Tetrahedron Letters 51 (2010) 863–867

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Ultrasound-assisted synthesis of symmetrical biaryls by palladium-catalyzed detelluration of 1,2-diarylditellanes

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ARTICLE INFO

Article history:
Received 2 November 2009
Revised 5 December 2009
Accepted 7 December 2009
Available online 11 December 2009

Keywords:
Detelluration reaction
Biaryls
Diarylditellurides

ABSTRACT

An ultrasound-assisted synthesis of functionalized symmetrical biaryls with electron-withdrawing or electron-donating substituents is described and illustrated by the palladium-catalyzed detelluration of 1,2-diarylditellanes. This procedure offers easy access to symmetrical biaryls in short reaction time and the products are achieved in good to excellent yields.

Biaryl scaffolds are important structural motifs for both synthetic and medicinal purposes. These scaffolds are also common structural features found in a large number of biologically important natural products.[1] Aside from their occurrence in complex natural products and pharmaceutical agents,[2] these compounds are also applied as chiral ligands,[3] liquid crystal materials,[4] and organic conductors.[5]

Several synthetic biaryl compounds have been reported to have diverse biological activities[6] such as antidiabetic,[7] anticancer,[8] antibacterial,[9] and γ-secretase inhibitory activity.[10] Some symmetric and asymmetric biaryls such as α-DDB (methyl 4,40-dimethoxy-5,6,50,60-dimethylenedioxy biphenyl-2,2-dicarboxylate) and bicyclol (Fig. 1) are used as leading hepatoprotective agents.[11] Recently, some biaryl scaffolds have been identified as a new class of antileishmanial agents.[12]

Aryl–aryl bond formation for the preparation of symmetrical and unsymmetrical biaryl compounds is one of the most useful and important tools in modern organic chemistry. The synthesis of some unsymmetrical biaryl compounds has been achieved by metal-catalyzed[13] and non-metal-catalyzed[14] approaches in the past few years. Symmetrical biaryls are traditionally obtained using the Ullmann reaction[15] and some other methods.[16] In the past decade, the synthesis of symmetrical biaryl scaffolds has continued using metal-assisted homocoupling of aryl halides,[17] boronic acids,[18] aryl Grignard reagents,[19] and arene diazonium salts.[20] Wong and Zhang reported the synthesis of these systems through the palladium-catalyzed homocoupling of aryl boronic acids, but this method requires phosphine or phosphate ligands and harsh reaction conditions.[21] In the past few years, Yamamoto et al. reported an efficient method to obtain symmetrical biaryls through

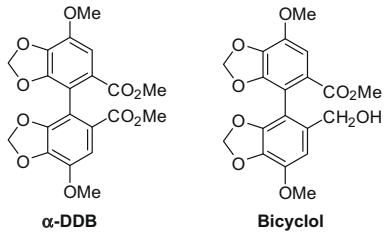

Figure 1. Structures of biologically active biaryl scaffolds.

Table 1
Study of the catalyst effect on detelluration of 1,2-diphenylditellane **1a**

Entry	Catalyst[a]	Yield[b] (%)
1	—	nr
2	$PdCl_2$	95
3	$Pd(AcO)_2$	82
4	Pd(dba)	20
5	$Pd(BzCN)_2$	62
6	$PdCl_2$(PEPPSI)	46
7	$Fe(acac)_3$	nr
8	$Cu(OAc)_2$	nr

Reaction conditions: diphenylditelluride (1 equiv), catalyst (10 mol %), Na_2CO_3 (2 equiv), Ag_2O (2 equiv), MeOH, irradiate in ultrasonic bath.
[a] 10 mol % of catalyst was used.
[b] The yields were determined by GC analysis.

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0040-4039/$ - see front matter © 2009 Published by Elsevier Ltd.
doi:10.1016/j.tetlet.2009.12.028

Table 2
Study of the effects of additive and base on the detelluration of 1,2-diphenylditellane **1a**

Entry	Base	Additive (equiv)	$Pd(PPh_3)_4$ (mol %)	Yield[a] (%)
1	—	AgOAc (2)	$PdCl_2$ (10)	nr
2	Na_2CO_3	AgOAc (2)	$PdCl_2$ (10)	95
3	Cs_2CO_3	AgOAc (2)	$PdCl_2$ (10)	92
4	$NaHCO_3$	AgOAc (2)	$PdCl_2$ (10)	72
5	DIPEA	AgOAc (2)	$PdCl_2$ (10)	79
6	Et_3N	AgOAc (2)	$PdCl_2$ 10)	84
7	Na_2CO_3	—	$PdCl_2$ (10)	nr
8	Na_2CO_3	AgOAc (2)	$PdCl_2$ (10)	95
9	Na_2CO_3	Ag_2O (2)	$PdCl_2$ (10)	98
10	Na_2CO_3	CuI (2)	$PdCl_2$ (10)	35
11	Na_2CO_3	Ag_2O (2)	$PdCl_2$ (10)	55
12	Na_2CO_3	Ag_2O (2)	$PdCl_2$ (8)	78
13	Na_2CO_3	Ag_2O (2)	$PdCl_2$ (10)	70

Reaction conditions: diphenylditelluride (1 equiv), $PdCl_2$ (10 mol %), base (2 equiv), additive (2 equiv), MeOH, irridiate in ultrasonic bath.
[a] The yields were determined by GC analysis.

