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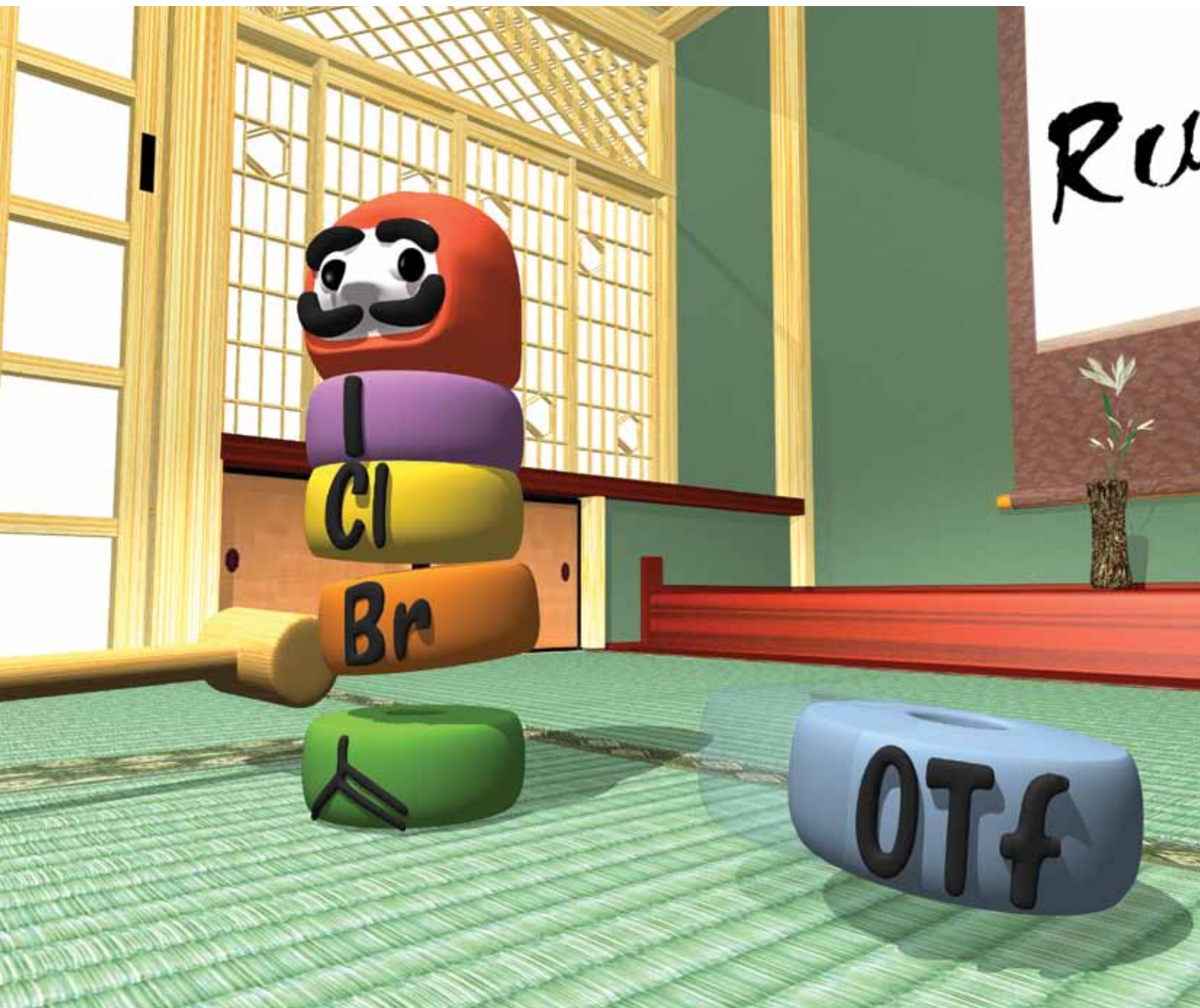
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Ruthenium-catalyzed transformation of alkenyl triflates to alkenyl halides†

Eiji Shirakawa,* Yusuke Imazaki and Tamio Hayashi*

In the presence of a ruthenium catalyst, alkenyl triflates were found to be transformed to the corresponding bromides, chlorides and iodides simply by treatment with a lithium halide (1.2 equiv.).

