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A Novel Enantioselective (2*Z*)-Alk-2-enylation of Aldehydes via an Allyl-Transfer Reaction from Chiral Allyl Donors Prepared from (+)-Isomenthone

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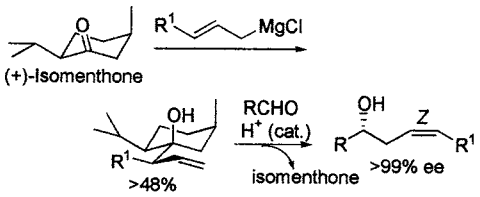
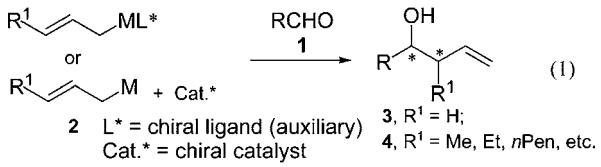
ABSTRACT



A highly enantioselective (2*Z*)-alk-2-enylation of aldehydes was successfully achieved by an allyl-transfer reaction from a chiral allyl donor, which was easily obtained by separation of a diastereomeric mixture of the corresponding homoallylic alcohol γ-adducts derived from (+)-isomenthone with alk-2-enylmagnesium chloride.

Asymmetric allylation of aldehydes (**1**, RCHO) is one of the most useful carbon−carbon bond formation reactions in organic synthesis because of the high and reactive functionality and high stereoselectivity.[1] For example, highly optically active homoallylic alcohols **3** [RC*H(OH)CH_2CH=CH_2] have been prepared by using allylic organometallic reagents **2** (CH_2=$CHCH_2$M; M = metal) with a stoichiometric amount of a chiral auxiliary[2] or a catalytic amount of a chiral promoter.[3] Furthermore, allylation reactions with γ-substituted organometallic reagent **2** (RCH=$CHCH_2$M; R = alkyl), in the presence of a chiral auxiliary or catalyst, afford the γ-adduct **4** diastereo- and enantioselectively.[4] This C−C bond formation reaction is particularly useful for the construction of vicinal stereogenic centers in a flexible hydrocarbon chain [eq 1].



(1)

Recently, we discovered an efficient stereoselective alk-2-enylation reaction of aldehydes to give the α-adduct **5**, in which no allyl(ic) metal nucleophiles are required and a homoallylic alcohol **6** served as an allyl donor in the presence of an acid catalyst. To understand this unusual allylation reaction, we proposed a reaction mechanism via a 2-oxonium [3,3]-sigmatropic rearrangement with a six-membered chair-like transition state (**TS-1**) as shown in Scheme 1, which we termed an "allyl-transfer reaction."[5a]

We succeeded in employing the allyl-transfer reaction to highly enantioselective (*E*)-alk-2-enylation of aldehydes to give optically pure (*E*)-α-adducts of homoallylic alcohols (*E*)-**7** using optically pure menthone as a chiral auxiliary.[5d,f] In this reaction, chiral allyl-donors **8** (γ-adducts of homoallylic alcohols) were prepared by reaction of alk-2-enylme-

(1) For reviews on the reaction using allyl(ic) metals: (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207−2293. (b) Marshall, J. A. In *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed.; Willey-VCH: New York, 2000; Vol. 1. For reviews on asymmetric allylation and related reactions: (c) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Willey-VCH: New York, 2000. (d) Chemler, S. R.; Roush, W. R. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Willey-VCH: New York, 2000.

