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REACTION OF *N*-TOSYLATED IMINES WITH α,β-ACETYLENIC KETONES VIA ORGANOZINC SPECIES

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A new procedure for stereoselective synthesis of trisubstituted alkenes by an one-pot, three-component reaction of* N*-tosylated imines with α,β-acetylenic ketones and organozinc species $CF_3COOZnEt$ was described. This reaction system provides β-branched Morita–Baylis–Hillman adducts with excellent yields in absence of any catalyst.

Keywords: α,β-Acetylenic ketones; $CF_3COOZnEt$; *N*-tosylated imines; trisubstituted alkenes

INTRODUCTION

Among the reactions in which C–C bonds are formed, the Morita–Baylis–Hillman reaction (MBH) is one of the most economical and important carbon–carbon bond-forming reactions.[1,2] The MBH adducts, which are allylic alcohol or allylic amine derivatives, play an important role in bringing latitude to organic synthesis and in the construction of molecular assemblies as useful intermediates.[3] However, this reaction suffers from slow reaction rates, which limit the scope of substrates.[4] Many methods to accelerate the reaction rate, such as change in catalyst, irradiation with microwaves, reaction under high pressure, and reaction in ionic liquids, have been developed.[5–7]

Organozinc reagents have been widely used in the conjugate addition to various reagents.[8–10] Nevertheless, the reaction of organozinc reagents with α,β-acetylenic ketones has not been reported thus far.[11,12] Recently, we reported a new procedure for synthesis of β-branched MBH adducts by the reaction of α,β-acetylenic ketones with organozinc species and aldehydes.[13] In continuation of our interest in exploring the reactivity and behavior of the organozinc species CF_3CO_2ZnR with electrophiles, we wanted to examine reactions of *N*-tosylated imines with α,β-acetylenic ketones and the organozinc species $CF_3COOZnEt$. Fortunately, $CF_3COOZnEt$ can react with

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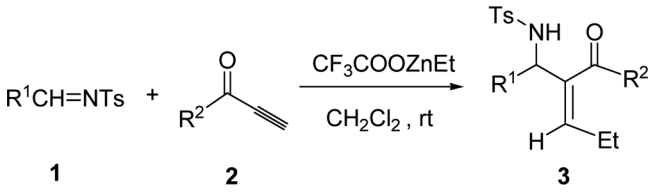


Scheme 1. The reaction of *N*-tosylated imines with α,β-acetylenic ketones in the presence of $CF_3COOZnEt$.

terminal α,β-acetylenic ketones and *N*-tosylated imines with good yields in absence of any catalyst (Scheme 1). Here we report these results.

RESULTS AND DISCUSSION

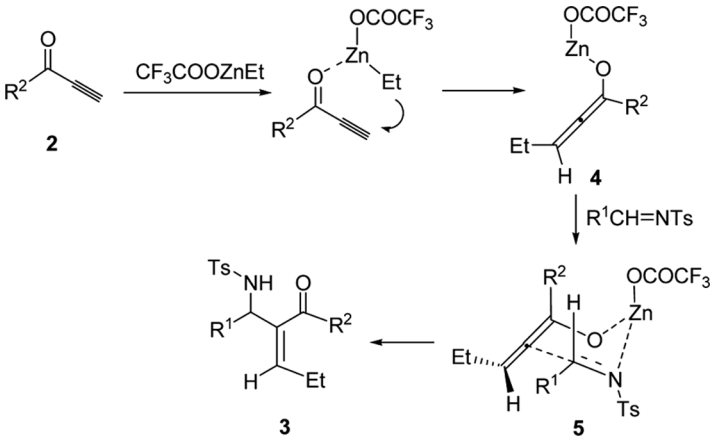
Initially, we carried out reactions using different quantities of reagents in CH_2Cl_2. The best results were obtained with a 1.0:1.5:1.5 ratio of *N*-tosylated imines, α,β-acetylenic ketones, and $CF_3COOZnEt$. Treatment of the in situ–generated CF_3CO_2ZnEt[13,14] with 1-phenylprop-2-yn-1-one and *N*-benzylidene-4-methylbenzenesulfonamide in CH_2Cl_2 at room temperature for 10 h generated β-substituted Baylis–Hillman adducts **3a** in 94% isolated yield (entry 1, Table 1). The reaction was performed in diethyl ether and tetrahydrofuran (THF) and gave the desired adducts **3a** in 5% and 21% respectively. Thus, CH_2Cl_2 was the solvent of choice.

