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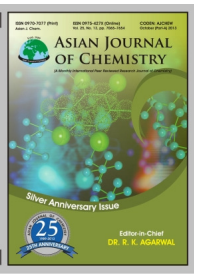

Effect of Increase in Steric Bulk of Aryllithium on Stereoselectivity of Boronate Complexes

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(S)-4,4,5,5-Tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane was reacted with 1-bromonaphthalene and ate-complex was synthesized and this resulted product acted as nucleophile. Stereoselectivity of ate-complex was determined by reacting with different electrophiles diisopropyl azodicarboxylate (DIAD), dibenzyl azodicarboxylate (DBAD) and tropylium tetrafluoroborate. Yields and enantiomeric ratios (e.r.) were measured at -78 ºC and room temperature. It was observed that the increase in steric bulk of aryl lithium (ArLi) resulted in the lower yields and enantiomeric ratios.

Key Words: *sec*-Boronic esters, Stereoselectivity, Steric bulk, 1-Bromonaphthalene, Boronate complexes, Electrophiles.

INTRODUCTION

Organic synthesis normally involves the combination of electrophiles and nucleophiles. Organometallic nucleophiles had been widely used in synthetic organic chemistry and there are many chiral examples of these useful reagents[1]. Boronate complexes had found wide applications in asymmetric synthesis. Kaiser *et al.*[2] synthesized boronate complex (99 % ee) with no racemization at boron through chirality transfer from a carbon. Lou *et al.*[3], Chong and Wu[4] as well as Goodman and Pellegrinet[5] synthesized more reactive boronate species by exchanging alkoxy groups with biphenols. Ichikawa *et al.*[6] synthesized 1,1-difluoroolefins from 1,1,1-trifluoroethyl *p*-toluenesulfonate in excellent yields *via* boron ate-complex. Similarly, ate-complexes in excellent yields were formed by reacting halomethylboronate derivatives with lithium ester enolates[7]. 1,5-Dienes had been prepard by reacting allylic boronate complexes with allylic halides[8].

Recently, Larouche-Gauthier *et al.*[9] converted secondary boronic esters into reactive nucleophiles by the addition of an aryl lithium reagent and the resulting boronate complexes reacted with a broad range of electrophiles with inversion of stereochemistry. Both secondary and benzylic boronic esters were reacted with a number of electrophiles like DIAD, DBAD, *etc*. Inversion of configuration was found during such reactions. Nucleophilic character of boronate complex was analyzed by using different aryl lithium (ArLi). Electronics of the aryl lithium was tuned to favour a certain pathway. Higher enantioselectivity was obtained when *bis*-trifluoromethyl aryl lithium was used for the synthesis of boronate complex.

In the recent study, it was estimated to investigate that whether an increase in steric bulk on the aryl lithium enhanced the nucleophilic character of boronate complex which may significantly influence both the yields and stereoselectivity. Moreover, 1-bromonaphthalene was used as aryl lithium for the production of boronate complex. The yields and stereoselectivity were determined by reacting boronate complex with a number of different electrophiles such as DIAD, DBAD and tropylium salt. Both yields and enantiomeric ratio were compared with the data published before[9].

EXPERIMENTAL

2,4,6-Triisopropylbenzoyl chloride was purchased from Alfa Aesar while 3-phenyl-1-propanol, *n*-butyl lithium (nBuLi), *sec*. butyl lithium solution (sBuLi) (1.6 M), methyl boronic acid, pinacol, sodium hydride (NaH) and 1-bromonaphthalene were purchased from Sigma Aldrich.All reagents were used as received. To avoid from moisture diethyl ether (Et_2O), acetonitrile and tetrahydrofuran (THF) were dried with 4 Å molecular sieves. The experiments were performed using schlenk line under nitrogen atmosphere in the absence of air and moisture.

