HI-Mediated Cyclization of *o*-Alkynylstyrenes

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o-Alkynylstyrenes cyclized in the presence of hydroiodic acid to yield polysubstituted iodoindenes. This reaction provides an efficient synthetic method for the preparation of polysubstituted iodoindenes.

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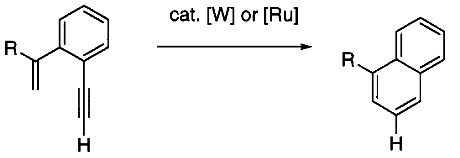
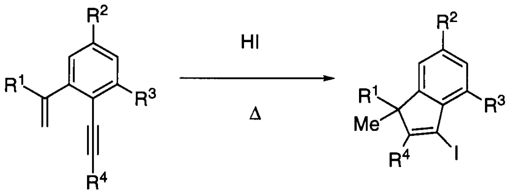
o-Ethynylstyrenes are useful precursors for the synthesis of bicyclic rings. Recent studies revealed that these compounds cyclized in the presence of transition metals to give naphthalene derivatives and related compounds in good yields (eq 1).[1] On the other hand, the cyclization of *o*-alkynylstyrenes has been studied to much less extent.[2] While we were studying the cyclization reaction of the *o*-alkynylstyrenes, we found that the cyclization reaction occurred in the presence of hydroiodic acid to yield an iodoindene. In this paper we report the preparation and HI-mediated cyclization of *o*-alkynylstyrenes (eq 2).



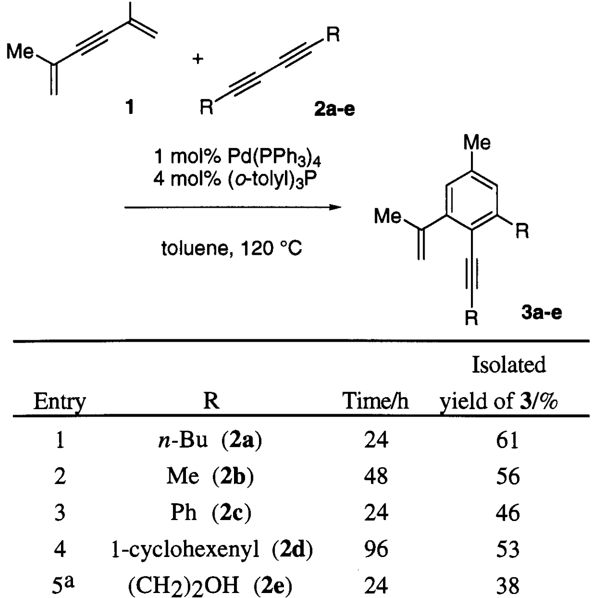
(1)



(2)

The preparation of *o*-alkynylstyrenes was carried out by the palladium catalyzed *cross*-benzannulation[3,4] of dienynes with diynes and the results are summarized in Table 1. 2,5-Dimethyl-1,5-hexadien-3-yne (**1**), which was prepared in one step by the Sonogashira coupling of 2-methyl-1-buten-3-yne with vinyl bromide, reacted in the presence of $Pd(PPh_3)_4$ and $(o\text{-tolyl})_3P$[3,4] with diyne **2a** to give polysubstituted *o*-alkynylstyrene **3a** in 61% yield (Table 1, entry 1). It was necessary to carry out the reaction at elevated temperature (120 °C), and the reactivity of **1** seems to be comparable to those of other 2,4-disubstituted enynes.[3,4] As is the case for the reaction of other conjugated enynes with diynes, the reaction proceeded in a highly regioselective manner, and **3a** was isolated as a single isomer. It is noteworthy that the *homo*-benzannulation product was not isolated, and the mode of the reaction of **1** with the diynes **2** was not affected by the presence of an additional olefinic moiety. The reactions of **1** with other diynes proceeded smoothly to give the corresponding products in good yields. Thus, the reaction of **1** with 2,4-hexadiyne **2b** gave **3b** (entry 2), and sterically hindered diynes such as **2c** and **2d** also reacted with **1** to give the polysubstituted *o*-ethynylstyrenes **3c** and **3d**, respectively, in moderate yields (entries 3, 4). The reaction proceeded even in the presence of hydroxyl group in the diyne moiety, though the yield of the product **3e** was low (38%) and a larger amount of the catalyst was employed for this reaction (entry 5). It may be possible to explain the lower yield of the product in terms of the complexation of the hydroxyl group to the palladium catalyst.

