Mapping the Melatonin Receptor. 4. Comparison of the Binding Affinities of a Series of Substituted Phenylalkyl Amides

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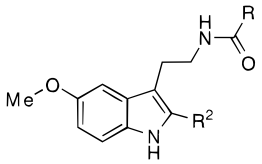
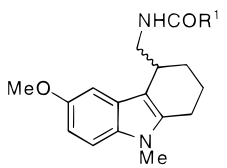
A series of 2-, 3-, and 4-substituted phenylalkyl amides were prepared as potential melatonin analogs in order to investigate the nature of the binding site of the melatonin receptor in chicken brain. The length of the alkyl chain was systematically varied from $n = 1$ to 4, and methoxyl substituents were incorporated into the phenyl ring at the 2-, 3-, and 4-positions. The maximum binding affinity was found to occur when $n = 3$ and when the methoxyl substituent was in the 3-position, the direct analog of the carbon framework of melatonin in which the 1,2-atoms of the indole ring have been removed. Whereas there was only a relatively small decrease in binding affinity for the corresponding 2-methoxy derivatives, 4-methoxyl substitution led to a large decrease in binding affinity, suggesting that the binding sites for the side chain and methoxyl group could not now be occupied at the same time. As in the indole analogs of melatonin, replacement of the methyl group of the amide by a longer alkyl chain led to an increase in binding affinity for ethyl and propyl with a subsequent decrease in binding affinity for butyl chains. Thus *N*-propanoyl-3-(3-methoxyphenyl)propanamine (**6f**) has a binding affinity of 5.6 nM, a remarkably high affinity for so simple a compound. Substitution of halogen for 3-methoxyl in the propanamide series gave a series of compounds with lower, but still substantial, binding affinities, the 3-chloro derivative **7e** showing the highest affinity, 113 nM. In the case of the 3-fluoro propanamides, a maximum in the binding affinity was not observed in the series synthesized, and these derivatives will merit further exploration. These results demonstrate the utility of simple, readily modified phenylalkylamines as a "framework" for studying the effect of changes in the nature and position of substituents on the melatonin receptor binding affinity.

Introduction

Despite the practical and clinical interest in melatonin (**1a**) (Figure 1), the hormone of the pineal gland, little is known about its mode of action or of the way in which it interacts with its receptor. High-affinity melatonin binding sites have been identified in central and, more recently, peripheral tissues,[1−5] and the receptor, termed Mel_1, has now been cloned from *Xenopus* melanophores, sheep, and humans.[6,7] A potential new role for melatonin has just been discovered by the observations that it is a natural ligand for a brain-specific nuclear receptor of the retinoic acid receptor family (RZRβ)[8] and for the α-subtype of RZR, which occurs in a range of tissues.[9] It has been shown[10] that activation of these receptors, which act as transcription factors, by melatonin can regulate the expression of genes containing an appropriate specific response element. It appears probable that Mel_1 and RZR receptors will have different characteristics, and we are attempting to model the binding of melatonin to the Mel_1 receptor and to use this model to design melatonin agonists and antagonists which can then be used to explore the functional requirements of other melatonin receptors. Such ligands may also be useful as tools to investigate the physiological roles of melatonin and may have utility in manipulating breeding cycles in commercially important species of livestock and in human medicine.[11,12]



1a R = Me, R^2 = H
1b R = Me, R^2 = I
1c R = Et, R^2 = H



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Variations of the acyl group on the C-3 side chain of melatonin had shown that acetyl was not the optimum group and that replacement by propanoyl or butanoyl effected an improvement in binding affinity.[13] We[14−16] have been exploring the spatial demands of the melatonin receptor in the chicken brain by synthesis of various types of indole and annelated indole derivatives and concluded that the orientation of the C-3 and C-5 substituents was a factor of major importance in the

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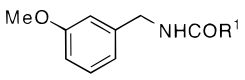
design of melatonin agonists, a finding reinforced by the difference in binding affinity of enantiomers of 4-substituted tetrahydrocarbazoles (*e.g.*, **2**).[15,17] In order to define the minimum requirements for a melatonin analog and further clarify the spatial requirements of the C-3 and C-5 substituents, we have prepared a series of phenylalkyl amides and investigated their binding affinities in the chicken brain radioligand binding assay. Previously, Copinga *et al.*[18] had reported that in a series of *N*-acyl-2-phenylethanamines the *N*-acetyl 2-methoxyl derivative had a somewhat higher binding affinity (K_i = 420 nM) than the corresponding 3-methoxyl derivative (K_i = 581 nM), with the 4-methoxyl derivative having a much lower binding affinity (K_i > 10 μM) than either. During the course of our investigations, Langlois *et al.*[19] reported the binding affinities for a series of substituted phenylethanamines and (2-methoxyphenyl)-ethanamines, with the *N*-propyl-(5-bromo-2-methoxyphenyl)ethanamine showing the highest affinity (K_i = 8 nM), and these authors again found that the 2-methoxyl derivative had a higher binding affinity than the corresponding 3-methoxyl derivative. We now report our findings.

Chemistry

(3-Methoxyphenyl)methyl amides **3** and (3,4-dimethoxyphenyl)ethylamides **4** were prepared by acylation of the commercially available amines. 3-(*x*-Methoxyphenyl)propionic acids were converted to the corresponding amides which were then reduced to the 3-(*x*-methoxyphenyl)propanamine or converted to the 2-(*x*-methoxyphenyl)ethanamine by Hofmann degradation. Acylation then gave the series of 2-(*x*-methoxyphenyl)ethyl amides **5** and 3-(*x*-methoxyphenyl)propyl amides **6**. 3-(*x*-Methoxyphenyl)propionic acids were reduced to the alcohol and mesylated, and the mesylate was displaced by cyanide. The resulting nitriles were reduced to the corresponding 4-(*x*-methoxyphenyl)butanamines which were then acylated to 4-(*x*-methoxyphenyl)butyl amides **7**. 3-(Halophenyl)propyl amides **8** were prepared by reduction of the corresponding cinnamamide and acylation of the resulting amine.



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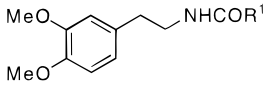

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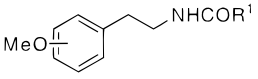

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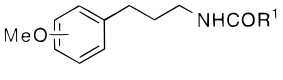

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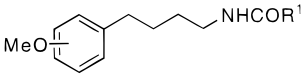

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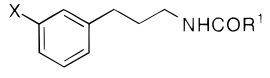

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Pharmacology

The affinity of the phenylalkyl amides at the melatonin binding site in chicken brain membranes was determined in a competition radioligand binding assay using 2-[^{125}I]iodomelatonin (**1b**). This radioligand binding assay was conducted as described previously by Sugden and Chong.[13]

Chicks (*Gallus domesticus*, White Leghorn, mixed sex) were obtained at 1 day of age and kept in a diurnal lighting cycle (L:D 12:12, lights on at 06.00) until killed between 14.00 and 15.00 h between 15 and 21 days of age. Chicks were killed by decapitation and whole brains removed, pooled, and rapidly frozen in liquid nitrogen. Frozen tissue was stored at −70 °C until used to prepare brain membranes. Brain membranes were prepared at *ca.* 3-month intervals using three to four chick brains from the frozen pool. All experiments performed on the series of phenylalkyl amides used the same preparation of membranes. Small variations in binding site density between different preparations have been noted.

Duplicate aliquots (60 μg) of brain membranes were incubated (25 °C, 60 min) with 60−70 pM 2-[^{125}I]-iodomelatonin (2200 Ci/mmol; DuPont U.K., Stevenage, U.K.) and a 10-fold dilution series of analogs. Cold melatonin (1 μM) was used to define nonspecific binding. Competion experiments were carried out once but used six concentrations of each analog in duplicate.

K_i was calculated from IC_{50} values determined in competition experiments using the Cheng−Prusoff equation. IC_{50} values were determined using the ALLFIT program.

Analogs were dissolved in methanol at 10 mM, stored at −20 °C in the dark, and diluted just before use with methanol. Methanol (0.1%) added to the binding assay had no effect on specific binding, but both total and nonspecific tubes contained methanol (0.1%).

Results and Discussion

The binding affinities for the (methoxyphenyl)alkylamines are shown in Table 1. The binding affinities are greatest for compounds of the **6** series with the 3-carbon alkyl chain. Both reduction of the chain length, as in compounds **3**−**5**, and increasing the chain length, as in compounds **7**, lead to a lowering of binding affinity. Propanamides of the **6** series have the same carbon framework as melatonin with the loss of the 1,2-indole atoms. Reducing the chain length to a single atom gave compounds **3** which had very poor affinity, which mirrors our experience with nortryptamine analogs.[20]

Comparison of compounds with the same alkyl chain length reveals that those isomers with the methoxyl group in the 3-position usually have the highest binding affinity. This again reflects the melatonin structure in the relative configuration of the two groups. Propyl amide **6e**, which is the exact analog of melatonin less the 1,2-indole atoms, has a binding affinity (63 nM) only 100-fold less than that of melatonin, a remarkably high binding affinity for such a simple system. The orientation of the two side chains can presumably duplicate the binding conformation of melatonin very closely, and the loss in affinity is probably due to the greater entropy requirement for **6e** to adopt the desired conformation than for melatonin. The likely binding conformation and the binding affinities for the compounds **6e**, melatonin (**1a**), *N*-acetyl-4-(aminomethyl)-6-methoxy-9-methyltetrahydrocarbazole (**2**),[15,17] and 2-acetamido-8-methoxytetralin (**9**)[18] are shown in Figure 1.[21]

While the 2-methoxyl compounds retained considerable binding affinity, as already shown by Copinga *et al.*[18] and Langlois *et al.*,[19] the 4-methoxyl derivatives had little affinity even with the optimum alkyl chain

