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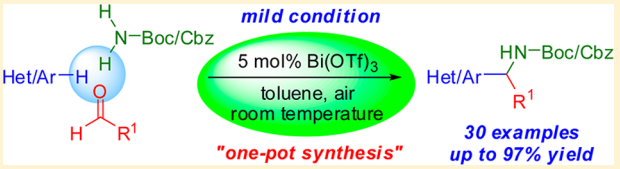
Bi(OTf)$_3$-Catalyzed One-Step Catalytic Synthesis of *N*-Boc or *N*-Cbz Protected α-Branched Amines

Jaray Jaratjaroonphong,* Surisa Tuengpanya, and Sureeporn Ruengsangtongkul

Department of Chemistry and Center of Excellence for Innovation in Chemistry, Faculty of Science, Burapha University, Chonburi 20131, Thailand

Supporting Information

ABSTRACT: In this paper, *N*-Boc and *N*-Cbz protected α-branched amines are synthesized directly from commercially available aromatic/heteroaromatic compounds, aldehydes, and *tert*-butyl or benzyl carbamate bearing a variety of substituents. Bismuth(III) triflate is found to be a highly effective catalyst for this one-pot, three-component coupling reaction. In addition, the use of mild reaction conditions, low catalytic loading, easy removal of the *N*-protective group, and one-step synthesis under "open-flask" are advantages of the present procedure.



INTRODUCTION

The α-branched amine skeleton represents a significant class of biologically active nitrogen compounds that are found in various natural products and drugs with well-recognized pharmacological properties (Figure 1).[1] In particular, they are the most promising therapeutic agents for neurological disorders like Alzheimers and Parkinson disease. As a consequence, the synthesis of α-branched amine derivatives has attracted comprehensive and continuous interest from synthetic organic chemists. Among a myriad of methods to approach functionalized α-branched amine, the aza-Friedel–Crafts reaction (AFCR) between electron-rich arenes and imine derivatives represents one of the most straightforward and atom-economic strategies to access a variety of corresponding α-branched amines.[2,3] Although great success has been achieved in such processes, the methods are multistep processes and require highly electrophilic imine acceptors such as ethyl glyoxylate imines,[4] and α-trifluoromethyl imines.[5] In contrast, the functionalized imines of aromatic aldehydes generally proceed to afford symmetrical triarylmethanes via a double Friedel–Crafts process due to the intrinsic instability of the intermediate benzylamine under the acidic reaction conditions.[6,7] Recently, several groups have reported a multicomponent aza-Friedel–Crafts reaction for the synthesis of α-branched amines in a one-step process without isolation of the imine intermediate under standard reaction conditions.[8−12] The reaction is well-established and practical, but the substrate scope is strictly limited to the indoles or 2-naphthols, amides or urea and nonenolizable, most notably, aryl aldehydes.[8−11] Moreover, there are disadvantages such as the use of expensive and corrosive reagents, high catalyst loading, long reaction times, strongly acidic conditions, low yields of products, and the use of microwave or ultrasonic irradiation.[8] Therefore, the development of a mild and efficient method utilizing aromatic and heteroaromatic systems, an amine source that easily removes the nitrogen-protecting group, a variety of aldehydes including both aromatic and aliphatic aldehydes, and easily available catalysts with high catalytic activity and short reaction times for the direct construction of α-branched amine scaffolds with multiple functional groups is still highly desirable.

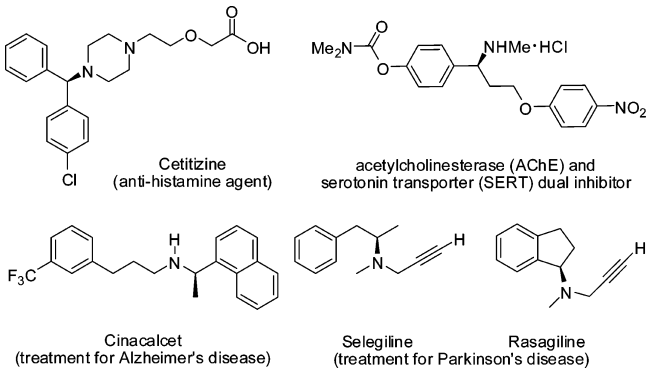


Figure 1. Representative examples of biologically active α-branched amines.

Recently, Bi(OTf)$_3$-catalyzed reactions have emerged as a versatile tool for developing syntheses due to their numerous advantages, namely, their relatively high efficiency, low toxicity, water compatibility, mild reaction conditions, and on eco-friendly catalytic reaction that is commercially available or can be easily prepared from commercially available starting materials.[13] Bi(OTf)$_3$ has been reported as catalyst for three-component Mannich–type reaction of a variety of in situ generated aldimines using aldehydes, anilines, and silyl enol ethers leading to the corresponding α-branched amines.[14a] Very recently, Manolikakes and co-workers reported an elegant work on Bi(OTf)$_3$-catalyzed three-component synthesis of

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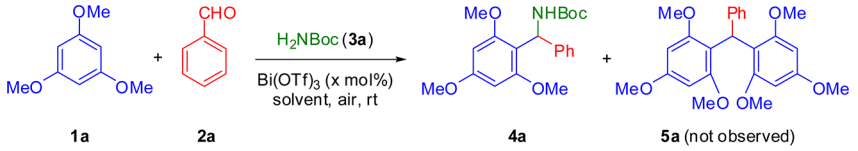
Table 1. Optimization of the Reaction Conditions[a,e]



1a 2a 4a 5a (not observed)

entry	$Bi(OTf)_3$ (mol %)	solvent	time (h)	4a, yield[b] (%)
1	5	CH_2Cl_2	2	88
2	5	$ClCH_2CH_2Cl$	2	88
3	5	MeOH	2	72
4	5	THF	2	89
5	5	CH_3CN	2	75
6	5	toluene	2	91
7	10	toluene	2	84
8	1	toluene	2	77
9	5	toluene	2	93[c]
10	0	toluene	48	[d]

[a]Reaction conditions: **1a** (1 mmol), **2a** (1.1 mmol), **3a** (1 mmol), $Bi(OTf)_3$, solvent (1 mL), room temperature. [b]Isolated yields. [c]The reaction was conducted under a N_2 atmosphere. [d]No reaction based on TLC analysis. [e]No side-product **5a** was observed.

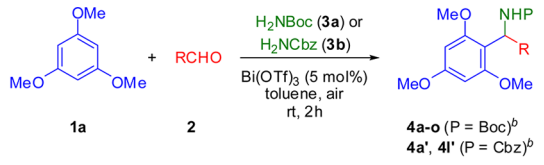
amidomethylated arenes/heteroarenes[14b] and α-amino acid derivatives[14c] from amides, arenes/heteroarenes, and formaldehyde or ethyl glyoxalate. In continuation of the development of useful synthetic methodologies for C−C and C−N bond-forming reactions,[12,15] here, we report an efficient $Bi(OTf)_3$-catalyzed one-pot, three-component aza-Friedel−Crafts reaction of aromatic/heteroaromatic compounds with *tert*-butyl or benzyl carbamates in combination with a wide variety of aldehydes under "open-flask" and mild conditions.

