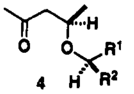
the direct formation of the β-alkoxy ketone is practically quite useful. It was soon realized that the combined use of diethylaluminum fluoride (1.2 equiv) and pentafluorophenol (2.4 equiv) was the most effective for a diastereoselective reductive cleavage reaction. The major isomer afforded a retentive product, and the observed high diastereoselectivity was similar to or better than that of reductive cleavages of acetals with aluminum hydride. As shown in Table II, several chiral acetals derived from aliphatic or aromatic ketones are applicable in good yields and with high diastereoselectivities.


4

In summary, this paper describes a new methodology for cationic *retentive* alkylation and reduction of acetals. The results reflect the unusual effect of a halophenol ligand on the reactivity of organoaluminum reagents. We also found that pentafluorophenol is an effective accelerator for Meerwein–Ponndorf–Verley reduction. Reduction of 4-*tert*-butylcyclohexanone with aluminum isopropoxide (3 equiv) in dichloromethane, for example, was very slow at 0 °C (<5% for 5 h), but in the presence of pentafluorophenol (1 equiv), the reduction was cleanly completed within 4 h at 0 °C. The question of why these reagents retain sufficient nucleophilicity is still open. It is possible that the *o*-halo-substituents of the phenoxide ligand may coordinate with the aluminum atom, thus increasing the nucleophilicity of the reagent. Whatever the reason, the combination of halophenol and organoaluminum reagent offers unique opportunities in organometallic reactions.[8]

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[8] A part of this work was financially supported by a Grant-in-Aid for Scientific Study from the Ministry of Education, Science and Culture of the Japanese Government. K.I. also acknowledges a JSPS Fellowship for Japanese Junior Scientists.

γ-Selective Cross-Coupling Reaction of Allyltrifluorosilanes: A New Approach to Regiochemical Control in Allylic Systems

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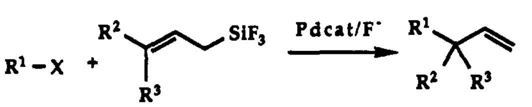
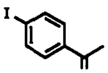
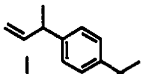
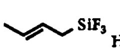
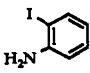
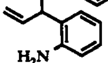
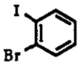
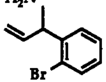
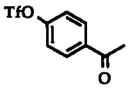
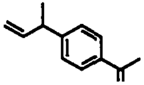
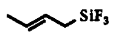
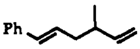
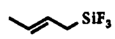
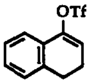
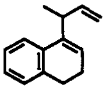
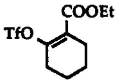
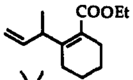
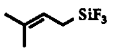
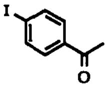
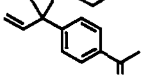
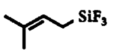
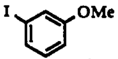
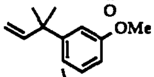
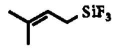
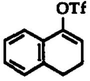
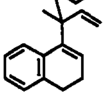
Although the cross-coupling reaction of allylmetals with vinylic, allylic, and aromatic electrophiles is a straightforward route to 1,4-dienes,[1] 1,5-dienes,[2] and allylic arenes,[3] low regioselectivity regarding organometallics has severely limited their synthetic application. Especially, no reliable allylmetal reagents with high γ-selectivity have been realized yet. We report herein that allyltrifluorosilanes,[4] when promoted by fluoride ion and a palladium catalyst,[5] undergo cross-coupling reactions with various electrophiles exclusively at the γ-carbon to give allylated products *in regiochemically pure forms* (Scheme I).[6]

Scheme I[a]



[a] R^1 = aryl, alkenyl, allyl; X = Br, I, OTf, OAc; R^2 = Me, R^3 = H; R^2 = Me, R^3 = Me.