With the optimal reaction conditions in hand, a variety of α,β-acetylenic ketones were then allowed to react with *N*-tosylated imines and CF_3CO_2ZnEt. These results are presented in Table 1. Both aliphatic and aromatic acetylenic ketones could be employed. The reaction of aromatic acetylenic ketones with *N*-tosylated imines proceeded smoothly and provided the corresponding products in good yields. The substituents on the benzene ring of aromatic acetylenic ketones seem to have no obvious effect on the yields. However, it should be noted that 1-(4-nitrophenyl)prop-2-yn-1-one provided the desired product **3l** in a moderate yield (52%) at room temperature (Table 1, entry 14), which was due to the high reactivity of the acetylenic ketone, leading to formation of the direct self-condensation product. [The 1,4-conjugate addition of $CF_3COOZnEt$ to α,β-acetylenic ketone generates an allenolate 4 (Scheme 2), which reacts with secondary α,β-acetylenic ketone to form a small amount of self-condensation products as by-products.] When the reaction temperature decreased to 0 °C, the yield of **3l** increased to 64%. Aliphatic α,β-acetylenic ketones, instead of aromatic α,β-acetylenic ketones, can also react with *N*-tosylated imines to provide the β-branched MBH adducts in moderate yields. The poor yields obtained might be ascribed to the lesser reactivity of aliphatic acetylenic ketones than that of aromatic acetylenic ketones. On the other hand, various *N*-tosylated imines were submitted to this reaction, and the corresponding products were obtained in good yields. The substituents on the benzene ring of *N*-tosylated imines seem to have no obvious effect on the yields. The stereochemistry of the β-branched Baylis–Hillman adducts was determined to be *Z* configuration for all cases in our reaction system as revealed by ^1H NMR analyses of the crude products. The *E*-isomer of the product was not observed from the ^1H and ^{13}C NMR spectra.

Table 1. Reactions of *N*-tosylated imines with α,β-acetylenic ketones and $CF_3COOZnEt$

Entry	R^1	R^2	Product	Yield[a] (%)
1	C_6H_5	C_6H_5	**3a**	94
2	C_6H_5	C_6H_5	**3a**	5[b]
3	C_6H_5	C_6H_5	**3a**	21[c]
4	C_6H_5	4-MeC_6H_4	**3b**	91
5	C_6H_5	4-$MeOC_6H_4$	**3c**	90
6	C_6H_5	4-ClC_6H_4	**3d**	86
7	C_6H_5	CH_3	**3e**	75
8	4-MeC_6H_4	C_6H_5	**3f**	85
9	4-MeC_6H_4	4-MeC_6H_4	**3g**	84
10	4-MeC_6H_4	4-$MeOC_6H_4$	**3h**	81
11	4-MeC_6H_4	4-FC_6H_4	**3i**	93
12	4-MeC_6H_4	4-ClC_6H_4	**3j**	89
13	4-MeC_6H_4	4-BrC_6H_4	**3k**	85
14	4-MeC_6H_4	4-$NO_2C_6H_4$	**3l**	52 (64)[d]
15	4-MeC_6H_4	CH_3	**3m**	73
16	4-MeC_6H_4	C_6H_{13}	**3n**	78
17	4-$MeOC_6H_4$	C_6H_5	**3o**	90
18	4-$MeOC_6H_4$	4-$MeOC_6H_4$	**3p**	88
19	4-$MeOC_6H_4$	4-BrC_6H_4	**3q**	86
20	4-$MeOC_6H_4$	CH_3	**3r**	74
21	4-ClC_6H_4	4-$MeOC_6H_4$	**3s**	92
22	4-ClC_6H_4	4-FC_6H_4	**3t**	95
23	2-ClC_6H_4	4-MeC_6H_4	**3u**	88
24	2-ClC_6H_4	4-BrC_6H_4	**3v**	87

[a]Yields after purification by column chromatography.
[b]Performed in Et_2O.
[c]Performed in THF.
[d]Performed at 0 °C.