RESULTS AND DISCUSSION

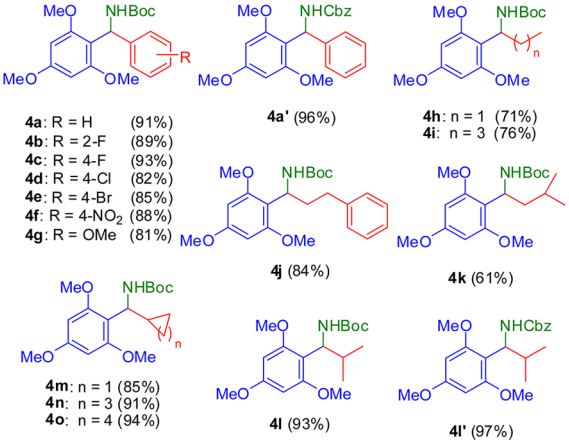
Our initial investigations employing 1,3,5-trimethoxybenzene (**1a**), benzaldehyde (**2a**), and *tert*-butyl carbamate (**3a**) as model substrates in combination with 5 mol % $Bi(OTf)_3$ as catalyst focused on the evaluation of the efficiency of various solvents under "open-flask" conditions (Table 1, entries 1−6). Among solvents tested, toluene seemed to be the most effective for this one-pot, three-component aza-Friedel−Crafts reaction (entry 6). A slightly lower yield was obtained when using CH_2Cl_2, $ClCH_2CH_2Cl$, and THF as a solvent. Encouraged by this result, we subsequently examined catalyst loading and reaction under a N_2 atmosphere. Regarding the quantity of the catalyst, we found that 5 mol % $Bi(OTf)_3$ resulted in a high yield, contrary to the use of 10 or 1 mol % $Bi(OTf)_3$ (entries 7−8). By comparison to the reaction in N_2, the reaction in air also produced the desired products (**4a**) with comparable yield (entries 6 and 9). These led to the confirmation that $Bi(OTf)_3$ is a highly efficient catalyst and highly tolerant of air as well as moisture. Under the reaction conditions, no side-product **5a** was observed. A control reaction in the absence of $Bi(OTf)_3$ gave no products, and starting materials were recovered (entry 10).

To evaluate the scope of this novel strategy for the synthesis of α-branched amines, a wide variety of aldehydes were reacted with 1,3,5-trimethoxybenzene (**1a**) and *tert*-butyl or benzyl carbamates in the presence of $Bi(OTf)_3$ (5 mol %) at room temperature using toluene as the reaction media. The experimental results are summarized in Scheme 1. In all cases, both aromatic aldehydes substituted with electron-donating or electron-withdrawing groups and enolizable aliphatic aldehydes underwent the multicomponent reaction smoothly to provide the desired products **4a−o** with good to excellent yields. Even isobutyraldehyde and cyclohexanecarbaldehyde as sterically fairly

Scheme 1. Scope with Respect to the Aldehyde Compounds[a,b]



1a 2 4a-o (P = Boc)[b] 4a', 4l' (P = Cbz)[b]



[a]Reaction conditions: **1** (1 mmol), **2** (1.1 mmol), **3** (1 mmol), $Bi(OTf)_3$ (5 mol %), toluene (1 mL), room temperature. [b]Isolated yields.

demanding precursors furnished α-branched amines **4l** and **4o**, respectively, in excellent yields. Compared to long chain aliphatic aldehydes, α-branched aliphatic aldehyde afforded higher yields of the desired products, probably due to the higher electrophilicity of the carbonyl group. We also used benzyl carbamate, serving as a nitrogen source, which cleanly provided the desired products **4a′** and **4l′** in excellent yields.

Encouraged by these results, the scope and generality of the reaction was further investigated with an array of electron-rich aromatic/heteroaromatic compounds, aldehydes, and *tert*-butyl or benzyl carbamates. The experimental results are summarized in Table 2. In all cases, both electron-rich aromatic and

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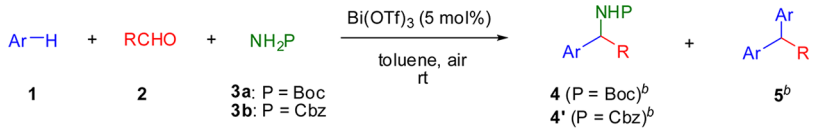
Table 2. Scope with Respect to the Electron-Rich Arenes and Carbamates[a,b,c,d,e]



1 **2** **3a**: P = Boc **3b**: P = Cbz **4** (P = Boc)[b] **4'** (P = Cbz)[b] **5**[b]

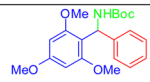
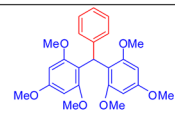
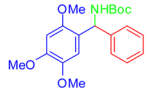
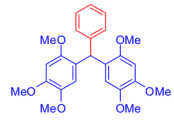
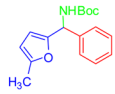
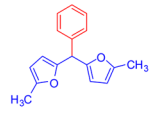
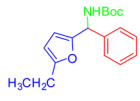
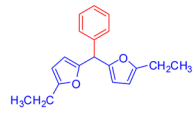
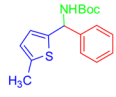
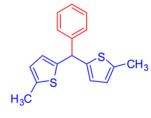
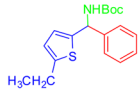
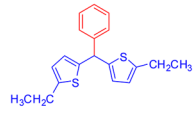
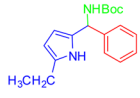
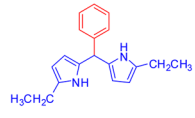
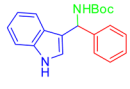
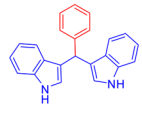
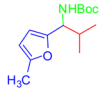
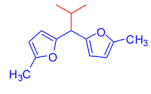
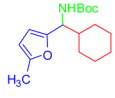
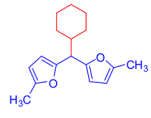
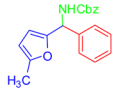
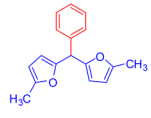
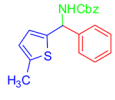
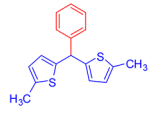
Entry	Arenes	Time (h)	α–Branched amines **4**		Yield (%)[b]	Triarylmethane **5**		Yield (%)[b]
1	**1a**	2		**4a**	91		**5a**	–
2	**1b**	2		**4p**	73		**5p**	8
3	**1c**	1		**4q**	79		**5q**	2
4	**1d**	1		**4r**	73		**5r**	–
5	**1e**	24		**4s**	53[c]		**5s**	7[c]
6	**1f**	24		**4t**	49[c]		**5t**	9[c]
7	**1g**	1 min		**4u**	–[d]		**5u**	65[d]
8	**1h**	10 min		**4v**	32[d]		**5v**	55[d]
9	**1c**	12		**4w**	74		**5w**	14
10	**1c**	12		**4x**	70		**5x**	12
11	**1c**	1		**4q′**	83		**5q**	16
12	**1e**	1		**4s′**	72[e]		**5s**	22[e]

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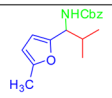
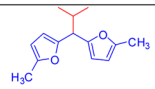
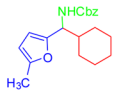
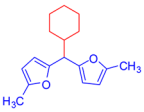
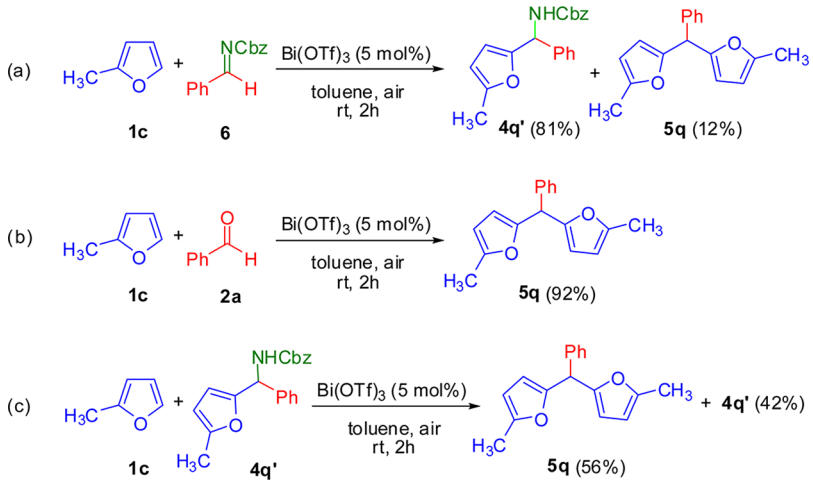
Table 2. continued

Entry	Arenes	Time (h)	α–Branched amines **4**		Yield (%)[b]	Triarylmethane **5**		Yield (%)[b]
13	**1c**	12		**4w′**	58		**5w**	38
14	**1c**	12		**4x′**	55		**5x**	32

[a]Reaction conditions: **1** (1 mmol), **2** (1.1 mmol), **3** (1 mmol), $Bi(OTf)_3$ (5 mol %), toluene (1 mL), room temperature. [b]Isolated yields. [c]The reaction was carried out using $Bi(OTf)_3$ (5 mol %) and arenes (1 mL) without solvent at room tempature. [d]The reaction was carried out using $Bi(OTf)_3$ (5 mol %) in toluene (15 mL) at 0 °C, dropwise. [e]The reaction was carried out using $Bi(OTf)_3$ (20 mol %) in toluene (1 mL) at room tempature.