Alkenyl halides are versatile reagents, which not only act as efficient alkenyl electrophiles but are also readily converted to strong alkenyl nucleophiles upon treating with a metal such as magnesium or lithium. Synthesis of alkenyl halides[1] from alkenyl triflates, which can be prepared regioselectively from readily available ketones or aldehydes,[2,3] is beneficial but no facile and general way has been reported.[4] Considering their high reactivity towards alkenyl triflates,[5] transition metal complexes are expected to have the potential to catalyze this transformation, but there have been no reports on the transition metal-catalyzed halogenation.[6] Here we report the ruthenium-catalyzed triflate–halide exchange on alkenes.
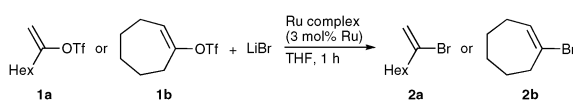
In the course of our investigation on the transition metal-catalyzed coupling of alkenyl triflates with Grignard reagents,[7] we found that a considerable amount of an alkenyl bromide was produced in the ruthenium-catalyzed reaction of the corresponding alkenyl triflate with a Grignard reagent contaminated with LiBr. We anticipated that the alkenyl bromide was produced from the triflate by the reaction with LiBr under ruthenium catalysis.

It was found that the bromination of 1-octen-2-yl triflate (**1a**) takes place selectively in the presence of a low valent ruthenium catalyst. Thus, the reaction of **1a** with LiBr (1.2 equiv.) in the presence of a ruthenium complex generated from Ru(acac)$_3$ (3 mol%) and EtMgBr (12 mol%) in THF at 20 °C for 1 h gave 1-octen-2-yl bromide (**2a**) in 98% yield (Table 1, entry 1). If Ru(acac)$_3$ is not treated with EtMgBr, **2a** is not produced (Table 1, entry 2), whereas a ruthenium(0) complex, Ru(cod)(cot), effectively catalyzed the bromination (Table 1, entry 3). These results show that some low valent ruthenium complexes are active catalysts. The reduction of readily available RuCl$_3$·nH$_2$O with zinc dust gave a catalyst of moderate activity, where the corresponding alkenyl chloride derived from the chloride of RuCl$_3$ was found to be a contaminant (Table 1, entries 4 and 5). The alkenyl chloride was obtained in a high yield by the use of LiCl instead of LiBr (Table 1, entry 6). The present halogenation was not observed with Ru$_3$(CO)$_{12}$ or Ru/C (entries 7 and 8). Cyclic triflate **1b**

was less reactive than **1a**; under the reaction conditions (20 °C, 1 h) where **1a** was fully consumed, only 8% of **1b** was converted (Table 1, entry 9). Three hours at 60 °C were required for completion of the bromination, although use of 1,10-phenanthroline (phen: 3 mol%) as a ligand reduced the reaction time to 1 h (entries 10 and 11). Addition of 2,2′-bipyridyl (bpy) also was effective, whereas PPh$_3$ severely inhibited the bromination (Table 1, entries 12 and 13).

Entries 1, 3, and 11 of Table 1 were selected as standard conditions for investigations of the substrate scope and referred to as methods A, B, and C, respectively, in Table 2. Method A, which employs Ru(acac)$_3$ and EtMgBr, works well for reactive triflates. 1-Alken-2-yl triflate **1c** underwent bromination in a similar efficiency to **1a** (Table 2, entry 1).‡ Chlorination and iodination of triflate **1c** proceeded well with