Table 1. Binding Affinity in Chicken Brain Assay of (Methoxyphenyl)alkyl Amides

compd	R^1	receptor binding, K_i (nM)
melatonin		0.59 ± 0.06
3a	Me	57 000 ± 8100
3b	Et	22 000 ± 2500
3c	Pr	13 000 ± 1500
4a	Me	870 ± 130
4b	Et	130 ± 21
4c	Pr	59 ± 9
5a, 2-OMe	Me	573 ± 68 420[a]
5b, 2-OMe	Et	135 ± 21 789[a]
5c, 2-OMe	Pr	69 ± 12 748[a]
5d, 2-OMe	Bu	16 000 ± 1600
5e, 3-OMe	Me	958 ± 108 581,[a] 253[b]
5f, 3-OMe	Et	62 ± 7
5g, 3-OMe	Pr	40 ± 6
5h, 3-OMe	Bu	741 ± 63
5i, 4-OMe	Me	>100 000 NE,[a] >1000[b]
5j, 4-OMe	Et	19 200 ± 5100
5k, 4-OMe	Pr	17 900 ± 5200
5l, 4-OMe	Bu	70 800 ± 4100
6a, 2-OMe	Me	1430 ± 310
6b, 2-OMe	Et	374 ± 80
6c, 2-OMe	Pr	442 ± 122
6d, 2-OMe	Bu	>100 000
6e, 3-OMe	Me	63 ± 4
6f, 3-OMe	Et	5.6 ± 1.7
6g, 3-OMe	Pr	5.5 ± 1.8
6h, 4-OMe	Me	14 000 ± 1600
6i, 4-OMe	Et	2900 ± 800
6j, 4-OMe	Pr	860 ± 210
7a, 2-OMe	Et	339 ± 54
7b, 2-OMe	Pr	116 ± 29
7c, 2-OMe	Bu	9190 ± 1260
7d, 3-OMe	Et	119 ± 25
7e, 3-OMe	Pr	208 ± 55
7f, 3-OMe	Bu	9670 ± 2660
7g, 4-OMe	Me	7300 ± 1300
7h, 4-OMe	Et	1400 ± 300
7i, 4-OMe	Pr	822 ± 192
7j, 4-OMe	Bu	7000 ± 1100

[a] Values from Copinga *et al.*, ref 18, for binding affinity in chicken retinal membranes. [b] Values from Langlois *et al.*, ref 19, for binding affinity in chicken brain membranes.

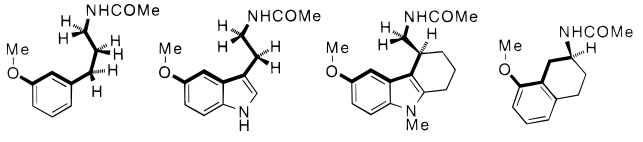


Figure 1. Postulated preferred conformations of melatonin and melatonin analogs in the chicken brain melatonin receptor and binding affinities in the chicken brain assay.

length. This indicates that while it may be possible to accommodate the change of the methoxyl to the 2-position by changing the length of the alkyl chain or modification of its conformation, such an accommodation is not readily possible for the 4-methoxyl derivatives, and binding at one or both sites may be compromised. As is clear from Table 1, the *relative positions* that the methoxyl group and side chain can adopt in these flexible molecules is more important than the actual length of the alkyl chain. Thus the ethyl amide **5f**, with the methoxyl in the 3-position, has 6-fold greater

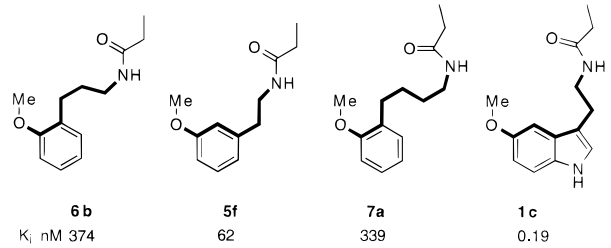


Figure 2. Comparison of *N*-propanoyl melatonin analogs in postulated preferred conformations and binding affinities in chicken brain assay.

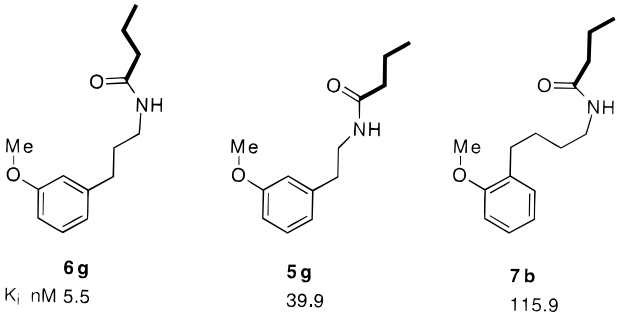


Figure 3. Binding affinities for phenylethyl amides, phenylpropyl amides, and phenylbutyl amides with optimal acylating group.

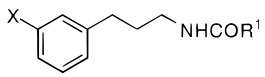
binding affinity than the 2-methoxy propanamide derivative **6b**. The 2-methoxy ethyl amide **5b** has a lower affinity than the 3-methoxy ethyl amide **5f**, presumably because the shorter ethanamine side chain makes simultaneous occupation of both sites more difficult. Further, the 2-methoxy butyl amide **7a** has a similar binding affinity to **6b**, indicating that the flexibility of the longer chain can now more readily accommodate the methoxyl and amide groups in the receptor, overcoming the greater entropic loss incurred by the longer alkyl chain (Figure 2).

The 2-(3,4-dimethoxyphenyl)ethanamines **4a**−**c** show similar or somewhat lower binding affinities than the corresponding 2-(3-methoxyphenyl)ethanamines **5e**−**g**; this small decrease in binding affinity may be due to the 3-methoxyl methyl group spending less time in the preferred binding conformation.

As with the indole melatonin analogs,[13] replacement of the acetyl group by propanoyl or butanoyl increases the affinity of the compounds (*e.g.*, **1c** $K_i = 0.19 \pm 0.06$ nM). This even occurs with methyl amide derivatives, despite their very poor affinity. It is, however, most strikingly seen by the changes that occur in the binding affinities of systems illustrated in Figures 1 and 2 on substitution of the methyl group by the most potent alkyl chain with respect to binding affinity (Figure 3).

The propyl derivative has the highest affinity in both the **5** (3-MeO) and **6** (3-MeO) series, and the propyl derivative **7b** has *ca.* 3 times the binding affinity of the ethyl derivative **7a**. These changes show the importance of the amide alkyl group in adjusting the binding of the alkyl side chain in these derivatives. This effect can partially override optimization of the chain length as seen by a comparison of the binding affinities of the (3-methoxyphenyl)ethyl amides **5e**−**h** with those of the 3-methoxy propyl amides **6e**−**g**. Thus, whereas **6e** has a 15-fold greater binding affinity than **5e**, when the amide alkyl side chain is optimized, **6g** (=**6f**) has only 7-fold greater binding affinity than **5g**. The lower

Table 2. Binding Affinity in Chicken Brain Assay of 3-(3-Halophenyl)propyl Amides



compd	X	R^1	receptor binding, K_i (nM)
melatonin			0.59 ± 0.06
8a	F	Me	1920 ± 330
8b	F	Et	740 ± 110
8c	F	Pr	434 ± 66
8d	Cl	Me	636 ± 134
8e	Cl	Pr	113 ± 33
8f	Cl	Bu	15 100 ± 2700
8g	Br	Me	852 ± 93
8h	Br	Et	318 ± 30
8i	Br	Pr	354 ± 74

affinity of **5a** compared to **5e** further indicates that with nonoptimal side chain binding the relative distance between the methoxyl and side chain becomes more important.

Interestingly, whereas we observe an 8-fold increase in binding across the series of (2-methoxyphenyl)ethyl amides **5a**−**c** in the chicken brain membrane binding assay (Table 1), Copinga *et al.*[18] did not observe any increase in binding in the chicken retinal membrane binding assay, the *N*-acetylethanamine **5a** having, in fact, the highest affinity. This may indicate a subtle difference in the amide binding region of these two receptors.

In the case of the butyl amides **7**, in the 3-methoxyl series there is a decrease in binding affinity on going from *N*-propanoyl, **7d**, to *N*-butanoyl, **7e**, whereas in the 2-methoxy series there is an increase in affinity on going from **7a** to **7b**. It thus appears that for the 3-methoxy butanamines the distance between the methoxyl and *N*-acyl groups is so large that the space in the binding "pocket" accommodating the *N*-acyl group is restricted. By contrast, the 2-methoxy butanamines, with the smaller interbond distance between two groups, appear to have less restriction on the "pocket" so that larger groups with increased van der Waals attractive components can be accommodated. The finding that the affinity of 4-methoxyl derivatives increases as the *N*-acylating group is changed from *N*-acetyl to *N*-butanoyl suggests that it is the amide side chain that is primarily bonding to the receptor in these compounds.

A number of propyl amides **8** were prepared in which the 3-methoxyl group was replaced by halogen, compounds similar to the 5-halo-substituted tryptamides.[22] The binding affinities for these compounds are shown in Table 2. In all cases there is a reduction of the binding affinity compared to the corresponding methoxyl system, but nevertheless, some of these compounds show considerable affinity for the melatonin receptor. The 3-chloro derivatives have the highest binding affinities, and these again show the effect of changing the acylating group, butanoyl being the most effective, whereas in the 3-bromo series the propanoyl and butanoyl show similar affinities. Unlike with the bromo and chloro derivatives, no maximum was observed in the 3-fluoro series, and further investigations seem merited to discover the preferred structure. Since the 2-methoxyl derivatives are similar in affinity to the 3-methoxyl derivatives, it would also appear desirable to investigate their 2-halo analogs.