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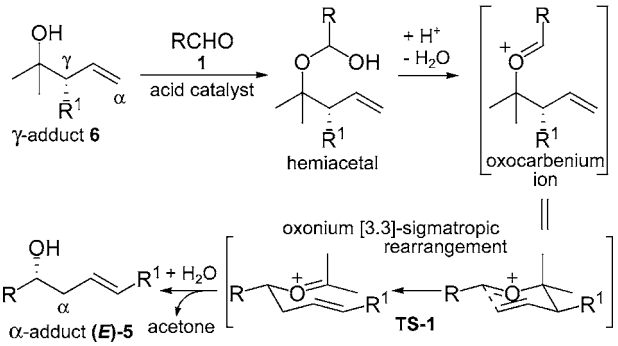
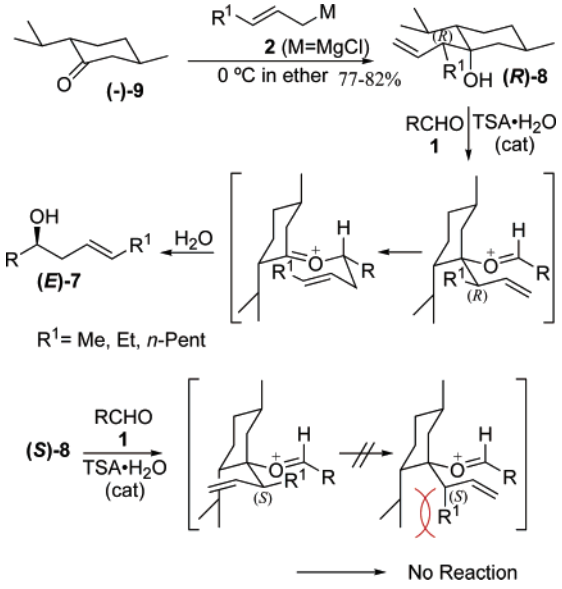
Scheme 1. Stereospecific Allyl-Transfer Reaction from γ-Adduct **6** to Aldehyde **1** to Give α-Adduct (*E*)-**5**



tallic reagents **2** (R ≠ H; M = MgCl, ZnBr, Ti(O*i*Pr)$_3$) with optically pure (−)- or (+)-menthone **9**, in which the desired chiral allyl donors (*R*)-**8** (assignment by analogy) were selectively obtained in 77−82% yield after column chromatography on silica gel. The minor product (*S*)-**8** did not react with aldehyde at all (Scheme 2).

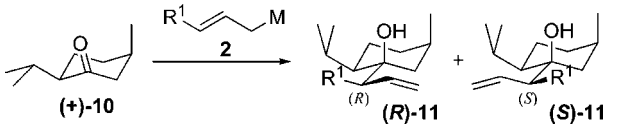
Scheme 2. Allyl-Transfer Reaction from (*R*)-**8** to Give (*E*,*R*)-**7**



In this paper, to extend the applicability of this asymmetric allyl-transfer reaction further, we used (+)-isomenthone **10** derived from inexpensive (+)-(1*S*,2*R*,5*R*)-isomethol (>99% ee) as a chiral auxiliary. Reaction of (+)-isomenthone **10** with alk-2-enylmetallic reagents **2** did not give a γ-adduct selectively, but gave an easily separable diastereomeric mixture of the corresponding γ-adducts **11** in good yield as shown in Table 1.

Surprisingly, we discovered that one of the isolated isomers served as an allyl donor for the (*Z*)-alk-2-enylation to give only the (*Z*)-olefin of the corresponding α-adduct (*Z*)-**5**, and the other isomer gave the corresponding (*E*)-olefin,

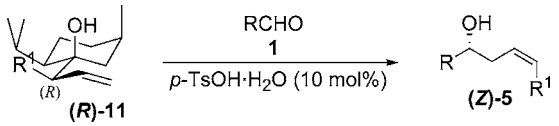
Table 1. Preparation of Allyl Donor **11** from (+)-Isomenthone[a]



			11 yield/%[b] (R_f value)[c]		
entry	R^1		(*R*)-**11**	(*S*)-**11**	*R*/*S*
1	Me	**b**	61 (0.41)	35 (0.51)	64/36
2	Et	**c**	52 (0.49)	40 (0.59)	56/44
3	*n*-Pent	**d**	48 (0.54)	47 (0.63)	51/49

[a] Reactions were performed with (+)-isomenthone (10 mmol) and alk-2-enylmagnesium chloride, derived from magnesium (15 mmol) and 1-chloroalk-2-ene (15 mmol), in THF at 0 °C for 2 h. [b] Isolated yield. [c] R_f value on TLC (Merk silica gel 60 F254, aluminum sheet) using a mixed solvent (hexane/ether = 10/1) as the eluent.

