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Hydrogen bond donor–acceptor–donor organocatalysis for conjugate addition of benzylidene barbiturates *via* complementary DAD–ADA hydrogen bonding†

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Franco King-Chi Leung, Jian-Fang Cui, Tsz-Wai Hui, Zhong-Yuan Zhou and Man-Kin Wong*

A new class of hydrogen bond donor–acceptor–donor (HB-DAD) organocatalysts has been developed for conjugate addition of benzylidene barbiturates. HB-DAD organocatalyst **1a** (featuring *para*-chloropyrimidine as the hydrogen bond acceptor (HBA), N–H as the hydrogen bond donor (HBD) and a trifluoroacetyl group as the electron withdrawing group (EWG)) is able to activate benzylidene barbiturates through complementary DAD–ADA hydrogen bonding. Using **1a** in benzylidene barbiturate conjugate addition, good yields were achieved. The relative rate constant ($k_{\text{rel}} = 2.9$) of **1a** in catalyzing the conjugate addition of benzylidene barbiturates and the binding constant ($K_{\text{A}} = 8936 (\pm 723) \text{ M}^{-1}$) of **1a** with benzylidene barbiturates were determined by NMR and UV/Vis. spectroscopy studies. The excellent correlation ($R^2 = 0.97$) between the relative rate constant and binding affinity of **1a** with benzylidene barbiturates provides support for the importance of DAD–ADA hydrogen bonding in organocatalysis.

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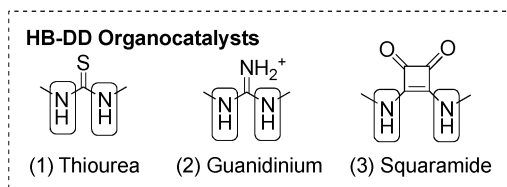
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Introduction

Hydrogen bond donor–donor (HB-DD) organocatalysis has largely been developed as efficient methodologies to achieve synthetic organic transformations.¹ Over time, significant advancements have been made in HB-DD organocatalysis employing thiourea,² guanidinium³ and squaramide-based⁴ HB-DD organocatalysts. Given the success of the HB-DD organocatalysis, it remains a great interest to explore new catalyst scaffolds for hydrogen bond-based organocatalysis.



Hydrogen bond donor–acceptor–donor (HB-DAD) and hydrogen bond acceptor–donor–acceptor (HB-ADA) systems are common in supramolecular chemistry, mainly acting as supramolecular linking units in non-covalent polymer

assembly.⁵ This class of hydrogen bonding system is of high utility in various applications in materials science because of its highly directional nature. In addition, these three complementary DAD–ADA hydrogen bondings are strong binding arrays.⁶ However, studies on the use of the complementary DAD–ADA hydrogen bonding in organocatalysis have rarely been explored.

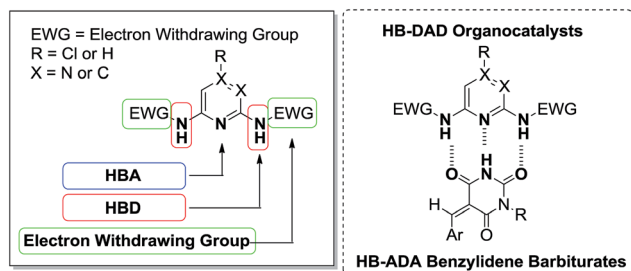
Along with our ongoing interest in the development of organocatalysis for organic synthesis⁷ and bioconjugation,⁸ we envision that this highly directional and strong complementary HB-DAD and HB-ADA systems could be developed as new catalyst scaffolds and efficient activation modes for hydrogen bond-based organocatalysis.

In this work, we have designed HB-DAD organocatalysts consisting of three components (1) hydrogen bond acceptor (HBA), (2) hydrogen bond donor (HBD), and (3) electron withdrawing group (EWG) (Scheme 1). The nitrogen atom in N-heterocyclic aromatic rings including chloro-pyrimidine, pyridine, and pyrazine were selected as HBA to give structurally diverse catalyst scaffolds. Nitrogen–hydrogen (N–H bond), one of the most electronegative hydrogen bonds, was chosen as HBD in the design. The electron withdrawing group could be used to tune the electrophilicity of the N–H bond.

