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First example of molecular iodine-catalyzed allylation and alkynylation of cyclic allylic acetates

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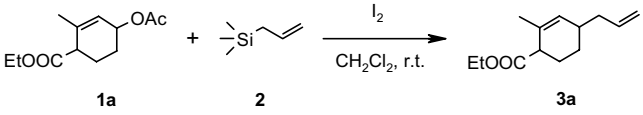
Abstract—Cyclic allylic acetates undergo smooth allylation and alkynylation with allyltrimethylsilane and alkynyl silanes in the presence of molecular iodine under mild conditions to afford the corresponding allylated and alkynylated cyclohexene derivatives in good yields with high selectivity.

The stereoselective addition of allylsilanes to aldehydes, referred to as the Sakurai–Hosomi reaction has been recognized as a particularly efficient method of carbon–carbon bond formation and has been extensively applied in organic synthesis, especially in natural product synthesis.[1,2] Acid catalyzed carbon–carbon bond forming reactions are of great significance in organic synthesis because of their high reactivity, selectivity and mild reaction conditions.[3] Allylic acetates are well-known carbon electrophiles capable of reacting with various nucleophiles and their ability to undergo nucleophilic substitution reactions contributes to their synthetic value.[4,5] However, there have been no reports on the allylation and alkynylation of allylic acetates with allyl/alkynyl silanes. Owing to its unique catalytic properties, iodine has been extensively used as a catalyst for a plethora of organic transformations.[6]

In continuation of our interest on the catalytic applications of elemental iodine for various organic transformations,[7] we report herein a novel and efficient protocol for the allylation and alkynylation of cyclic allylic acetates with allyl and alkynyl silanes using iodine as the catalyst. Thus treatment of 4-ethoxycarbonyl-3-methyl-2-cyclohexenyl acetate **1a** with allyltrimethylsilane **2** in the presence of 5 mol% of molecular iodine resulted in the formation of ethyl 4-allyl-2-methyl-2-cyclohexene-1-carboxylate **3a** in 86% yield (Scheme 1).



1a **2** **3a**

Scheme 1.

Similarly, various cyclohexenyl acetates underwent smooth allylation with allyltrimethylsilane to afford the corresponding allylated cyclohexenyl derivatives in high yields (Table 1, entries **d**, **f**, **i** and **l**). In all cases, the reactions proceeded smoothly at room temperature and were complete within 30–40 min. No γ-substitution was observed (as a result of allylic rearrangement, S_N2' type substitution) under the reaction conditions. The acetate group was simply replaced by the allylic functionality in a S_N2 manner. Further, treatment of 2-ethyl-4-ethoxycarbonyl-3-methyl-2-cyclohexenyl acetate **1d** with 2-[(trimethylsilyl)ethynyl]benzene **4** gave ethyl 3-ethyl-2-methyl-4-(2-phenyl-1-ethynyl)-2-cyclohexene-1-carboxylate **3j** in 75% yield (Scheme 2).

Analogous to 2-[(trimethylsilyl)ethynyl]benzene, 1-trimethylsilyl-1-hexyne also reacted efficiently with various cyclic allylic acetates to give the respective alkynylated