A number of these phenylalkyl amides show remarkably high binding affinities for such simple molecules, suggesting that the active site on the melatonin receptor is highly organized around a small cavity when the messenger molecule is docked in position. The low water solubility of melatonin and its analogs suggests that the pocket is largely lipophilic with hydrogen bonding to the amide and methoxyl side chains, the former probably acting both as donor and acceptor. van der Waals attractive interactions with the side chains of amino acids in the receptor protein, the amide alkyl group, and the aromatic indole ring are also probably involved, the latter probably through $\pi-\pi$ stacking aromatic rings. The small molecule binding site in G-protein-coupled receptors is thought to involve residues in the hydrophobic transmembrane domains.[23] Receptor mutagenesis and structure−activity studies have indicated that binding involves hydrogen bonding between ligand hydroxyl groups and specific amino acids in the fifth transmembrane helix of the receptor and $\pi-\pi$ bonding in the sixth transmembrane helix. Most of the receptors so far examined have natural ligands which are more basic than melatonin, and if one compares these ligands with melatonin, then amide replaces amine and methoxyl replaces hydroxyl. The recent cloning of the melatonin receptor[6,7,24,25] allows for comparison with these receptors. Immediately striking is the absence in the sequence of cloned melatonin receptors of the conserved serine residues in the predicted fifth transmembrane helix, which have been suggested to interact with the hydroxyl groups of catecholamines.[23,26] Of the residues in the putative fifth transmembrane domain of melatonin receptors, a conserved histidine (211) could conceivably substitute for serine and act as a proton donor to the C-5 methoxyl group of melatonin.[27] Mutagenesis studies have indicated that a conserved aspartate residue in the third transmembrane helix provides the counterion for the basic amine of agonists and antagonists, and again this residue is not found in the cloned melatonin receptors but is replaced by a methionine. A phenylalanine in the sixth transmembrane domain, conserved in all receptors which bind aromatic biogenic amine ligands, is thought to interact with the aromatic ring of the ligand. There are two phenylalanine residues conserved in the sixth putative transmembrane domain of all the cloned melatonin receptors together with a conserved tryptophan residue, all of which would be suitable for $\pi-\pi$ stacking. Clearly the acetylation of the amine residue and the methylation of the hydroxyl group impose on melatonin different binding requirements compared to those of biogenic amines, and it may be that the ligand binding site of melatonin differs considerably from that of these compounds.

Experimental Section

Melting points were determined on a Reichert or Electrothermal melting point apparatus and are uncorrected. Mass spectra were recorded on a VG7070H mass spectrometer with a Finnigan Incos II data system or on a VG ZAB-2F mass spectrometer. Only molecular ions (M^+), base peaks, and the next two peaks due to ions of maximum abundance are given. IR spectra were recorded on a Perkin-Elmer PE-983 or Perkin-Elmer 1605 FTIR spectrophotometer using KBr pellets unless stated otherwise. ^{1}H NMR spectra were recorded in $CDCl_3$ unless stated otherwise on a Varian VXR-400 spectrometer, and the spectra are reported in δ. ^{13}C NMR spectra were

recorded at 100 MHz on a Varian VXR-400 spectrometer and are reported in δ. Microanalyses were carried out by the Microanalytical Section, Department of Chemistry, University College London.

Merck Kieselgel 60 F_{254} plates were used for analytical TLC and visualized with ultraviolet light or developed with *p*-anisaldehyde. Flash column chromatography was performed using Sorbsil C60-A silica gel (40−60 μm) as the stationary phase. Spinning plate chromatography (SPC) was carried out using Merck silica gel 60 PF_{254} with calcium sulfate.

General Procedure for Acylation. Except where otherwise indicated, the amine in dry dichloromethane (3.5 mL) was treated with triethylamine (0.25 mL) at 0 °C. The appropriate anhydride (1.3 equiv) or acid chloride (1.3 equiv) was then added dropwise at the same temperature, and the resulting reaction mixture was left stirring at room temperature for 2 h. The solution was then poured into a separatory funnel, CH_2Cl_2 was added, and the yellow organic layer was washed with H_2O (20 mL), 2 N HCl (2 × 20 mL), saturated aqueous $NaHCO_3$ (2 × 20 mL), and brine. After drying over $MgSO_4$, the solvent was evaporated under reduced pressure to give the crude product, which was chromatographed (SPC or flash column) to give the desired amide.

***N*-Acetyl-(3-methoxyphenyl)methanamine (3a).** 3-Methoxybenzylamine (1.4 g, 10 mmol) was treated with acetic anhydride (1.0 mL) in triethylamine (5 mL) and dichloromethane (20 mL). Purification by SPC eluting with CH_2Cl_2 gave **3a** as colorless crystals (1.40 g, 7.8 mmol, 78 %): mp 58−59 °C; ^{1}H NMR δ 2.00 (s, 3H), 3.78 (s, 3H), 4.36 (m, 2H), 6.10 (br s, 1H), 6.79−6.85 (m, 3H), 7.20−7.27 (m, 1H); ^{13}C NMR δ 23.1, 43.6, 55.2, 112.8, 113.4, 119.9, 129.6, 139.8, 159.8, 170.1; IR 3245, 3081, 1651, 1561, 1245, 755 cm^{-1}; EIMS *m*/*z* 179, 120 (100), 107. Anal. ($C_{10}H_{13}NO_2$) C, H, N.

***N*-Propanoyl-(3-methoxyphenyl)methanamine (3b).** 3-Methoxybenzylamine (1.40 g, 10 mmol) was treated with propanoic anhydride (1.0 mL) in triethylamine (5 mL) and dichloromethane (20 mL). Purification by SPC eluting with CH_2Cl_2:methanol gave **3b** as colorless crystals (1.30 g, 6.8 mmol, 68%): mp 57−58 °C: ^{1}H NMR δ 1.08 (t, 3H, J = 7.6 Hz), 2.15 (q, 2H, J = 7.5 Hz), 3.70 (s, 3H), 4.27 (m, 2H), 6.60 (br s, 1H), 6.72−6.78 (m, 3H), 7.14−7.18 (m, 1H); ^{13}C NMR δ 9.7, 23.1, 43.6, 55.1, 112.8, 113.3, 119.9, 129.5, 140.1, 159.6, 174.0; IR 3238, 3076, 1650, 1555, 1249, 750 cm^{-1}; EIMS *m*/*z* 193, 120 (100), 107. Anal. ($C_{11}H_{15}NO_2$) C, H, N.

***N*-Butanoyl-(3-methoxyphenyl)methanamine (3c).** 3-Methoxybenzylamine (1.40 g, 10 mmol) was treated with butanoic anhydride (1.0 mL) in triethylamine (5 mL) and dichloromethane (20 mL). Purification by SPC eluting with CH_2Cl_2 gave **3c** as pale yellow crystals (1.5 g, 7.3 mmol, 73%): mp 36−37 °C; ^{1}H NMR δ 0.89 (t, 3H, J = 7.3 Hz), 1.57−1.63 (m, 2H), 2.11 (t, 2H, J = 7.1 Hz), 3.71 (s, 3H), 4.30 (m, 2H), 6.60 (br s, 1H), 6.73−6.79 (m, 3H), 7.15−7.18 (m, 1H); ^{13}C NMR δ 13.5, 19.0, 38.2, 43.0, 54.9, 112.4, 113.0, 119.6, 129.3, 140.0, 159.5, 173.0; IR 3247, 3082, 1653, 1554, 1240, 759 cm^{-1}; EIMS *m*/*z* 207, 120 (100), 107. Anal. ($C_{12}H_{17}NO_2$) C, H, N.

***N*-Acetyl-2-(3,4-dimethoxyphenyl)ethanamine (4a).** 2-(3,4-Dimethoxyphenyl)ethanamine (1.80 g, 10 mmol) was treated with acetic anhydride (1.0 mL) in triethylamine (5 mL) and dichloromethane (20 mL). Purification by SPC eluting with CH_2Cl_2 gave **4a** as colorless crystals (1.80 g, 8.2 mmol, 82%): mp 95−96 °C; ^{1}H NMR δ 1.90 (s, 3H), 2.72 (t, 2H, J = 7.0 Hz), 3.44 (dt, 2H, J = 6.1, 7.0 Hz), 3.82 (s, 3H), 3.82 (s, 3H), 5.65 (br s, 1H), 6.67 (s, 1H), 6.69 (d, 1H, J = 7.8 Hz), 6.76 (d, 1H, J = 7.9 Hz); ^{13}C NMR δ 23.2, 35.1, 40.7, 55.7, 55.8, 111.2, 111.7, 120.5, 131.2, 147.5, 148.9, 170.0; IR 3245, 3080, 1655, 1550, 1242, 750 cm^{-1}; EIMS *m*/*z* 223, 164 (100), 151. Anal. ($C_{12}H_{17}NO_3$) C, H, N.

***N*-Propanoyl-2-(3,4-dimethoxyphenyl)ethanamine (4b).** 2-(3,4-Dimethoxyphenyl)ethanamine (1.8 g, 10 mmol) was treated with propanoic anhydride (1.0 mL) in triethylamine (5 mL) and dichloromethane (20 mL). Purification by SPC eluting with CH_2Cl_2 gave **4b** as a colorless oil (1.50 g, 6.2 mmol, 62%) which solidified in the cold: mp 43−44 °C; ^{1}H NMR δ 1.06 (t, 3H, J = 7.5 Hz), 2.10 (q, 2H, J = 7.6 Hz), 2.69 (t, 2H, J = 7.0 Hz), 3.41 (dt, 2H, J = 6.1, 7.0 Hz), 3.78 (s, 3H), 3.79 (s, 3H), 5.73 (br s, 1H), 6.65−6.67 (m, 2H), 6.73 (d, 1H, J = 8.6 Hz); ^{13}C NMR δ 9.8, 29.5, 35.1, 40.5, 55.6, 55.7, 111.1, 111.7, 120.4, 131.3, 147.4, 148.8, 173.7; IR 3243, 3082, 1654, 1553, 1240, 750 cm^{-1}; EIMS *m*/*z* 237, 164 (100), 151. Anal. ($C_{13}H_{19}NO_3$) C, H, N.

