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Vanadium(IV) tetrachloride catalyzed oxidative homo-coupling of aryl lithium under mild reaction condition

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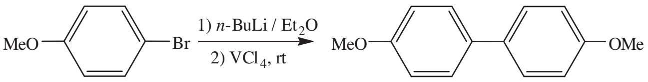
ABSTRACT

A novel efficient strategy to prepare symmetrical diaryls via VCl_4 catalyzed homo-coupling of aryl lithium has been developed. In which, organometallic reagent *n*-BuLi was applied as the strong base to form aryl lithium from aryl halogen in anhydrous diethyl ether, then it was followed by the addition of catalytic amount of VCl_4 at room temperature to afford diaryls. All the diaryls have been characterized by ^1H and ^{13}C NMR.

Carbon–carbon bond formation of aryl–aryl by homo-/cross-coupling reactions has been extensively investigated for decades in order to develop highly efficient and environmentally friendly strategies, as well as the construction of pharmaceuticals, natural products, and new materials.[1] Ullmann reaction as a convenient method has been widely applied to prepare aryl–aryl complexes.[2] Especially, palladium/nickel complexes—transition-metal oxidants catalyzed oxidative homo-coupling of aryl-metal reagents has offered symmetrical biaryl backbones, for example, Suzuki reaction (aryl boronic acid),[3] Sonogashira reaction (aryl stannanes),[4] and arylzinc.[5] Recently, the iron-catalyzed homo-coupling reaction of aryl Grignard reagent has attracted the profound interest from synthetic chemists, for example, in the presence of a stoichiometric amount of 1,2-dichloroethane.[6] However, iron-catalyzed aryl magnesium method was not well available for the low activity of chlorobenzene. Additionally, aryl magnesium also could be oxidized by oxygen or alternative organic molecules to perform homo-coupling reaction and generate diaryl,[7] such as $TiCl_4$.[8] Oxovanadium(V) catalytic activity has been investigated, though.[9] Moreover, vanadium(III) reagent VCl_3 has been performed to catalyze homo-coupling of aryl bromide in the presence of two stoichiometric amounts of Mg in THF with moderate yield.[6] Cp_2VCl_2 catalyzed meso-selective pinacol coupling reaction has also been reported.[10]

However, VCl_4 as catalyst for homo-coupling of aryl lithium has not been reported so far.[11] In order to investigate the catalytic activity of VCl_4, and solve the low activity of aryl chloride via aryl Grignard reagent method, as well as avoid the usage of organic oxidant and precious transition metal catalyst, herein an efficient and convenient method involving vanadium(IV) tetrachloride as catalyst for oxidative homo-coupling of aryl lithium to prepare diaryls has been developed under mild reaction condition (Scheme 1). Neither stoichiometric transition-metal, nor oxidant, such as oxygen, 1,2-dihalogen compounds, was required.



Scheme 1. VCl_4 catalyzed aryl lithium oxidative homo-coupling.

Commercially available red-brown liquid VCl_4 was directly applied as homogeneous catalyst in diethyl ether at room temperature. The general procedure is described as follows.[12] Under dried dinitrogen atmosphere, aryl halogen was treated with equiv *n*-BuLi in anhydrous diethyl ether for one hour to result in aryl lithium. The reaction period depended on the activity of aryl halogen, for example, aryl chloride with further one hour. After the addition of catalytic amount of VCl_4, the mixture was stirred at rt for hours to afford the symmetrical diaryls. The coupling reaction was monitored by thin layer chromatography till completion or no obvious changing. The moderate yields could be partially ascribed to trace H_2O in commercial aryl halogens, which have not been dried or freshly distilled. As Table 1 showed, electron-donating group led to better yield, such as OCH_3 (Table 1, entries 1, 7). In the absence of *n*-BuLi, the mixture of phenyl bromide with VCl_4 did not result in biphenyl even after stirring for 24 h at room temperature. Also, it is

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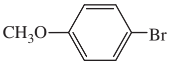
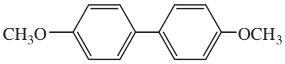
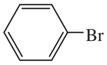
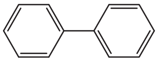
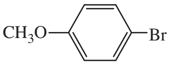
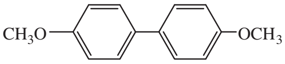
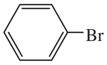
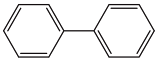
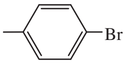
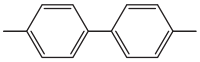
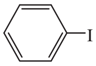
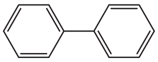
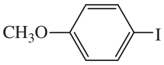
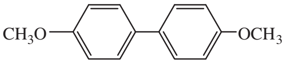
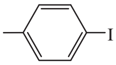
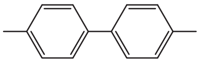
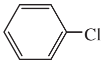
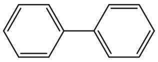
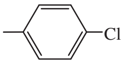
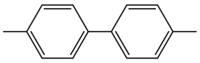
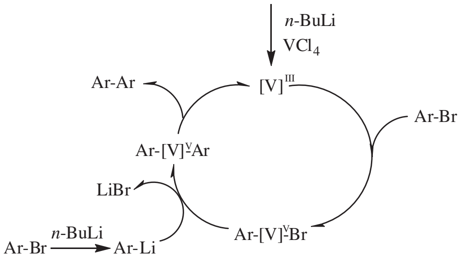
Table 1
Preparation of diaryls catalyzed by VCl_4 in diethyl ether at room temperature[a]

