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Nickel-catalyzed reductive allylation of aryl bromides with allylic acetates[†]

Xiaozhan Cui,‡^a Shulin Wang,‡^a Yuwei Zhang,‡^b Wei Deng,^a Qun Qian*^a and Hegui Gong*^a

This paper highlights Ni-catalyzed allylation of electron-rich aryl bromides with a variety of substituted allylic carbonates using zinc as the terminal reductant, affording *E*-alkenes regioselectively in good to excellent yields by the addition of aryl to the less hindered allylic carbon. The electron-deficient aryl bromides and chlorides are also highly efficient coupling partners.

Introduction

Allylic arylation is generally achieved *via* transition-metal-catalyzed coupling of aryl-metallic reagents with allylic electrophiles and allyl-metallic reagents with aryl electrophiles;¹⁻⁴ numerous well-established synthetic methods, in particular asymmetric versions, have been developed.³ On the other hand, reductive coupling of two electrophiles⁵⁻⁷ including allylation of aryl halides with allylic electrophiles affords an alternative choice by its facile carbon–carbon bond formation without pre-preparation of organometallic nucleophiles.⁸⁻¹⁰ Although recent years have seen significant progress in advancing the nickel and cobalt-catalyzed reductive allylic arylation,^{8,9} the present methods still suffer from limited substrate scope and a lack of enantioselective studies on the 1,3-disubstituted allylic electrophiles.

For instance, our previous studies have disclosed an efficient method for the coupling of electron-rich and electron-deficient aryl bromides with unsubstituted allylic acetate (Scheme 1, method A).^{9a} The Ni-catalyzed conditions seem to be more effective than the analogous Co-catalyzed reductive and Fe-catalyzed domino Kumada methods.^{8,9} However, low or

^aDepartment of Chemistry, Shanghai University, 99 Shang-Da Road, Shanghai 200444, China. E-mail: Hegui_gong@shu.edu.cn; Tel: +86 21 6613 2410

200444, China. E-mail: Hegui_gong@snu.euu.ch, 1et. +80.210015.2410

trace amounts of yields result when this method is applied to substituted allylic acetates.

Recently, Weix and co-workers reported a similar Ni-catalyzed protocol in which a variety of substituted allylic acetates undergo highly efficient coupling with mainly aryl iodides (Scheme 1, method B).^{9b} Allylation of aryl bromides, however, appears to be limited to those bearing electron-withdrawing groups with a much reduced coupling efficiency. In addition, no examples of the corresponding coupling of aryl chlorides have been reported. Therefore, systematic studies of the coupling of substituted allylic acetates with aryl halides, particularly less reactive aryl bromides and chlorides with varying electronic properties, are still in need.

In this paper, we present our continuing efforts toward efficient Ni-catalyzed reductive allylation of aryl halides with emphasis on the coupling of electron-deficient and electronrich aryl bromides and activated aryl chlorides with various substituted allylic acetates (Scheme 1, method C). The use of pyridinylimidazole ligand **3a** (Fig. 1) and additives is critical in the present study. In addition, we disclose the first asymmetric version of the allylic arylation through the coupling of two electrophiles, although the coupling efficiency and enantio-selectivity are still low.



Scheme 1 Ni-catalyzed coupling of allylic acetates with aryl halides.^{8,9}

^bCollege of Chemistry and Molecular Engineering, Zhengzhou University, 100 Science Road, Zhengzhou 450001, China

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[‡]These authors contributed equally.



Results and discussion

Our initial allylation of aryl bromides with unsubstituted allyl acetate suggests that 4,4'-di-*t*BuBipy **1a** was optimal (Scheme 1). However, when the same reaction conditions were used for the reaction of **8** with 2 equiv. of 1-ethyl allylic acetate, only 20% of the allylated arene **9** was isolated. The coupling with methyl 4-bromobenzoate only produced trace amounts of the desired product. To improve the coupling efficiency, we screened a variety of ligands for the coupling of electron-rich arylbromide **8** with 1.5 equiv. of allylic acetate (Table 1), and eventually determined that ligand **3a** was able to generate the coupling product **9** in 76% yield at 60 °C (Table 1, entry 2). By the use of 2 equiv. of allylic acetate, the allylated aryl product was obtained in 87% yield (entry 1). Other nickel