***N*-Butanoyl-2-(3,4-dimethoxyphenyl)ethanamine (4c).** 2-(3,4-Dimethoxyphenyl)ethanamine (1.80 g, 10 mmol) was treated with butanoic anhydride (1.0 mL) in triethylamine (5 mL) and dichloromethane (20 mL). Purification by SPC eluting with CH_2Cl_2 gave **4c** as a colorless oil (1.70 g 6.8 mmol, 68%) which solidified in the cold: mp 48.5−49.5 °C; ^{1}H NMR δ 0.89 (t, 3H, J = 7.3 Hz), 1.58−1.69 (m, 2H), 2.08 (t, 2H, J = 7.3 Hz), 2.74 (t, 2H, J = 7.0 Hz), 3.47 (dt, 2H, J = 6.4, 6.7 Hz), 3.84 (s, 6H), 5.43 (br s, 1H), 6.69 (s, 1H), 6.70 (d, 1H, J = 7.3 Hz), 6.78 (d, 1H, J = 7.6 Hz); ^{13}C NMR δ 13.7, 19.1, 35.3, 38.7, 40.6, 55.8, 55.9, 111.2, 111.8, 120.6, 131.4, 147.6, 149.0, 173.0; IR 3240, 3087, 1652, 1549, 1239, 746 cm^{-1}; EIMS *m*/*z* 251, 164 (100), 151. Anal. ($C_{14}H_{21}NO_3$) C, H, N.

***N*-Acetyl-2-(2-methoxyphenyl)ethanamine (5a).**[18] 2-(2-Methoxyphenyl)ethanamine (0.15 g, 1 mmol) was treated with acetic anhydride (0.5 mL) in triethylamine and dichloromethane to give **5a** as colorless crystals (0.17 g, 0.9 mmol, 88%): mp 84−85 °C (lit.[18] mp 77−78 °C); ^{1}H NMR δ 1.93 (s, 3H), 2.84 (t, 2H, J = 6.6 Hz), 3.48 (dt, 2H, J = 6.6, 6.7 Hz), 3.85 (s, 3H), 5.72 (br s, 1H), 6.87−6.94 (m, 2H), 7.14 (d, 1H, J = 7.5 Hz), 7.24 (dd, 1H, J = 7.8, 8.0 Hz); ^{13}C NMR δ 23.3, 30.1, 39.8, 55.2, 110.3, 120.5, 127.8, 130.6, 127.3, 157.4, 170.0; IR 3266, 3080, 1650, 1561, 1245, 755 cm^{-1}; EIMS *m*/*z* 193, 134 (100), 121, 91 (100). Anal. ($C_{11}H_{15}NO_2$) C, H, N.

***N*-Propanoyl-2-(2-methoxyphenyl)ethanamine (5b).**[18] 2-(2-Methoxyphenyl)ethanamine (0.15 g, 1.0 mmol) was treated with propanoic anhydride (0.5 mL) in triethylamine and dichloromethane to give **5b** as colorless crystals (0.19 g, 0.9 mmol, 92%): mp 53−54 °C (lit.[18] mp 47−49 °C); ^{1}H NMR δ 1.09 (t, 3H, J = 7.7 Hz), 2.12 (q, 2H, J = 7.6 Hz), 2.81 (t, 2H, J = 6.7 Hz), 3.46 (dt, 2H, J = 5.6, 6.5 Hz), 3.82 (s, 3H), 5.68 (br s, 1H), 6.84−6.90 (m, 2H), 7.10 (dd, 1H, J = 1.6, 7.5 Hz), 7.20 (m, 1H); ^{13}C NMR δ 9.8, 29.8, 30.1, 39.8, 55.2, 110.3, 120.7, 127.8, 130.6, 127.4, 157.4, 173.0; IR 3268, 3073, 1641, 1540, 1247, 759 cm^{-1}; EIMS *m*/*z* 207, 134 (100), 121, 91 (100). Anal. ($C_{12}H_{17}NO_2$) C, H, N.

***N*-Butanoyl-2-(2-methoxyphenyl)ethanamine (5c).** 2-(2-Methoxyphenyl)ethanamine (0.15 g, 1.0 mmol) was treated with butanoic anhydride (0.5 mL) in triethylamine and dichloromethane. Purification by SPC eluting with CH_2Cl_2:1% methanol gave **5c** as a colorless oil (0.15 g, 0.7 mmol, 68%) (lit.[18] mp 45−47 °C): ^{1}H NMR δ 0.91 (t, 3H, J = 7.4 Hz), 1.61 (s, 2H), 2.09 (t, 2H, J = 7.9 Hz), 2.83 (t, 2H, J = 6.8 Hz), 3.48 (dt, 2H, J = 5.7, 6.7 Hz), 3.83 (s, 3H), 5.83 (br s, 1H), 6.86 (d, 1H, J = 8.3 Hz), 6.90 (m, 1H), 7.12 (dd, 1H, J = 1.3, 7.2 Hz), 7.22 (m, 1H); ^{13}C NMR δ 13.7, 19.0, 30.1, 38.6, 39.6, 55.2, 110.2, 120.6, 127.7, 130.5, 127.3, 157.3, 172.9; IR (film) 3268, 3064, 1650, 1558, 1241, 750 cm^{-1}; EIMS *m*/*z* 221, 134 (100), 121, 91 (100). Anal. ($C_{13}H_{19}NO_2$) Calcd: C, 70.55; H, 8.65; N, 6.33. Found: C, 70.09; H, 8.33; N, 6.30.

***N*-Pentanoyl-2-(2-methoxyphenyl)ethanamine (5d).** 2-(2-Methoxyphenyl)ethanamine (0.15 g, 1.0 mmol) was treated with valeroyl chloride (0.5 mL) in triethylamine and dichloromethane. Purification by SPC eluting with CH_2Cl_2:1% methanol gave **5d** as a colorless oil (0.15 g, 0.6 mmol, 64%): ^{1}H NMR δ 0.88 (t, 3H, J = 7.4 Hz), 1.28 (m, 2H), 1.55 (m, 2H), 2.10 (t, 2H, J = 7.7 Hz), 2.83 (t, 2H, J = 6.8 Hz), 3.46 (dt, 2H, J = 5.8, 6.6 Hz), 3.81 (s, 3H), 5.90 (br s, 1H), 6.84−6.90 (m, 2H), 7.11 (dd, 1H, J = 7.3 Hz), 7.19 (m, 1H); ^{13}C NMR δ 13.7, 22.2, 27.7, 30.0, 36.4, 39.6, 55.1, 110.2, 120.5, 127.3, 127.7, 130.4, 157.3, 173.0; IR (film) 3268, 3064, 1650, 1558, 1241, 750 cm^{-1}; EIMS *m*/*z* 235, 134 (100), 121, 91 (100). Anal. ($C_{14}H_{21}NO_2$) C, H, N.

***N*-Acetyl-2-(3-methoxyphenyl)ethanamine (5e).**[18,19] 2-(3-Methoxyphenyl)ethanamine (0.45 g, 2.6 mmol) was treated with acetic anhydride (1 mL) in triethylamine and dichloromethane. Purification by SPC eluting with CH_2Cl_2:5% methanol gave **5e** as a pale yellow oil (0.35 g, 1.8 mmol, 70%): ^{1}H NMR δ 1.90 (s, 3H), 2.75 (t, 2H, J = 7.0 Hz), 3.47 (q, 2H, J = 5.9, 7.0 Hz), 3.76 (s, 3H), 5.73 (br s, 1H), 6.70−6.80 (m, 3H), 7.19 (dd, 1H, J = 7.7, 7.9 Hz); ^{13}C NMR δ 23.3, 35.6, 40.5, 55.1, 111.7, 114.4, 121.0, 129.6, 140.5, 159.7, 170.1; IR (film)

3292, 2935, 1644, 1440, 1224 cm^{-1}; EIMS *m/z* 193, 134 (100), 121, 57 (100). Anal. ($C_{11}H_{15}NO_2$) C, H, N.

***N*-Propanoyl-2-(3-methoxyphenyl)ethanamine (5f).** 2-(3-Methoxyphenyl)ethanamine (0.45 g, 2.6 mmol) was treated with propanoic anhydride (1.0 mL) in triethylamine and dichloromethane. Purification by SPC with CH_2Cl_2:2% methanol gave **5f** as a yellow oil (0.37 g, 1.8 mmol, 69%): ^{1}H NMR δ 1.11 (t, 3H, J = 7.7 Hz), 2.17 (q, 2H, J = 7.5 Hz), 2.77 (t, 2H, J = 7.0 Hz), 3.48 (q, 2H, J = 6.0, 7.0 Hz), 3.77 (s, 3H), 5.78 (br s, 1H), 6.72−6.77 (m, 3H), 7.20 (dd, 1H, J = 7.7, 7.8 Hz); ^{13}C NMR δ 9.8, 29.6, 35.6, 40.4, 55.0, 111.7, 114.3, 120.9, 129.5, 140.5, 159.6, 173.8; IR (film) 3290, 2940, 1645, 1443, 1226 cm^{-1}; EIMS *m/z* 207, 134 (100), 121, 57. Anal. ($C_{12}H_{17}NO_2$) Calcd: C, 69.53; H, 8.27; N, 6.76. Found: C, 68.47; H, 8.03; N, 5.66.

***N*-Butanoyl-2-(3-methoxyphenyl)ethanamine (5g).** 2-(3-Methoxyphenyl)ethanamine (0.45 g, 2.6 mmol) was treated with butanoic anhydride (1.0 mL) in triethylamine and dichloromethane. Purification by SPC eluting with CH_2Cl_2:2% methanol gave **5g** as a yellow oil (0.45 g, 2.0 mmol, 78%): ^{1}H NMR δ 0.89 (t, 3H, J = 7.4 Hz), 1.60 (m, 2H), 2.07 (t, 2H, J = 7.4 Hz), 2.76 (t, 2H, J = 6.9 Hz), 3.48 (q, 2H, J = 6.0, 6.9 Hz), 3.76 (s, 3H), 5.58 (br s, 1H), 6.70−6.76 (m, 3H), 7.19 (dd, 1H, J = 7.8, 8.0); ^{13}C NMR δ 13.7, 19.1, 35.7, 38.6, 40.3, 55.1, 111.8, 114.3, 121.0, 129.5, 140.5, 159.7, 172.9; IR (film) 3299, 2963, 1638, 1440, 1223 cm^{-1}; EIMS *m/z* 221, 134 (100), 121, 57. Anal. ($C_{13}H_{19}NO_2$) Calcd: C, 70.55; H, 8.65; N, 6.33. Found: C, 69.67; H, 8.49; N, 6.30.