Table I. Cross-Coupling Reactions of Allyltrifluorosilanes with Various Electrophiles Mediated by Palladium Catalyst and Fluoride Ion in THF

Entry	Allylsilane	Substrate	Conditions[a]	Product	Yield(%)[b]
1			A 80 °C, 19 h		95
2			B 100 °C, 25 h		53
3			B 100 °C, 37 h		78
4			C 100 °C, 12 h		96
5			A 60 °C, 5 h		54
6			C 100 °C, 12 h		85
7			C 120 °C, 24 h		98
8			B 100 °C, 46 h		70
9			B 100 °C, 33 h		51
10			C 120 °C, 46 h		83

[a] Reactions were carried out in sealed tubes under the following conditions. A: $Pd(PPh_3)_4$ (2–5 mol %) and TBAF (1.0 equiv) were used. B: $Pd(PPh_3)_4$ (5 mol %) was used. After the addition of TBAF (1.0 equiv), additional TBAF (0.5 equiv) was introduced at intervals of 10 h. C: $Pd(OAc)_2$ (5 mol %), dppb (10 mol %), and TASF (1.0 equiv) were used. [b] Isolated.

Our results summarized in Table I clearly demonstrate that a wide range of electrophiles such as organic halides, triflates, and an acetate can effectively take part in this coupling reaction. For example, the cross coupling of (*E*)-crotyltrifluorosilane with 4-iodoacetophenone in the presence of 1 equiv of tetrabutylammonium fluoride (TBAF) and 5 mol % of $Pd(PPh_3)_4$ in tetrahydrofuran (THF) at 80 °C (in a sealed tube) proceeded with complete γ-attack, giving 3-(4-acetylphenyl)-1-butene in 95% yield (entry 1).[7] With an appropriate Pd catalyst, fluoride ion, and reaction conditions (see footnotes of Table I), (*E*)-crotyltri-

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[1] (a) Lipshutz, B. H.; Elworthy, T. R. *J. Org. Chem.* **1990**, *55*, 1695 and references cited therein. For the cross coupling of higher order allylic cuprates with alkyl halides, see: (b) Lipshutz, B. H.; Crow, R.; Dimock, S. H.; Ellsworth, E. L. *J. Am. Chem. Soc.* **1990**, *112*, 4063.

[2] (a) Godschlax, J.; Stille, J. K. *Tetrahedron Lett.* **1980**, *21*, 2599. (b) **1983**, *24*, 1905. (c) Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Am. Chem. Soc.* **1981**, *103*, 1969. (d) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1.

[3] Kosugi, M.; Sasaki, K.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 301.

[4] Various types of allyltrifluorosilanes are conveniently prepared via a copper-catalyzed coupling of trichlorosilane with the corresponding allyl chlorides and fluorination of the resulting allyltrichlorosilanes using SbF_3: (a) Kira, M.; Hino, T.; Sakurai, H. *Tetrahedron Lett.* **1989**, *30*, 1099. (b) Furuya, N.; Sukawa, T. *J. Organomet. Chem.* **1975**, *96*, C1.

[5] For the cross-coupling reaction of organosilicon compounds promoted by palladium catalyst and fluoride ion, see: (a) Hatanaka, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1990**, *112*, 7793. (b) Hatanaka, Y.; Hiyama, T. *Tetrahedron Lett.* **1990**, *31*, 2719 and references cited therein.

[6] With the aid of a Lewis acid catalyst, allyltrimethylsilane couples with tertiary chlorides only: (a) Fleming, I.; Paterson, I. *Synthesis* **1979**, 446. (b) Sasaki, T.; Usuki, A.; Ohno, M. *Tetrahedron Lett.* **1978**, 4925.

[7] The following procedure is representative (Table I, entry 1). A tetrahydrofuran (THF) solution of tetrabutylammonium fluoride (1.0 M, 3.0 mL, 3.0 mmol, purchased from Aldrich Chemical Co.) was added to 4-iodoacetophenone (490 mg, 2.0 mmol), (*E*)-crotyltrifluorosilane (420 mg, 3.0 mmol), and $Pd(PPh_3)_4$ (62 mg, 0.05 mmol) dissolved in THF (10 mL) at room temperature under an argon atmosphere. The reaction mixture was then heated to 80 °C for 19 h. Concentration and purification by column chromatography (silica gel) using ethyl acetate/hexane (1:10) gave 3-(4-acetylphenyl)-1-butene (341 mg, 95%).