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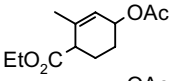
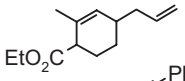
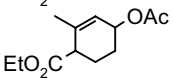
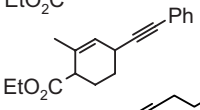
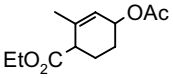
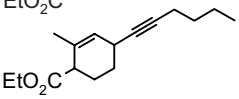
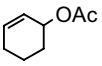
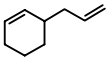
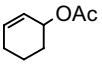
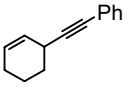
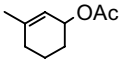
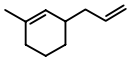
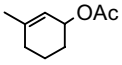
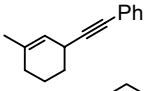
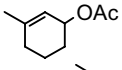
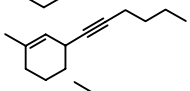
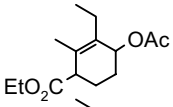
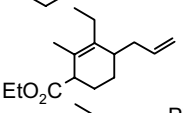
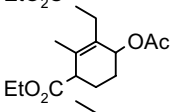
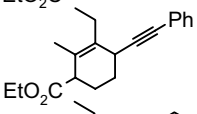
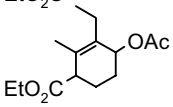
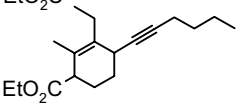
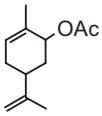
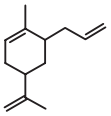
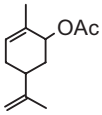
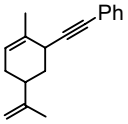
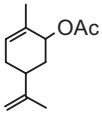
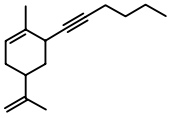
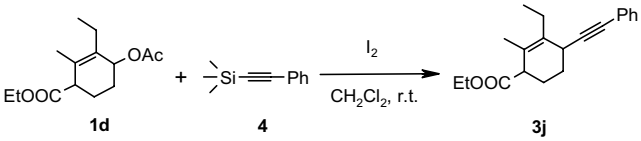
Table 1. Iodine-catalyzed allylation and alkynylation of cyclic allylic acetates

Entry	Allylic acetate	Product[a]	Time (min)	Yield (%)[b]
a			40	86
b			45	72
c			50	70
d			30	82
e			35	75
f			35	90
g			40	80
h			45	78
i			35	87
j			50	75
k			60	72
l			30	89
m			40	82
n			45	80

[a] All products were characterized by ^{1}H NMR, IR and mass spectroscopy.
[b] Yield refers to the isolated pure products after column chromatography.



Scheme 2.

cyclohexenyl derivatives. However, alkynylsilanes afforded lower yields compared to allylsilanes. This method is compatible with the ester and alkene moieties present in the starting materials. Simple cyclohexyl acetates failed to undergo either allylation or alkynylation under the reaction conditions. Similarly, acyclic allylic acetates such as 3-phenyl-(*E*)-2-propenyl acetate and (*E*)-2-butenyl acetate did not give the desired products. This method was only successful with cyclic allylic acetates. As solvent, dichloromethane appeared to give the best results. In the absence of catalyst, the reaction did not yield any product even after a long reaction time. All products were characterized by ^{1}H, ^{13}C NMR, IR and mass spectroscopy.

Interestingly, a catalytic amount of TMSI was also found to be equally effective for this conversion. However, the use of allyltri-*n*-butyltin in place of allyltrimethylsilane did not yield any product under these reaction conditions, perhaps because iodine does not interact with allyltri-*n*-butyltin. No additives or acidic promoters were required for the reaction to proceed. The catalyst is readily available at low cost and is highly efficient in promoting allylations and alkynylations. The scope and generality of this process is illustrated with respect to various allylic acetates and the results are presented in Table 1.[8]

In summary, we have described a novel and efficient protocol for the allylation and alkynylation of cyclic allylic acetates using cheap and readily available elemental iodine as catalyst. In addition to its efficiency, simplicity and mild reaction conditions, this method provides high yields of products with high selectivity, which makes it a useful and attractive process for the synthesis of allylated and alkynylated cyclohexenyl acetates.