Table 1. Palladium-catalyzed *cross*-benzannulation of **1** with diynes **2**



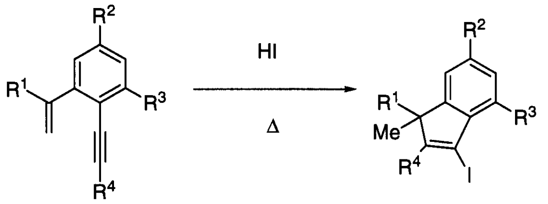
Entry	R	Time/h	Isolated yield of **3**/%
1	*n*-Bu (**2a**)	24	61
2	Me (**2b**)	48	56
3	Ph (**2c**)	24	46
4	1-cyclohexenyl (**2d**)	96	53
5[a]	$(CH_2)_2OH$ (**2e**)	24	38

[a]Larger amounts of $Pd(PPh_3)_4$ (5 mol%) and $(o\text{-tolyl})_3P$ (20 mol%) were used.

We treated the alkynylstyrenes under various conditions and found that the cyclization reaction occurred in the presence of a protic acid. Though *o*-alkynylstyrene **3a** did not cyclize in the presence of protic acids such as HCl, HBr, or CF_3SO_3H, the cyclization reaction proceeded smoothly in the presence of hydroiodic acid and the results are summarized in Table 2. Thus, compound **3a** cyclized in the presence of 1 equiv of HI (condition A) to yield iodoindene **4a** in 53% yield. The reaction also proceeded smoothly in the presence of chlorotrimethylsilane/sodium iodide (condition B),[5] and **4a** was isolated in 73% yield. The reaction of other alkynylstyrenes (**3f–h**) also proceeded efficiently, and the yields of the products were generally higher when the reaction was carried out under condition B (entries 3–8).

While we were monitoring the reaction by gas chromatography, we observed the formation of an intermediate during the reaction. In order to investigate the mechanism of this reaction, we isolated the intermediate by carrying out the reaction in toluene[6] and isolated iodovinylbenzene **5**.[7] Compound **5** react-

Table 2. HI-mediated cyclization of *ortho*-alkynylstyrenes

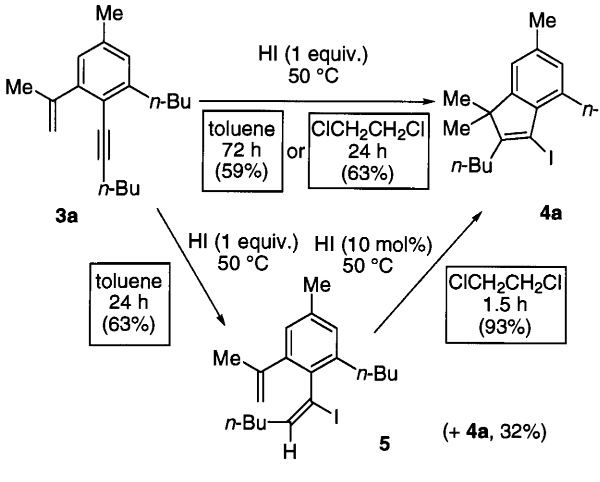


3a (R^1, R^2 = Me, R^3, R^4 = n-C_4H_9) **4a, 4f-h**
3f (R^1 = Ph, R^2, R^3 = H, R^4 = n-C_6H_{13})
3g (R^1 = Me, R^2, R^3 = H, R^4 = n-C_6H_{13})
3h (R^1 = Me, R^2, R^3, R^4 = H)

Entry	Compound	Reaction condition[a]	Time/h	Isolated yield of **4**/%
1	**3a**	A	24	53
2		B	4	73
3	**3f**	A	24	69
4		B	1	72
5	**3g**	A	24	45
6		B	3	57
7	**3h**	A	24	57
8		B	3	19[b]

[a] Condition A: a mixture of a 0.1 M (1 M = 1 mol dm^{-3}) solution of **3** in 1,2-dichloroethane and 57% (w/w) hydroiodic acid (1 equiv) was heated at 50 °C under Ar. Condition B: a mixture of a 0.7 M solution of **3** in 1,2-dichloroethane, NaI (1.2 equiv.), Me_3SiCl (1.2 equiv.), and H_2O (0.6 equiv.) was heated at 50 °C under Ar. [b] The yield was estimated by NMR.