Scheme 2. Mechanistic Experiments



heteroaromatic compounds, except for pyrrole and indole, proved to be very effective, leading to the selective formation of α-branched amine adducts in moderate to good yields. Compared to 1,3,5-trimethoxybenzene (**1a**), the less sterically electron-rich arene, 1,2,4-trimethoxybenzene (**1b**) gave a slightly lower yield of the aza-Friedel–Crafts products and triarylmethane **5q** was obtained as a minor product via a double Friedel–Crafts reaction (entries 1–2). Not only aromatic nucleophiles but also heteroaromatic nucleophiles like 2-methylfuran (**1c**) or 2-ethylfuran (**1d**) were equally good to satisfactory in affording α-branched amine derivatives **4q** and **4r** in modest yields (entries 3–4). 2-Methylthiophene (**1e**) and 2-ethylthiophene (**1f**), which is known to be a poorly reactive substrate,[16] gave satisfactory product yields, although an excess of the thiophene substrate was employed to accomplish the reaction (entries 5–6). In constrast, heteroaromatic compounds containing nitrogen atoms such as 2-ethylpyrrole (**1g**) and indole (**1h**) evolve according to a double Friedel–Crafts reaction to give triarylmethane as a major product. These might be due to the intrinsic instability of α-branched amine derivatives under our conditions (entries 7–8).[6] We then tested the efficiency of this reaction with the enolizable aldehydes, isobutyraldehyde (entry 9), and cyclohexanecarbaldehyde (entry 10). Gratifyingly, the reactions with 2-methylfuran and *tert*-butyl carbamate were converted into the desired products in moderate yields. Finally, the reaction employing benzyl cabamate with heteroaromatic compounds and aldehydes also afforded *N*-Cbz protected α-branched amines in good yields but with an increase in triarylmethane formation (entries 11–14).

In order to aid our interpretation of the mechanism, a series of experiments were performed as outlined in Scheme 2. Initially, we found that α-branched amine **4q′** and triarylmethane **5q** were found in the reaction of 2-methylfuran with *N*-Cbz imine **6** in the presence of 5 mol % $Bi(OTf)_3$, strongly indicating that the three-component coupling reaction proceeded via *N*-Boc or *N*-Cbz imine intermediates, which generated in situ under the reaction conditions (Scheme 2a). To gain a more thorough understanding of triarylmethane formation under our conditions, the reaction of 2-methylfuran with benzaldehyde (Scheme 2b) and with desired product **4q′** (Scheme 2c) were also carried out. The compound **5q** was obtained in both cases, indicating that aldehyde and diarylmethyl carbamate act as good alkylating agents of Friedel–Crafts reaction.

On the basis of the literature information[7,11,12] and our experimental results, a plausible explanation of the mechanism is depicted in Scheme 3. The first step is the formation of **I**, which is formed by coordination of the aldehyde to $Bi(OTf)_3$. Condensation of **I** with benzyl carbamate gives the resulting activated *N*-Cbz imine **II**. The nucleophilic addition of 2-methylfuran (**1c**) attacks the resulting imine **II**, leading to the formation of the desired amine **4**. Further, the formation of triarylmethane **5** could be explained by addition of a second 2-methylfuran to the reactive intermediate **V**, which is generated by Bi(III)) ion catalyzed carbamate elimination of **4** and/or by dehydration of **IV**. A structure like intermediate **V**

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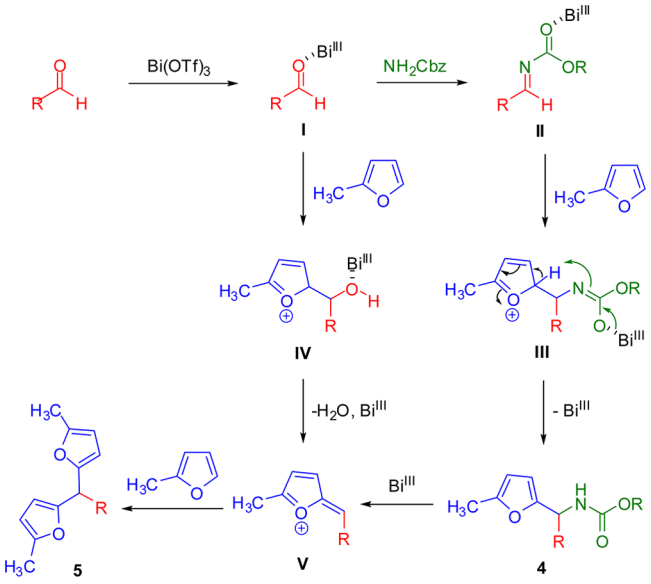
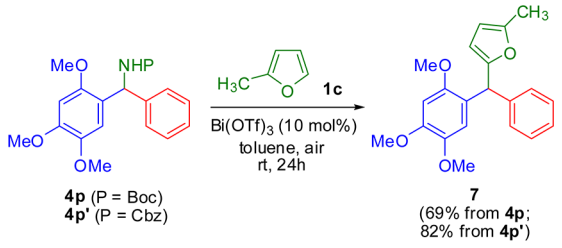
Scheme 3. Plausible Reaction Mechanism



is proposed by other researchers for the reaction of indole with aldehydes[17] and imines.[6b,e,11]

The synthetic utility of this transformation was demonstrated by derivation of the corresponding diarylmethyl carbamate to unsymmetrical triarylmethane (Scheme 4). Friedel–Crafts type

Scheme 4. Synthesis of an Unsymmetrical Triarylmethane



substitution reactions of **4p** and **4p′** occurred cleanly by treatment with 2-methylfuran in the present of 10 mol % $Bi(OTf)_3$ in toluene at room temperature to afford unsymmetrical triarylmethane **7** in 69% and 82% yields, respectively.

CONCLUSIONS

In summary, we have successfully developed a one-pot, three-component aza-Friedel–Crafts reaction of electron-rich arenes with a variety of aldehydes and *tert*-butyl or benzyl carbamate, providing an efficient approach for the direct construction of the corresponding *N*-Boc and *N*-Cbz protected α-branched amines in the presence of a catalytic amount of $Bi(OTf)_3$. The reactions were also applicable to enolizable aliphatic aldehydes as well as to various heteroaromatic compounds. In addition, the use of mild reaction conditions, low catalytic loading, easy removal of the *N*-protective group,[18,19] and one-step synthesis are advantages of the present procedure. The further development of asymmetric reaction is ongoing and will be reported in due course.

EXPERIMENTAL SECTION

General Procedure. All isolated compound were characterized on the basis of ^{1}H NMR and ^{13}C NMR spectroscopic data, IR spectra, and HRMS data. ^{1}H NMR and ^{13}C NMR chemical shifts are reported in ppm using tetramethylsilane (TMS) as an internal standard or the residual nondeuterated solvent peak as an internal standard.

