Iridium-Catalyzed Regioselective Reaction of 1-Naphthols with Alkynes at the *peri*-Position

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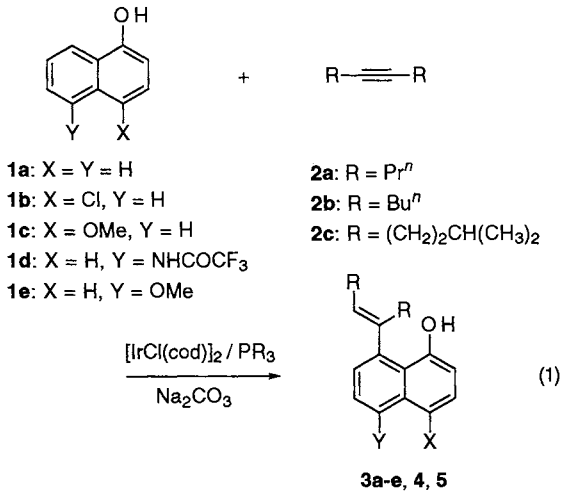
1-Naphthols efficiently couple with internal alkynes in the presence of an iridium catalyst to selectively afford the corresponding 8-substituted 1-naphthol derivatives.

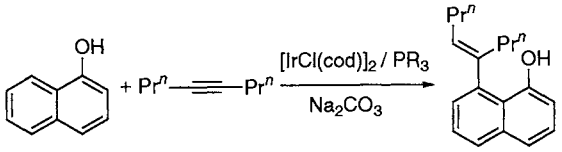
The activation of C-H bonds in organic compounds by transition-metal complexes is currently one of the most significant subjects in organometallic chemistry. An effective strategy to regioselectively activate an aromatic C-H bond by transition-metal complexes is to introduce a functional group having ligating ability at an appropriate position of a given aromatic substrate.[1] Recently, a number of catalytic coupling reactions of aromatic compounds bearing carbonyl or nitrogen-containing groups with alkenes and/or alkynes involving such a C-H bond activation mode as the key step have also been successfully developed.[2,3] Meanwhile, we have recently reported that intermolecular arylation reactions of 2-phenylphenols and 1-naphthols with aryl halides using palladium catalysts can regioselectively take place at the spatially neighboring positions of phenolic function to give 2-(2'-arylphenyl)phenols and 8-aryl-1-naphthols, respectively.[4] The coordination of phenolic oxygen to intermediary arylpalladium species is consider to be the key for the reactions via C-H bond cleavage.[5] The latter reaction using 1-naphthols seems to be of particular interest since it has been known to be difficult to achieve direct C-C coupling at their 8-position owing to *peri*-strain.[6] In the course of our study to extend this unique substitution reaction, we found that 1-naphthols also react efficiently with internal alkynes in the presence of an iridium catalyst to give the corresponding 8-substituted products (Eq. 1).



3a-e, 4, 5

When 1-naphthol (**1a**) (2 mmol) was treated with 4-octyne (**2a**) (2 mmol) in the presence of $[IrCl(cod)]_2$ (0.01 mmol, 0.5 mol%), PPh_3 (0.04 mmol), and Na_2CO_3 (0.1 mmol) in refluxing toluene for 5 h, a small amount of 8-[(*E*)-1-propyl-1-pentenyl]-1-naphthol (**3a**) was produced (Entry 1 in Table 1).[7] Reaction efficiency was found to be sensitive to the identity of added phosphine ligands. Thus, the use of $P(o\text{-Tol})_3$ in place of PPh_3 improved the product yield up to 64% (Entry 2). Since the reaction using $P(cyclo\text{-}C_6H_{11})_3$ gave a similar result (Entry 3), sterically hindered phosphine ligands appear to be suitable for the present reaction. Expectedly, in the case using a further bulky phosphine, PBu^t_3, **3a** was formed in a yield of 83% within 2 h (Entry 4). While increase in the amount of PBu^t_3 to 0.09 mmol did not affect the product yield (Entry 5), the coupling was suppressed by elimination of Na_2CO_3 (Entry 6). The reaction was sluggish in refluxing benzene (Entry 7). In our previous study, it has been shown that the cross-coupling of salicylaldehydes with alkynes can efficiently take place by using $[RhCl(cod)]_2$-dppf-Na_2CO_3 catalyst system.[5c,d] For the present reaction, however, either this or $[RhCl(cod)]_2$-PBu^t_3-Na_2CO_3 system was ineffective.

