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Rhodium-catalyzed direct *ortho*-alkenylation of phenyl sulfones with alkynes utilizing sulfonyl function as modifiable directing group

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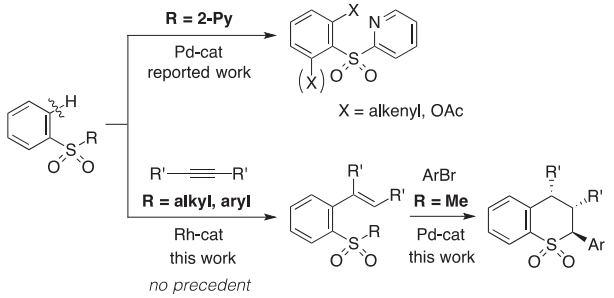
ABSTRACT

The *ortho*-selective alkenylation of phenyl sulfones with alkynes proceeds effectively in the presence of a cationic Cp*-rhodium(III) catalyst together with an appropriate carboxylic acid involving regioselective C–H bond cleavage directed by the sulfonyl function. An (*ortho*-alkenylated phenyl) methyl sulfone prepared by this hydroarylation method undergoes palladium-catalyzed α-arylation and subsequent diastereoselective cyclization to directly produce the corresponding thiochromane 1,1-dioxide derivatives.

1. Introduction

Transition-metal-catalyzed direct C–H functionalization reactions of aromatic substrates have received much attention as environmentally-benign synthetic methods, because they provide atom- and step-economical routes from simple arenes to functionalized aromatic molecules.[1] Especially, the chelation-assisted version involving a C–H bond cleavage step with the assistance of a directing group, which leads to regioselective *ortho*-substitution, is highly useful in precise synthesis. As typical directing groups, oxygen- and nitrogen-containing groups have been utilized. Besides them, sulfur-containing functions are beginning to be employed as directing groups. Several examples for sulfide- and sulfoxide-directed C–H functionalization reactions have been recently reported by us[2] and others.[3] However, the utilization of sulfonyl groups, which can be readily introduced onto aromatic rings via electrophilic sulfonylation, has been less explored. So far, the palladium-catalyzed *ortho*-alkenylation[4] and –acetoxylation[5] employing a (2-pyridyl)sulfonyl group have been examined, the efficiency and selectivity being less acceptable. In these examples, coordination of the pyridyl function rather than the sulfonyl moiety seems to be the key for the *ortho*-functionalization. Other sulfonyl groups containing no pyridyl moiety have, to our knowledge, never been utilized as effective directing groups. During our continuous studies of rhodium-catalyzed C–H functionalization,[1t] we succeeded in finding that simple phenyl sulfones undergo direct alkenylation upon treatment with internal alkynes[2,6] in the presence of a rhodium catalyst through C–H bond cleavage directed by their sulfonyl group to produce *ortho*-alkenylated phenyl sulfones (Scheme 1). In these reactions, simple alkyl- and aryl sulfonyl functions without any pyridyl group could act as effective directing groups. Various *ortho*-substituted phenyl sulfone derivatives have recently drawn much attention because of their biological activities as well as their utilities as useful ligands for transition-metals.[7] Therefore, the present reaction provides a straightforward



Scheme 1. *ortho* C–H Functionalization of phenyl sulfones.

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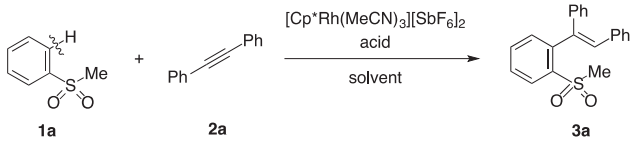
approach toward such an important class of compounds. Furthermore, the sulfonyl directing group was found to be readily modified after the *ortho*-alkenylation through palladium-catalyzed α-arylation[8,9] and subsequent diastereoselective cyclization to afford the corresponding 2-arylthiochromane 1,1-dioxide derivatives. These new findings are described herein.