Synthesis and characterization of 3-phenylpropyl-2,4,6-triisopropylbenzoate: (3): A solution of 2,4,6-Triisopropylbenzoyl chloride **(1)** (5 g, 18.7 mmol, 1.0 eq in Et_2O 50 mL) was added dropwise over 10 min to a stirred solution of NaH (822.8 mg, 20.57 mmol, 1.1 eq, 60 % suspension in mineral oil) and 3-phenyl-1-propanol **(2)** (2.82 mL, 21.505 mmol, 1.15 eq) in Et_2O (50 mL) at room temperature. The resulting mixture was stirred at room temperature for 16 h.

Then, 1 M $HCl_{(aq)}$ (100 mL) was added and resulting mixture was stirred vigorously for 5 min. The two layers were separated and aqueous layer was extracted with EtOAc (2 × 100 mL). The organic extracts were washed with saturated $NaHCO_3$ solution and then with saturated NaCl solution and dried with $MgSO_4$ and evaporated under reduced pressure to give the crude product **(3)** as light yellow oil (3.98 g, yield: 79.7 %). The reaction is given in Fig. 1.

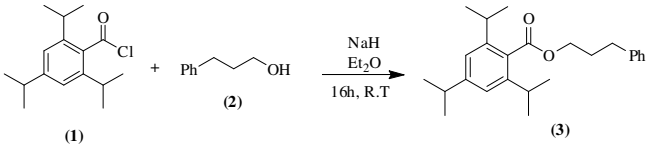


Fig. 1. Synthesis of 3-phenylpropyl-2,4,6-triisopropylbenzoate

Product **(3)** was characterized through ^{1}H NMR, ^{13}C NMR and functional groups were confirmed through IR. This crude product was used for the synthesis of (S)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane **(4)**.

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.34-7.28 (2H, m, 2 × ArH), 7.25-7.18 (3H, m, 3 × ArH), 7.02 (s, 2H, s, 2 × ArH), 4.33 (2H, t, J = 6.5 Hz, OCH_2), 2.95-2.83 (3H, m, 3 × -$CH(CH_3)_2$), 2.77-2.73 (2H, m, $ArCH_2$), 2.09-2.03 (2H, m, CH_2CH_2Ar), 1.27 (12H, d, J = 7.0 Hz,2 × $(CH_3)_2CH$), 1.26 (6H, d, J = 7.0 Hz, $(CH_3)_2CH$).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 170.9 (1C, C=O), 150.1 (1C, $ArCCH(CH_3)_2$), 144.8 (2C, 2 × $ArCCH(CH_3)_2$), 141.1 (1C, $ArCCH_2$), 130.6 (1C, ArCC=O), 128.5 (2C,2 × ArCHCCH), 128.4 (2C, 2 × $ArCHCCH_2$), 126.1 (1C,ArCH), 120.9 (2C, ArCH), 64.3 (1C,OCH_2), 34.4 (1C, $CH(CH_3)_2$), 32.4 (1C,CH_2Ar), 31.6 (1C, OCH_2CH_2), 30.4 (2C, 2 ×$CH(CH_3)_2$), 24.2 (4C, 2 × $(CH_3)_2CH$), 24.0 (2C, $(CH_3)_2CH$).

IR (film): ν_{max} (cm^{-1}) 3026 (sp^2 C-H Stretch), 2960, 2869 (sp^3 C-H stretch), 1723 (C=O stretch), 1460 (sp^2 C=C stretch), 1249 (sp^3 C-O Stretch), 876, 744, 698 (sp^2 C-H oop bending). Finally, the structure of 3-phenylpropyl-2,4,6-triisopropyl benzoate (**3**) had been proved from ^{1}H NMR, ^{13}C NMR and IR results.