Benzylidene barbiturates are biologically active compounds⁹ and synthetic building blocks.¹⁰ We considered benzylidene barbiturates as HB-ADA substrates because of (1) the imide group functioning as HB-ADA moiety and (2) the electron

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Scheme 1 Design of HB-DAD organocatalysts containing (1) HBA, (2) HBD, and (3) electron withdrawing group. Complementary DAD-ADA hydrogen bonding between HB-DAD organocatalysts and HB-ADA benzylidene barbiturates.

deficient alkene unit amenable for nucleophilic attack. The complementary hydrogen bonding mode of HB-DAD organocatalysts and HB-ADA benzylidene barbiturates is depicted in Scheme 1.

In 2011, Spange and co-workers found that a gradual adjustment of electrophilicity of a barbiturate merocyanine is achieved through cooperative DAD-ADA hydrogen bond.^{11a} Substituent effects of HB-DAD receptors are transmitted to the reactive center of electrophilic HB-ADA substrates so that a fine adjustment of their reactivity would be possible.^{11b,c}

In the present work, we developed a organocatalytic conjugate addition of benzylidene barbiturates with 2-methylfuran catalyzed by HB-DAD organocatalysts through the complementary DAD-ADA hydrogen bonding. Kinetic studies of

HB-DAD organocatalysts in catalyzing conjugate addition of benzylidene barbiturates and binding constant studies of HB-DAD organocatalysts with HB-ADA benzylidene barbiturates were conducted. The excellent correlation between the binding constants and relative rate constants of HB-DAD organocatalysts provides support for HB-DAD as the catalyst scaffold in organocatalysis.

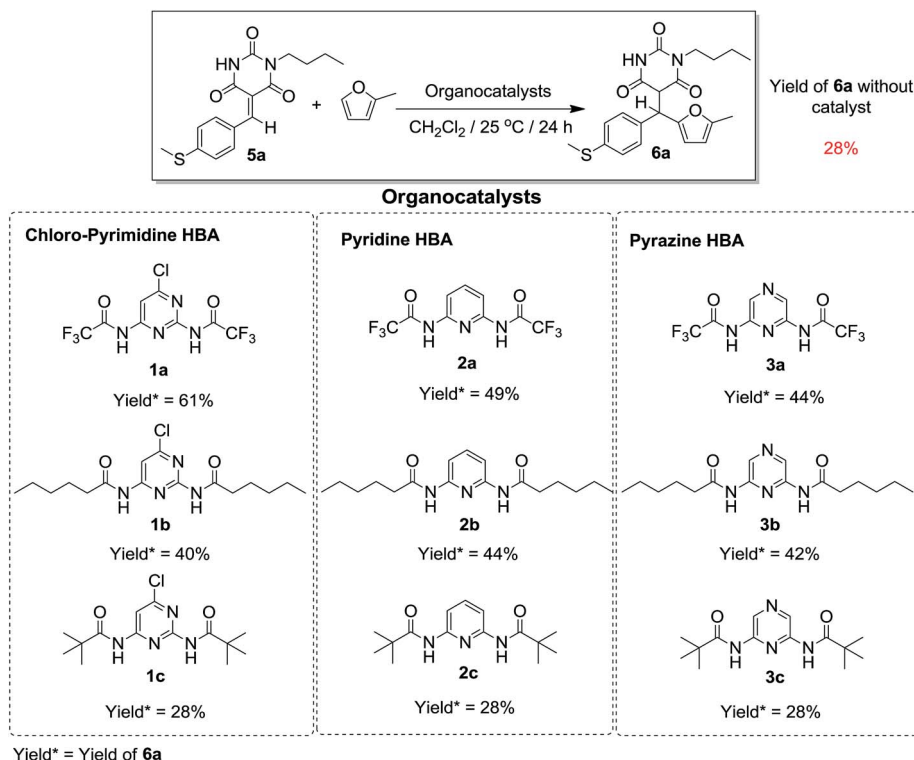
Results and discussion

Preparation of HB-DAD organocatalysts 1–4 and HB-ADA benzylidene barbiturates 5 and 7

