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Aldol reactions catalyzed by organocatalysts derived from 1,1′-Bi-2-napthol and amino acids

Anusha Bade, Yupu Qiao and Allan D. Headley*

Department of Chemistry, Texas A&M University-Commerce, Commerce, TX 75429-3011, USA

ABSTRACT

Organocatalysts derived from 1,1′-Bi-2-naphthol (BINOL) and amino acids have been developed and synthesized via a simple straightforward two-step reaction sequence using chiral BINOL and α-amino acids as starting materials. These catalysts are used to catalyze the direct asymmetric *syn*-aldol reactions of various aromatic aldehydes and hydroxyacetone. Owing to a favorable Z-enamine conformer of the hydroxyacetone and various non-bonded interactions, the *syn*-product was the favored product. Reactions involving aromatic aldehydes with substituents in the 2-position showed slight enantioselectivity.

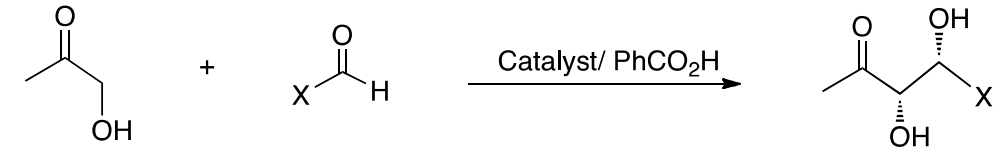
KEYWORDS: asymmetric catalysis, amino acids, aldol reaction

1. INTRODUCTION

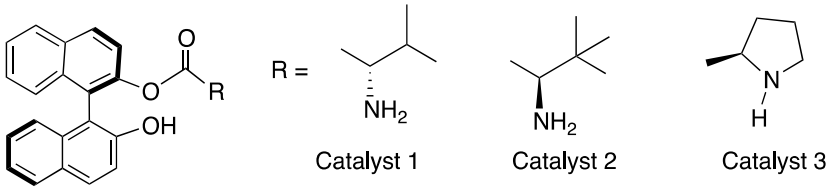
The development of appropriate chiral amines to serve as effective catalysts for asymmetric reactions has created an interesting challenge for chemists over the years [1]. Catalysts that mimic the enzymatic enamine catalysis in biological systems have gained the interest of synthetic chemists [2]. The excellent stereocontrol that results from the direct asymmetric aldol reaction in biological systems is key for the enzymatic aldolase reaction [3]. In recent years, the application of amino acid derivatives as organocatalysts has received much attention owing to their stereochemical selectivity for some direct aldol reactions [4]. In addition, they are readily available and relatively cheap. Through the pioneering work of List *et al.* [5], a better understanding of enamine-based catalysis has been achieved and there has been widespread development and use of enamine-based catalysts for a wide variety of asymmetric reactions [6]. Compared to secondary amine-based catalysts, such as proline-type catalysts, several types of primary amine-based organocatalysts have been developed and effectively used to catalyze asymmetric reactions [7]. These types of catalysts are gaining widespread use to catalyze various enamine-based reactions.

Recently, 1,1′-binaphthyl derived compounds like 1,1′-Bi-2-naphthol (BINOL); 2,2′-bis (diphenylphosphinoamino) - 1,1′-binaphthyl (BINAM); and 2,2′-bis(diphenylphosphino) - 1,1′-binaphthyl BINAP which belong to C_2-symmetry ligands [8] have gained popularity in organic catalysis because of their axial stereochemical property [9]. BINOL and its derivatives are extensively studied as catalysts for different asymmetric synthesis [10] and different types of reactions, including Mannich reactions [11], Strecker reactions [12], Diels-Alder reaction, Michael reaction, and aldol reactions [13]. There are various advantages for the use of chiral BINOL derivatives as catalysts; they are relatively cheap and applicable to a broad spectrum of asymmetric reactions [14]. BINOL has a versatile backbone, which can be modified easily to result in compounds of different electronic and steric properties, which can then influence the asymmetric outcomes of the reactions they catalyze. Resulting from the work of Akiyama [15] and Terada [16], chiral BINOL phosphates and other derivatives

*Corresponding author: allan.headley@tamuc.edu



X = napthyl and various substituted phenyl groups.



