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$Bi(OTf)_3$–Catalyzed Multicomponent α–Amidoalkylation Reactions

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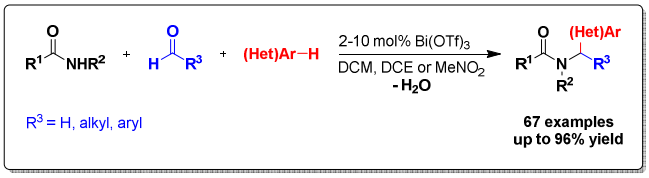
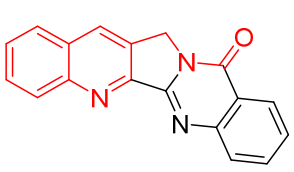
A bismuth(III) triflate catalyzed three–component synthesis of α–substituted amides starting from amides, aldehydes and (hetero)arenes is reported. The reaction has a broad substrate scope, encompassing formaldehyde as well as aryl and alkyl aldehydes. Low catalyst loadings are required and water is formed as only side product. Scope and limitation of this method will be discussed.



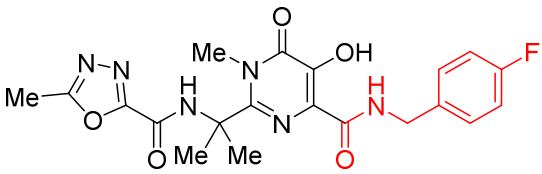
INTRODUCTION

Amino– and amidoalkyl moieties are important structural motifs in organic synthesis and pharmaceutical chemistry.[1-3] α–Substituted amides, in particular amidoalkylated arenes and heteroarenes, are found in many important natural products and biological active molecules such as luotonin–A[2], an alkaloid or the antiretroviral Raltegravir[3] (**Figure 1**).

Figure 1. Amidoalkylated Moieties in Biologically Active Molecules



Luotonin-A



Raltegravir

An important approach for the synthesis of this structural motif is the addition of nucleophilic (hetero)arenes to electrophilic carbon–nitrogen double bonds. Especially, three–component *aza*–Friedel–Crafts type amidoalkylations with *in situ* generated acylimines or acyliminium ions provide a useful synthetic tool for the synthesis of α–substituted amides.[4,5] The *in situ* preparation of these reactive imine compounds from an aldehyde and an amide represents an atom–economical methodology[6] for the synthesis of amidoalkylated (hetero)arenes.

Generating water as only side product, these reactions could meet the requirements of modern sustainable organic synthesis.[7] However, most common procedures require stoichiometric amounts of Lewis or Brønsted acids[8] or are limited to the reaction of electron–rich aromatics and heteroaromatics, such as indole and naphthol.[9-12]

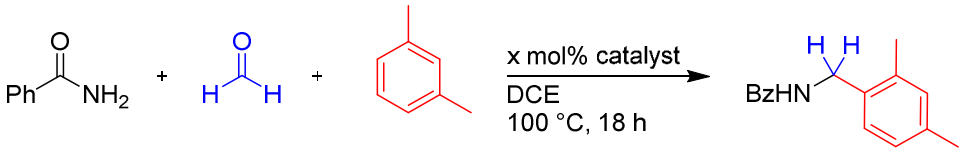
Our interest in developing novel multicomponent reactions for the rapid synthesis of pharmaceutical active molecules[13-15] has led us to closer examination of these three–component reactions. In the course of our investigations, we were able to develop a $Bi(OTf)_3$–catalyzed three–component reaction between amides, formaldehyde and arenes. This reaction provides straightforward access to amidomethylated arenes and heteroarenes.[13] Recently the group of *Jaratjaroonphong* reported a similar $Bi(OTf)_3$-catalyzed three-component reaction between carbamates, aldehydes and arenes.[16] However, this reaction is limited to very electron-rich trimethoxybenzene derivatives or reactive heteroarenes such as furan, thiophen or indol.[17] Herein, we wish to report the extension of our method to aryl and alkyl aldehydes as well as scope and limitations of the corresponding reactions and mechanistic investigations.

RESULTS & DISCUSSION

1. Three–Component Reaction with Formaldehyde

We started our investigations with the identification of a suitable catalyst using the reaction between benzamide (**1**), paraformaldehyde (**2**) and *m*–xylene (**3**), a moderately reactive arene, as test system (**Table 1**). From a multitude of tested metal triflates and Bi(III)–salts (entries 1–3) only $Bi(OTf)_3$ efficiently catalyzed the transformation even at low catalyst loadings (entries 4–8, 61–85% yield). Since $Bi(OTf)_3$ is commercially available, non–toxic, air and moisture stable, it is a very attractive catalyst.[18-20] Performing the reaction in nitromethane led to an increased yield. Best results could be achieved with 2.5 mol% $Bi(OTf)_3$ (entry 5, 85% yield). Replacement of paraformaldehyde by aq. formalin solution as formaldehyde source furnished the product in comparable yield (entry 7 and 8). TfOH, a possible byproduct of the hydrolysis of $Bi(OTf)_3$, displayed reduced catalytic activity (entry 9). To exclude a possible hidden Brønsted acid catalysis, the reaction was performed in presence of the selective proton scavenger 2,6–di–*tert*–butyl–pyridine (dbpy) (entry 10).[21] Since no significant decrease in catalytic activity was observed, the Bi(III)–species is assumed to be the active catalyst.[22] In all cases the amidoalkylated product was obtained as a mixture of regioisomers (15:1 *ortho/para*- vs. *ortho/ortho*-substitution)

Table 1. Formaldehyde — Survey of Catalysts[a,b]



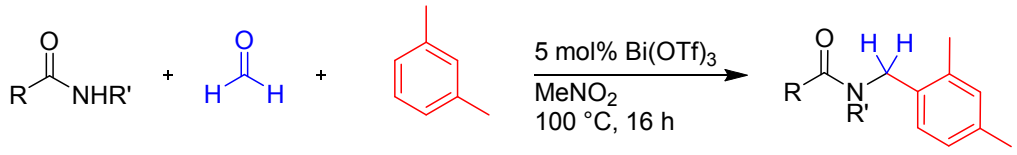
1 1.0 equiv. **2** 1.2 equiv. **3** 3.0 equiv. **4**

entry	catalyst [mol%]	yield [%]
1	$M(OTf)_x$ (5.0) M = Cu, Zn, In, Sc, Mg, Yb, etc.	< 5
2	$BiBr_3$ (5.0)	< 5
3	$BiCl_3$ (5.0)	< 5
4	$Bi(OTf)_3$ (1.0)[c,d]	71
5	$Bi(OTf)_3$ (2.5)[c,d]	85
6	$Bi(OTf)_3$ (5.0)[c]	61
7	$Bi(OTf)_3$ (5.0)[c,d]	84
8	$Bi(OTf)_3$ (5.0)[c,d,e]	79
9	TfOH (5.0)	10
10	$Bi(OTf)_3$ (5.0) + dbpy (10.0)[c,d]	75

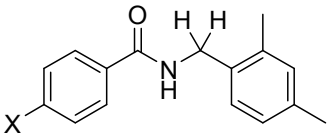
[a] General reaction conditions: Benzamide (1.0 equiv.), paraformaldehyde (1.2 equiv.), *m*–xylene (3.0 equiv.), catalyst (x mol%). [b] Isolated yield of analytical pure product. [c] Obtained as a 15:1 mixture of regioisomers. [d] Reaction in $MeNO_2$. [e] Reaction with aqueous formalin.

With the optimized conditions established, the scope of reaction was examined (**Scheme 1**). Conversion of substituted benzamides led to the products **6a** and **6b** in 65–70% yield. With carbamates as amide component, the corresponding *N*–protected amidomethylarenes **6c** and **6d** were obtained in 45% and 71% yield respectively. Deprotection of such products would offer a straightforward access to *α*–aminomethylarenes, which are found in various bioactive substances.[23] Reactions with various alkylamides furnished the corresponding amidoalkylated products in good to excellent yields. Acid sensitive functionalities, such as an acrylamide, were well tolerated (product **6e**). With exception of oxazolidin–2–one (product **6j**) secondary amides did not react under the standard conditions. Similar regioselectivities are observed for all different amide components.

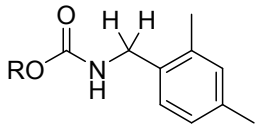
Scheme 1. Formaldehyde — Variation of Amides[a]



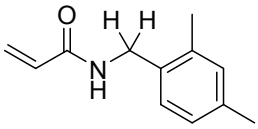
5 1.0 equiv. **2** 1.2 equiv. **3** 3.0 equiv. **6**



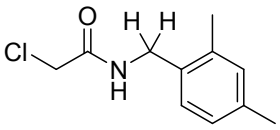
6a: X = OMe 65%
6b: X = Br 70% (24:1)[b]



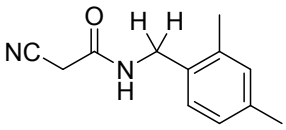
6c: R = Et 71%[b,c]
6d: R = Bn 45% (14:1)[b,c]



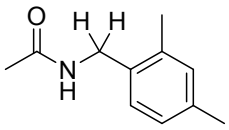
6e
55% (13:1)[b]



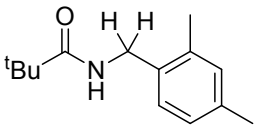
6f
73% (18:1)[b]



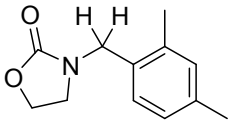
6g
96% (11:1)[b]



6h
51% (15:1)[b]



6i
77% (17:1)[b]

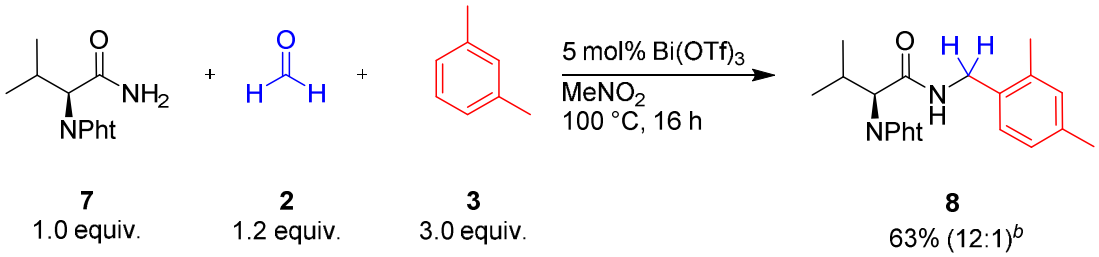


6j
71% (> 25:1)[b]

[a] Isolated yield of analytical pure product. [b] Obtained as mixture of regioisomers, ratio of regioisomers given in parentheses. [c] Reaction at 60 °C.

Also highly functionalized amides are suitable substrates for this three–component reaction, Thus, the reaction of the protected valinamide **7** provided the amino acid derivate **8** in 63% yield (**Scheme 2**).[24]

Scheme 2. Reaction of Phthalyl–Protected Valinamide[a]

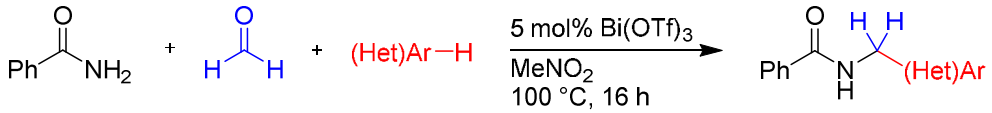


7 1.0 equiv. **2** 1.2 equiv. **3** 3.0 equiv. **8** 63% (12:1)[b]

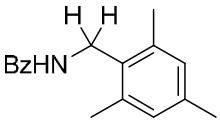
[a] Isolated yield of analytical pure product. [b] Obtained as mixture of regioisomers, ratio of regioisomers given in parentheses.

Next, reactions with different aromatic components were examined. Various electron rich arenes such as mesitylene, anisole and its halogenated derivatives furnished the desired *α*–amidoalkylated products in good to excellent yields (**10a–h**, 42–88% yield). In general the *α*–amidomethylated arenes were obtained with high regioselectivity. Only with anisole as arene, a 1:3 mixture of *ortho*– and *para*–substituted regioisomers, typical for electrophilic aromatic substitutions,[25] was obtained. Unprotected phenols or acid labile ester functionalities were well tolerated under the reaction conditions (products **10m** and **10j**). The reaction with sterically hindered pivaloyl amide proceeded in a chemoselective manner and the amidoalkylated product **10k** was obtained in 66% yield. Less electron–rich arenes, such as toluene or benzene, did not react even under more forcing conditions. In the case of electron–rich heteroarenes lower reaction temperatures were required to avoid direct addition of the heteroarene to formaldehyde. Several electron rich heteroaromatics gave the corresponding amidomethylated products in 33–94% yield (**Scheme 3**, products **10o–s**). For some of these reactions considerably higher yields could be obtained with aq. formalin as aldehyde source (**10o, 10q, 10s**). Regioselective amidoalkylation at the more reactive 2-position over the 3-position was observed for benzofuran and thiophene.

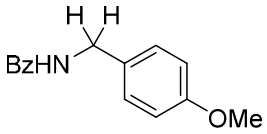
Scheme 3. Formaldehyde — Variation of (Hetero)Arenes[a]



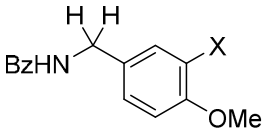
1 1.0 equiv. | **2** 1.2 equiv. | **9** 3.0 equiv. | **10**



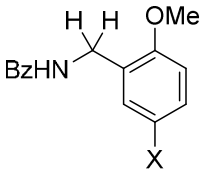
10a
73%



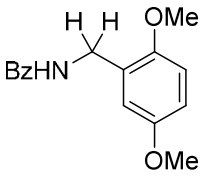
10b
68% (3:1)[b]



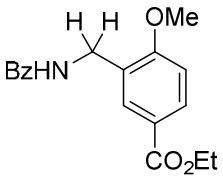
10c: X = Cl 84%
10d: X = Br 88%
10e: X = I 79%



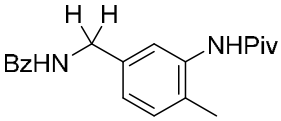
10f: X = Cl 83%
10g: X = Br 77%
10h: X = I 64%



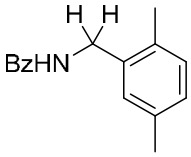
10i
42%[c,d]



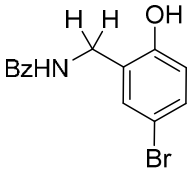
10j
87%



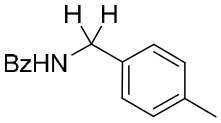
10k
66%



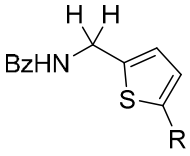
10l
37%



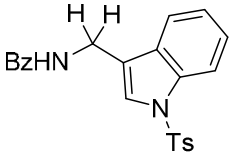
10m
68%[c,d]



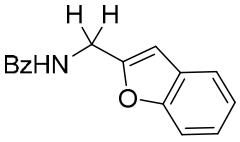
10n
0%



10o: R = Me 64% (12:1)[b,e,f]
10p: R = Br 94%[c]
10q: R = Cl 69%[f,g]



10r
76% (14:1)[b,f,g]



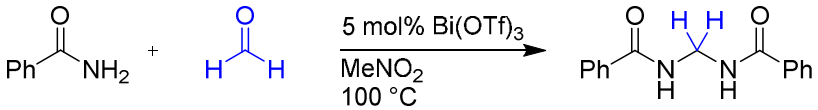
10s
70% (24:1)[b,f,g]

[a] Isolated yield of analytical pure product. [b] Obtained as mixture of regioisomers, ratio of regioisomers given in parentheses. [c] Reaction at 80 °C. [d] 4.0 equiv. of arene. [e] Reaction at r.t. [f] Reaction with aqueous formalin. [g] Reaction at 40 °C.

1.1. Mechanistic Consideration

For the development of the three–component reaction, the *in situ* generation of a reactive acylimine species as electrophilic amidoalkylating agent was assumed to be the first crucial step. Therefore we investigated the two–component reaction between formaldehyde and benzamide, which should lead to the corresponding acylimine or acyiminium ion. However, we were not able to detect or isolate any acylimine species.[26] The only product we could obtain from the two–component reaction was bisamide **11**, derived from a two–fold addition of benzamide to formaldehyde. This bisamide is formed very rapidly in almost quantitative yield (**Scheme 4**).

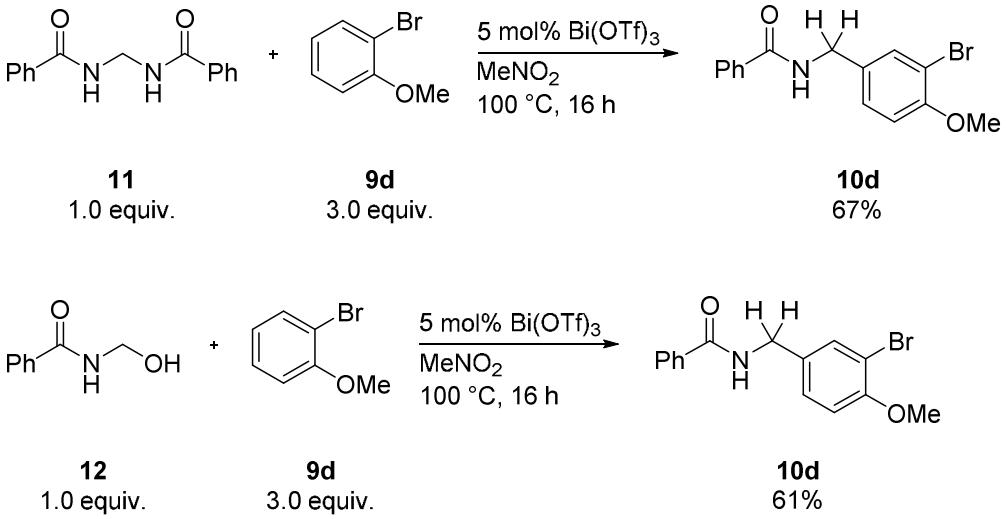
Scheme 4. Formation of Bisamide



1 1.0 equiv. **2** 1.2 equiv. **11**

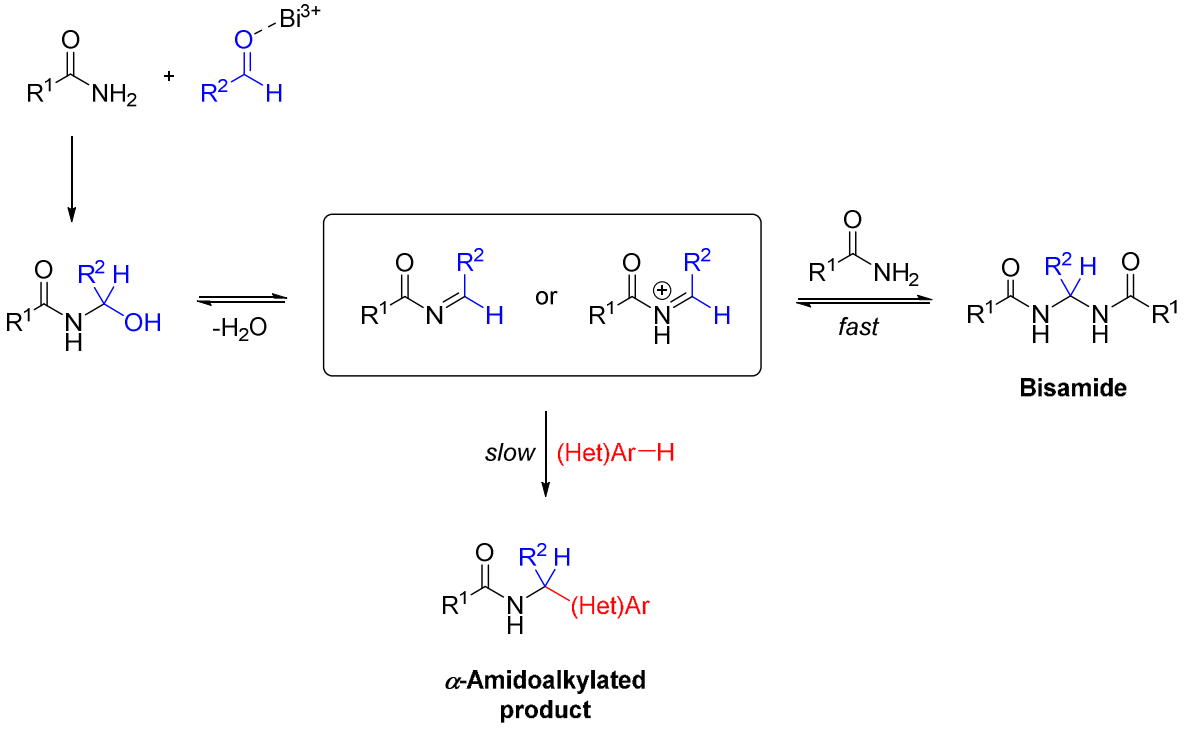
In the case of the three–component reactions we were able to observe the same rapid formation of the bisamide and a slower subsequent conversion of the bisamide to the product during the course of the reaction. It is worth mentioning, that we could observe the formation of this bisamide during our initial catalyst screenings with almost every tested Lewis– or Brønsted acid.[27] Some Brønsted acids, e.g. TfOH, could catalyzed the bisamide formation even more efficiently than $Bi(OTf)_3$. Treatment of the bisamide **11** with 2–bromoanisole as nucleophilic arene component in the presence of 5 mol% $Bi(OTf)_3$ furnished the expected amidoalkylated product **10d** in 67% yield (**Scheme 5**). The analogous N,O–aminal **12**, the formal mono–addition product of benzamide to formaldehyde, reacts in a similar manner. Treatment of **12** with bromoanisole in the presence of 5 mol% $Bi(OTf)_3$ leads to the formation of the amidoalkylation product in 61% yield. No other tested Lewis– or Brønsted acid could catalyze those two transformations with comparable efficiency.