Table 1 Effect of ruthenium catalysts in the bromination of alkenyl triflates[a]

| Entry	1	Catalyst	Additive (mol%)	T/°C	Conv. (%)[b]	Yield (%)[b]
1	**1a**	Ru(acac)$_3$	EtMgBr (12)	20	>99	98
2	**1a**	Ru(acac)$_3$	—	20	<1	<1
3	**1a**	Ru(cod)(cot)	—	20	>99	99
4	**1a**	RuCl$_3$·nH$_2$O	Zn (15)	20	27	26
5[c]	**1a**	RuCl$_3$·nH$_2$O	Zn (15)	60	>99	93[d]
6[e]	**1a**	RuCl$_3$·nH$_2$O	Zn (15)	60	>99	97[f]
7	**1a**	Ru$_3$(CO)$_{12}$	—	20	<1	<1
8	**1a**	Ru/C	—	20	<1	<1
9	**1b**	Ru(acac)$_3$	EtMgBr (12)	20	8	7
10[c]	**1b**	Ru(acac)$_3$	EtMgBr (12)	60	>99	96
11	**1b**	Ru(acac)$_3$	EtMgBr (12), phen[g] (3)	60	>99	96
12	**1b**	Ru(acac)$_3$	EtMgBr (12), bpy[h] (3)	60	93	90
13	**1b**	Ru(acac)$_3$	EtMgBr (12), PPh$_3$ (6)	60	4	4

[a] The reaction was carried out in THF (1.0 mL) for 1 h under a nitrogen atmosphere using an alkenyl triflate (**1a** or **1b**: 0.25 mmol) and LiBr (0.30 mmol) in the presence of a ruthenium complex (3 mol% of Ru). **1a** was contaminated with 5% of the corresponding 2-alken-2-yl triflates. [b] Determined by ^{1}H NMR. In the reaction of **1a**, the product contained ≤5% of the corresponding 2-alken-2-yl bromides and the yield of **2a** was estimated based on the 1-alken-2-yl triflate (**1a**). [c] Reaction time = 3 h. [d] The corresponding chloride also was produced in 4% yield. [e] LiCl was used instead of LiBr. Reaction time = 6 h. [f] The corresponding chloride was obtained. [g] phen = 1,10-phenanthroline. [h] bpy = 2,2′-bipyridyl.

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† Electronic supplementary information (ESI) available: Experimental details and NMR spectra. See DOI: 10.1039/b907761h

Table 2 Ruthenium-catalyzed halogenation of alkenyl triflates[a]

$$R^1\underset{R^2}{\overset{}{=}}OTf \;+\; LiX \;\;\xrightarrow[\text{THF}]{\text{Ru complex (3 mol%)}}\;\; R^1\underset{R^2}{\overset{}{=}}X$$

1 : 1.2   **1**   **2**   X = Br, Cl, I

Entry		X	Method	$T/°C$	Time/h	Yield (%)[b]
1	MeO–C₆H₄–CH₂CH₂–C(=CH₂)OTf **1c**[c]	Br	A	20	1	97[d]
2	**1c**[c]	Cl	A[e]	60	1	93[d]
3	**1c**[c]	I	B	20	3	98[f]
4	CH₂=C(Ph)OTf **1d**	Br	A	20	1	90
5	n-C₇H₁₅CH=CHOTf **1e**	Br	C[g]	60	24	98[h]
6	(MeO–C₆H₄–CH=)C(CH₃)OTf **1f**[i]	Br	A	20	12	94[j]
7	cycloheptenyl–OTf **1b**	Cl	A[e]	60	3	98
8	**1b**	I	B	60	3	91
9	cyclohexenyl–OTf **1g**	Br	C	60	24	91
10	6-Me-cyclohexenyl–OTf **1h** (**1h**:**1i** = 98:2)	Br	C	60	24	91[k]
11	2-Me-cyclohexenyl–OTf **1i** (**1i**:**1h** = 98:2)	Br	C	60	24	99[l]
12	cyclopentenyl–OTf **1j**	Br	C	60	24	91
13	2-naphthyl–OTf **1k**	Br	C[g]	60	24	97
14	Ph–C≡C–CH₂CH₂–C(=CH₂)OTf **1l**[m]	Br	A	20	6	79[n]
15	BocN-piperidinyl–OTf **1m**	Br	C[g]	60	24	91
16	dioxolane-cyclohexenyl–OTf **1n**	Br	C[g]	60	24	91

