Iridium-Catalyzed Addition Reactions of Ethynylsilane to Quinolines and Isoquinolines Activated by Acyl Chloride

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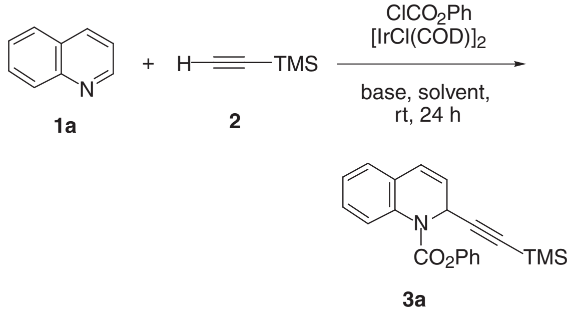
Addition reactions of ethynyltrimethylsilane to various quinolines and isoquinolines activated by acyl chloride are catalyzed with a few Ir-complexes to afford 2-trimethylsilylethynyl-1,2-dihydroquinolines and 1-trimethylsilylethynyl-1,2-dihydroisoquinolines in good to high yields.

Addition reactions of organometallic reagents to azaaromatic compounds have been of great importance for synthesizing a variety of physiologically interesting nitrogen heterocyclic compounds, including alkaloids.[1] Among them, alkyne addition reaction to quinolines activated by acyl chlorides have attracted much attention for synthesis of Dynemicin A possessing antitumor activity.[2] All of these reactions, however, utilize stoichiometric amounts of alkynyl organometallic reagents.[2,3] We wish to report here Ir-catalyzed addition reactions of ethynylsilane to quinolines and isoquinolines activated by acyl cholride.[4]

When quinoline (**1a**) activated by phenyl chloroformate was treated with ethynyltrimethylsilane (**2**) in the presence of $[IrCl(COD)]_2$ (5 mol %) in THF, 2-(2-trimethylsilylethynyl)-1,2-dihydroquinoline (**3a**) was obtained in 13% yield. However, addition of base (1 equiv.) greatly improved the yield of **3a** (Scheme 1). The results on the base and the solvent used are summarized in Table 1.



Scheme 1.

As shown in Table 1, addition of 2,6-lutidine (1 equiv.) as the base gave the best result and THF was the solvent of choice. We next examined the amount of the catalyst and a couple of Ir-complexes in order to find more effective catalytic system. The results are summarized in Table 2, indicating that the amount of the catalyst can be reduced to 1 mol % at elevated reaction temperature with high chemical yield (Run 3). It is also shown that other Ir–COD complexes are effective (Runs 4,5), while Cp*–Ir complex is not (Run 6).

Since the catalytic system seemed to be optimized in our hand, various quinolines with functional groups were subjected to the present catalytic system (Scheme 2). The results are summarized in Table 3.[5]

Table 1. Ir-catalyzed addition reactions of **2** to **1a** activated by phenyl chloroformate

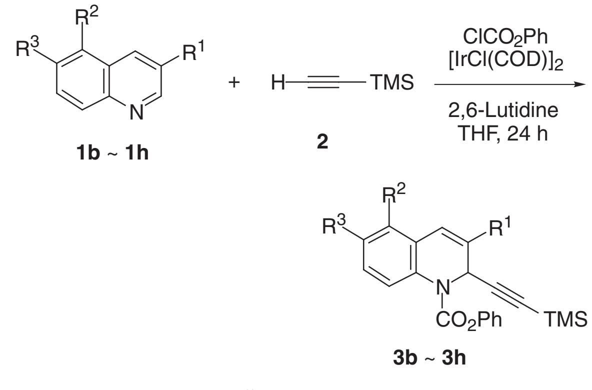
Run	Base	Solvent	Yield / %[a]
1	none	THF	13
2	Et_3N	THF	32
3	2,4,6-collidine	THF	66
4	2,6-lutidine	THF	74
5	2,6-lutidine	CH_3CN	13
6	2,6-lutidine	Et_2O	10

[a]Isolated yield.

Table 2. Ir-catalyzed addition reactions of **2** to **1a** activated by phenyl chloroformate under various conditions

Run	Catalyst	Amount / mol %	Temp / °C	Yield / %[a]
1	$[IrCl(COD)]_2$	5	rt	74
2	$[IrCl(COD)]_2$	5	50	85
3	$[IrCl(COD)]_2$	1	65	81
4	$[Ir(OMe)(COD)]_2$	1	65	74
5	$[Ir(OPh)(COD)]_2$	1	65	79
6	$[Cp^*IrCl_2]_2$	1	65	43[b]

[a]Isolated yield. [b]NMR yield.



Scheme 2.