***N*-Pentanoyl-2-(3-methoxyphenyl)ethanamine (5h).** 2-(3-Methoxyphenyl)ethanamine (0.45 g, 2.6 mmol) was treated with valeroyl chloride (0.70 mL) in triethylamine and dichloromethane. Purification by SPC eluting with CH_2Cl_2:1% methanol gave **5h** as a yellow oil (0.52 g, 2.2 mmol, 85%): ^{1}H NMR δ 0.82 (t, 3H, J = 7.3 Hz), 1.25 (m, 2H), 1.50 (m, 2H), 2.08 (t, 2H, J = 7.8 Hz), 2.73 (t, 2H, J = 7.0 Hz), 3.42 (q, 2H, J = 5.9, 7.1 Hz), 3.72 (s, 3H), 6.05 (br s, 1H), 6.68−6.72 (m, 3H), 7.15 (dd, 1H, J = 7.6, 7.9 Hz); ^{13}C NMR δ 13.6, 22.2, 27.7, 35.6, 36.2, 40.3, 54.9, 111.5, 114.2, 120.8, 129.3, 140.4, 159.5, 173.1; IR (film) 3283, 2967, 1645, 1441, 1228 cm^{-1}; EIMS *m/z* 235, 134 (100), 121, 57 (100). Anal. ($C_{14}H_{21}NO_2$) Calcd: C, 71.45; H, 9.00; N, 5.95. Found: C, 70.73; H, 8.82; N, 5.88.

***N*-Acetyl-2-(4-methoxyphenyl)ethanamine (5i).**[18,19] 2-(4-Methoxyphenyl)ethanamine (0.50 g, 3.0 mmol) was treated with acetic anhydride (0.30 mL) in triethylamine and dichloromethane. Purification by SPC eluting with CH_2Cl_2:5% methanol gave **5i** as colorless crystals (0.5 g, 2.6 mmol, 86%): mp 83.5−84.5 °C (lit.[18] mp 85−86 °C); ^{1}H NMR δ 1.96 (s, 3H), 2.78 (t, 2H, J = 7.3 Hz), 3.48 (dt, 2H, J = 5.9, 7.1 Hz), 3.81 (s, 3H), 5.97 (br s, 1H), 6.87 (d, 2H, J = 8.7 Hz), 7.13 (d, 2H, J = 8.6 Hz); ^{13}C NMR δ 23.1, 34.6, 40.8, 55.1, 113.9, 129.5, 130.7, 158.1, 170.1; IR 3287, 3087, 1638, 1515, 1251 cm^{-1}; EIMS *m/z* 193, 134 (100), 121 (100), 78. Anal. ($C_{11}H_{15}NO_2$) C, H, N.

***N*-Propanoyl-2-(4-methoxyphenyl)ethanamine (5j).** 2-(4-Methoxyphenyl)ethanamine (0.50 g, 3.0 mmol) was treated with propanoic anhydride (0.40 mL) in triethylamine and dichloromethane. Purification by SPC eluting with CH_2Cl_2: 2% methanol gave **5j** as colorless crystals (0.4 g, 1.9 mmol, 64%): mp 79−80 °C; ^{1}H NMR δ 1.11 (t, 3H, J = 7.7 Hz), 2.17 (q, 2H, J = 7.5 Hz), 2.74 (t, 2H, J = 7.0 Hz), 3.44 (q, 2H, J = 5.9, 7.1 Hz), 3.76 (s, 3H), 5.60 (br s, 1H), 6.82 (d, 2H, J = 8.7 Hz), 7.07 (d, 2H, J = 8.7 Hz); ^{13}C NMR δ 9.8, 29.6, 34.7, 40.6, 55.1, 113.9, 129.6, 130.8, 158.1, 173.7; IR 3295, 3066, 1639, 1513,1250 cm^{-1}; EIMS *m/z* 207, 134 (100), 121 (100), 78. Anal. ($C_{12}H_{17}NO_2$) C, H, N.

***N*-Butanoyl-2-(4-methoxyphenyl)ethanamine (5k).** 2-(4-Methoxyphenyl)ethanamine (0.50 g, 3.0 mmol) was treated with butanoic anhydride (0.5 mL) in triethylamine and dichloromethane. Purification by SPC eluting with CH_2Cl_2:1% methanol gave **5k** as colorless crystals (0.55 g, 2.5 mmol, 83%): mp 89.5−90.5 °C; ^{1}H NMR δ 0.89 (t, 3H, J = 7.4 Hz), 1.59 (m, 2H), 2.07 (t, 2H, J = 7.8 Hz), 2.72 (t, 2H, J = 7.0 Hz), 3.44 (q, 2H, J = 5.9, 7.0 Hz), 3.76 (s, 3H), 5.60 (br s, 1H), 6.81 (d, 2H, J = 8.7 Hz), 7.07 (d, 2H, J = 8.6 Hz); ^{13}C NMR δ 13.7, 19.1, 34.7, 38.6, 40.6, 55.2, 113.9, 129.6, 130.8, 158.1, 172.9; IR 3285, 3066, 1640, 1518, 1255 cm^{-1}; EIMS *m/z* 221, 134 (100), 121, (100), 78. Anal. ($C_{13}H_{19}NO_2$) C, H, N.

***N*-Pentanoyl-2-(4-methoxyphenyl)ethanamine (5l).** 2-(4-Methoxyphenyl)ethanamine (0.50 g, 3.0 mmol) was treated with valeroyl chloride (0.40 mL) in triethylamine and dichloromethane. Purification by SPC eluting with CH_2Cl_2 gave **5l** as colorless crystals (0.50 g, 2.1 mmol, 71%): mp 77−78 °C; ^{1}H NMR δ 0.85 (t, 3H, J = 7.4 Hz), 1.26 (m, 2H), 1.53 (m, 2H), 2.08 (t, 2H, J = 7.6 Hz), 2.71 (t, 2H, J = 7.0 Hz), 3.42 (q, 2H, J = 6.1, 6.9 Hz), 3.74 (s, 3H), 5.74 (br s, 1H), 6.79 (d, 2H, J = 8.7 Hz), 7.06 (d, 2H, J = 8.7 Hz); ^{13}C NMR δ 13.8, 22.3, 27.8, 34.7, 36.5, 40.7, 55.2, 113.9, 129.6, 130.9, 158.1, 173.2; IR 3290, 3042, 1636, 1499, 1253 cm^{-1}; EIMS *m/z* 235, 134 (100), 121 (100), 78. Anal. ($C_{14}H_{21}NO_2$) C, H, N.

***N*-Acetyl-3-(2-methoxyphenyl)propanamine (6a).** 3-(2-Methoxyphenyl)propanamine (0.40 g, 2.4 mmol) was treated with acetic anhydride (0.3 mL) in triethylamine and dichloromethane to give **6a** as a colorless oil (0.27 g, 1.0 mmol, 43%): ^{1}H NMR δ 1.77 (m, 2H), 1.93 (s, 3H), 2.63 (t, 2H, J = 7.3 Hz), 3.21 (dt, 2H, J = 6.0, 7.0 Hz), 3.78 (s, 3H), 6.33 (br s, 1H), 6.81 (d, 1H, J = 8.2 Hz), 6.86 (dd, 1H, J = 7.4, 7.5 Hz), 7.09 (d, 1H, J = 7.4 Hz), 7.13 (m, 1H); ^{13}C NMR δ 23.0, 27.2, 29.3, 39.0, 55.0, 110.0, 120.3, 127.1, 129.5, 129.6, 157.1, 170.0; IR (film) 3264, 3073, 1646, 1560, 1243 cm^{-1}; EIMS *m/z* 207, 148 (100), 135. Anal. ($C_{12}H_{17}NO_2$) C, H, N.

***N*-Propanoyl-3-(2-methoxyphenyl)propanamine (6b).** 3-(2-Methoxyphenyl)propanamine (0.40 g, 2.4 mmol) was treated with propanoic anhydride (0.3 mL) in triethylamine and dichloromethane to give **6b** as a colorless oil (0.47 g, 1.7 mmol, 71%): ^{1}H NMR δ 1.10 (t, 3H, J = 7.6 Hz), 1.75 (m, 2H), 2.14 (t, 2H, J = 7.6 Hz), 2.61 (t, 2H, J = 7.3 Hz), 3.20 (dt, 2H, J = 5.9, 6.9 Hz), 3.76 (s, 3H), 6.31 (br s, 1H), 6.79 (d, 1H, J = 7.2 Hz), 6.83 (m, 1H), 7.08 (d, 1H, J = 7.3 Hz), 7.13 (m, 1H); ^{13}C NMR δ 9.7, 27.1, 27.2, 29.4, 38.7, 54.9, 109.9, 120.2, 126.9, 129.5, 129.6, 157.0, 173.7; IR (film) 3292, 3070, 1652, 1552, 1244; EIMS *m/z* 221, 148 (100), 135. Anal. ($C_{13}H_{19}NO_2$) Calcd: C, 70.55; H, 8.65; N, 6.33. Found: C, 70.03; H, 8.59; N, 6.25.

***N*-Butanoyl-3-(2-methoxyphenyl)propanamine (6c).** 3-(2-Methoxyphenyl)propanamine (0.40 g, 2.4 mmol) was treated with butanoic anhydride (0.4 mL) in triethylamine and dichloromethane to give **6c** as a yellow oil (0.50 g, 2.1 mmol, 89%): ^{1}H NMR δ 0.91 (t, 3H, J = 7.3 Hz), 1.57 (m, 2H), 1.75 (m, 2H), 2.10 (t, 2H, J = 7.3 Hz), 2.62 (t, 2H, J = 7.6 Hz), 3.22 (dt, 2H, J = 6.2, 6.7 Hz), 3.79 (s, 3H), 5.75 (br s, 1H), 6.81−6.88 (m, 2H), 7.07−7.18 (m, 2H); ^{13}C NMR δ 13.7, 19.1, 27.2, 29.7, 38.7, 38.8, 55.2, 110.2, 120.5, 127.2, 129.8, 129.7, 157.2, 172.8; IR (film) 3312, 3045, 1650, 1550, 1240 cm^{-1}; EIMS *m/z* 235, 148 (100), 135. Anal. ($C_{14}H_{21}NO$) C, H, N.