[a] The reaction was carried out in THF (1.0 mL) under a nitrogen atmosphere using an alkenyl triflate (**1**: 0.25 mmol) and LiX (0.30 mmol). Method A: Ru(acac)$_3$ (3 mol%) and EtMgBr (12 mol%). Method B: Ru(cod)(cot) (3 mol%). Method C: Ru(acac)$_3$ (3 mol%), phen (3 mol%), and EtMgBr (12 mol%). [b] Isolated yield based on **1**. [c] Containing 9% of the 2-alken-2-yl triflates. [d] Containing 9% of the 2-alken-2-yl halides. [e] BuMgCl was used instead of EtMgBr. [f] Containing 8% of the 2-alken-2-yl iodides. [g] Twice the amount of the ruthenium complex and additives were used. [h] $E:Z = 50:50$. [i] $E:Z = 60:40$. [j] $E:Z = 64:36$. [k] 6-Me:2-Me = 98:2. [l] 2-Me:6-Me = 98:2. [m] Containing 19% of the 2-alken-2-yl triflates. [n] Containing 9% of the 2-alken-2-yl bromides.
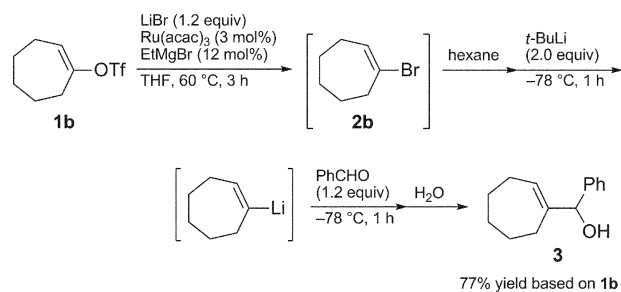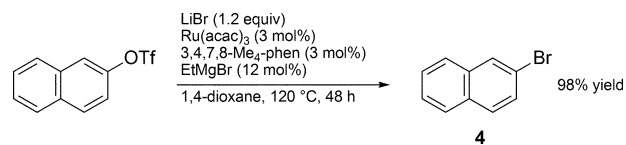

Scheme 1

a modified method A using LiCl and Ru(acac)$_3$–BuMgCl and method B employing LiI and Ru(cod)(cot), respectively (Table 2, entries 2 and 3). α-Phenylvinyl triflate (**1d**) was as reactive as **1a** (Table 2, entry 4). Interestingly, the bromination of linear triflate **1e** was much slower even at 60 °C with method C and a one to one $E:Z$ mixture was formed from the E isomer of **1e** (Table 2, entry 5). A disubstituted vinyl triflate underwent bromination (Table 2, entry 6). Chlorination and iodination of cyclic triflate **1b** proceeded with high selectivity in high yields (Table 2, entries 7 and 8). Other cyclic triflates were also brominated in high yields (Table 2, entries 9–13). Migration of double bonds during the bromination did not take place (Table 2, entries 10 and 11). Alkyne, carbamate, and acetal moieties were compatible with the bromination (Table 2, entries 14–16).

Alkenyl halides thus obtained can be further transformed to alkenyl nucleophiles,[8] which react with electrophiles in the same flask. For example, triflate **1b** was transformed to bromide **2b**, which, after dilution with hexane, was treated successively with t-butyllithium (2.0 equiv.) and benzaldehyde (1.2 equiv.) to give allyl alcohol **3** in 77% yield based on **1b** (Scheme 1).

The bromination using a modified method C was found to be applicable to 2-naphthyl triflate (Scheme 2). Thus, 2-naphthyl bromide (**4**) was obtained in 98% yield by the reaction using 3,4,7,8-tetramethyl-1,10-phenanthroline and 1,4-dioxane as a ligand and a solvent, respectively, at an elevated temperature (120 °C). Unfortunately, the reaction of p-tolyl triflate did not give the corresponding bromide under the same conditions.