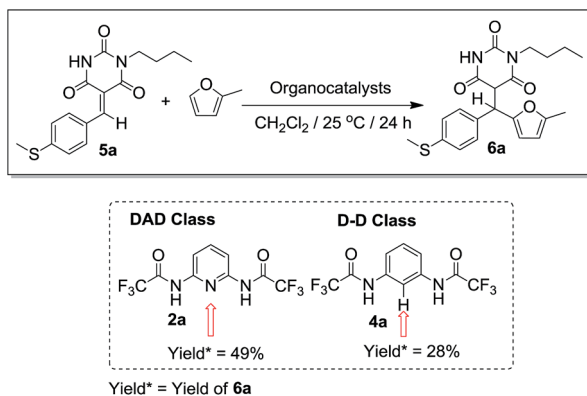
HB-DAD organocatalysts **1a–c** and **3a–c** were prepared by amide coupling of 2,6-diamino-4-chloropyrimidine/2,6-diaminopyrazine with acid chlorides/anhydrides and obtained in 18–68% isolated yield. In addition, **1a** was characterized by X-ray crystallography (see ESI†). HB-DAD organocatalysts **2a**,¹² **2b**,¹³ **2c**,¹⁴ **4a**,¹⁵ **4b**, and **4c**¹⁶ were synthesized according to literature reports. HB-ADA benzylidene barbiturates **5** and **7** were prepared by condensation of barbiturate acid derivatives with various benzaldehydes and obtained in 24–95% isolated yield. The *E/Z* ratio of the alkene moieties of **5** and **7** were found to be 1 : 1 by NMR studies.

Catalytic activities of HB-DAD organocatalysts 1–3 in conjugate addition of benzylidene barbiturates

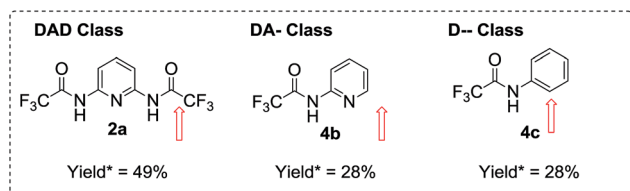
As shown in Scheme 2, the catalytic activity of 20 mol% of **1a** in conjugate addition of benzylidene barbiturate **5a** (0.05 mmol) and 2-methylfuran (0.05 mmol) at 25 °C in 24 h were



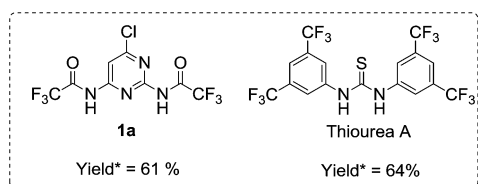
Scheme 2 Catalytic activities of HB-DAD organocatalysts 1–3 in conjugate addition of **5a**.



Scheme 3 2a and 4a in catalyzing conjugate addition of 5a.



Scheme 4 2a, 4b and 4c in catalyzing conjugate addition of 5a.



Scheme 5 1a and thiourea A in catalyzing conjugate addition of 5a.

investigated. Adduct **6a** was obtained in 61% yield, using toluene as internal standard determined by ^1H NMR studies. In the absence of **1a**, **6a** was obtained in 28% yield.

To optimize the reaction conditions of the conjugate addition of benzylidene barbiturate **5a** with 2-methylfuran, reaction temperature, choice of solvents, and amount of HB-DAD organocatalyst **1a** used were studied (see ESI[†]). The conjugate addition in the presence of 20 mol% of **1a** in CH_2Cl_2 at 25 °C in 24 h was found to be the optimized reaction conditions. The catalytic activities of a variety of HB-DAD organocatalysts **1–3** towards conjugate addition of benzylidene barbiturate **5a** were examined accordingly (Scheme 2).

Using **1a** with trifluoroacetyl group as the EWG, adduct **6a** was obtained in 61% yield. Yet, 40% yield of **6a** was obtained using **1b** (bearing hexanoyl group as the EWG). The results indicated that the electron withdrawing trifluoroacetyl group is important to achieve high catalytic activity.¹⁷ **1c** with pivaloyl group as the EWG gave no enhancement to yield of **6a**. These findings indicated that the steric effect of the pivaloyl group would lead to poor catalytic activity in the reaction. Hence, the activating effect of the EWG on the catalytic activities of

HB-DAD organocatalysts is in the order of **1a**-trifluoroacetyl group > **1b**-hexanoyl group > **1c**-pivaloyl group. Interestingly, this trend of activating effect of the EWG on the catalytic activities of **1** also applies for HB-DAD organocatalysts **2** and **3**.

Using **1a** with chloro-pyrimidine as the HBA, adduct **6a** was obtained in 61% yield while **2a** with pyridine as the HBA gave 49% yield of **6a**. The reaction using **3a** with pyrazine as the HBA gave only 44% yield of **6a**. These results indicated that the activating effect of HBA on catalytic activities of HB-DAD organocatalysts is in the order of **1a**-chloro-pyrimidine > **2a**-pyridine > **3a**-pyrazine.