***N*-Pentanoyl-3-(2-methoxyphenyl)propanamine (6d).** 3-(2-Methoxyphenyl)propanamine (0.40 g, 2.4 mmol) was treated with valeroyl chloride (0.4 mL) in triethylamine and dichloromethane to give **6d** as a pale yellow oil (0.45 g, 1.8 mmol, 75%): ^{1}H NMR δ 0.87 (t, 3H, J = 5.5 Hz), 1.26 (m, 2H), 1.55 (m, 2H), 1.74 (m, 2H), 2.10 (t, 2H, J = 7.9 Hz), 2.60 (t, 2H, J = 7.3 Hz), 3.19 (dt, 2H, J = 6.2, 6.6 Hz), 3.77 (s, 3H), 5.90 (br s, 1H), 6.79−6.85 (m, 2H), 7.06−7.15 (m, 2H); ^{13}C NMR δ 13.7, 20.6, 22.2, 27.2, 29.6, 36.4, 38.8, 55.1, 110.1, 120.4, 127.1, 129.5, 129.7, 157.1, 173.0; IR 3311, 3046, 1648, 1553, 1241 cm^{-1}; EIMS *m/z* 249, 148 (100), 135. Anal. ($C_{15}H_{23}NO_2$) C, H, N.

***N*-Acetyl-3-(3-methoxyphenyl)propanamine (6e).** 3-(3-Methoxyphenyl)propanamine (0.20 g, 1.2 mmol) was treated with acetic anhydride (0.2 mL) in triethylamine and dichloromethane to give **6e** as a colorless oil (0.20 g, 1.0 mmol, 81%) after SPC eluting with CH_2Cl_2:1% methanol: ^{1}H NMR δ 1.78 (m, 2H), 1.90 (s, 3H), 2.58 (t, 2H, J = 7.8 Hz), 3.22 (dt, 2H, J = 6.7, 7.1 Hz), 3.74 (s, 3H), 5.90 (br s, 1H), 6.69−6.75 (m, 3H), 7.15 (m, 1H); ^{13}C NMR δ 23.1, 30.9, 33.2, 39.1, 55.0, 111.1, 114.0, 120.6, 129.3, 143.0, 159.5, 170.1; IR 3260, 3072, 1642, 1542, 1240 cm^{-1}; EIMS *m/z* 207, 148 (100), 135. Anal. ($C_{12}H_{17}NO_2$) C, H, N.

***N*-Propanoyl-3-(3-methoxyphenyl)propanamine (6f).** 3-(3-Methoxyphenyl)propanamine (0.20 g, 1.2 mmol) was treated with propanoic anhydride (0.2 mL) in triethylamine and dichloromethane to give **6f** as a colorless oil (0.25 g, 1.1 mmol, 94%) after SPC with CH_2Cl_2:1% methanol: ^{1}H NMR δ 1.10 (t, 3H, J = 7.4 Hz), 1.81 (m, 2H), 2.13 (q, 2H, J = 7.7

Hz), 2.60 (t, 2H, J = 7.9 Hz), 3.26 (dt, 2H, J = 6.2, 7.0 Hz), 3.76 (s, 3H), 5.54 (br s, 1H), 6.68−6.78 (m, 3H), 7.17 (m, 1H); ^{13}C NMR δ 9.9, 29.7, 31.0, 33.3, 39.1, 55.2, 111.3, 114.0, 120.8, 129.4, 143.1, 159.6, 173.7; IR 3294, 3056, 1651, 1550, 1242 cm^{-1}; EIMS m/z 221, 148 (100), 135. Anal. ($C_{13}H_{19}NO_2$) C, H, N.

***N*-Butanoyl-3-(3-methoxyphenyl)propanamine (6g).** 3-(3-Methoxyphenyl)propanamine (0.20 g, 1.2 mmol) was treated with butanoic anhydride (0.2 mL) in triethylamine and dichloromethane to give **6g** as a colorless oil (0.20 g, 0.9 mmol, 71%) after purification by SPC eluting with CH_2Cl_2:1% methanol: ^{1}H NMR δ 0.90 (t, 3H, J = 5.1 Hz), 1.60 (m, 2H), 1.78 (m, 2H), 2.08 (t, 2H, J = 7.3 Hz), 2.57 (t, 2H, J = 7.4 Hz), 3.23 (dt, 2H, J = 6.2, 7.0 Hz), 3.74 (s, 3H), 5.80 (br s, 1H), 6.68−6.76 (m, 3H), 7.17 (m, 1H); ^{13}C NMR δ 13.6, 19.1, 31.0, 33.2, 38.5, 39.0, 55.0, 111.0, 114.0, 120.6, 129.3, 143.0, 159.5, 173.1; IR 3310, 3042, 1647, 1548, 1244 cm^{-1}; EIMS m/z 235, 148 (100), 135. Anal. ($C_{14}H_{21}NO_2$) Calcd: C, 71.45; H, 9.00; N, 5.95. Found: C, 71.01; H, 8.79; N, 5.85.

***N*-Acetyl-3-(4-methoxyphenyl)propanamine (6h).** 3-(4-Methoxyphenyl)propanamine (0.70 g, 4.2 mmol) was treated with acetic anhydride (0.4 mL) in triethylamine and dichloromethane to give **6h** as a colorless solid (0.37 g, 1.8 mmol, 43%): mp 48−49 °C; ^{1}H NMR δ 1.76 (m, 2H), 1.91 (s, 3H), 2.55 (t, 2H, J = 7.9 Hz), 3.22 (dt, 2H, J = 5.9, 7.1 Hz), 3.74 (s, 3H), 5.80 (br s, 1H), 6.79 (d, 2H, J = 8.7 Hz), 7.05 (d, 2H, J = 8.6 Hz); ^{13}C NMR δ 23.2, 31.3, 32.3, 39.2, 55.2, 113.7, 129.1, 133.4, 157.7, 170.1; IR 3308, 3067, 1640, 1540, 1238 cm^{-1}; EIMS m/z 207, 148 (100), 135. Anal. ($C_{12}H_{17}NO_2$) Calcd: C, 69.53; H, 8.28; N, 6.76. Found: C, 68.83; H, 8.14; N, 6.57.

***N*-Propanoyl-3-(4-methoxyphenyl)propanamine (6i).** 3-(4-Methoxyphenyl)propanamine (0.70 g, 4.2 mmol) was treated with propanoic anhydride (0.55 mL) in triethylamine and dichloromethane to give **6i** as a colorless solid (0.48 g, 2.2 mmol, 52%): mp 56−57 °C; ^{1}H NMR δ 1.10 (t, 3H, J = 7.6 Hz), 1.78 (m, 2H), 2.13 (q, 2H, J = 7.6 Hz), 2.57 (t, 2H, J = 7.6 Hz), 3.25 (dt, 2H, J = 6.2, 6.9 Hz), 3.76 (s, 3H), 5.42 (br s, 1H), 6.79 (d, 2H, J = 8.5 Hz), 7.06 (d, 2H J = 8.4 Hz); ^{13}C NMR δ 9.8, 29.7, 31.4, 32.3, 39.1, 55.2, 113.8, 129.2, 133.4, 157.8, 173.4; IR 3290, 3035, 1653, 1551, 1240 cm^{-1}; EIMS m/z 221, 148 (100), 135. Anal. ($C_{13}H_{19}NO_2$) C, H, N.

***N*-Butanoyl-3-(4-methoxyphenyl)propanamine (6j).** 3-(4-Methoxyphenyl)propanamine (0.70 g, 4.2 mmol) was treated with butanoic anhydride (0.70 mL) in triethylamine and dichloromethane to give **6j** as a colorless solid (0.65 g, 2.8 mmol, 66%): mp 53−54 °C; ^{1}H NMR δ 0.90 (t, 3H, J = 7.4 Hz), 1.60 (m, 2H), 1.76 (m, 2H), 2.08 (t, 2H, J = 7.1 Hz), 2.56 (t, 2H, J = 7.7 Hz), 3.23 (dt, 2H, J = 6.1, 7.0 Hz), 3.75 (s, 3H), 5.70 (br s, 1H), 6.79 (d, 2H, J = 8.5 Hz), 7.06 (d, 2H, J = 8.4 Hz); ^{13}C NMR δ 13.7, 19.1, 31.4, 32.3, 38.6, 39.0, 55.1, 113.7, 129.1, 133.4, 157.7, 172.9; IR 3310, 3026, 1648, 1556, 1232 cm^{-1}; EIMS m/z 235, 148 (100), 135. Anal. ($C_{14}H_{21}NO_2$) C, H, N.

***N*-Propanoyl-4-(2-methoxyphenyl)butanamine (7a).** 4-(2-Methoxyphenyl)butanamine (0.21 g, 1.18 mmol) was treated with propionic anhydride (0.17 g, 0.17 mL, 1.30 mmol) in triethylamine and dichloromethane. Chromatography of the crude product eluting with petroleum ether and then petroleum ether:EtOAc (45:55) gave **7a** (0.24 g, 1.0 mmol, 85%) as a pale yellow oil: ^{1}H NMR δ 1.12 (t, 3H, J = 7.6 Hz), 1.49−1.54 (m, 2H), 1.55−1.61 (m, 2H), 2.16 (q, 2H, J = 7.6 Hz), 2.60 (t, 2H, J = 7.1 Hz), 3.23−3.28 (m, 2H), 3.79 (s, 3H), 5.45 (br s, 1H), 6.81−7.17 (m, 4H); ^{13}C NMR δ 9.95, 27.1, 28.9, 29.4, 29.8, 39.3, 55.2, 110.2, 120.35, 127.0, 129.8, 130.5, 157.4, 173.6. Anal. ($C_{14}H_{21}NO_2$) C, H, N.