At present, we do not have convincing evidence to clarify the reaction mechanism, but the stereochemical outcome in the reaction of **1e** and the reactivity order of triflates tempt us to discuss it. In the nickel-catalyzed halogen exchange with alkenyl halides to give stereo-retained products, σ-bond metathesis between Ni–X and C(alkenyl)–X′ bonds is considered to be the key step.[6b] It is unlikely that the present halogenation proceeds in a similar mechanism because the reaction of **1e** gave a mixture of stereoisomers (Table 2, entry 5).[9] Another possible catalytic cycle, which consists of oxidative addition of

Scheme 2

an alkenyl triflate, ligand exchange between OTf and X, and reductive elimination of the halide,[10] also seems incompatible with the production of stereoisomers. The much higher reactivity of α-substituted vinyl triflate **1a** than β-substituted **1e**, together with the *E–Z* isomerization of **1e** may indicate an involvement of cationic or radical species in the catalytic cycle.

In conclusion, we have disclosed a transformation of alkenyl triflates to the corresponding halides using a ruthenium complex and a lithium halide as a catalyst and a halide source, respectively.

Notes and references

‡ A representative procedure for halogenation of alkenyl triflates (Table 2, entry 1): to a THF solution (0.97 mL) of Ru(acac)$_3$ (3.0 mg, 7.5 μmol) and LiBr (26 mg, 0.30 mmol) placed in an oven-dried 20 mL Schlenk tube, was added ethylmagnesium bromide (1.0 M THF solution, 0.030 mL, 30 μmol). After stirring for 10 min at room temperature, 4-(4-methoxyphenyl)-1-buten-2-yl triflate (**1c**, containing 9% of (*E*)- and (*Z*)-1-(4-methoxyphenyl)-2-buten-3-yl triflates, 77.5 mg, 0.250 mmol) was added at 20 °C and stirring was continued for 1 h. Purification by passing through a pad of silica gel using hexane : AcOEt (10 : 1) as an eluent gave 2-bromo-4-(4-methoxyphenyl)-1-butene as a colorless oil (containing (*E*)- and (*Z*)-3-bromo-1-(4-methoxyphenyl)-2-butenes, 58.3 mg, 97% yield).

1 Elimination of hydrogen halides from 1,1- or 1,2-dihaloalkanes, and hydrometalation of alkynes followed by halogenolysis of the resulting alkenyl metals are two major methods to prepare alkenyl halides.
2 Several methods to prepare alkenyl halides directly from ketones are known though regioselective synthesis from dissymmetric ketones is difficult. For examples, see: (*a*) R. C. Larock, *Comprehensive Organic Transformations*, Wiley-VCH, New York, 2nd edn, 1999, pp. 722–724 and p. 302. For a recent example, which is applicable to a relatively wide range of ketones, see: (*b*) A. Spaggiari, D. Vaccari, P. Davoli, G. Torre and F. Prati, *J. Org. Chem.*, 2007, **72**, 2216–2219.
3 Regioselective preparation of alkenyl triflates from dissymmetric ketones through the corresponding enolates followed by trimethyl-stannylation with the aid of a transition metal and halogenolysis is frequently used as a reliable method for transformation from ketones to alkenyl halides in natural product synthesis. For recent examples, see: (*a*) P. B. Hurley and G. R. Dake, *J. Org. Chem.*, 2008, **73**, 4131–4138; (*b*) H. Kim, H. Lee, D. Lee, S. Kim and