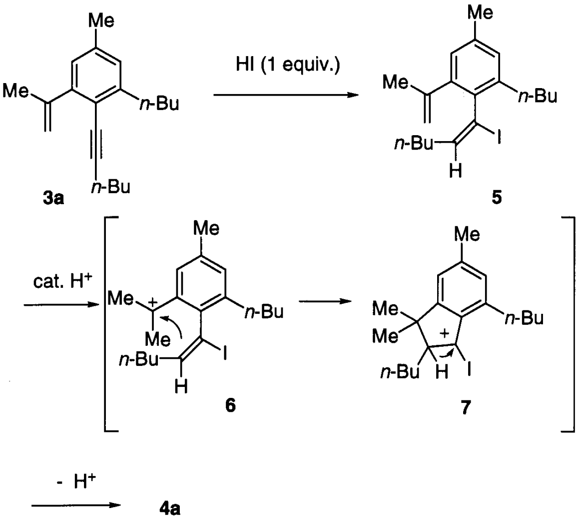
ed in the presence of a catalytic amount of hydroiodic acid to yield **4a** in good yield (eq 3).



(3)

Based on these results, we currently assume the mechanism of the cyclization as shown in Scheme 1. Thus, the regioselective addition of hydrogen iodide to **3a** would occur to give the intermediate **5**, which would be protonated to give the benzyl cation **6**. Subsequent cyclization would yield the iodobenzyl cation **7**. Proton would be eliminated from **7** and the iodoindene **4a** would be formed as the final product.

Scheme 1.



In summary, we found that the cyclization of *o*-alkynylstyrenes proceeds smoothly in the presence of hydroiodic acid under mild conditions. This reaction complements the previously known synthetic methods for the preparation of polysubstituted iodoindenes.

References and Notes

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2 A palladium-mediated cyclization of *o*-alkynylstyrenes has been reported. See, W. Münzenmaier and H. Straub, *Synthesis* **1976,** 49.

3 a) V. Gevorgyan, A. Takeda, M. Homma, N. Sadayori, U. Radhakrishnan, and Y. Yamamoto, *J. Am. Chem. Soc.*, **121**, 6391 (1999). b) V. Gevorgyan, A. Takeda, Y. Yamamoto, *J. Am. Chem. Soc.*, **119,** 11313 (1997).

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6 The rate of the reaction was much slower in this solvent.

7 Spectroscopic data of **5**: colorless oil, ^1H NMR (300 MHz, $CDCl_3$) δ 6.94 (d, 1H, *J* = 1.8 Hz), 6.80 (d, 1H, *J* = 1.5 Hz), 6.44 (t, 1H, *J* = 7.2 Hz), 5.13–5.11 (m, 1H), 4.92–4.91 (m, 1H), 2.66–2.57 (m, 2H), 2.30 (s, 3H), 2.12 (s, 3H), 1.79–1.16 (m, 8H), 0.96 (t, 3H, *J* = 7.2 Hz), 0.83 (t, 3H, *J* = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.5, 144.8, 143.0, 140.3, 137.7, 134.5, 128.5, 126.9, 115.2, 93.7, 32.7, 32.5, 32.4, 30.5, 24.1, 23.0, 22.4, 21.3, 14.0, 13.9; IR (neat) 3080, 3015, 2957, 2928, 2858, 1715, 1632, 1601, 1456, 1377, 1340, 1313, 1265, 1244, 1209, 1180, 1136, 1038, 968, 932, 895, 860, 818, 762, 719, 631 cm^{-1}; HRMS Found 396.1313. Calcd for $C_{20}H_{29}I$: 396.1313. Anal. Found: C, 60.52; H, 7.62%. Calcd for $C_{20}H_{29}I$: C, 60.61; H, 7.37%. The geometry of the double bond was determined by the observation of the coupling constant between the olefinic proton of **8**, which was prepared by the reduction (Bu_3SnH–$Pd(PPh_3)_4$) of **5**.