2. Results and discussion

In an initial attempt, methyl phenyl sulfone (**1a**) (0.5 mmol) was treated with diphenylacetylene (**2a**) (0.25 mmol) in the presence of $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.01 mmol) and PivOH (0.1 mmol, PivOH=pivalic acid) in chlorobenzene (1 mL) at 140 °C for 24 h under N_2. As a result, (*E*)-2-(1,2-diphenylethenyl)phenyl methyl sulfone (**3a**) was formed in 23% yield (entry 1 in Table 1). Increasing the amount of **1a** to 0.75 mmol somewhat improved the yield of **3a** to 42% (entry 2). It is conceivable that the addition of an excess amount of **1a** stands by the relatively low coordination ability of **1a**. While a similar result was obtained in $C_6H_5CF_3$ (entry 3), the reaction efficiencies were low in *o*-dichlorobenzene and diglyme (entries 4 and 5). The use of 1-$AdCO_2H$ (0.1 mmol, 1-$AdCO_2H$=1-adamantanecarboxylic acid) in place of PivOH significantly enhanced the yield of **3a** up to 66% (entry 6). In contrast, $C_6F_5CO_2H$ was less effective to decrease the reaction efficiency (entry 7). In the absence of any acids, the reaction hardly proceeded (entry 8). In addition, it was confirmed that a neutral rhodium complex, $[Cp^*RhCl_2]_2$, did not show any catalytic activity at all (entry 9).

Table 1
Reaction of methyl phenyl sulfone (**1a**) with diphenylacetylene (**2a**)[a]



1a 2a 3a

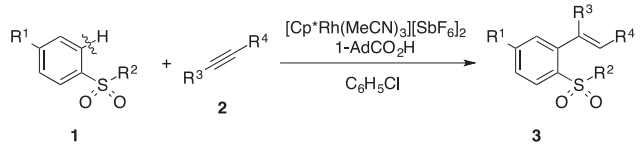
Entry	Acid	Solvent	Yield of **3a** (%)[b]
1[c]	PivOH[d]	C_6H_5Cl	23
2	PivOH	C_6H_5Cl	42
3	PivOH	$C_6H_5CF_3$	43
4	PivOH	*o*-$C_6H_4Cl_2$	21
5	PivOH	Diglyme	7
6	1-$AdCO_2H$[e]	C_6H_5Cl	66 (63)
7	$C_6F_5CO_2H$	C_6H_5Cl	14
8	—	C_6H_5Cl	5
9[f]	1-$AdCO_2H$	C_6H_5Cl	0

[a] Reaction conditions: **1a** (0.75 mmol), **2a** (0.25 mmol), $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.01 mmol), acid (0.1 mmol), in solvent (1 mL) at 140 °C for 24 h under N_2, unless otherwise noted.
[b] GC yield based on the amount of **2a** used. Value in parentheses indicates yield after purification.
[c] Using **1a** (0.5 mmol).
[d] PivOH=pivalic acid.
[e] 1-$AdCO_2H$=1-adamantanecarboxylic acid.
[f] Using $[(Cp^*RhCl_2)_2]$ (0.005 mmol) in place of $[Cp^*Rh(MeCN)_3][SbF_6]_2$.

