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The first example of alkynylation of propargylic alcohols with alkynylsilanes catalyzed by molecular iodine

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Abstract

Aryl propargyl alcohols undergo smooth alkynylation with alkynylsilanes in the presence of 10 mol % of iodine under mild and neutral conditions to produce 1,4-diynes in excellent yields with high selectivity. The use of readily available molecular iodine makes this method simple, convenient, cost-effective and practical.

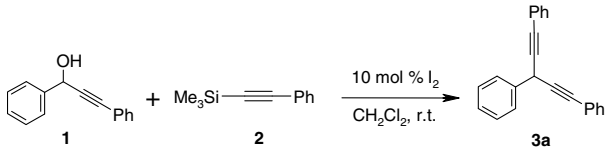
Keywords: Aryl propargyl alcohols; Alkynylation; Molecular iodine; 1,4-Diynes

The stereoselective addition of allylsilanes to aldehydes, referred to as the Sakurai–Hosomi reaction has been recognized as an efficient method for carbon–carbon bond formation and has been applied extensively in organic synthesis, especially in natural products synthesis.[1,2] Lewis 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] Aryl propargylic methanols are well-known carbon electrophiles capable of reacting with various nucleophiles and their ability to undergo nucleophilic substitution reactions contributes largely to their synthetic value.[4,5] However, there have been no reports on the direct nucleophilic substitution of aryl propargylic alcohols with alkynyltrimethylsilane.

Molecular iodine has received considerable attention in organic synthesis because of its high tolerance to air and moisture, low-cost, nontoxic nature and ready availability, affording the corresponding products with high selectivity in excellent yields. The mild Lewis acidity associated with iodine has led to its use in organic synthesis using catalytic to stoichiometric amounts.[6]

In continuation of our interest on the use of molecular iodine for various transformations,[7] we herein report for the first time, a direct and metal-free nucleophilic substitution of aryl propargyl alcohols with alkynylsilanes using molecular iodine as a novel catalyst. As a preliminary study, 1,3-diphenyl-2-propyn-1-ol (**1**) was treated with phenyl(trimethylsilyl)acetylene (**2**) in the presence of 10 mol % of molecular iodine. The reaction went to completion at room temperature in 3 h and the product, 1,4-diyne **3a** was obtained in 96% yield (Scheme 1).

Other alkynylsilanes such as 1,4-bis(trimethylsilyl)-butadiyne and bis(trimethylsilyl)acetylene also reacted well with 1,3-diphenyl-2-propyn-1-ol under the influence of molecular iodine (Table 1, entries b and c). The remarkable catalytic activity of iodine provided the incentive for further study of reactions with various other propargyl alcohols. Aryl propargyl methanols such as 3-phenyl-1-(thien-2-yl)prop-2-yn-1-ol, and 1-(2,5-dimethoxyphenyl)-



Scheme 1. Preparation of product **3a**.

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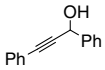
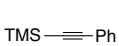
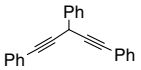
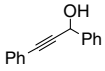
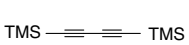
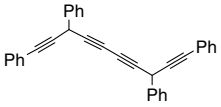
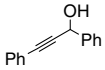
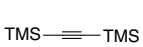
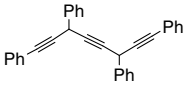
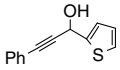
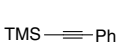
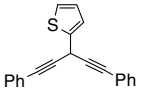
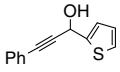
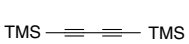
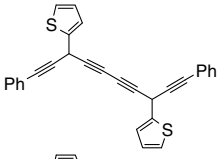
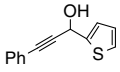
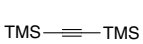
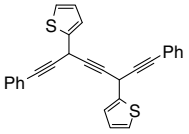
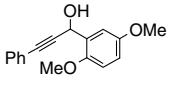
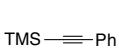
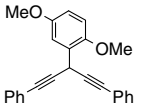
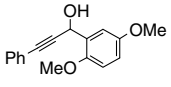
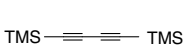
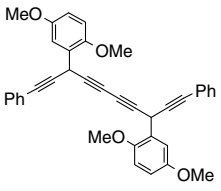
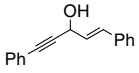
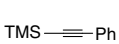
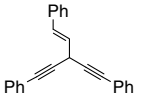
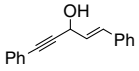
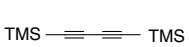
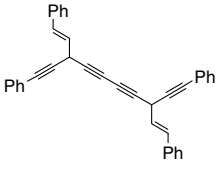
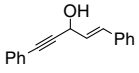
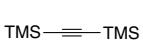
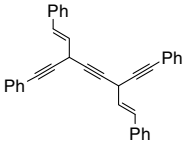
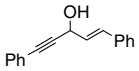
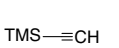
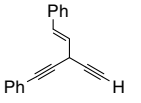
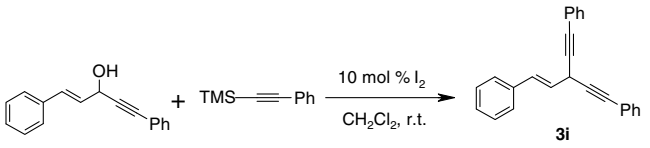
Table 1
Iodine-catalyzed alkynylation of propargylic alcohols

Entry	Propargyl alcoho	TMS–alkyne	Product[a]	Time (h)	Yield[b] (%)
a				3.0	96
b				3.5	90
c				3.0	93
d				1.5	97
e				2.0	96
f				3.0	95
g				2.0	93
h				2.5	90
i				2.5	90
j				3.5	88
k				3.0	90
l				4.0	80

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



Scheme 2. Preparation of **3i**.