Scheme 1. Aldol reactions catalyzed by various BINOL organocatalysts.

have gained widespread use in various catalytic systems, including the Mannich reaction, Friedel-Crafts [17] Strecker, cycloaddition reaction and reductive aminations [18].

The organocatalytic aldol reaction has become a widely utilized reaction for the generation of new C-C bonds [19] and as a result, is an ideal type reaction to test the effectiveness of newly developed catalysts. Many bio-organic transformations in nature are accomplished via this type of reaction [20]. They are the key reactions for the biosynthesis of carbohydrates, keto acids and some amino acids [21]. This type of reaction is of extreme importance since it provides an efficient method to synthesize optically active β-hydroxy carbonyls. These reactions, which involve the addition of an enolyzable carbonyl compound with itself or with other carbonyl compounds, generate optically active β-hydroxy carbonyl compounds, which are structural motifs found in carbohydrates, alkaloids, antibodies, and terpenes [22]. In this research, aldol reactions involving hydroxyacetone and different aromatic aldehydes are examined using various organocatalysts derived from 1,1′-Bi-2-naphthol (BINOL) and amino acids (Scheme 1).

2. EXPERIMENTAL

General methods: Unless otherwise stated, chemicals were directly used as received from Alfa Aesar, Aldrich, TCI. Dichloromethane (DCM) was distilled over CaH_2. TLC was accomplished using aluminum backed TLC plates and flash chromatography was done using silica gel. The synthesis of the monoesters was carried out by coupling the commercially available BINOL with Boc-protected α-amino acids followed by deprotection with TFA/CH_2Cl_2 or with HCl/Dioxane.

Boc protected Catalyst 1: N-Boc-D-Valine (1.089 g, 5mmol), DCC (1.031 g, 1 equiv, 5mmol) and DMAP (0.061 g, 0.1 equiv, 0.5 mmol) were mixed in dry DCM (15 ml) and the mixture was stirred at 0 °C for 30 min. Then, to the above solution, (R)-BINOL (1.431 g, 1 equiv, 5 mmol) dissolved in dry DCM (20 ml) was added dropwise over 20 min at the same temperature. After completing the addition of the BINOL solution, the mixture was stirred for 17 hr at room temperature. The mixture was extracted with DCM (3 × 15 ml). The organic layers were combined and dried over Na_2SO_4 and concentrated under reduced pressure and purified by flash chromatography using 10% of EtOAc in hexanes to obtain the Boc protected Catalyst **1** in 56% yield that was used in the next step. $[\alpha]^{22}$ = 16.2 (c = 0.48, DCM); m.p = 98-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.12-7.76 (m, 4H), 7.56-7.00 (m, 8H), 5.44-5.16 (bs, 1H), 4.65-4.16 (d, 1H), 1.50-1.28 (s, 9H), 0.56-0.40 (d, 3H), 0.18-0.03 (d, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ = 172.2, 155.9, 152.1, 148.0, 133.6, 133.5, 132.6, 131.3, 130.7, 129.3, 128.5, 128.2, 127.8, 127.1, 126.7, 125.9, 124.6, 123.9, 123.3, 121.9, 118.5, 114.2, 58.5, 30.5, 28.5, 19.0, 16.3.

Catalyst 1: To the Boc-protected product (0.8645 g, 1.77 mmol) was added 20% TFA/CH_2Cl_2

and then neutralized to pH 7 with $NaHCO_3$. The aqueous phase was then extracted 3 times using DCM (15 ml), separated and dried over Na_2SO_4 and purified using 1.5% MeOH in DCM to afford the Catalyst **1** as a white solid in 63% yield. M.P: 70-75 °C; $[\alpha]^{22}_D$ = +12.0 (c = 0.51, DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.10-7.79 (m, 4H), 7.55-7.00 (m, 8H), 3.09-3.05 (d, 1H), 1.42-1.30 (m, 1H), 0.64-0.54 (d, 3H), 0.35-0.25 (d, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.0, 152.2, 148.0, 133.7, 133.6, 132.5, 131.0, 130.7, 129.2, 128.5, 128.2, 127.8, 127.0, 126.6, 125.9, 124.6, 123.8, 121.8, 118.7, 114.1, 60.0, 31.3, 19.2, 16.3.