***N*-Butanoyl-4-(2-methoxyphenyl)butanamine (7b).** 4-(2-Methoxyphenyl)butanamine (0.21 g, 1.18 mmol) was treated with butyric anhydride (0.21 g, 0.21 mL, 1.30 mmol) in triethylamine and dichloromethane. Chromatography of the crude product eluting with petroleum ether and then petroleum ether: EtOAc (50:50) gave **7b** (0.24 g, 0.94 mmol, 80%) as a pale yellow oil: ^{1}H NMR δ 0.91 (t, 3H, J = 7.4 Hz), 1.49−1.54 (m, 2H), 1.55−1.59 (m, 2H), 1.60−1.66 (m, 2H), 2.10 (t, 2H, J = 7.3 Hz), 2.60 (t, 2H, J = 7.6 Hz), 3.24−3.28 (m, 2H), 3.79 (s, 3H), 5.47 (br s, 1H), 6.81−7.17 (m, 4H); ^{13}C NMR δ 13.8, 19.2, 27.1, 29.4, 29.8, 38.8, 39.3, 55.2, 110.2, 120.3, 127.0, 129.8, 130.5, 157.4, 172.85. Anal. ($C_{15}H_{23}NO_2$) C, H, N.

***N*-Pentanoyl-4-(2-methoxyphenyl)butanamine (7c).** 4-(2-Methoxyphenyl)butanamine (0.21 g, 1.18 mmol) was treated with valeric anhydride (0.24 g, 0.26 mL, 1.30 mmol) in triethylamine and dichloromethane. Chromatography of the crude product eluting with petroleum ether and then petroleum ether:EtOAc (65:35) gave **7c** (0.25 g, 1.0 mmol, 82%) as a yellow oil: ^{1}H NMR δ 0.89 (t, 3H, J = 7.3 Hz), 1.31 (m, 2H, J = 7.6 Hz), 1.49−1.52 (m, 2H), 1.53−1.57 (m, 2H), 1.58−1.62 (m, 2H), 2.12 (t, 2H, J = 7.4 Hz), 2.60 (t, 2H, J = 7.1 Hz), 3.23−3.28 (m, 2H), 3.79 (s, 3H), 5.42 (br s, 1H), 6.81−7.18 (m, 4H); ^{13}C NMR δ 13.8, 22.4, 27.1, 27.9, 29.4, 29.8, 36.7, 39.3, 55.2, 110.2, 120.35, 127.0, 129.8, 130.5, 157.4, 173.0. Anal. ($C_{16}H_{25}NO_2$) C, H, N.

***N*-Propanoyl-4-(3-methoxyphenyl)butanamine (7d).** 4-(3-Methoxyphenyl)butanamine (0.20 g, 1.2 mmol) was treated with propionic anhydride (0.17 g, 0.17 mL, 1.30 mmol) in triethylamine and dichloromethane. Chromatography eluting with petroleum ether and then petroleum ether:EtOAc (45:55) gave pure **7d** (0.23 g, 1.0 mmol, 80%) as a pale yellow oil: ^{1}H NMR δ 1.12 (t, 3H, J = 7.6 Hz), 1.48−1.54 (m, 2H), 1.58−1.64 (m, 2H), 2.15 (q, 2H, J = 7.6 Hz), 2.58 (t, 2H, J = 7.3 Hz), 3.23 (q, 2H, J = 7.2 Hz), 3.77 (s, 3H), 5.45 (br s, 1H), 6.69−7.19 (m, 4H); ^{13}C NMR δ 9.9, 28.5, 29.2, 29.7, 35.45, 39.25, 55.1, 110.95, 114.2, 120.8, 129.2, 143.7, 159.55, 173.7. Anal. ($C_{14}H_{21}NO_2$) C, H, N.

***N*-Butanoyl-4-(3-methoxyphenyl)butanamine (7e).** 4-(3-Methoxyphenyl)butanamine (0.20 g, 1.2 mmol) was treated with butyric anhydride (0.21 g, 0.21 mL, 1.30 mmol) in triethylamine and dichloromethane. Chromatography eluting initially with petroleum ether and then with petroleum ether: EtOAc (50:50) gave pure **7e** (0.25 g, 1.0 mmol, 82%) as a pale yellow oil: ^{1}H NMR δ 0.90 (t, 3H, J = 7.3 Hz), 1.47−1.53 (m, 2H), 1.57−1.62 (m, 2H), 1.62−1.66 (m, 2H), 2.10 (t, 2H, J = 7.3 Hz), 2.57 (t, 2H, J = 7.6 Hz), 3.23 (q, 2H, J = 7.1 Hz), 3.76 (s, 3H, MeO), 5.60 (br s, 1H), 6.69−7.18 (m, 4H); ^{13}C NMR δ 13.7, 19.2, 28.45, 29.15, 35.45, 38.7, 39.2, 55.1, 111.0, 114.15, 120.75, 129.2, 143.7, 159.5, 173.1. Anal. ($C_{15}H_{23}NO_2$) C, H, N.

***N*-Pentanoyl-4-(3-methoxyphenyl)butanamine (7f).** 4-(3-Methoxyphenyl)butanamine (0.20 g, 1.2 mmol) was treated with valeric anhydride (0.24 g, 0.26 mL, 1.30 mmol) in triethylamine and dichloromethane. Chromatography eluting initially with petroleum ether and then with petroleum ether: EtOAc (65:35) gave pure **7f** (0.27 g, 1.0 mmol, 85%) as a yellow oil: ^{1}H NMR δ 0.89 (t, 3H, J = 7.3 Hz), 1.31 (m, 2H), 1.27−1.36 (m, 2H), 1.46−1.60 (m, 2H), 1.62−1.66 (m, 2H), 2.12 (t, 2H, J = 7.6 Hz), 2.59 (t, 2H, J = 7.4 Hz), 3.22−3.26 (m, 2H), 3.77 (s, 3H), 5.38 (br s, 1H), 6.70−7.19 (m, 4H); ^{13}C NMR δ 13.8, 22.4, 27.9, 28.5, 29.2, 35.5, 36.6, 39.3, 55.1, 111.0, 114.2, 120.8, 129.3, 143.75, 159.7, 173.05. Anal. ($C_{16}H_{25}NO_2$) C, H, N.

***N*-Acetyl-4-(4-methoxyphenyl)butanamine (7g).** 4-(4-Methoxyphenyl)butanamine (0.20 g, 1.1 mmol) was treated with acetic anhydride (0.2 mL) in triethylamine and dichloromethane. SPC eluting with CH_2Cl_2:1% methanol and trituration with ether gave **7g** as a pale yellow solid (0.2 g, 0.9 mmol, 81%): mp 39−40 °C; ^{1}H NMR δ 1.48 (m, 2H), 1.57 (m, 2H), 1.91 (s, 3H), 2.53 (t, 2H, J = 6.7 Hz), 3.20 (m, 2H, J = 6.7, 6.4 Hz), 3.75 (s, 3H), 5.72 (br s, 1H), 6.78 (d, J = 8.5 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 7.04 (d, J = 8.5 Hz, 2H); ^{13}C NMR δ 23.2, 28.8, 29.0, 34.5, 39.4, 55.2, 113.7, 129.2, 134.1, 157.7, 170.1; EIMS m/z 221, 162, 121 (100), 57. Anal. ($C_{13}H_{19}NO_2$) Calcd: C, 70.56; H, 8.66; N, 6.33. Found: C, 69.76; H, 8.14; N, 6.11.

***N*-Propanoyl-4-(4-methoxyphenyl)butanamine (7h).** 4-(4-Methoxyphenyl)butanamine (0.20 g, 1.1 mmol) was treated with propanoic anhydride (0.2 mL) in triethylamine and dichloromethane. SPC eluting with CH_2Cl_2:1% methanol and trituration with ether gave **7h** as a pale yellow solid (0.24 g, 1.0 mmol, 91%): mp 31−33 °C; ^{1}H NMR δ 1.11 (t, 2H, J = 7.6 Hz), 1.46−1.51 (m, 2H), 1.54−1.60 (m, 2H), 2.14 (q, 2H, J = 7.6 Hz), 2.54 (t, 2H, J = 7.2 Hz), 3.18−3.24 (m, 2H), 3.75 (s, 3H), 5.65 (br s, 1H), 6.78 (d, 2H, J = 8.7 Hz), 7.04 (d, 2H, J = 8.4 Hz); ^{13}C NMR δ 10.0, 28.9, 29.2, 29.8, 34.6, 39.4, 55.3, 113.8,

129.3, 134.2, 157.8, 173.8; IR 3294, 2939, 1649, 1510, 1243 cm^{-1}; EIMS *m/z* 235, 162, 121 (100), 57. Anal. ($C_{14}H_{21}NO_2$) Calcd: C, 71.45; H, 9.00; N, 5.95. Found: C, 70.66; H, 8.80; N, 5.78.

***N*-Butanoyl-4-(4-methoxyphenyl)butanamine (7i).** 4-(4-Methoxyphenyl)butanamine (0.20 g, 1.1 mmol) was treated with butanoic anhydride (0.3 mL) in triethylamine and CH_2Cl_2. SPC eluting with CH_2Cl_2:1% MeOH gave **7i** as a pale yellow solid (0.2 g, 0.8 mmol, 72%): mp 60−61 °C; ^{1}H NMR δ 0.92 (t, 3H, J = 7.4 Hz), 1.51 (m, 2H), 1.60 (m, 2H), 1.64 (m, 2H), 2.11 (t, 2H, J = 7.3 Hz), 2.55 (t, 2H, J = 7.3 Hz), 3.24 (m, 2H), 3.77 (s, 3H), 5.78 (br s, 1H), 6.80 (d, 2H, J = 8.6 Hz), 7.06 (d, 2H, J = 8.7 Hz); ^{13}C NMR δ 13.7, 19.1, 28.8, 29.0, 34.4, 39.1, 38.6, 55.1, 113.6, 129.1, 134.1, 157.6, 173.0; IR 3292, 2944, 1647, 1515, 1240 cm^{-1}; EIMS *m/z* 249, 162, 121 (100), 57. Anal. ($C_{15}H_{23}NO_2$) C, H, N.