Table 1 Optimization for the coupling of 1	
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MeO MeO MeO 8 (0.15	Br + OAc (0.3 mmol) Br + OAc (0.3 mmol) 0	OMe 9
Entry ^a	Variation from the "standard" conditions	Yield ^b (%)
1	None	87
2	1.5 equiv. of allylic acetate	76
3	1.5 equiv. of allylic acetate; 3b instead of 3a	74
4	1.5 equiv. of allylic acetate; 3c instead of 3a	73
5	1.5 equiv. of allylic acetate; 3b instead of 3a	66
6	1.5 equiv. of allylic acetate; 5a instead of 3a	76
7	1.5 equiv. of allylic acetate; 5b instead of 3a	60
8	1.5 equiv. of allylic acetate; 5c instead of 3a	73
9	1.5 equiv. of allylic acetate; 1a instead of 3a	67
10	1.5 equiv. of allylic acetate; 1b instead of 3a	Trace
11	1.5 equiv. of allylic acetate; 1c instead of 3a	50
12	1.5 equiv. of allylic acetate; 4a instead of 3a	63
13	1.5 equiv. of allylic acetate; 4b instead of 3a	Trace
14	1.5 equiv. of allylic acetate; 4c instead of 3a	10
15	1.5 equiv. of allylic acetate; 6 instead of 3a	45
16	80 °C, instead of 60 °C	72
17	$Ni(acac)_2$, instead of NiI_2	63
18	No Bu_4NBr	63

^{*a*} Reaction conditions: **8** (100 mol%, 0.15 M in DMA, allyl acetate (200 mol%), NiI₂ (10 mol%), Zn (200 mol%), ligand (10 mol%), MgCl₂ (0.15 mmol)-pyridine-Bu₄NBr (1:1:1), DMA (1 mL). ^{*b*} Isolated yields.

 Table 2
 Scope of the allylic acetates

R	Br + allylic acetate (2 equiv) BRB(100%), Zn (200%) DMA, 60 °C				
			Yield ^{b} for R =		
Entry ^a	Allylic acetate	Product	MeO	MeOOC	
1	Ph OAc	Ar Ph	10 (86%)	18 (87%)	
2	OAc	Ar	11 (81%)	19 (75%)	
3	OAc	Ar	12 (83%)	20 (91%)	
4	nPr OAc	<i>n</i> Pr Ar	13 (83%)	21 (85%)	
5	Ph OAc	Ph	14 (87%)	22 (90%)	
6	OAc	Ar	15 (94%)	23 (86%)	
7	PhOAc	Ph	16 (80%)	24 (94%)	
8	Ph OAc	Ph	17 (40%)	25 (45%)	

^{*a*} Reaction conditions: as in Table 1, entry 1. ^{*b*} Isolated yields.

sources (e.g., Ni(acac)₂, entry 17) were not satisfactory. It was interesting that without Bu_4NBr , a significant decrease of the yield was observed (entry 18). We speculated that the role of MgCl₂ and Bu_4NBr is possibly to activate zinc powder by removal salts on its surface.^{9a}

With the optimized conditions in hand, coupling of 4-methoxy-1-bromobenzene with a variety of substituted allylic acetates gave allylated products **10–16** in fairly good yields (Table 2). The electron-deficient methyl 4-bromobenzoate also demonstrated high reactivity with the substituted allylic acetates, giving products **18–24** in excellent yields (Table 2). The addition of aryl groups to the less substituted carbon terminus of the allylic acetates accounted for the regioselectivity of the coupling process. However, coupling of the sterically more hindered 1-methyl-3-phenyl-allylic acetate with both 4-methoxy-1bromobenzene and methyl 4-bromobenzoate generated products **17** and **25** in moderate yields (entry 8).