D. Kim, *J. Am. Chem. Soc.*, 2007, **129**, 2269–2274; (*c*) S. Schiltz, C. Ma, L. Ricard and J. Prunet, *J. Organomet. Chem.*, 2006, **691**, 5438–5443; (*d*) I. Martínez, P. E. Alford and T. V. Ovaska, *Org. Lett.*, 2005, **7**, 1133–1135; (*e*) J. L. Hubbs and C. H. Heathcock, *J. Am. Chem. Soc.*, 2003, **125**, 12836–12843; (*f*) L. A. Paquette and F.-T. Hong, *J. Org. Chem.*, 2003, **68**, 6905–6918.
4 Transformation of alkenyl triflates to iodides by treatment with MgI$_2$ in CS$_2$ or cyclohexane is reported to be applicable to a certain scope of triflates but not to simple ones such as 1-cyclopentenyl triflate. (*a*) A. G. Martínez, R. M. Alvarez and A. G. Fraile, *Synthesis*, 1986, 222–224. The halogenation of alkenyl triflates has been reported for those having an electron-donating group at the α-position or those derived from 1,3-dicarbonyl compounds. For examples, see: (*b*) J. K. Stille and M. P. Sweet, *Organometallics*, 1990, **9**, 3189–3191; (*c*) H. Tanaka, Y. Nishioka, Y. Kameyama, S. Sumida, H. Matsuura and S. Torii, *Chem. Lett.*, 1995, **24**, 709–710; (*d*) H. Salim, X. Chen and Z. Rappoport, *J. Phys. Org. Chem.*, 2001, **14**, 778–787; (*e*) K. Kamei, N. Maeda and T. Tatsuoka, *Tetrahedron Lett.*, 2005, **46**, 229–232.
5 (*a*) K. Ritter, *Synthesis*, 1993, 735–762; (*b*) I. L. Baraznenok, V. G. Nenajdenko and E. S. Balenkova, *Tetrahedron*, 2000, **56**, 3077–3119.
6 Nickel- or copper-catalyzed halogen exchange reactions in alkenyl halides have been reported. (*a*) K. Takagi, N. Hayama and S. Inokawa, *Chem. Lett.*, 1978, **7**, 1435–1436; (*b*) T. T. Tsou and J. K. Kochi, *J. Org. Chem.*, 1980, **45**, 1930–1937; (*c*) H. Suzuki, M. Aihara, H. Yamamoto, Y. Takamoto and T. Ogawa, *Synthesis*, 1988, 236–238.
7 (*a*) E. Shirakawa, T. Sato, Y. Imazaki, T. Kimura and T. Hayashi, *Chem. Commun.*, 2007, 4513–4515; (*b*) E. Shirakawa, Y. Imazaki and T. Hayashi, *Chem. Lett.*, 2008, **37**, 654–655.
8 Transformation of alkenyl triflates to alkenyl metals of Sn, B, and Si in the presence of a transition metal catalyst has been reported. For Sn, see ref. 3. For other examples, see: (*a*) S. Matsubara, J. Hibino, Y. Morizawa, K. Oshima and H. Nozaki, *J. Organomet. Chem.*, 1985, **285**, 163–172; (*b*) W. D. Wulff, G. A. Peterson, W. E. Bauta, K.-S. Chan, K. L. Faron, S. R. Gilbertson, R. W. Kaesler, D. C. Yang and C. K. Murray, *J. Org. Chem.*, 1986, **51**, 277–279; (*c*) K. Takahashi, J. Takagi, T. Ishiyama and N. Miyaura, *Chem. Lett.*, 2000, **29**, 126–127; (*d*) M. Murata, Y. Oyama, S. Watanabe and Y. Masuda, *Synthesis*, 2000, 778–780.
9 Stereoisomeric mixtures of 1-deuterio-1-octen-2-yl triflate of different compositions (*E* : *Z* = 71 : 29 and 20 : 80) were transformed to the corresponding bromide in similar isomer ratios (*E* : *Z* = 47 : 53 and 53 : 47, respectively).
10 This cycle has not been reported to be operative, which is probably due to the reluctant reductive elimination step, which is known to take place only under special conditions. (*a*) A. H. Roy and J. F. Hartwig, *J. Am. Chem. Soc.*, 2001, **123**, 1232–1233; (*b*) A. H. Roy and J. F. Hartwig, *J. Am. Chem. Soc.*, 2003, **125**, 13944–13945; (*c*) A. H. Roy and J. F. Hartwig, *Organometallics*, 2004, **23**, 1533–1541.