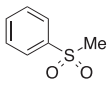
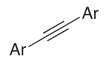
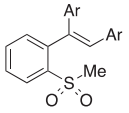
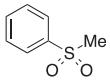
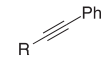
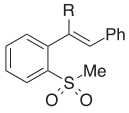
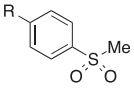
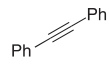
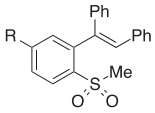
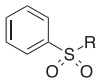
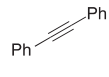
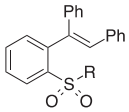
With the effective reaction conditions in hand, we next examined the substrate scope for the reaction of phenyl sulfones **1** with alkynes **2** (Table 2). The reactions of 4,4′-disubstituted diphenylacetylenes **2b**–**d** with **1a** gave the corresponding *ortho*-alkenylated phenyl sulfones **3b**–**d** in moderate to good yields (entries 1–3). Unsymmetrical alkynes, 1-phenyl-1-hexyne (**2e**) and 1-phenyl-1-propyne (**2f**), also reacted with **1a** to produce **3e** and **3f**, albeit with moderate to low yields (entries 4 and 5). Notably, no other regioisomers were detected by GC–MS at all in these cases. In contrast, treatment of ethyl 3-phenylpropiolate with **1a** did not give a desired coupling product at all.

The reactions using a series of 4-substituted phenyl sulfones **1b**–**e** with **2a** were also examined. Treatment of methyl (4-methylphenyl) sulfone (**1b**) with **2a** under standard conditions gave **3g** in 57% yield (entry 6). In contrast, the reactions of 4-methoxy- (**1c**), 4-phenoxy- (**1d**), and 4-chloro- (**1e**) substituted phenyl sulfones were somewhat sluggish. These reactions could be conducted more effectively by increasing the catalyst loading and reaction temperature in *o*-dichlorobenzene to produce **3h**–**j** in 38–59% yields (entries 7–9). Ethyl phenyl sulfone (**1f**) and diphenyl sulfone (**1g**) underwent *ortho*-alkenylation upon treatment with **2a** under standard conditions to afford **3k** and **3l** in 51 and 65% yields, respectively (entries 10 and 11).

Table 2
Reaction of phenyl sulfones **1** with alkynes **2**[a]



1 2 3

entry	1	2	product, % yield
			
1	**1a**	**2b**: Ar = 4-ClC_6H_4	**3b**: Ar = 4-ClC_6H_4, 77
2		**2c**: Ar = 4-$CF_3C_6H_4$	**3c**: Ar = 4-$CF_3C_6H_4$, 59
3		**2d**: Ar = 4-MeC_6H_4	**3d**: Ar = 4-MeC_6H_4, 46
			
4	**1a**	**2e**: R = ^{n}Bu	**3e**: R = ^{n}Bu, 47
5		**2f**: R = Me	**3f**: R =Me, 26
			
6	**1b**: R = Me	**2a**	**3g**: R = Me, 57
7[b]	**1c**: R = OMe		**3h**: R = OMe, 59
8[b]	**1d**: R = OPh		**3i**: R = OPh, 41
9[b]	**1e**: R = Cl		**3j**: R = Cl, 38
			
10	**1f**: R = Et	**2a**	**3k**: R = Et, 51
11	**1g**: R = Ph		**3l**: R = Ph, 65

[a] Reaction conditions: 1 (0.75 mmol), 2 (0.25 mmol), $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.01 mmol), 1-$AdCO_2H$ (0.1 mmol), in C_6H_5Cl (1 mL) at 140 °C for 24 h under N_2, unless otherwise noted.
[b] Using $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.02 mmol) in o-$C_6H_4Cl_2$ (1 mL) at 150 °C.

As described above, 4-chloro-substituted phenyl sulfone **1e** showed significantly lower reactivity than that of unsubstituted **1a** (entry 9 in Table 2). Therefore, we expected that unsymmetrically substituted (4-chlorophenyl) phenyl sulfone (**1h**) would react with **2a** selectively on the more reactive unsubstituted phenyl ring. However, unexpectedly, treatment of **1h** with **2a** under standard conditions gave an almost 1:1 mixture of possible alkenylated products **3m** and **3m′** (Scheme 2).

The reaction of (4-acetylaminophenyl) methyl sulfone (**1i**) with **2a** exclusively gave (4-acetylamino-3-alkenylphenyl) methyl sulfone (**3n′**). Thus, the hydrogen at the *ortho*-position of the acetylamino function[10] in **1i** is highly reactive compared to that at the