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Ir-Catalyzed Substitution of Propargylic-type Esters with Enoxysilanes

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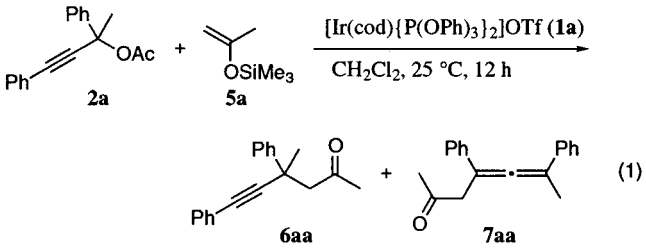
Because an acetylenic carbon−carbon triple bond plays a pivotal role in a variety of transformations,[1] the Nicholas reaction[2] has been widely accepted as a powerful tool for the construction of complex molecules.[3] Among some successful catalytic reactions to form propargylic derivatives,[4] a Ru-catalyzed process[4c] is available for carbon−carbon bond formation similar to the Nicholas reaction, where more than a stoichiometric amount of $Co_2(CO)_8$ is required. However, with this method, the substrate is limited to terminal acetylenic compounds.

We previously found that [Ir(cod)$(PR_3)_2$]OTf (**1**) modified by H_2 behaves as an active catalyst in Mukaiyama-type aldol coupling,[5] Michael coupling,[6] and the allylic substitution.[7] An enoxysilane behaves as a nucleophile in all of these reactions. These facts prompted us to design Ir-catalyzed reactions of a propargylic-type alcohol with an enoxysilane. We found that enoxysilanes work as good nucleophiles to form β-alkynyl carbonyl compounds in the presence of a catalytic amount of **1**. We describe here the successful results and scope of these reactions.

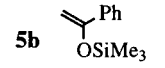
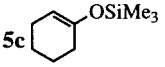
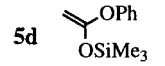
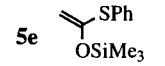
The acetoxy group of **2a** was readily substituted at 25 °C to form **6aa** in 82% yield by simple stirring of **2a** (0.5 mmol), enoxysilane (**5a**, 1.0 mmol), and **1a** (0.005 mmol), which was activated preliminarily with molecular H_2 (eq 1). Allenyl-type product **7aa** was not detected at all in this reaction. An additional product was the enyne **8a**, which is considered an elimination product. Other cationic complexes, [Ir(cod)$(PPh_3)_2$]OTf (**1b**) and [Ir(cod)(binap)]OTf, were also effective without any change in regioselectivity for this substitution, albeit they required a longer time than **1a** for the complete consumption of **2a**.



(1)

The presence of an excess amount of **5a** is crucial for sufficient conversion of **2a**. The use of 3 or 4 equiv of **5a** gave increased yields of **6aa** even with a short reaction time (entries 2 and 3 in Table 1). The rate of the reaction was appreciably accelerated with carbonate **3a** ($R^1 = R^2 = Ph$, $R^3 = Me$), although the formation of **8a** inevitably increased (entry 4 in Table 1). Other enoxysilanes, **5b**, **5c**, **5d**, and **5e**, were also suitable for the present transformation. Unfortunately, allenyl isomer **7ac** (**6ac**:**7ac** ≈ 90:10) was concomitantly formed in the reaction of **5c** (entry 6 in Table 1). This implies that bulkiness at the nucleophilic site affects the regioselectivity of this substitution.

Table 1. Ir-Catalyzed Reactions of **2a** with **5**[a]

entry	enoxysilane	mole ratio **5**/**2a**	reaction time (h)	yield (%) **6**	yield (%) **8a**
1	**5a**	2	12	**aa** 82	6
2	**5a**	3	6	**aa** 95	4
3	**5a**	4	6	**aa** 89	2
4[b]	**5a**	2	5	**aa** 84	13
5	**5b** 	4	6	**ab** 95	trace
6	**5c** 	2	24	**ac** 89[c]	2
7	**5d** 	4	6	**ad** 97	0
8	**5e** 	4	4	**ae** 93	0

[a] Reactions were carried out on a 0.5 mmol scale at 25 °C in a CH_2Cl_2 solution containing 1 mol % of **1a** activated by H_2. [b] Methyl carbonate **3a** was used instead of **2a**. [c] Isolated as a mixture of **6ac** and **7ac** (**6ac**:**7ac** ≈ 90:10).

In contrast to Nicholas reactions, a catalyst species derived from only 1 mol % of **1a** makes it possible to achieve the corresponding transformation. Thus, this procedure was applied to other types of propargylic esters **2**, **3**, and **4**, and enoxysilanes **5**. The results are summarized in Table 2. The regioselectivity that preferred the propargylic product was retained in substrates bearing *n*-butyl, Me_3-Si, or H instead of the phenyl group of **2a** (entries 1, 4, and 5 in Table 2). The presence of alkyl groups on the propargyl carbon of **2** seems to increase the proportion of the elimination route leading to **8**. In fact, **2e** and **2f** gave **8e** and **8f**, respectively, as major products in the reactions with 2 mol equiv of **5a**. However, the route to form **8** was remarkably suppressed using 4 equiv of **5a** and by low temperature (entries 6, 7, and 11 in Table 2). The yields of the substitution products seem to reflect the order of the reactivity of enoxysilanes: **5a** < **5d** < **5e** (entries 6, 8, 9, 10, 12, and 13 in Table 2).[8] The number of substituents on the propargyl carbon affects the susceptibility of **2** with **5**. When an aryl group was the sole substituent on the propargyl carbon, the reactions proceeded at an acceptable rate and with a sufficient yield of **6** (entries 14−16 in Table 2). However, **2i** ($R^1 = Ph$, $R^2 = Me$, $R^3 = H$) and **2j** ($R^1 = Ph$, $R^2 = R^3 = H$) did not react at all with **5a**. The starting **2i** and **2j** were recovered intact under conditions analogous to the reaction of **2e**. The desired transformation was accomplished using