Synthesis and characterization of (S)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane: (4): To a solution of primary 2,4,6-triisopropyl benzoate **(3)** (2.5 g, 6.82 mmol, 1.0 eq) and (-) sparteine (1.88 mL, 8.184 mmol, 1.2 eq) in Et_2O (25 mL) at -78 ºC was added sBuLi (1.3 M in 92:8 cyclohexane/hexane, 6.82 mmol, 1.0 eq) dropwise. The resulting brown mixture was stirred for 4 h at -78 ºC before boronic ester (1.16 g, 8.16 mmol, 1.2 eq) was added dropwise. The reaction mixture was further stirred at -78 ºC for 1 h, allowed to warm to room temperature and refluxed for 16 h. The reaction mixture was allowed to room temperature and carefully quenched with water. Et_2O was added, the layers were separated and the aqueous phase was extracted with Et_2O. The combined layers were washed with 1 N HCl, 1 N NaOH, water and brine, dried ($MgSO_4$), concentrated and purified by column chromatography (SiO_2) to obtain the pure secondary boronic ester **(4)** (1.83g, yield: 73.1 %) as colourless oil. The reaction is given in Fig. 2.

Complete characterization was done by taking ^{1}H NMR, ^{13}C NMR and IR. Fine peaks confirmed the purity of the product **(4)** and it was used as starting material for reaction (Fig. 3).

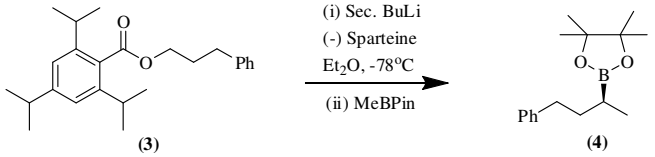


Fig. 2. Synthesis of (S)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane

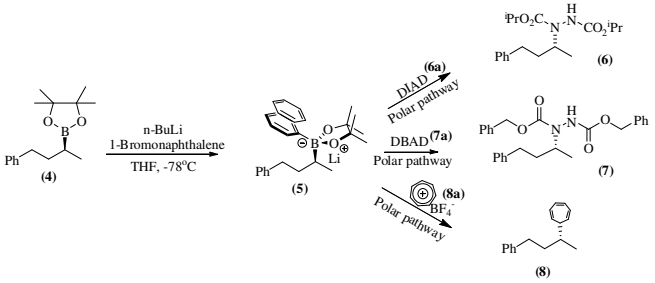


Fig. 3. Synthesis of boronate complex and reaction with electrophiles (E^+) (**6a, 7a, 8a**)

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.25 - 7.32 (2H, m,2 × ArH) 7.15-7.25 (3H, m, 3 × ArH) 2.66 (2H, t, J = 8.19 Hz, $ArCH_2$) 1.76-1.89 (1H, m, CHHCHB) 1.56-1.68 (1H, m, CHHCHB) 1.28 (12H, s, 2 × $C(CH_3)_2$) 1.09-1.17 (1H, m, $BCHCH_3$) 1.03-1.09 (3H, m, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.0 (1C, $ArCCH_2$), 128.4 (2C, 2 × ArCH), 128.2 (2C, ArCH), 125.5 (1C,ArCH), 82.89 (2C, 2 × $C(CH_3)_2$), 35.3 (1C, $ArCH_2$), 35.3 (1C,CHB), 24.8 (1C, CH_2CHB), 24.7 (4C, 2 × $(CH_3)_2C$), 15.4 (1C, CH_3). ^{11}B NMR (96.23 MHz, none) δ ppm 33.4.

IR (film): ν_{max} (cm^{-1}) 3026 (sp^2 C-H Stretch), 2977, 2927, 2856 (sp^3 C-H Stretch), 1496, 1461(sp^2 C=C Stretch), 1249, 1165, 1142, 1111 (sp^3C-O stretch), 861, 848, 745, 697(sp^2 C-H oop bending).

Hence, from ^{1}H NMR, ^{13}C NMR and IR results, the structure of (S)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane had proved.

