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Zinc Triflate Catalyzed C-Benzylation: Chemo- and Regioselective Route to Amido Substituted Diaryl and Arylheteroarylmethanes

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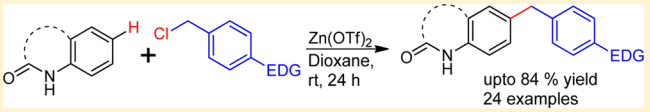
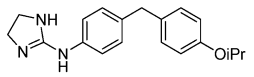
Supporting Information

ABSTRACT: An unprecedented zinc triflate catalyzed selective C-benzylation of anilides and heteroaryl amides with benzyl chlorides having electron-donating group at *para*-position is reported. The protocol offers moderate to high yield of *para*-amido substituted diaryl and arylheteroaryl-methanes, uses cheap and easily available benzyl chlorides as the benzylating agent, catalytic amount of zinc triflate, and takes place under ambient conditions. Aminodiarylmethane derivatives can be obtained by hydrolysis of the corresponding amides. The methodology has also been applied for preparing dimethoxydiarylmethanes in good yields, which are the key precursors for synthesis of phenolic natural products.

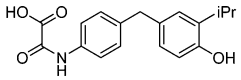


INTRODUCTION

Diarylmethanes are important constituents of agrochemicals, natural products, supramolecular structures, fine and bulk chemicals.[1,2] They are key precursors for the synthesis of fluorenyl-based electroactive and photoactive oligomers and polymers.[3] Specifically, amido, amino, and methoxy substituted diaryl- and arylheteroaryl-methane motifs are an integral part of a number of biologically potent compounds.[4] As shown in Figure 1, they exhibit diverse activities such as prostacyclin



PGI_2 anatgonist (inflammation and pain)



Arteriosclerosis and hypercholesterolaemia

Figure 1. Biologically important substituted diarylmethanes.

receptor antagonist for pain and inflammation, for treatment of arteriosclerosis and hypercholesterolemia, and nonsteroidal nuclear receptor inhibitors.[5] Therefore, the development of mild, efficient and economical methods for their synthesis is an important goal for organic chemists.

The classical approaches toward amine substituted diaryl-methane synthesis involve addition reaction of aromatic amines with styrene,[6] reduction of diarylketones having an amine group[7] or transition metal assisted cross coupling reactions of aromatic bromides having an amine group with benzylzinc reagents.[8] An ancient approach uses cheaply available 4,4′-diaminodiphenylmethane, and involves its selective mono-acetylation followed by diazotization.[9] The diazonium salt is then replaced by hydroxy group, and alkylated to yield the 4-amido-4′-methoxydiarylmethanes. While the above methods suffer from harsh reaction conditions, employing direct benzylation strategy between aryl amines and benzyl halides also fails, and instead of producing amine substituted diarylmethanes, yields the *N*-benzylated product.[10] To prevent *N*-benzylation, anilides are often used as substrates since they are less nucleophilic than amines. However, even they yield *N*-benzylated product when subjected to base promoted benzylation with benzyl halides.[11] Under acid mediated conditions employing benzyl alcohols as benzylating agents, acids such as pTSA[12] furnish a mixture of 5-benzylated and 5,*N*-dibenzylated oxindoles (Figure 2), while with others like

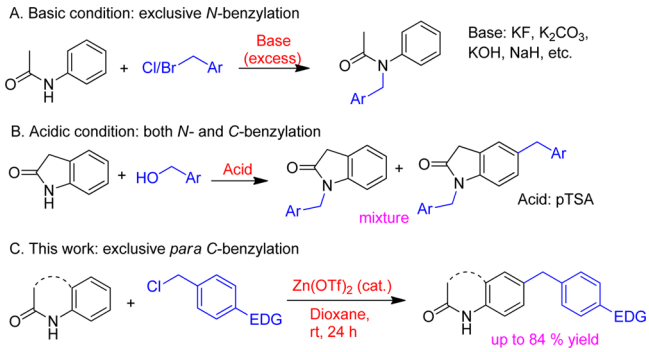


Figure 2. Literature procedures for C/N-benzylation of anilides vs our approach.

Al-grafted MCM-41, a complex mixture of both *N*-benzylated and *ortho*- and *para*- C-benzylated products is obtained.[12b] Apparently, with the current methods available, it is almost impossible to perform *para*-selective C-benzylation of anilides. As an attempt to lift this limitation, herein, we demonstrate an exclusive C-benzylation of anilides and heteroaryl amides with benzyl chlorides using zinc triflate as the catalyst under ambient conditions. This is the first report showing the use of benzyl halides as C-benzylating agents under acidic conditions.

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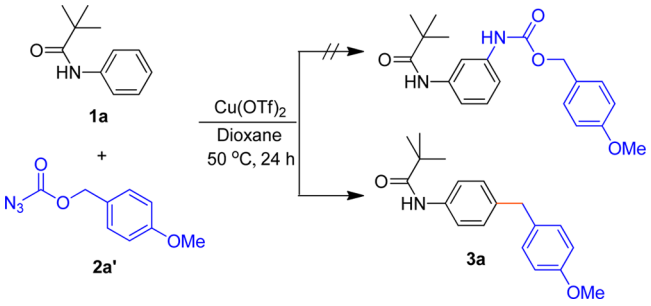
RESULTS AND DISCUSSION

The benzylation was discovered accidently during our endeavors of carrying out copper triflate mediated *meta*-selective amidation of pivaloylanilide (**1a**) using 4-methoxy benzyl azidoester (**2a′**) in dioxane at 50 °C (Scheme 1). While

Scheme 1. $Cu(OTf)_2$ Catalyzed Reaction of Pivaloylanilide with Azido Ester



we did not get the desired product, an unexpected product was isolated in 30% yield, and the reaction did not go to completion even after stirring for 24 h. The spectroscopic characterization showed the product to be *N*-[4-(4-methoxybenzyl)phenyl]-2,2-dimethylpropanamide (**3a**). Intrigued by this observation, we checked if there were any previous reports on C-benzylation of anilides using copper catalyst. Since no precedence to a similar work was found, and realizing its potential in making molecules with diaryl methane motif, we decided to explore the reaction in further details.