General Procedure for the Synthesis of α-Branched Amines 4. To a toluene solution (1 mL) of electron-rich arene (1.0 mmol), freshly distilled aldehyde (1.1 mmol), and *tert*-butyl or benzyl carbamate (1.0 mmol) in a test tube open to air at room temperature was added $Bi(OTf)_3$ (0.05 mmol). After the reaction was stirred until completion (TLC analysis), the reaction mixture was quenched with aqueous $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, and filtered. The filtrate was evaporated (aspirator then vacuo) to give a crude product, which was purified by radial chromatography (SiO_2, 100% hexane to 30% EtOAc/hexane as eluent) to give the corresponding α-branched amines **4** and/or triarylmethane **5** as a byproduct.

*tert-Butyl Phenyl(2,4,6-trimethoxyphenyl)methylcarbamate (**4a**).* White solid; mp 132–133 °C; yield 338.7 mg (91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.24 (m, 4H), 7.17–7.16 (m, 1H), 6.60 (d, J = 10.2 Hz, 1H), 6.27 (d, J = 10.2 Hz, 1H), 6.17 (s, 2H), 3.83 (s, 3H), 3.79 (s, 6H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6, 158.6, 155.7, 143.6, 127.9, 126.1, 125.9, 111.2, 91.2, 79.0, 55.9, 55.4, 48.2, 28.6; IR (film): ν_{max} 3456 (N-H), 1713, 1593, 1494, 1455, 1419, 1365, 1234, 1205, 1154, 1127, 1042, 1017, 951 cm^{-1}; HRMS (EI-TOF) calcd for $C_{21}H_{27}NO_5Na$ $[M + Na]^+$ 396.1787, found 396.1782.

*Benzyl[(2,4,6-trimethoxyphenyl)phenylmethyl]carbamate (**4a′**).* Pale yellow oil; yield 390.8 mg (96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.17 (m, 10H), 6.68 (d, J = 10.1 Hz, 1H), 6.52 (d, J = 10.1 Hz, 1H), 6.17 (s, 2H), 5.18 (q, J = 12.1 Hz, 1H), 5.12 (q, J = 12.1 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 158.5, 156.2, 142.9, 136.8, 128.5, 128.3, 128.1, 127.9, 126.0, 126.0, 110.7, 91.2, 66.7, 55.9, 55.3, 48.9; IR (film): ν_{max} 3444 (N-H), 1722, 1609, 1593, 1497, 1455, 1332, 1230, 1205, 1152, 1127, 1036, 1027, 951 cm^{-1}; HRMS (EI-TOF) calcd for $C_{24}H_{25}NO_5$ $[M]^+$ 407.1733, found 407.1727.

*tert-Butyl[(2,4,6-trimethoxyphenyl)-2-fluorophenylmethyl]-carbamate (**4b**).* White solid; mp 128–129 °C; yield 348.4 mg (89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (t, J = 7.7 Hz, 1H), 7.15 (q, J = 6.1 Hz, 1H), 7.03 (t, J = 7.4 Hz, 1H), 6.93 (t, J = 9.4 Hz, 1H), 6.77 (d, J = 9.9 Hz, 1H), 6.14 (s, 2H), 6.07 (d, J = 9.9 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 6H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 160.5 ($^1J_{C\text{-}F}$ = 247.0 Hz), 158.7, 155.1, 130.0 ($^2J_{C\text{-}F}$ = 14.0 Hz), 128.2 ($^3J_{C\text{-}F}$ = 4.0 Hz), 127.9 ($^3J_{C\text{-}F}$ = 8.0 Hz), 123.1 ($^4J_{C\text{-}F}$ = 2.0 Hz), 115.4 ($^2J_{C\text{-}F}$ = 22.0 Hz), 110.0, 91.2, 79.2, 55.9, 55.3, 44.0, 28.5 (CH_3); IR (film): ν_{max} 3457 (N-H), 1717, 1609, 1593, 1492, 1457, 1229, 1205, 1154, 1130, 1041 cm^{-1}; HRMS (EI-TOF) calcd for $C_{21}H_{26}FNO_5$ Na $[M + Na]^+$ 414.1693, found 414.1687.

*tert-Butyl[(2,4,6-trimethoxyphenyl)-4-fluorophenylmethyl]-carbamate (**4c**).* White solid; mp 119–121 °C; yield 364.0 mg (93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (dd, J = 8.1, 5.7 Hz, 2H), 6.92 (t, J = 8.7 Hz, 2H), 6.55 (d, J = 10.0 Hz), 6.25 (d, J = 10.0 Hz, 1H), 6.17 (s, 2H), 3.83 (s, 3H), 3.79 (s, 6H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7 ($^1J_{C\text{-}F}$ = 242.0 Hz), 161.0, 158.7, 155.9, 139.6 ($^4J_{C\text{-}F}$ = 2.0 Hz), 127.8 ($^3J_{C\text{-}F}$ = 8.0 Hz), 114.8 ($^2J_{C\text{-}F}$ = 21.0 Hz), 111.2, 91.5, 79.4, 56.2, 55.6, 48.0, 28.8 (CH_3); IR (film): ν_{max} 3455 (N-H), 1712, 1609, 1493, 1457, 1366, 1221, 1205, 1155, 1126, 1042, 1016, 952 cm^{-1}; HRMS (EI-TOF) calcd for $C_{21}H_{26}FNO_5Na$ $[M + Na]^+$ 414.1693, found 414.1687.

*tert-Butyl[(2,4,6-trimethoxyphenyl)-4-chlorophenylmethyl]-carbamate (**4d**).* White solid; mp 114–115 °C; yield 334.5 mg (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22–7.17 (m, 4H), 6.55 (d, J = 10.0 Hz, 1H), 6.22 (d, J = 10.0 Hz, 1H), 6.16 (s, 2H), 3.82 (s, 3H), 3.79 (s, 6H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 158.4, 155.5, 142.2, 131.7, 127.9, 127.4, 110.5, 91.1, 79.2, 55.8, 55.3, 47.7, 28.5; IR (film): ν_{max} 3455 (N-H), 1713, 1609, 1594, 1491, 1456, 1205, 1154, 1128, 1014 cm^{-1}; HRMS (EI-TOF) calcd for $C_{21}H_{27}ClNO_5$ $[M + H]^+$ 408.1578, found 408.1572.

*tert-Butyl[(2,4,6-trimethoxyphenyl)-4-bromophenylmethyl]-carbamate (**4e**).* White solid; mp 133–135 °C; yield 384.4 mg (85%).

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^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 6.53 (d, J = 9.9 Hz, 1H), 6.21 (d, J = 9.9 Hz, 1H), 6.16 (s, 2H), 3.83 (s, 3H), 3.79 (s, 6H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 158.4, 155.6, 142.8, 130.9, 127.9, 119.9, 110.5, 91.1, 79.3, 55.9, 55.4, 47.80, 28.5; IR (film): ν_{max} 3453 (N-H), 1713, 1610, 1493, 1205, 1154, 1128, 1010 cm^{-1}; HRMS (EI-TOF) calcd for $C_{21}H_{26}BrNO_5Na$ [M + Na]$^+$ 474.0892, found 474.0887.

*tert-Butyl[(2,4,6-trimethoxyphenyl)-4-nitrophenylmethyl]-carbamate (**4f**).* Yellow solid; mp 161−163 °C; yield 368.2 mg (88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 8.7 Hz, 2H), 7.42 (d, J = 8.7 Hz, 2H), 6.64 (d, J = 9.7 Hz, 1H), 6.20 (d, J = 9.7 Hz, 1H), 6.16 (s, 2H), 3.83 (s, 6H), 3.80 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1, 158.3, 155.5, 151.6, 146.4, 126.6, 123.1, 109.7, 91.1, 79.6, 55.8, 55.3, 48.0, 28.4; IR (film): ν_{max} 3450 (N-H), 1712, 1607, 1492, 1347, 1205, 1154, 1120, 1043 cm^{-1}; HRMS (EI-TOF) calcd for $C_{21}H_{27}N_2O_7$ [M + H]$^+$ 419.1818, found 419.1815.