Reaction of boronic ester (4) with electrophiles (6a, 7a, 8a)

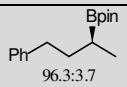
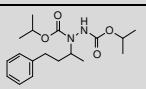
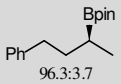
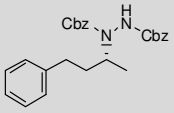
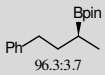
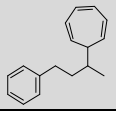
General procedure: To a solution of 1-bromo naphthalene (0.028 g, 0.138 mmol, 1.2 eq) in THF (1.2mL) at -78 ºC was added nBuLi (1.6 M in hexanes, 0.138 mmol, 1.2 eq) dropwise. The mixture was stirred for 1 h at -78 ºC before a solution of boronic ester **(4)** (0.03 g, 0.115 mmol, 1.0 eq) in THF (0.6 mL) was added dropwise. The reaction mixture was stirred for 1 h at -78 ºC to give the boronate complex solution **(5)**. Then electrophile (E^+) **(6a, 7a, 8a)** (0.287mmol, 1.2 eq) was added dropwise and resulting mixture was stirred for 18 h at -78 ºC. Then saturated solution of $NaHCO_3$ (3 mL) and Et_2O was added and layers were separated. Aqueous phase was extracted with Et_2O; the organic layers were combined, washed with brine, dried ($MgSO_4$), concentrated and purified by column chromatography (SiO_2, 1:3 EtOAc/pet. ether) to give desired product as colourless oil **(6**, **8)** and yellowish oil **(7)**.

Synthesis and characterization of (R)-diisopropyl 1-(4-phenylbutan-2-yl)hydrazine-1,2-dicarboxylate: (6): Boronate complex **(5)** was reacted with DIAD **(6a)** (0.058 g, 0.287 mmol, 2.5 eq) to synthesize (R)-diisopropyl 1-(4-phenylbutan-2-yl)hydrazine-1,2-dicarboxylate **(6)** as

TABLE-1
DATA OF STARTING MATERIALS

Entry	Starting material	Colour	Yield (%)
1	3-Phenylpropyl-2, 4, 6-triisopropyl benzoate	Light yellow oil	79.7
2	(S)-4,4,5,5-Tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane	Colourless oil	73.1

TABLE-2
EFFECT OF INCREASE IN STERIC BULK ON ENANTIOSELECTIVITY

Entry	Boronic Ester	Electrophile	Product	1-Bromonaphthalene (At –78 ºC)			1-Bromonaphthalene (At R.T)		
				Yield (%)	e.r (%)	e.s (%)	Yield (%)	e.r (%)	e.s (%)
1		DIAD		31	66:34	35	65	62:38	26
2		DBAD		–	–	–	44	53:47	06
3				40	88:12	82	38	90:10	88

colourless oil (yields mentioned in Table-2 entry 1). Diastereomeric ratios was determined from ^{1}H NMR and enantiomeric ratio was calculated from chiral HPLC. Results were investigated at two different conditions at -78 ºC and room temperature.

^{1}H NMR (500 MHz, DMSO-d_6, 90 ºC) δ ppm 9.16-8.94 (1H, m, NH), 7.32-7.09 (5H, m, 5 × ArH), 4.17 (1H, br s, NCH), 2.63-2.37 (2H, m, $ArCH_2CH_2$), 1.68 (1H, br s, $ArCH_2CHH$), 1.51 (1H, br s, Ar CH_2CHH), 1.20 (12H, d, J = 13.93Hz), 1.02 (3H, br s, $CHCH_3$).

^{13}C NMR (125 MHz, DMSO-d_6, 90 ºC) δ ppm 156.9 (1C, HNCO), 155.6 (1C, NCO), 142.7 (1C, ArC), 128.8 (2C, 2 × ArCH), 128.6 (2C, 2 × ArCH), 126.1 (1C, ArCH), 69.2 (1C, NCOOCH), 68.6 (1C, HNCOOCH), 53.5 (1C, CH_3CHN), 36.2 (1C, CH_3CHNCH_2), 32.6 (1C, $CH_3CHNCH_2CH_2$), 22.4 (2C, $(CH_3)_2CHOOCN$), 22.3 (2C, $(CH_3)_2CHOOCNH$), 18.3 (1C, $NCHCH_3$).