The importance of hydrogen bond donors and acceptors in HB-DAD organocatalyst scaffolds

To investigate the importance of hydrogen bond donors and acceptors of HB-DAD organocatalysts in catalyzing the conjugate addition, hydrogen bond organocatalysts including D-D class **4a**, DA-class **4b** and D-class **4c** were employed for conjugate addition of benzylidene barbiturate **5a** by 2-methylfuran.

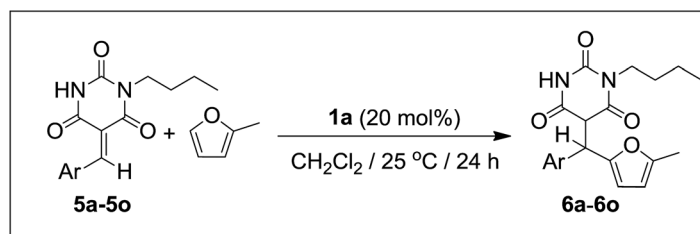
Using **4a**, adduct **6a** was obtained in 28% yield. In contrast, the reaction using **2a** gave adduct **6a** in 49% yield (Scheme 3). Note that **2a** has a nitrogen atom yet **4a** bears a C-H bond. Thus, the nitrogen atom (HBA) of **2a** in the DAD-ADA hydrogen bonding is essential to give catalytic activities on conjugate addition of **5a**.

Conjugate addition of **5a** using DA-class **4b** (bearing one trifluoroacetamide group) and nitrogen atom (HBA) and D-class **4c** (bearing one trifluoroacetamide group) gave adduct **6a** in 28% yield (Scheme 4). As a comparison, **2a** (bearing HB-DAD catalyst scaffold) gave 49% yield. The higher yield of **2a** than **4b** and **4c** indicated that the trifluoroacetamide group and nitrogen atom are important for the catalysis.

Using HB-DD organocatalyst thiourea A (3,5-bis(trifluoromethyl)phenyl thiourea),¹⁸ adduct **6a** was obtained in 64% yield (Scheme 5) while using HB-DAD organocatalyst **1a** gave 61%. The results indicated that **1a** afforded comparable catalytic activity to thiourea A in conjugate addition of **5a**.

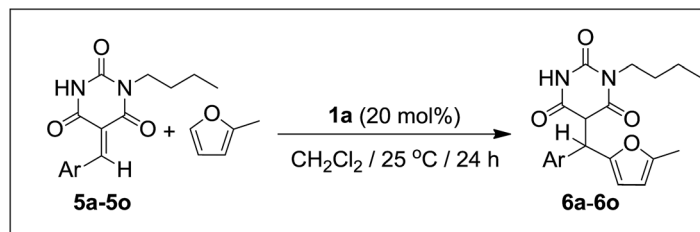
Substrate scope of conjugate addition of benzylidene barbiturates 5 and 7

The substrate scope of conjugate addition was examined by using a variety of benzylidene barbiturates. Treatment of a series of benzylidene barbiturates **5a–o** with 2-methylfuran furnished the corresponding adducts **6a–o** (Table 1). As shown, the conjugate additions were conducted in the presence of 20 mol% of **1a** at 25 °C in 24 h. The **1a**-catalyzed conjugate addition worked well for electron rich benzylidene barbiturates **5a–h** with good yield (Table 1; entries 1–8) because of the low background NMR yield of the reactions. Particularly, **1a**-catalyzed conjugate addition of **5b** and **5e–5h** bearing *para*-alkoxy phenyl groups afforded good yield (entries 2 and 5–8) while the conjugate addition of **5d** bearing an *ortho*-methoxy phenyl group could give even higher yield (entry 4). In contrast, **5c** bearing a *meta*-methoxy phenyl group gave a higher value of background NMR yield (65%), probably due to the methoxy

Table 1 Substrate scope of **1a**-catalyzed conjugate addition of benzylidene barbiturates **5a–5o**

Entry ^a	Substrate	Ar	Product	Isolated yield (%)	NMR yield ^b (%)	Background NMR yield ^{b,c} (%)
1	5a		6a	55	61	28
2	5b		6b	52	57	25
3	5c		6c	78	80	65
4	5d		6d	25	22	7
5	5e		6e	30	30	17
6	5f		6f	16	20	7
7	5g		6g	65	70	31
8	5h		6h	47	50	21
9	5i		6i	66	69	30
10	5j		6j	73	71	36
11	5k		6k	79	84	60
12	5l		6l	35	38	16
13	5m		6m	95	96	87
14	5n		6n	95	97	76

Table 1 (Contd.)