3-phenylprop-2-yn-1-ol underwent smooth coupling with alkynylsilanes to produce the corresponding 1,4-diynes in excellent yields (Table 1, entries d–h). In addition, doubly activated (*E*)-1,5-diphenyl-1-penten-4-yn-3-ol also underwent facile nucleophilic substitution with alkynylsilanes to furnish the respective 1,4-enediynes (Scheme 2, Table 1, entries i–l).

In all the cases, the reactions proceeded smoothly at room temperature under the influence of 10 mol % of iodine. This method is compatible with aryl alkyl ethers, alkynes and alkenes present in the molecule. It should be noted that alkynylation of all the substrates led exclusively to the formation of propargylic products and no traces of allenic side products were detected. As a solvent, dichloromethane gave the best results compared to THF, 1,4-dioxane and acetonitrile. All the products were characterized by ^{1}H, ^{13}C NMR, IR and mass spectrometry. The scope and generality of this process are illustrated in Table 1.[8]

However, in the absence of iodine, the reaction did not proceed even after a long reaction time. Interestingly, the use of a catalytic amount of TMSI was found to be an equally effective catalyst for this conversion. However, the use of alkynyltri-*n*-butyltin in place of the alkynylsilane did not yield the desired product under these reaction conditions, perhaps because iodine does not interact with allyltri-*n*-butyltin. Thus, the combination of allyltrimethylsilane and iodine is a useful system for alkynylation of propargyl alcohols.[9] No additives or activators are required for the activation of the –OH group. The advantages of this method are the ready availability of alcohols and no salt formation.

In summary, we have described a novel and an efficient protocol for the alkynylation of aryl propargyl alcohols using molecular iodine as the catalyst. In addition to its efficiency, simplicity and mild reaction conditions, this method provides excellent yields of 1,4-diynes with high selectivity, which makes it a useful and attractive process for the direct substitution of propargyl alcohols with alkynylsilanes.

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8. *General procedure*: To a stirred solution of 3-phenyl-1-thien-2-ylprop-2-yn-1-ol (1 mmol) and phenyl(trimethylsilyl)acetylene (1 mmol) in dichloromethane (10 mL), iodine (10 mol %) was added at 0 °C and the mixture was stirred for the appropriate time at this temperature. After complete conversion as indicated by TLC, the reaction mixture was quenched with water (10 mL) and extracted with dichloromethane (3 × 15 mL). The combined extracts were washed with a 15% solution of aqueous sodium thiosulfate, dried over anhydrous Na_2SO_4 concentrated in vacuo and purified by column chromatography on silica gel (Merck 60–120 mesh, ethyl acetate–hexane, 1:9) to afford pure 2-(3-phenyl-1-phenylethynylprop-2-ynyl)thiophene. Spectral data for selected products:
2-(1,5-Diphenylpenta-1,4-diyn-3-yl)thiophene (d): Liquid, IR (KBr): *v* 3063, 2922, 2853, 1734, 1632, 1441, 1233, 1073, 1031, 839, 755, 695, 599 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$,): δ 7.60 (q, 2H, $J = 1.6$ Hz), 7.27–7.40 (m, 10H), 7.10 (t, 1H, $J = 4.5$ Hz), 5.80 (s, 1H). ^{13}C NMR (proton decoupled, 75 MHz, $CDCl_3$): δ 132.0, 131.7, 128.8, 128.6, 128.4, 127.1, 126.9, 126.6, 126.4, 125.8, 125.3, 100.1, 99.8, 52.5. EIMS: *m/z*: ($M+H^+$): 299. ESI-HRMS calcd for $C_{13}H_9S$ (M^+-101): 197.0424. Found: 197.0419.
1,4-Dimethoxy-2-(1,5-diphenylpenta-1,4-diyn-3-yl)benzene (g): Liquid, IR (KBr): *v* 2924, 2854, 1723, 1602, 1496, 1457, 1235, 1046, 751 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.77 (s, 3H), 3.88 (s, 3H), 5.66 (s, 1H), 6.56 (s, 1H), 6.85–6.75 (m, 3H), 7.63–7.09 (m, 9H). ^{13}C NMR (proton decoupled, 75 MHz, $CDCl_3$): δ 127.7, 127.5, 127.1, 126.5, 123.5, 123.1, 122.8, 113.9, 112.8, 112.1, 57.7, 56.5, 55.6. ESIMS: *m/z*: (M^+): 352. ESI-HRMS calcd for $C_{25}H_{21}O_2$ ($M+H^+$): 353.0943. Found: 353.0931.
1,5-Diphenyl-3-(2-phenylethynyl)pent-1-ene-4-yne (i): Liquid, IR (KBr): *v* 3023, 2923, 2854, 2167, 1630, 1485, 1440, 1283, 1096, 1026, 950, 855, 756, 694, 648, 610 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.20 (d, 1H, $J = 9.8$ Hz), 6.40–6.60 (m, 2H), 7.10–7.55 (m, 15H). ^{13}C NMR (proton decoupled, 75 MHz, $CDCl_3$ + DMSO): δ 167.1, 151.5, 99.0, 33.2, 30.5, 30.3, 28.3, 27.4, 23.7, 21.3, 12.9. EIMS *m/z*: ($M+H^+$): 319. ESI-HRMS calcd for $C_{17}H_{13}$ (M^+-101): 217.1017. Found: 217.1018.
9. (a) Sakurai, H.; Sasaki, K.; Hosomi, A. *Tetrahedron Lett.* **1981**, *22*, 745–748; (b) Jung, M. E.; Blumenkopf, T. A. *Tetrahedron Lett.* **1978**, *19*, 3657–3660.