Boc protected Catalyst 2: Utilizing the procedure outlined in the literature [23], Boc protected L-*tert*-Leucine (0.5 g, 2 mmol) was combined with DCC (0.516 g, 1.5 equiv, 2.5 mmol) and DMAP (0.0244 g, 0.1 equiv, 0.2 mmol) and mixed in dry DCM (15 ml) and the mixture was stirred at 0 °C for 30 min. (R)-BINOL (0.687 g, 1.2 equiv, 2.4 mmol) dissolved in dry DCM (20 ml) was added dropwise for over 20 mins at the room temperature. After adding the solution, the mixture was stirred for 17 hr at 0 °C, followed by extraction with DCM (3 × 15 ml). The organic layers were combined and dried over Na_2SO_4 and concentrated under reduced pressure and purified by flash chromatography using 10% of EtOAc in hexanes to obtain the Boc protected catalyst **2** in 80% yield, which was further used in the next step. $[\alpha]^{22}$ = -0.5 (c = 0.27, DCM); m.p = 168-169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08-7.78 (m, 4H), 7.54-7.00 (m, 8H), 5.33 (s, 1H), 4.83-4.75 (d, 1H), 4.0-3.92 (d, 1H), 1.45 (s, 9H), 0.49 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.1, 155.8, 152.1, 148.3, 133.8, 133.7, 132.5, 131.1, 130.6, 129.4, 128.5, 128.2, 127.6, 126.9, 126.6, 126.0, 124.8, 123.7, 123.3, 121.9, 118.6, 114.4, 80.2, 62.7, 33.9, 28.5, 26.0.

Catalyst 2: To the Boc-protected catalyst **2** (0.7321 g, 1.4 mmol) was added 10 ml of 4 M HCl in 1,4-Dioxane. After 1 hour, the reaction was concentrated under reduced pressure, followed by neutralization to pH 7 with $NaHCO_3$. The reaction was extracted 3 times using DCM (15 ml), separated and dried over Na_2SO_4 and purified using 1.5% MeOH in DCM to afford the Catalyst **2** as a white solid in 60% yield (0.3234 g, 0.8 mmol). M.P: 90-95 °C; $[\alpha]_D^{22}$ = +10.0 (c = 0.53), DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.12-7.89 (m, 4H), 7.56-7.0 (m, 8H), 2.88 (s, 1H), 0.75-0.59 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.7, 152.0, 148.1, 133.7, 132.4, 131.1, 130.7, 129.2, 128.5, 128.2, 127.8, 127.0, 126.6, 125.9, 124.7, 123.9, 121.8, 118.5, 114.4, 63.6, 34.0, 26.0.

Boc protected Catalyst 3: Utilizing the procedure outlined above, Boc-protected Catalyst **3** was obtained in 55% yield M.P: 193-196 °C; $[\alpha]_D^{22}$ = -4.29 (c = 0.14, DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.12-7.79 (m, 4H), 7.56-7.0 (m, 8H), 6.0-5.70 (bs, 1H), 5.4-5.1 (bs, 1H), 4.25-4.05 (dd, 1H), 3.13-2.9 (m, 2H), 1.76-1.58 (m, 1H), 1.56-1.38 (d, 9H), 1.56-1.10 (m, 1H), 0.92-0.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.3, 172.0, 152.3, 151.9, 147.9, 133.8, 133.6, 132.5, 131.2, 130.6, 130.7, 130.4, 129.2, 128.6, 128.5, 128.1, 128.0, 127.8, 127.4, 127.2, 126.8, 126.7, 126.3, 126.0, 125.8, 125.0, 124.8, 124.0, 123.7, 123.3, 122.3, 121.5, 118.7, 118.3, 114.0, 59.1, 59.0, 46.5, 46.2, 30.12, 29.3, 28.7, 28.6, 23.5, 22.6.