*tert-Butyl[(2,4,6-trimethoxyphenyl)-4-methoxyphenylmethyl]-carbamate (**4g**).* White solid; mp 112−113 °C; yield 327.9 mg (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, J = 8.6 Hz, 2H), 6.79 (d, J = 8.6 Hz, 2H), 6.55 (d, J = 10.2 Hz, 1H), 6.27 (d, J = 10.2 Hz, 1H), 6.17 (s, 2H), 3.82 (s, 3H), 3.79 (s, 6H), 3.77 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.4, 158.5, 158.0, 155.6, 135.7, 127.1, 113.3, 111.1, 91.2, 78.9, 55.9, 55.3, 55.1, 47.8, 28.5; IR (film): ν_{max} 3456 (N-H), 1712, 1609, 1593, 1510, 1495, 1465, 1365, 1246, 1205, 1154, 1126, 1038 cm^{-1}; HRMS (EI-TOF) calcd for $C_{22}H_{29}NO_6Na$ [M + Na]$^+$ 426.1893, found 426.1887.

*tert-Butyl[(2,4,6-trimethoxyphenyl)propyl]carbamate (**4h**).* White solid; mp 85−87 °C; yield 230.9 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.14 (s, 2H), 5.81 (d, J = 10.1 Hz, 1H), 5.23 (q, J = 7.7 Hz, 1H), 3.83 (s, 6H), 3.81 (s, 3H), 1.82−1.68 (m, 2H), 1.45 (s, 9H), 0.83 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0, 158.7, 155.6, 111.2, 91.0, 78.5, 55.8, 55.3, 47.2, 28.7, 28.5, 11.0; IR (film): ν_{max} 3458 (N-H), 1713, 1610, 1592, 1497, 1456, 1364, 1230, 1205, 1171, 1155, 1138, 1060, 1042 cm^{-1}; HRMS (EI-TOF) calcd for $C_{17}H_{28}NO_5$ [M + H]$^+$ 326.1967, found 326.1971.

*tert-Butyl[(2,4,6-trimethoxyphenyl)pentyl]carbamate (**4i**).* White solid; mp 74−76 °C; yield 267.2 mg (76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.13 (2H, s), 5.79 (1H, d, J = 10.2 Hz), 5.30 (1H, q, J = 8.5 Hz), 3.83 (s, 6H), 3.81 (s, 3H), 1.76−1.64 (2H, m), 1.44 (9H, s), 1.30−1.25 (3H, m), 1.15−1.13 (1H, m), 0.85 (3H, t, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 158.5, 155.4, 111.4, 90.9, 78.4, 55.7, 55.2, 45.7, 35.5, 28.5, 28.4, 22.5, 14.0; IR (film): ν_{max} 3458 (N-H), 1713, 1610, 1593, 1496, 1456, 1365, 1205, 1172, 1154, 1138, 1041 cm^{-1}; HRMS (EI-TOF) calcd for $C_{19}H_{32}NO_5$ [M + H]$^+$ 354.2280, found 354.2275.

*tert-Butyl[(2,4,6-trimethoxyphenyl)-3-phenylpropyl]carbamate (**4j**).* Colorless oil; yield 338.8 mg (84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28−7.23 (m, 2H), 7.17−7.13 (m, 3H), 6.14 (s, 2H), 5.86 (d, J = 10.2 Hz, 1H), 5.42 (q, J = 7.6 Hz, 1H), 3.83 (s, 6H), 3.82 (s, 3H), 2.73−2.65 (m, 1H), 2.51−2.43 (m, 1H), 2.14−2.07 (m, 1H), 2.02−1.94 (m, 1H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.4, 158.8, 155.8, 143.0, 136.4, 128.6, 128.4, 125.7, 111.2, 91.2, 79.0, 56.1, 55.6, 46.2, 37.8, 33.2, 28.8; IR (film): ν_{max} 3454 (N-H), 1172, 1609, 1592, 1495, 1455, 1365, 1260, 1204, 1151, 1119, 1043 cm^{-1}; HRMS (EI-TOF) calcd for $C_{23}H_{32}NO_5$ [M + H]$^+$ 402.2280, found 402.2275.

*tert-Butyl[(2,4,6-trimethoxyphenyl)-3-methylbutyl]carbamate (**4k**).* White solid; mp 91−93 °C; yield 215.4 mg (61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.13 (s, 2H), 5.72 (d, J = 10.2 Hz, 1H), 5.41 (q, J = 7.7 Hz, 1H), 3.83 (s, 6H), 3.80 (s, 3H), 1.70−1.63 (m, 1H), 1.57−1.48 (m, 1H), 1.44 (m, 10H), 0.95 (d, J = 6.5 Hz, 3H), 0.90 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 158.4, 155.3, 111.8, 90.9, 78.4, 55.7, 55.2, 45.0, 44.1, 28.5, 25.3, 22.7; IR (film): ν_{max} 3458 (N-H), 1712, 1610, 1593, 1496, 1456, 1365, 1219, 1205, 1155, 1110, 1042 cm^{-1}; HRMS (EI-TOF) calcd for $C_{19}H_{32}NO_5$ [M + H]$^+$ 354.2280, found 354.2275.

*tert-Butyl[(2,4,6-trimethoxyphenyl)-2-methylpropyl]carbamate (**4l**).* White solid; mp 127−129 °C; yield 316.6 mg (93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.12 (s, 2H), 5.75 (d, J = 10.4 Hz, 1H), 4.97 (t, J = 10.2 Hz, 1H), 3.81 (s, 6H), 3.80 (s, 3H), 2.05−1.98 (m, 1H), 1.42 (s, 9H), 1.00 (d, J = 6.6 Hz, 3H), 0.69 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 158.7, 155.8, 111.3, 91.0, 78.4, 55.8, 55.3, 51.8, 33.3, 28.5, 19.8; IR (film): ν_{max} 3458 (N-H), 1714, 1609, 1592, 1497, 1456, 1365, 1230, 1205, 1154, 1101, 1040, 1009 cm^{-1}; HRMS (EI-TOF) calcd for $C_{18}H_{30}NO_5$ [M + H]$^+$ 340.2124, found 340.2118.

*Benzyl[(2,4,6-trimethoxyphenyl)-2-methylpropyl]carbamate (**4l′**).* Colorless oil; yield 363.5 mg (97%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.31 (m, 5H), 6.14 (s, 2H), 6.03 (d, J = 10.4 Hz, 1H), 5.16 (d, J = 12.2 Hz, 1H), 5.05 (q, J = 11.3 Hz, 2H), 3.82 (s, 9H), 2.11−2.07 (m, 1H), 1.04 (d, J = 6.6 Hz, 3H), 0.73 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0, 158.6, 156.3, 137.0, 128.4, 128.2, 127.9, 110.8, 91.0, 66.4, 55.7, 55.3, 52.6, 33.0, 19.9, 19.6; IR (film): ν_{max} 3448 (N-H), 1723, 1609, 1592, 1502, 1455, 1227, 1205, 1143, 1102 cm^{-1}; HRMS (EI-TOF) calcd for $C_{21}H_{27}NO_5Na$ [M + Na]$^+$ 396.1787, found 396.1768.