Table 2. Allyl-Transfer Reaction from (*R*)-**11** to Give Homoallylic Alcohol α-Adduct (*Z*)-**5**[a]

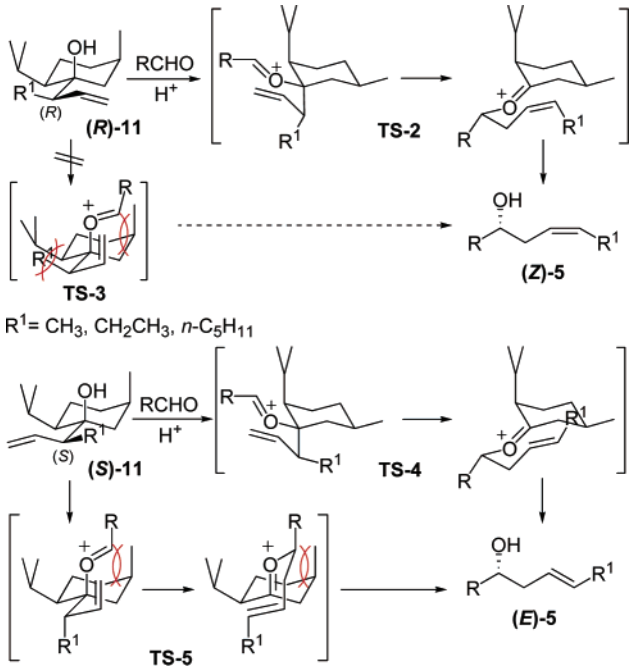


	(*R*)-**11**		RCHO **1**		(*Z*)-**5**		
entry	R^1	mol equiv		R		yield, %[b,c]	
1	**b**	CH_3	1.0	**u**	$PhCH_2CH_2$	**5bu**	69 (>99)
2	**b**	CH_3	2.0	**u**	$PhCH_2CH_2$	**5bu**	88 (>99)
3[d]	**b**	CH_3	2.0	**v**	Ph	**5bv**	68 (>99)
4	**b**	CH_3	2.0	**w**	$BnO(CH_2)_5$	**5bw**	88 (>99)
5	**b**	CH_3	2.0	**x**	$PhSCH_2CH_2$	**5bx**	90 (>99)[e]
6	**c**	C_2H_5	1.0	**u**	$PhCH_2CH_2$	**5cu**	88 (>99)
7	**c**	C_2H_5	2.0	**u**	$PhCH_2CH_2$	**5cu**	92 (>99)
8[d]	**c**	C_2H_5	2.0	**v**	Ph	**5cv**	74 (>99)
9	**c**	C_2H_5	1.0	**w**	$BnO(CH_2)_5$	**5cw**	77 (>99)
10	**c**	C_2H_5	1.5	**w**	$BnO(CH_2)_5$	**5cw**	90 (>99)
11	**c**	C_2H_5	1.0	**x**	$PhSCH_2CH_2$	**5cx**	77 (>99)[e]
12	**c**	C_2H_5	1.5	**x**	$PhSCH_2CH_2$	**5cx**	88 (>99)[e]
13	**d**	n-C_5H_{11}	1.0	**u**	$PhCH_2CH_2$	**5du**	89 (>99)
14[d]	**d**	n-C_5H_{11}	2.0	**v**	Ph	**5dv**	78 (>99)
15	**d**	n-C_5H_{11}	1.0	**w**	$BnO(CH_2)_5$	**5dw**	90 (>99)
16	**d**	n-C_5H_{11}	1.0	**x**	$PhSCH_2CH_2$	**5dx**	93 (>99)[e]

[a] Reactions were performed with allyl donor **11**, 1 mmol (2.0 equiv), 0.75 mmol (1.5 equiv), or 0.5 mmol (1.0 equiv), aldehyde (0.5 mmol), and *p*-TsOH·H_2O (10 mol % to aldehyde) in CH_2Cl_2 (1 mL), at 20 °C for 20 h, unless otherwise noted. [b] Isolated yield. [c] Values in parentheses show % ee of the product, determined by HPLC analysis (CHIRALCEL OD, 5% ^{i}PrOH in hexane as the eluent) unless otherwise noted. >99 means that no signal of the corresponding enantiomer was observed. [d] *p*-TsOH·H_2O (40 mol %) was used. [e] Determined by HPLC analysis (CHIRALCEL OJ, 2% ^{i}PrOH in hexane as the eluent).