Extensive optimization studies were taken up with **1a** as the substrate, and variations in the catalyst, solvent, time and temperature were done (Table 1). First, to ascertain the role of copper triflate as a Lewis acid, reaction between **1a** and **2a′** was carried out using the conventional Lewis acid aluminum trichloride (0.2 equiv) in dichloroethane at 60 °C (entry 1). The reaction was found to fail completely, and **3a** was not seen even after stirring for 24 h. However, on increasing the catalyst loading from 0.2 equiv to 1.2 equiv (entry 2), the desired product was obtained, albeit in low yield (25%). Further, on changing the benzylating agent from azidoester to 4-methoxybenzyl chloride (**2a**), no product was obtained even at elevated temperatures (80 °C, entry 3). With $Cu(OTf)_2$ as the catalyst, however, the reaction between **1a** and **2a** yielded **3a** in 28% yield (entry 4). These preliminary experiments confirmed the potential of $Cu(OTf)_2$ over $AlCl_3$ as a catalyst in promoting C-benzylation with benzyl chlorides. Motivated by the results, we next explored several other Lewis acids such as $Yb(OTf)_3$, $Sc(OTf)_3$, $Zn(OTf)_2$, and $In(OTf)_3$ in dioxane at 80 °C (entry 6–9). With these Lewis acid catalysts, the yield of **3a** was found to increase (44–57%); however, formation of substantial amount of dibenzylated product was also seen (26–40%). Since $Zn(OTf)_2$ happened to be the cheapest of all the triflates examined, it was selected for further studies. Bringing down the reaction temperature from 80 °C to ambient conditions resulted in an increase in the yield of monobenzylated product **3a** to 69%, and drastically reduced the dibenzylated product formation (entry 10). Pleased with this finding, we next monitored the reaction by lowering the catalytic loading to 10 mol %. Although, this resulted in a slight drop in the yield of **3a** (entry 11), increasing the reaction time up to 24 h helped in escalating the yield of **3a** up to 84% (entry 12). Applying identical reaction conditions on **2a′** in place of **2a** did not give any product (entry 13). Next, to assess the necessity of methoxy group in this reaction, reaction with unsubstituted benzyl chloride was carried out. As expected, no product was seen in this case (entry 12). Screening of solvents such as acetonitrile, THF, DCM, DMF, DMSO and toluene was done, and all were found to be inferior to 1,4-dioxane (entry 14–19). In fact, the reaction was completely inhibited with coordinating solvents like DMF and DMSO (entries 17

Table 1. Optimization Table for C-Benzylation of Anilide[a]

entry	X	catalyst (equiv)	solvent	temp °C (time, h)	% yield[b] (dibenzylated)
1	N_3CO_2	$AlCl_3$, (0.2)	DCE	60 (24)	0
2	N_3CO_2	$AlCl_3$, (1.2)	DCE	60 (16)	25
3	Cl	$AlCl_3$, (1.2)	DCE	80 (16)	0
4	N_3CO_2	$Cu(OTf)_2$, (0.2)	Dioxane	80 (16)	34
5	Cl	$Cu(OTf)_2$, (0.2)	Dioxane	80 (16)	28
6	Cl	$Yb(OTf)_3$, (0.2)	Dioxane	80 (16)	57 (26)
7	Cl	$Sc(OTf)_3$, (0.2)	Dioxane	80 (16)	44 (40)
8	Cl	$Zn(OTf)_2$, (0.2)	Dioxane	80 (16)	48 (37)
9	Cl	$In(OTf)_3$, (0.2)	Dioxane	80 (16)	53 (32)
10	Cl	$Zn(OTf)_2$, (0.2)	Dioxane	RT (16)	69 (5)
11	Cl	$Zn(OTf)_2$, (0.1)	Dioxane	RT (16)	65 (5)
12	Cl	$Zn(OTf)_2$, (0.1)	Dioxane	RT (24)	84 (5), 0[c]
13	N_3CO_2	$Zn(OTf)_2$, (0.1)	Dioxane	RT (24)	0
14	Cl	$Zn(OTf)_2$, (0.1)	CH_3CN	RT (24)	48 (5)
15	Cl	$Zn(OTf)_2$, (0.1)	THF	RT (24)	48 (2)
16	Cl	$Zn(OTf)_2$, (0.1)	DCM	RT (24)	49 (13)
17	Cl	$Zn(OTf)_2$, (0.1)	DMF	RT (24)	0
18	Cl	$Zn(OTf)_2$, (0.1)	DMSO	RT (24)	0
19	Cl	$Zn(OTf)_2$, (0.1)	Toluene	RT (24)	14 (31)
20[d]	Cl	$Zn(OTf)_2$, (0.1)	Dioxane	RT (24)	5
21[e]	Cl	$Zn(OTf)_2$, (0.1)	Dioxane	RT (24)	0
22[f]	Cl	$Zn(OTf)_2$, (0.1)	Dioxane	RT (24)	64 (15)
23[g]	Cl	$Zn(OTf)_2$, (0.1)	Dioxane	RT (24)	63 (14)
24	Cl	pTSA (0.2)	Dioxane	RT (18)	0
25	Cl	pTSA (0.2)	Dioxane	90 (18)	0
26[h]	OH	pTSA (0.05)	CH_3NO_2	90 (18)	33
27[h]	OH	pTSA (0.2)	CH_3NO_2	90 (18)	40

[a] **1a** (1.0 equiv), benzylating reagent (1.2 equiv) and catalyst in solvent. [b] HPLC yield of **3a**. [c] benzyl chloride was used in place of 4-methoxy benzyl chloride (**2a**). [d] K_3PO_4 (1.1 equiv) was used as base. [e] Et_3N (1 equiv) was used as base. [f] Acetic acid (2.0 equiv) was used as additive. [g] Trifluoroacetic acid (2.0 equiv) was used as additive. [h] **1a** (1.0 equiv), 4-methoxybenzyl alcohol (1.0 equiv), pTSA in nitromethane.

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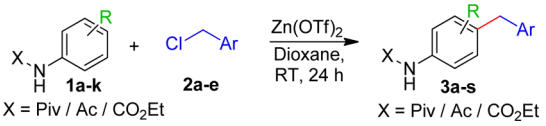
and 18). Addition of bases such as K_3PO_4 and Et_3N was detrimental to the reaction, and did not yield any product (entries 20 and 21), which is reasonable since they tend to quench the acid catalysis by coordinating with zinc ion. Addition of acids such as acetic acid and TFA, dropped the yield of **3a** due to significant formation of disubstituted products (entries 22 and 23). Replacing $Zn(OTf)_2$ with pTSA as the acid catalyst, however, failed to yield the desired product (entries 24 and 25). The literature conditions[12] employing 4-methoxybenzyl alcohol and pTSA as the catalyst, when applied to **1a** as the substrate, yielded the desired product **3a** in only 33% yield along with unreacted **1a** (entry 26). The yield did not improve much on increasing the catalyst loading from 5 mol % to 20 mol % (entry 27), demonstrating the higher efficiency of $Zn(OTf)_2$ over pTSA in catalyzing the reaction.