IR (film): ν_{max} (cm^{-1}) 3294 (br N-H stretch), 3026 (sp^2 C-H stretch), 2980, 2934 (sp^3 C-H stretch),1752, 1707(C=O stretch), 1495, 1455, 1410 (sp^2 C=C stretch), 1231, 1180, 1108 (sp^3 C-O stretch), 760, 700 (sp^2 C-H oop bending).

HPLC separation conditions: Chiralpak IB column with guard, 2.0 % iPrOH in hexane, flow rate: 0.7 mL/min, 20 ºC; tR 12.7 min for (R)-enantiomer (major) and tR 14.6 min for (S)-enantiomer (minor). Enantiomeric ratio = 66:34 for -78 ºC and 62:38 for room temperature.

At the end, the structure of (R)-diisopropyl 1-(4-phenylbutan-2-yl)hydrazine-1,2-dicarboxylate has been proved from ^{1}H NMR, ^{13}C NMR and IR results.

Synthesis and characterization of (R)-dibenzyl 1-(4-phenylbutan-2-yl)hydrazine-1,2-dicarboxylate: (7): (R)-Dibenzyl 1-(4-phenylbutan-2-yl)hydrazine-1,2-dicarboxylate **(7)** (yields mentioned in Table-2 entry 2) was synthesized by reacting boronate complex **(5)** with DBAD **(7a)** (0.085 g, 0.287 mmol, 2.5 eq). DBAD was added as solution in acetonitrile. The product **(7)** was completely characterized by ^{1}H and ^{13}C NMR and chiral HPLC. Both yields and enantiomeric ratio's were lower (Table-2, entry 2) than reported literature.

^{1}H NMR (500 MHz, DMSO-d_6, 90 ºC) δ ppm 9.19 (1H, s, NH), 7.34 (10H, s, 10 × ArH), 7.23 (2H, d, J = 6.96 Hz, 2×ArH), 7.16 (3H, d, J = 7.33 Hz, 3 × ArH), 5.12 (4H, s, 2 × OCH_2), 4.26-4.13 (1H, m, $NCHCH_3$), 2.70-2.54 (2H, m, CH_2CH_2CHN), 1.90-1.75 (1H, m, $CH_2CHHCHN$), 1.67-1.52 (1H, m, $CH_2CHHCHN$), 1.11(3H, d, J = 6.23 Hz, $CHNCH_3$)

^{13}C NMR (125 MHz, DMSO-d_6, 90 ºC) δ ppm 157.9 (1C, HNCO), 155.8 (1C, NCO), 142.5 (1C, ArC), 137.1 (2C, 2 × ArC), 128.9 (2C, 2 × ArC), 128.8 (2C, 2 × ArC), 128.7 (2C, 2 × ArC), 128.6 (2C, 2 × ArC), 128.4 (2C, 2 × ArC), 128.1 (2C, 2 × ArC), 127.8 (2C, 2 × ArC), 126.1 (1C, ArC), 67.4 (1C, CH_2OOCN), 66.8 (1C, CH_2OOCNH), 51.7 (1C, $NCCH_3$), 36.6 (1C, CH_2CHNCH_3), 32.6 (1C, CH_2CH_2CHN), 18.3 (1C, CH_3)

IR (film): ν_{max} (cm^{-1}) 3288 (br N-H stretch), 3063, 3031 (sp^2C-H stretch), 2934, 2857 (sp^3 C-H stretch),1751, 1712 (C=O stretch),1497, 1455 (sp^2 C=C stretch), 1257, 1220, 1115, 1055 (sp^3C-O Stretch), 747, 697 (sp^2 C-H oop bending).

