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One-Pot Self-Condensation of Phenylboronic Acid with Phenols and Aldehydes

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An efficient procedure is developed for additive-free condensation of boronic acid with phenols and various aromatic and aliphatic aldehydes under solvent-free conditions.

Key Words: Benzodioxaborinine, Boronic acid, Phenols, Aldehydes, Solvent-free.

INTRODUCTION

Condensation of phenols and aldehydes with boronic acid is a well-known method for the synthesis of dioxaborins. The products are precursors for facile *ortho* substitution of phenols[1], preparation of quinone methides for Diels-Alder cycloadditions[2] and protection of diols[3,4]. The usefulness of the reaction also arises from the application of the dioxaborins as key intermediates for preparation of a variety of natural and synthetic products such as saligenol derivatives[5], polycyclic chromans[6,7], cannabinoids[8], precocene and robustadial derivatives[9], decaline portion of (+)-compactin[10], (+) decursinol[11] and thielocin[12].

The scope of the process, primarily reported by Peer under acid catalysis for formaldehyde in refluxing benzene[13], was later improved by Nagata using optimized reaction conditions and employing other aldehydes[5]. Dufresne *et al.* also offered a more efficient synthetic procedure by using dichlorophenylborane[14]. However, the available methods are either conducted under environmentally unsafe conditions[1,5], are limited to the condensation of phenols with more reactive aldehydes[14], or needs labor and time consuming procedures to make the starting reagents[15-17]. Due to environmental and economic reasons, solvent-free reactions have been of huge interest in synthetic organic chemistry in the last two decades[18-21]. In the framework of our investigations on the development of environmentally friendly procedures[22-25], we recently communicated a solid supported synthesis of dioxaborines under microwave irradiation[26]. We now wish to report a general procedure for the title reaction applicable to the condensation of both aliphatic and various aromatic aldehydes with different phenols in absence of solvent, additive, or external stimulant (**Scheme-I**).

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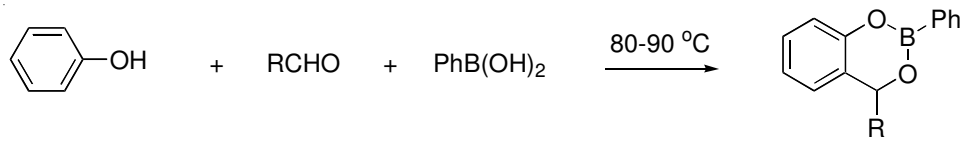


Scheme-I

EXPERIMENTAL

All reported yields are isolated yields. IR spectra were recorded on a FT-IR Bruker Vector 22 infrared spectrophotometer using KBr disks. NMR spectra were recorded on FT-NMR Bruker Ultra ShieldTM (500 MHz) or FT-NMR Bruker AC 80 MHz as $CDCl_3$ solutions with TMS as internal reference. GC-MS spectra were obtained on Fisons 8000 Trio instrument at ionization potential of 70 eV. Elemental analyses were performed using a Thermo Finnigan Flash EA 1112 instrument.

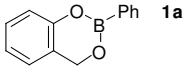
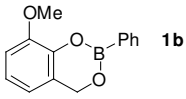
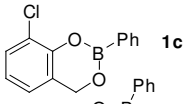
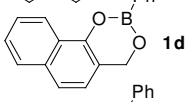
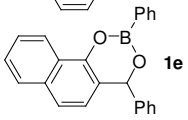
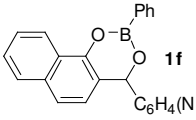
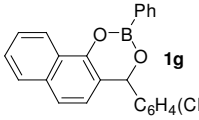
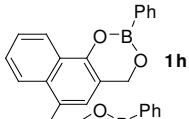
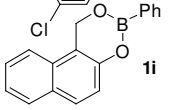
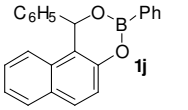
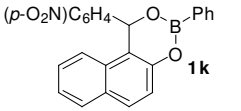
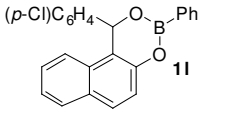
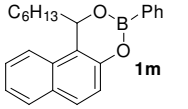
General procedure: A solvent-free mixture of a phenol (1.0 mmol), phenylboronic acid (1.2 mmol) and an aldehyde (1.1 mmol) was thoroughly ground in a mortar. The mixture was transferred to a flask and the flask was heated at 80-90 ºC in an oven for the time period specified in Table-1. The course of the reaction was monitored by TLC. The mixture was cooled to room temperature and the product was separated by column chromatography using 1:4 EtOAc/hexane solution. Products **1g**, **1h** and **1l** were characterized based on their spectroscopic and elemental analysis data. All other products were known and their specifications were compared with the literature data[2,5,26].