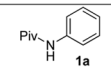
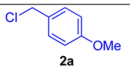
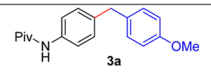
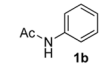
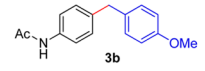
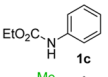
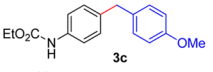
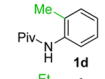
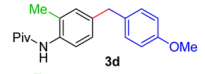
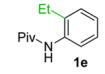
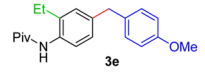
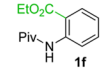
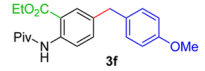
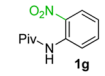
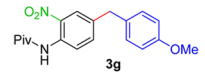
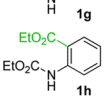
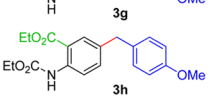
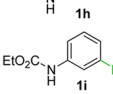
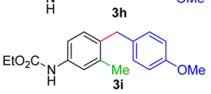
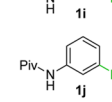
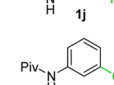
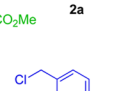
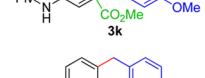
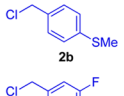
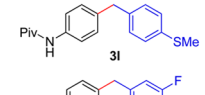
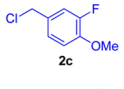
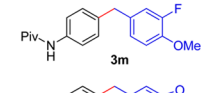
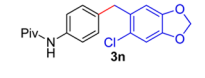
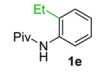
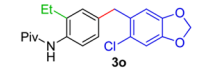
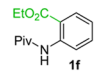
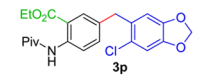
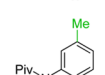
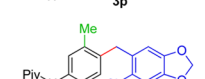
The optimized conditions for obtaining the monosubstituted product were found to be with methoxy substituted benzyl chloride, and 10 mol % $Zn(OTf)_2$ at room temperature for 24 h. To explore the versatility of this method, the substrate scope was tested by using various amides and benzylating agents (Table 2). Under the optimized reaction condition, changing the amide from *N*-pivaloyl (**1a**) to *N*-acetyl (**1b**) resulted in a drop in the yield of diarylmethane amide from 76% (**3a**) to 53% (**3b**). However, with carbamate in place of amide, as in ethyl phenyl carbamate (**1c**), the highest yield of benzylated product (**3c,** 84%) was isolated. With *ortho*-methyl and ethyl derivatives of pivaloylamide, products **3d** and **3e** were isolated in similar yields as with the unsubstituted counterpart **3a**.

Presence of electron withdrawing ester group at *ortho*-position to the amide resulted in slightly lower yield of the corresponding diarylmethane derivative (**3f**). In fact, with very strong electron withdrawing substituent like nitro, no trace of the desired product **3g** was seen even on heating the contents at 100 °C for 24 h, suggesting that highly electron deficient arenes are not suitable for this reaction. In general, it was found that ethyl phenyl carbamate gave higher product yields (**3c**, **3h**, **3i**) compared to those obtained from the corresponding pivaloyl amide (**3a**, **3f**, **3j**) as the starting substrate, again indicative of electron rich arenes to facilitate the reaction. After evaluating the effect of *ortho*-substituent on reaction yield, we shifted our focus toward the *meta*-position, which is closest to the reaction center. Lower yields were obtained with substituents at the *meta*-position (**3j, 3k**) compared to those occupying *ortho*-position (**3d, 3f**). While the effect was less pronounced with small substituents like methyl (**3d** and **3j**), the disparity increased with bulkier ester group (**3f** and **3k**). The significant drop in reaction yield is governed both by the steric and electronic effects of ester group, which not only reduces the electron density at *para*-position of anilide but also makes the approach of incoming electrophile difficult. The reaction of **1a** with 4-trifluoromethoxybenzyl chloride (**2e**) was attempted but failed to yield the desired product **3s**, suggesting the inability of trifluoromethoxy group in assisting the departure of chloride, thus inhibiting the formation of the reactive intermediate species discussed later.

During optimization studies it became clear that *para*-methoxy group on benzyl chloride was necessary for facilitating the reaction (Table 1, entry 3). Going further, reactivity pattern with respect to other substituents on benzyl chloride was examined. Reaction was found to work well with other *para*-substituted benzylating reagents such as 4-methylsulfanylbenzyl chloride (**2b**), 3-fluoro-4-methoxybenzyl chloride (**2c**) and 5-chloro-6-(chloromethyl)-1,3-benzodioxole (**2d**), and gave the

Table 2. Substrate Scope with Anilide Derivatives and Benzyl Chlorides[a]



Entry	Arylamide (1)	Benzyl chloride (2)	Product (3)	Yield[a]
1				76 %
2		2a		53 %
3		2a		84 %
4		2a		72 %
5		2a		73 %
6		2a		68 %
7		2a		0 %[b]
8		2a		75 %
9		2a		71 %
10		2a		65 %
11		2a		58 %
12	1a			64 %
13	1a			74 %
14	1a			70 %
15		2d		75 %
16		2d		67 %
17		2d		65 %
18		2d		60 %
19	1a			0 %

[a]**1** (1.0 equiv), **2** (1.2 equiv), and $Zn(OTf)_2$ (10 mol %) in 1,4-dioxane (2.0 mL) were stirred at room temperature for 24 h. % Yields are isolated yields. [b]Reaction was performed at 100 °C for 24 h.

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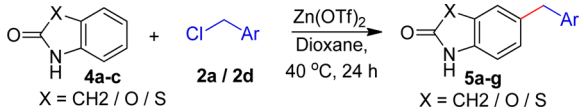
desired products (**3l**-**3r**) in moderate yields. The lower product yield of **3l** (64%) compared to **3a** (76%) is due to weaker electron donation ability of sulfur compared to oxygen. Interestingly, a comparable yield of **3m** was obtained, even on introduction of electron withdrawing fluoro substituent *ortho*- to the methoxy. Further, the yield of the product, **3n** obtained with **2d** was found comparable to that of **3l** obtained with **2b**. This might be due to compensation of steric and electron withdrawing effect of chloro substituent by additional alkoxy subtituent at *meta*-position in **2d**.

The reaction was extended to heterocyclic substrates (**4**) such as 2-oxoindole, benzoxazolone, and benzothiazolone as well (Table 3). A C-5 alkylation of oxoindole, and a C-6

Table 3. Substrate Scope with Heterocyclic Derivatives[a]



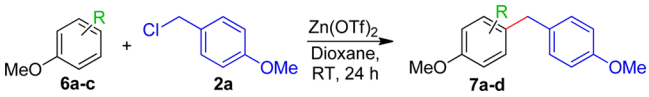
Entry	Amide (4)	Benzyl chloride (2)	Product	Yield[a]
1	4a	2a	5a	64 %
2	4b	2a	5b	74 %
3	4c	2a	5c	72 %
4	4a	2d	5d	55 %
5	4b	2d	5e	59 %
6	4c	2d	5f	59 %
7	4d	2a	5g	72 %

[a]**4** (1.0 equiv), **2** (1.2 equiv), and $Zn(OTf)_2$ (10 mol %) in 1,4-dioxane (2.0 mL) were stirred at 40 °C for 24 h. % Yields are isolated yields.

alkylation in case of benzoxazolone and benzothiazolone took place to yield the substituted aryl-heteroarylmethanes (**5a**−**5f**) in moderate yields, with an optimal reaction temperature of 40 °C. The only preceding report on a one-step C-5 alkylation of oxindole employed benzyl alcohol and *p*TSA at 90 °C yielding a mixture of **5a** and *N*-benzylated **5a**.[12] Hence the above result, furnishing an exclusive C-5 alkylation in one step under acid catalysis is a useful method. Benzylation of 1,3-dimethyluracil gave 5-(4-methoxybenzyl)-1,3-dimethylpyrimidine-2,4-(1*H*,3*H*)-dione (**5g**) in 72% yield. These 5-benzyl uracil derivatives are biologically important as antiviral agents, and for inhibiting the mammalian enzyme uridine phosphorylase responsible for degradation of floxuridine, a known anticancer drug.[13]

