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Ru-catalyzed *ortho*-oxidative alkenylation of 2-arylbenzo[*d*]thiazoles in aqueous solution of anionic surfactant sodium dodecylbenzenesulfonate (SDBS)

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ABSTRACT

A mild and efficient Ru-catalyzed *ortho*-oxidative alkenylation of 2-arylbenzo[*d*]thiazoles through twofold C-H bond functionalization in aqueous solution of anionic surfactant sodium dodecylbenzenesulfonate (SDBS) has been developed using activated olefins as coupling partner. The protocol could be carried out smoothly on a gram scale, recyclable, and applicable to 2-arylthiazoles.

1. Introduction

Benzo[*d*]thiazoles are ubiquitous structural scaffolds in biologically natural products, agrochemicals, and pharmaceuticals that exhibit remarkable antitumor, antiviral, and antimicrobial activities.[1] In particular, 2-arylbenzo[*d*]thiazoles are widely found in a broad range of pharmaceutically active molecules.[2] For example, aryl hydrocarbon receptor agonist 2-(4-amino-3-methylphenyl)-5-fluorobenzothiazole (5F 203) can induce oxidative stress triggering DNA damage and cytoglobin up-regulation in human breast cancer cells (Fig. 1).[2a] 2-(4-*N*-[^{11}C]methylaminophenyl)-6-hydroxybenzothiazole (^{11}C PIB), is an β-amyloid PET imaging tracer for Alzheimer's disease diagnosis.[2b] In addition, 2-(3,4-dimethoxyphenyl)-5-fluorobenzothiazole (GW 610) shows potent and selective inhibitory activity against lung, colon, and breast cancer cell lines.[2g]

Directing group-assisted transition-metal-catalyzed *ortho* C–H functionalization reactions have been achieved considerable progress in organic and medicinal chemistry in the past decades.[3,4] To date, diverse functional groups including pyridine, amide, anilide, imine, imidazoline, pyrazole, oxazoline, cyano, amine, carboxylic acid, ester, ketone, and hydroxyl groups, have been used as directing groups for various C–H bond functionalizations to construct various C–C and C–X (X = O, N, halogens) bonds. Recently, we and other groups have reported many transition-metal-catalyzed benzothiazole directed *ortho* C–H bond functionalization,[4] including arylation,[4a] alkylation,[4b] acetoxylation,[4c] halogenation,[4d,e] amination,[4f] acylation,[4g-j] hydroxylation,[4k,l] nitration,[4m] trifluoromethylthiolation,[4n] and cyanation.[4o]

During the past decades, transition-metal-catalyzed C–H bond alkenylation have emerged as powerful strategies for the step-economical synthesis of unsaturated and conjugated molecules. In contrast, great success has been achieved with expensive 4d transition-metal catalysts, such as rhodium[5] or palladium[6] complexes. Recently, considerable progress has been made in this field through less expensive ruthenium[7–11] or iron[12] species catalyzed C–H coupling reaction with alkenes, as reported by Miura,[7] Ackermann,[8] Jeganmohan,[9] Dixneuf,[10] and Lei[12b] group.

It is well known that water is the ideal green solvent for organic reaction, because of its abundance, nonflammable, nontoxic, and inexpensiveness. Furthermore, great achievements showed that water could enhance the reactivities and selectivities of some reactions.[13] Given our recent interest in oxidative alkenylation-cyclization of aryl sulfonamides with acrylates,[14] and the Suzuki-

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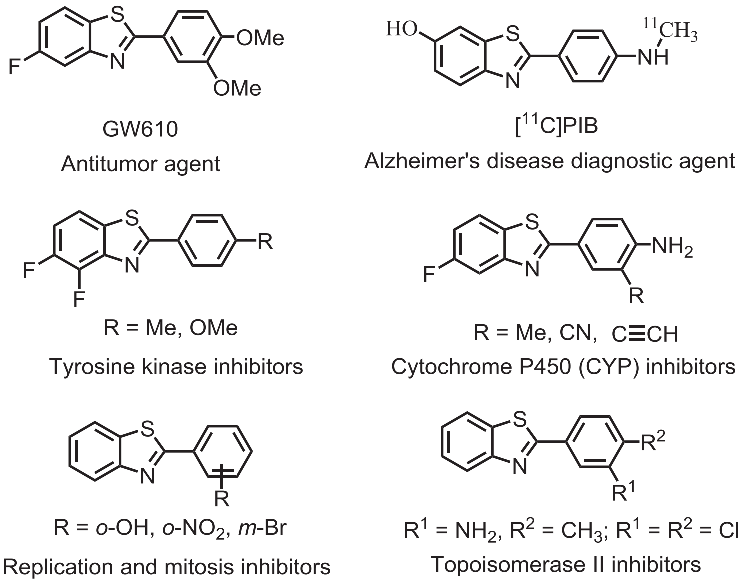