Catalyst 3: Utilizing the procedure outlined earlier, catalyst **3** was afforded in 35% yield. M.P: 45-55 °C; $[\alpha]_D^{22}$ = -7.20 (c = 0.59, DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.10-7.70 (m, 4H), 7.52-6.86 (m, 8H), 4.26-3.90 (m, 1H), 3.09-2.74 (m, 2H), 2.26-2.10 (m, 1H), 2.00-1.62 (m, 1H), 1.56-1.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.6, 168.1, 152.9, 152.4, 146.5, 133.8, 133.7, 133.5, 132.4, 131.2, 130.7, 130.0, 129.5, 128.9, 128.5, 128.4, 128.3, 127.4, 127.0, 126.6, 126.5, 124.8, 124.6, 124.3, 124.0, 123.6, 121.5, 118.3, 118.1, 113.2, 112.1, 59.2, 59.1, 46.1, 45.8, 28.7, 28.1, 23.7, 23.0.

General procedure for aldol reactions: Catalyst **2** (15.96 mg, 0.04 mmol), hydroxyacetone (0.027 ml, 0.4 mmol), 4-nitrobenzaldehyde (0.03 g, 0.2 mmol) and benzoic acid (9.76 mg, 0.08 mmol) were mixed in 0.4 ml of DMF at room temperature for the time indicated in the tables, followed by purification by flash chromatography using EA/Hexanes in 1:4 ratio to afford the aldol adducts.

(3S,4R)-3,4-dihydroxy-4-(4-nitrophenyl)butan-2-one (6a): Yield = 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 4.42 (m, 1H), 5.23 (m, 1H), 7.56-7.68 (d, 2H), 8.19-8.32 (d, 2H); HPLC (Chiralpak AD-H, iPrOH/Hexanes = 1:4, flow rate = 0.8 ml/ min, λ = 254nm, 21 °C) t_{major}(syn) = 11.72 min, t_{minor}(syn) = 14.93 min; *ee* = 30%; syn/anti = 3:1.

(3S,4R)-3,4-dihydroxy-4-(3-nitrophenyl) butan-2-one (6b): Yield = 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 4.40-4.47 (m, 1H), 5.22-5.28 (m, 1H), 7.52-7.60 (m, 1H), 7.76-7.81 (m, 1H), 8.13-8.20 (m, 1H), 8.30-8.35 (m, 1H); HPLC (Chiralpak AD-H, iPrOH/Hexanes = 1:4, flow rate = 0.8 ml/min, λ = 254 nm, 21 °C) t_{major} (syn) = 10.35 min, t_{minor}(syn) = 13.33 min; *ee* = 31%; syn/anti = 3.1:1.

(3S,4R)-3,4-dihydroxy-4-(2-nitrophenyl)butan-2-one (6c): Yield = 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (s, 3H), 4.54-4.60 (d, 1H), 5.88 (m, 1H), 7.47-7.54 (m, 1H), 7.65-7.74 (m, 1H), 7.79-7.84 (m, 1H), 8.06-8.12 (m, 1H); HPLC (Chiralpak AD-H, iPrOH/Hexanes = 1:4, flow rate = 0.8 ml/min, λ = 254 nm, 21 °C) t_{major} (syn) = 12.64 min, t_{minor}(syn) = 11.93 min; *ee* = 43%, syn/anti = 2.7:1.

(3S,4R)-4-(4-bromophenyl)-3,4-dihydroxybutan-2-one (6d): Yield = 45%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.28 (s, 3H), 4.30-4.34 (d, 1H), 4.95-5.10 (d, 1H), 7.26-7.34 (m, 2H), 7.46-7.54 (m, 2H); (Chiralpak AD-H, iPrOH/Hexanes = 10:90, flow rate = 1.0 ml/min, λ = 220 nm, 21 °C) t_{major} (syn) = 13.56 min, t_{minor} (syn) = 18.04 min; *ee* = 18%; syn/anti = 3.5:1.