***N*-Pentanoyl-4-(4-methoxyphenyl)butanamine (7j).** 4-(4-Methoxyphenyl)butanamine (0.20 g, 1.1 mmol) was treated with valeroyl chloride (0.3 mL) in triethylamine and CH_2Cl_2. SPC eluting with CH_2Cl_2 gave **7j** as a pale yellow solid (0.25 g, 85%): mp 58−59 °C; ^{1}H NMR δ 0.86 (t, 3H, J = 7.4 Hz), 1.25−1.31 (m, 2H), 1.43−1.50 (m, 2H), 1.51−1.58 (m, 4H), 2.10 (t, 2H, J = 7.4 Hz), 2.52 (t, 2H, J = 7.2 Hz), 3.20 (m, 2H), 3.72 (s, 3H), 6.00 (br s, 1H), 6.77 (d, 2H, J = 8.7 Hz), 7.02 (d, 2H, J = 8.7 Hz); ^{13}C NMR δ 13.7, 22.3, 27.8, 28.8, 29.0, 34.4, 36.4, 39.1, 55.1, 113.6, 129.1, 134.1, 157.6, 173.1; IR 3282, 2952, 1649, 1514, 1242 cm^{-1}; EIMS *m/z* 263, 162, 121 (100), 57. Anal. ($C_{16}H_{25}NO_2$) C, H, N.

***N*-Acetyl-3-(3-fluorophenyl)propanamine (8a).** Acetic anhydride (0.058 g, 0.57 mmol) was added to 3-(3-fluorophenyl)propanamine (0.080 g, 0.52 mmol) in triethylamine and dichloromethane. SPC eluting with CH_2Cl_2:1% MeOH gave **8a** (0.070 g, 0.36 mmol, 69%) as a yellow oil: ^{1}H NMR δ 1.77−1.85 (m, 2H), 1.94 (s, 3H), 2.62 (t, 2H, J = 7.40 Hz), 3.25 (q, 2H), 5.55 (br s, 1H), 6.84−6.93 (m, 3H), 7.18 −7.22 (m, 1H); EIMS *m/z* 196 (100), 149, 109.

***N*-Propanoyl-3-(3-fluorophenyl)propanamine (8b).** Propionic anhydride (0.077 g, 0.60 mmol) was added to 3-(3-fluorophenyl)propanamine (0.080 g, 0.52 mmol) in triethylamine and dichloromethane. SPC eluting with CH_2Cl_2:1% MeOH gave **8b** (0.061 g, 0.29 mmol, 55%) as a yellow oil: ^{1}H NMR δ 1.11 (t, 3H, J = 7.58 Hz), 1.77−1.85 (m, 2H), 2.12−2.18 (m, 2H), 2.62 (t, 2H, J = 7.36 Hz), 3.24−3.29 (m, 2H), 5.45 (br s, 1H), 6.84−6.87 (m, 2H), 6.93 (d, 1H, J = 7.58 Hz), 7.18−7.23 (m, 1H); EIMS *m/z* 210 (100), 109, 57.

***N*-Butanoyl-3-(3-fluorophenyl)propanamine (8c).** Butanoic anhydride (0.088 g, 0.57 mmol) was added to 3-(3-fluorophenyl)propanamine (0.080 g, 0.52 mmol) in triethylamine and dichloromethane. SPC eluting with CH_2Cl_2 gave **8c** (0.049 g, 0.22 mmol, 43%) as a yellow oil: ^{1}H NMR δ 0.92 (t, 3H, J = 7.33 Hz), 1.58−1.68 (m, 2H), 1.74−1.86 (m, 2H), 2.1 (m, 2H), 2.64 (t, 2H, J = 7.5 Hz), 3.24−3.29 (m, 2H), 5.45 (br s, 1H), 6.85−6.9 (m, 2H), 6.94 (d, 1H, J = 7.58 Hz), 7.20−7.26 (m, 1H); EIMS *m/z* 224 (100), 109, 71.

***N*-Acetyl-3-(3-chlorophenyl)propanamine (8d).** Acetic anhydride (0.077 g, 0.8 mmol) was added to 3-(3-chlorophenyl)-propanamine (0.125 g, 0.74 mmol) in triethylamine and dichloromethane. SPC eluting with CH_2Cl_2:1% MeOH gave **8d** (0.11 g, 0.52 mmol, 70%) as a yellow oil: ^{1}H NMR δ 1.78−1.86 (m, 2H), 1.98 (s, 3H), 2.62 (t, 2H, J = 7.8 Hz), 3.26−3.29 (m, 2H), 5.6 (br s, 1H), 7.05 (d, 1H, J = 7.25 Hz), 7.15−7.22 (m, 3H); ^{13}C NMR δ 23.2, 30.9, 32.8, 39.1, 126.3, 126.4, 128.3, 129.7, 134.0, 143.7, 170.0; EIMS *m/z* 212 (100), 170, 149, 125, 85.

***N*-Butanoyl-3-(3-chlorophenyl)propanamine (8e).** Butyric anhydride (0.21 g, 0.21 mL, 1.30 mmol) was added to 3-(3-chlorophenyl)propanamine (0.20 g, 1.2 mmol) in triethylamine and dichloromethane. Chromatography eluting with petroleum ether and then with petroleum ether:AcOEt (1:1) gave pure **8e** (0.20 g, 0.9 mmol, 74%) as a pale yellow oil: ^{1}H NMR δ 0.94 (t, 3H, J = 7.4 Hz), 1.65 (m, 2H), 1.82 (qt, 2H, J = 7.4 Hz), 2.13 (t, 2H, J = 7.3 Hz), 2.62 (t, 2H, J = 7.4 Hz), 3.26−3.31 (m, 2H), 5.61 (br s, 1H), 7.05−7.22 (m, 4H); ^{13}C NMR δ 13.78, 19.19, 31.13, 32.97, 38.75, 39.00, 126.19, 126.57, 128.44, 129.70, 134.18, 143.52, 173.02. Anal. ($C_{13}H_{18}ClNO$) C, H, N.

***N*-Pentanoyl-3-(3-chlorophenyl)propanamine (8f).** Valeric anhydride (0.24 g, 0.26 mL, 1.30 mmol) was added to 3-(3-chlorophenyl)propanamine (0.20 g, 1.2 mmol) in triethylamine and dichloromethane. Chromatography eluting with petroleum ether and then with petroleum ether:EtOAc (7:3) gave pure **8f** (0.24 g, 0.96 mmol, 80%) as a yellow oil: ^{1}H NMR δ 0.89 (t, 3H, J = 7.4 Hz), 1.32 (m, 2H, J = 7.5 Hz), 1.57 (qt, 2H, J = 7.7 Hz), 1.80 (qt, 2H, J = 7.3 Hz), 2.12 (t, 2H, J = 7.5 Hz), 2.60 (t, 2H, J = 7.4 Hz), 3.23−3.28 (m, 2H), 5.46 (br s, 1H), 7.03−7.24 (m, 4H); ^{13}C NMR δ 13.79, 22.40, 27.84, 31.11, 32.97, 36.58, 39.00, 126.18, 126.55, 128.42, 129.69, 134.18, 143.50, 173.13. Anal. ($C_{14}H_{20}ClNO$) C, H, N.

***N*-Acetyl-3-(3-bromophenyl)propanamine (8g).** Acetic anhydride (0.066 g, 0.60 mmol) was added to 3-(3-bromophenyl)propanamine (0.12 g, 0.56 mmol) in triethylamine and dichloromethane. SPC eluting with CH_2Cl_2:1% MeOH gave **8g** (0.09 g, 0.36 mmol, 64%) as a yellow oil: ^{1}H NMR δ 1.75−1.85 (m, 2H), 1.95 (s, 3H), 2.60 (t, 2H, J = 7.6 Hz), 3.25 (m, 2H), 5.6 (br s, 1 H), 7.07−7.30 (m, 4H); ^{13}C NMR δ 23.4, 31.2, 32.9, 39.3, 122.5, 127.1, 129.1, 130.5, 131.4, 143.8, 170.2; EIMS *m/z* 258 (M^++ 1), 256, 178, 149, 85 (100).

***N*-Propanoyl-3-(3-bromophenyl)propanamine (8h).** Propionic anhydride (0.077 g, 0.60 mmol) was added to 3-(3-bromophenyl)propanamine (0.12 g, 0.56 mmol) in triethylamine and dichloromethane. SPC eluting with CH_2Cl_2:1% MeOH gave **8h** (0.09 g, 0.34 mmol, 61%) as a yellow oil: ^{1}H NMR δ 1.05−1.96 (m, 3H), 1.76−1.88 (m, 2H), 2.05−2.20 (m, 2H), 2.93−3.07 (m, 2H), 3.20−3.29 (m, 2H), 5.42 (br s, 1H), 7.04−7.39 (m, 4H); EIMS *m/z* 272 (M^++1), 270, 236, 136, 91.

***N*-Butanoyl-3-(3-bromophenyl)propanamine (8i).** Butyric anhydride (0.10 g, 0.60 mmol) was added to 3-(3-bromophenyl)propanamine (0.12 g, 0.56 mmol) in triethylamine and dichloromethane. SPC eluting with CH_2Cl_2:1% MeOH gave **8i** (0.07 g, 0.25 mmol, 45%) as a pale yellow oil: ^{1}H NMR δ 0.80−0.98 (m, 3H), 1.55−1.65 (m, 2H), 1.72−1.85 (m, 2H), 2.04−2.15 (m, 2H), 2.53−2.63 (m, 2H), 3.20−3.29 (m, 2H), 5.6 (br s, 1H), 7.02−7.4 (m, 4H); ^{13}C NMR δ 13.7, 19.7, 31.1, 33.3, 35.7, 38.5, 39.1, 122.4, 127.2, 129.1, 130.0, 143.8, 173.05; EIMS *m/z* 284 (M^++ 1), 282, 206, 149, 71.

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