HPLC separation conditions: Chiralpak IB column with guard, 5.0 % iPrOH in hexane, flow rate: 0.7 mL/min, 20 ºC; tR 32.2 min for (R)-enantiomer (major) and tR 37.9 min for (S)-enantiomer (minor). Enantiomeric ratio = 53:47 at room temperature.

Synthesis and characterization of (R)-7-(4-phenylbutan-2-yl)cyclohepta-1,3,5-triene: (8): Boronate complex **(5)** was reacted with tropylium tetrafluoroborate **(8a)** (0.053 g, 0.287 mmol, 2.5 eq) to synthesize (R)-7-(4-phenylbutan-2-yl)-cyclohepta-1,3,5-triene **(8)** (yields given in Table-2 entry 3). For characterization ^{1}H and ^{13}C NMR were studied; and enantiomeric ratio was calculated from chiral HPLC. Reaction was done at -78ºC and room temperature.

^{1}H NMR (301 MHz, $CDCl_3$) δ ppm 7.35-7.25 (2H, m, 2 × ArH) 7.22-7.15 (3H, m, 3 × ArH) 6.68-6.64 (2H, m, 2 × =CH) 6.23-6.16 (2H, m, 2 × =CH) 5.26 (2H, dt, J = 9.23, 6.27Hz, 2 × =CH) 2.77-2.68 (1H, m, $ArCHHCH_2$) 2.56 (1H, ddd, J = 13.69, 10.15, 6.48Hz, $ArCHHCH_2$) 2.00-1.90 (1H, m, $ArCH_2CHH$) 1.89-1.80 (1H, m, $ArCH_2CHH$) 1.60-1.49 (1H, m, $CH(CH)_2$) 1.41-1.34 (1H, m, $CHCH_3$) 1.11 (3H, d, J = 6.60 Hz, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 142.7 (1C, $ArCCH_2$) 130.7 (1C, =CH) 128.3 (2C, 2 × ArCH) 128.2 (2C, 2 × ArCH) 125.6(1C, =CH) 124.8 (2C, 2 × =CH) 124.6 (1C, ArCH) 124.2 (2C, 2 × =CH) 44.5 (1C, $C(CH_2)_2$) 36.4 (1C, CH_2CHCH_3) 34.2 (1C, CH_2CHCH_3) 33.2 (1C, $CH_2CH_2CHCH_3$) 16.9(1C, CH_3)

IR (film): ν (cm^{-1}) 3019 (sp^2 C-H stretch), 2955, 2926, 2857 (sp^3 C-H stretch),1496, 1454 (sp^2 C=C stretch), 744, 697 (sp^2 C-H oop bending).

HPLC separation conditions: Chiralpak IA column with guard, 100 % hexanes, flow rate: 0.3 mL/min, 4 ºC; tR 25.3 min for (S)-enantiomer (minor) and tR 26.4 min for (R)-enantiomer (major). enantiomeric ratio = 88:12 at -78ºC and 90:10 at room temperature.

Synthesis and characterization of (S)-4-phenylbutan-2-ol (9)

Oxidation of (S)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane: (4): A solution of 3 M NaOH/ 30 % H_2O_2 (2:1 v/v, 1mL) was added dropwise to a solution of (S)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (0.03 g, 0.115 mmol) in THF/Et_2O (1:1 v/v, 1 mL) at 0 ºC under vigorous stirring. The reaction mixture was allowed to warm to room temperature and further stirred for 2 h. Et_2O and water was added and phases were separated. The aqueous phase was extracted with Et_2O. The combined organic layers were washed with brine, dried ($MgSO_4$), concentrated and purified by column chromatography (SiO_2) to obtain the pure secondary alcohol as colourless oil (0.025 g, yield: 83.9 %).