(3S,4R)-4-(2-bromophenyl)-3,4-dihydroxybutan-2-one (6e): Yield = 60%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.43 (s, 3H), 4.42-4.52 (d, 1H), 5.44-5.52 (d, 1H), 7.10-7.26 (m, 1H), 7.32-7.44 (m, 1H), 7.46-7.68 (m, 1H), 7.84-8.02 (m, 1H); HPLC (Chiralpak AD-H, iPrOH/Hexanes = 10:90, flow rate = 1.0 ml/min, λ = 220 nm, 21 °C) t_{major} (syn) = 17.13 min, t_{minor}(syn) = 16.22 min; *ee* = 22%; syn/anti = 2.5:1.

(3S,4R)-3,4-dihydroxy-4-(naphthalen-2-yl)butan-2-one (6f): Yield = 30%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 4.46-4.52 (d, 1H), 5.12-5.22 (d, 1H), 7.43-8.07 (m, 7H); HPLC (Chiralpak AD-H, iPrOH/Hexanes = 10:90, flow rate = 1.0 ml/min, λ = 254 nm, 21 °C) t_{major} (syn) = 21.67 min, t_{minor}(syn) = 36.12 min; *ee* = 21%; syn/anti = 3.3:1.

(3S,4R)-3,4-dihydroxy-4-(naphthalen-1-yl)butan-2-one (6g): Yield = 26%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 4.54-4.56 (d, 1H), 5.82-5.86 (d, 1H), 7.25-8.14 (m, 7H); HPLC (Chiralpak AD-H, iPrOH/Hexanes = 10:90, flow rate = 1.0 ml/min, λ = 254 nm, 21 °C) t_{major} (syn) = 21.22 min, t_{minor}(syn) = 27.69 min; *ee* = 41%; syn/anti = 2.8:1.

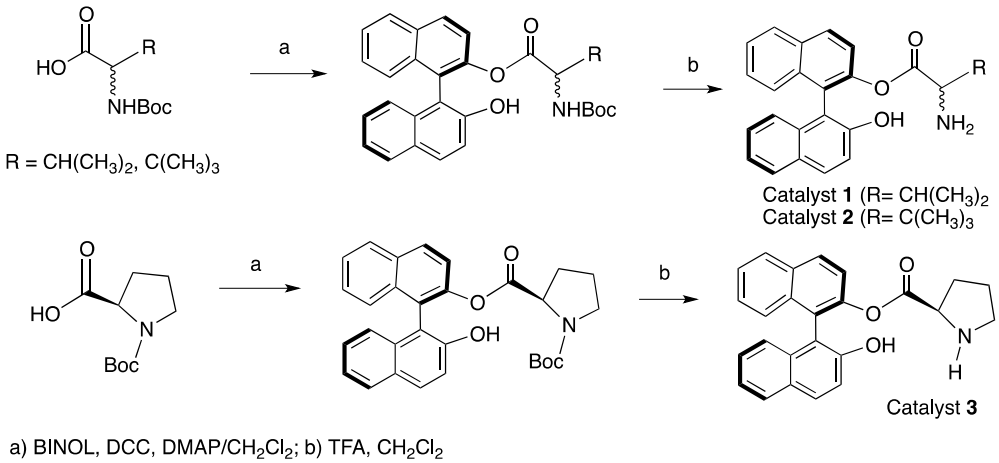
3. RESULTS AND DISCUSSION

A new series of organocatalysts derived from 1,1′-Bi-2-naphthol and amino acids has been synthesized and are shown in Scheme 2.

These catalysts were then screened using various reaction conditions for the aldol reaction of hydroxyacetone and 4-nitrobenzaldehyde and the results are shown in Table 1.