Acknowledgements

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References and notes

1. (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207; (b) Marshall, J. A. *CHEMTRACTS* **1992**, *5*, 75.
2. (a) Colvin, E. *Silicon in Organic Synthesis*; Butterworth: London, 1981; p 97; (b) Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200; (c) Langkopf, E.; Schinzer, D. *Chem. Rev.* **1995**, *95*, 1375.
3. Kobayashi, S. *Eur. J. Org. Chem.*, **1999**, 15.
4. (a) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: London, **1985**; Review: (b) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1992**, *3*, 1089–1122; (c) Trost, B. M.; van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395–422.
5. For general reviews on palladium catalyzed allylic substitution, see: (a) Godleski, S. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford; (b) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1173–1180; (c) Dawson, G. J.; Williams, J. M. J.; Coote, S. J. *Tetrahedron: Asymmetry*, **1995**, 2535–2546, and references therein.
6. (a) Deka, N.; Kalita, D. J.; Borah, R.; Sharma, J. C. *J. Org. Chem.* **1997**, *62*, 1563; (b) Vaino, A. R.; Szarek, W. A. *Synlett* **1995**, 1157; (c) Lipshutz, B. H.; Keith, J. *Tetrahedron Lett.* **1998**, *39*, 2495.
7. (a) Yadav, J. S.; Reddy, B. V. S.; Hashim, S. R. *J. Chem. Soc., Perkin Trans. 1*, **2000**, 3025; (b) Yadav, J. S.; Reddy, B. V. S.; Sabitha, G.; Reddy, G. S. K. K. *Synthesis*, **2000**, 1532; (c) Kumar, H. M. S.; Reddy, B. V. S.; Reddy, E. J.; Yadav, J. S. *Chem. Lett.* **1999**, 857; (d) Yadav, J. S.; Reddy, B. V. S.; Rao, C. V.; Chand, P. K.; Prasad, A. R. *Synlett* **2001**, 1638.
8. General procedure: To a stirred solution of the allylic acetate (1 mmol) and iodine (5 mol%) in dichloromethane (10 mL), allyl- or alkynyl-trimethylsilane (2 mmol) was added slowly dropwise at 0 °C and the mixture allowed to stir at room temperature for the appropriate time (Table 1). After complete conversion as indicated by TLC, the reaction mixture was quenched with water (15 mL) and extracted with dichloromethane (2×15 mL). The combined organic extracts were washed with a 15% solution of aq sodium thiosulfate, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting product was purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane, 1:9) to afford the pure allyl or alkynyl derivative (Table 1, entry **3h**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.31 (d, 1H, J = 3.6 Hz), 2.95 (m, 1H), 2.13 (m, 4H), 1.84 (t, 2H, J = 7.2 Hz), 1.76 (t, 2H, J = 8.0 Hz), 1.64 (s, 3H), 1.44 (m, 4H), 0.96 (t, 3H, J = 6.8 Hz). EIMS:*m*/*z*: 176 [M^+], 134, 95, 91, 43. HRMS (LSIMS): calcd for $C_{13}H_{20}$ [M^+]: 176.1565, found: 176.1563. (entry **3l**): IR (KBr): υ 3055, 3027, 2907, 1597, 1440, 1108, 967 cm^{-1} 1H NMR (200 MHz, $CDCl_3$): δ 5.76 (m, 1H), 5.38 (brs, 1H), 4.98 (dd, 2H, J = 2.0, 4.2 Hz), 4.67 (s, 2H), 2.35 (m, 1H), 2.18 (m, 1H), 2.02 (m, 3H), 1.87 (m, 1H), 1.71 (s, 3H), 1.69 (s, 3H), 1.42 (m, 1H). ^{13}C NMR (50 MHz, proton decoupled): 20.5, 21.6, 30.4, 35.4, 36.9, 38.6, 76.2, 108.1, 115.5, 121.7, 137.8, 149.9, 216.1. EIMS: *m*/*z*: 176 [M^+], 174, 134, 107, 93, 91, 69, 54, 42. HRMS (LSIMS): calcd for $C_{13}H_{20}$ [M^+]: 176.1565, found: 176.1562. $[\alpha]^{25}$ −2.27 (*c* 0.55 $CHCl_3$). (entry **3m**): ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.36–7.25 (m, 5H), 5.46 (brs, 1H), 4.72 (s, 2H), 3.14 (brs, 1H), 2.49 (m, 1H), 2.32 (m, 2H), 2.15 (m, 2H), 1.78 (s, 3H) 1.85 (s, 3H). EIMS: *m*/*z*: 236 [M^+], 194, 160, 119, 92, 41. HRMS (LSIMS): calcd for $C_{18}H_{20}$ [M^+]: 236.1565, found: 236.1560. $[\alpha]^{25}$ −5.5 (*c* 0.50 $CHCl_3$).