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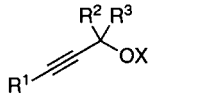
Table 2. Ir-Catalyzed Reactions of Propargylic Esters with **5**[a]

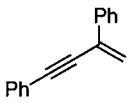
	propargylic ester					product (%)	
entry		R^1	R^2	R^3	enoxysilane[b]	**6**	**7**
1	**2b**	^{n}Bu	Ph	Me	**5a** (2)	**ba**	84	0
2	**2b**	^{n}Bu	Ph	Me	**5a** (4)	**ba**	94	0
3	**3b**	^{n}Bu	Ph	Me	**5a** (2)	**ba**	84	0
4	**2c**	Me_3Si	Ph	Me	**5a** (4)	**ca**	86	5[c]
5	**2d**	H	Ph	Me	**5a** (4)	**da**	81	0
6	**2e**	Ph	Me	Me	**5a** (4)	**ea**	66	3[c]
7[d]	**2e**	Ph	Me	Me	**5a** (4)	**ea**	84	4[c]
8	**2e**	Ph	Me	Me	**5d** (4)	**ed**	83	0
9	**2e**	Ph	Me	Me	**5e** (4)	**ee**	88	0
10	**2f**	Ph	$-(CH_2)_5-$		**5a** (4)	**fa**	33	0
11[e]	**2f**	Ph	$-(CH_2)_5-$		**5a** (4)	**fa**	72	0
12	**2f**	Ph	$-(CH_2)_5-$		**5d** (4)	**fd**	38	4[c]
13	**2f**	Ph	$-(CH_2)_5-$		**5e** (4)	**fe**	77	0
14[f]	**2g**	Ph	Ph	H	**5a** (2)	**ga**	93	0
15	**2g**	Ph	Ph	H	**5a** (3)	**ga**	95	0
16	**2h**	Ph	Naph[g]	H	**5a** (2)	**ha**	86	0
17[h]	**4i**	Ph	Me	H	**5a** (4)	**ia**	72	5[c]
18[i]	**4j**	Ph	H	H	**5a** (4)	**ja**	68	1[c]
19	**2k**	Ph	Ph	Ph	**5a** (2)	**ka**	34[c]	55
20	**2k**	Ph	Ph	Ph	**5b** (2)	**kb**	40[c]	56
21	**2k**	Ph	Ph	Ph	**5c** (2)	**kc**	0	86
22	**2k**	Ph	Ph	Ph	**5d** (2)	**kd**	49	39[c]
23	**2k**	Ph	Ph	Ph	**5e** (2)	**ke**	54	33[c]
24	**2l**	H	Ph	Ph	**5a** (2)	**la**	8	77[j]

[a] Reactions were carried out on a 0.5 mmol scale at 25 °C in a CH_2Cl_2 solution containing 1 mol % of **1a** activated by H_2. They were stopped when propargylic esters disappeared (4−24 h). [b] The number in parentheses shows the molar equivalents of **5** used. [c] Estimated from the ^{1}H NMR spectrum of the sample isolated as a mixture of **6** and **7**. [d] At 0 °C for 26 h. [e] At −20 °C for 24 h in the presence of 2 mol % of **1a**. [f] At 50 °C for 16 h. [g] 1-Naphthyl. [h] At 50 °C for 5 h in the presence of 2 mol % of **1a**. [i] At 80 °C for 2 h in the presence of 2 mol % of **1a**. [j] Allenyl product **7la** changed to dienone **9** during column chromatography on SiO_2.

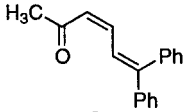
the corresponding phosphate, **4i** and **4j**, as a starting substrate under forcing conditions (entries 17 and 18 in Table 2).



2; X = Ac
3; X = CO_2Me
4; X = $P(=O)(OEt)_2$



8a



9

In sharp contrast to the above results, reverse selectivity in the regiochemistry of the substitution was observed in the reaction of **2k** and **2l**, which have two phenyl groups on the propargyl carbon (entries 19−21 and 24 in Table 2). In particular, **7kc** was isolated as the sole product in the reaction of **2k** with **5c** (entry 21 in Table 2). Ketene acetal **5d** and ketene monothioacetal **5e** retained the preferential formation of **6k** in reactions with **2k** (entries 22 and 23 in Table 2). The ratio of **6k** in the products increased with an increase in the nucleophilicity of **5**. On the other hand, steric bulkiness at the nucleophilic site is advantageous for the formation of **7**. Because the contribution of the allenyl form in the cation derived from **2k** is estimated to be 10−30% on the basis of ^{13}C NMR,[9] the selective formation of **7kc** implies the participation of thermodynamic factors. Regioselectivity aside, the present substitution of propargylic esters seems to be enhanced by the cation-stabilizing effects of the substituent on the propargyl carbon. This speculation is based on the reactivity order, **2k** > **2a** > **2b** > **2h** = **2g** > **2f** ≈ **2e**, which is roughly estimated by comparing the reaction times. The intervention of certain cationic species derived from **2** is supported by the finding that racemic **6ga** was obtained as the sole product in the respective reactions of (*S*)-**2g** (69% ee) and racemic **2g** with **5a**.

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Supporting Information Available: Experimental procedures and analytical data for new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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