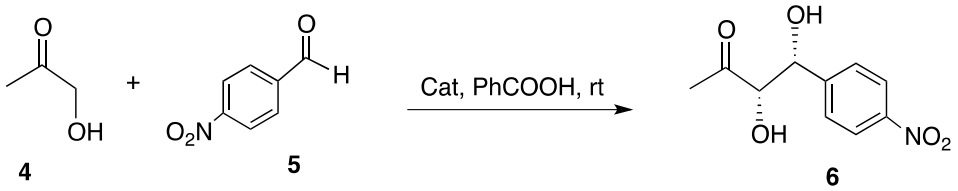
It is obvious from Table 1 that Catalyst **2** is the best catalyst, compared to the other two catalysts. Even though it does not give the highest yields, it resulted in the highest diasteroselectivities. Both catalysts **1** and **2** contain the primary amine, but **1** contains the *iso*-propyl group; whereas, catalyst **2** contains a bulkier *tert*-butyl group. The larger size of the R group for catalyst **2** (*tert*-butyl), compared to that of catalyst **1** (*iso*-propyl), contributes to it being a more effective catalyst compared to catalyst **1**. Based on these results, we proceeded to test catalyst **2** using different reaction conditions for the same reaction and the results are shown in Table 2.

The reaction of hydroxyacetone with 4-nitrobenzaldehyde catalyzed by Catalyst **2** was first examined using various solvents, without an acid additive (entries 1-6). Even though the best yield was obtained in DMF, the stereoselectivity was poor (entry 3). For the conditions considered without an acid additive, the best enantioselectivity was obtained in THF (entry 1). Catalyst **2** was then screened in which different amounts of acid additive were used and different solvents considered (entries 7-15). From the results shown, the best enantio/diastereoselectivity combination was obtained in DMF and 40 mol% acid (entry 13). These results demonstrate that in the presence of acid additive, there was an improvement in the yield of the reaction, and a slight improvement in enantioselectivity, but a slight decrease in diastereoselectivity. It was observed that increasing the acid concentration resulted in higher yields, but poorer enantioselectivity (entries 14 and 15).



Scheme 2. Synthesis of organocatalysts derived from 1,1′-Bi-2-naphthol (BINOL) and amino acids.

Table 1. Screening and optimization of reaction conditions and catalysts for the aldol reaction of hydroxyacetone and 4-nitrobenzaldehyde. Structures of the catalysts are shown in Scheme 1.



Entry	Catalyst[a]	Solvent	Time/hr	Yield (%)[b]	*ee* (%)[c]	syn/anti[d]
1	**1**	Hexane	60	63	1.5	3.5:1
2	**1**	iPrOH	60	65	7	2.3:1
3	**1**	MeOH	96	22	5	3:1
4	**1**	THF	60	53	11	4:1
5	**1**	DMF	96	30	2	3.3:1
6	**2**	THF	60	7	8	2.8:1
7	**2**	**THF**	**48**	**18**	**28**	**4:1**
8	**3**	THF	60	7	10	2:1

[a] 10 mol% of catalyst used; [b] yields of isolated product; [c] determined by ^{1}H NMR; [d] determined by chiral HPLC.

Based on these results, Catalyst **2**, along with the reaction conditions shown in entry 13 of Table 2, were used to test the scope of the reaction, and the results are shown in Table 3.

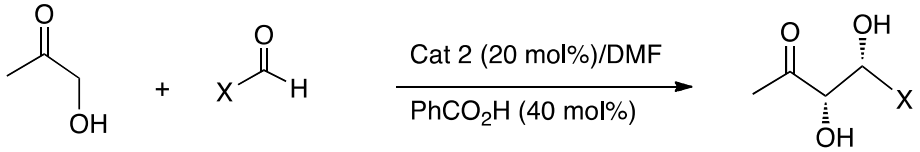
Even though the enantioselectivities shown in Table 3 are not the best, there are some observations that are worth noting. First, the major product is the *syn*-product. One explanation for this observation is that the more stable conformation of the enamine [24], which is formed between hydroxyacetone and Catalyst **2**, is the *syn* conformer, where the N-H forms a hydrogen bond to the hydroxyl group. Another observation is that the highest enantioselectivity is for the 2-nitrobenzaldehyde, compared to 4-nitrobenzaldehyde (entries 1 and 3). Similarly, 1-naphthaldehyde resulted in higher enantioselectivity, compared to the 2-napthaldehyde (entries 6 and 7), and likewise for 2-bromobenzaldehyde, compared