Scheme 2. Plausible mechanism for the reaction.

Based on the works of Kitamura et al.[15] and Taniguchi et al.,[16] a plausible mechanism of the reaction was proposed, as shown in Scheme 2. The first step of the reaction is the 1,4-conjugate addition of the organozinc species $CF_3COOZnEt$ to α,β-acetylenic ketone to form an active allenolate intermediate **4**. The *N*-tosylated imine coordinates with the zinc atom, which serves to orient *N*-tosylated imines for attack on allenolate. Therefore, the steric interaction between *N*-tosylated imine R^1 group and Et at the β-position of the allenolate dominates the stereochemistry of this reaction. The *N*-tosylated imine attacks the allenolate from the less hindered side of the allenolate **4** to provide *Z*-isomer as the product.

In conclusion, an efficient method for the synthesis of functionalized trisubstituted olefins has been developed. The reactions of *N*-tosylated imines with α,β-acetylenic ketones and organozinc species CF_3CO_2ZnEt proceed smoothly in the absence of any catalyst. The procedure can be subjected to aliphatic and aromatic α,β-acetylenic ketones, which affords β-branched MBH adducts in moderate to excellent yields.

EXPERIMENTAL

General Procedure: Reaction of *N*-Tosylated Imines with α,β-Acetylenic Ketones and CF_3CO_2ZnEt

CF_3COOH (58 μL, 0.75 mmol) slowly was added dropwise via syringe to a solution of Et_2Zn (80 μL, 0.75 mmol) in 2 mL CH_2Cl_2 at 0 °C under N_2. After stirring for 30 min at 0 °C, *N*-tosylated imines (0.5 mmol) were added, and then acetylenic ketone (0.75 mmol) was added. The mixture was stirred for 10 h at room temperature until thin-layer chromatography (TLC) indicated complete consumption of the starting *N*-tosylated imines. The reaction was quenched by saturated aqueous NH_4Cl and extracted with Et_2O (3×10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to an oily residue. The desired product was isolated by silica-gel chromatography with petroleum ether/EtOAc (5:1–3:1).

Spectral Data

Compound 3a. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.80 (t, $J = 7.5$ Hz, 3H), 1.68 – 1.80 (m, 2H), 2.42 (s, 3H), 5.26 (d, $J = 7.8$ Hz, 1H), 5.82 (t, $J = 7.5$ Hz, 1H), 6.08 (d, $J = 7.8$ Hz, 1H), 7.17 – 7.24 (m, 7H), 7.31 – 7.40 (m, 2H), 7.53 (t, $J = 7.5$ Hz, 1H), 7.61 (d, $J = 6.9$ Hz, 2H), 7.73 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.5, 23.4, 62.1, 126.9, 127.3, 127.7, 128.56, 128.58, 129.1, 129.5, 133.5, 136.8, 137.6, 137.9, 138.6, 138.8, 143.2, 199.1. IR (neat): 3284, 1648, 1596, 1449, 1330, 1238, 1161 cm^{-1}. HRMS (EI) calcd. for $C_{18}H_{18}NO$ ($M-Ts^+$): 264.1388; found 264.1392.

Compound 3b. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.72 (t, $J = 7.5$ Hz, 3H), 1.64 (m, 2H), 2.33 (s, 3H), 2.34 (s, 3H), 5.19 (d, $J = 7.8$ Hz, 1H), 5.69 (t, $J = 7.5$ Hz, 1H), 6.14 (d, $J = 7.8$ Hz, 1H), 7.12 – 7.17 (m, 9H), 7.46 (d, $J = 8.1$ Hz, 2H), 7.66 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.2, 21.4, 21.7, 23.3, 62.0, 126.9, 127.2, 127.5, 128.4, 129.2, 129.3, 129.4, 134.9, 136.8, 137.86, 137.92, 138.8,

143.0, 144.5, 198.7. IR (neat): 3285, 3028, 1622, 1604, 1414, 1341, 1162, 1094 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{20}NO$ ($M-Ts^+$): 278.1545; found 278.1541.