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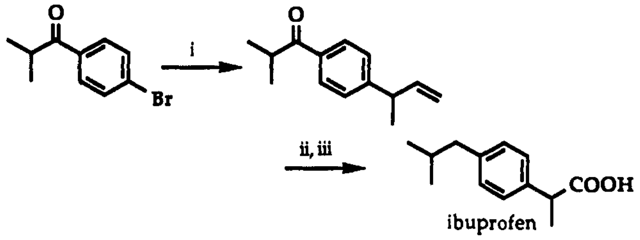
Scheme II[a]



[a] (i) (*E*)-Crotyltrifluorosilane, $Pd(PPh_3)_4$ (5 mol %), TBAF (1.0 equiv), THF, 100 °C, 90 h, 95%; (ii) $KMnO_4$, $NaIO_4$, K_2CO_3, *t*-BuOH, H_2O, 0 °C, 2 h, 70%; (iii) $HSiEt_3$, CF_3COOH, room temperature, 24 h, 78%.

fluorosilane afforded isomerically pure γ-coupled products.[8,9,10] Similar conditions were successfully applied to the allylation of both aryl triflates and an allyl acetate, achieving the cross couplings at the γ-carbon of crotyltrifluorosilane exclusively (entries 4 and 5). The use of the $Pd(OAc)_2$ (5 mol %)/1,4-bis(diphenylphosphino)butane (dppb) (10 mol %) system[11] coupled with tris(diethylamino)sulfonium difluorotrimethylsilicate (TASF)[12] (1.0 equiv) as a F^- source was found particularly effective for γ-selective cross couplings with enol triflates (entries 6 and 7).

Under typical conditions, (3-methyl-2-butenyl)trifluorosilane also smoothly coupled with aryl halides or enol triflates at the sterically crowded γ-carbon to afford 3-substituted 3-methyl-1-butenes in good yields (entries 8-10). These results sharply contrast with the fact that coupling reactions of higher order 3-methyl-2-butenylcuprate with enol triflate take place with complete α-attack.[1a]

High chemoselectivity also deserves special comment. Ester and ketone carbonyls and even an amino group were tolerated. The C-I bond reacted in preference to the C-Br bond of 2-bromo-1-iodobenzene as seen in the example of entry 3.

The synthetic utility of this process was well demonstrated by the synthesis of ibuprofen (Scheme II).[13] Oxidative cleavage of the C=C bond of isomerically pure γ-coupled product has provided a facile route to this potent antiinflammatory agent with good overall yield.

In conclusion, γ-selective allylation of organic halides, triflates, and acetate has been realized using allyltrifluorosilanes together with a Pd catalyst and fluoride ion. The reaction reported here should give a unique solution to the long-standing problem of regiochemical control in allylic coupling. The high γ-selectivity of allyltrifluorosilanes as compared with other allylic organometallic compounds may be explained in terms of the enhanced nucleophilicity of the γ-carbon of the intermediate pentacoordinate allylic silicates[14] formed from nucleophilic attack of fluoride ion on allyltrifluorosilanes.

Supplementary Material Available: Spectral and analytical data of new compounds and literature references or registry numbers of known compounds (3 pages). Ordering information is given on any current masthead page.

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(8) The reaction of (*E*)-crotyltrifluorosilane with 4-bromoacetophenone mediated by $Pd(PPh_3)_4$/TBAF under the same conditions gave a small amount of α-coupled product with a 1:6.2 ratio of α:γ products.

(9) The kinds of silyl groups in the allylsilanes strongly influenced both the regioselectivity and the yields of the coupled products. Thus, the reaction of (*E*)-crotyltriethoxysilane or (*E*)-crotyltrimethylsilane with 4-iodoacetophenone gave a mixture of α- and γ-coupled products. Although 3-(trimethylsilyl)-1-propene effectively coupled with cinnamyl bromide under the influence of Pd catalyst and fluoride ion, this reaction could not be applied to vinylic and aromatic substrates: Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918.

(10) The reaction of crotyltrifluorosilane with (*E*)-1-iodo-1-octene under the influence of $Pd(PPh_3)_4$/TBAF afforded ca. 20–30% yields of γ-coupled product with the recovery of a considerable amount of the starting material.