For the determination of enantiomeric ratio, (S)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane **(4)** was oxidized into (S)-4-phenylbutan-2-ol **(9)** by following method mentioned in Fig. 4.

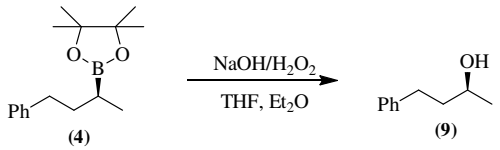


Fig. 4. Oxidation of (S)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.32-7.25 (2H, m, 2 × ArH), 7.23-7.16 (3H, m, 3 × ArH), 3.84 (1H, dq, J = 12.44, 6.21 Hz, CHOH), 2.81-2.63 (2H, m, $ArCH_2CH_2$), 1.82-1.74 (2H, m, $ArCH_2$), 1.40 (1H, br s, OH), 1.24 (3H, d, J = 6.0 Hz, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 142.0 (1C, ArC), 128.3 (4C, 4 × ArCH), 125.8 (1C, ArCH), 67.5 (1C, CHOH), 40.8 (1C, CH_2CH_2CHOH), 32.1 (1C, CH_2CHOH), 23.6 (1C, CH_3).

IR (film): ν_{max} (cm^{-1}) 3354 (br O-H stretch), 3026 (sp^2 C-H stretch), 2966, 2926, 2857 (sp^3 C-H stretch),1495, 1454 (sp^2 C=C stretch), 745, 698 (sp^2 C-H oop bending). The structure of (S)-4-phenylbutan-2-ol was proved from ^{1}H NMR, ^{13}C NMR and IR results.

HPLC separation conditions: Chiralpak IB column with guard, 3.0 % iPrOH in hexane, flow rate: 0.7 mL/min, 20 ºC; tR 16.5 min for (R)-enantiomer (minor) and tR 23 min for (S)-enantiomer (major). Enantiomeric ratio = 96.3:3.7.

Equipments: Varian NMR (400 MHz) spectrometer (model DMX 400) was used for ^{1}H and ^{13}C NMR measurements. For protons, the chemical shifts were measured relative to tetramethylsilane (TMS) at δ = 0 ppm. Chiral HPLC was used for the determination of enantiomeric ratios (e.r.).

RESULTS AND DISCUSSION

3-Phenylpropyl-2,4,6-triisopropyl benzoate**(3)** was synthesized in excellent yields by reacting 2,4,6-triisopropylbenzoyl chloride **(1)** with 3-phenyl-1-propanol **(2)** at given conditions (Fig. 1). Secondary boronic ester namely S)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane **(4)** (Table-1, entry 2) was selected for investigations. And it was formed (Fig. 2) by lithiation-borylation reaction from 3-phenylpropyl-2,4,6-triisopropyl benzoate **(3)** (Table-1, entry 1). Yield for this reaction was good. Product **(4)** was used as starting material for the production of boronate complex.

In order to increase the steric bulk 1-bromonaphthalene was selected. Boronate complex **(5)** was synthesized by reacting (S)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane **(4)** with 1-bromo naphthalene in specific mentioned conditions in Fig. 3. Formation of boronate complex was confirmed by ^{11}B NMR.

The compound **5** behaved as nucleophile and enantioselectivity was checked by reacting with different electrophiles **(6a, 7a, 8a)**. Electrophiles were added as a solution in acetonitrile. These reactions resulted in inversion of configuration. In JACS publication[9], after formation of boronate complex, the electrophiles were added at room temperature but in recent study stereoselectivity boronate complex was investigated with these three electrophiles **(6a, 7a, 8a)**at both room tempe-rature and at -78 ºC.