*tert-Butyl[(2,4,6-trimethoxyphenyl)cyclopropylmethyl]carbamate (**4m**).* White solid; mp 105−107 °C; yield 287.5 mg (85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.16 (s, 2H), 5.95 (d, J = 10.2 Hz, 1H), 4.68 (t, J = 9.7 Hz, 1H), 3.83 (s, 3H), 3.81 (s, 6H), 1.44 (s, 9H), 1.37−1.33 (m, 1H), 0.56−0.52 (m, 1H), 0.44−0.41 (m, 1H), 0.35−0.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0, 158.3, 155.6, 111.6, 91.0, 78.5, 55.8, 55.3, 49.9, 28.5, 17.0, 3.7, 3.1; IR (film): ν_{max} 3460 (N-H), 1712, 1610, 1593, 1495, 1456, 1205, 1154, 1111, 1041, 1017 cm^{-1}; HRMS (EI-TOF) calcd for $C_{18}H_{27}NO_5Na$ [M + Na]$^+$ 360.1787, found 360.1787.

*tert-Butyl[(2,4,6-trimethoxyphenyl)cyclopentylmethyl]carbamate (**4n**).* White solid; mp 116−118 °C; yield 333.1 mg (91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.13 (s, 2H), 5.79 (d, J = 10.4 Hz, 1H), 5.12 (t, J = 10.4 Hz, 1H), 3.83 (s, 3H), 3.81 (s, 6H), 2.38−2.32 (m, 1H), 1.76−1.68 (m, 2H), 1.61−1.56 (m, 1H), 1.54−1.43 (m, 12H), 1.27−1.20 (m, 1H), 1.17−1.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 158.8, 155.9, 112.2, 91.3, 78.6, 56.0, 55.5, 50.0, 45.8, 30.4, 29.8, 28.8, 26.9, 23.9; IR (Nujol-mull): ν_{max} 3458 (N-H), 1712, 1609, 1592, 1497, 1455, 1365, 1230, 1204, 1163, 1152, 1117, 1040, 1011 cm^{-1}; HRMS (EI-TOF) calcd for $C_{20}H_{32}NO_5$ [M + H]$^+$ 366.2280, found 366.2275.

*tert-Butyl[(2,4,6-trimethoxyphenyl)cyclohexylmethyl]carbamate (**4o**).* White solid; mp 138−140 °C; yield 357.8 mg (94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.12 (s, 2H), 5.74 (d, J = 10.3 Hz, 1H), 5.03 (t, J = 10.0 Hz, 1H), 3.81 (s, 6H), 3.80 (s, 3H), 1.94−1.91 (br m, 1H), 1.75−1.59 (br m, 4H), 1.43 (s, 9H), 1.26−1.04 (br m, 5H), 0.97−0.91 (br m, 1H; ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 158.6, 155.7, 110.7, 90.8, 78.3, 55.7, 55.2, 50.6, 42.5, 30.0, 29.8, 28.5, 26.4, 26.2; IR (film): ν_{max} 3458 (N-H), 1713, 1609, 1592, 1496, 1454, 1364, 1204, 1172, 1143, 1112, 1039, 1009 cm^{-1}; HRMS (EI-TOF) calcd for $C_{21}H_{34}NO_5$ [M + H]$^+$ 380.2437, found 380.2431.

*tert-Butyl[(2,4,5-trimethoxyphenyl)phenylmethyl]carbamate (**4p**).* White solid; mp 91−93 °C; yield 272.6 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29−7.18 (m, 5H), 6.82 (s, 1H), 6.53 (s, 1H), 6.00 (br d, J = 8.0 Hz, 1H), 5.67 (br d, J = 5.8 Hz, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 3.70 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7, 151.6, 149.3, 143.3, 142.8, 128.5, 127.0, 126.8, 122.0, 113.4, 98.8, 79.8, 57.0, 56.7, 56.5, 55.3, 28.5; IR (film): ν_{max} 3368 (N-H), 1710, 1510, 1455, 1366, 1275, 1260, 1206, 1168, 1034 cm^{-1}; HRMS (EI-TOF) calcd for $C_{21}H_{27}NO_5Na$ [M + Na]$^+$ 396.1787, found 396.1781.

*tert-Butyl[2-(5-methylfuryl)phenylmethyl]carbamate (**4q**).* White solid; mp 73−75 °C; yield 227.5 mg (79%). ^{1}H NMR (400 MHz, $CDCl_3$): 7.38−7.28 (m, 5H), 5.99 (br s, 1H), 5.90 (br s, 2H), 5.30 (br s, 1H), 2.27 (s, 3H), 1.46 (br s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.2, 152.5, 152.4, 140.7, 128.8, 127.8, 127.2, 108.4, 106.4, 80.2, 53.0, 28.7, 13.9; IR (film): ν_{max} 3338 (N-H), 1706, 1496, 1455, 1367, 1243, 1168, 1046, 1021, 964, 879, 784, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{17}H_{21}NO_3Na$ [M + Na]$^+$ 310.1419, found 310.1418.

*tert-Butyl[2-(5-ethylfuryl)phenylmethyl]carbamate (**4r**).* Yellow solid; mp 75−77 °C; yield 220.0 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.26 (m, 5H), 5.98 (br s, 1H), 5.89 (br d, J = 3.1 Hz, 2H), 5.28 (br s, 1H). 2.61 (q, J = 7.5 Hz, 2H), 1.45 (br s, 9H), 1.20 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.8, 154.9, 152.0, 140.4, 128.5, 127.5, 126.9, 107.9, 104.4, 79.9, 52.8, 28.4 (3 × CH_3),

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21.4, 12.0; IR (film): ν_{max} 3338 (N-H), 1705, 1496, 1455, 1367, 1246, 1168, 1046, 1013 cm^{-1}: HRMS (ESI-TOF) calcd for $C_{18}H_{23}NO_3Na$ $[M + Na]^+$ 324.1576, found 324.1579.

*tert-Butyl[2-(5-methylthienyl)phenylmethyl]carbamate (**4s**).* Pale yellow solid; mp 105−109 °C; yield 160,8 mg (53%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.37−7.27 (m, 5H), 6.57−6.55 (m, 2H), 6.02 (br s, 1H), 5.21 (br s, 1H), 2.42 (s, 3H), 1.44 (br s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 143.8, 141.9, 139.7, 128.6, 127.6, 126.8, 125.3, 124.7, 80.0, 54.6, 28.4 (3 × *C*H_3), 15.3; IR (film): ν_{max} 3357 (N-H), 1691, 1515, 1367, 1173, 1019 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{17}H_{21}NO_2SNa$ $[M + Na]^+$ 326.1191, found 326.1190.

*tert-Butyl[3-(5-ethylthienyl)phenylmethyl]carbamate (**4t**).* White solid; mp 77−81 °C; yield 154.2 mg (49%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.40−7.30 (m, 5H), 6.60 (s, 2H), 6.05 (br s, 1H), 5.26 (br s, 1H), 2.80 (q, J = 7.5 Hz, 2H), 1.46 (br s, 9H), 1.29 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 146.9, 143.0, 141.4, 128.1, 127.2, 126.4, 124.7, 122.4, 79.5, 54.2, 27.9 (3 × *C*H_3), 23.1, 15.4; IR (film): ν_{max} 3332 (N-H), 1702, 1494, 1455, 1366, 1246, 1166, 1016 cm^{-1}: HRMS (ESI-TOF) calcd for $C_{18}H_{23}NO_2SNa$ $[M + Na]^+$ 340.1347, found 340.1346.

*tert-Butyl[(3-indolyl)phenylmethyl]carbamate (**4v**).* Orange solid; mp 131−135 °C; yield 101.9 mg (32%). ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (br s, 1H), 7.55 (d, J = 7.3 Hz, 1H), 7.43−7.35 (m, 5H), 7.31−7.28 (m, 2H), 7.23 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.77 (br s, 1H), 6.24 (br d, J = 7.2 Hz, 1H), 5.25 (br s, 1H), 1.48 (br s, 9H); ^{13}C NMR (100 MHz, $CDCI_3$): δ 155.2, 142.0, 136.7, 128.4, 127.1, 126.8, 125.9, 123.2, 122.4, 119.8, 119.5, 118.0, 111.3, 79.6, 51.7, 28.4 (3 × *C*H_3); IR (film): ν_{max} 3407, 3327, 1693, 1495, 1455, 1367, 1244, 1166, 1017 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{20}H_{22}N_2O_2Na$ $[M + Na]^+$ 345.1579, found 345.1577.