Scheme 5. Two–Component Reactions with Preformed Acylimine–Precursors



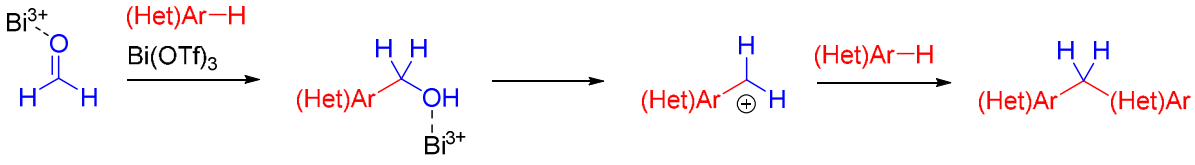
Based on those experiments we assume the following mechanism as shown in **Scheme 6**. In the first step the amide adds to the aldehyde to afford an aminal. Elimination of water leads to the formation of a reactive acylimine or acyliminium species.[28] This electrophilic species reacts immediately with a second molecule of the amide in *aza*-amidoalkylation to furnish the observed and isolated bisamide. Considering the higher nucleophilicity of the amide nitrogen, the fast addition of a second amide to the acylimine is not surprising. Under the reaction conditions, the bisamide, favoured under kinetic control, can decompose to form the acylimine. In the presence of a suitable nucleophilic arene, the electrophilic acylimine can react in an *aza*–Friedel–Crafts reaction to afford the amidoalkylated product containing a thermodynamically stable C-C-bond. The unique catalytic activity of $Bi(OTf)_3$ can be explained by two reasons. On the one hand $Bi(OTf)_3$, although easily hydrolyzed,[20b,] does not lose its catalytic activity in the presence of higher amounts of water.[19] On the other hand $Bi(OTf)_3$ is a strong Lewis acid and could further activate the formed acylimine towards the addition of nucleophiles.[29]

Scheme 6. Proposed Mechanism of the Three–Component *α*–Amidoalkylation Reaction



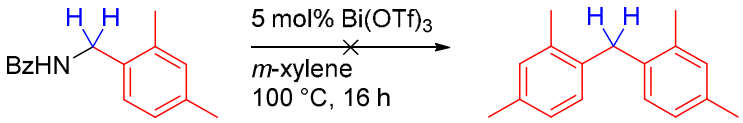
During our studies we often observed the formation of bis(hetero)arylmethane derivatives, especially for reactions with more reactive (hetero)arenes such as thiophene, furan or *N*-tosylindole.[30] Since we were never able to isolate the amidoalkylation products of very reactive heteroarenes, such as indole, we cannot rule out that these products decompose under our reaction conditions. Control experiments showed, that these side–products arise from the direct addition of two (hetero)arenes to the aldehyde, presumably via *in situ* formed benzyl cations (**Scheme 7**).[31]

Scheme 7. Side Reaction with Electron–Rich (Hetero)arenes



The amidoalkylated products proved to be stable under our reaction conditions. Prolonged treatment of **4** with excess *m*–xylene in the presence of 5 mol% $Bi(OTf)_3$ did not lead to the formation of any diarylmethane (**Scheme 8**).

Scheme 8. Stability of Amidoalkylated Products

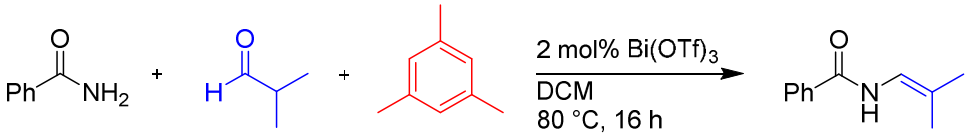


4

2. Three–Component Reaction with Alkylaldehydes

Encouraged by the results of the *α*–amidoalkylation reaction with formaldehyde, we turned our attention to reactions with simple alkylaldehydes. Unfortunately, the reaction of benzamide (**1a**), isobutyraldehyde (**13**) and mesitylene (**9a**) led to the selective formation of enamide **14** in 75% yield (**Scheme 9**).[32]

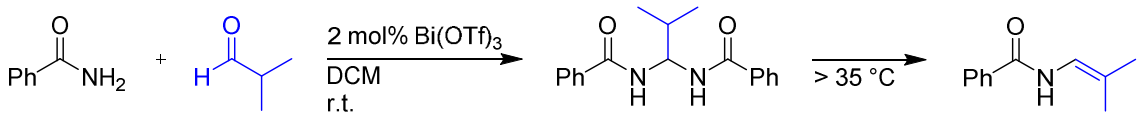
Scheme 9. Multicomponent Reactions with Alkylaldehydes Fail at Elevated Temperatures



1 1.2 equiv. **13** 1.0 equiv. **9a** 3.0 equiv. **14** 75%

Therefore the corresponding two–component reaction between benzamide and isobutyraldehyde was investigated in more detail (**Scheme 10**). These investigations revealed a rapid formation of the corresponding bisamide **15** in the presence of $Bi(OTf)_3$ even at room temperature. However, this bisamide is not stable at elevated temperatures. At temperatures above 35 °C formation of the enamide occurs, presumably via elimination of one molecule of benzamide.[33] Enamide **14** is stable in the presence of $Bi(OTf)_3$ at temperatures below 100 °C. In the presence of stronger acids or at higher temperatures dimerization and polymerization of the enamide is observed.

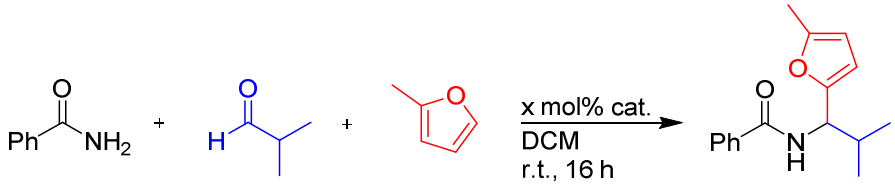
Scheme 10. Two–Component–Reaction between Benzamide and Isobutyraldehyde



1 **13** **15** **14**

From these results we can draw two conclusions. One the one hand, alkylaldehydes are not suitable aldehyde components for our amidoalkylation reactions with moderately nucleophilic arenes. On the other hand, the formation of bisamide **15** clearly shows that a reactive acylimine species is formed even at room temperature. Therefore, trapping of the electrophilic acylimine with more reactive, electron–rich (hetero)arenes at temperatures below 35 ºC should be possible. With these considerations in mind we investigated the three–component reaction between benzamide (**1**), isobutyraldehyde (**13**) and 2–methylfuran (**16**) as more nucleophilic arene component (**Table 2**).[17] Indeed, $Bi(OTf)_3$ can efficiently catalyze this reaction at 2–5 mol% catalyst loading. The yield of the reaction can be improved by a slight modification of the reaction protocol. Slow addition of the nucleophilic component over 2 h leads to an increased yield and decreased direct addition of the arene to the aldehyde.

Table 2. Alkylaldehydes — Survey of Catalysts[a,b]



1 1.2 equiv. **13** 1.0 equiv. **16** 3.0 equiv. **17**

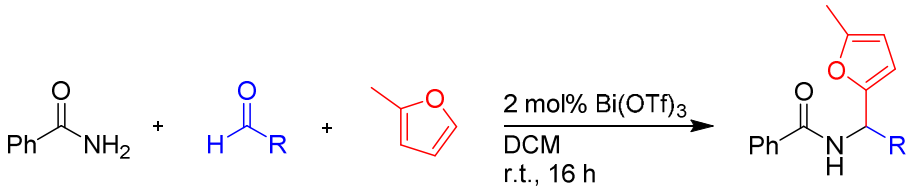
entry	catalyst [mol%]	yield [%]
1	$Bi(OTf)_3$ (0.5)	–
2	$Bi(OTf)_3$ (1.0)	–
3	$Bi(OTf)_3$ (2.0)	44
4	$Bi(OTf)_3$ (2.0)[c]	61
5	$Bi(OTf)_3$ (5.0)	35
6	$BiCl_3$ (5.0)	–

7	$BiNO_3$ (5.0)	–	

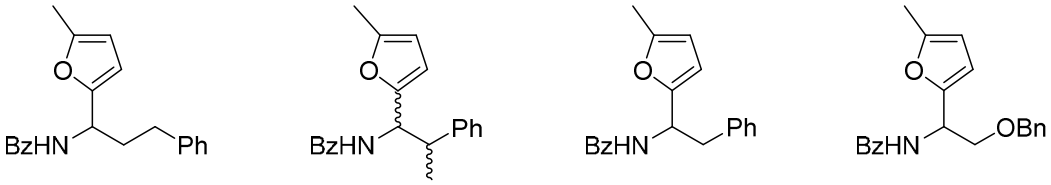
[a] General reaction conditions: Benzamide (1.2 equiv.), isobutyraldehyde (1.0 equiv.), 2–methylfuran (3.0 equiv.), $Bi(OTf)_3$ (x mol%). [b] Isolated yield of analytical pure product. [c] The arene was added dropwise over a period of 2 h to the reaction mixture.

With the optimized conditions in hand, we investigated reactions with different alkylaldehydes. In general the desired amidoalkylated products were obtained in moderate to high yields (**Scheme 11**). In the case of 2–benzyloxyacetaldehyde the corresponding 1,2–aminoalcohol **19d** could be isolated in 77% yield. Reactions of alkylaldehydes bearing a stereocenter in α–position, furnished the amides **19b** and **19f** in good yields and moderate to high diastereoselectivities.

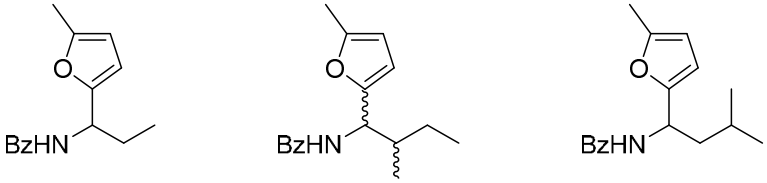
Scheme 11. Alkylaldehydes — Variation of Aldehydes[a]



1 1.2 equiv. **18** 1.0 equiv. **16** 3.0 equiv. **19**



19a 81%[b] **19b** 53% (*d.r.* 7:1)[c,d] **19c** 45%[e] **19d** 77%[e]

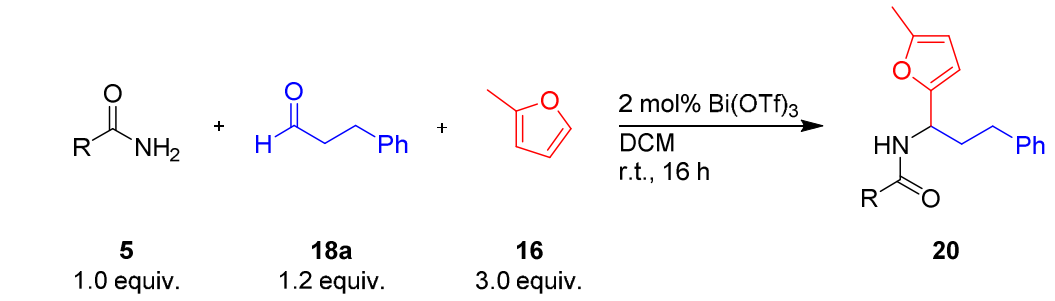


19e 53%[e] **19f** 72% (*d.r.* 2:1)[d,e] **19g** 66%[e]

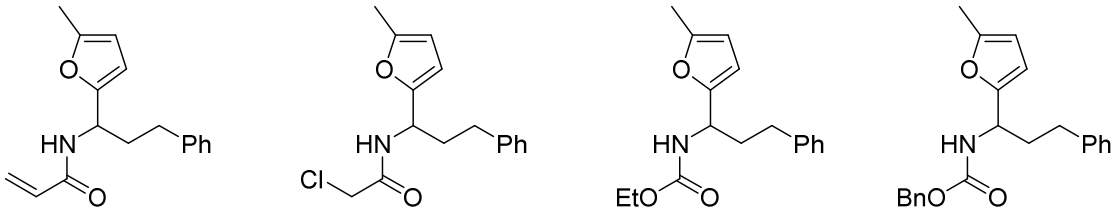
[a] Isolated yield of analytical pure product. [b] The reaction mixture was cooled to 0° C, then the arene was added. [c] The arene was added dropwise over a period of 1 h to the reaction mixture. [d] Obtained as mixture of diastereomers, ratio of diastereomers given in parentheses. [e] The arene was added dropwise over a period of 2 h to the reaction mixture. Pht = *N*–phthalyl.

Different amides and carbamates are suitable amide components for this three–component reaction. The reaction with alkyl amides or various carbamates leads to the formation of amidoalkylated furans in 32–76% yield (**Scheme 12**). *Tert*–butyl carbamate is a suitable substrate for this transformation (product **20e**).

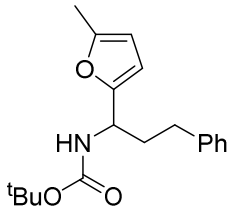
Scheme 12. Alkylaldehydes — Variation of Amides [a]



5 1.0 equiv. **18a** 1.2 equiv. **16** 3.0 equiv. **20**



20a 59%[b] **20b** 32%[b,c] **20c** 47%[d] **20d** 45%[d]

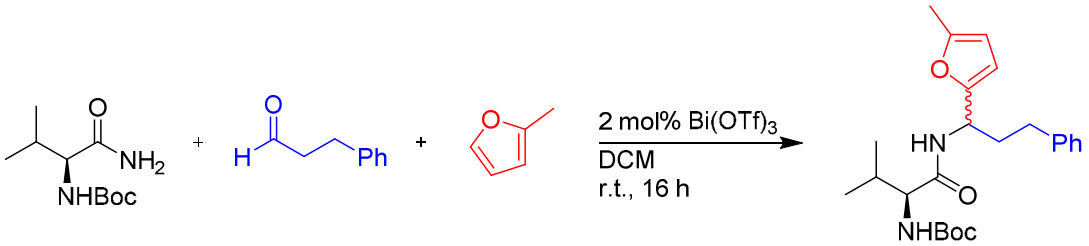


20e 76%[e]

[a] Isolated yield of analytical pure product. [b] The arene was added dropwise over a period of 2 h to the reaction mixture. [c] The bis(heteroaryl)phenylpropane species was formed as major product. [d] The reaction mixture was cooled to 0° C, then the arene was added. [e] The arene was added dropwise over a period of 1 h to the reaction mixture.

The acid–sensitive *Boc*–functionality is well tolerated under the very mild reaction conditions **(Scheme 13**). The reaction of Boc–protected valinamide **21** furnished the corresponding product **22** in 62% yield and with a 2:1 diastereoselectivity .

Scheme 13. Alkylaldehydes — Reaction of *Boc*–Protected Valinamide[a,b,c]

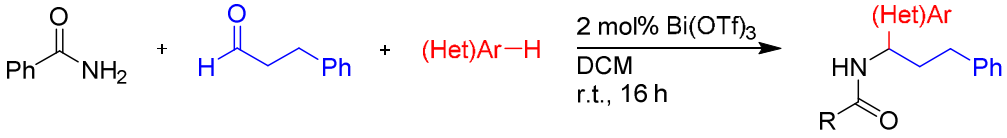


21 1.0 equiv. | **18a** 1.2 equiv. | **16** 3.0 equiv. | **22** 62% (*d.r.* 2:1)

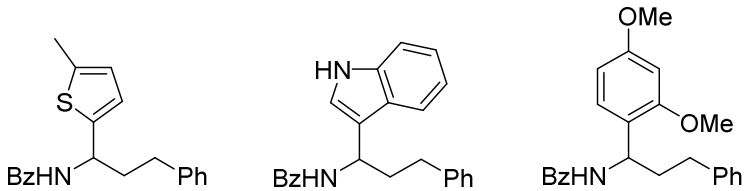
[a] Isolated yield of analytical pure product. [b] The arene was added dropwise over a period of 2 h to the reaction mixture. [c] Obtained as mixture of diastereomers, ratio of diastereomers given in parentheses.

As indicated above, three–component reactions with alkylaldehydes are limited to electron–rich arenes and heteroarenes. Therefore the reaction of 2–methylthiophene and 1,3–dimethoxybenzene furnished the products **23a** and **23c** in 61 and 58% yield **(Scheme 14)**. Further examination of this three–component reaction revealed a second limitation. Very reactive heteroarenes, such as indole or pyrrole, are not suitable substrates for this transformation. In the case of such highly reactive aromatic components only direct addition to the aldehyde is observed.

Scheme 14. Alkylaldehydes — Variation of (Hetero)Arenes[a]



1 1.0 equiv. | **18a** 1.2 equiv. | **9** 3.0 equiv. | **23**



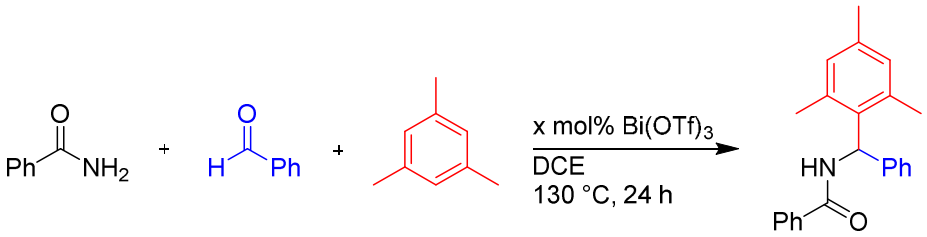
23a 61%[b,c] | **23b** 0%[d] | **23c** 58%[e]

[a] Isolated yield of analytical pure product. [b] Reaction at 35 °C. [c] 5 mol% $Bi(OTf)_3$. [d] The bis(heteroaryl)phenylpropane species was formed. [e] The reaction mixture was cooled to 0° C, then the arene was added.

3. Three–Component Reaction with Arylaldehydes

We next turned our attention to reactions with arylaldehydes as aldehyde component. In this case enamide formation is not possible. During preliminary experiments rapid formation of the bisamide intermediate was observed at temperatures higher than 50 °C. The reaction between benzamide (**1**), benzaldehyde (**24**) and mesitylene (**9a**) was chosen as model system to investigate the influence of various reaction parameters (**Table 3**). Surprisingly, high temperatures of 130 °C were required for efficient product formation. Best yields were obtained using 10 mol% $Bi(OTf)_3$ (entry 4, 71%). We attribute these forcing reaction conditions with the decreased electrophilicity of *N*–acylimines derived from arylaldehydes. Comparable results in yields were provided either by lengthening of the reaction time to 48 h or performing the reaction at 150 °C (entry 2–3, 63 and 60% yield). Addition of Brønsted acids, such as TfOH, did not affect the yield (entry 5).

Table 3. Arylaldehydes — Optimization of Catalysts[a,b]



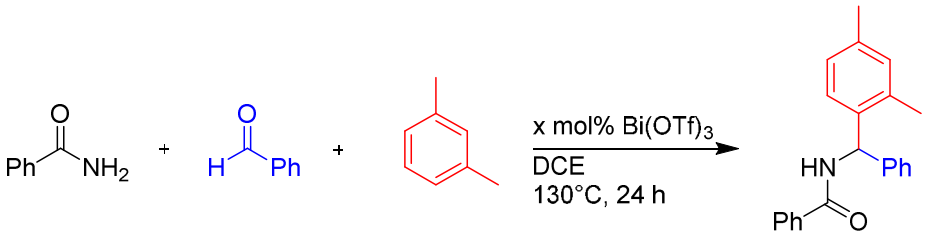
1 1.0 equiv. | **24** 1.2 equiv. | **9a** 3.0 equiv. | **25**

entry	catalyst [mol%]	yield [%]
1	$Bi(OTf)_3$ (5.0)	23
2	$Bi(OTf)_3$ (5.0)[c]	63
3	$Bi(OTf)_3$ (5.0)[d]	60
4	$Bi(OTf)_3$ (10.0)	71
5	$Bi(OTf)_3$ (5.0) + TfOH (5.0)	25

[a] General reaction conditions: Benzamide (1.0 equiv.), benzaldehyde (1.2 equiv.), mesitylene (3.0 equiv.), $Bi(OTf)_3$ (x mol%), 130 °C, 24 h. [b] Isolated yield of analytical pure product. [c] Reaction time: 48 h. [d] Reaction at 150 °C.