(*E*)-**5**. We believe that the former is the first, direct, and enantioselective (*Z*)-alk-2-enylation reaction of an aldehyde to give the corresponding enantiomerically pure (*Z*)-homoallylic alcohol. Here, we predict that (*R*)-**11** serves as the allyl donor, as shown in Scheme 3. The (*E*)-alk-2-enylation is similar to an allyl-transfer reaction derived from (2*R*,5*R*)-

Scheme 3. Configuration of **11** (Assignment by Analogy) which Gives **(*Z*)-5** via Allyl-Transfer Reaction



(+)-menthone having the 5-epi configuration of (2*R*,5*S*)-(+)-isomenthone. From this, it is very reasonable to assume that (*S*)-**11** will give (*E*)-**5**.

Note that if the methyl substituent takes an equatorial configuration in a transition state such as **TS-2**, the isopropyl substituent has to be an axial conformation. In this case, there is a strong steric hindrance preventing the transition state **TS-3**, due to both the methyl and isopropyl substituents on the isomenthane ring. Therefore, the formation of (*Z*)-**5** via transition state **TS-2** is the most reasonable route. The formation of (*E*)-**5** via both transition states **TS-4** and **TS-5** seems to be favorable.

In summary, an asymmetric alk-2-enylation reaction of aldehydes by a *p*-TsOH·H_2O catalyzed allyl-transfer reaction from (+)-isomenthone adducts as chiral allyl-donors gave (*E*)- and (*Z*)-homoallylic alcohol α-adducts, via a six-membered chairlike transition state, in good yield with >99% ee. This is the first example of an asymmetric (*Z*)-alk-2-enylation of aldehydes. The chiral allyl donors were conveniently prepared using an environmentally friendly Grignard reagent with easily available (+)-isomenthone. Therefore, there was no need to prepare an allylmetallic reagent such as allyltin by transmetalation with a Grignard reagent and so on. Finally, it is noteworthy that the conformational analysis of the six-membered chairlike transition state is

(2) Chiral *B*-allylborane: (a) Racherla, U. S.; Brown, H. C. *J. Org. Chem.* **1991**, *56*, 401−404. (b) Williams, D. R.; Clark, M. P.; Emde, U.; Berliner, M. A. *Org. Lett*. **2000**, *2*, 3023−3026. (c) Lachance, H.; Lu, X.; Gravel, M.; Hall, D. G. *J. Am. Chem. Soc*. **2003**, *125*, 10160−10161. Allyltin having chiral ligand: (d) Otera, J.; Yoshinaga, Y.; Yamaji, T.; Yoshioka, T.; Kawasaki, Y. *Organometallics* **1985**, *4*, 1213−1218. Allyltin with a chiral auxiliary: (e) Mukaiyama, T.; Minowa, N.; Oriyama, T.; Narasaka, K. *Chem. Lett*. **1986**, 97−100. (f) Boldrini, G. P.; Lodi, L.; Tagliavini, Tarasco, C.; E.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem*. **1987**, *52*, 5447−5452. (g) Boga, C.; Savoia, D.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Ogranometal. Chem*. **1988**, *353*, 177−183. (h) Kobayashi, S.; Nishio, K. *Tetrahedron Lett*. **1995**, *36*, 6729−6732. (i) Yamada, K.; Tozawa, T.; Nishida, M.; Mukaiyama, T. *Bull. Chem. Soc. Jpn*. **1997**, *70*, 2301−2308. Allyl bromide and metallic indium with a chiral auxiliary: (j) Loh, T.-P.; Zhou, J.-R.; Yin, Z. *Org. Lett*. **1999**, *1*, 1855−1857. (k) Loh, T.-P.; Zhou, J.-R. *Tetrahedron Lett*. **1999**, *40*, 9115−9118. (l) Loh, T.-P.; Zhou, J.-R. *Tetrahedron Lett*. **1999**, *40*, 9333−9336. Allyltitanium complexed with a chiral auxiliary: (m) Bouzbouz, S.; Cossy, J. *Org. Lett*. **2000**, *2*, 501−504. (n) Bouzbouz, S.; Popkin, M. P.; Cossy, J. *Org. Lett*. **2000**, *2*, 3449−3451. (o) Cossy, J.; Willis, C.; Bellosta, V.; Bouzbouz, S. *Synlett* **2000**, 1461−1463. Allylsilane with chiral auxiliary or catalyst: (p) Denmark, S. E.; Coe, D. M.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem*. **1994**, *59*, 6161−6163. (q) Zhang, L. C.; Sakurai, H.; Kira, M. *Chem. Lett*. **1997**, 129−130. (r) Kubota, K.; Leighton, J. L. *Angew. Chem., Int. Ed*. **2003**, *42*, 946−948. (s) Kinnaird, J. W. A.; Ng, P. Y.; Kubota, K.; Wang, X.; Leighton, J. L. *J. Am. Chem. Soc*. **2002**, *124*, 7920−7921. (t) Duthaler, R. O.; Hafner, A. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 43−45.