Entry ^a	Substrate	Ar	Product	Isolated yield (%)	NMR yield ^b (%)	Background NMR yield ^{b,c} (%)
15	5o		6o	98	99	99

^a Reaction conditions: **5a-5o** (0.05 mmol), 2-methylfuran (0.05 mmol), **1a** (0.01 mmol), CH₂Cl₂ (1 mL), 25 °C, 24 h. ^b Yields were determined by ¹H NMR of the crude product using toluene as the internal standard. ^c Without addition of **1a**.

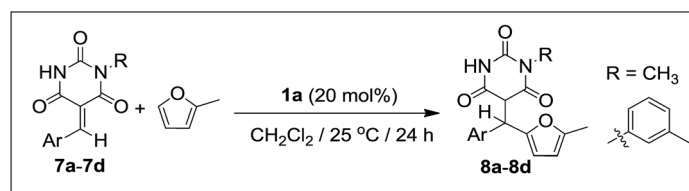
group in the *meta*-position contributes less positive mesomeric effect. The results indicated that benzylidene barbiturates bearing electron donating groups could lead to better yield because of the lower background yield.

Interestingly, **5i** bearing an isopropyl phenyl group, **5j** bearing a *t*-butyl phenyl group and **5l** bearing a naphthalene group led to the corresponding adducts in good yield (entries 9,10 and 12) and low background NMR yield (16–36%). However, **5k** bearing a phenyl group afforded 60% background NMR yield (entry 11). Note that the alkyl- and aryl-substituents on the phenyl ring of benzylidene barbiturates have positive

inductive and mesomeric effect on the phenyl rings. In this connection, benzylidene barbiturates bearing electron donating groups led to better yield with low background yield.

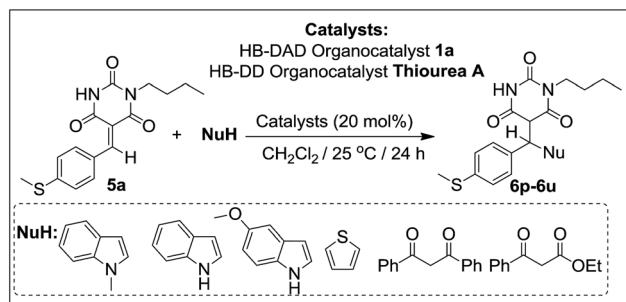
Conjugate additions of **5m-o** bearing electron deficient substituents –Cl, –Br and –CN gave high background NMR yield (76–99%) (entries 13–15). These findings indicated that the electrophilicity of benzylidene barbiturates was a crucial factor in governing the yield in the reaction.

We further examined the scope of this reaction by changing the substituents on the barbiturate acid moiety of benzylidene barbiturates **7a-d** to give the corresponding adducts **8a-d**

Table 2 Substrate scope of **1a**-catalyzed conjugate addition of benzylidene barbiturates **7a-7d**

Entry ^a	Substrate	R	Ar	Product	Isolated yield (%)	NMR yield ^b (%)	Background NMR yield ^{b,c} (%)
1	7a	CH ₃		8a	20	25	5
2	7b	CH ₃		8b	20	18	6
3	7c			8c	46	48	27
4	7d			8d	75	73	61

^a Reaction conditions: **7a-7d** (0.05 mmol), 2-methylfuran (0.05 mmol), **1a** (0.01 mmol), CH₂Cl₂ (1 mL), 25 °C, 24 h. ^b Yields were determined by ¹H NMR of the crude product using toluene or ethyl acetate as the internal standard. ^c Without addition of **1a**.



Scheme 6 1a and thiourea A in catalyzing conjugate addition of 5a with nucleophiles.

(Table 2). Benzylidene barbiturates 7a and 7b (R = methyl) afforded good yield (Table 2, entries 1 and 2). In contrast, conjugate additions of 7c and 7d (R = *m*-tolyl) gave high background NMR yield (27–61%; entries 3 and 4). The difference in the background NMR yield was possibly due to the increased electrophilicity of benzylidene barbiturates (7c and 7d) (*i.e.*, *m*-tolyl group giving negative mesomeric effect on the benzylidene barbiturates).

Furthermore, we examined the scope of nucleophiles (1-methylindole, indole, 5-methoxyindole, thiophene, dibenzoylmethane and ethylbenzylacetate) in 1a- and thiourea A-catalyzed conjugate additions of 5a. However, no yield increase of the reaction was observed using 1a or thiourea A (Scheme 6 and Table S4 and S5†). In this regard, 1a and thiourea A have shown similar behavior in catalyzing conjugate addition of 5a.