As shown in Table 4, the reaction conditions were further explored to test if benzylation of anisole and its derivatives could as well be mediated by $Zn(OTf)_2$. We were delighted to find that the reaction of anisole (**6a**) with **2a** (1.2 equiv) in the

Table 4. C-Benzylation of Anisole Derivatives[a]



Entry	Starting	Reagent	Product	Yield[a]
1	6a	2a	7a	71 %
2	6b	2a	7b	57 %
3	6c	2a	7c	62 %
4	6a	2a[b]	7d	59 %
5	7d	BBr_3, CH_2Cl_2, r.t., Demethylation[15a]	Natural product	

[a]**6** (1.0 equiv), **2** (1.2 equiv), and $Zn(OTf)_2$ (10 mol %) in 1,4-dioxane (2.0 mL) were stirred at room temperature for 24 h. % Yields are isolated yields. [b]4-Methoxybenzyl chloride (4.0 equiv) was used.

presence of $Zn(OTf)_2$ (10 mol %) at room temperature yielded dimethoxydiarylmethane (**7a**) in 71% yield. With *ortho*-chloro and *ortho*-bromo substituted anisole derivatives, slightly lower yield of products (**7b**, **7c**) were obtained. On increasing the amount of **2a** to 4 equiv, dibenzylation took place at *ortho*- and *para*-positions of anisole and **7d** was obtained in 59% yield. The ability to control mono- and dibenzylation adds to the synthetic utility of this protocol which has been illustrated by demethylation of **7d** to yield the naturally occurring 2,4-bis(4-hydroxybenzyl)phenol. The methodology provides a facile access to these molecules, as the earlier reports on their synthesis involve either the use of benzyl alcohols with phosphorus pentoxide on solid supports giving low *ortho*-*para* selectivity, or base promoted reaction of 4-methoxybenzyl halides in excess anisole,[14] or transition metal catalyzed cross couplings using benzylborane, aryltrialkoxysilane and aryllithium as coupling partners.[15] This natural product has recently been reported to be an inhibitor of heat shock transcription factor 1, and also enhances the effectiveness of conventional anticancer agents such as cisplatin and placlitaxel.[16]

To understand the mechanism of reaction, control experiments were carried out. Addition of TEMPO (1 equiv) to the reaction of **1a** and **2a** did not quench the reaction, and the desired product **3a** was isolated suggesting that the reaction did not follow a free radical path. It was evident that the electron donating *para*-substituent in benzyl chloride played a crucial role in this reaction, as no product was formed in its absence (entry 12, Table 1), or its replacement with poor electron donor like trifluoromethoxy group. Based on these experimental findings and literature information, two reaction pathways could be postulated as shown in Scheme 2. In one probable scenario, **2a** gets converted to reactive intermediate, methyl (4-methylidenecyclohexa-2,5-dien-1-ylidene) oxonium (**8**),[17] which undergoes electrophilic aromatic substitution reaction with anilide **1a** at the *para*-position and yields **3a**. Alternatively, it gets converted to 4-methoxybenzyl triflate (**8′**),

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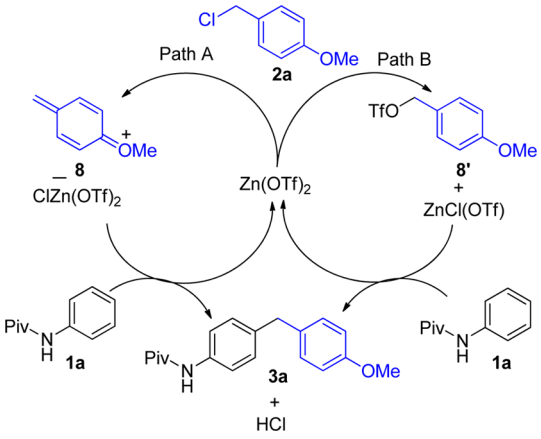
Scheme 2. Plausible Mechanism



which thereafter undergoes *para*-benzylation to yield **3a**. To identify the active intermediate, time-dependent UV−vis analysis of the reaction mixture was performed (Supporting Information). Addition of $Zn(OTf)_2$ to **2a** in dioxane showed appearance of a new peak at 292 nm indicating the formation of a new species, believed to be either **8** or **8′**. In order to confirm the reactive species, a time-dependent ^1H NMR study was done (Figure 3). ^1H NMR of **2a** in CD_3CN showed peaks at 7.4−6.9, 4.6, and 3.8 δ corresponding to aromatic, benzylic and methoxy protons, respectively. Addition of $Zn(OTf)_2$ (10 mol %) to above solution showed appearance of additional peaks in all the three regions suggesting formation of multiple species after 10 min. The benzylic region showed two new signals at 4.54 and 4.95 δ corresponding to protons of 4-methoxybenzyl alcohol and the more deshielded 4-methoxybenzyl triflate, respectively. On addition of **1a** to this solution, the ^1H NMR recorded after 1 min showed a decrease in the intensity of peak at 4.95 δ suggesting that 4-methoxybenzyl triflate which was generated as the reactive species during the reaction was getting consumed on addition of **1a**. Increasing the reaction time to 10 min resulted in further decrease in the intensity of the peak at 4.95 δ due to its conversion to the product **3a**. Based on these observations, we believe that the reaction goes via formation of **8′** as the active intermediate.

CONCLUSIONS

Through this work, we demonstrate a facile and versatile method for *para*-selective C-benzylation of anilides mediated by $Zn(OTf)_2$ under ambient conditions. The protocol is quite robust, uses catalytic amount of inexpensive $Zn(OTf)_2$, easily available methoxysubstituted benzyl chlorides as benzylating agents, and provides moderate to high yield of amido substituted diaryl and arylheteroaryl methane derivatives. The reaction conditions are favorable for regioselective mono- and dibenzylation of arylmethyl ethers as well. Benzyltriflate generated in situ is believed to be the reactive intermediate for effecting mild benzylation. The strategy offers significant synthetic utility, as hydrolysis of the amide provides an easy access to *para*-substituted aminodiarylmethane derivatives.

EXPERIMENTAL SECTION

General Experimental Details. ^1H NMR and ^{13}C NMR spectra were recorded on 400 MHz spectrometer. Chemical shifts (δ) are reported in parts per million downfield from TMS as an internal standard or residual solvent. All organic solvents and reagents were used as received from commercial sources. The starting materials such as substituted 2,2-dimethyl-*N*-phenylpropanamides,[18] and *N*-phenylacetamide[19] were prepared using the literature reported procedures whereas substituted ethyl phenyl carbamates were synthesized using modified procedure (mentioned below). The reported yields are the actual isolated yields of pure materials. Flash chromatography was performed on prepacked silica gel columns. Achiral HPLC analysis was performed on HPLC system using C18 HPLC column (5.0 μm, 4.6 mm × 250 mm) and acetonitrile and formic acid (0.1% v/v in water) as gradient eluting solvent system.