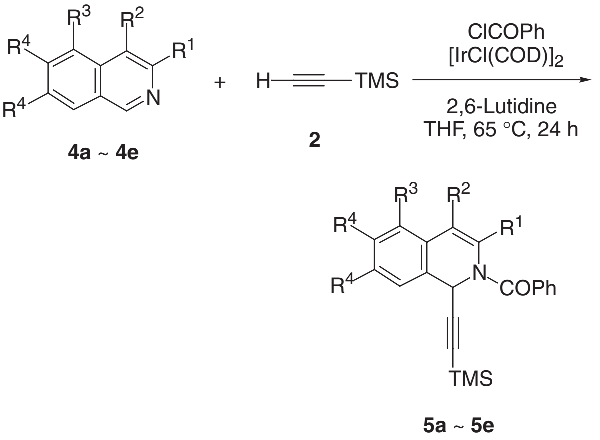
When an electron-donating group was substituted in quinoline ring, the reactions took place smoothly (Runs 1, 7). On the other hand, when an electron-withdrawing group was placed on the ring, addition of AgOTf improved the yields of the adducts (Runs 2–6), probably owing to the facilitation of the formation of quinolinium ions.[6]

The Ir-catalyzed addition reactions of **2** to isoquinolines were sluggish, but we found that the reactions proceeded when benzoyl chloride was used as an activator (Scheme 3). The re-

Table 3. Ir-catalyzed addition reactions of **2** to various quinolines activated by phenyl chloroformate[a]

Run	R^1	R^2	R^3	Amount of Catalsyt /mol %	Additive /mol %	Temp / °C	Product	Yield / %[b]
1	Me	H	H	1	—	65	**3b**	79
2	Br	H	H	1	—	65	**3c**	13
3	Br	H	H	5	AgOTf (10)	rt	**3c**	80
4	CN	H	H	5	AgOTf (10)	rt	**3d**	58
5	H	NO_2	H	5	AgOTf (10)	rt	**3e**	65
6	H	H	NO_2	1	AgOTf (5)	65	**3f**	70
7	H	H	OMe	1	—	65	**3g**	71
8[c]	H	H	OH	1	AgOTf (5)	65	**3h**[d]	69

[a]A solution of quinoline (1.0 mmol) and phenyl chloroformate (1.5 mmol) (and AgOTf, if any) in THF (1 mL) was stirred for 30 min and then to this solution were added 2,6-lutidine (1.0 mmol), **2** (1.5 mmol) and $[IrCl(COD)]_2$ (1–5 mol %). The mixture was stirred at the temperature indicated for 24 h. After usual work-up, column chromatography on silica-gel gave the product. [b]Isolated yield. [c]2.5 equiv. of $ClCO_2Ph$ was used. [d]The product was phenyl carbonate ester of the adduct.



Scheme 3.

sults are summarized in Table 4. In these reactions, 5 mol % of the iridium complex was needed in order to obtain good yields of the adducts. In similar to the above, an electron-withdrawing substituent on isoquinoline ring retarded the reaction and addition of AgOTf (0.1 equiv.) improved the yield (Runs 3, 4).

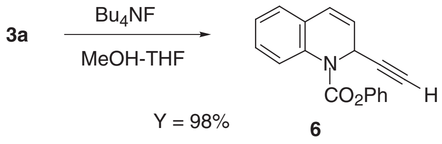
The trimethylsilylethynyl substituted 1,2-dihydroquinolines and -isoquinolines thus obtained could be valuable synthetic intermediates, because several transformations of alkynylsilanes have been well known.[7] For example, desilation of **3a** with TBAF gave 1-ethynyl-1,2-dihydroquinoline (**6**) in almost quantitative yield, as shown in Scheme 4.

In summary, we have shown the first iridium-catalyzed addition reactions of ethynyltimethylsilane to azaaromatic compounds, providing a new catalytic pathway to obtain 2-trimethylsilylethynyl-1,2-dihydroquinolines and 1-trimethylsilylethynyl-1,2-dihydroisoquinolines in good to high yields.[8]

Table 4. Ir-catalyzed addition reactions of **2** to various isoquinolines activated by benzoyl chlorode[a]

Run	R^1	R^2	R^3	R^4	Product	Yield / %[b]
1	H	H	H	H	**5a**	82
2	Me	H	H	H	**5b**	80
3[c]	H	Br	H	H	**5c**	66
4[c]	H	H	NO_2	H	**5d**	61
5	H	H	H	OMe	**5e**	81

[a]5 mol % of $[IrCl(COD)]_2$ was used. [b]Isolated yield. [c]AgOTf (0.1 equiv.) was added.



Scheme 4.

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8 The reactions with alkynes other than **2** were unsuccessful.

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