Extension of the allylation approach to other aryl halides was also pursued *via* coupling with various substituted allylic acetates, generating products **26–35** (Table 3). The reaction tolerated a wide array of functional groups, including amide, aryl chloride, aldehyde, ether, ester, and even arenol. In general, high coupling yields were observed regardless of the electronic properties of the aryl halides and the substitution patterns of the allylic acetates (entries 1–10). Whereas the coupling of electron-deficient **1**-(4-bromophenyl)ethanone with 2 equiv. of allylic acetate delivered the product **33** in 89% yield, the use of 1.5 equiv. of allylic acetate only resulted in 52% yield (entry 8). Aryl chlorides bearing electron-withdrawing groups were also effective. The coupling of methyl 4-chlorobenzoate with 3-phenyl allylic acetate delivered the product **22** in 82% yield

Table 3 Scope of the aryl halides



 a Reaction conditions: as in Table 1, entry 1. b Isolated yields. c 1.5 equiv. of allylic acetate was used. d Aryl chloride was used.

(entry 11). It was interesting to note that the coupling of methyl 4-chlorobenzoate with 1,3-disubstituted allylic acetates, *e.g.*, 1-methyl-3-phenyl allyl acetate, generated the desired product **25** in 61% yield (entry 12).

Finally, we investigated whether it was possible to achieve enantioselectivity for the coupling of methyl 4-bromobenzoate and (E)-4-phenylbut-3-en-2-yl acetate using a chiral tridentate pybox ligand 7. Although a moderate yield was obtained, 10% of enantiomeric excess was observed. To the best of our knowledge, this is the first time that enantioselectivity was observed from direct reductive coupling of aryl halides with allylic electrophiles (Scheme 2).



Scheme 2 Asymmetric coupling of 1,3-disubstituted allyl acetate





To understand the details of the reaction, we first examined whether an *in situ* Negishi process is possible. Coupling of an organozinc reagent prepared from dimethyl 4-bromophthalate with cinnamyl acetate in the absence of zinc powder did not give an allylation product.¹¹ In addition, coupling of methyl 4-bromobenzoate and cinnamyl acetate as in Table 2, entry 5, but in the absence of ligand mainly gave recovered starting materials. These results suggest that *in situ* formation of organozinc/Negishi process is not likely to occur.

According to the stoichiometric studies of allylic-Ni(I) with aryl halides reported by Corey and Heghdus, a Ni(I) to Ni(III) process may account for the catalytic pathways in the present study.^{12,13} Similar to the Ni-catalyzed reductive allylic alkylation in our previous studies,^{7b} we propose the following catalytic pathways. One electron reduction of the π -allyl-Ni(II) formed from oxidative addition of allyl acetate to Ni(0) generates allyl-Ni(I) intermediate.¹⁴ Oxidative addition of aryl bromide to allyl-Ni(I) species results in allyl-Ni(III)-Ar. Subsequent reductive elimination gives the product and generates a Ni(I) intermediate which can be reduced to Ni(0) by Zn (Scheme 3).

Conclusions

In conclusion, an efficient Ni-catalyzed method for the allylation of aryl halides has been developed using the unprecedented **3a** as a ligand. The reaction demonstrates excellent functional group tolerance and broad substrate scope for a variety of substituted allylic acetates and aryl halides including electron-rich aryl bromides and electron-deficient aryl bromides and chlorides. The allylation method displays excellent regioselectivities by the addition of aryl groups to the less hindered allylic carbon. In addition, although low ee was observed for the **1**,3-disubstituted allylic acetate, it represents the first asymmetric version of direct reductive coupling of two electrophiles wherein *in situ* organometallic reagents may not be involved.