*Representative Procedure for Preparation of Ethyl Phenyl Carbamate (**1c**).* Ethyl chloroformate (61 μL, 6.45 mmol) was slowly added to a stirred solution of aniline (500 mg, 5.38 mmol) and triethylamine (1.1 mL, 8.07 mmol) in dry DCM (20 mL) at 0 °C. The resulting reaction mixture was stirred at 10 °C for 2 h. After completion of reaction, it was diluted with DCM (80 mL) and washed with water (50 mL), 6N aq. HCl (50 mL) and brine (50 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under a vacuum to get crude product contaminated with *N*,*N*′-diphenyl urea. It was then stirred in hexanes (50 mL) and filtered. The filtrate was concentrated under reduced pressure to get the pure title product. The ester and methyl substituted carbamates (**1h** and **1i**) were prepared following above-mentioned procedure.

*Representative Procedure for Preparation of Amido Substituted Diarylmethanes (**3a**−**3s**).* **2a** (46 μL, 0.339 mmol) was added to a

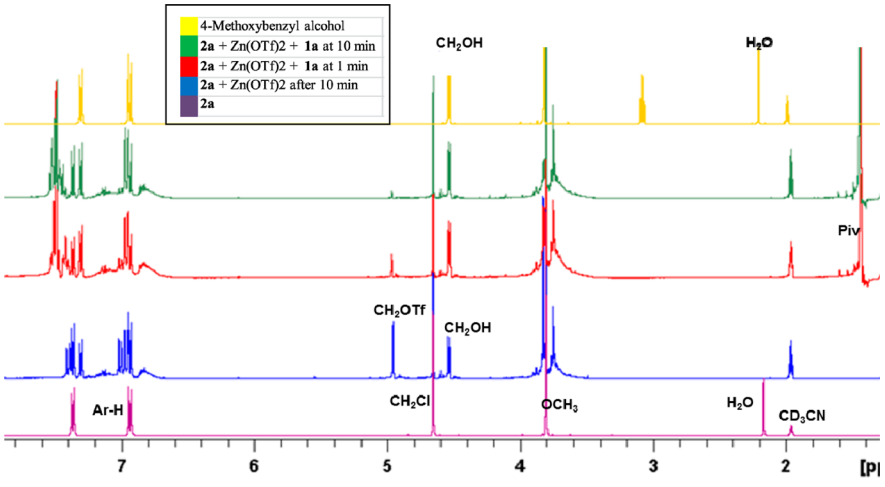


Figure 3. Time dependent overlay of ^1H NMR spectra of reaction of **1a**, **2a** and $Zn(OTf)_2$ in CD_3CN. 4-Methoxybenzyl chloride and 4-methoxybenzyl alcohol have been included for comparison.

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stirred solution of **1a** (50 mg, 0.282 mmol) and $Zn(OTf)_2$ (10 mg, 0.028 mmol) in dry 1,4-dioxane (2.0 mL) at room temperature. The resulting reaction mixture was stirred at same temperature for 24 h. After completion of reaction, it was diluted with EtOAc (50 mL) and washed with saturated aqueous $NaHCO_3$ solution (25 mL) and brine (25 mL). Organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under a vacuum to get crude compound, which was purified by column chromatography using EtOAc:hexanes as eluting medium.

*Representative Procedure for Preparation of Aryl-heteroarylmethanes (**5a**–**5g**).* **2a** (61 μL, 0.451 mmol) was added to a stirred solution of 1,3-dihydro-2*H*-indol-2-one (50 mg, 0.376 mmol) and $Zn(OTf)_2$ (10 mg, 0.038 mmol) in dry 1,4-dioxane (2.0 mL) at room temperature. The resulting reaction mixture was stirred at 40 °C for 24 h. After completion of reaction, it was diluted with EtOAc (50 mL) and washed with saturated aqueous $NaHCO_3$ solution (25 mL) and brine (25 mL). Organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under a vacuum to get crude compound, which was purified by column chromatography using EtOAc:hexanes as eluting medium.

*Representative Procedure for Preparation of 4,4′-Dimethoxydiarylmethanes (**7a**–**7c**).* **2a** (75 μL, 0.556 mmol) was added to a stirred solution of anisole (51 μL, 0.463 mmol) and $Zn(OTf)_2$ (17 mg, 0.046 mmol) in dry 1,4-dioxane (2.0 mL) at room temperature. The resulting reaction mixture was stirred at room temperature for 24 h. It was then diluted with EtOAc (50 mL) and washed with saturated aqueous $NaHCO_3$ solution (25 mL) and brine. Organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under a vacuum to get crude compound, which was purified by column chromatography using EtOAc:hexanes as eluting medium.

*Procedure for Preparation of 1-Methoxy-2,4-bis(4-methoxybenzyl)benzene (**7d**).* **2a** (75 μL, 3.704 mmol) was added to a stirred solution of anisole (101 μL, 0.926 mmol) and $Zn(OTf)_2$ (34 mg, 0.093 mmol) in dry 1,4-dioxane (3.0 mL) at room temperature. The resulting reaction mixture was stirred at room temperature for 24 h. After completion of reaction, it was diluted with EtOAc (50 mL) and washed with saturated aqueous $NaHCO_3$ solution (25 mL) and brine (25 mL). Organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under a vacuum to get crude compound, which was purified by column chromatography using EtOAc:hexanes as eluting medium.

Characterization Data. *N-[4-(4-Methoxybenzyl)phenyl]-2,2-dimethylpropanamide (**3a**).* White solid; 76% yield (64 mg); melting point 129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.43 (d, J = 8.5 Hz, 2H), 7.28 (br. s., 1H), 7.12 (d, J = 8.5 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 8.7 Hz, 2H), 3.88 (s, 2H), 3.77 (s, 4H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.5, 157.9, 137.5, 136.0, 133.3, 129.8, 129.3, 120.1, 113.9, 55.3, 40.4, 39.5, 27.6. HRMS-ESI exact mass calcd. for $C_{19}H_{23}NNaO_2^+$ $[M + Na]^+$ requires m/z 320.1629, found m/z 320.1621.

*N-[4-(4-Methoxybenzyl)phenyl]acetamide (**3b**).* White solid; 53% yield (50 mg); melting point 116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.39 (d, J = 8.4 Hz, 2H), 7.29 (br. s., 1H), 7.12–6.06 (m, 4H), 6.83–6.80 (d, J = 8.8 Hz, 2H), 3.88 (s, 2H), 3.78 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 167.2, 156.9, 136.6, 134.8, 132.2, 128.8, 128.3, 119.1, 112.9, 54.2, 39.4, 23.5. HRMS-ESI exact mass calcd. for $C_{16}H_{17}NNaO_2^+$ $[M + Na]^+$ requires m/z 278.1151, found m/z 278.1153.

*Ethyl [4-(4-methoxybenzyl)phenyl]carbamate (**3c**).* Orange solid; 84% yield (72 mg); melting point 72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.28 (d, J = 8.0 Hz, 2H), 7.09 (t, J = 8.4 Hz, 4H), 6.82 (d, J = 8.4 Hz, 2H), 6.56 (br. s., 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.87 (s, 2H), 3.78 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 158.0, 153.7, 136.7, 135.9, 133.3, 129.8, 129.4, 118.9, 113.9, 61.2, 55.3, 40.3, 14.6. HRMS-ESI exact mass calcd. for $C_{17}H_{19}NNaO_3^+$ $[M + Na]^+$ requires m/z 308.1262, found m/z 308.1257.