Time course experiments using 20 mol% of HB-DAD organocatalysts 1a, 1b, 1c, 2a, 2b, and 3a in conjugate additions of 5a (0.025 mmol; 0.05 M) with 2-methylfuran (0.25 mmol; 0.5 M) to give adduct 6a in CDCl₃ at 25 °C in 120 min were monitored by ¹H NMR.^{19,20} As shown in Fig. 1, the reaction orders were nearly constant over time indicating the absence of product inhibition. Using 1a gave adduct 6a in 66% yield while using 2a gave adduct 6a in 56% yield. Both 1b and 2b were found to be catalytically active, giving 6a in 52% and 49% yields, respectively. In addition, the conjugate addition using 3a could lead to adduct 6a in 44% yield. However, 1c was found to be inactive to catalyze conjugate addition of 5a with 2-methylfuran (yield = 22%). With reference to the increasing acidity of the HBD (N–H) moieties of HB-DAD organocatalysts, the reaction rate is in the order of 1a > 2a > 1b > 2b > 3a.

Kinetic studies of HB-DAD organocatalysts

With a 10-fold excess of 2-methylfuran, all the conjugate additions of 5a were regarded as pseudo-first-order, and the corresponding rate constant k_{obs} were determined and depicted in Table 3. For the determination of k_{obs} , the kinetics data was plotted as $\ln[5a]$ against the reaction time.¹⁹ The rate constant k_{obs} was determined by the negative slope of the plot (see ESI†).

On the basis of the rate constant (k_{obs}), the relative rate constant (k_{rel}) of HB-DAD organocatalysts were calculated.^{20,21} The relative rate constant (k_{rel}) of 1a-catalyzed conjugate addition of 5a was 2.9 (Table 3; entry 1). The relative rate constant suggests that 20 mol% of HB-DAD organocatalyst 1a increases the conjugate addition rate by a factor of = 2.9. The k_{rel} of 2a was 2.2 (entry 4) while the k_{rel} of 3a was calculated as 1.2 (entry 6). In addition,

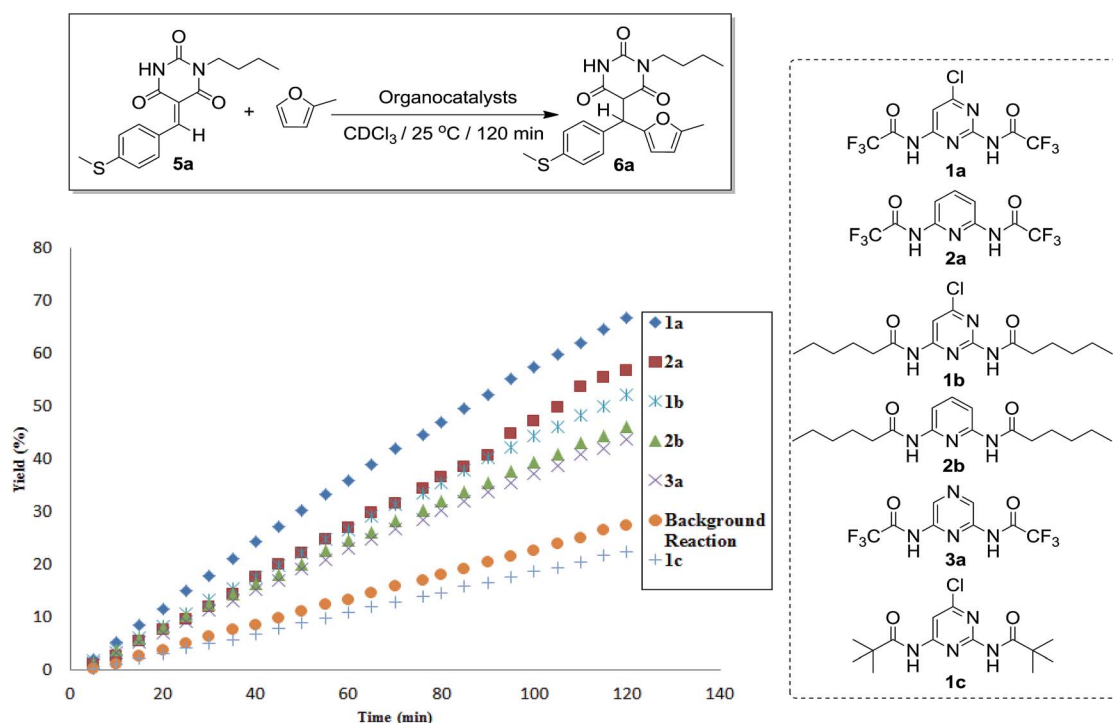


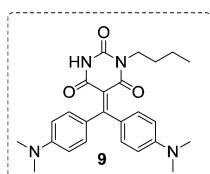
Fig. 1 Time course experiments of HB-DAD organocatalyst-catalyzed conjugate addition of 5a with 2-methylfuran.