(3) Allyltributyltin with chiral catalyst: (a) Yanagisawa, A.; Nakashima, H.; Ishiba, A.; Yamamoto, H. *J. Am. Chem. Soc*. **1996**, *118*, 4723−4724. (b) Weigand, S.; Brückner, R. *Chem. Eur. J*. **1996**, *2*, 1077−1084. (c) Cozzi, P. G.; Orioli, P.; Tagliavini, E.; Umani-Ronchi, A. *Tetrahedron Lett*. **1997**, *38*, 145−148. (d) Lipshutz, B. H.; James, B.; Vance, S.; Carrico, I. *Tetrahedron Lett*. **1997**, *38*, 753−756. (e) Yu, C.-M.; Choi, H.-S.; Jung, W.-H.; Kim, H.-J.; Shin, J. *Chem. Commun*. **1997**, 761−762. (f) Motoyama, Y.; Narusawa, H.; Nishiyama, H. *J. Chem. Soc., Chem. Commun*. **1999**, 131−132. (g) Doucet, H.; Santelli, M. *Tetrahedron: Asymmetry* **2000**, *11*, 4163−4169. (h) Loh, T.-P.; Zhou, I.-R. *Tetrahedron Lett*. **2000**, *41*, 5261−5264. (i) Brenna, E.; Scaramelli, L.; Serra, S. *Synlett* **2000**, 357−358. (j) Denmark, S. E.; Wynn, T. *J. Am. Chem. Soc*. **2001**, *123*, 6199−6200. (k) Kurosu, M.; Lorca, M. *Tetrahedron Lett*. **2002**, *43*, 1765−1769. (l) Kii, S.; Maruoka, K. *Tetrahedron Lett*. **2001**, *42*, 1935−1939. (m) Hanawa, H.; Hashimoto, T.; Maruoka, K. *J. Am. Chem. Soc*. **2003**, *125*, 1708−1709. Excess allyltributyltin or tetraallyltin with chiral catalyst (allylation of ketones): (n) Casolari, S.; D'Addario, D.; Tagliavini, E. *Org. Lett*. **1999**, *1*, 1061−1063. (o) Waltz, K. M.; Gavenonis, J.; Walsh, P. J. *Angew. Chem., Int. Ed*. **2002**, *41*, 3697−3699. Allylsilane with chiral catalyst: (p) Gauthier, D. R., Jr.; Carreira, E. M. *Angew. Chem., Int. Ed. Engl*. **1996**, *35*, 2363−2365. (q) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc*. **2000**, *122*, 12021−12022. (r) Yamasaki, S.; Fujii, K.; Wada, R.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc*. **2002**, *124*, 6536−6537. (s) Malkov, A. V.; Orsini, M.; Pernazza, D.; Muir, K. W.; Langer, V.; Meghani, P.; Kocovsky, P. *Org. Lett*. **2002**, *4*, 1047−1049. (t) Malkov, A. V.; Dufková, L.; Farrugia, L.; Kocovsky, P. *Angew. Chem., Int. Ed*. **2003**, *42*, 3674−3677. Allylbromide and metallic Mn with chiral $Cr^{(II)}$[salen]-catalyst: (u) Bandini, M.; Cozzi, P. G.; Melchiorre, P.; Umani-Ronchi, A. *Angew. Chem., Int. Ed*. **1999**, *38*, 3357−3359. (v) Suzuki, T.; Kinoshita, A.; Kawada, H.; Nakada, M. *Synlett* **2003**, 570−572. (w) Inoue, M.; Suzuki, T.; Nakada, M. *J. Am. Chem. Soc*. **2003**, *125*, 1140−1141.