*N-[4-(4-Methoxybenzyl)-2-methylphenyl]-2,2-dimethylpropanamide (**3d**).* Light yellow solid; 72% yield (59 mg); melting point 104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (d, J = 8.0 Hz, 1H), 7.17 (br. s., 1H), 7.08 (d, J = 8.8 Hz, 2H), 7.02 (d, J = 8.0 Hz, 1H), 6.97 (s, 1H), 6.81 (d, J = 8.8 Hz, 2H), 3.85 (s, 2H), 3.78 (s, 3H), 2.20 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.4, 157.9, 138.2, 133.8, 133.3, 130.8, 129.8, 129.0, 127.2, 123.0, 113.9, 55.3, 40.5, 39.7, 27.7, 17.7. HRMS-ESI exact mass calcd. for $C_{20}H_{25}NNaO_2^+$ $[M + Na]^+$ requires m/z 334.1777, found m/z 334.1778.

*N-[2-Ethyl-4-(4-methoxybenzyl)phenyl]-2,2-dimethylpropanamide (**3e**).* Light yellow liquid; 73% yield (58 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.74 (d, J = 8.0 Hz, 1H), 7.23 (br. s., 1H), 7.08 (d, J = 8.4 Hz, 2H), 7.03–7.01 (m, 1H), 6.99 (d, J = 1.6 Hz, 1H), 6.81 (d, J = 8.8 Hz, 2H), 3.87 (s, 2H), 3.78 (s, 3H), 2.54 (q, J = 7.6 Hz, 2H), 1.32 (s, 9H), 1.21 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.5, 157.9, 138.4, 134.8, 133.3, 133.2, 129.8, 129.0, 127.2, 123.6, 113.9, 55.3, 40.6, 39.7, 27.7, 24.5, 14.0. HRMS-ESI exact mass calcd. for $C_{21}H_{27}NNaO_2^+$ $[M + Na]^+$ requires m/z 348.1931, found m/z 348.1934.

*Ethyl 2-[(2,2-dimethylpropanoyl)amino]-5-(4-methoxybenzyl)-benzoate (**3f**).* White solid; 68% yield (50 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.27 (br. s., 1H), 8.68 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 2.3 Hz, 1H), 7.34 (dd, J = 2.4, 8.7 Hz, 1H), 7.07 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 4.37 (q, J = 7.0 Hz, 2H), 3.90 (s, 2H), 3.78 (s, 3H), 1.40 (t, J = 7.2 Hz, 3H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 177.8, 168.4, 158.1, 140.2, 135.3, 135.1, 132.9, 130.8, 129.7, 120.6, 115.4, 113.9, 61.3, 55.3, 40.3, 40.2, 27.6, 14.2. HRMS-ESI exact mass calcd. For $C_{22}H_{27}NNaO_4^+$ $[M + Na]^+$ requires m/z 392.1835, found m/z 392.1832.

*N-[4-(4-Methoxybenzyl)-2-nitrophenyl]-2,2-dimethylpropanamide (**3g**).* Compound was not formed even in traces, and could not be characterized.

*Ethyl 2-[(ethoxycarbonyl)amino]-5-(4-methoxybenzyl)benzoate (**3h**).* Colorless liquid; 75% yield (57 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.40 (s, 1H), 8.34 (d, J = 8.6 Hz, 1H), 7.84 (d, J = 2.3 Hz, 1H), 7.33 (dd, J = 2.3, 8.6 Hz, 1H), 7.08 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 4.36 (q, J = 7.2 Hz, 2H), 4.21 (q, J = 7.2 Hz, 2H), 3.89 (s, 2H), 3.78 (s, 3H), 1.39 (t, J = 7.2 Hz, 3H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 168.1, 158.1, 153.8, 140.1, 135.0, 134.5, 132.9, 130.8, 129.7, 119.1, 114.8, 114.0, 61.3, 61.1, 55.3, 40.1, 14.5, 14.2. HRMS-ESI exact mass calcd. for $C_{20}H_{23}NNaO_5^+$ $[M + Na]^+$ requires m/z 380.1459, found m/z 380.1468.

*Ethyl [4-(4-methoxybenzyl)-3-methylphenyl]carbamate (**3i**).* Colorless liquid; 71% yield (59 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.19 (s, 1H), 7.13 (dd, J = 2.5, 8.3 Hz, 1H), 7.01 (d, J = 8.3 Hz, 3H), 6.80 (d, J = 8.6 Hz, 2H), 6.50 (br. s., 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.86 (s, 2H), 3.77 (s, 3H), 2.20 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.9, 153.7, 137.4, 136.1, 134.6, 132.5, 130.4, 129.6, 120.7, 116.4, 113.8, 61.1, 55.2, 37.9, 19.7, 14.6. HRMS-ESI exact mass calcd. for $C_{18}H_{21}NNaO_3^+$ $[M + Na]^+$ requires m/z 322.1424, found m/z 322.1414.

*N-[4-(4-Methoxybenzyl)-3-methylphenyl]-2,2-dimethylpropanamide (**3j**).* White solid; 65% yield (53 mg); melting point 109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.39 (d, J = 2.8 Hz, 1H), 7.29–7.24 (m, 1H), 7.04 (d, J = 8.3 Hz, 1H), 7.00 (d, J = 8.8 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 3.88 (s, 2H), 3.77 (s, 3H), 2.20 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.5, 157.8, 137.4, 136.3, 135.3, 132.5, 130.3, 129.5, 121.8, 117.5, 113.8, 55.3, 39.6, 38.0, 27.7, 19.7. HRMS-ESI exact mass calcd. for $C_{20}H_{26}NO_2^+$ $[M + H]^+$ requires m/z 312.1958, found m/z 312.1958.

*Methyl 5-[(2,2-dimethylpropanoyl)amino]-2-(4-methoxybenzyl)-benzoate (**3k**).* White solid; 58% yield (44 mg); melting point 119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.98 (d, J = 2.5 Hz, 1H), 7.70 (dd, J = 2.5, 8.3 Hz, 1H), 7.35 (br. s., 1H), 7.17 (d, J = 8.5 Hz, 1H), 7.04 (d, J = 8.8 Hz, 2H), 6.79 (d, J = 8.8 Hz, 2H), 4.26 (s, 2H), 3.82 (s, 3H), 3.77 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.7, 167.6, 157.8, 138.5, 136.2, 133.1, 132.1, 130.2, 129.8, 123.5, 121.9, 113.7, 55.2, 52.1, 39.6, 38.2, 27.6. HRMS-ESI exact mass calcd. for $C_{21}H_{25}NNaO_4^+$ $[M + Na]^+$ requires m/z 378.1683, found m/z 378.1675.

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*2,2-Dimethyl-N-{4-[4-(methylsulfanyl)benzyl]phenyl}-propanamide (**3l**).* White solid; 64% yield (57 mg); melting point 120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.44 (d, J = 8.4 Hz, 2H), 7.28 (br. s., 1H), 7.18 (d, J = 8.3 Hz, 2H), 7.12 (d, J = 8.3 Hz, 2H), 7.10−7.06 (d, J = 8.4 Hz, 2H), 3.90 (s, 2H), 2.45 (s, 3H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.5, 138.3, 136.9, 136.2, 135.7, 129.4, 129.4, 127.2, 120.2, 40.7, 39.6, 27.6, 16.3. HRMS-ESI exact mass calcd. for $C_{19}H_{23}NNaOS^+$ $[M + Na]^+$ requires m/z 336.1388, found m/z 336.1392.