Compound 3c. ^1H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.80 (t, $J=7.5$ Hz, 3H), 1.70 (m, 2H), 2.41 (s, 3H), 3.75 (s, 3H), 5.21 (d, $J=7.5$ Hz, 1H), 5.82 (t, $J=7.5$ Hz, 1H), 6.03 (d, $J=7.5$ Hz, 1H), 6.74 (d, $J=8.7$ Hz, 2H), 7.12 (d, $J=8.7$ Hz, 2H), 7.22 (d, $J=8.1$ Hz, 2H), 7.38 (t, $J=7.5$ Hz, 2H), 7.53 (d, $J=7.5$ Hz, 1H), 7.65 (d, $J=7.5$ Hz, 2H), 7.71 (d, $J=8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.5, 23.3, 55.2, 61.2, 113.9, 127.2, 128.2, 128.5, 129.1, 129.4, 130.9, 133.4, 137.1, 137.5, 137.8, 138.0, 143.1, 159.0, 199.1. IR (neat): 3283, 1710, 1647, 1596, 1571, 1508, 1455, 1421, 1323, 1258, 1160 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{20}NO_2$ ($M-Ts^+$): 294.1494; found 294.1493.

Compound 3d. ^1H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.73 (t, $J=7.5$ Hz, 3H), 1.55 – 1.70 (m, 2H), 2.34 (s, 3H), 5.22 (d, $J=8.4$ Hz, 1H), 5.76 (t, $J=7.5$ Hz, 1H), 6.13 (d, $J=8.4$ Hz, 1H), 7.09 – 7.15 (m, 7H), 7.25 – 7.29 (m, 2H), 7.51 (d, $J=8.7$ Hz, 2H), 7.63 (d, $J=8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.5, 23.4, 61.7, 126.9, 127.2, 127.7, 128.6, 128.9, 129.5, 130.5, 135.8, 136.8, 137.8, 138.3, 138.6, 140.0, 143.2, 197.8. IR (KBr): 3292, 1625, 1588, 1449, 1402, 1340, 1231, 1161 cm^{-1}. HRMS (EI) calcd. for $C_{18}H_{17}NOCl$ ($M-Ts^+$): 298.0999; found 298.0994.

Compound 3e. ^1H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.94 (t, $J=7.5$ Hz, 3H), 2.07 (s, 3H), 2.22 (m, 2H), 2.39 (s, 3H), 5.15 (d, $J=8.9$ Hz, 1H), 5.65 (d, $J=8.9$ Hz, 1H), 5.73 (t, $J=7.5$ Hz, 1H), 7.28 – 7.10 (m, 7H), 7.65 (d, $J=8.1$ Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.7, 21.5, 23.1, 31.9, 61.6, 126.7, 127.3, 127.6, 128.6, 129.5, 138.1, 138.8, 139.1, 142.0, 143.3, 203.2. IR (KBr): 2963, 1656, 1494, 1418, 1330, 1262, 1160 cm^{-1}. HRMS (EI) calcd. for $C_{13}H_{16}NO$ ($M-Ts^+$): 202.1232; found 202.1235.

Compound 3f. ^1H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.65 (t, $J=7.5$ Hz, 3H), 1.58 (m, 2H), 2.13 (s, 3H), 2.27 (s, 3H), 5.09 (d, $J=7.5$ Hz, 1H), 5.90 (t, $J=7.5$ Hz, 1H), 6.33 (d, $J=7.5$ Hz, 1H), 7.03 (d, $J=8.1$ Hz, 2H), 7.09 (d, $J=8.1$ Hz, 2H), 7.20 (d, $J=8.1$ Hz, 2H), 7.38 (t, $J=7.5$ Hz, 2H), 7.53 (t, $J=7.5$ Hz, 1H),7.66 (d, $J=7.5$ Hz, 2H), 7.70 (d, $J=8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.1, 21.5, 23.4, 61.7, 126.9, 127.3, 128.6, 129.2, 129.3, 129.5, 133.5, 135.8, 137.0, 137.4, 137.6, 137.9, 138.4, 143.1, 199.1. IR (KBr): 3293, 1623, 1595, 1509, 1425, 1382, 1332, 1156 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{20}NO$ ($M-Ts^+$): 278.1545; found 278.1543.