Table 2. Screening of catalyst **2** under different conditions using the aldol reaction of hydroxyacetone and 4-nitrobenzaldehyde shown in Table 1.

Entry	Catalyst (mol%)	PhCOOH (mol%)	Solvent	Time (hr)	Yield[a] (%)	*ee* (%)[b]	dr[c] (syn:anti)
1	10	-	THF	48	18	28	4:1
2	10	-	MeOH	48	18	23	7:1
3	10	-	DMF	48	34	20	2:1
4	10	-	DMSO	5d	-	-	-
5	10	-	H_2O	4d	trace	n.d	n.d
6	10	-	THF/ H_2O	2.5d	8	R	n.d
7	10	20	THF	48	22	17	4:1
8	10	40	THF	48	18	18	4:1
9	10	100	THF	48	44	11	2.4:1
10	20	20	THF	48	40	24	4:1
11	20	40	THF	48	60	22	3.2:1
12	20	20	DMF	48	70	28	3.3:1
13	**20**	**40**	**DMF**	**48**	**65**	**30**	**3:1**
14	20	80	DMF	48	75	16	2.6:1
15	20	120	DMF	48	90	23	2.3:1

[a] yields of isolated product; [b] determined by chiral HPLC; [c] determined by ^{1}H NMR.

Table 3. Scope of catalyst **2** for the asymmetric aldol reaction involving hydroxyacetone and various substituted benzaldehydes.



Entry	X	Product	Time	Yield (%)[a]	*ee* (%)[b]	syn/anti[c]
1	4-$NO_2C_6H_4$	**6a**	48h	65	30	3:1
2	3-$NO_2C_6H_4$	**6b**	48h	65	31	3.1:1
3	2-$NO_2C_6H_4$	**6c**	48h	65	43	2.7:1
4	4-BrC_6H_4	**6d**	5 days	45	18	3.5:1
5	2-BrC_6H_4	**6e**	4 days	60	22	2.5:1
6	2-Naphthyl	**6f**	4 days	30	21	3.3:1
7	1-Naphthyl	**6g**	4 days	26	41	2.8:1

[a] yields of isolated product; [b] determined by chiral HPLC; [c] determined by ^{1}H NMR.

to 4-bromobenzaldehyde (entries 4 and 5). Even though these enantioselectivities are low, one explanation is that there are possible interactions of the group in the 2-position of the benzaldehyde with the acidic hydrogen of the OH group of the enamine catalyst. Such interactions would contribute to making the transition states for the reactions involving 2-substituted benzaldehydes slightly more stable than 4-stubstituted benzaldehydes, where such interactions would not be possible.

4. CONCLUSIONS

In summary, a new series of organocatalysts derived from 1,1′-Bi-2-naphthol and amino acids has been developed and synthesized via a two-step reaction sequence using chiral binaphthol and D-α-amino acid as starting materials. These catalysts are used to catalyze the direct asymmetric *syn*-aldol reactions of various aromatic aldehydes and dihydroxyacetone to give various aldol products. The organocatalysts derived from 1,1′-Bi-2-naphthol and *tert*-leucine resulted in moderate yields for a fairly broad scope of reactions. Owing to a favorable Z-enamine conformer of the hydroxyacetone and various non-bonded interactions, the *syn*-product was the favored product, and the reactions involving aromatic aldehydes with substituents in the 2-position showed slight enantioselectivity. Further studies are being carried out in which different catalysts are being developed using a wider rage of L and D amino acids as precursors to better understand the factors that dictate the stereochemical outcome of these type reactions.

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