*N-[4-(3-Fluoro-4-methoxybenzyl)phenyl]-2,2-dimethylpropanamide (**3m**).* White solid; 74% yield (66 mg); melting point 125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.45 (d, J = 8.5 Hz, 2H), 7.28 (bs, 1H), 7.12 (d, J = 8.5 Hz, 2H), 6.88−6.84 (m, 3H), 3.86 (d, J = 1.0 Hz, 2H), 3.85 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.5, 151.2, 146.0, 145.9, 136.7, 136.3, 134.4, 134.3, 129.3, 124.3, 124.2, 120.2, 116.6, 116.4, 113.5, 113.5, 56.4, 40.3, 39.6, 27.6. HRMS-ESI exact mass calcd. for $C_{19}H_{22}FNNaO_2^+$ $[M + Na]^+$ requires m/z 338.1529, found m/z 338.1527.

*N-{4-[(6-Chloro-1,3-benzodioxol-5-yl)methyl]phenyl}-2,2-dimethylpropanamide (**3n**).* White solid; 70% yield (68 mg); melting point 144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.45 (d, J = 8.5 Hz, 2H), 7.28 (br. s., 1H), 7.13 (d, J = 8.5 Hz, 2H), 6.84 (s, 1H), 6.58 (s, 1H), 5.93 (s, 2H), 3.95 (s, 2H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.5, 146.7, 146.7, 136.3, 135.6, 131.7, 129.3, 125.5, 120.1, 110.3, 109.8, 101.6, 39.6, 38.4, 27.6. HRMS-ESI exact mass calcd. for $C_{19}H_{20}ClNNaO_3^+$ $[M + Na]^+$ requires m/z 368.1030, found m/z 368.1023.

*N-{4-[(6-Chloro-1,3-benzodioxol-5-yl)methyl]-2-ethylphenyl}-2,2-dimethylpropanamide (**3o**).* White solid; 75% yield (68 mg); melting point 134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.77 (d, J = 8.6 Hz, 1H), 7.25 (br. s., 1H), 7.04−6.99 (m, 2H), 6.84 (s, 1H), 6.58 (s, 1H), 5.93 (s, 2H), 3.94 (s, 2H), 2.56 (q, J = 7.6 Hz, 2H), 1.33 (s, 9H), 1.22 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.5, 146.7, 146.6, 136.5, 134.8, 133.5, 131.8, 129.0, 127.2, 125.4, 123.5, 110.3, 109.8, 101.6, 39.7, 38.5, 27.7, 24.5, 14.0. HRMS-ESI exact mass calcd. for $C_{21}H_{24}ClNNaO_3^+$ $[M + Na]^+$ requires m/z 396.1333, found m/z 396.1336.

*Ethyl 5-[(6-chloro-1,3-benzodioxol-5-yl)methyl]-2-[(2,2-dimethylpropanoyl)amino] benzoate (**3p**).* Colorless liquid; 67% yield (56 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.29 (br. s., 1H), 8.69 (d, J = 8.8 Hz, 1H), 7.89 (d, J = 2.3 Hz, 1H), 7.33 (dd, J = 2.4, 8.7 Hz, 1H), 6.85 (s, 1H), 6.56 (s, 1H), 5.94 (s, 2H), 4.38 (q, J = 7.2 Hz, 2H), 3.97 (s, 2H), 1.41 (t, J = 7.1 Hz, 3H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 177.8, 168.3, 146.8, 140.4, 135.0, 133.5, 131.3, 130.9, 125.5, 120.6, 115.4, 110.2, 109.9, 101.7, 61.4, 40.3, 38.3, 27.6, 14.2. HRMS-ESI exact mass calcd. for $C_{22}H_{24}ClNNaO_5^+$ $[M + Na]^+$ requires m/z 440.1246, found m/z 440.1235.

*N-{4-[(6-Chloro-1,3-benzodioxol-5-yl)methyl]-3-methylphenyl}-2,2-dimethylpropanamide (**3q**).* White solid; 65% yield (61 mg); melting point 129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.44 (d, J = 2.8 Hz, 1H), 7.29−7.24 (m, 1H), 6.95 (d, J = 8.3 Hz, 1H), 6.86 (s, 1H), 6.34 (s, 1H), 5.91 (s, 2H), 3.91 (s, 2H), 2.20 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.5, 146.8, 146.5, 137.6, 136.6, 133.6, 131.1, 130.1, 125.5, 121.9, 117.6, 109.7, 109.7, 101.6, 39.6, 36.0, 27.6, 19.6. HRMS-ESI exact mass calcd. for $C_{20}H_{22}ClNNaO_3^+$ $[M + Na]^+$ requires m/z 382.1179, found m/z 382.1180.

*Methyl 2-[(6-chloro-1,3-benzodioxol-5-yl)methyl]-5-[(2,2-dimethylpropanoyl)amino]benzoate (**3r**).* White solid; 60% yield (51 mg); melting point 97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.06 (d, J = 2.5 Hz, 1H), 7.71 (dd, J = 2.5, 8.5 Hz, 1H), 7.39 (d, J = 1.3 Hz, 1H), 7.06 (d, J = 8.5 Hz, 1H), 6.85 (s, 1H), 6.40 (s, 1H), 5.92 (s, 2H), 4.32 (s, 2H), 3.84 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.7, 167.4, 146.7, 146.5, 136.6, 136.5, 131.7, 131.7, 130.2, 125.5, 123.7, 122.0, 110.0, 109.7, 101.6, 52.1, 39.6, 36.6, 27.7. HRMS-ESI exact mass calcd. for $C_{21}H_{21}ClNO_5^+$ $[M + H]^+$ requires m/z 404.1259, found m/z 404.1272.

*2,2-dimethyl-N-{4-[4-(trifluoromethoxy)benzyl]phenyl}-propanamide (**3s**).* Compound was not formed even in traces, and could not be characterized.

*5-(4-Methoxybenzyl)-1,3-dihydro-2H-indol-2-one (**5a**).* White solid; 64% yield (61 mg); melting point 167 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 10.25 (s, 1H), 7.11 (d, J = 8.8 Hz, 2H), 7.03−6.96 (m, 2H), 6.83 (d, J = 8.5 Hz, 2H), 6.71 (d, J = 7.8 Hz, 1H), 3.79 (s, 2H), 3.70 (s, 3H), 3.40 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ (ppm) 176.8, 158.0, 142.1, 135.1, 134.2, 130.0, 127.9, 126.5, 125.1, 114.3, 109.3, 55.5, 40.4, 36.2. HRMS-ESI exact mass calcd. for $C_{16}H_{15}NO_2^+$ $[M + H]^+$ requires m/z 254.1176, found m/z 254.1177.