4-(4-Chlorophenyl)-2-phenyl-4*H*-naphtho[1,2-d][1,3,2]dioxaborinine (**1g**, $C_{23}H_{16}BClO_2$). White solid in 75 % yield; m.p. 160-161 ºC; ^{1}H NMR ($CDCl_3$) δ: 6.28 (s, 1H), 6.87 (d, 1H, *J* = 8.0 Hz), 7.29 (s, 5H), 7.39-7.80 (m, 6H), 8.02-8.11 (m, 2H), 8.45-8.55 (m, 1H); ^{13}C NMR ($CDCl_3$) δ: 75.4, 119.1, 122.3, 123.3, 124.1, 125.5, 126.8, 127.3, 128.1, 128.2, 128.3, 129.4, 129.5, 132.3, 134.5, 134.8, 135.1, 141.6, 144.2; IR (KBr, ν_{max}, cm^{-1}): 3066, 3041, 2360, 2331, 1595, 1494, 1440, 1390, 1320, 1197, 1112, 1093, 1022; MS (70 eV) m/z (%) 373, 372, 370 (M^+), 369, 335, 266, 259, 231, 202, 155, 127, 104, 77; Calcd. (%) for $C_{23}H_{16}BClO_2$: C, 74.53; H,4.35. Found (%): C, 74.47; H, 4.37.

6-Chloro-2-phenyl-4*H*-naphtho[1,2-d][1,3,2]dioxaborinine (**1h**, $C_{17}H_{12}BClO$). White solid in 88 % yield; m.p. 114-6 ºC; ^{1}H NMR ($CDCl_3$) δ: 5.26 (s, 2H), 7.12-7.19 (m, 1H), 7.45-7.82 (m, 5H), 7.98-8.32 (m, 4H); ^{13}C NMR ($CDCl_3$) δ: 63.2, 117.0, 122.3, 122.6, 124.8, 126.3, 126.6, 1126.8, 27.3, 127.9, 128.3, 131.2, 132.2, 134.9, 143.6; IR (KBr, ν_{max}, cm^{-1}): 3064, 3047, 2340, 2290, 1600, 1467, 1377, 1320, 1253, 1124, 1068, 1028; MS (70 eV) m/z (%) 297, 296, 294 (M^+), 190, 162, 127, 104, 77; Calcd. (%) for $C_{17}H_{12}BClO$: C, 69.32; H, 4.11. Found (%): C, 69.20; H, 4.10.

1-(4-Chlorophenyl)-3-phenyl-1*H*-naphtho[2,1-d][1,3,2]dioxaborinine (**1l**, $C_{23}H_{16}BClO_2$). White solid in 85 % yield; m.p. 140-142 ºC; ^{1}H NMR ($CDCl_3$) δ: 6.72 (s, 1H), 7.25 (s, 5H), 7.26-7.51 (m, 6H), 7.71-8.10 (m, 4H); ^{13}C NMR ($CDCl_3$)

TABLE-1
SOLVENT-FREE SYNTHESIS OF DIOXABORININES

Entry	Phenol	Aldehyde	Product	Time (h)	Yield (%)[a]
1	phenol	HCHO	 **1a**	18	75
2	2-methoxyphenol	HCHO	 **1b**	18	60
3	2-chlorophenol	HCHO	 **1c**	18	60
4	naphthalen-1-ol	HCHO	 **1d**	3	98
5	naphthalen-1-ol	C_6H_5CHO	 **1e**	18	65
6	naphthalen-1-ol	*p*-NO_2-C_6H_4CHO	 **1f**	18	85
7	naphthalen-1-ol	*p*-Cl-C_6H_4CHO	 **1g**	18	75
8	4-chloronaphthalen-1-ol	HCHO	 **1h**	3	88
9	naphthalen-2-ol	HCHO	 **1i**	3	98
10	naphthalen-2-ol	C_6H_5CHO	 **1j**	18	80
11	naphthalen-2-ol	*p*-NO_2-C_6H_4CHO	 **1k**	18	83
12	naphthalen-2-ol	*p*-Cl-C_6H_4CHO	 **1l**	18	85
13	naphthalen-2-ol	*n*-$C_6H_{13}CHO$	 **1m**	18	82

[a] isolated yields

δ: 73.1, 116.6, 119.7, 122.9, 124.9, 127.6, 128.3, 129.2, 129.5, 129.6, 120.4, 130.8, 130.9, 131.3, 132.2, 134.8, 135.0, 141.0, 147.6; IR (KBr, ν_{max}, cm^{-1}): 3066, 3024, 2900, 1597, 1348, 1249, 1095; MS (70 eV) m/z (%) 373, 370 (M^+), 336, 266, 260, 231, 202, 155, 127, 104, 77; Calcd. (%) for $C_{23}H_{16}BClO_2$: C, 74.53; H,4.35. Found (%): C, 74.42; H, 4.28.

RESULTS AND DISCUSSION

A variety of aldehydes were subjected to condense with phenylboronic acid and different phenols under solvent-free conditions (Table-1). Reaction of phenol and its derivatives with paraformaldehyde took 18 h to give moderate amounts of products **1a-c** (entries 1-3). Naphthol derivatives gave higher yields of their respective products. It took only 3 h for paraformaldehyde to nearly quantitatively give **1d** in reaction with 1-naphthol (entry 4). Aromatic aldehydes took longer time to give similar results in reaction with naphthalen-1-ol (entries 5-7). Comparable results were obtained for the reactions of other naphthol substrates (entries 8-12). Finally, *n*-heptanal was subjected to the conditions to examine the reactivity of aliphatic aldehydes giving product **1m** after 18 h (entry 13).

Conclusion

In summary, a new procedure is offered which provides an efficient condensation of boronic acid with phenols and aldehydes without using any solvent or additive.

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