also employed to afford **2j** in >99% isolated yield.

The results of a reductive coupling of alkenes and ketones with triethylsilane are shown in Scheme 2. The reaction of oallylacetophenone (1k) took place efficiently to afford the corresponding silyl-protected 1-methyl-1-indanol (2k) in 98% isolated yield and >99:1 dr. The syn-conformation between the silyl ether and the methyl groups in 2k was confirmed by comparison with reports in the literature after desilylation with TBAF.^{14,15} The substituted allyl group was also employed at 60 °C, giving 2I in >99% isolated yield.

Preliminary results of the expansion of the presented reaction to an enantioselective version are given in Scheme 3.¹⁴ Chiral NHC ligands generated in situ by treating the imidazolinium salts (Ln•HBF₄) with t-BuOK were applied in this reaction. The reductive coupling of **1a** and triethylsilane was catalyzed by 5 mol% of Ni(cod)₂ and L1 at room temperature for 24 h in 1,4-dioxane and provided 2a in 92% isolated yield, >99:1 dr, and 15% ee. The enantiomeric excess of 2a was determined using supercritical fluid chromatography (SFC) after converting it into 2-methyl-1-indanol (3a) through desilylation using TBAF.¹⁴ A novel ligand L2 was prepared according to the procedures of L1 reported by Montgomery et al.,¹⁶ and the system utilizing **L2** afforded further improved results (98% isolated yield, >99:1 dr, and 38% ee). The absolute configuration of (15,25)-2a was confirmed by comparing the specific rotation of corresponding desilylation product (15,25)-**3a** with data found in the literature.^{13b}

This intramolecular reductive coupling might proceed through oxidative cyclization of an aldehyde and an alkene affording an oxanickelacycle intermediate as shown in Scheme 1.¹⁷ The oxidative cyclization process would be promoted by a Lewis acidic silane reagent.^{2e,3a} The following σ -bond



Scheme 2 Reductive coupling of ketones and alkenes with triethylsilane

metathesis and reductive elimination might give the product. Analogous mechanisms proceeding through by a hickel a state intermediates were proposed in the reductive coupling reaction of aldehydes and alkynes.¹⁸

In conclusion, the nickel(0)/NHC-catalyzed diastereoselective intramolecular reductive coupling of alkenes and aldehydes with hydrosilanes was demonstrated. A variety of silyl-protected 1-indanol derivatives were prepared in excellent yields with perfect diastereoselectivities. A corresponding reductive coupling with ketones was also achieved. The preliminary results on the enantioselective reductive coupling were shown, in which the target indanol was obtained with a perfect diastereoselectivity and a promising enantioselectivity. Further development of this enantioselective process is ongoing in our group.

This work was supported by Grants-in-Aid for Young Scientists (A) (25708018) and Grants-in-Aid for Scientific Research on Innovative Area "Precise Formation of a Catalyst Having a Specified Field for Use in Extremely Difficult Substrate Conversion Reactions" (15H05803) and "Stimuli-responsive Chemical Species" (15H00943) from MEXT and by ACT-C from JST. Y.H. acknowledges support from the Frontier Research Base for Global Young Researchers, Osaka University, on the Program of MEXT. Y.H. expresses her special thanks for the Research Fellowship for Young Scientists from JSPS.

Notes and references

- 1 For selected recent reviews and books on the nickel(0)catalyzed reactions via nickelacycle intermediates, see: (a) M. Ohashi, Y. Hoshimoto and S. Ogoshi, Dalton Trans., 2015, 44, 12060; (b) Y. Hoshimoto, M. Ohashi and S. Ogoshi, Acc. Chem. Res., 2015, 48, 1746; (c) S. Z. Tasker, E. A. Standley and T. F. Jamison, Nature, 2014, 509, 299; (d) J. Montgomery, Organonickel Chemistry, in Organometallics in Synthesis: Fourth Manual, ed. B. H. Lipshutz, Wiley, Hoboken, N.J., 2013, pp. 319-428; (e) J. C. Leung and M. J. Krische, Chem. Sci., 2012, 3, 2202; (f) Modern Organonickel Chemistry; ed. Y. Tamaru, Wiely-VCH, Weinheim, 2005.
- 2 For selected recent reviews on nickel(0)-catalyzed reductive coupling reactions, see: (a) E. A. Standley, S. Z. Tasker, K. L. Jensen and T. F. Jamison, Acc. Chem. Res., 2015, 48, 1503; (b) E. P. Jackson, H. A. Malik, G. J. Sormunen, R. D. Baxter, P. Liu, H. Wang, A.-R. Shareef and J. Montgomery, Acc. Chem.



Scheme 3 Enantioselective reductive coupling of 1a with triethylsilane



COMMUNICATION

Published on 04 April 2016. Downloaded by George Washington University on 04/04/2016 15:58:32.