Compound 3g. ^1H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.72 (t, $J=7.5$ Hz, 3H), 1.64 (m, 2H), 2.21 (s, 3H), 2.33 (s, 3H), 2.34 (s, 3H), 5.66 (d, $J=7.8$ Hz, 1H), 5.70 (t, $J=7.5$ Hz, 1H), 6.12 (d, $J=7.8$ Hz, 1H), 6.95 (d, $J=7.8$ Hz, 2H), 7.07 – 7.12 (m, 6H), 7.50 (d, $J=8.1$ Hz, 2H), 7.65 (d, $J=8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.2, 21.0, 21.4, 21.7, 23.2, 61.7, 126.8, 127.2, 129.1, 129.16, 129.22, 129.3, 135.0, 135.8, 137.0, 137.1, 137.7, 137.9, 143.0, 144.4, 198.6. IR (KBr): 3268, 1626, 1602, 1513, 1427, 1384, 1341, 1262, 1161 cm^{-1}. HRMS (EI) calcd. for $C_{20}H_{22}NO$ ($M-Ts^+$): 292.1701; found 292.1694.

Compound 3h. ^1H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.80 (t, $J=7.5$ Hz, 3H), 1.63 – 1.82 (m, 2H), 2.28 (s, 3H), 2.42 (s, 3H), 3.88 (s, 3H), 5.17 (d, $J=7.5$ Hz, 1H),

5.72 (t, $J = 7.5$ Hz, 1H), 6.10 (d, $J = 7.5$ Hz, 1H), 6.85 (d, $J = 8.7$ Hz, 2H), 7.01 (d, $J = 8.1$ Hz, 2H), 7.11 (d, $J = 8.1$ Hz, 2H), 7.22 (d, $J = 8.1$ Hz, 2H), 7.64 (d, $J = 8.7$ Hz, 2H), 7.72 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.0, 21.5, 23.2, 55.5, 61.8, 113.8, 126.8, 127.3, 129.1, 129.4, 130.4, 131.7, 135.8, 137.0, 137.1, 137.2, 137.9, 143.0, 164.0, 197.5. IR (neat): 3428, 1956, 1682, 1493, 1453, 1372, 1212 cm^{-1}. HRMS (EI) calcd. for $C_{20}H_{22}NO_2$ ($M-Ts^+$): 308.1651; found 308.1653.

Compound 3i. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.77 (t, $J = 7.5$ Hz, 3H), 1.60 – 1.75 (m, 2H), 2.23 (s, 3H), 2.37 (s, 3H), 5.13 (d, $J = 7.5$ Hz, 1H), 5.76 (d, $J = 7.5$ Hz, 2H), 5.79 (t, $J = 7.8$ Hz, 2H), 6.95 – 7.03 (m, 6H), 7.18 (d, $J = 8.1$ Hz, 2H), 7.61 – 7.68 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.0, 21.5, 23.3, 61.5, 115.6, 115.9, 126.8, 127.3, 129.2, 129.4, 131.8, 132.0, 133.8, 135.6, 137.0, 137.4, 137.8, 143.2, 197.4. IR (neat): 3435, 1683, 1611, 1585, 1512, 1249, 1174 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{19}NOF$ ($M-Ts^+$): 296.1451; found 296.1450.

Compound 3j. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.77 (t, $J = 7.5$ Hz, 3H), 1.58 – 1.74 (m, 2H), 2.23 (s, 3H), 2.37 (s, 3H), 5.13 (d, $J = 7.5$ Hz, 1H), 5.77 (d, $J = 7.5$ Hz, 1H), 5.80 (t, $J = 7.5$ Hz, 1H), 6.93 – 7.04 (m, 4H), 7.18 (d, $J = 8.4$ Hz, 2H), 7.30 (d, $J = 8.7$ Hz, 2H), 7.53 (d, $J = 8.7$ Hz, 2H), 7.65 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.1, 21.5, 23.4, 61.4, 126.8, 127.3, 128.9, 129.2, 129.3, 129.4, 130.6, 125.6, 136.9, 137.5, 137.8, 138.2, 140.0, 143.2, 197.7. IR (neat): 3298, 1635, 1587, 1509, 1421, 1340, 1231, 1160 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{19}NOCl$ ($M-Ts^+$): 312.1155; found 312.1154.