(11) Phosphine ligands affect the regioselectivity of the reactions. $Pd(PPh_3)_4$/TBAF resulted in low regioselectivity for the enol triflates (α:γ = 1:1-3), and a fair amount of reduced substrate was formed. Use of 1,1'-bis(diphenylphosphino)ferrocene or 1,3-bis(diphenylphosphino)propane in place of dppb led to nonregioselective coupling. These observations suggest that a (σ-allyl)palladium species (Kurosawa, H.; Emoto, M.; Urabe, A.; Miki, K.; Kasai, N. *J. Am. Chem. Soc.* **1985**, *107*, 8253) is a catalytic key intermediate. If the (σ-allyl)palladium species underwent reductive elimination before rearranging to a (π-allyl)palladium species, high γ-selectivity would be achieved. It is well-known that the rate of reductive elimination of an organopalladium species is strongly influenced by the coordinating phosphine ligand: Gillie, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4933.

(12) Middleton, W. J. U.S. Pat. 3940402, 1976; *Chem. Abstr.* **1976**, *85*, P6388j. Cf.: Middleton, W. J. *Org. Synth.* **1985**, *64*, 221. Commercially available tris(dimethylamino)sulfonium difluorotrimethylsilicate is much less reactive than tris(diethylamino)sulfonium difluorotrimethylsilicate mainly due to poor solubility in the reaction media.

(13) Rieu, J. P.; Boucherle, A.; Cousse, H.; Mouzin, G. *Tetrahedron* **1986**, *42*, 4095.

(14) (a) Sakurai H. *Synlett* **1989**, 1. (b) Kira, M.; Sato, K.; Sakurai, H.; Hada, M.; Izawa, M.; Ushio, J. *Chem. Lett.* **1991**, 387.

Reaction of Second-Row Transition-Metal Atoms with Methane

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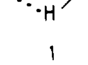
In this communication the first systematic ab initio study is presented, in which all the steps in a chemical reaction have been investigated for a whole row of transition-metal atoms. The reactivities of naked metal atoms are not only of interest as such but are also relevant for a detailed understanding of reaction mechanisms of ligated complexes. Recently, experimental results for the reactions of neutral metal atoms have become available,[1] whereas earlier studies were only concerned with the reactivities of metal cations.[2]

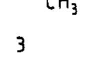
Probably the most important aspect, which has been highlighted by the above-mentioned experimental studies and also several theoretical studies,[3] is the large importance of the atomic spectrum for the reactivity. Exactly how these spectra influence the reactivities is best understood by studying sequences of transition-metal atoms. The most important results from a study of this type, the oxidative addition of methane to the whole sequence of second-row transition-metal atoms, are discussed here. This reaction is of great present interest, mainly as the first step in the catalytic conversion of the abundant and nonreactive alkanes into more useful products. One of the first metals experimentally observed to insert into unactivated C-H bonds was rhodium,[4] and therefore the second row was chosen for this study.

Four regions on the potential energy surface for the reaction of each atom have been studied. The first region is for the reactants. The second region is for the molecular precursor $M-CH_4$ complex **1**. The third region is the transition state **2** for the reaction, and the fourth region is the $MHCH_3$ product region



1

2



3

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(1) (a) Klabunde, K. J.; Jeong, Gi Ho; Olsen, A. W. In *Selective Hydrocarbon Activation: Principles and Progress*; Davies, J. A., Watson, P. L., Greenberg, A., Liebman, J. F., Ed.; VCH Publishers: New York, 1990; pp 433–466. (b) Ritter, D.; Weisshaar, J. C. *J. Am. Chem. Soc.* **1990**, *112*, 6425. (c) Mitchell, S. A.; Hackett, P. A. *J. Chem. Phys.* **1990**, *93*, 7822.

(2) See for example: Armentrout, P. B.; Beauchamp, J. L. *Acc. Chem. Res.* **1989**, *22*, 315.

(3) (a) Blomberg, M.; Brandemark, U.; Pettersson, L.; Siegbahn, P. *Int. J. Quantum Chem.* **1983**, *23*, 855. (b) Walch, S. P.; Bauschlicher, C. W. Jr. *J. Chem. Phys.* **1983**, *78*, 4597. (c) Low, J. J.; Goddard, W. A., III *J. Am. Chem. Soc.* **1984**, *106*, 8321.

(4) (a) Jones, W. D.; Feher, F. J. *J. Am. Chem. Soc.* **1982**, *104*, 4240. (b) Sakakura, T.; Sodeyama, T.; Sasaki, K.; Wada, K.; Tanaka, M. *J. Am. Chem. Soc.* **1990**, *112*, 7221.

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