The use of TfOH as Brønsted–acid additive in the three–component reaction with less reactive *m*–xylene led to considerable higher yield (**Table 4**, entry 1 and 3). Best yields of **26** were obtained by an additional increase of temperature to 150 °C (entry 4).

Table 4. Arylaldehydes — Use of TfOH Elevates Yield in the Case of *m*–Xylene[a,b]



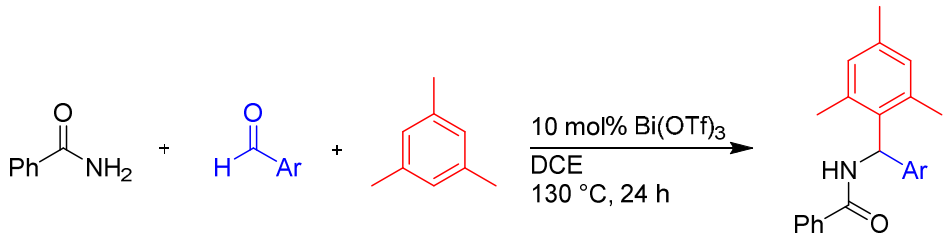
1 1.0 equiv. **24** 1.2 equiv. **3** 3.0 equiv. **26**

entry	catalyst [mol%]	yield [%]
1	$Bi(OTf)_3$ (5.0)[c]	43
2	$Bi(OTf)_3$ (10.0)	35
3	$Bi(OTf)_3$ (5.0) + TfOH (5.0)[d,e]	58
4	$Bi(OTf)_3$ (5.0) + TfOH (5.0)[e,f]	76

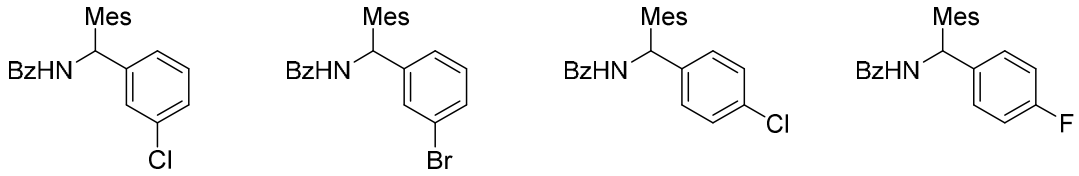
[a] General reaction conditions: Benzamide (1.0 equiv.), benzaldehyde (1.2 equiv.), mesitylene (3.0 equiv.), $Bi(OTf)_3$ (x mol%), 130 °C, 24 h. [b] Isolated yield of analytical pure product. [c] Reaction time: 48 h. [d] Reaction at 100 °C. [e] Benzamide (1.2 equiv.), benzaldehyde (1.0 equiv.). [f] Reaction at 150 °C.

With the optimized reaction conditions at hand, we examined reactions with various arylaldehydes (**Scheme 15**). Arylaldehydes bearing halogenes in *meta* and *para* position afforded the products in good yields (**28a**–**d**, 54–72% yield). Reaction with 2–chloro–5–nitrobenzaldehyde provided the product **28e** in 66% yield. The *α*–amidoalkylated product **28f** of naphthylaldehyde was isolated in 29% yield.

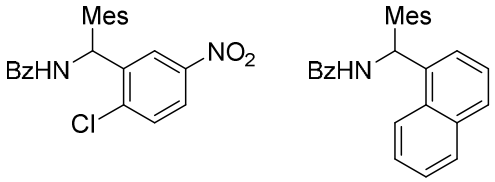
Scheme 15. Arylaldehydes — Variation of Aldehydes[a]



1 1.0 equiv. **27** 1.2 equiv. **9a** 3.0 equiv. **28**



28a 54% **28b** 54% **28c** 72% **28d** 64%

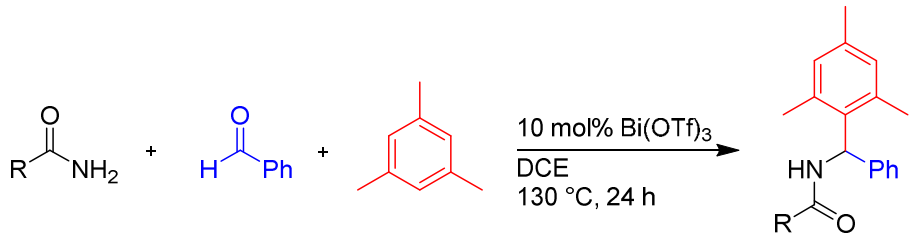


28e 66% **28f** 29%

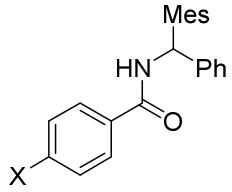
[a] Isolated yield of analytical pure product. Mes = mesityl (2,4,6–trimethylphenyl).

As shown in **Scheme 16** variation of the amide component afforded the desired products **29a–d**; **29f–g** in 33–89% yield. In the case of arylaldehydes, carbamates are not suitable amide components. Only in the case of urethane, the desired product **29g** was formed, albeit in only 33% yield. Most likely carbamates are not stable under these conditions.

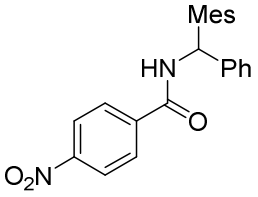
Scheme 16. Arylaldehydes — Variation of Amides[a]



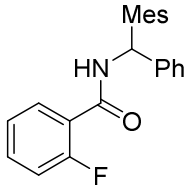
5 1.0 equiv. **24** 1.2 equiv. **9b** 3.0 equiv. **29**



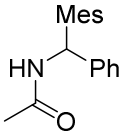
29a: X = OMe 39%
29b: X = Br 56%



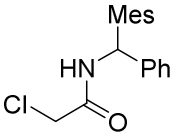
29c 67%



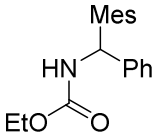
29d 73%



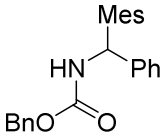
29e 0%



29f 89%[b]



29g 33%

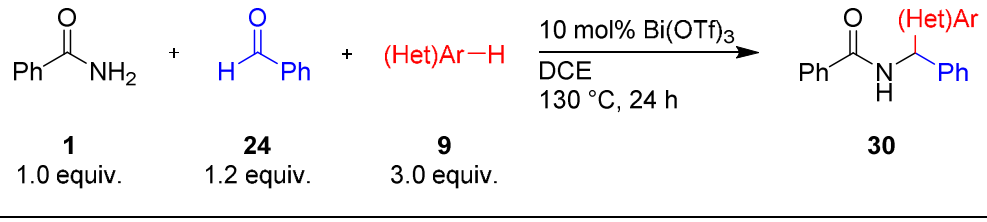


29h 0%

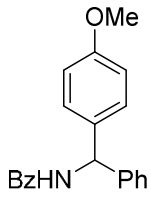
[a] Isolated yield of analytical pure product. [b] Reaction at 100 °C. Mes = mesityl (2,4,6–trimethyl–phenyl).

Next we investigated reactions with various arenes (**Scheme 17**). Anisole and its halogenated derivatives gave the desired amidoalkylated products **30a–d** in 25–40% yield. Only in the case of 3,5–*di*–methylanisole the α–substituted amide was isolated in a satisfactory yield of 74%. In general, reactions with various electron–rich heterocycles were not successful. The intermediate species is efficiently generated at 50 °C, but the high reactivity of the heteroarenes promotes synthesis of the direct addition products at these temperatures. Best results were achieved with 2–bromothiophene (**30f**, 36% yield). The high reactivity of the heteroarenes leads to a rapid direct addition to the aldehyde temperatures below 50 ºC, necessary for the acylimine formation.

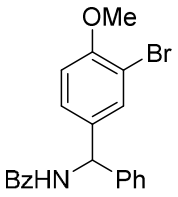
Scheme 17. Arylaldehydes — Variation of (Hetero)Arenes[a]



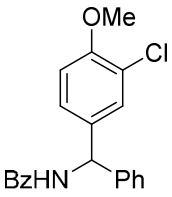
1 1.0 equiv. **24** 1.2 equiv. **9** 3.0 equiv. **30**



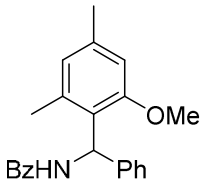
30a
25% (4:1)[b,c]



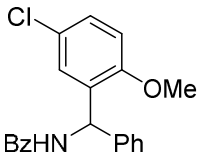
30b
35%[d,e]



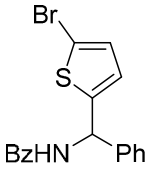
30c
40%



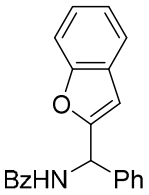
30d
74%



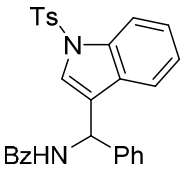
30e
0%



30f
36%[f]



30g
9%[g]



30h
0%

[a] Isolated yield of analytical pure product. [b] Obtained as mixture of regioisomers, ratio of regioisomers given in parentheses. [c] Reaction at 100 °C. [d] Reaction with 5 mol% $Bi(OTf)_3$. [e] Reaction with 5 mol% TfOH. [f] Reaction at 80 °C. [g] Reaction at 50 °C.

CONCLUSIONS

In summary, a general $Bi(OTf)_3$–catalyzed multicomponent between amides, aldehydes and arenes was developed. Formaldehyde, alkylaldehydes and arylaldehydes were successfully employed as aldehyde compounds. Scope and limitations for all three types of aldehyde components were investigated.

These practical and operational simple multicomponent reactions provide straightforward and versatile access to α–amidoalkylated (hetero)arenes. The use of the nontoxic catalyst and generation of water as only side product constitute a valuable approach towards the concept of sustainable chemistry.

EXPERIMENTAL SECTION

General Considerations

Solvents for reactions and column chromatography were obtained from different commercial suppliers in > 97 % purity and used as received. *Reagents:* (S)–*N*–(2,4–Dimethylbenzyl)–3–methyl–2–(1,3–dioxoisoindolin–2–yl)butanamide[34], *N*–benzyl–2–oxoacetamide[35], ethyl–4–methoxybenzoate[36], 3,5–dimethylanisole[37], 2–methylpivalanilide[38], 3– ethylpivalanilide[38], *N*–tosylindole[39] and *N*–tosylpyrrole[40], were synthesized according to literature. All other starting materials were purchased from commercial sources and used without further purification. Anhydrous $Bi(OTf)_3$ was obtained from different providers and used directly. No special precautions were taken to avoid exposure of $Bi(OTf)_3$ to moisture. Therefore we cannot rule out the formation of $Bi(OTf)_3 \cdot xH_2O$ during storage. Indeed depending on the provider and storage time (or even the time for weighting out a defined amount for elemental analysis) $Bi(OTf)_3$ contained up to six molecules of water. However no changes in catalytic activity and yield even upon prolonged storage (>1 year) were observed. Therefore the amount of $Bi(OTf)_3$ used is always calculated on anhydrous $Bi(OTf)_3$. The actual catalyst loading for particular reactions might be slightly lower, depending on the batch quality and storage time. *Column chromatography* was performed with Silica 0.04–0.063 mm/ 230–400 mesh. Thin layer chromatography was done using aluminum plates coated with SiO_2. The spots were visualized by ultraviolet light, iodine or CAM. *NMR spectroscopy:* ^{1}H– and ^{13}C–NMR spectra were recorded at 300 or 400 MHz and 75 or 101 MHz, respectively. *Mass spectrometry spectra* (MS) were measured using ESI (electrospray ionization) coupled to a quadrupole mass mass analyzer. *High resolution mass spectra* (MALDI-HRMS) were measured using MALDI (matrix-assisted laser desorption/ionization) coupled to an ion trap mass spectrometer. Melting points are uncorrected. All yields refer to isolated yields of compounds estimated to be > 95% pure as determined by ^{1}H–NMR or elementary analysis.

Typical Procedures

All reactions were performed in vials sealed with a screw cap to avoid evaporation of the solvent. For reactions performed at room temperature the screw cap can be replaced with a rubber septum. For reaction performed at temperatures below the boiling point of the solvent culture tubes with a PTFE lined screw cap were used. For reaction performed at or above the boiling point of the solvent special thick-walled pressure tubes have to be used.

TP 1 — Reactions with Formaldehyde

A 10 mL screw cap vial was charged with $Bi(OTf)_3$ (5 mol%), amide (1.0 equiv), formaldehyde (1.2 equiv), (hetero)arene (3–4 equiv.) and nitromethane and closed with a Teflon lined screw cap. The reaction mixture was stirred at 25–100 °C for the specified time. After cooling to room temperature the reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by column chromatography (hexane/EtOAc) afforded the analytically pure product.

TP 2 — Reactions with Arylaldehydes

A 10 mL screw cap vial was charged with $Bi(OTf)_3$ (10 mol%), amide (1.0 equiv), arylaldehyde (1.2 equiv), (hetero)arene (3–4 equiv.) and nitromethane and closed with a Teflon lined screw cap. The reaction mixture was stirred at 50–130 °C for the specified time. After cooling to room temperature the reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by column chromatography (hexane/EtOAc) afforded the analytically pure product.

N–(2,4–Dimethylbenzyl)benzamide (**4**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), *m*–xylene (0.74 mL, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 5 mol%) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (403 mg, 84%, ratio of regioisomers 15:1). m.p.: 94 –95 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks are listed only for major regioisomer): δ = 7.77 (d, J = 8 Hz, 2H), 7.51 – 7.47 (m, 1H), 7.44 – 7.40 (m, 2H), 7.19 (d, J = 8 Hz, 1H), 7.04 – 7.00 (m, 2H), 6.17 (bs, 1H), 4.61 (d, J = 5 Hz, 2H), 2.34 (s, 3H), 2.32 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz) (peaks are listed only for major regioisomer): δ = 167.3, 137.8, 136.7, 134.6, 132.9, 131.6, 129.1, 128.7, 128.7, 127.0, 127.0, 42.3, 21.1, 19.1. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{16}H_{18}NO$ 240.14, found 240.40. EA (%): Calcd.: C 80.30 H 7.16 N 5.85 found: C 80.13 H 7.06 N 5.78. IR (cm^{-1}): 3284 (m), 1626 (s), 1578 (m), 1524 (m), 1487 (w), 1474 (w), 1363 (w), 1308 (m), 1281 (m), 1219 (w), 1182 (w), 1144 (w), 1057 (w), 1055 (w), 1026 (w), 968 (w), 920 (w), 877 (w), 831 (w), 823 (m), 800 (m), 769 (m), 704 (w), 690 (s), 660 (w). R_f(hexane/ EtOAc 4:1) = 0.3.

N–(2,4–Dimethylbenzyl)–4–methoxybenzamide (**6a**) was synthesized according to TP 1 from 4–methoxybenzamide (76 mg, 0.5 mmol), paraformaldehyde (19 mg, 0.6 mmol), m–xylene (0.24 mL, 2.0 mmol, 4 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol) in nitromethane (2 mL) at 80 °C for 24 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as

colorless solid (87 mg, 65%). m.p.: 134–135 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.73 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.03 – 6.99 (m, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 6.07 (bs, 1H), 4.58 (d, *J* = 5.1 Hz, 2H), 3.84 (s, 3H), 2.33 (s, 3H), 2.32 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 166.8, 162.3, 137.8, 136.7, 133.1, 131.6, 129.1, 128.9, 127.0, 126.8, 113.9, 55.5, 42.3, 21.1, 19.1. MS (ESI) m/z: Calcd. for $C_{17}H_{19}NO_2Na$ 292.13; found 292.21 $[M+Na]^+$. EA (%): Calcd.: C 75.81 H 7.11 N 5.20; found: C 75.61 H 6.91 N 5.10. IR (cm^{-1}): 3284 (m), 1618 (s), 1574 (w), 1531 (m), 1497 (m), 1462 (m), 1408 (w), 1367 (w), 1304 (m), 1281 (m), 1250 (s), 1176 (m), 1111 (w), 1032 (m), 968 (w), 533 (w), 883 (w), 843 (m), 823 (s), 771 (m), 683 (w). R_f (hexane/ EtOAc 4:1) = 0.1.

N–(2,4–Dimethylbenzyl)–4–bromobenzamide (**6b**) was synthesized according to TP 1 from 4–bromobenzamide (400 g, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), *m*–xylene (0.74 mL, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (448 mg, 70%, ratio of regioisomers 24:1). m.p.: 174–175 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks are listed only for major regioisomer): *δ* = 7.63 (d, *J* = 7.6 Hz, 2H), 7.55 (d, *J* = 7.5 Hz, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.04 – 7.00 (m, 2H), 6.12 (bs, 1H), 4.59 (d, *J* = 5.1 Hz, 2H), 2.33 (s, 3H), 2.32 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): *δ* = 166.3, 138.0, 136.7, 133.4, 132.6, 132.0, 131.7, 129.2, 128.7, 127.1, 126.3, 42.4, 21.2, 19.1. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{16}H_{17}BrNO$ 318.04, found 318.00. EA (%): Calcd.: C 60.39 H 5.07 N 4.40 found: C 60.23 H 5.02 N 4.21. IR (cm^{-1}): 3286 (w), 2906 (w), 1626 (s), 1589 (w), 1529 (m), 1481 (m), 1358 (w), 1304 (w), 1277 (w), 1180 (w), 1146 (w), 1072 (w), 1009 (m), 972 (w), 881 (w), 843 (m), 823 (m), 771 (w), 756 (w), 677 (w). R_f (hexane/ EtOAc 4:1) = 0.4.

Ethyl–2,4–dimethylbenzylcarbamate (**6c**) was synthesized according to TP 1 from urethane (45 mg, 0.5 mmol), paraformaldehyde (19 mg, 0.6 mmol), *m*–xylene (0.18 mL, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol, 5 mol%) in nitromethane (2 mL) at 60 °C for 24 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colourless solid (73 mg, 71%). m.p.: 54–55 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): *δ* = 7.13 (d, *J* = 7.4 Hz, 1H), 6.99 – 6.97 (m, 2H), 4.76 (bs, 1H), 4.32 (d, *J* = 5.2 Hz, 2H), 4.14 (q, *J* = 6.9, 6.9 Hz, 2H), 2.31 (s, 6H), 1.25 (t, *J* = 7.0 Hz, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): *δ* = 156.6, 137.5, 136.2, 133.3, 131.5, 128.5, 126.9, 61.0, 43.0, 21.1, 19.0, 14.8. MS (ESI) m/z: $[M+Na]^+$ Calcd. for $C_{12}H_{17}NO_2Na$ 230.12, found 230.23. HRMS (MALDI) m/z: $[M+H]^+$ Calcd. for $C_{12}H_{18}NO_2$ 208.1332, found 208.1333. IR (cm^{-1}): 3321 (m), 2979 (m), 2921 (w), 1686 (s), 1617 (w), 1525 (m), 1479 (m), 1470 (m), 1375 (m), 1356 (m), 1301 (m), 1243 (s), 1160 (m),

1128 (m), 1047 (s), 965 (m), 925 (m), 880 (m), 822 (s), 780 (m), 638 (m), 580 (s), 550 (m), 505 (m). R_f (hexane/ EtOAc 4:1) = 0.4.

Benzyl–2,4–dimethylbenzylcarbamate (**6d**) was synthesized according to TP 1 from benzylcarbamate (76 mg, 0.5 mmol), paraformaldehyde (19 mg, 0.6 mmol), *m*–xylene (0.18 mL, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol, 5 mol%) in nitromethane (2 mL) at 60 °C for 24 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (61 mg, 45%, ratio of regioisomers 14:1). m.p.: 74–76 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks are listed only for major regioisomer): δ = 7.36 – 7.30 (m, 5H), 7.12 (d, J = 7.5 Hz, 1H), 6.99 – 6.97 (m, 2H), 5.13 (s, 2H), 4.85 (bs, 1H), 4.35 (d, J = 5.5 Hz, 2H), 2.30 (s, 3H), 2.29 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz) (compound exists as a mixture of rota– and regioisomers, peaks are not assigned): δ = 156.3, 137.5, 136.7, 136.2, 133.1, 131.5, 128.7, 128.5, 128.3, 128.0, 126.9, 126.8, 66.9, 43.2, 21.1, 19.0. MS (ESI) m/z: $[M+Na]^+$ Calcd. for $C_{17}H_{19}NO_2Na$ 292.13, found 292.21. EA (%): Calcd.: C 75.81 H 7.11 N 5.20; found: C 75.67 H 7.09 N 4.97. IR (cm^{-1}): 3318 (w), 2946 (w), 2921 (w), 1683 (s), 1519 (s), 1505 (s), 1463 (m), 1453 (m), 1379 (w), 1356 (m), 1303 (w), 1241 (s), 1159 (w), 1118 (m), 1080 (w), 1047 (s), 1028 (m), 1003 (w), 965 (m), 925 (w), 912 (m), 881 (w), 852 (m), 823 (m), 780 (m), 756 (s), 719 (m), 706 (m), 693 (m), 627 (m), 588 (s), 568 (m), 538 (m), 504 (m), 468 (m). R_f (hexane/ EtOAc 4:1) = 0.5.