GW610
Antitumor agent

[^{11}C]PIB
Alzheimer's disease diagnostic agent

R = Me, OMe
Tyrosine kinase inhibitors

R = Me, CN, C≡CH
Cytochrome P450 (CYP) inhibitors

R = *o*-OH, *o*-NO_2, *m*-Br
Replication and mitosis inhibitors

$R^1 = NH_2$, $R^2 = CH_3$; $R^1 = R^2 = Cl$
Topoisomerase II inhibitors

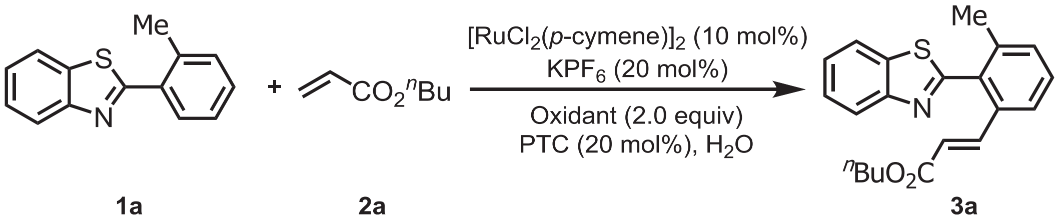
Fig. 1. Selected bioactive examples containing 2-aryl-benzothiazole scaffold.

Miyaura coupling reaction[15a] and the tandem synthesis 2-aminobenzothiazoles[15b] in aqueous, we would like to report our recent efforts towards Ru-catalyzed *ortho*-oxidative alkenylation of 2-arylbenzo[*d*]thiazoles through twofold C—H bond functionalization in aqueous solution of anionic surfactant sodium dodecylbenzenesulfonate (SDBS).

2. Results and discussion

We commenced the dehydrogenative alkenylation of 2-(*o*-tolyl)

Table 1
Optimization of Ru-catalyzed *ortho*-oxidative alkenylation of 2-(*o*-tolyl)benzo[*d*]thiazole **1a** with butyl acrylate **2a**.[a]



Entry	Oxidant (x equiv)	PTC[c]	Yield (%)[b]
1	$Cu(OAc)_2\cdot H_2O$ (2.0)	–	14
2	$Cu(OAc)_2\cdot H_2O$ (2.0)	PEG 200	30
3	AgOAc (2.0)	PEG 200	20
4	Ag_2CO_3 (2.0)	PEG 200	25
5	$K_2S_2O_8$ (2.0)	PEG 200	Trace
6	CuBr (2.0)	PEG 200	Trace
7	$Cu(OAc)_2\cdot H_2O$ (2.0)	18-Crown-6	Trace
8	$Cu(OAc)_2\cdot H_2O$ (2.0)	TMAF	35
9	$Cu(OAc)_2\cdot H_2O$ (2.0)	CTAC	25
10	$Cu(OAc)_2\cdot H_2O$ (2.0)	SDS	22
11	$Cu(OAc)_2\cdot H_2O$ (2.0)	SDBS	48
12	$Cu(OAc)_2\cdot H_2O$ (3.0)	SDBS	60
13	$Cu(OAc)_2\cdot H_2O$ (4.0)	SDBS	84
14[d]	$Cu(OAc)_2\cdot H_2O$ (2.0)	SDBS	90
15[e]	$Cu(OAc)_2\cdot H_2O$ (2.0)	SDBS	60
16[f]	$Cu(OAc)_2\cdot H_2O$ (2.0)	SDBS	80
17	$Cu(OAc)_2\cdot H_2O$ (0.5)	SDBS	43
18	$Cu(OAc)_2\cdot H_2O$ (0.2)	SDBS	16

[a] Reaction conditions: 2-(*o*-tolyl)benzo[*d*]thiazole **1a** (0.2 mmol), butyl acrylate **2a** (0.4 mmol, 2.0 equiv), $[RuCl_2(p\text{-cymene})]_2$ (10 mol%), additive (KPF_6, 20 mol%), phase transfer catalyst (PTC, 20 mol%), stirred at 80 °C for 24 h in H_2O (2 mL).

[b] Yield based on **1a**.

[c] TMAF: tetramethylammonium fluoride; CTAC: hexadecyl trimethyl ammonium chloride; SDS: sodium dodecyl sulfate; SDBS: sodium dodecylbenzenesulfonate.

[d] SDBS (40 mol%).

[e] Using $AgSbF_6$ as additive instead of KPF_6.

[f] At 60 °C.