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Notes and references

- For selected reviews on allylic substitutions, see: (a) Z. Lu and S. Ma, Angew. Chem., Int. Ed., 2008, 47, 258–297;
 (b) K. Geurts, S. P. Fletcher, A. W. van Zijl, A. J. Minnaard and B. L. Feringa, Pure Appl. Chem., 2008, 80, 1025–1037;
 (c) C. A. Falciola and A. Alexakis, Eur. J. Org. Chem., 2008, 3765–3780; (d) H. Yorimitsu and K. Oshima, Angew. Chem., Int. Ed., 2005, 44, 4435–4439; (e) B. M. Trost, J. Org. Chem., 2004, 69, 5813–5837.
- 2 For selected examples of aryl-allyl formation from aryl-M, using Pd/Suzuki: (a) C. Li, J. Xing, J. Zhao, P. Huynh, W. Zhang, P. Jiang and Y. J. Zhang, Org. Lett., 2012, 14, 390-393; (b) D. Li, T. Tanaka, H. Ohmiya and M. Sawamura, Org. Lett., 2010, 12, 3344-3347: H. Ohmiya, Y. Makida, D. Li, M. Tanabe and (*c*) M. Sawamura, J. Am. Chem. Soc., 2010, 132, 879-889; Pd/Stille: (d) F. K. Sheffy, J. P. Godschalx and J. K. Stille, J. Am. Chem. Soc., 1984, 106, 4833-4840; (e) A. C. Albéniz, P. Espinet and B. Martín-Ruiz, Chem.-Eur. J., 2001, 7, 2481; Pd/Hiyama: (f) K. H. Shukla and P. DeShong, J. Org. Chem., 2008, 73, 6283-6291; Kumada: (g) H. Yasui, K. Mizutani, H. Yorimitsu and K. Oshima, Tetrahedron, 2006, **62**, 1410-1415; (h) Y. Kiyotsuka, Y. Katayama, H. P. Acharya, T. Hyodo and Y. Kobayashi, J. Org. Chem., 2009, 74, 1939–1951; Ar-In: (i) R. Riveiros, R. Tato, J. P. Sestelo and L. A. Sarandeses, Eur. J. Org. Chem., 2012, 3018-3023; Negishi: (j) A. Krasovskiy, V. Malakhov, A. Gavryushin and P. Knochel, Angew. Chem., Int. Ed., 2006, 45, 6040-6044.
- 3 For the asymmetric and enantiospecific allylation of aryl metals, see: (a) D. Polet, X. Rathgeb, C. A. Falciola, J.-B. Langlois, S. E. Hajjaji and A. Alexakis, Chem.-Eur. J., 2009, 15, 1205-1216; (b) Rh-Negishi: P. A. Evans and D. Uraguchi, J. Am. Chem. Soc., 2003, 125, 7158-7159; (c) K. B. Selim, K.-I. Yamada and K. Tomioka, Chem. Commun., 2008, 5140-5142; (d) A. Alexakis, S. E. Hajjaji, D. Polet and X. Rathgeb, Org. Lett., 2007, 9, 3393; (e) E. Gomez-Bengoa, N. M. Heron, M. T. Didiuk, C. A. Luchaco and A. H. Hoveyda, J. Am. Chem. Soc., 1998, 120, 7649-7650; (f) M. A. Kacprzynski, T. L. May, S. A. Kazane and A. H. Hoveyda, Angew. Chem., Int. Ed., 2007, 46, 4554-4558.
- 4 For selected examples of aryl-allyl formation from allyl-M, see: (a) K. Lee, H. Kim, J. Mo and P. H. Lee, *Chem.-Asian J.*, 2011, 6, 2147–2157; (b) W. Su, S. Urgaonkar and J. G. Verkade, *Org. Lett.*, 2004, 6, 1421–1424; (c) S. Doherty, J. G. Knight, C. H. Smyth, R. W. Harrington and W. Clegg,

Organometallics, 2007, **26**, 6453–6461; (*d*) M. Al-Masum and S. Alam, *Tetrahedron Lett.*, 2009, **50**, 5201.