Table 1. Reaction of 1-naphthol (**1a**) with 4-octyne (**2a**)[a]



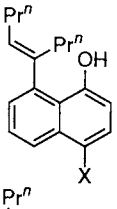
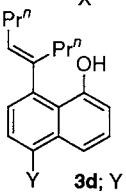
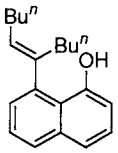
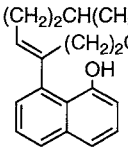
1a **2a** **3a**

Entry	PR_3 (mmol)	Time / h	Yield of **3a**[b] / %[c]
1	PPh_3 (0.04)	5	2
2	$P(o\text{-Tol})_3$ (0.04)	5	64
3	$P(cyclo\text{-}C_6H_{11})_3$ (0.04)	5	56
4	PBu^t_3 (0.03)	2	83
5	PBu^t_3 (0.09)	5	84
6[d]	PBu^t_3 (0.03)	2	tr.
7[e]	PBu^t_3 (0.03)	50	45

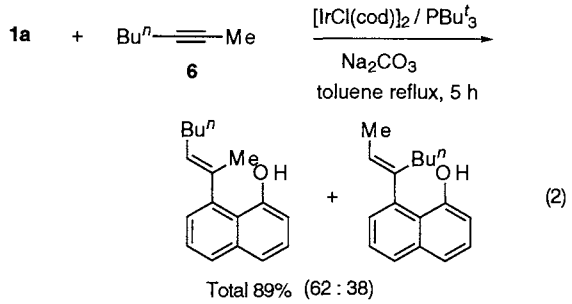
[a]Reaction conditions: **1a** (2 mmol), **2a** (2 mmol), $[IrCl(cod)]_2$ (0.01 mmol), Na_2CO_3 (0.1 mmol), in refluxing toluene (5 cm^3) under nitrogen. [b]The structure was unambiguously determined by its 2D-NMR spectra and NOE experiments. [c]GLC yield. [d]Reaction in the absence of Na_2CO_3. [e]Reaction in refluxing benzene (5 cm^3).

Table 2 summarizes the results for the reactions of a number of substituted 1-naphthols and of internal alkynes. All of examined 1-naphthols bearing electron-withdrawing or -donating groups at 4- or 5-position **1b-e** with **2a** gave the corresponding 8-substituted products **3b-e**. The reactions of **1a** using alkynes **2b** and **2c** in place of **2a** also gave compounds **4** and **5**. The reaction of **1a** with an unsymmetrical alkyne, 2-heptyne (**6**), gave a mixture of two regioisomers (Eq. 2).

Table 2. Reaction of 1-naphthols **1** with alkynes **2**[a]

1	2	Time / h	Product[b]	Yield / %[c]
1b	**2a**	2	 **3b**; X = Cl	93 (42)[d]
1c	**2a**	3	**3c**; X = OMe	67 (54)[d]
1d	**2a**	2	 **3d**; Y = $NHCOCF_3$	85 (44)[d]
1e	**2a**	5	**3e**; Y = OMe	82 (42)[d]
1a	**2b**	2	 **4**	73 (41)
1a	**2c**	2	 **5**	75 (61)

[a]Reaction conditions: **1** (2 mmol), **2** (2 mmol), $[IrCl(cod)]_2$ (0.01 mmol), PBu^t_3 (0.03 mmol), Na_2CO_3 (0.1 mmol) in refluxing toluene (5 cm^3) under nitrogen. [b]Satisfactory spectra were obtained in measurements of ^1H and ^{13}C NMR and MS. [c]GLC yield. Value in parentheses indicates yield after isolation. [d]Isolated after acetylation with Ac_2O in pyridine.



The present reaction may involve initial coordination of **1** to a chloroiridium(I) species to form a naphtholate complex accompanied by liberation of HCl and then oxidative addition of the aromatic C-H bond at 8-position to the metal center to give an arylhydridoiridium(III) species as the key steps.[8] A possible role of the added base, Na_2CO_3, seems to be removal of initially formed HCl, as was proposed for the rhodium-catalyzed reaction of salycylaldehydes.[5c,d] The origin of high efficiency of sterically hindered phosphines as ligand, however, is not definitive at the present stage.

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References and Notes

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7 Typical experimental procedure: A mixture of **1a** (288 mg, 2 mmol), **2a** (220 mg, 2 mmol), $[IrCl(cod)]_2$ (7 mg, 0.01 mmol), PBu^t_3 (6 mg, 0.03 mmol), Na_2CO_3 (11 mg, 0.1 mmol), and 1-methylnaphthalene (ca. 100 mg, internal standard) in refluxing toluene (5 cm^3) was stirred under nitrogen for 2 h. After cooling, the reaction mixture was extracted with diethyl ether, and dried over sodium sulfate. GLC and GLC-MS analyses confirmed formation of **3a** in 83% yield. Product **3a** (303 mg, 60%) was also isolated by column chromatography on silica gel using hexane-ethyl acetate as eluent. **3a**: oil; ^1H NMR (400 MHz, $CDCl_3$) δ = 0.88 (3H, t, J = 7.3 Hz), 1.01 (3H, t, J = 7.3 Hz), 1.25-1.45 (2H, m), 1.53 (2H, qt, J = 7.3, 7.3 Hz), 2.22-2.65 (4H, m), 5.80 (1H, t, J = 7.3 Hz), 6.93 (1H, dd, J = 1.2, 7.3 Hz), 7.03 (1H, dd, J = 1.2, 7.1 Hz), 7.32-7.36 (2H, m), 7.40 (1H, dd, J = 1.2, 8.3 Hz), 7.60 (1H, s), 7.72 (1H, dd, J = 1.2, 8.3 Hz). MS *m/z* 254 (M^+).

8 A similar arylhydridometal intermediate was proposed in the rhodium-catalyzed coupling of 1,2-diaryldiazenes with alkynes: see Ref. 3b.