N–(2,4–Dimethylbenzyl)–2–acrylamide (**6e**) was synthesized according to TP 1 from acrylamide (142 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), *m*–xylene (0.74 mL, 6.0 mmol, 3.0 equiv.) und $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (207 mg, 55%, ratio of regioisomers 13:1). m.p.: 122–123 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks are listed only for major regioisomer): δ = 7.14 – 7.12 (m, 1H), 7.01 – 6.68 (m, 2H), 6.31 (dd, J = 17.0, 1.5 Hz, 1H), 6.12 – 6.08 (m, 1H), 5.65 (dd, J = 10.2, 1.5 Hz, 1H), 4.48 (d, J = 5.4 Hz, 2H), 2.31 (s, 3H), 2.30 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz) (peaks are listed only for major regioisomer): δ = 165.3, 137.8, 136.6, 132.7, 131.6, 130.8, 129.1, 127.0, 126.7, 41.8, 38.5, 21.1, 19.0. MS (ESI) m/z: $[M+Na]^+$ Calcd. for $C_{12}H_{15}NONa$ 212.11, found 212.17. EA (%): Calcd.: C 76.16 H 7.99 N 7.40 found: C 76.02 H 7.79 N 7.32. IR (cm^{-1}): 3286 (m), 2916 (w), 1653 (s), 1620 (s), 1537 (m), 1464 (w), 1404 (w), 1352 (w), 1304 (w), 1234 (s), 1046 (m), 995 (s), 145 (s), 879 (w), 822 (m), 775 (w), 688 (m). R_f (hexane/ EtOAc 4:1) = 0.1.

N–(2,4–Dimethylbenzyl)–2–chloroacetamide (**6f**) was synthesized according to TP 1 from 2–chloroacetamide (187 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), *m*–xylene (0.74 mL, 6.0 mmol, 3.0 equiv.) und $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colourless solid (308 mg, 73%, ratio of regioisomers 18:1). m.p.: 120–121 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz) (peaks are listed only for major regioisomer): δ = 7.13 (d, J = 7.5 Hz, 1H), 7.02 – 7.00 (m, 2H), 6.63 (bs, 1H), 4.45 (d, J = 5.4 Hz, 2H), 4.09 (s, 2H), 2.32 (s, 3H), 2.30 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz) (peaks are listed only for major regioisomer): δ = 165.7, 138.0, 136.5, 132.0, 131.6, 128.9, 127.1, 42.7, 42.0, 21.1, 19.1. MS (ESI) m/z: $[M]^+$ Calcd. for $C_{11}H_{14}ClNO$ 211.08, found 211.40. EA (%): Calcd.: C 62.41 H 6.67 N 6.62; found: C 62.33 H 6.57 N 6.43. IR (cm^{-1}): 3282 (m), 3003 (w), 1645 (s), 1541 (m), 1466 (w), 1416 (w), 1362 (w), 1319 (w), 1225 (m), 1157 (w), 1061 (w), 1034 (w), 995 (w), 124 (w), 879 (w), 820 (m), 771 (w), 702 (s), 667 (m). R_f (hexane/ EtOAc 4:1) = 0.3.

N–(2,4–Dimethylbenzyl)–2–cyanoacetamide (**6g**) was synthesized according to TP 1 from 2–cyanoacetamide (168 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), *m*–xylene (0.74 mL, 6.0 mmol, 3.0 equiv.) und $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colourless solid (387 mg, 96%, ratio of regioisomers 11:1). m.p.: 136–137 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks only for major regioisomer listed): δ = 7.11 (d, J = 7.6 Hz, 1H), 7.03 – 7.00 (m, 2H), 6.15 (bs, 1H), 4.44 (d, J = 5.3 Hz, 2H), 3.37 (s, 2H), 2.32 (s, 3H), 2.30 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz) (peaks not assigned to regioisomers): δ = 160.5, 138.3, 136.5, 131.8, 131.5, 129.1, 128.8, 127.2, 114.7, 52.3, 42.5, 25.9, 21.1, 19.9, 19.1. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{12}H_{15}N_2O$ 203.12, found 203.40. EA: Calcd.: C 71.26 H 6.98 N 13.85; found: C 71.28 H 7.05 N 13.66. IR (cm^{-1}): 3275 (m), 1647 (w), 1645 (s), 1571 (m), 1504 (w), 1468 (w), 1367 (m), 1365 (m), 1325 (w), 1232 (m), 1066 (w), 991 (w), 922 (w), 876 (w), 822 (m), 793 (m), 768 (w), 687 (m). R_f (hexane/ EtOAc 1:1) = 0.5.

N–(2,4–Dimethylbenzyl)acetamide (**6h**) was synthesized according to TP 1 from acetamide (29 mg, 0.5 mmol), paraformaldehyde (19 mg, 0.6 mmol), *m*–xylene (0.18 mL, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol, 5 mol%) in nitromethane (2 mL) at 100 °C for 8 h. Purification by chromatography (hexane/EtOAc 1:1) yielded the product as colorless solid (45 mg, 51%, ratio of regioisomers 15:1). m.p.: 110–112 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks are listed only for major regioisomer): δ = 7.11 (d, J = 7.6 Hz, 1H), 7.01 – 6.98 (m, 2H), 5.54 (bs, 1H), 4.39 (d, J = 5.3 Hz, 2H), 2.31 (s, 3H), 2.29 (s, 3H), 1.99 (s, 3H). ^{13}C–

NMR ($CDCl_3$, 75 MHz) (peaks are not assigned to regioisomers): δ = 169.8, 137.7, 137.6, 136.5, 134.0, 132.9, 131.5, 129.0, 158.6, 128.1, 127.0, 41.8, 38.6, 23.3, 23.2, 21.1, 19.8, 19.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{11}H_{16}NO$ 178.12, found 178.21 . EA (%): Calcd.: C 74.54 H 8.53 N 7.90; found: C 74.20 H 8.65 N 7.75. IR (cm^{-1}): 3289 (w), 3000 (w), 2920 (w), 2871 (w), 1689 (w),1634 (s), 1538 (s), 1463 (s), 1377 (s), 1352 (w), 1300 (w), 1275 (s), 1215 (w), 1159 (w), 1124 (w), 1092 (m), 1037 (w), 998 (m), 951 (w), 886 (w), 816 (s), 770 (w), 713 (s), 617 (m), 598 (s), 573 (s), 552 (w), 508 (w), 467(s). R_f(hexane/ EtOAc 1:1) = 0.2.

N–(2,4–Dimethylbenzyl)–2,2,2–trimethylacetamide (**6i**) was synthesized according to TP 1 from 2,2,2–trimethylacetamide (202 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), *m*–xylene (0.74 mL, 6.0 mmol, 3.0 equiv.) und $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100°C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (337 mg, 77%, ratio of regioisomers 17:1). m.p.: 85–86 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks are listed only for major regioisomer): δ = 7.10 (d, J = 8 Hz, 1H), 7.01 – 6.98 (m, 2H), 5.67 (bs, 1H), 4.39 (d, J = 5 Hz, 2H), 2.31 (s, 3H), 2.28 (s, 3H), 1.21 (s, 9H). ^{13}C–NMR ($CDCl_3$, 101 MHz) (peaks are listed only for major regioisomer): δ = 178.1, 137.6, 136.6, 133.2, 131.5, 128.9, 126.9, 41.9, 38.9, 27.8, 21.1, 19.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{14}H_{22}NO$ 220.17, found 220.80. EA (%): Calcd.: C 76.67 H 9.65 N 6.39; found: C 76.42 H 9.75 N 6.11. IR (cm^{-1}): 3317 (m), 2954 (w), 1633 (s), 1539 (m), 1504 (w), 1425 (w), 1365 (w), 1296 (w), 1225 (w), 1213 (m), 1005 (m), 931 (w), 866 (w), 814 (m), 787 (m), 702 (w), 677 (m). R_f(hexane/ EtOAc 1:1) = 0.4.

3–(2,4–Dimethylbenzyl)oxazolidin–2–one (**6j**) was synthesized according to TP 1 from oxazolidin–2–one (44 mg, 0.5 mmol), paraformaldehyde (19 mg, 0.6 mmol), *m*–xylene (0.18 mL, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol) in nitromethane (2 mL) at 100 °C for 6 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless oil (73 mg, 71 %, ratio of regioisomers >25:1). ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.08 (d, J = 7.6 Hz, 1H), 7.02 – 6.98 (m, 2H), 4.42 (s, 2H), 4.30 – 4.26 (m, 2H), 3.38 – 3.34 (m, 2H), 2.31 (s, 3H), 2.31 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 158.3, 138.1, 136.9, 131.7, 130.7, 129.3, 126.9, 61.9, 46.5, 44.1, 21.1, 19.1. MS (ESI) m/z: $[M+Na]^+$ Calcd. for $C_{12}H_{15}NO_2Na$ 228.10, found 227.80. EA (%): Calcd.: C 70.22 H 7.37 N 6.82; found: C 69.94 H 7.35 N 6.74. IR (cm^{-1}): 3491 (w), 2919 (w), 1740 (s), 1616 (w), 1484 (m), 1424 (s), 1376 (m), 1355 (m), 1320 (w), 1252 (s), 1204 (m), 1185 (m), 1158 (m), 1119 (m), 1067 (s), 1034 (s), 975 (m), 954 (m), 921 (m), 878 (w), 833 (m), 803 (m), 778 (m), 760 (s), 728 (m), 717 (m), 693 (m), 652 (m), 581 (m), 538 (w), 490 (m). R_f(hexane/ EtOAc 4:1) = 0.1.

N–(2,4–Dimethylbenzyl)–3–methyl–2–(1,3–dioxoisoindolin–2–yl)butanamide (**8**) was synthesized according to TP 1 from (S)–3–methyl–2–(1,3–dioxoisoindolin–2–yl)butanamide (123 mg, 0.5 mmol), paraformaldehyde (19 mg, 0.6 mmol), *m*–xylene (0.18 mL, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol, 5 mol%) in nitromethane (2 mL) at 100 °C for 24 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless, very viscous foam (115 mg, 63%, mixture of regioisomers as determined by analytical HPLC 12:1). ^{1}H–NMR ($CDCl_3$, 400 MHz) (mixture of regioisomer and rotamers, peaks are not assigned): δ = 7.87 – 7.85 (m, 2H), 7.76 – 7.74 (m, 2H), 7.09 (d, J = 7.6 Hz, 1H), 7.03 – 7.02 (m, 1H), 6.98 – 6.94 (m, 2H), 4.49 – 4.42 (m, 2H), 4.35 – 4.31 (m, 1H), 2.85 – 2.85 (m, 1H), 2.29 (s, 3H), 2.26 (s, 3H), 1.10 (d, J = 6.7 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz) (mixture of regioisomer and rotamers, peaks are not assigned): δ = 168.6, 168.6, 137.5, 136.3, 134.6, 132.7, 131.5, 131.5, 128.7, 128.6, 128.0, 127.0, 123.8, 63.3, 41.7, 38.6, 27.8, 21.1, 20.0, 19.8, 19.6, 19.1. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{22}H_{25}N_2O_3$ 365.19, found 365.90. EA (%): Calcd.: C 72.50 H 6.64 N 7.69; found: C 72.20 H 6.60 N 7.58. IR (cm^{-1}): 3329 (w), 2966 (m), 2926 (w), 2874 (w), 1770 (m), 1706 (s), 1660 (m), 1615 (m), 1530 (m), 1467 (m), 1381 (s), 1355 (s), 1332 (s), 1288 (m), 1225 (m), 1192 (m), 1172 (m), 1157 (m), 1123 (w), 1070 (s), 1014 (m), 988 (m), 961 (w), 927 (w), 888 (m), 817 (m), 791 (m), 716 (s), 660 (m), 627 (m), 575 (m), 560 (m), 530 (s). R_f(hexane/ EtOAc 4:1) = 0.2.

N–(2,4,6–Trimethylbenzyl)benzamide (**10a**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), mesitylene (0.83 mL, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 5 mol%) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (371 mg, 73%). m.p.: 151–152 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.73 (d, J = 8.1 Hz, 2H), 7.48 (t, J = 7.1 Hz, 1H), 7.40 (t, J = 7.5 Hz, 2H), 6.91 (s, 2H), 5.89 (bs, 1H), 4.64 (d, J = 4.4 Hz, 2H), 2.37 (s, 6H), 2.29 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.5, 137.9, 137.7, 136.6, 134.5, 131.6, 130.9, 129.7, 129.4, 128.7, 127.0, 38.9, 21.1, 19.8. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{20}NO$ 254.15, found 254.40. EA (%): Calcd.: C 80.60 H 7.56 N 5.53; found: C 80.72 H 7.65 N 5.13. IR (cm^{-1}): 3296 (m), 1626 (s), 1578 (m), 1516 (s) 1471 (m), 1377 (w), 1269 (w), 1178 (w), 1076 (w), 1022 (w), 906 (w), 854 (m), 802 (m), 771 (w), 692 (s), 660 (w). R_f(hexane/ EtOAc 4:1) = 0.3.

N–(2–Methoxybenzyl)benzamide (**10b**) was synthesized according to TP 1 from benzamide (61 mg, 0.5 mmol), formalin (45 µL, 37 wt% solution in H_2O, 0.6 mmol), anisole (0.22 mL, 2.0 mmol, 4 equiv.) and $Bi(OTf)_3$ (16 mg, 0.1 mmol, 5 mol%) in nitromethane (2 mL) at

100 °C for 24 h. Purification by chromatography (hexane/EtOAc 9:1→4:1) yielded the product as yellow solid (82 mg, 68%, ratio of regioisomers 3:1). m.p.: 110–111 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks are listed only for *para*–regioisomer): δ = 7.75 – 7.71 (m, 2H), 7.47 – 7.30 (m, 3H), 7.24 – 7.22 (m, 2H), 6.92 – 6.81 (m, 2H,), 6.33 (bs, 1H), 4.55 (d, J = 5.5 Hz, 2H), 3.77 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz) (peaks are not assigned to *ortho* and *para*–isomer): δ = 167.4, 137.2, 136.1, 135.7, 134.6, 131.6, 130.1, 129.9, 129.5, 128.7, 128.7, 127.2, 127.1, 127.1, 125.9, 125.6, 44.1, 43.3, 20.6, 19.9, 19.5, 15.1. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{15}H_{16}NO_2$ 242.12, found 242.40. EA (%): Calcd.: C 74.67 H 6.27 N 5.81; found: C 74.44 H 6.26 N 5.63. IR (cm^{-1}): 1300 (w), 3223 (w), 3055 (w), 2924 (w), 2831 (w), 1630 (s), 1546 (w), 1539 (m), 1489 (m), 1460 (c), 1429 (w), 1350 (w), 1296 (m), 1238 (s), 1176 (m), 1109 (m), 1072 (w), 1032 (s), 172 (w), 926 (w), 812 (m), 752 (s), 694 (s), 667 (s). R_f(hexane/ EtOAc 4:1) = 0.2.

N–(3–Chloro–4–methoxybenzyl)benzamide (**10c**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), 2–chloroanisol (0.76 mL, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 5 mol%) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as yellow solid (462 mg, 84%). m.p.: 117–118 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.79 – 7.77 (m, 2H), 7.51 – 7.47 (m, 1H), 7.43 – 7.39 (m, 2H), 7.35 (d, J = 2 Hz, 1H), 7.20 (dd, $J1$ = 2 Hz, $J2$ = 8 Hz, 1H), 6.87 (d, J = 8 Hz, 1H), 6.57 (bs, 1H), 4.54 (d, J = 6 Hz, 2H), 3.87 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.5, 154.6, 134.3, 131.8, 131.6, 129.9, 128.7, 127.5, 127.1, 122.7, 112.3, 56.3, 43.2. MS (ESI) m/z: [M+H] Calcd. for $C_{15}H_{15}ClNO_2$ 276.08, found 276.00 $^{+}$. EA (%): Calcd.: C 65.34 H 5.12 N 5.08; found: C 65.05 H 5.10 N 4.91. IR (cm^{-1}): 3311 (w), 3242 (w), 3059 (w), 3010 (w), 2943 (w), 2927 (w), 2833 (w), 1626 (m), 1574 (w), 1541 (s), 1504 (m), 1462 (w), 1427 (w), 1354 (w), 1282 (s), 1182 (w), 1147 (w), 1063 (s), 1094 (m), 974 (m), 937 (w), 872 (m), 814 (m), 756 (m), 698 (s), 654 (w). R_f(hexane/ EtOAc 4:1) = 0.1.

N–(3–Bromo–4–methoxybenzyl)benzamide (**10d**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), 2–bromoanisole (0.74 mL, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as yellow solid (563 mg, 88%) m.p.: 112–113 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.79 – 7.77 (m, 2H), 7.52 (d, J = 7.5 Hz, 1H), 7.49 – 7.47 (m, 1H), 7.43 – 7.39 (m, 2H), 7.27 – 7.24 (m, 1H), 6.84 (d, J = 6.8 Hz, 1H), 6.58 (bs, 1H), 4.54 (d, J = 4.5 Hz, 2H), 3.87 (s, 3H). ^{13}C–NMR

($CDCl_3$, 101 MHz): δ = 167.5, 155.5, 134.3, 133.0, 132.1, 131.7, 128.7, 128.3, 127.1, 112.2, 111.9, 56.4, 43.1. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{15}H_{15}BrNO_2$ 320.03, found 320.00. EA (%): Calcd.: C 56.27 H 4.41 N 4.37; found: C 56.08 H 4.39 N 4.25. IR (cm^{-1}): 3307 (w), 3240 (w), 3055 (w), 3008 (w), 2964 (w), 2926 (w), 2831 (w), 1626 (m), 1539 (s), 1493 (s), 1460 (w), 1427 (w), 1402 (w), 1352 (w), 1261 (s), 1259 (s), 1180 (w), 1147 (w), 1061 (w), 1024 (m), 1022 (m), 170 (w), 137 (w), 885 (w), 860 (w), 814 (m), 754 (m), 698 (s), 667 (w). R_f(hexane/ EtOAc 4:1) = 0.1.

N–(3–Iodo–4–methoxybenzyl)benzamide (**10e**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), 2–iodoanisole (0.78 mL, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (578 mg, 79%). m.p.: 106–107 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.79 – 7.76 (m, 3H), 7.50 (t, J = 7.3 Hz, 1H), 7.43 (t, J =7.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 1H), 6.78 (d, J = 8.4 Hz, 1H), 6.42 (bs, 1H), 4.54 (d, J = 5.7 Hz, 2H), 3.87 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.4, 157.8, 139.1, 134.4, 132.6, 131.8, 129.5, 128.8, 127.1, 111.1, 86.3, 56.6, 43.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{15}H_{15}INO_2$ 368.01, found 368.40. EA (%): Calcd.: C 49.07 H 3.84 N 3.81; found: C 49.03 H 3.88 N 3.66. IR (cm^{-1}): 3280 (w), 3030 (w), 2927 (w), 2831 (w), 1626 (s), 1578 (w), 1527 (m), 1485 (m), 1460 (m), 1400 (w), 1363 (w), 1288 (m), 1250 (m), 1225 (m), 1178 (w), 1144 (w), 1074 (w), 1047 (m), 1018 (m), 978 (w), 922 (w), 887 (w), 841 (w), 798 (m), 692 (s), 667 (m). R_f(hexanes/ EtOAc 4:1) = 0.1.

N–(5–Chloro–2–methoxybenzyl)benzamide (**10f**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), 4–chloroanisole (0.73 mL, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (459 mg, 83%). m.p.: 138–139 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.77 (d, J = 8.0 Hz, 2H), 7.48 (t, J = 7.0 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.31 (bd, J = 2.1 Hz, 1H), 7.22 (dd, J = 8.7, 2.3 Hz, 1H), 6.81 (d, 1H, J = 8.7 Hz), 6.65 (bs, 1H), 4.60 (d, J = 6.0 Hz, 2H), 3.86 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.3, 156.3, 134.7, 131.6, 129.7, 128.7, 128.6, 128.2, 127.1, 125.8, 111.7, 55.9, 39.5. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{15}H_{15}ClNO_2$ 276.08, found 275.90. EA (%): Calcd.: C 65.34 H 5.12 N 5.08; found: C 65.19 H 5.07 N 4.93. IR (cm^{-1}): 3269 (m), 3055 (w), 1624 (m), 1576 (m), 1543 (m), 1487 (m), 1443 (w), 1423 (w), 1352 (w), 1294 (w), 1254 (w), 1244 (m), 1176 (w), 1174 (w), 1126 (m), 1053 (w), 1049 (w), 1026 (m), 989 (w), 930 (w), 877 (w), 806 (m), 692 (s), 667 (w). R_f(hexane/ EtOAc 4:1) = 0.1.