*6-(4-Methoxybenzyl)-1,3-benzoxazol-2(3H)-one (**5b**).* White solid; 74% yield (70 mg); melting point 159 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 11.49 (br. s., 1H), 7.17−7.10 (m, 3H), 6.98 (d, J = 1.0 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 3.87 (s, 2H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ (ppm) 157.5, 154.4, 143.4, 135.9, 133.2, 129.5, 128.2, 123.7, 113.8, 109.5, 109.4, 54.9. HRMS-ESI exact mass calcd. for $C_{15}H_{13}NNaO_3^+$ $[M + Na]^+$ requires m/z 278.0787, found m/z 278.0787.

*6-(4-Methoxybenzyl)-1,3-benzothiazol-2(3H)-one (**5c**).* White solid; 72% yield (65 mg); melting point 173 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 11.78 (br. s., 1H), 7.39 (d, J = 1.8 Hz, 1H), 7.16−7.08 (m, 3H), 7.04−7.00 (m, 1H), 6.84 (d, J = 8.5 Hz, 2H), 3.85 (s, 2H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ (ppm) 170.4, 158.1, 136.9, 134.9, 133.7, 130.1, 127.3, 123.9, 122.9, 114.3, 111.9, 55.5. HRMS-ESI exact mass calcd. for $C_{15}H_{13}NNaO_2S^+$ $[M + Na]^+$ requires m/z 294.0543, found m/z 294.0549.

*5-[(6-Chloro-1,3-benzodioxol-5-yl)methyl]-1,3-dihydro-2H-indol-2-one (**5d**).* Brown solid; 55% yield (62 mg); melting point 230 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 10.30 (s, 1H), 7.05 (s, 1H), 7.03−6.97 (m, 2H), 6.92 (s, 1H), 6.72 (d, J = 7.6 Hz, 1H), 6.04 (s, 2H), 3.88 (s, 2H), 3.42 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ (ppm) 176.3, 146.6, 146.5, 141.9, 132.5, 131.9, 127.4, 126.0, 124.4, 124.2, 110.5, 109.4, 108.8, 101.8, 37.7, 35.7. HRMS-ESI exact mass calcd. for $C_{16}H_{12}ClNNaO_3^+$ $[M + Na]^+$ requires m/z 324.0410, found m/z 324.0398.

*6-[(6-Chloro-1,3-benzodioxol-5-yl)methyl]-1,3-benzoxazol-2(3H)-one (**5e**).* White solid; 59% yield (66 mg); melting point 196 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 11.54 (bs, 1H), 7.13 (d, J = 1.3 Hz, 1H), 7.06 (s, 1H), 7.02−6.95 (m, 3H), 6.04 (s, 2H), 3.96 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ (ppm) 154.4, 146.6, 143.4, 133.7, 131.4, 128.5, 124.2, 123.6, 110.5, 109.5, 109.4, 101.8, 37.8. HRMS-ESI exact mass calcd. for $C_{15}H_{10}ClNNaO_4^+$ $[M + Na]^+$ requires m/z 326.0191, found m/z 326.0190.

*6-[(6-Chloro-1,3-benzodioxol-5-yl)methyl]-1,3-benzothiazol-2(3H)-one (**5f**).* White solid; 59% yield (62 mg); melting point 234 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 11.81 (br s, 1H), 7.38 (d, J = 1.8 Hz, 1H), 7.14−7.08 (m, 1H), 7.07−7.00 (m, 2H), 6.96 (s, 1H), 6.04 (s, 2H), 3.94 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ (ppm) 170.4, 147.2, 147.1, 135.1, 134.8, 131.8, 127.2, 124.8, 123.9, 122.8, 111.9, 111.1, 110.0, 102.3, 38.2. For $C_{15}H_{11}ClNO_3S^+$ $[M + H]^+$ requires m/z 320.0145, found m/z 320.0142.

*5-(4-Methoxybenzyl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (**5g**).* White solid; 72% yield (67 mg); melting point 80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.15 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 6.69 (s, 1H), 3.79 (s, 3H), 3.60 (s, 2H), 3.36 (s, 3H), 3.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.5, 157.3, 150.7, 138.7, 129.2, 129.1, 113.2, 113.1, 54.2, 35.9, 31.3, 27.0. HRMS-ESI exact mass calcd. for $C_{14}H_{16}N_2O_3^+$ $[M + H]^+$ requires m/z 261.1234, found m/z 261.1235.

*1,1′-Methanediylbis(4-methoxybenzene) (**7a**).* White solid; 71% yield (75 mg); melting point 53 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.09 (d, J = 8.6 Hz, 4H), 6.82 (d, J = 8.8 Hz, 4H), 3.86 (s, 2H), 3.78 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.9, 133.7, 129.7, 113.9, 55.3, 40.1. HRMS-ESI exact mass calcd. for $C_{15}H_{16}NaO_2^+$ $[M + Na]^+$ requires m/z 251.1042, found m/z 251.1042.

*2-Chloro-1-methoxy-4-(4-methoxybenzyl)benzene (**7b**).* White solid; 57% yield (53 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.17 (d, J = 2.3 Hz, 1H), 7.08 (d, J = 8.8 Hz, 2H), 7.01 (dd, J = 2.3, 8.3 Hz, 1H), 6.85−6.81 (m, 3H), 3.86 (s, 3H), 3.83 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 158.1, 153.3, 134.9, 132.9, 130.5, 129.8, 127.9, 122.3, 114.0, 112.1, 56.2, 55.3, 39.9. HRMS-ESI

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exact mass calcd. for $C_{15}H_{15}ClO_2^+$ $[M]^+$ requires m/z 262.0755, found m/z 262.0760.

*2-Bromo-1-methoxy-4-(4-methoxybenzyl)benzene (**7c**).* Colorless liquid; 62% yield (51 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.35 (d, J = 2.3 Hz, 1H), 7.10−7.03 (m, 3H), 6.85−6.78 (m, 3H), 3.86 (s, 3H), 3.83 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.0, 153.1, 134.3, 132.5, 131.8, 128.7, 127.6, 112.9, 110.9, 110.5, 55.24, 54.2, 38.7. HRMS-ESI exact mass calcd. for $C_{15}H_{15}BrNaO_2^+$ $[M + Na]^+$ requires m/z 329.0148, found m/z 329.0147.

*1-Methoxy-2,4-bis(4-methoxybenzyl)benzene (**7d**).* Colorless liquid; 59% yield (190 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.10 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 6.95 (dd, J = 2.4, 8.2 Hz, 1H), 6.90 (d, J = 2.3 Hz, 1H), 6.82−6.78 (m, 4H), 6.76 (d, J = 8.3 Hz, 1H), 3.86 (s, 2H), 3.81 (s, 2H), 3.79−3.74 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.8, 157.7, 155.7, 133.8, 133.4, 133.2, 130.8, 129.9, 129.8, 129.7, 127.4, 113.8, 113.7, 110.5, 55.5, 55.3, 55.2, 40.1, 35.0. HRMS-ESI exact mass calcd. for $C_{23}H_{24}NaO_3^+$ $[M + Na]^+$ requires m/z 371.1616, found m/z 371.1617.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01646.

Copies of ^{1}H and ^{13}C NMR spectra for all the synthesized compounds, and UV−vis data. (PDF)

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Notes

The authors declare no competing financial interest.

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