(4) Asymmetric 1-methylallylation and related reactions: By chiral catalyst with tributylcrotyltin: (a) Marshall, J. A.; Tang, Y. *Synlett* **1992**, 653−654. By chiral catalyst with crotylsilane: (b) Furuta, K.; Mouri, M.; Yamamoto, H. *Synlett* **1991**, 561−582. (c) Yanagisawa, A.; Kageyama, H.; Nakatsuka, Y.; Asakawa, K.; Matsumoto, Y.; Yamamoto, H. *Angew. Chem., Int. Ed*. **1999**, *38*, 3701−3703. (d) Aoki, S.; Mikami, K.; Terada, M.; Nakai, T. *Tetrahedron* **1993**, *49*, 1783−1792. (e) Iseki, K.; Mizuno, S.; Kuroki, Y.; Kobayashi, Y. *Tetrahedron Lett*. **1998**, *39*, 2767−2770. (f) Nakajima, M.; Saito, M.; Shiro, M.; Hashimoto, S.-i. *J. Am. Chem. Soc*. **1998**, *120*, 6419−6420. (g) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc*. **2001**, *123*, 9488−9489. By $Cr^{(II)}$[salen]-catalyst with crotyl bromide and metallic Mn: (h) Bandini, M.; Cozzi, P. G.; Umani-Ronchi, A. *Angew. Chem., Int. Ed*. **2000**, *39*, 2327−2330. Noncatalytic reaction by a stoichiometric amount of chiral *B*-crotylborane reagents: (i) Roush, W. R.; Halterman, R. L. *J. Am. Chem. Soc*. **1986**, *108*, 294−296. (j) Roush, W. R.; Ando, K.; Powers, D. B.; Halterman, R. L.; Palkowitz, A. D. *Tetrahedron Lett*. **1988**, *29*, 5579−5582. (k) Garcia, J.; Kim, B. M.; Masamune, S. *J. Org. Chem*. **1987**, *52*, 4831−4832. (l) Brown, H. C.; Jadhav, R. K. *Tetrahedron Lett*. **1984**, *25*, 1215−1218. (m) Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc*. **1986**, *108*, 293−294. (n) Jadhav, P. K.; Bhat, K. S.; Perumal, T.; Brown, H. C. *J. Org. Chem*. **1986**, *51*, 432−439. (o) Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem*. **1989**, *54*, 1570−1576. (p) Ref 2c. By a stoichiometric amount of crotyltitanium complex with a chiral auxiliary: (q) BouzBouz, S.; Cossy, J. *Org. Lett*. **2001**, *3*, 3995−3998.

(5) (a) Nokami, J.; Yoshizane, K.; Matsuura, H.; Sumida, S. *J. Am. Chem. Soc*. **1998**, *120*, 6609−6610. (b) Sumida, S.; Ohga, M.; Mitani, J.; Nokami, J. *J. Am. Chem. Soc*. **2000**, *122*, 1310−1313. (c) Nokami, J.; Anthony, L.; Sumida, S. *Chem. Eur. J*. **2000**, *6*, 2909−2913. (d) Nokami, J.; Ohga, M.; Nakamoto, H.; Matsubara, T.; Hussain, I.; Kataoka, H. *J. Am. Chem. Soc*. **2001**, *123*, 9168−9169. (e) Nokami, J.; Nomiyama, K.; Matsuda, S.; Imai, N.; Kataoka, H. *Angew. Chem., Int. Ed*. **2003**, *42*, 1273−1275.

useful to estimate the reactivity and stereochemistry of this reaction.

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Supporting Information Available: Experimental procedures and complete characterization (^{1}H and ^{13}C NMR, IR, and mass spectra or elemental analysis) for compounds **5** and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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