*tert-Butyl[2-(5-methylfuryl)-2-methylpropyl]carbamate (**4w**).* Yellow oil; yield 209.7 mg (74%). ^1H NMR (400 MHz, $CDCl_3$): δ 6.01 (br d, J = 2.1 Hz, 1H), 5.88 (br d, J = 2.1 Hz, 1H), 4.89 (br d, J = 7.9 Hz, 1H), 4.49 (br t, J = 7.9 Hz, 1H), 2.27 (s, 3H), 2.10−2.05 (m, 1H), 1.46 (s, 9H), 0.94 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.4, 152.6, 151.0, 106.9, 105.8, 79.3, 54.4, 32.3, 28.4, 19.1, 18.4, 13.5; IR (film): ν_{max} 3347 (N-H), 1705, 1499, 1390, 1366, 1240, 1171, 1020 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{24}NO_3$ $[M + H]^+$ 254.1756, found 254.1751.

*tert-Butyl[2-(5-methylfuryl)cyclohexylmethyl]carbamate (**4x**).* Yellow solid; mp 89−91 °C; yield 205.4 mg (70%). ^1H NMR (400 MHz, $CDCl_3$): δ 6.00 (br d, J = 1.6 Hz, 1H), 5.87 (br d, J = 1.6 Hz, 1H), 4.89 (br d, J = 8.7 Hz), 4.49 (br t, J = 8.3 Hz), 2.27 (s, 3H), 1.81−1.64 (m, 5H), 1.53−1.51 (m, 1H), 1.45 (s, 9H), 1.29−1.11 (m, 3H), 1.04−0.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.4, 152.4, 151.0, 106.9, 105.7, 79.3, 53.7, 42.0, 29.7, 29.0, 28.4, 26.3, 26.0, 13.5; IR (film): ν_{max} 3350 (N-H), 1702, 1499, 1451, 1366, 1245, 1171, 1054, 1019 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{17}H_{28}NO_3$ $[M + H]^+$ 294.2069, found 294.2066.

*Benzyl[2-(5-methylfuryl)phenylmethyl]carbamate (**4q′**).* Yellow solid; mp 83−87 °C; yield 265.5 mg (83%). ^1H NMR (400 MHz, $CDCl_3$): 7.38−7.28 (m, 10H), 6.00−5.90 (br m, 3H), 5.56 (br s, 1H), 5.15 (q, J = 12.2 Hz, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 152.0, 151.3, 139.5, 136.0, 128.2, 127.4, 126.6, 108.1, 105.8, 66.7, 52.9, 13.2: IR (film): ν_{max} 3321 (N-H), 1702, 1498, 1455, 1220, 1404, 1026 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{20}H_{19}NO_3Na$ $[M + Na]^+$ 344.1263, found 344.1258.

*Benzyl[2-(5-methylthienyl)phenylmethyl]carbamate (**4s′**).* Pale yellow solid; mp 99−103 °C; yield 242.9 mg (72%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.34 (brm, 10H), 6.60 (d, J = 7.1 Hz, 2H), 6.11 (br d, J = 6.7 Hz, 1H), 5.49 (br s, 1H), 5.14 (q, J = 12.3 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 143.1, 141.3, 139.9, 136.3, 128.6, 128.5, 128.1, 127.8, 126.8, 125.5, 124.8, 67.0, 55.1, 15.3; IR (film): ν_{max} 3308 (N-H), 1690, 1533, 1242, 1028 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{20}H_{19}NO_2SNa$ $[M + Na]^+$ 360.1034, found 360.1032.

*Benzyl[2-(5-methylfyryl)-2-methylpropyl]carbamate (**4w′**).* Yellow oil; yield 167.0 mg (58%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.39−7.34 (m, 5H), 6.04 (br d, J = 1.7 Hz, 1H), 5.89 (br d, J = 1.7 Hz, 1H), 5.16−5.13 (m, 3H), 4.56 (t, J = 8.2 Hz, 1H), 2.27 (s, 3H), 2.13−2.08 (m, 1H), 0.96 (d, J = 6.7 Hz, 3H), 0.90 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.9, 152.0, 152.0, 136.5, 128.5, 128.3, 128.1, 107.2, 105.8, 66.8, 55.1, 32.2, 19.1, 18.5, 13.5; IR (film): ν_{max} 3347 (N-H), 1705, 1499, 1390, 1366, 1240, 1171, 1020 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{17}H_{22}NO_3$ $[M + H]^+$ 288.1600, found 288.1605.

*Benzyl[2-(5-methylfyryl)cyclohexylmethyl]carbamate (**4x′**).* Yellow oil; yield 180.1 mg (55%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.37 (brm, 5H), 6.03 (br s, 1H), 5.88 (br s, 1H), 5.15−5.11 (m, 3H), 4.56 (br t, J = 8.0 Hz, 1H), 2.27 (s, 3H), 1.84−1.64 (m, 5H), 1.60−1.45 (m, 1H), 1.28−1.12 (m, 3H), 1.06−0.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 152.4, 151.7, 137.0, 129.0, 128.62, 128.58, 107.7, 106.3, 67.3, 54.8, 42.3, 30.1, 29.6, 26.7, 26.4, 14.0; IR (film): ν_{max} 3328 (N-H), 1702, 1507, 1451, 1240, 1215, 1055, 1022 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{20}H_{26}NO_3$ $[M + H]^+$ 328.1913, found 328.1907.

*Bis(2,4,5-trimethoxyphenyl)phenylmethane (**5p**).*[15a] White solid; mp 129−133 °C; yield 17.0 mg (8%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.28−7.24 (m, 2H), 7.18 (m, 1H), 7.07 (d, J = 7.6 Hz, 2H), 6.56 (s, 2H), 6.44 (s, 2H), 6.10 (s, 1H), 3.90 (s, 6H), 3.68 (s, 6H), 3.65 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.9, 148.4, 144.6, 143.1, 129.3, 128.3, 126.1, 124.9, 115.0, 98.8, 57.4, 57.0, 56.4, 42.9; IR (Nujol-mull): ν_{max} 1729, 1509, 1464, 1394, 1317, 1275, 1259, 1206, 1178, 1035, 764, 750 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{28}O_6Na$ $[M + Na]^+$ 447.1784, found: 447.1760.

*Bis[(5-methyl)-2-furyl]phenyl Methane (**5q**).*[15b,20] Yellow oil; yield 3.0 mg (2%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.28 (br m, 5H), 5.91 (br d, J = 4.3 Hz, 4H), 5.37 (s, 1H), 2.28 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.8, 151.4, 140.0, 128.39, 128.36, 126.9, 108.1, 106.0, 45.1, 13.6; IR (film): ν_{max} 1603, 1561, 1494, 1452, 1218, 1022, 778 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{17}H_{17}O_2$ $[M + H]^+$ 253.1229, found 253.1223.

*Bis[(5-methyl)-2-thienyl]phenyl Methane (**5s**).*[15,20a,c] Pale yellow oil; yield 10.0 mg, (7%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.27 (m, 5H), 6.64 (br d, J = 3.3 Hz, 2H), 6.61 (br d, J = 3.3 Hz, 2H), 5.70 (s, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 143.9, 139.1, 128.5, 128.4, 127.0, 125.7, 124.6, 47.9, 15.4; IR (film): ν_{max} 1600, 1493, 1451, 1404, 1228, 1167, 1029, 796 cm^{-1}.