Compound 3k. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.77 (t, $J = 7.5$ Hz, 3H), 1.70 (m, 2H), 2.23 (s, 3H), 2.37 (s, 3H), 5.13 (d, $J = 7.5$ Hz, 1H), 5.78 (t, $J = 7.5$ Hz, 1H), 5.82 (d, $J = 7.5$ Hz, 1H), 6.97 – 7.03 (m, 4H), 7.18 (d, $J = 8.1$ Hz, 2H), 7.44 – 7.49 (m, 4H), 7.65 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.1, 21.5, 23.4, 61.3, 126.8, 127.2, 128.7, 129.3, 129.4, 130.6, 131.9, 135.6, 136.3, 136.9, 137.4, 137.7, 138.2, 143.2, 197.9. IR (neat): 3441, 2923, 1633, 1596, 1505, 1422, 1340, 1227, 1160 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{19}NOBr$ ($M-Ts^+$): 356.0650; found 356.0648.

Compound 3l. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.79 (t, $J = 7.5$ Hz, 3H), 1.66 – 1.73 (m, 2H), 2.22 (s, 3H), 2.37 (s, 3H), 5.19 (d, $J = 7.5$ Hz, 1H), 5.74 (t, $J = 7.8$ Hz, 1H), 5.97 (d, $J = 7.5$ Hz, 1H), 6.95 – 6.99 (m, 4H), 7.18 (d, $J = 7.8$ Hz, 2H), 7.65 (d, $J = 7.8$ Hz, 2H), 7.74 (d, $J = 8.4$ Hz, 2H), 8.17 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.1, 21.6, 23.6, 61.3, 123.9, 126.8, 127.3, 129.5, 129.6, 130.0, 135.4, 137.0, 137.7, 137.9, 139.6, 142.3, 143.5, 150.5, 197.4. IR (neat): 3234, 2964, 1665, 1560, 1524, 1431, 1345, 1262, 1239, 1158 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{19}N_2O_3$ ($M-Ts^+$): 323.1396; found 323.1400.

Compound 3m. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.94 (t, $J = 7.5$ Hz, 3H), 2.05 (s, 3H), 2.14 (m, 2H), 2.26 (s, 3H), 2.37 (s, 3H), 5.10 (d, $J = 8.9$ Hz, 1H), 5.65 (d, $J = 8.9$ Hz, 1H), 5.73 (t, $J = 7.5$ Hz, 1H), 6.98 – 7.01 (m, 4H), 7.19 (d, $J = 8.1$ Hz, 2H), 7.63 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.7, 21.1, 21.5, 23.1, 31.9, 61.3, 126.6, 127.3, 129.3, 129.5, 136.1, 137.4, 138.1, 138.9, 141.7, 143.2, 203.2. IR (neat): 3240, 2920, 2837, 1655, 1428, 1334, 1164 cm^{-1}. HRMS (EI) calcd. for $C_{14}H_{18}NO$ ($M-Ts^+$): 216.1388; found 216.1387.

Compound 3n. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.83 (t, $J = 7.2$ Hz, 3H), 0.91 (t, $J = 7.5$ Hz, 3H), 1.04 – 1.22 (m, 6H), 1.25 – 1.36 (m, 2H), 1.96 – 2.17 (m, 4H), 2.27 (s, 3H), 2.38 (s, 3H), 5.09 (d, $J = 8.7$ Hz, 1H), 5.61 (t, $J = 7.5$ Hz, 1H), 5.72 (d, $J = 8.7$ Hz, 1H), 6.98 – 7.02 (m, 4H), 7.19 (d, $J = 8.1$ Hz, 2H), 7.64 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.8, 14.1, 21.1, 21.5, 22.5, 23.0, 23.6, 28.7, 31.6, 44.1, 61.3, 126.8, 127.3, 129.3, 129.5, 136.0, 137.4, 137.1, 139.4, 139.5, 143.2, 206.8. IR (neat): 3297, 1658, 1512, 1418, 1339, 1161 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{28}NO$ ($M-Ts^+$): 286.2171; found 286.2166.