N–(5–Bromo–2–methoxybenzyl)benzamide (**10g**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), 4–bromoanisole (0.75 mL, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (494 mg, 77%). m.p.: 123–124 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.78 – 7.75 (m, 2H), 7.53 – 7.40 (m, 4H), 7.38 – 7.35 (m, 1H), 6.76 (d, J = 9 Hz, 1H), 6.61 (bs, 1H), 4.61 (d, J = 6 Hz, 2H), 3.86 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 167.3, 156.8, 134.7, 132.6, 131.6, 131.6, 128.7, 128.6, 127.1, 113.1, 112.2, 55.9, 39.5. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{15}H_{15}BrNO_2$ 320.03, found 320.00. EA (%): Calcd.: C 56.27 H 4.41 N 4.37; found: C 56.15 H 4.52 N 4.27. IR (cm^{-1}): 3265 (w), 3055 (w), 1624 (m), 1576 (m), 1541 (m), 1489 (m), 1443 (w), 1421 (w), 1398 (w), 1350 (w), 1292 (w), 1244 (m), 1176 (w), 1174 (w), 1120 (w), 1055 (w), 1051 (w), 1024 (m), 987 (w), 131 (w), 856 (w), 806 (m), 692 (s), 667 (w). R_f(hexanes/ EtOAc 4:1) = 0.2.

N–(5–Iodo–2–methoxybenzyl)benzamide (**10h**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), 4–iodoanisole (1.40 g, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (465 mg, 64%). m.p.: 117–118 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.78 – 7.74 (m, 2H), 7.63 (d, J = 2.3 Hz, 1H), 7.58 – 7.40 (m, 4H), 6.66 (d, J = 8.6 Hz, 1H), 6.59 (bs, 1H), 4.58 (d, J = 5.9 Hz, 2H), 3.86 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 167.3, 157.7, 138.4, 137.8, 134.7, 131.6, 129.0, 128.7, 127.1, 112.9, 83.1, 55.8, 39.4. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{15}H_{15}INO_2$ 368.01, found 368.40. EA (%): Calcd.: C 49.07 H 3.84 N 3.81; found: C 49.18 H 3.89 N 3.69. IR (cm^{-1}): 3267 (w), 3061 (w), 3008 (w), 2947 (w), 2835 (w) 2158 (w), 1992 (w), 1633 (s), 1551 (w), 1539 (s), 1495 (f), 458 (m), 1433 (m), 1360 (w), 1309 (m), 1279 (m), 1263 (m), 1242 (w), 1215 (s), 1118 (m), 1151 (w), 1059 (w), 1045 (m), 1020 (m), 993 (w), 924 (w) 906 (w), 879 (m), 825 (m), 795 (s), 710 (s), 665 (w). R_f(hexanes/ EtOAc 4:1) = 0.1.

N–(3,6–Dimethoxybenzyl)benzamide (**10i**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), 1,4–dimethoxybenzene (1.128 g, 8.0 mmol, 4 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 5 mol%) in nitromethane (4 mL) at 80 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as yellow solid (0.18 g, 42%). m.p.: 101–102 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.76 (d, J = 8 Hz, 2H), 7.48 (t, J = 7 Hz, 1H), 7.41 (t, J = 7 Hz, 2H), 6.94 (d,

J = 2 Hz, 1H), 6.84 – 6.78 (m, 2H), 6.68 (bs, 1H), 4.62 (d, J = 6 Hz, 2H), 3.84 (s, 3H), 3.76 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.1, 153.6, 151.8, 134.7, 131.3, 128.5, 127.2, 126.9, 115.9, 113.3, 111.4, 55.9, 55.8, 40.1. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{16}H_{18}NO_3$ 272.1, found 272.4. EA (%): Calcd.: C 70.83 H 6.32 N 5.16; found: C 70.92 H 6.21 N 5.11. IR (cm^{-1}): 3267 (m), 3062 (w), 3008 (w), 2949 (w), 2833 (w), 2154 (w), 1996 (w), 1952 (w), 1633 (s), 1579 (w), 1539 (s), 1495 (s), 1458 (m), 1431 (m), 1360 (w), 1309 (s), 1279 (m), 1242 (w), 1215 (s), 1180 (m), 1149 (w), 1115 (m), 1059 (w), 1045 (s), 1020 (s), 993 (m), 924 (w), 874 (w), 879 (m), 825 (m), 795 (s), 710 (s), 667 (w). R_f (Hexane/EtOAc 4:1): 0.1.

Ethyl–3–((benzamido)methyl)–4–methoxybenzoate (**10j**) was synthesized according to TP 1 from benzamide (61 mg, 0.5 mmol), paraformaldehyde (19 mg, 0.6 mmol), ethyl–4–methoxybenzoate (0.25 mL, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol) in nitromethane (2 mL) at 100 °C for 24 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colourless solid (135 mg, 87%). m.p.: 127–129 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 8.03 – 7.99 (m, 2H), 7.78 – 7.75 (m, 2H), 7.50 – 7.46 (m, 1H), 7.42 – 7.40 (m, 2H), 6.92 (d, J = 8.5 Hz, 1H), 6.60 (bs, 1H), 4.67 (d, J = 5.9 Hz, 2H), 4.33 (q, J = 7.1 Hz, 2H), 3.94 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.4, 166.4, 161.4, 134.8, 131.5, 131.4, 131.2, 128.7, 127.1, 126.3, 123.2, 110.1, 60.9, 55.9, 39.9, 14.5. MS (ESI) m/z: $[M+Na]^+$ Calcd. for $C_{18}H_{19}NO_4Na$ 336.12, found 336.25. HRMS (MALDI) m/z: $[M+H]^+$ Calcd. for $C_{18}H_{20}NO_4$ 314.1387, found 314.1389. IR (cm^{-1}): 3279 (w), 2978 (w), 1710 (s), 1626 (s), 1611 (m), 1578 (m), 1549 (m), 1504 (m), 1491 (w), 1462 (w), 1446 (w), 1413 (w), 1361 (m), 1314 (s), 1264 (s), 1174 (m), 1125 (s), 1050 (w), 1022 (s), 993 (w), 931 (w), 909 (w), 875 (w), 832 (m), 768 (s), 695 (s), 672 (m), 628 (m), 607 (w), 539 (w), 510 (w).R_f(hexane/ EtOAc 4:1) = 0.1.

N–(4–Methyl–3–pivalamido)benzamide (**10k**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), *N–o–*tolylpivalamide (1.15 g, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (430 mg, 66%). m.p.: 170–171 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.78 (d, J = 7.8 Hz, 3H), 7.49 (t, J = 7.2 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.23 (bs, 1H), 7.18 – 7.16 (m, 2H), 6.45 (bs, 1H), 4.56 (d, J = 5.6 Hz, 2H), 2.23 (s, 3H), 1.34 (s, 9H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 176.7, 167.4, 135.4, 134.9, 134.5, 131.7, 130.3, 129.6, 128.7, 127.1, 126.5, 123.5, 43.9, 39.9, 27.9, 17.8. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{20}H_{25}N_2O_2$ 325.19, found 325.60. HRMS (MALDI) m/z: $[M+H]^+$ Calcd. for $C_{20}H_{25}N_2O_2$ 325.1916, found 325.1914. IR

(cm^{-1}): 3307 (b), 2953 (w), 1643 (s), 1558 (w), 1541 (m), 1506 (s), 1417 (w), 1309 (w), 1221 (w), 1178 (w), 1051 (w), 1005 (w), 984 (w), 980 (w), 930 (w), 849 (w), 802 (m), 737 (w), 694 (s), 667 (w). R_f(hexane/ EtOAc 1:1) = 0.3.

N–(2,5–Dimethylbenzyl)benzamide (**10l**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), *p*–xylene (0.74 mL, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 5 mol%) in nitromethane (4 mL) at 100 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (177 mg, 37%). m.p.: 113–114 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.79 – 7.78 (m, 2H), 7.52 – 7.48 (m, 1H), 7.45 – 7.40 (m, 2H), 7.12 – 7.09 (m, 2H), 7.04 (d, J = 8 Hz, 1H), 6.22 (bs, 1H), 4.61 (d, J = 5 Hz, 2H), 2.34 (s, 3H), 2.32 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.1, 135.8, 135.5, 134.4, 133.4, 131.5, 130.6, 129.6, 129.6, 128.6, 126.9, 42.4, 20.9, 18.6. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{16}H_{18}NO$ 240.1, found 240.4. EA (%): Calcd.: C 80.30 H 7.16 N 5.85; found: C 80.28 H 7.05 N 5.76. IR (cm^{-1}): 2290 (m), 2912 (w), 1626 (s), 1578 (m), 1531 (s), 1460 (w), 1360 (w), 1308 (m), 1298 (w), 1236 (w), 1180 (w), 1147 (w), 1074 (w), 1053 (w), 1028 (w), 1001 (w), 970 (w), 922 (w), 864 (w), 856 (w), 814 (m), 712 (w), 694 (s), 669 (w). R_f (Hexane/EtOAc 4:1) = 0.3.

N–(5–Bromo–2–hydroxybenzyl)benzamide (**10m**) was synthesized according to TP 1 from benzamide (61 mg, 0.5 mmol), paraformaldehyde (19 mg, 0.6 mmol), 4–bromophenol (346 mg, 2.0 mmol, 4 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol) in nitromethane (2 mL) at 80 °C for 24 h. Purification by chromatography (hexane/EtOAc 9:1→4:1) yielded the product as colorless solid (104 mg, 68%). m.p.: 154–156 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 9.67 (bs, 1H), 7.78 – 7.76 (m, 2H), 7.56 – 7.52 (m, 1H), 7.46–7.42 (m, 2H), 7.31 – 7.29 (m, 2H), 6.98 (bs, 1H), 6.85 (d, J = 8.6 Hz, 1H), 4.50 (d, J = 6.6 Hz, 2H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 170.0, 155.4, 133.4, 133.0, 132.7, 132.5, 129.0, 127.4, 126.3, 120.2, 111.5, 40.8. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{14}H_{13}BrNO_2$ 306.01, found 306.05. EA (%): Calcd.: C 54.92 H 3.95 N 4.58: found: C 54.58 H 3.93 N 4.41. IR (cm^{-1}): 3343 (w), 2598 (w), 1682 (w), 1615 (w), 1545 (s), 1481 (s), 1392 (m), 1352 (w), 1310 (m), 1268 (m), 1254 (s), 1222 (m), 1180 (w), 1117 (m), 1081 (w), 1032 (w), 1002 (w), 972 (w), 932 (w), 907 (w), 817 (s), 789 (m), 738 (w), 711 (s), 690 (s), 630 (s), 551 (m), 516 (s), 492 (w). R_f (hexane/ EtOAc 4:1) = 0.1

N–((5–Methylthiophen–2–yl)methyl)benzamide (**10o**) was synthesized according to TP 1 from benzamide (73 mg, 0.6 mmol), formalin (37 µL, 37 wt% solution in H_2O, 0.5 mmol), 2–methylthiophene (0.15 mL, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol,

5 mol%) in nitromethane (2 mL) at 25 °C for 24 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as yellow solid (74 mg, 64%, mixture of regioisomers 12:1). m.p.: 105–107 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks are listed only for major regioisomer): δ = 7.81 – 7.75 (m, 2H), 7.52 – 7.48 (m, 1H), 7.46 – 7.41 (m, 2H), 6.82 (bd, J = 3.3 Hz, 1H), 6.61 – 6.60 (m, 1H), 6.36 (s, 1H), 4.73 (d, J = 5.5 Hz, 2H), 2.46 (s, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.2, 140.2, 138.4, 134.4, 131.7, 128.7, 127.1, 126.3, 125.0, 39.3, 15.5. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{13}H_{14}NOS$ 232.08, found 232.60. EA (%): Calcd.: C 67.50 H 5.66 N 6.06 S 13.86; found: C 67.47 H 5.52 N 5.91 S 14.14. IR (cm^{-1}): 3345 (m), 3060 (w), 2917 (w), 2856 (w), 1630 (s), 1602 (m), 1576 (m), 1538 (s), 1490 (s), 1445 (m), 1424 (m), 1350 (m), 1325 (m), 1294 (s), 1260 (m), 1216 (m), 1190 (m), 1153 (m), 1101 (w), 1075 (m), 1049 (m), 1032 (m), 1003 (w), 976 (m), 930 (w), 866 (m), 808 (m), 797 (s), 742 (m), 711 (s), 686 (s), 662 (m), 600 (s), 556 (s), 499 (m). R_f(hexane/ EtOAc 4:1) = 0.2.

N–(5–Bromothiophen–3–yl)benzamide (**10p**) was synthesized according to TP 1 from benzamide (242 mg, 2.0 mmol), paraformaldehyde (72 mg, 2.4 mmol), 2–bromothiophene (0.6 mL, 6.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol) in nitromethane (4 mL) at 80 °C for 16 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as yellow solid (558 mg, 94%). m.p.: 117–118 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.79 – 7.78 (m, 1H), 7.77 – 7.76 (m, 1H), 7.54 – 7.48 (m, 1H), 7.45 – 7.40 (m, 2H), 6.90 (d, J = 4 Hz, 1H), 6.79 – 6.78 (m, 1H), 6.53 (bs, 1H), 4.71 (d, J = 6 Hz, 2H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.4, 142.8, 134.0, 131.9, 129.7, 128.8, 127.1, 126.7, 112.0, 39.2. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{12}H_{11}BrNOS$ 295.97, found 295.90. HRMS (MALDI) m/z: $[M+H]^+$ Calcd. for $C_{12}H_{11}BrNOS$ 295.9745, found 295.9748.. IR (cm^{-1}): 3278 (w), 3055 (w), 2924 (w), 1626 (m), 1601 (w), 1552 (w), 1531 (s), 1489 (m), 1441 (m), 1417 (m), 1354 (w), 1292 (m), 1255 (e), 1205 (m), 1142 (m), 1051 (w), 1047 (m), 182 (m), 157 (m), 330 (w), 783 (m), 739 (m), 688 (s). R_f(hexane/ EtOAc 4:1) = 0.3.

N–((5–Chlorothiophen–2–yl)methyl)benzamide (**10q**) was synthesized according to TP 1 from benzamide (61 mg, 0.6 mmol), formalin (45 µL, 37 wt% solution in H_2O, 0.6 mmol), 2–chlorothiophene (0.14 mL, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol, 5 mol%) in nitromethane (2 mL) at 40 °C for 24 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (86 mg, 69%). m.p.: 109–110 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz): δ = 7.78 – 7.76 (m, 2H), 7.53 – 7.51 (m, 1H), 7.43 (t, J = 7.5 Hz, 2H), 6.80 (d, J = 3.7 Hz, 1H), 6.76 (d, J = 3.7 Hz, 1H), 6.51 (bs, 1H), 4.70 (d, J = 5.8 Hz, 2H).

^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.4, 139.9, 134.1, 131.9, 129.9, 128.8, 127.1, 125.9, 125.7, 39.3. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{12}H_{11}ClNOS$ 252.02, found 252.50. HRMS (MALDI) m/z: Calcd. for $C_{12}H_{11}ClNOS$ 252.0244 $[M+H]^+$, found 252.0243. IR (cm^{-1}): 3317 (w), 1683 (w), 1629 (s), 1602 (m), 1577 (m), 1550 (s), 1534 (s), 1490 (s), 1453 (m), 1418 (m), 1356 (w), 1296 (m), 1258 (m), 1207 (m), 1189 (w), 1161 (w), 1146 (w), 1057 (w), 1035 (w), 1026 (w), 996 (m), 967 (m), 929 (w), 792 (m), 739 (w), 689 (s), 664 (m), 641 (m), 616 (m), 565 (m), 533 (w), 482 (w). R_f(hexane/ EtOAc 4:1) = 0.2.

N–((1–Tosyl–1H–indol–3–yl)methyl)benzamide (**10r**) was synthesized according to TP 1 from benzamide (61 mg, 0.6 mmol), formalin (45 µL, 37 wt% solution in H_2O, 0.6 mmol), 1–tosyl–1*H*–indole (407 mg, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol) in nitromethane (2 mL) at 40 °C for 24 h. Purification by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (155 mg, 76%, ratio of regioisomers 14:1). m.p.: 157–159 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks only for major isomer listed): δ = 7.99 (d, J = 8.3 Hz, 1H), 7.79 – 7.74 (m, 4H), 7.61 – 7.56 (m, 2H), 7.51 – 7.47 (m, 1H), 7.41 (t, J = 7.5 Hz, 2H), 7.36 – 7.32 (m, 1H), 7.23 (d, J = 8.6 Hz, 3H), 6.29 (bs, 1H), 4.77 (d, J = 5.5 Hz, 2H), 2.33 (d, J = 8.5 Hz, 3H). ^{13}C–NMR ($CDCl_3$, 101 MHz) (peaks are not assigned to regioisomers): δ = 167.5, 145.3, 135.5, 135.4, 134.3, 131.8, 130.1, 129.7, 128.8, 127.1, 127.0, 125.3, 124.6, 123.6, 119.9, 119.4, 113.9, 35.3, 21.7. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{21}N_2O_3S$ 405.13, found 405.70. EA (%): Calcd.: C 68.30 H 4.98 N 6.93 S 7.93; found: C 67.90 H 4.91 N 6.63 S 7.75. IR (cm^{-1}): 1639 (m), 1602 (w), 1578 (w), 1537 (m), 1490 (m), 1447 (m), 1424 (w), 1371 (s), 1327 (w), 1295 (m), 1273 (m), 1252 (m), 1207 (m), 1187 (m), 1172 (s), 1119 (s), 1093 (m), 1047 (m), 1016 (m), 987 (m), 963 (m), 805 (m), 788 (m), 757 (s), 749 (m), 711 (m), 695 (m), 665 (s), 622 (m), 589 (s), 582 (s), 568 (s), 543 (s), 533 (s), 494 (m). R_f(hexane/ EtOAc 4:1) = 0.1.

N–(Benzofuran–3–yl)benzamide (**10s**) was synthesized according to TP 1 from benzamide (61 mg, 0.5 mmol), formalin (45 µL, 37 wt% solution in H_2O , 0.6 mmol), benzofuran (0.16 mL, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (16 mg, 0.025 mmol, 5 mol%) in nitromethane (2 mL) at 40 °C for 24 h. Purification by chromatography (cyclohexane/EtOAc 9:1→4:1) yielded the product as white solid (88 mg, 70%, ratio of regioisomers: 24:1). m.p.: 127–128 °C. ^{1}H–NMR ($CDCl_3$, 400 MHz) (peaks are listed only for major regioisomer): δ = 7.81 (d, J = 8 Hz, 2H), 7.52 – 7.51 (m, 2H), 7.45 – 7.43 (m, 3H), 7.27 – 7.21 (m, 2H), 6.67 (s, 1H), 6.63 (bs, 1H), 4.79 (d, J = 6 Hz, 2H). ^{13}C–NMR ($CDCl_3$, 101 MHz): δ = 167.5, 155.1, 154.0, 134.2, 131.9, 128.8, 128.4, 127.2, 124.4, 123.0, 121.2, 111.3, 104.6, 37.6. MS (ESI) m/z: $[M+H]^+$ Calcd. for

$C_{16}H_{14}NO_2$ 252.10, found 252.40. **HRMS** (MALDI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{14}NO_2$ 252.1019, found 252.1021. IR (cm^{-1}): 3304 (w), 3049 (w), 1626 (m), 1578 (w), 1525 (m), 1489 (m), 1448 (m), 1361 (w), 1279 (m), 254 (w), 1219 (w), 1178 (m), 1076 (w), 1051 (w), 984 (w), 980 (m), 935 (m), 873 (m), 800 (m), 731 (w), 727 (w), 692 (s). R_f (hexane/ EtOAc 4:1) = 0.2.