- 5 For selected examples of C(sp³)-C(sp²) coupling without *in situ* organometallic reagents: (a) F. Wu, W. Lu, Q. Qian, Q. Ren and H. Gong, Org. Lett., 2012, 14, 3044; (b) H. Yin, C. Zhao, H. You, Q. Lin and H. Gong, Chem. Commun., 2012, 48, 7034; (c) D. A. Everson, B. A. Jones and D. J. Weix, J. Am. Chem. Soc., 2012, 134, 6146-6159; (d) C.-S. Yan, Y. Peng, X.-B. Xu and Y.-W. Wang, Chem.-Eur. J., 2012, 18, 6039-6048; (e) M. Durandetti, J.-Y. Nédélec and J. Périchon, J. Org. Chem., 1996, 61, 1748-1755.
- 6 For selected examples of C(sp³)-C(sp²) coupling via in situ organometallic formation: (a) A. Krasovskiy, C. Duplais and B. H. Lipshutz, J. Am. Chem. Soc., 2009, 131, 15592; (b) W. M. Czaplik, M. Mayer and A. J. von Wangelin, Angew. Chem., Int. Ed., 2009, 48, 607; (c) M. Amatore and C. Gosmini, Chem. Commun., 2008, 5019; (d) C. Duplais, A. Krasovskiy, A. Wattenberg and B. H. Lipshutz, Chem. Commun., 2010, 562; (e) W. M. Czaplik, M. Mayer and A. J. von Wangelin, Synlett, 2009, 2931.
- 7 For selected examples of reductive C(sp³)-C(sp³) coupling, see: (a) X. Yu, T. Yang, S. Wang, H. Xu and H. Gong, Org. Lett., 2011, 13, 2138; (b) Y. Dai, F. Wu, Z. Zang, H. You and H. Gong, Chem.-Eur. J., 2012, 16, 808; (c) S. M. Goldup, D. A. Leigh, R. T. McBurney, P. R. McGonigal and A. Plant, Chem. Sci., 2010, 1, 383; (d) X. Qian, A. Auffrant, A. Felouat and C. Gosmini, Angew. Chem., Int. Ed., 2011, 50, 10402.
- 8 (*a*) P. Gomes, C. Gosmini and J. Périchon, *Org. Lett.*, 2003,
 5, 1043–1045; (*b*) M. Mayer, W. M. Czaplik and A. Jacobi von Wangelin, *Adv. Synth. Catal.*, 2010, 352, 2147;
 (*c*) P. H. Lee, D. Seomoon, K. Lee, S. Kim, H. Kim, H. Kim, E. Shim, M. Lee, S. Lee, M. Kim and M. Sridhar, *Adv. Synth. Catal.*, 2004, 346, 1641–1645.
- 9 (a) S. Wang, Q. Qian and H. Gong, Org. Lett., 2012, 14, 3352–3355; (b) L. L. Anka-Lufford, M. R. Prinsell and D. J. Weix, J. Org. Chem., 2012, 77, 9989.
- 10 For selected reviews on Ni-catalyzed cross-coupling of alkyl electrophiles, see: (a) A. Rudolph and M. Lautens, *Angew. Chem., Int. Ed.*, 2009, **48**, 2656–2670; (b) A. C. Frisch and M. Beller, *Angew. Chem., Int. Ed.*, 2005, **44**, 674–688; (c) X. Hu, *Chem. Sci.*, 2011, **2**, 1867–1886.
- 11 See the ESI^+ for details.
- 12 (a) L. S. Hegedus and D. H. P. Thompson, J. Am. Chem. Soc., 1985, 107, 5663–5669; (b) E. J. Corey and M. F. Semmelhack, J. Am. Chem. Soc., 1967, 89, 2755–2757.
- 13 Though not directly relevant, Ar-Ar coupling *via* Ni^I/Ni^{III} is known: (a) T. T. Tsou and J. K. Kochi, *J. Am. Chem. Soc.*, 1979, **101**, 7547–7560; (b) I. Colon and D. R. Kelsey, *J. Org. Chem.*, 1986, **51**, 2627–2637; (c) C. Amatore and A. Jutand, *Organometallics*, 1988, 7, 2203–2214; (d) A. Klein, Y. H. Budnikova and O. G. Sinyashin, *J. Organomet. Chem.*, 2007, **692**, 3156–3166.
- 14 Reduction of π-allyl Nickel(II) to π-allyl Nickel(I) by Zn has been proposed: S. Ikeda, K. Suzuki and K. Odashima, *Chem. Commun.*, 2006, 457–459.