Compound 3o. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.80 (t, $J = 7.5$ Hz, 3H), 1.70 (m, 2H), 2.41 (s, 3H), 3.75 (s, 3H), 5.21 (d, $J = 7.5$ Hz, 1H), 5.82 (t, $J = 7.5$ Hz, 1H), 6.03 (d, $J = 7.5$ Hz, 1H), 6.74 (d, $J = 8.7$ Hz, 2H), 7.12 (d, $J = 8.7$ Hz, 2H), 7.22 (d, $J = 8.1$ Hz, 2H), 7.38 (t, $J = 7.5$ Hz, 2H), 7.53 (d, $J = 7.5$ Hz, 1H), 7.65 (d, $J = 7.5$ Hz, 2H), 7.71 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.5, 23.3, 55.2, 61.2, 113.9, 127.2, 128.2, 128.5, 129.1, 129.4, 130.9, 133.4, 137.1, 137.5, 137.8, 138.0, 143.1, 159.0, 199.1. IR (neat): 3215, 1633, 1511, 1436, 1330, 1243, 1158 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{20}NO_2$ ($M-Ts^+$): 294.1494; found 294.1493.

Compound 3p. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.74 (t, $J = 7.5$ Hz, 3H), 1.60 – 1.74 (m, 2H), 2.35 (s, 3H), 3.70 (s, 3H), 3.82 (s, 3H), 5.11 (d, $J = 7.5$ Hz, 1H), 5.65 (t, $J = 7.5$ Hz, 1H), 6.04 (d, $J = 7.5$ Hz, 1H), 6.67 (d, $J = 8.4$ Hz, 2H), 6.79 (d, $J = 8.7$ Hz, 2H), 7.07 (d, $J = 8.7$ Hz, 2H), 7.16 (d, $J = 8.1$ Hz, 2H), 7.58 (d, $J = 8.7$ Hz, 2H), 7.65 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.4, 23.2, 55.2, 55.5, 61.5, 113.78, 113.80, 127.2, 128.1, 129.4, 130.3, 130.9, 131.7, 136.8, 137.0, 137.9, 143.0, 158.9, 164.0, 197.6. IR (neat): 3278, 1600, 1509, 1421, 1341, 1253, 1161, 1094 cm^{-1}. HRMS (EI) calcd. for $C_{20}H_{22}NO_3$ ($M-Ts^+$): 324.1600; found 324.1598.

Compound 3q. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.78 (t, $J = 7.5$ Hz, 3H), 1.63 – 1.79 (m, 2H), 2.39 (s, 3H), 3.73 (s, 3H), 5.18 (d, $J = 8.1$ Hz, 1H), 5.81 (t, $J = 7.8$ Hz, 1H), 6.03 (d, $J = 8.1$ Hz, 1H), 6.70 (d, $J = 8.4$ Hz, 2H), 7.05 (d, $J = 8.4$ Hz, 2H), 7.18 (d, $J = 8.1$ Hz, 2H), 7.47 – 7.51 (m, 4H), 7.66 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.3, 21.5, 23.3, 55.2, 60.9, 113.9, 127.2, 128.2, 128.8, 129.4, 130.6, 130.7, 131.9, 136.2, 137.0, 137.7, 137.9, 143.2, 159.1, 198.0. IR (neat): 3313, 2929, 1635, 1581, 1510, 1399, 1340, 1252 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{19}NO_2Br$ ($M-Ts^+$): 372.0599; found 372.0598.

Compound 3r. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.94 (t, $J = 7.5$ Hz, 3H), 2.05 (s, 3H), 2.14 (m, 2H), 2.39 (s, 3H), 3.75 (s, 3H), 5.10 (d, $J = 8.7$ Hz, 1H), 5.65 (d, $J = 8.7$ Hz, 1H), 5.73 (t, $J = 7.5$ Hz, 1H), 6.73 (d, $J = 8.7$ Hz, 2H), 7.03 (d, $J = 8.7$ Hz, 2H), 7.21 (d, $J = 8.1$ Hz, 2H), 7.64 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.8, 21.6, 23.1, 31.9, 55.4, 61.0, 114.0, 127.3, 128.0, 129.5, 131.2, 138.1, 139.1, 141.3, 143.2, 159.1, 203.4. IR (neat): 3284, 1660, 1608, 1511, 1424, 1335, 1249 cm^{-1}. HRMS (EI) calcd. for $C_{14}H_{18}NO_2$ ($M-Ts^+$): 232.1338; found 232.1342.