N,N'–Methylen–bis–benzamide (**11**)

Benzamide (3.00 g, 25 mmol, 2.0 equiv.), paraformaldehyde (0.41 g, 12 mmol, 1.0 equiv.) and H_2SO_4 (1 drop) in toluene (25 mL) were refluxed in a Dean–Stark apparatus. After cooling to 0 °C the mixture was filtrated, the crude residue washed with toluene and dried in high vacuum. The product was obtained as colourless solid, sufficiently pure for further transformations (2.77 g, 91%). ^{1}H–NMR (DMSO, 250 MHz): δ = 9.07 – 9.02 (m, 2H), 7.92 – 7.89 (m, 4H), 7.53 – 7.42 (m, 6H), 4.89 – 4.85 (m, 2H). Analytical data are consistent with literature.[27]

N–Hydroxymethylenbenzamide (**12**)

A 50 mL round bottom flask was charged with benzamide (7.00 g, 46.0 mmol, 1.2 equiv.), K_2CO_3 (0.20 g, 1.5 mmol, 3 mol%) and formalin (4.1 mL, 37 wt% solution in H_2O, 55.0 mmol, 1.0 equiv.) in H_2O (7 mL). The reaction was stirred at 50 °C until everything was disolved. After cooling to r.t. the mixture was filtrated. Purification of the crude residue by recrystallization from ethanol yielded the product as colourless solid, sufficiently pure for further transformations (1.33 g, 19%). ^{1}H–NMR (DMSO, 250 MHz): δ = 9.14 – 9.10 (m, 1H), 7.88 (d, J = 8 Hz, 2H), 7.54 7.44 (m, 3H), 5.66 (bs, 1H), 4.72 – 4.70 (m, 2H). Analytical data are consistent with literature.[41]

N–(2–Methyl–1–propen–1–yl)benzamide (**14**) was isolated during the attempted preparation of *N*–(2–methyl–1–(2,4,6–trimethylbenzyl)propyl)benzamide. A 10 mL flask was charged with benzamide (72 mg, 0.6 mmol), isobutyraldehyde (42 µL, 0.5 mmol), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCE (2 mL). The reaction mixture was stirred at 80 °C for 16 h. After cooling to room temperature the reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by column chromatography (hexane/EtOAc 4:1) afforded **14** (66 mg, 75%) as colourless solid. ^{1}H–NMR ($CDCl_3$, 250 MHz): δ = 7.80 – 7.77 (m, 2H), 7.54 – 7.41 (m, 4H), 6.76 – 6.72 (m, 1H), 1.77 (s, 3H), 1.71 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 164.3, 134.4, 131.8, 128.8, 127.1, 117.5, 116.5, 22.7, 16.8. Analytical data are consistent with literature.[42]

N–(2–Methyl–1–(5–methylfuran–2–yl)propyl)benzamide (**17**)

A 10 mL flask was charged with benzamide (72 mg, 0.6 mmol), isobutyraldehyde (42 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (2 mL). 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) in DCM (2 mL) was added over 2 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 9:1) yielded the product as colourless solid (78 mg, 61%). m.p.: 82–84 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.81 – 7.77 (m, 2H), 7.53 – 7.41 (m, 3H), 6.42 (bd, J = 8.9 Hz, 1H), 6.08 (d, J = 3.0 Hz, 1H), 5.89 – 5.87 (m, 1H), 5.09 – 5.03 (m, 1H), 2.27 (s, 3H), 2.24 – 2.17 (m, 1H), 1.02 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.7 Hz, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.8, 151.9, 151.4, 134.9, 131.6, 128.7, 127.1, 107.8, 106.1, 53.4, 32.6, 19.4, 19.0, 13.7. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{16}H_{20}NO_2$ 258.2, found 258.5. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{16}H_{19}NO_2K$ 296.1048, found 296.1047. IR (cm^{-1}): 3337 (w), 2966 (m), 2923 (m), 1639 (s), 1603 (w), 1580 (m), 1565 (m), 1533 (s), 1492 (m), 1463 (m), 1383 (w), 1361 (m), 1346 (m), 1311 (m), 1269 (m), 1219 (m), 1149 (m), 1111 (w), 1055 (m), 1033 (s), 1018 (m), 1002 (m), 948 (w), 883 (w), 821 (w), 802 (w), 787 (s), 772 (m), 716 (m), 694 (s), 666 (m), 627 (m), 601 (m), 510 (w), 471 (w). R_f (hexane/ EtOAc 4:1): 0.3.

N–(1–(5–Methylfuran–2–yl)–3–phenylpropyl)benzamide (**19a**)

A 10 mL screw–cap vial was charged with benzamide (73mg, 0.6 mmol), 3–phenylpropionaldehyde (69 µL, 0.5 mmol), $Bi(OTf)_3$ (7 mg, 0.025 mmol, 2 mol%) and DCM (2 mL). The mixture was cooled to 0°C and 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) was added. The reaction was stirred at r.t. for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 4:1) yielded the product as yellow oil (130 mg, 81%). ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.75 – 7.72 (m, 2H), 7.51 – 7.39 (m, 3H), 7.31 – 7.26 (m, 2H), 7.21 – 7.19 (m, 3H), 6.40 (bd, J = 8.5 Hz, 1H), 6.14 (d, J = 3.0 Hz, 1H), 5.92 – 5.90 (m, 1H), 5.33 (q., J = 7.3 Hz, 1H), 2.75 – 2.65 (m, 2H), 2.30 – 2.21 (m, 5H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.6, 152.2, 151.8, 141.5, 134.6, 131.6, 128.6, 128.6, 128.5, 127.1, 126.1, 107.6, 106.2, 47.8, 35.8, 32.5, 13.7. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{22}NO_2$ 320.2, found 320.5. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{21}H_{21}NO_2K$ 358.1204, found 358.1207. IR (cm^{-1}): 3322 (w), 1634 (s), 1602 (w), 1577 (m), 1527 (s), 1487

(m), 1454 (m), 1437 (m), 1354 (w), 1327 (m), 1289 (m), 1217 (m), 1200 (w), 1158 (w), 1093 (w), 1074 (m), 1062 (w), 1020 (m), 951 (m), 841 (w), 793 (m), 787 (m), 766 (m), 754 (w), 743 (m), 706 (s), 691 (s), 666 (m), 629 (m), 615 (m), 579 (m), 545 (m), 510 (w), 490 (m), 468 (w). R_f (hexane/ EtOAc 4:1): 0.3.

N–(1–(5–Methylfuran–2–yl)–2–phenylpropyl)benzamide (**19b**)

A 10 mL flask was charged with benzamide (72 mg, 0.6 mmol), 2–phenylpropionaldehyde (68 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (2 mL). 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) in DCM (2 mL) was added over 1 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 9:1) yielded the product as yellow solid (85 mg, 53%, ratio of diastereomers: 7:1). m.p.: 132–134 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz) (peaks are listed only for major diasteromer): δ = 7.79 – 7.75 (m, 2H), 7.51 – 7.41 (m, 3H), 7.27 – 7.19 (m, 3H), 7.10 – 7.07 (m, 2H), 6.47 (bd, J = 9.2 Hz, 1H), 5.85 (d, J = 3.1 Hz, 1H), 5.78 – 5.77 (m, 1H), 5.45 (q, J = 9.2, 7.7 Hz, 1H), 3.34 (quint., J = 7.2 Hz, 1H), 2.20 (s, 3H), 1.42 (d, J = 7.1 Hz, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz) (peaks are listed only for major diastereomer): δ = 166.6, 151.3, 150.6, 142.7, 134.7, 131.7, 128.7, 128.2, 128.7, 127.1, 126.8, 108.7, 106.1, 53.1, 44.2, 18.2, 13.6. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{22}NO_2$ 320.2, found 320.6. HRMS (MALDI) m/z: $[M+Na]^+$ Calcd. for $C_{21}H_{21}NO_2Na$ 342.1465, found 342.1465. IR (cm^{-1}): 3300 (w), 3061 (w), 3029 (w), 2970 (w), 2923 (w), 1635 (s), 1602 (w), 1579 (w), 1530 (m), 1489 (m), 1453 (m), 1375 (w), 1330 (m), 1288 (w), 1220 (w), 1183 (w), 1144 (w), 1075 (w), 1050 (w), 1020 (m), 1000 (w), 965 (w), 950 (w), 910 (w), 866 (w), 784 (m), 762 (m), 698 (s), 666 (m), 616 (w), 551 (w). R_f (hexane/ EtOAc 4:1): 0.4.

N–(1–(5–Methylfuran–2–yl)–2–phenylethyl)benzamide (**19c**)

A 10 mL flask was charged with benzamide (72 mg, 0.6 mmol), 2–phenylacetaldehyde (59 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (2 mL). 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) in DCM (2 mL) was added over 2 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 9:1) yielded the product

as colourless solid (68 mg, 45%). m.p.: 130–132 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.73 – 7.70 (m, 2H), 7.50 – 7.38 (m, 3H), 7.28 – 7.18 (m, 3H), 7.14 – 7.11 (m, 2H), 6.37 (bd, J = 8.3 Hz, 1H), 5.96 (d, J = 3.1 Hz, 1H), 5.86 – 5.85 (m, 1H), 5.51 (q, J = 7.8 Hz, 1H), 3.31 – 3.17 (m, 2H), 2.30 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.6, 151.7, 151.5, 137.3, 134.6, 131.7, 129.5, 128.7, 128.5, 127.1, 126.8, 107.9, 106.3, 49.2, 40.4, 13.8. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{20}H_{20}NO_2$ 306.15, found 306.00. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{20}H_{19}NO_2K$ 344.1047, found 344.1047. IR (cm^{-1}): 3300 (w), 3062 (w), 1637 (s), 1603 (w), 1579 (m), 1533 (s), 1490 (s), 1454 (w), 1296 (w), 1219 (w), 1081 (w), 1038 (w), 1026 (w), 787 (w), 697 (s). R_f(hexane/ EtOAc 4:1): 0.3.

N–(2–(Benzyloxy)–1–(5–methylfuran–2–yl)ethyl)benzamide (**19d**)

A 10 mL flask was charged with benzamide (72 mg, 0.6 mmol), benzyloxyacetaldehyde (72 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (4 mL). 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) in DCM (2 mL) was added over 2 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 9:1) yielded the product as yellow oil (129 mg, 77%). ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.77 – 7.74 (m, 2H), 7.46 – 7.36 (m, 3H), 7.29 – 7.22 (m, 5H), 6.70 (bd, J = 8.2 Hz, 1H), 6.15 (d, J = 3.1 Hz, 1H), 5.89 – 5.88 (m, 1H), 5.49 – 5.43 (m, 1H), 4.53 (d, J = 2.4 Hz, 2H), 3.91 – 3.86 (m, 1H), 3.81 – 3.76 (m, 1H), 2.24 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.8, 151.7, 150.6, 138.0, 134.4, 131.7, 128.6, 128.5, 127.8, 127.8, 127.2, 108.0, 106.4, 73.2, 70.6, 47.7, 13.7. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{22}NO_3$ 336.2, found 336.3. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{21}H_{21}NO_3K$ 374.1153, found 374.1156. IR (cm^{-1}): 3321 (w), 3063 (w), 3031 (w), 2923 (w), 2866 (w), 1722 (m), 1642 (s), 1602 (m), 1579 (m), 1521 (s), 1486 (m), 1453 (m), 1362 (m), 1270 (m), 1248 (m), 1208 (m), 1177 (m), 1158 (m), 1098 (s), 1072 (s), 1026 (s), 1001 (m), 929 (m), 800 (m), 737 (m), 711 (s), 695 (s), 609 (m), 571 (m). R_f(hexane/ EtOAc 4:1): 0.2.

N–(1–(5–Methylfuran–2–yl)propyl)benzamide (**19e**)

A 10 mL flask was charged with benzamide (72 mg, 0.6 mmol), propanal (37 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (4 mL). 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) in DCM (2 mL) was added over 2 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 22 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with

additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 9:1) yielded the product as yellow oil (65 mg, 53%). ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.80 – 7.76 (m, 2H), 7.52 – 7.38 (m, 3H), 6.38 (bd, J = 8.3 Hz, 1H), 6.11 (d, J = 3.0 Hz, 1H), 5.89 – 5.88 (m, 1H), 5.16 (q, J = 7.4 Hz, 1H), 2.27 (s, 3H), 1.98 – 1.87 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.7, 152.4, 151.7, 134.8, 131.6, 128.7, 127.1, 107.8, 106.2, 49.3, 27.4, 13.7, 10.6. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{15}H_{18}NO_2$ 244.13, found 244.00. HRMS (MALDI) m/z: $[M-H]^+$ Calcd. for $C_{15}H_{16}NO_2$ 242.1181, found 242.1177. IR (cm^{-1}): 3311 (w), 2968 (w), 2935 (w), 2876 (w), 1726 (w), 1635 (s), 1602 (w), 1578 (m), 1531 (s), 1489 (m), 1458 (w), 1447 (w), 1385 (w), 1329 (m), 1297 (m), 1244 (w), 1216 (w), 1186 (w), 1153 (w), 1125 (w), 1103 (w), 1074 (w), 1021 (m), 1000 (w), 949 (w), 931 (w), 855 (w), 785 (m), 768 (w), 710 (m), 691 (s), 662 (m), 615 (m), 571 (w), 550 (w). R_f (hexane/ EtOAc 4:1): 0.4.). Analytical data are consistent with literature.[43]

N–(2–Methyl–1–(5–methylfuran–2–yl)butyl)benzamide (**19f**)

A 10 mL flask was charged with benzamide (72 mg, 0.6 mmol), 2–methylbutyraldehyde (56 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (4 mL). 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) in DCM (2 mL) was added over 2 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 9:1) yielded the product as yellow oil (98 mg, 72%, ratio of diastereomers 2:1). ^{1}H–NMR ($CDCl_3$, 300 MHz) (peaks are not assigned to diastereomers): δ = 7.80 – 7.77 (m, 2H), 7.53 – 7.40 (m, 3H), 6.46 – 6.37 (m, 1H), 6.07 (t, J = 3.5 Hz, 1H), 5.89 – 5.87 (m, 1H), 5.23 – 5.10 (m, 1H), 2.27 (s, 3H), 2.02 – 1.93 (m, 1H), 1.59 – 1.40 (m, 1H), 1.22 – 1.11 (m, 1H), 1.00 – 0.89 (m, 6H). ^{13}C–NMR ($CDCl_3$, 75 MHz) (peaks are not assigned to diastereomers): δ = 166.8, 166.7, 152.2, 151.8, 151.4, 134.9, 131.6, 128.7, 128.7, 127.1, 107.9, 107.5, 106.1, 52.3, 52.0, 38.9, 26.3, 25.8, 15.8, 15.3, 13.7, 11.7, 11.6. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{22}NO_2$ 272.2, found 272.4. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{17}H_{21}NO_2K$ 310.1204, found 310.1204. IR (cm^{-1}): 3300 (w), 3061 (w), 2963 (w), 2925 (w), 2876 (w), 1635 (s), 1603 (w), 1579 (m), 1529 (s), 1488 (m), 1462 (m), 1381 (w), 1328 (m), 1287 (m), 1261 (m), 1220 (m), 1187 (w), 1142 (w), 1075 (w), 1020 (m), 1001 (w), 964 (w), 951 (w), 911 (w), 877 (w), 783 (s), 731 (m), 709 (s), 692 (s), 666 (m), 616 (m), 573 (m), 521 (w). R_f (hexane/ EtOAc 4:1): 0.4.

N–(3–Methyl–1–(5–methylfuran–2–yl)butyl)benzamide (**19g**)

A 10 mL flask was charged with benzamide (72 mg, 0.6 mmol), isovaleraldehyde (55 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (4 mL). 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) in DCM (2 mL) was added over 2 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 9:1 → 4:1) yielded the product as colourless solid (90 mg, 66%). m.p.: 111–113 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.79 – 7.76 (m, 2H), 7.51 – 7.38 (m, 3H), 6.31 (bd, J = 8.5 Hz, 1H), 6.11 (d, J = 3.0 Hz, 1H), 5.88 – 5.87 (m, 1H), 5.34 (q, J = 16.2, 7.8 Hz, 1H), 2.26 (s, 3H), 1.82 – 1.75 (m, 2H), 1.68 – 1.54 (m, 1H), 1.00 – 0.94 (m, 6H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.5, 152.9, 151.6, 134.7, 131.6, 128.7, 127.1, 107.1, 106.2, 46.2, 43.4, 25.2, 22.7, 22.7, 13.7. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{22}NO_2$ 272.2, found 272.8. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{17}H_{21}NO_2K$ 310.1204, found 310.1205. IR (cm^{-1}): 3300 (w), 3062 (w), 2955 (w), 2925 (w), 2869 (w), 1634 (s), 1603 (w), 1579 (m), 1532 (s), 1490 (m), 1469 (m), 1448 (w), 1385 (w), 1367 (w), 1331 (m), 1289 (m), 1220 (m), 1187 (w), 1148 (w), 1076 (w), 1037 (w), 1021 (m), 1001 (w), 953 (w), 937 (w), 869 (w), 782 (s), 693 (s), 666 (m), 647 (m), 616 (m), 555 (w). R_f(hexane/ EtOAc 4:1): 0.5.

N–(1–(5–Methylfuran–2–yl)–3–phenylpropyl)acrylamide (**20a**)

A 10 mL flask was charged with acrylamide (76 mg, 1.0 mmol), 3–phenylpropionaldehyde (69 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (2 mL). 2–methylfuran (59 µL, 0.6 mmol, 1.2 equiv.) in DCM (2 mL) was added over 2 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 4:1) yielded the product as colourless solid (78 mg, 59%). m.p.: 76–78 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.29 – 7.24 (m, 2H), 7.19 – 7.15 (m, 3H), 6.28 (dd, J = 17.0, 1.5 Hz, 1H), 6.11 – 6.02 (m, 2H), 5.95 (bd, J = 8.6 Hz, 1H), 5.88 – 5.87 (m, 1H), 5.63 (dd, J = 10.2, 1.5 Hz, 1H), 5.17 (q, J = 7.4 Hz, 1H), 2.68 – 2.57 (m, 2H), 2.26 (s, 3H), 2.20 – 2.10 (m, 2H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 164.7, 152.0, 151.8, 141.5, 130.9, 128.5, 128.5, 126.9, 126.1, 107.6, 106.2, 47.4, 35.8, 32.4, 13.7. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{20}NO_2$ 270.2, found 270.5. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{17}H_{19}NO_2K$ 308.1047, found 308.1049. IR (cm^{-1}): 3267 (w), 3062

(w), 3027 (w), 2923 (w), 2861 (w), 1655 (s), 1625 (m), 1535(s), 1496 (m), 1454 (m), 1407 (m), 1384 (w), 1314 (w), 1278 (w), 1239 (m), 1219 (m), 1066 (w), 1020 (m), 984(m), 957 (m), 846 (w), 785 (m), 748 (m), 698 (s), 567 (w), 495 (m). R_f(hexane/ EtOAc 7:3): 0.3.

2–Chloro–N–(1–(5–methylfuran–2–yl)–3–phenylpropyl)acetamide (**20b**)

A 10 mL flask was charged with 2–chloroacetamide (91 mg, 1.0 mmol), 3–phenylpropionaldehyde (69 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (2 mL). 2–methylfuran (0.05 mL, 1.5 mmol, 3.0 equiv.) in DCM (2 mL) was added over 2 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 9:1) yielded the product as yellow oil (46 mg, 32%). ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.31 – 7.28 (m, 2H), 7.21 – 7.16 (m, 3H), 6.76 (bd, J = 8.5 Hz, 1H), 6.10 (d, J = 3.1 Hz, 1H), 5.91 – 5.90 (m, 1H), 5.09 (quart., J = 7.4 Hz, 1H), 4.04 (s, 2H), 2.66 – 2.60 (m, 2H), 2.28 (s, 3H), 2.23 – 2.12 (m, 2H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 165.1, 152.1, 151.4, 141.2, 128.6, 128.5, 126.2, 107.8, 106.2, 47.7, 42.8, 35.5, 32.4, 13.7. MS (ESI) m/z: $[M+Na]^+$ Calcd. for $C_{16}H_{18}ClNO_2Na$ 314.1, found 314.3. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{16}H_{18}ClNO_2K$ 330.0658, found 330.0658. IR (cm^{-1}): 3280 w), 3062 (w), 3027 (w), 2923 (w), 2863 (w), 2076 (w), 1657 (s), 1603 (w), 1527 (m), 1496 (m), 1454 (m), 1410 (w), 1384 (w), 1334 (w), 1219 (m), 1176 (w), 1154 (w), 1055 (m), 1033 (m), 1020 (m), 938 (w), 783 (s), 749 (m), 698 (s), 564 (m), 485 (m). R_f(hexane/ EtOAc 4:1): 0.4.

Ethyl–(1–(5–methylfuran–2–yl)–3–phenylpropyl)carbamate (**20c**)

A 10 mL screw–cap vial was charged with urethane (45 mg, 0.6 mmol), 3–phenylpropionaldehyde (69 µL, 0.5 mmol), $Bi(OTf)_3$ (7 mg, 0.025 mmol, 2 mol%) and DCM (2 mL). The mixture was cooled to 0°C and 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) was added. The reaction was stirred at r.t. for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 12:1 → 9:1 → 4:1) yielded the product as yellow oil (68 mg, 47%). ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.28 – 7.24 (m, 2H), 7.18 – 7.15 (m, 3H), 6.04 (bd, J = 2.8 Hz, 1H), 5.87 – 5.85 (m, 1H), 5.05 – 4.81 (m, 1H), 4.81 – 4.66 (m, 1H), 4.11 (q, J = 7.1 Hz, 2H), 2.67 – 2.56 (m, 2H), 2.24 (s, 3H), 2.12 – 2.03 (m, 2H), 1.22 (t, J = 7.1 Hz, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 156.7, 152.7, 151.7,

141.5, 128.5, 126.1, 107.1, 106.1, 61.1, 49.1, 36.2, 32.3, 14.7, 13.7. MS (ESI) m/z: $[M+Na]^+$ Calcd. for $C_{17}H_{21}NO_3Na$ 310.1, found 310.3. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{17}H_{21}NO_3K$ 326.1153, found 326.1154. IR (cm^{-1}): 3319 (w), 3062 (w), 3027 (w), 2981 (w), 2924 (w), 2863 (w), 1693 (s), 1604 (w), 1514 (m), 1497 (m), 1454 (m), 1376 (w), 1329 (m), 1240 (s), 1219 (s), 1172 (m), 1133 (w), 1047 (s), 1033 (m), 1020 (s), 960 (w), 909 (w), 875 (w), 845 (w), 779 (s), 749 (m), 699 (s), 558 (m), 505 (m). R_f(hexane/ EtOAc 4:1): 0.6.