Table 3 Rate constants determined by ^1H NMR studies

Entry	Catalyst	$k_{\text{obs}} \times 10^{-4} (\text{s}^{-1})$	$k_{\text{cat}} \times 10^{-4} (\text{s}^{-1})$	k_{rel}
1	1a	1.48	1.11	2.9
2	1b	1.05	0.67	1.8
3	1c	0.37	-0.01	-0.03
4	2a	1.22	0.84	2.2
5	2b	0.90	0.52	1.4
6	3a	0.82	0.44	1.2
7	—	0.38	$k_{\text{uncata}} = 0.38$	—

Table 4 Binding constants of HB-DAD organocatalysts

Entry	Catalyst	$K_{\text{A}} (\text{M}^{-1})$
1	1a	8936 (± 723)
2	1b	6447 (± 380)
3	2a	7747 (± 367)
4	2b	4895 (± 1019)



studies were employed. In these studies, binding constants were monitored with UV/Vis. spectroscopy titration experiments.^{11,22}

The linearized Scatchard plot was used in determining the binding constants of **1a**, **1b**, **2a**, and **2b** with barbiturate **9** (see ESI[†]). The binding constant ($K_{\text{A}} = 8936 (\pm 723) \text{ M}^{-1}$; Table 4, entry 1) was obtained for **1a**. These results indicated that using the trifluoroacetyl group as the EWG led to a significant increase in the binding affinity. Notably, chloro-pyrimidine is a better HBA than pyridine in achieving high binding affinity. With the increasing acidity of HBD (N-H) moieties in HB-DAD organocatalysts, the stability of hydrogen bonding complexes is in the order of **1a** > **2a** > **1b** > **2b**.

Correlation of rate constants and binding constants of HB-DAD organocatalysts

A gradually escalating trend of relative rate constants of conjugate addition of **5a** was obtained in kinetic studies while increasing trend in binding affinity was also determined in binding studies. Particularly, a correlation was observed between kinetic and binding studies. The natural logarithm of the binding constants and relative rate constants were listed in Table S8 (see ESI[†]).^{20b} By plotting of $\ln K_{\text{A}}$ against $\ln k_{\text{rel}}$ of HB-DAD organocatalysts, a linear correlation ($R^2 = 0.97$) was obtained (Fig. 2). The results indicated that a higher binding constant gave a higher relative rate of the conjugate addition.

Conclusion

In summary, we have developed new hydrogen bond-based organocatalysis using HB-DAD catalyst scaffold in catalyzing the conjugate addition of benzylidene barbiturates. The catalytic activities of HB-DAD organocatalyst **1a** were comparable to thiourea A. The catalytic activities of the HB-DAD catalyst scaffolds were supported by the correlation of rate constants and binding constants. This work would lay down a foundation for the development of chiral HB-DAD organocatalysts for asymmetric catalysis.

Experimental section

General procedure for synthesis of HB-DAD organocatalysts **1a** and **3a**

A mixture of 2,6-diamino-N-heterocyclic compounds (1.0 mmol) and trifluoroacetic anhydride (3.0 mmol) in CH_2Cl_2 (10 mL) was stirred under nitrogen atmosphere at room temperature for 24 h. The reaction mixture was added with water (5 mL) and extracted with ethyl acetate (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, and concentrated. The residue was purified by flash column chromatography on silica gel using ethyl acetate-hexane as eluent to give **1a** (58% yield) and **3a** (68% yield).