Res., 2015, **48**, 1736; (c) K. Tanaka and Y. Tajima, *Eur. J. Org. Chem.*, 2012, **20**, 3715; (d) M. Jeganmohan and C.-H. Cheng, *Chem. – Eur. J.*, 2008, **14**, 10876; (e) S.-S. Ng, C.-Y. Ho, K. D. Schleicher and T. F. Jamison, *Pure Appl. Chem.*, 2008, **80**, 929; (f) R. M. Moslin, K. Miller-Moslin and T. F. Jamison, *Chem. Commun.*, 2007, 4441; (g) J. Montgomery, *Angew. Chem.*, *Int. Ed.*, 2004, **43**, 3890; (h) S.-i. Ikeda, *Angew. Chem.*, *Int. Ed.*, 2003, **42**, 5120; (i) J. Montgomery, *Acc. Chem. Res.*, 2000, **33**, 467.

- 3 (a) S. Ogoshi, M.-a. Oka and H. Kurosawa, J. Am. Chem. Soc., 2004, 126, 11802. (b) Y. Hoshimoto, Y. Hayashi, H. Suzuki, M. Ohashi and S. Ogoshi, Angew. Chem., Int. Ed., 2012, 51, 10812.
- 4 (a) C.-Y. Zhou, S.-F. Zhu, L.-X. Wang and Q.-L. Zhou, *J. Am. Chem. Soc.*, 2010, **132**, 10955; (b) K. M. Miller, W.-S. Huang and T. F. Jamison, *J. Am. Chem. Soc.*, 2003, **125**, 3442; (c) W.-S. Huang, J. Chan, T. F. Jamison, *Org. Lett.*, 2000, **2**, 4221; (d) X.-Q. Tang and J. Montgomery, *J. Am. Chem. Soc.*, 2000, **122**, 6950; (e) X.-Q. Tang and J. Montgomery, *J. Am. Chem. Soc.*, 1999, **121**, 6098; (f) E. Oblinger and J. Montgomery, *J. Am. Chem. Soc.*, 1997, **119**, 9065.
- 5 Nickel(0)-catalyzed reductive coupling of 1,6-enynes and aldehydes, see: R. M. Moslin, K. M. Miller and T. F. Jamison, *Tetrahedron*, 2006, **62**, 7598 and references therein.
- 6 N. Saito, Y. Sugimura and Y. Sato, *Org. Lett.*, 2010, **12**, 3494 and references therein.
- 7 (a) S.-S. Ng and T. F. Jamison, J. Am. Chem. Soc., 2005, 127, 7320; (b) S.-K. Kang and S.-K. Yoon, Chem. Commun., 2002, 2634; (c) J. Montgomery and M. Song, Org. Lett., 2002, 4, 4009.
- 8 K. Ogata, Y. Atsuumi and S.-i. Fukuzawa, *Org. Lett.*, 2010, **12**, 4536.
- 9 (a) K. Ogata, A. Toh, D. Shimada and S.-i. Fukuzawa, *Chem. Lett.*, 2012, **41**, 157; (b) K. Ogata, Y. Atsuumi, D. Shimada and S.-i. Fukuzawa, *Angew. Chem.*, *Int. Ed.*, 2011, **50**, 5896.
- (a) M. Ohashi, T. Kawashima, T. Taniguchi, K. Kikushima and S. Ogoshi, *Organometallics*, 2015, **34**, 1604; (b) M. Ohashi, H. Shirataki, K. Kikushima and S. Ogoshi, *J. Am. Chem. Soc.*, 2015, **137**, 6496.
- Nickel(0)-catalyzed reductive coupling with ketones, see ref.
 and: (a) W. Fu, M. Nie, A. Wang, Z. Cao and W. Tang, Angew. Chem., Int. Ed., 2015, 54, 2520; (b) K. M. Miller and T. F. Jamison, Org. Lett., 2005, 7, 3077; (c) J. Chan and T. F. Jamison, J. Am. Chem. Soc., 2004, 126, 10682.
- 12 Y. Hoshimoto, Y. Hayashi, H. Suzuki, M. Ohashi and S. Ogoshi, Organometallics, 2014, **33**, 1276.
- (a) P. A. Marshall and R. H. Prager, *Aust. J. Chem.*, 1979, **32**, 1251; (b) R. Fernández, A. Ros, A. Magriz, H. Dietrich and J. M. Lassaletta, *Tetrahedron*, 2007, **63**, 6755.
- 14 See the Supplementary Information for details.
- 15 N. M. Kablaoui and S. L. Buchwald, J. Am. Chem. Soc., 1996, 118, 3182.
- 16 M. R. Chaulagain, G. J. Sormunen and J. Montgomery, J. Am. Chem. Soc., 2007, 129, 9568.
- 17 A mechanism initiated by oxidative addition of hydrosilane to nickel(0) yielding nickel(II) hydrido silyl complex is unlikely. Stoichiometric treatment of hydrosilane with **TNSI** was examined at room temperature and no observable change was confirmed by NMR spectroscopy.
- 18 (a) E. P. Jackson and J. Montgomery, J. Am. Chem. Soc., 2015, 137, 958; (b) M. T. Haynes II, P. Liu, R. D. Baxter, A. J. Nett, K. N. Houk and J. Montgomery, J. Am. Chem. Soc., 2014, 136, 17495; (c) P. Liu, P. McCarren, P. H.-Y. Cheong, T. F. Jamison and K. N. Houk, J. Am. Chem. Soc., 2010, 132, 2050; (d) N. Saito, T. Katayama and Y. Sato, Org. Lett., 2008, 10, 3829.

Page 4 of 4

View Article Online DOI: 10.1039/C6CC01915C