Entry	ArX	Product	Time (h)	Yield[b] (%)
1			12	72
2			12	64 [c]
3			24	0 [d]
4			12	70
5			12	68
6			10	81
7			10	86
8			10	80
9			12	61
10			12	63

[a] Reaction condition: aryl halogen (4 mmol), *n*-BuLi (4 mmol), diethyl ether (20 ml), VCl_4 (10 mg, 1%), room temperature.
[b] Isolated yield.
[c] Reaction condition: metal lithium (28 mg, 4 mmol), phenyl bromide (0.5 ml, 4 mmol), Et_2O (20 ml), room temperature 2 h; VCl_4 (10 mg), 12 h.
[d] No *n*-BuLi, only VCl_4 with aryl bromide.

common that treatment of phenyl bromide with *n*-BuLi only affords phenyllithium, rather than diaryls. Therefore, the limitations of requirement of electronically activated aryl iodide precursors and a stoichiometric amount of transition metal salts have been overcome. This methodology has been proved to be applicable to construct symmetrical diaryls from various aryl halogen substrates. Especially, this method made it possible to generate aryl lithium reagents from electronically deactivated aryl chloride under mild reaction condition. Although, in consideration of high reactivity of *n*-BuLi, the substrates bearing active functional groups such as –OH, –CHO, –CN, –COOEt etc. have not been attempted yet. Additionally, there is no alternative oxidant required in the catalytic process, for example, $ClCH_2CH_2Cl$, or oxygen.

A tentative mechanism is proposed as Scheme 2. According to the catalytic mechanism of vanadium(V) complexes ($VO(OR)_2Cl$) and related investigations of VCl_4 with *n*-BuLi,[9] VCl_4 was assumed to firstly form active [V(III)] intermediate with *n*-BuLi, which then conducted oxidative addition with aryl bromide to generate Ar[V(V)]Br. It was followed by transmetalation with Ar-Li to result in LiBr and Ar[V(V)]Ar. Reductive elimination of Ar[V(V)]Ar afforded diaryls and active substrate [V(III)]. Solid evidence related to the intermediates should be carried out, though.



Scheme 2. Proposed mechanism for VCl_4 catalyzed aryllithium oxidative homo-coupling.

Interestingly, metallic lithium used as lithiation reagent has also been successfully demonstrated by reaction with phenyl bromide (entry 3), though the yield was not so satisfactory. The detailed procedure was described as below. At room temperature, the mixture of equiv aryl bromide and metal lithium wire was stirred for hours till solid metal disappeared, then it was followed by the addition of catalytic amount of VCl_4 to give biphenyl after hours' vigorously stirring at rt and purification by flash chromatography.

The advantages of this strategy are obvious, available for aryl chloride, mild reaction condition, as well as no application of expensive transition metal and organic ligands. Also, there is no necessity to prepare organoborate via aryl bromide with *n*-BuLi.[13] The optimization including catalytic loading, reaction temperature, time, and solvents, will be considered further. While the expansion scope of this new methodology to alkyl lithium substrates, mixed aryl halogen, bicyclic aromatic systems such as naphthalene substrates, as well as metallic lithium as lithiation reagent, are under the way.

In conclusion, an efficient and versatile strategy to prepare symmetrical biaryls via vanadium(IV) tetrachloride catalyzed oxidative homo-coupling of aryl lithium has been successfully demonstrated for the first time. In which, *n*-BuLi was used as the lithiation reagent to prepare aryl lithium, and catalytic amount of vanadium(IV) tetrachloride was involved in oxidative homo-coupling of aryl lithium to afford symmetrical biaryls at room temperature. Importantly, this method overcame the drawback of the preparation of Grignard reagent from low active aryl chloride. Specially, no stoichiometric amount of transition-metal or organic oxidant is required. This method allows an easy and practical way for the construction of symmetrical aryl–aryl.

Acknowledgments

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12. *General Procedures, 4,4'-Dimethoxybiphenyl:* All the reactions were performed under dinitrogen atmosphere with standard Schlenk techniques. At 0 °C, to the solution of bromoanisole (0.5 ml, 4 mmol) in anhydrous Et_2O (20 ml), *n*-BuLi (1.6 M/hexane, 2.5 ml, 4 mmol) was added dropwise. After stirred at rt for 1 h, red liquid VCl_4 (5.5 µl, 10 mg, 0.052 mmol, 1.3%) was added. The mixture was stirred at rt for further 12 h. During this period, the reaction mixture was monitored by TLC till completion or no significant changing. After all the volatiles were evaporated in vacuum, the residue was extracted by petroleum ether and purified by flash chromatography (SiO_2) to give the desired product as white powder. Yield: 310 mg (72%). ^1H NMR (300 MHz): δ 7.41 (d, $J = 3$ Hz, 4H), 6.88 (d, $J = 3$ Hz, 4H), 3.77 (s, 6H). ^{13}C NMR: 156.9, 131.9, 126.1, 112.7, 54.
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