General procedure for synthesis of HB-DAD organocatalysts **1b**, **1c**, **3b** and **3c**

A mixture of 2,6-diamino-N-heterocyclic compounds (1.0 mmol), acid chloride (2.5 mmol), 4-dimethylaminopyridine

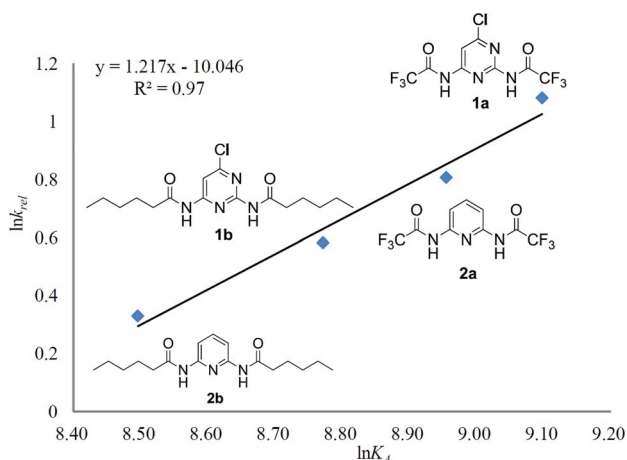


Fig. 2 Correlation of natural logarithm rate constants and binding constants of HB-DAD organocatalysts.

the k_{rel} of **1b** and **2b** were 1.8 and 1.4, respectively (entries 2 and 5). The k_{rel} of **1c** was -0.03 (entry 3), meaning that 20 mol% of **1c** gave no catalytic activity to conjugate addition of **5a** with 2-methylfuran. These results indicated that the more electron deficient EWG (trifluoroacetyl group) afforded the higher catalytic activities than using the hexanoyl group as the EWG.

Binding studies of HB-DAD organocatalysts

To quantify the binding affinity of HB-DAD organocatalysts and HB-ADA benzylidene barbiturate derivatives, binding constant

(0.2 mmol) and triethylamine (2.5 mmol) in CH_2Cl_2 (10 mL) was stirred under nitrogen atmosphere at room temperature for 24 h. The reaction mixture was treated with water (5 mL) and extracted with ethyl acetate (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, and concentrated. The residue was purified by flash column chromatography on silica gel using ethyl acetate–hexane as eluent to give **1b** (15% yield), **1c** (62% yield), **3b** (58% yield) and **3c** (58% yield).

General procedure for synthesis of benzylidene barbiturates

A mixture of barbiturate acid (2.0 mmol) and benzaldehyde (2.0 mmol) in EtOH (10 mL) was refluxed for 2–12 h. The reaction mixture was allowed to cool to room temperature and filtered to obtain solid/crystalline crude products. The residue was purified by flash column chromatography on silica gel using ethyl acetate–hexane as eluent to give benzylidene barbiturates in 24–95% yield.

Procedure for catalytic conjugate additions of benzylidene barbiturates

A mixture of benzylidene barbiturates **5** (0.05 mmol), 2-methylfuran (0.05 mmol) and HB-DAD organocatalyst **1a** (0.01 mmol) in CH_2Cl_2 (1 mL) was stirred at 25 °C for 24 h. The product yield was determined by crude ^1H NMR with toluene (0.02 mmol) as internal standard. The reaction mixture was concentrated. The residue was purified by flash column chromatography on silica gel using ethyl acetate–hexane as eluent to obtain isolated yield.

Kinetics study

All reactions were conducted with 0.025 mmol of benzylidene barbiturate **5a**, 0.25 mmol of 2-methylfuran, 0.03 mmol of dichloromethane (internal standard) and 20 mol% of HB-DAD organocatalysts. Stock solutions of **5a** (0.083 M; 0.05 mmol of **5a** in 0.6 mL of CDCl_3) and the HB-DAD organocatalysts (0.05 M; 0.01 mmol of HB-DAD organocatalysts in 0.2 mL of CDCl_3) were prepared in 2 mL vials. A NMR tube was charged with 0.3 mL of **5a** stock solution followed by 0.1 mL of HB-DAD organocatalysts stock solution and 1.98 μL of dichloromethane. The mixture was made up to 0.5 mL with CDCl_3 . After adding 22.3 μL of 2-methylfuran, the first NMR spectrum was taken 5 min after the addition. Additional NMR spectra were recorded every 5 min for a total of 120 min.

Binding study

Ten graduated flasks (5 mL) were added with 0.5 mL of stock solution of barbiturate **9** (2×10^{-4} M; 2×10^{-2} mmol of barbiturate **9** in 100.0 mL of CH_2Cl_2) (final concentration: 2×10^{-5} M) and 0, 20, 40, 80, 160, 320, 640, 1260, 2560, 3000 μL (corresponding to a 2–290 fold excess) of a stock solution of HB-DAD organocatalysts (9.67×10^{-3} M; 9.67×10^{-2} mmol of HB-DAD organocatalysts in 10.0 mL of CH_2Cl_2), and filled up to 5 mL with CH_2Cl_2 . The change in absorbance was monitored and evaluated by linearized Scatchard plot. The given values of K_A were the average of two runs.

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