Table 3
Study of the solvent effect on the detelluration of 1,2-diphenylditellane **1a**

Entry	Solvent	Yield[a] (%)
1	MeOH	98
2	MeCN	38
3	THF	35
4	1,4-Dioxane	17
5	Toluene	23

Reaction conditions: diphenylditelluride (1 equiv), $PdCl_2$ (10 mol %), Na_2CO_3 (2 equiv), Ag_2O (2 equiv), solvent, irradiate in ultrasonic bath.
[a] The yield was determined by GC analysis.

the homocoupling of aryl boronic acids, but this method suffers from low yields with electron-withdrawing functionalities as aryl boronic acids.[22]

Organotellurium compounds have undergone remarkable development as intermediates in synthetic organic chemistry. Organotellurium compounds have been used instead of halogens as electrophilic partners in some palladium-catalyzed cross-coupling reactions.[23,24] Recently, we reported the synthesis of symmetrical biaryls[25] through the palladium-catalyzed homocoupling of *n*-butyl aryltellurides, which proceeds in a few minutes using ultrasonic waves as a source of energy. The ultrasound effects are attributed to a physical process called cavitation.[26]

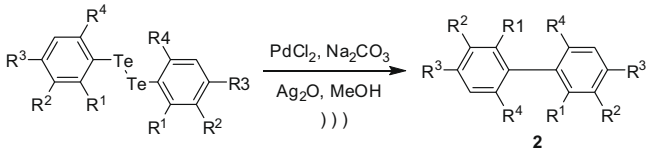
Herein, we report a new protocol for the synthesis of symmetrical biaryls using a palladium-catalyzed detelluration reaction of functionalized 1,2-diaryldiltellanes with ultrasonic waves as a source of energy. The strength of the procedure lies in the formation of a C–C bond and the introduction of electron-donor or -acceptor functionalities into the products.

The approach to prepare biaryl compounds **2a–i** was based on a palladium-catalyzed detelluration reaction of functionalized 1,2-diaryldiltellanes **1a–i**. The parent precursors 1,2-diaryldiltellanes **1a–j** were conveniently prepared in high yields through the Grignard reaction of aryl halides followed by the addition of tellurium and oxidation by air.[27]

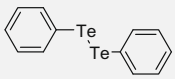
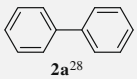
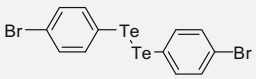
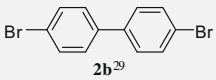
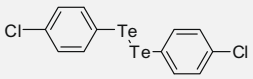
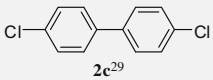
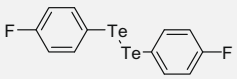
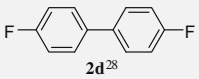
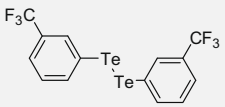
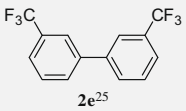
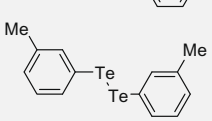
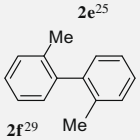
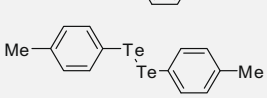
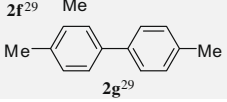
Initially, we optimized the conditions for the detelluration of functionalized 1,2-diaryldiltellanes **1**. In order to find appropriate conditions for the detelluration reaction of 1,2-diaryldiltellanes, 1,2-diphenylditellane **1a** was selected as a model substrate and a variety of conditions were screened, as described in Tables 1–3. The reactions were monitored by TLC or GC.

Initially, we surveyed palladium catalysts for this detelluration reaction. We attempted reactions with some palladium (Table 1,

Table 4
Detelluration of functionalized 1,2-diaryldiltellanes **1a–j**



2

Entry	Diaryldiltellurides (**1**)	Biaryls (**2**)	Reaction time (min)	Yield[a] (%)
a		 **2a**[28]	30	95
b		 **2b**[29]	30	92
c		 **2c**[29]	30	88
d		 **2d**[28]	25	82
e		 **2e**[25]	45	84
f		 **2f**[29]	45	78
g		 **2g**[29]	30	83