Resulting products **(6, 7, 8)**were extracted with diethyl ether and purified through column chromatography. ^{1}H NMR and ^{13}C NMR for (R)-diisopropyl 1-(4-phenylbutan-2-yl)-hydrazine-1,2-dicarboxylate **(6)**, (R)-dibenzyl 1-(4-phenylbutan-2-yl)hydrazine-1,2-dicarboxylate **(7)** and (R)-7-(4-phenylbutan-2-yl)cyclohepta-1,3,5-triene **(8)** were collected for their characterization. Diastereomeric ratios (d.r) were determined from ^{1}H NMR while enantiomeric ratios (e.r) were determined by chiral HPLC.

In case of (R)-diisopropyl 1-(4-phenylbutan-2-yl)hydrazine-1,2-dicarboxylate **(6)**, yield was quite low (31 %) at -78 ºC but at room temperature yield (65 %) was comparatively better. By comparing enantiomeric ratio's at both temperatures, enantiomeric ratio's were found slightly lower at room temperature than -78 ºC (Table-2, Entry 1). When compared with literature published before[9] both the yields and enantioselectivities, slight increase in enantiomeric ratio was found but yield was reasonably low.

For (R)-dibenzyl 1-(4-phenylbutan-2-yl)hydrazine-1,2-dicarboxylate **(7)**, reaction was performed only at room temperature and results were very discouraging. Yield was slightly lower but enantiomeric ratio was much lower than reported (Table-2 entry 2).

Results were investigated at two different conditions at -78 ºC and room temperature for (R)-7-(4-phenylbutan-2-yl)-cyclohepta-1,3,5-triene **(8)**. At both temperatures, yields were

quite lower and enantiomeric ratio's were slightly lower than reported. At room temperature, yield was found quite low but at -78 ºC yield was comparatively better. But when we compared enantiomeric ratio's at both temperatures, it was slightly higher at R.T than -78 ºC (Table-2, Entry 3). After comparing both the yields and enantioselectivities with literature published before[9], we found that increase in steric bulk resulted in lower yields and enantioselectivities at both conditions of temperatures.

Conclusion

From this study, it was found that temperature significantly affected both yields and enantioselectivities. For (R)-diisopropyl 1-(4-phenylbutan-2-yl)hydrazine-1,2-dicarboxylate **(6)** (Table-2, entry 1), it was found that the enantiomeric ratio was slightly better at -78 ºC, but the yield was lower. For (R)-dibenzyl 1-(4-phenylbutan-2-yl)hydrazine-1,2-dicarboxylate **(7)** (Table-2, entry 2), the result was quite surprising and no significant stereoselectivity was observed. For (R)-7-(4-phenylbutan-2-yl)cyclohepta-1,3,5-triene **(8)** (Table-2, entry 3), the enantiomeric ratio's were comparable at room temperature and at -78 ºC. Secondly, after comparing data with literature, it was found that with the increase in steric bulk on ArLi had played no significant role to enhance the yield and enantiomeric ratio's.

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REFERENCES

1. S. Davey, *J. Am. Chem. Soc.* **133**, 16794 (2011).
2. P.F. Kaiser, J.M. White and C.A. Hutton, *J. Am. Chem. Soc*., **130**, 16450 (2008).
3. S. Lou, P.N. Moquist and S.E. Schaus, *J. Am. Chem. Soc*., **128**, 12660 (2006).
4. M.J. Chong and T.R. Wu, *J. Am. Chem. Soc.,* **127**, 3244 (2005).
5. J.M. Goodman and S.C. Pellegrinet, *J. Am. Chem. Soc*., **128**, 3116 (2005).
6. J. Ichikawa, T. Sonoda, H. Kobayashi and H. Kobayashi, *Tetrahedron*, **30**, 1641 (1989).
7. R.J. Mears and A. Whiting, *Tetrahedron,* **49**, 177 (1993).
8. Y. Yamamoto and K. Maruyama, *J. Am. Chem. Soc.,* **100**, 6282 (1978).
9. R. Larouche-Gauthier, T.G. Elford and V.K. Aggarwal, *J. Am. Chem. Soc*., **133**, 16794 (2011).