Benzyl–(1–(5–methylfuran–2–yl)–3–phenylpropyl)carbamate (**20d**)

A 10 mL screw–cap vial was charged with benzyl carbamate (76 mg, 0.6 mmol), 3–phenylpropionaldehyde (69 µL, 0.5 mmol), $Bi(OTf)_3$ (7 mg, 0.025 mmol, 2 mol%) and DCM (2 mL). The mixture was cooled to 0°C and 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) was added. The reaction was stirred at r.t. for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 12:1 → 9:1 → 4:1) yielded the product as colourless solid (79 mg, 45%). m.p.: 67-69 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.37 – 7.15 (m, 10H), 6.06 (d, J = 3.0 Hz, 1H), 5.89 – 5.87 (m, 1H), 5.16 – 5.01 (m, 3H), 4.83 – 4.78 (m, 1H), 2.67 – 2.60 (m, 2H), 2.26 (s, 3H), 2.17 – 2.07 (m, 2H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 155.8, 152.4, 151.8, 141.5, 136.6, 128.7, 128.6, 128.5, 128.3, 126.1, 107.2, 106.1, 67.0, 49.3, 36.1, 32.4, 13.7. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{22}H_{24}NO_3$ 350.18, found 350.00. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{22}H_{23}NO_3K$ 388.1310, found 388.1317. IR (cm^{-1}): 3265 (w), 1683 (s), 1585 (w), 1539 (s), 1497 (m), 1454 (m), 1441 (m), 1386 (w), 1358 (w), 1324 (m), 1289 (s), 1257 (s), 1242 (s), 1218 (s), 1197 (m), 1155 (m), 1138 (m), 1090 (m), 1041 (s), 1019 (s), 995 (m), 967 (m), 943 (m), 931 (m), 911 (m), 779 (s), 746 (s), 724 (m), 697 (s), 621 (m), 589 (m), 578 (m), 512 (m), 485 (m), 459 (s). R_f(hexane/ EtOAc 4:1): 0.3.

tert–Butyl–(1–(5–methylfuran–2–yl)–3–phenylpropyl)carbamate (**20e**)

A 10 mL flask was charged with *tert*–butylcarbamate (70 mg, 0.6 mmol), 3–phenylpropionaldehyde (69 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (2 mL). 2–Methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) in DCM (2 mL) was added over 1 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 9:1)

yielded the product as yellow oil (120 mg, 76%). ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.30 – 7.16 (m, 5H), 6.04 (d, J = 3.0 Hz, 1H), 5.88 – 5.87 (m, 1H), 4.76 (d, J = 18.4 Hz, 3H), 2.67 – 2.61 (m, 2H), 2.26 (s, 3H), 2.14 – 2.03 (m, 2H), 1.45 (s, 9H). ^{13}C–NMR ($CDCl_3$, 75 MHz) δ = 155.3, 153.0, 151.6, 141.7, 128.6, 128.5, 126.0, 106.9, 106.1, 48.8, 36.4, 32.4, 28.5, 28.5, 13.7. MS (ESI) m/z: $[M+Na]^+$ Calcd. for $C_{19}H_{25}NO_3Na$ 338.2, found 338.4. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{19}H_{25}NO_3K$ 354.1472, found 354,1476. IR (cm^{-1}): 3347 (w), 3028 (w), 2979 (w), 2932 (w), 1697 (s), 1603 (m), 1497 (m), 1454 (m), 1392 (m), 1367 (s), 1248 (s), 1153 (s), 1047 (m), 1024 (s), 856 (m), 749 (s), 699 (s), 546 (m), 493 (m). R_f (hexane/ EtOAc 4:1): 0.6.

tert–Butyl–((2S)–3–methyl–1–((1–(5–methylfuran–2–yl)–3–phenylpropyl)amino)–1–oxobutan–2–yl)carbamate (**22**)

A 10 mL flask was charged with (S)–*tert*–Butyl–(1–amino–3–methyl–1–oxobutan–2–yl)carbamate (130 mg, 0.6 mmol), 3–phenylpropionaldehyde (69 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (2 mL). 2–methylfuran (0.14 mL, 1.5 mmol, 3.0 equiv.) in DCM (2 mL) was added over 2 h via syringe pump to the solution. The reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 9:1) yielded the product as colourless solid (128 mg, 62%, ratio of diastereomers 2:1). m.p.: 85–87 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.30 – 7.15 (m, 5H), 6.23 – 6.15 (m, 1H), 6.06 – 6.04 (m, 1H), 5.87 – 5.86 (m, 1H), 5.10 – 5.04 (m, 2H), 3.91 – 3.81 (m, 1H), 2.65 – 2.58 (m, 2H), 2.26 – 2.24 (m, 3H), 2.17 – 2.08 (m, 2H), 1.43 (s, 9H), 0.99 – 0.89 (m, 6H). ^{13}C–NMR ($CDCl_3$, 75 MHz) (peaks are not assigned to diastereomers): δ = 170.8, 156.0, 152.0, 151.8, 141.4, 128.6, 128.5, 126.1, 126.1, 107.4, 106.2, 106.1, 80.0, 60.6, 47.3, 47.2, 35.8, 35.6, 32.4, 30.9, 28.4, 19.5, 19.3, 17.9, 13.7, 13.6. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{24}H_{35}N_2O_4$ 415.26, found 415.15. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{24}H_{34}N_2O_4K$ 453.2150, found 453.2142. IR (cm^{-1}): 3681 (w), 3301 (w), 2966 (m), 2924 (m), 2872 (w), 2845 (w), 2248 (w), 1683 (m), 1649 (s), 1604 (w), 1517 (m), 1497 (m), 1454 (m), 1391 (m), 1366 (m), 1298 (m), 1246 (m), 1167 (s), 1053 (m), 1033 (m), 1018 (m), 878 (w), 850 (w), 784 (m), 731 (s), 698 (s), 647 (m), 566 (w), 517 (m), 493 (m), 462 (m). R_f (hexane/ EtOAc 4:1): 0.4.

N–(1–(5–Methylthiophen–2–yl)–3–phenylpropyl)benzamide (**23a**)

A 10 mL screw–cap vial was charged with benzamide (73mg, 0.6 mmol), 3–phenylpropionaldehyde (69 µL, 0.5 mmol), 2–methylthiophene (0.15 mL, 1.5 mmol, 3.0 equiv.), $Bi(OTf)_3$ (16 mg, 0.025 mmol, 5 mol%) and DCM (6 mL). The reaction was stirred at 35 °C for 16 h. After cooling to room temperature the reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 4:1) yielded the product as colourless solid (102 mg, 61%). m.p.: 152–154 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.70 (d, J = 7.7 Hz, 2H), 7.52 – 7.39 (m, J = 14.7, 7.3 Hz, 3H), 7.31 – 7.16 (m, 5H), 6.82 (d, J = 3.3 Hz, 1H), 6.62 (d, J = 3.0 Hz, 1H), 6.23 (bd, J = 8.2 Hz, 1H), 5.46 (q, J = 7.4 Hz, 1H), 2.75 (t, J = 7.9 Hz, 2H), 2.46 (s, 3H), 2.40 – 2.25 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 166.6, 143.2, 141.5, 139.2, 134.5, 131.7, 128.7, 128.7, 128.6, 127.1, 126.2, 125.1, 124.8, 49.7, 38.3, 32.7, 15.5. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{22}NOS$ 336.1, found 336.4. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{21}H_{21}NOSK$ 374.0975, found 374.0975. IR (cm^{-1}): 3288 (w), 3061 (w), 3027 (w), 2920 (w), 2858 (w), 2244 (w), 1633 (s), 1602 (m), 1579 (m), 1530 (s), 1489 (s), 1453 (m), 1327 (m), 1288 (m), 1229 (m), 1184 (w), 1158 (w), 1075 (m), 1044 (w), 1029 (m), 1001 (w), 908 (m), 869 (w), 844 (w), 798 (m), 730 (s), 694 (s), 647 (m), 616 (m), 531 (m), 492 (m). R_f(hexane/ EtOAc 4:1) = 0.5.

N–(1–(2,4–Dimethoxyphenyl)–3–phenylpropyl)–benzamide (**23c**)

A 10 mL screw–cap vial was charged with benzamide (73 mg, 0.6 mmol), 3–phenylpropionaldehyde (69 µL, 0.5 mmol) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCM (2 mL)). The solution was stirred at 25 °C for 5 min. and cooled to 0 °C. Then 1,3–dimethoxybenzene (0.20 mL, 1.5 mmol, 3.0 equiv.) was added. The mixture was stirred at 25 °C for 16h. The reaction mixture was diluted with EtOAc and filtered over a short plug of celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by chromatography (hexane/EtOAc 4:1) yielded the product as colorless solid (109 mg, 58%). m.p.: 125–127 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.73 – 7.69 (m, 2H), 7.45 – 7.36 (m, 3H), 7.27 – 7.13 (m, 7H), 6.49 – 6.42 (m, 2H), 5.30 (q, J = 7.5 Hz, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 2.72 – 2.51 (m, 2H), 2.34 – 2.10 (m, 2H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.3, 160.4, 158.4, 142.0, 135.2, 131.3, 130.1, 128.6, 128.5, 128.4, 127.0, 125.9, 122.0, 104.3, 99.6, 55.6, 55.5, 52.6, 37.1, 33.1. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{24}H_{26}NO_3$ 376.19, found 376.33. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{24}H_{25}NO_3K$ 414.1466, found 414.1462. IR (cm^{-1}): 3315 (w), 2999 (w), 2835 (w), 1634 (s), 1616 (m), 1591 (m), 1578 (w), 1527 (s), 1505 (s), 1448 (m), 1419

(m), 1361 (m), 1299 (m), 1260 (s), 1209 (s), 1175 (m), 1157 (s), 1126 (s), 1080 (m), 1037 (s), 922 (m), 871 (w), 819 (s), 803 (m), 786 (m), 725 (s), 692 (s), 680 (s), 633 (m), 546 (m), 508 (m), 475 (m). R_f(hexane/ EtOAc 4:1): 0.2. Analytical data are consistent with literature.[43]

N–(Mesityl(phenyl)methyl)benzamide (**25**) was synthesized according to TP 2 from benzamide (121 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), mesitylene (0.38 mL, 2.7 mmol, 2.7 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (235 mg, 71%). m.p.: 75–77 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.84 – 7.81 (m, 2H), 7.53 – 7.40 (m, 3H), 7.29 – 7.19 (m, 3H), 7.17 – 7.14 (m, 2H), 7.00 (bd, J = 8.6 Hz, 1H), 6.89 – 6.85 (m, 3H), 2.31 (s, 6H), 2.28 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.8, 141.2, 137.4, 136.9, 134.8, 134.5, 131.8, 130.3, 128.8, 128.7, 127.1, 126.9, 126.1, 52.2, 21.1, 21.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{24}NO$ 330.19, found 330.32. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{23}H_{23}NOK$ 368.1411, found 368.1410. IR (cm^{-1}): 2918 (w), 1640 (m), 1600 (w), 1579 (w), 1513 (s), 1482 (s), 1376 (w), 1344 (w), 1272 (m), 1192 (w), 1127 (w), 1028 (w), 906 (w), 860 (w), 803 (w), 789 (w), 727 (s), 707 (s), 697 (m), 687 (m), 663 (w), 650 (w), 620 (w), 592 (m), 533 (m). R_f (hexane/ EtOAc 4:1): 0.5. Analytical data are consistent with literature.[12]

N–((2,4–Dimethylphenyl)(phenyl)methyl)benzamide (**26**) was synthesized according to TP 2 benzamide (145 mg, 1.2 mmol), benzaldehyde (99 µL, 1.2 mmol), *m*–xylene (0.37 mL, 3.0 mmol, 3.0 equiv.), $Bi(OTf)_3$ (33 mg, 0.05 mmol, 5 mol%) and TfOH (4 µL, 0.05 mmol, 5 mol%) in DCE (4 mL) at 150 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (239 mg, 76%). m.p.: 154–156 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.83 – 7.80 (m, J = 6.9, 1.6 Hz, 2H), 7.54 – 7.41 (m, 3H), 7.33 – 7.25 (m, 5H), 7.06 – 6.86 (m, 3H), 6.64 – 6.46 (m, 2H), 2.33 (s, 3H), 2.31 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.4, 141.3, 137.4, 136.7, 136.5, 134.4, 131.9, 131.8, 128.8, 128.8, 127.6, 127.5, 127.2, 127.0, 127.0, 54.4, 21.1, 19.6. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{22}H_{22}NO$ 316.17, found 316.32. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{22}H_{21}NOK$ 354.1255, found 354.1251. IR (cm^{-1}): 3344 (w), 2919 (w), 1628 (s), 1576 (m), 1524 (s), 1498 (m), 1486 (s), 1379 (w), 1360 (m), 1303 (m), 1278 (m), 1237 (m), 1211 (w), 1135 (w), 1075 (m), 1053 (w), 1030 (m), 978 (w), 930 (w), 853 (w), 819 (s), 805 (m), 738 (s), 713 (s), 702 (s), 689 (s), 663 (m), 646 (m), 620 (m), 586 (s), 563 (m), 542 (m). R_f (hexane/ EtOAc 4:1): 0.5.

N–((3–Chlorophenyl)(mesityl)methyl)benzamide (**28a**) was synthesized according to TP 2 from benzamide (121 mg, 1.0 mmol), 3–chlorobenzaldehyde (0.14 mL, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (196 mg, 54%). m.p.: 130–132 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.85 – 7.82 (m, 2H), 7.54 – 7.44 (m, 3H), 7.26 – 7.16 (m, 3H), 7.08 – 7.02 (m, 1H), 6.97 (bd, J = 8.5 Hz, 1H), 6.91 (s, 2H), 6.82 (bd, J = 8.6 Hz, 1H), 2.31 (s, 9H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 167.0, 143.8, 137.8, 136.8, 134.8, 134.3, 134.2, 132.0, 130.5, 130.0, 128.9, 127.2, 127.1, 126.2, 124.3, 51.8, 21.1, 21.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}ClNO$ 364.15, found 364.28. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{23}H_{22}ClNOK$ 402.1022, found 402.1024. IR (cm^{-1}): 1640 (s), 1600 (w), 1580 (m), 1570 (m), 1512 (s), 1481 (s), 1443 (m), 1423 (m), 1379 (w), 1336 (m), 1272 (m), 1236 (w), 1207 (w), 1190 (m), 1146 (w), 1128 (w), 1099 (w), 1073 (w), 1055 (m), 1033 (m), 1001 (w), 893 (w), 861 (m), 795 (w), 762 (s), 746 (m), 713 (s), 703 (m), 685 (s), 665 (w), 650 (m), 595 (s), 551 (m), 523 (m), 486 (w). R_f(hexane/ EtOAc 4:1): 0.6.

N–((3–Bromophenyl)(mesityl)methyl)benzamide (**28b**) was synthesized according to TP 2 from benzamide (121 mg, 1.0 mmol), 3–bromobenzaldehyde (0.14 mL, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (222 mg, 54%). m.p.: 139–141 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.88 – 7.78 (m, 2H), 7.57 – 7.40 (m, 3H), 7.42 – 7.33 (m, 1H), 7.32 – 7.30 (m, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.12 – 7.05 (m, 1H), 6.99 – 6.96 (m, 1H), 6.91 (s, 2H), 6.79 (bd, J = 8.6 Hz, 1H), 2.30 (s, 9H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 167.0, 144.1, 137.8, 136.8, 134.3, 134.2, 132.0, 130.5, 130.3, 130.2, 129.1, 128.9, 127.2, 124.9, 123.1, 51.8, 21.1, 21.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}BrNO$ 408.10, found 408.68. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{23}H_{22}BrNOK$ 446.0516, found 446.0504. IR (cm^{-1}): 2967 (w), 1640 (s), 1580 (m), 1512 (s), 1481 (s), 1272 (m), 1055 (m), 1033 (s), 861 (m), 760 (s), 709 (s), 687 (s), 675 (m), 595 (s), 548 (m). R_f(hexane/ EtOAc 4:1): 0.5.

N–((4–Chlorophenyl)(mesityl)methyl)benzamide (**28c**) was synthesized according to TP 2 from benzamide (121 mg, 1.0 mmol), 4–chlorobenzaldehyde (172 mg, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (261 mg, 72%). m.p.: 62–64 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ =

7.83 – 7.81 (m, 2H), 7.56 – 7.43 (m, 3H), 7.28 – 7.26 (m, 1H), 7.25 – 7.24 (m, 1H), 7.11 – 7.07 (m, 2H), 6.96 – 6.90 (m, 3H), 6.79 (bd, J = 8.3 Hz, 1H), 2.29 (s, 9H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.9, 140.0, 137.8, 136.8, 134.4, 132.8, 132.0, 130.5, 128.9, 128.8, 127.6, 127.1, 51.8, 21.1, 21.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}ClNO$ 364.15, found 364.28. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{23}H_{22}ClNOK$ 402.1022, found 402.1017. IR (cm^{-1}): 3313 (w), 2921 (w), 1638 (m), 1579 (w), 1508 (m), 1483 (s), 1378 (w), 1343 (w), 1311 (m), 1178 (w), 1150 (w), 1091 (m), 1058 (m), 1033 (m), 1013 (m), 909 (w), 850 (m), 824 (m), 799 (m), 768 (m), 709 (s), 691 (s), 658 (m), 601 (m), 577 (m), 562 (m), 532 (m), 499 (m). R_f (hexane/ EtOAc 4:1): 0.6.

N–((4–Fluorophenyl)(mesityl)methyl)benzamide (**28d**) was synthesized according to TP 2 from benzamide (121 mg, 1.0 mmol), 4–fluorobenzaldehyde (0.13 mL, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (243 mg, 64%). m.p.: 60–62 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.84 – 7.81 (m, 2H), 7.53 – 7.43 (m, 3H), 7.14 – 7.09 (m, 2H), 7.00 – 6.95 (m, 3H), 6.90 (s, 2H), 6.81 (bd, J = 8.5 Hz, 1H), 2.30 (s, 6H), 2.29 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.9, 163.6, 160.3, 137.6, 137.0 (d, J = 3.1 Hz), 136.8, 134.6, 134.3, 131.9, 130.5, 128.9, 127.8 (d, J = 8.0 Hz), 127.1, 115.7, 115.4, 51.7, 21.1, 21.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}FNO$ 348.18, found 348.32. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{23}H_{22}FNOK$ 386.1317, found 386.1316. IR (cm^{-1}): 3301 (w), 2921 (w), 1639 (m), 1601 (w), 1580 (w), 1505 (s), 1481 (m), 1378 (w), 1310 (w), 1222 (m), 1157 (m), 1098 (w), 1057 (w), 1033 (m), 1014 (m), 849 (m), 833 (m), 804 (w), 770 (m), 710 (m), 691 (m), 661 (m), 612 (m), 585 (m), 533 (m), 503 (m), 459 (m). R_f (hexane/ EtOAc 4:1): 0.6.

N–((2–Chloro–5–nitrophenyl)(mesityl)methyl)benzamide (**28e**) was synthesized according to TP 2 from benzamide (121 mg, 1.0 mmol), 2–chloro–5–nitrobenzaldehyde (190 mg, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (269 mg, 66%). m.p.: 220–222 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 8.34 (dd, J = 2.6, 0.7 Hz, 1H), 8.11 – 8.07 (m, 1H), 7.85 – 7.82 (m, 2H), 7.58 – 7.44 (m, 4H), 6.87 (bs, 2H), 6.80 (d, J = 6.6 Hz, 1H), 6.51 (bd, J = 6.6 Hz, 1H), 2.28 (s, 3H), 2.21 (s, 6H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 167.1, 146.7, 141.6, 140.2, 138.5, 137.1, 133.5, 132.3, 131.9, 131.4, 131.0, 129.0, 127.3, 124.1, 123.4, 52.8, 21.6, 21.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{22}ClN_2O_3$ 409.13, found 409.30. HRMS (MALDI)

m/z: $[M+K]^+$ Calcd. for $C_{23}H_{21}ClN_2O_3K$ 447.0872, found 447.0871. IR (cm^{-1}): 2921 (w), 1640 (s), 1595 (w), 1580 (w), 1513 (s), 1481 (s), 1423 (w), 1379 (w), 1342 (m), 1318 (w), 1273 (m), 1238 (w), 1207 (w), 1190 (w), 1147 (w), 1129 (w), 1099 (w), 1073 (w), 1055 (w), 1033 (m), 1001 (w), 909 (w), 889 (w), 861 (m), 795 (w), 762 (m), 742 (m), 713 (s), 685 (s), 650 (w), 595 (m), 552 (m), 523 (m), 486 (w), 458 (w). R_f(hexane/ EtOAc 4:1): 0.5.