*Bis[(5-ethyl)-2-thienyl]phenyl Methane (**5t**).* Pale yellow oil; yield 14.0 mg (9%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.39−7.31 (br m, 5H), 6.68 (br d, 4H), 5.76 (s, 1H), 2.84 (q, J = 7.5 Hz, 4H), 1.33 (t, J = 7.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3, 144.4, 143.5, 128.03, 127.95, 126.6, 125.1, 122.2, 47.5, 23.1, 15.4; IR (film): ν_{max} 1600, 1493, 1452, 1377, 1316, 1260, 1220, 1074, 1015, 945, 802, 737, 699 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{19}H_{20}S_2Na$ $[M + Na]^+$ 335.0904, found 335.0901.

*Bis[(5-ethyl)-2-pyrrolyl]phenyl Methane (**5u**).* Brown oil; yield 91 mg (65%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (br s, 1H), 7.37−7.26 (m, 5H), 5.86 (br s, 2H), 5.79 (br s, 2H), 5.40 (s, 1H), 2.59 (q, J = 7.5 Hz, 4H), 1.24 (t, J = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 134.2, 131.4, 128.8, 128.7, 127.1, 107.4, 104.3, 44.5, 21.1, 13.8; IR (film): ν_{max} 3164 (N-H), 1688, 1584, 1495, 1404, 1329, 1275, 1228, 1035, 958, 764 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{19}H_{22}N_2$ $[M]^+$ 278.1783, found 278.1785.

*Bis[(1H-indol-3-yl]phenyl Methane (**5v**).*[20d] Orange solid; mp 93−97 °C; yield 88.4 mg (55%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (br s, 2H), 7.42−7.36 (m, 6H), 7.32−7.30 (m, 2H), 7.23−7.17 (m, 3H), 7.02 (t, J = 7.5 Hz, 2H), 6.69 (br d, J = 1.5 Hz), 5.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3, 136.9, 129.0, 128.5, 127.3, 126.5, 123.9, 122.2, 120.2, 119.8, 119.5, 111.4, 40.5; IR (Nujol-mull): ν_{max} 3414 (N-H), 1601, 1492, 1456, 1417, 1337, 1265, 1217, 1152, 1093, 1010, 793, 743 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{18}N_2Na$ $[M + Na]^+$ 345.1368, found 345.1360.

*Bis-1,1-[(5-methyl)-2-furyl]-2-methylpropane (**5w**).*[20c] Colorless oil; yield 15.3 mg (14%). ^1H NMR (400 MHz, $CDCl_3$): δ 6.00 (br s, 2H), 5.89 (br s, 2H), 3.70 (d, J = 7.8 Hz, 1H), 2.34−2.28 (m, 7H), 0.92 (d, J = 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.0, 151.0, 107.5, 106.5, 47.0, 32.5, 21.4, 14.3; IR (film): ν_{max} 1614, 1563, 1451, 1387, 1369, 1220, 1022, 1000, 966, 782 cm^{-1}.

*Bis[(5-methyl)-2-furyl]cyclohexylmethane (**5x**).* Pale yellow oil; yield 15.5 mg (12%). ^1H NMR (400 MHz, $CDCl_3$): δ 5.99 (d, J = 2.4 Hz, 2H), 5.88 (br d, J = 2.4 Hz, 2H), 3.71 (d, J = 8.7 Hz, 1H), 2.29 (s, 6H),

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1.98−1.94 (m, 1H), 1.73−1.60 (m, 5H), 1.30−1.12 (m, 3H), 1.01−0.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 153.2, 150.3, 106.7, 105.8, 45.5, 41.4, 31.2, 26.4, 26.3, 13.6; IR (film): ν_{max} 1615, 1561, 1449, 1400, 1220, 1021, 1000, 772 cm^{-1}; HRMS (EI-TOF) calcd for $C_{17}H_{22}O_2Na$ $[M + Na]^+$ 281.1517, found 281.1504.

The Reaction of 2-Methylfuran (1c) with *N*-Cbz Imine 6. To a toluene solution (1 mL) of 2-methylfuran (1.0 mmol) and *N*-Cbz-imine **6** (1.0 mmol) in a test tube open to air at room temperature was added $Bi(OTf)_3$ (0.05 mmol). After the reaction was stirred until completion (TLC analysis), the reaction mixture was quenched with aqueous $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, and filtered. The filtrate was evaporated (aspirator then vacuo) to give a crude product, which was purified by radial chromatography (SiO_2, 100% hexane to 30% EtOAc/hexane as eluent) to give the corresponding α-branched amines **4q′** (260.3 mg, 81%) and triarylmethane **5q** (15.1 mg, 12%).

The Reaction of 2-Methylfuran (1c) with Benzaldehyde (2a). To a toluene solution (1 mL) of 2-methylfuran (2.0 mmol) and benzaldehyde (1.0 mmol) in a test tube open to air at room temperature was added $Bi(OTf)_3$ (0.05 mmol). After the reaction was stirred until completion (TLC analysis), the reaction mixture was quenched with aqueous $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, and filtered. The filtrate was evaporated (aspirator then vacuo) to give a crude product, which was purified by radial chromatography (SiO_2, 100% hexane to 30% EtOAc/hexane as eluent) to give triarylmethane **5q** (232.0 mg, 92% yield).

The Reaction of 2-Methylfuran (1c) with α-Branched Amine 4q′. To a toluene solution (1 mL) of 2-methylfuran (1.0 mmol) and α-branched amine **4q′** (1.0 mmol) in a test tube open to air at room temperature was added $Bi(OTf)_3$ (0.05 mmol). After the reaction was stirred until completion (TLC analysis), the reaction mixture was quenched with aqueous $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, and filtered. The filtrate was evaporated (aspirator then vacuo) to give a crude product, which was purified by radial chromatography (SiO_2, 100% hexane to 30% EtOAc/hexane as eluent) to give triarylmethane **5q** (141.3 mg, 56% yield) and α-branched amine **4q′** (106.0 mg. 42%) was recovered.

General Procedure for the Synthesis of Unsymmetrical Triarylmethane 7. To a toluene solution (1 mL) of α-branched amines **4p** or **4p′** (0.4 mmol) and 2-methylfuran (0.4 mmol) in a test tube open to air at room temperature was added $Bi(OTf)_3$ (0.04 mmol). After the reaction was stirred until completion (TLC analysis), the reaction mixture was quenched with aqueous $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, and filtered. The filtrate was evaporated (aspirator then vacuo) to give a crude product, which was purified by radial chromatography (SiO_2, 100% hexane to 30% EtOAc/hexane as eluent) to give the corresponding unsymmetrical triarylmethane 7 (93.4 mg, 69% from **4p** and 111.0 mg, 82% from **4p′**).

*2-Methyl-5-[phenyl(2,4,5-trimethoxyphenyl)methyl]furan (**7**).* Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.17 (m, 5H), 6.62 (s, 1H), 6.56 (s, 1H), 5.88 (br d, J = 2.0 Hz, 1H), 5.79 (s, 1H) 5.74 (br d, J = 2.8 Hz, 1H), 3.90 (s, 3H), 3.76 (s, 3H), 3.73 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.1, 151.2, 148.5, 143.1, 142.3, 128.6, 128.2, 126.3, 122.4, 114.1, 108.8, 105.9, 98.1, 56.8, 56.7, 56.1, 43.1, 13.6; IR (film): ν_{max} 3104.1, 3026, 3001, 2936, 2832, 1610, 1561, 1509, 1464, 1453, 1438, 1397, 1316, 1210, 1036, 701 cm^{-1};; HRMS (EI-TOF) calcd for $C_{21}H_{22}O_4Na$ $[M + Na]^+$ 361.1416, found 361.1412.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of all prepared products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: jaray@buu.ac.th (J.J.).

Notes

The authors declare no competing financial interest.

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