N–(Mesityl(naphthalen–2–yl)methyl)benzamide (**28f**) was synthesized according to TP 2 from benzamide (121 mg, 1.0 mmol), 1–naphthaldehyde (0.16 mL, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as yellow oil (110 mg, 29%). ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 8.07 – 8.04 (m, 1H), 7.92 – 7.88 (m, 1H), 7.83 – 7.75 (m, 3H), 7.51 – 7.33 (m, 7H), 7.26 – 7.23 (m, 1H), 6.92 (s, 2H), 6.75 (bd, J = 7.8 Hz, 1H), 2.36 (s, 6H), 2.30 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.0, 137.1, 136.9, 134.8, 134.4, 134.1, 133.8, 131.7, 130.6, 129.0, 129.0, 128.8, 127.1, 126.9, 126.2, 126.0, 125.3, 123.9, 51.9, 21.8, 21.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{27}H_{26}NO$ 380.20, found 380.36. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{27}H_{25}NOK$ 418.1568, found 418.1556. IR (cm^{-1}): 3300 (w), 2921 (w), 2243 (w), 1638 (s), 1600 (w), 1579 (w), 1508 (s), 1481 (s), 1397 (w), 1373 (w), 1348 (w), 1298 (w), 1262 (w), 1238 (w), 1150 (w), 1074 (w), 1033 (m), 907 (m), 852 (m), 800 (m), 778 (s), 728 (s), 709 (s), 691 (s), 647 (m), 624 (w), 602 (m), 563 (m), 534 (m), 506 (m). R_f(hexane/ EtOAc 4:1): 0.5.

N–(Mesityl(phenyl)methyl)–4–methoxybenzamide (**29a**) was synthesized according to TP 2 from 4–methoxybenzamide (154 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (140 mg, 39%). m.p.: 184–186 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 8.88 (bd, J = 8.6 Hz, 1H), 8.30 (dd, J = 7.8, 1.8 Hz, 1H), 7.49 – 7.43 (m, 1H), 7.31 – 7.28z (m, 1H), 7.24 – 7.17 (m, 3H), 7.13 – 7.05 (m, 2H), 6.99 (d, J = 8.3 Hz, 1H), 6.89 (s, 2H), 3.94 (s, 3H), 2.33 (s, 6H), 2.28 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 164.8, 157.7, 142.0, 137.1, 136.9, 135.6, 133.0, 132.9, 130.2, 128.6, 126.6, 126.0, 121.6, 121.5, 111.4, 56.1, 51.7, 21.0, 20.8. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{24}H_{26}NO_2$ 360.20, found 360.36. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{24}H_{25}NO_2K$ 398.1517, found 398.1512. IR (cm^{-1}): 2967 (w), 1632 (m), 1598 (m), 1518 (m), 1345 (m), 1292 (m), 1260 (m), 1186 (m), 1062 (s), 1033 (s), 1016 (s), 867 (m), 850 (m), 807 (m), 781 (w), 698 (s), 623 (m), 584 (m). R_f (hexane/ EtOAc 4:1): 0.4.

4–Bromo–N–(mesityl(phenyl)methyl)benzamide (**29b**) was synthesized according to TP 2 from 4–bromobenzamide (206 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (228 mg, 56%). m.p.: 163–165 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.72 – 7.69 (m, 2H), 7.61 – 7.57 (m, 2H), 7.33 – 7.24 (m, 3H), 7.16 (d, J = 1.3 Hz, 2H), 6.97 (d, J = 8.5 Hz, 1H), 6.91 (s, 2H), 6.80 (bd, J = 8.4 Hz, 1H), 2.30 (s, 6H), 2.30 (s, 9H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 165.9, 141.0, 137.5, 136.9, 134.6, 133.3, 132.1, 130.4, 128.8, 128.7, 127.1, 126.5, 126.1, 52.3, 21.1, 21.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}BrNO$ 408.10, found 408.22. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{23}H_{22}BrNOK$ 446.0516, found 446.0507. IR (cm^{-1}): 2922 (w), 1636 (m), 1589 (m), 1568 (w), 1516 (s), 1493 (w), 1477 (s), 1448 (m), 1378 (w), 1343 (m), 1309 (m), 1269 (m), 1146 (w), 1127 (w), 1111 (w), 1074 (w), 1051 (w), 1028 (w), 1011 (m), 891 (w), 856 (w), 843 (m), 792 (w), 754 (s), 733 (s), 698 (s), 650 (w), 594 (m), 535 (m), 524 (m), 497 (w). R_f (hexane/ EtOAc 9:1): 0.7.

N–(Mesityl(phenyl)methyl)–4–nitrobenzamide (**29c**) was synthesized according to TP 2 from 4–nitrobenzamide (169 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as yellow solid (251 mg, 67%). m.p.: 161–163 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 8.31 (d, J = 8.9 Hz, 2H), 7.99 (d, J = 8.9 Hz, 2H), 7.35 – 7.29 (m, 3H), 7.16 – 7.14 (m, 2H), 6.99 (d, J = 8.5 Hz, 1H), 6.96 – 6.84 (m, 3H), 2.31 (s, 6H), 2.30 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 164.9, 149.9, 140.5, 140.1, 137.8, 136.9, 134.2, 130.5, 128.9, 128.3, 127.3, 126.1, 124.1, 52.7, 21.1, 21.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}N_2O_3$ 375.17, found 375.32. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{23}H_{22}N_2O_3K$ 413.1262, found 413.1263. IR (cm^{-1}): 1665 (m), 1639 (m), 1614 (w), 1600 (m), 1516 (s), 1493 (m), 1479 (s), 1448 (m), 1380 (w), 1341 (m), 1325 (w), 1304 (m), 1273 (w), 1206 (w), 1156 (w), 1112 (w), 1095 (w), 1048 (w), 1028 (w), 910 (w), 871 (w), 852 (m), 821 (w), 788 (w), 781 (w), 754 (m), 734 (s), 719 (m), 698 (s), 648 (w), 620 (w), 597 (m), 548 (m), 533 (m), 506 (m). R_f (hexane/ EtOAc 4:1): 0.6.

2–Fluoro–N–(mesityl(phenyl)methyl)benzamide (**29d**) was synthesized according to TP 2 from 2–fluorobenzamide (142 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at

130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless oil (254 mg, 73%). ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 8.19 – 8.13 (m, 1H), 7.66 – 7.59 (m, 1H), 7.47 – 7.39 (m, 1H), 7.29 – 7.02 (m, 8H), 6.87 (s, 2H), 2.29 (s, 6H), 2.25 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 162.8 (d, J = 3.4 Hz), 162.6, 159.3, 141.1, 137.3, 136.9, 134.9, 133.5 (d, J = 9.5 Hz), 132.5 (d, J = 2.1 Hz), 130.3, 128.7, 126.9, 125.9, 125.0 (d, J = 3.2 Hz), 120.9 (d, J = 11.0 Hz), 116.1 (d, J = 25.1 Hz), 52.0, 21.0, 20.8. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{23}FNO$ 348.18, found 348.32. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{23}H_{22}FNOK$ 386.1317, found 386.1318. IR (cm^{-1}): 3028 (w), 2967 (w), 2919 (w), 1664 (s), 1614 (m), 1582 (w), 1512 (s), 1494 (s), 1478 (s), 1448 (m), 1378 (w), 1346 (w), 1302 (m), 1285 (m), 1205 (m), 1155 (w), 1135 (w), 1095 (m), 1058 (w), 1030 (m), 958 (w), 908 (w), 846 (m), 821 (m), 779 (m), 754 (s), 726 (s), 697 (s), 641 (m), 598 (s), 577 (w), 547 (m), 532 (m), 504 (s). R_f(hexane/ EtOAc 4:1): 0.7.

2–Chloro–N–(mesityl(phenyl)methyl)acetamide (**29f**) was synthesized according to TP 2 from 2–chloroacetamide (94 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 100 °C for 24 h. Purification by chromatography (hexane:EtOAc 12:1 → 9:1) yielded the product as yellow oil (270 mg, 89%). ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.45 (bd, J = 9.1 Hz, 1H), 7.29 – 7.18 (m, 3H), 7.09 – 7.06 (m, 2H), 6.86 (s, 2H), 6.77 (d, J = 9.1 Hz, 1H), 4.16 (d, J = 15.2 Hz, 1H), 4.03 (d, J = 15.2 Hz, 1H), 2.25 (s, 3H), 2.23 (s, 6H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 165.3, 140.3, 137.4, 136.8, 134.2, 130.2, 128.7, 127.1, 125.8, 51.8, 42.9, 20.9, 20.8. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{18}H_{21}ClNO$ 302.13, found 302.24. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{18}H_{20}ClNOK$ 340.0865, found 340.0865. IR (cm^{-1}): 3301 (w), 3028 (w), 2958 (w), 2920 (w), 2865 (w), 1654 (s), 1611 (m), 1584 (w), 1517 (s), 1494 (s), 1448 (m), 1409 (m), 1378 (m), 1319 (w), 1259 (m), 1192 (w), 1148 (w), 1085 (w), 1062 (w), 1030 (m), 984 (w), 910 (w), 848 (m), 807 (w), 771 (m), 732 (s), 697 (s), 647 (m), 634 (m), 619 (m), 581 (m), 565 (m), 532 (m), 496 (m), 465 (m). R_f(hexane/ EtOAc 4:1): 0.4.

Ethyl–(mesityl(phenyl)methyl)carbamate (**29g**) was synthesized according to TP 2 from urethane (92 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as yellow oil (98 mg, 33%). ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.31 – 7.22 (m, 3H), 7.16 – 7.13 (m, 2H), 6.88 (s, 2H), 6.52 (bd, J = 9.1 Hz, 1H), 5.40 (bd, J = 8.5 Hz, 1H), 4.21 – 4.11 (m, 2H), 2.29 (s, 3H), 2.22 (s, 6H), 1.27 (t, J = 7.1 Hz, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ =

156.7, 141.7, 137.3, 136.8, 135.4, 130.2, 128.6, 126.8, 125.9, 61.2, 53.4, 21.0, 20.9, 14.8. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{19}H_{24}NO_2$ 298.18, found 298.05. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{19}H_{23}NO_2K$ 336.1360, found 336.1355. IR (cm^{-1}): 3347 (w), 2977 (w), 2919 (w), 1703 (s), 1611 (w), 1583 (w), 1494 (s), 1448 (m), 1377 (m), 1330 (m), 1297 (m), 1245 (m), 1220 (s), 1172 (m), 1117 (m), 1077 (m), 1046 (s), 1023 (s), 963 (w), 935 (w), 913 (w), 887 (w), 848 (m), 796 (w), 775 (m), 733 (s), 697 (s), 633 (m), 601 (m), 542 (m), 528 (m), 496 (m), 458 (m). R_f (hexane/ EtOAc 4:1): 0.4.

N–((4–Methoxyphenyl)(phenyl)methyl)benzamide (**30a**) was synthesized according to TP 2 benzamide (121 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), anisole (0.30 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 100 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (80 mg, 25%, ratio of regioisomers 4:1). m.p.: 172–174 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz) (peaks are listed only for major regioisomer): δ = 7.84 – 7.80 (m, 2H), 7.51 – 7.44 (m, 3H), 7.38 – 7.29 (m, 5H), 7.23 – 7.20 (m, 2H), 6.90 – 6.85 (m, 2H), 6.65 – 6.60 (m, 1H), 6.41 (d, J = 7.7 Hz, 1H), 3.80 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz) (peaks are not assigned to regioisomers): δ = 166.6, 159.2, 141.8, 134.4, 133.8, 131.8, 131.6, 129.8, 129.2, 128.9, 128.9, 128.8, 128.7, 128.4, 127.6, 127.5, 127.2, 127.1, 126.8, 121.3, 114.3, 111.8, 57.1, 55.8, 55.5, 55.0. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{20}NO_2$ 318.15, found 318.28. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{21}H_{19}NO_2K$ 356.1047, found 356.1047. IR (cm^{-1}): 3305 (w), 3061 (w), 2955 (w), 1629 (s), 1600 (w), 1578 (m), 1535 (m), 1509 (m), 1490 (m), 1461 (w), 1360 (w), 1314 (m), 1246 (m), 1203 (w), 1175 (m), 1112 (w), 1081 (w), 1031 (m), 1001(w), 934 (w), 908 (w), 865 (w), 827 (m), 799 (w), 782 (w), 746 (w), 698 (s), 662 (m), 618 (w), 573 (m), 509 (w). R_f (hexane/ EtOAc 4:1): 0.5. Analytical data are consistent with literature.[12]

N–((3–Bromo–4–methoxyphenyl)(phenyl)methyl)benzamide (**30b**) was synthesized according to TP 2 benzamide (121 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), 2–bromoanisole (0.38 mL, 3.0 mmol, 3.0 equiv.), $Bi(OTf)_3$ (33 mg, 0.05 mmol, 5 mol%) and TfOH (4 µL, 0.05 mmol, 5 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (114 mg, 35%). m.p.: 146–148 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.83 – 7.80 (m, 2H), 7.52 – 7.42 (m, 4H), 7.37 – 7.20 (m, 6H), 6.86 (d, J = 8.5 Hz, 1H), 6.63 (bd, J = 7.7 Hz, 1H), 6.37 (d, J = 7.7 Hz, 1H), 3.88 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.6, 155.4, 141.2, 135.3, 134.2, 132.4, 131.9, 129.0, 128.8, 128.0, 127.9, 127.6, 127.2, 112.2, 112.1, 56.7, 56.5. MS (ESI) m/z:

$[M+H]^+$ Calcd. for $C_{21}H_{19}BrNO_2$ 396.06, found 397.91. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{21}H_{18}BrNO_2K$ 434.0153, found 434.0146. IR (cm^{-1}): 3279 (w), 2981 (w), 1633 (s), 1601 (w), 1578 (m), 1525 (m), 1489 (s), 1457 (m), 1438 (w), 1401 (w), 1356 (w), 1315 (m), 1303 (m), 1278 (m), 1257 (s), 1204 (w), 1184 (m), 1157 (w), 1083 (w), 1053 (m), 1022 (m), 1001 (w), 936 (w), 884 (w), 847 (w), 812 (m), 804 (m), 784 (w), 740 (m), 702 (s), 681 (m), 663 (m), 641 (m), 617 (m), 582 (s). R_f(hexane/ EtOAc 4:1): 0.2.

N–((3–Chloro–4–methoxyphenyl)(phenyl)methyl)benzamide (**30c**) was synthesized according to TP 2 benzamide (121 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), 2–chloroanisole (0.38 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (142 mg, 40%). m.p.: 144–146 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.83 – 7.80 (m, 2H), 7.52 – 7.15 (m, 9H), 7.19 – 7.15 (m, 1H), 6.89 (d, *J* = 8.5 Hz, 1H), 6.63 (bd, *J* = 7.5 Hz, 1H), 6.37 (d, *J* = 7.7 Hz, 1H), 3.89 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): *δ* = 166.6, 154.5, 141.2, 134.9, 134.2, 131.9, 129.3, 129.0, 128.8, 128.0, 127.6, 127.2, 127.1, 122.9, 112.3, 56.8, 56.4. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{19}ClNO_2$ 352.11, found 352.24. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{21}H_{18}ClNO_2K$ 390.0658, found 390.0651. IR (cm^{-1}): 3297 (w), 3060 (w), 1631 (s), 1601 (w), 1578 (w), 1528 (m), 1500 (s), 1491 (s), 1458 (w), 1404 (w), 1356 (w), 1305 (m), 1279 (m), 1257 (s), 1205 (w), 1186 (w), 1159 (w), 1085 (w), 1063 (m), 1023 (m), 1002 (w), 948 (w), 937 (w), 891 (w), 878 (w), 813 (m), 803 (w), 784 (w), 739 (w), 703 (s), 693 (s), 619 (w), 610 (w), 586 (s), 547 (w). R_f(hexane/ EtOAc 4:1): 0.2.

N–((2–Methoxy–4,6–dimethylphenyl)(phenyl)methyl)benzamide (**30d**) was synthesized according to TP 2 benzamide (121 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), 3,5–dimethylanisol (408 mg, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 130 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as yellow oil (255 mg, 74%). ^{1}H–NMR ($CDCl_3$, 300 MHz): *δ* = 8.01 (bd, *J* = 9.5 Hz, 1H), 7.84 – 7.81 (m, 2H), 7.50 – 7.41 (m, 3H), 7.28 – 7.17 (m, 5H), 6.91 (d, *J* = 9.5 Hz, 1H), 6.73 (s, 1H), 6.64 (s, 1H), 3.70 (s, 3H), 2.50 (s, 3H), 2.33 (s, 3H). ^{13}C–NMR ($CDCl_3$, 75 MHz): *δ* = 166.5, 158.1, 142.1, 138.5, 137.8, 135.0, 131.5, 128.7, 128.3, 127.2, 126.7, 126.4, 125.0, 124.6, 111.1, 55.9, 50.7, 21.6, 20.4. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{24}NO_2$ 346.18, found 346.32. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{23}H_{23}NO_2K$ 384.1360, found 384.1356. IR (cm^{-1}): 1657 (s), 1611 (m), 1602 (m), 1580 (m), 1508 (s), 1481 (s), 1464 (s), 1447 (m), 1380 (w), 1346 (m), 1304 (s), 1265 (m), 1234 (m), 1183 (m), 1154

(m), 1134 (m), 1093 (s), 1050 (m), 1029 (m), 1001 (m), 971 (w), 937 (w), 914 (w), 891 (w), 833 (m), 800 (m), 733 (s), 710 (s), 695 (s), 668 (m), 639 (m), 606 (s), 592 (s), 568 (s), 518 (m). R_f(hexane/ EtOAc 4:1): 0.4.

N–((5–Bromothiophen–2–yl)(phenyl)methyl)benzamide (**30f**) was synthesized according to TP 2 benzamide (121 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), 2–bromothiophene (0.29 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 80 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (133 mg, 36%). m.p.: 159–161 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.82 – 7.79 (m, 2H), 7.53 – 7.34 (m, 7H), 6.90 (d, J = 3.8 Hz, 1H), 6.72 (bd, J = 7.7 Hz, 1H), 6.63 (dd, J = 3.8, 1.0 Hz, 1H), 6.55 (d, J = 7.9 Hz, 1H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.5, 147.4, 140.3, 134.0, 132.1, 129.9, 129.1, 128.9, 128.5, 127.3, 127.2, 126.5, 112.2, 53.7. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{18}H_{15}BrNOS$ 372.01, found 372.44. HRMS (MALDI) m/z: $[M+Na]^+$ Calcd. for $C_{18}H_{14}BrNOSNa$ 393.9872, found 393.9887. IR (cm^{-1}): 3282 (w), 3030 (w), 1640 (s), 1602 (w), 1578 (w), 1521 (m), 1488 (m), 1455 (w), 1439 (m), 1359 (m), 1311 (m), 1271 (w), 1248 (w), 1214 (m), 1195 (w), 1155 (w), 1084 (w), 1050 (w), 1029 (w), 966 (m), 925 (w), 902 (w), 820 (w), 801 (m), 784 (m), 721 (m), 700 (s), 691 (s), 666 (m), 645 (m), 615 (m), 568 (m), 551 (w), 500 (w), 478 (m). R_f(hexane/ EtOAc 4:1): 0.4.

N–(Benzofuran–2–yl(phenyl)methyl)benzamide (**30g**) was synthesized according to TP 2 benzamide (121 mg, 1.0 mmol), benzaldehyde (0.12 mL, 1.2 mmol), benzofuran (0.32 mL, 3.0 mmol, 3.0 equiv.) and $Bi(OTf)_3$ (66 mg, 0.1 mmol, 10 mol%) in DCE (4 mL) at 50 °C for 24 h. Purification by chromatography (hexane/EtOAc 12:1 → 9:1) yielded the product as colourless solid (30 mg, 9%). m.p.: 137–139 °C. ^{1}H–NMR ($CDCl_3$, 300 MHz): δ = 7.86 – 7.83 (m, 2H), 7.53 – 7.30 (m, 12H), 7.28 – 7.19 (m, 1H), 6.92 (bd, J = 8.1 Hz, 1H), 6.67 – 6.64 (m, 2H). ^{13}C–NMR ($CDCl_3$, 75 MHz): δ = 166.7, 156.1, 155.3, 139.0, 134.1, 132.0, 129.0, 128.8, 128.3, 128.2, 127.4, 127.3, 124.5, 123.1, 121.3, 111.5, 105.0, 52.1. MS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{22}H_{18}NO_2$ 328.13, found 328.26. HRMS (MALDI) m/z: $[M+K]^+$ Calcd. for $C_{22}H_{17}NO_2K$ 366.0891, found 366.0888. IR (cm^{-1}): 3318 (w), 1630 (s), 1600 (m), 1577 (w), 1537 (s), 1490 (m), 1454 (m), 1329 (m), 1284 (w), 1270 (m), 1254 (s), 1203 (w), 1168 (m), 1142 (m), 1104 (w), 1081 (m), 1029 (w), 1002 (w), 966 (m), 904 (m), 857 (w), 823 (m), 802 (m), 752 (s), 742 (s), 725 (s), 711 (s), 697 (s), 690 (s), 647 (s), 624 (m), 615 (m), 585 (m), 565 (m), 461 (m). R_f(hexane/ EtOAc 4:1): 0.3.

ASSOCIATED CONTENT

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

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Notes

The authors declare no competing financial interest.

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