Compound 3s. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.76 (t, $J = 7.5$ Hz, 3H), 1.60 – 1.70 (m, 2H), 2.39 (s, 3H), 3.85 (s, 3H), 2.17 (d, $J = 7.5$ Hz, 1H), 5.66 (t, $J = 7.8$ Hz, 1H), 6.30 (d, $J = 7.5$ Hz, 1H), 6.83 (d, $J = 9.0$ Hz, 2H), 7.13 – 7.17 (m, 4H), 7.19 (d, $J = 8.1$ Hz, 2H), 7.58 (d, $J = 8.7$ Hz, 2H), 7.66 (d, $J = 8.1$ Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.2, 21.5, 23.4, 55.6, 61.6, 113.9, 127.2, 128.3, 128.6, 129.5, 131.7, 132.2, 133.4, 136.3, 137.5, 137.8, 138.0, 143.3, 164.2, 197.3. IR (neat): 3278, 1647, 1596, 1491, 1421, 1334, 1258 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{19}NO_2Cl$ ($M-Ts^+$): 328.1104; found 328.1099.

Compound 3t. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.76 (t, $J = 7.5$ Hz, 3H), 1.63 – 1.73 (m, 2H), 2.38 (s, 3H), 5.15 (d, $J = 7.8$ Hz, 1H), 5.75 (t, $J = 7.8$ Hz, 1H), 5.97 (d, $J = 7.8$ Hz, 1H), 6.99 – 7.26 (m, 8H), 7.56 – 7.65 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.2, 21.5, 23.5, 61.2, 115.8, 116.1, 127.2, 128.4, 129.1, 129.5, 131.8, 132.0, 133.6, 136.4, 137.3, 137.7, 138.8, 143.5, 197.2. IR (KBr): 3303, 1625, 1605, 1510, 1421, 1385, 1342, 1253 cm^{-1}. HRMS (EI) calcd. for $C_{18}H_{16}NOFCl$ ($M-Ts^+$): 318.0885; found 318.0882.

Compound 3u. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.74 (t, $J = 7.5$ Hz, 3H), 1.56 – 1.75 (m, 2H), 2.36 (s, 6H), 5.52 (d, $J = 7.5$ Hz, 1H), 5.58 (t, $J = 8.1$ Hz, 1H), 6.38 (d, $J = 7.5$ Hz, 1H), 7.03 – 7.22 (m, 6H), 7.27 – 7.35 (m, 2H), 7.49 (d, $J = 8.1$ Hz, 2H), 7.69 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.2, 21.5, 21.8, 23.5, 58.9, 127.1, 127.3, 128.9, 129.1, 129.2, 129.3, 129.4, 129.5, 132.4, 134.3, 134.7, 136.0, 137.4, 138.7, 143.2, 144.8, 198.9. IR (neat): 3286, 1654, 1603, 1444, 1338, 1239, 1162 cm^{-1}. HRMS (EI) calcd. for $C_{19}H_{19}NOCl$ ($M-Ts^+$): 312.1155; found 312.1152.

Compound 3v. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 0.74 (t, $J = 7.5$ Hz, 3H), 1.60 – 1.71 (m, 2H), 2.34 (s, 3H), 5.49 (d, $J = 7.5$ Hz, 1H), 5.61 (t, $J = 7.5$ Hz, 1H), 6.15 (d, $J = 7.5$ Hz, 1H), 7.05 – 7.20 (m, 6H), 7.41–7.47 (m, 4H), 7.65 (d, $J = 8.1$ Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ, ppm: 13.2, 21.5, 23.4, 58.9, 115.7, 116.0, 127.2, 127.4, 129.1, 129.2, 129.5, 129.6, 131.8, 131.9, 132.4, 134.2, 135.8, 137.4, 139.0, 143.3, 197.7. IR (neat): 3284, 1660, 1583, 1444, 1335, 1160 cm^{-1}. HRMS (EI) calcd. for $C_{18}H_{16}NOClBr$ ($M-Ts^+$): 376.0104; found 376.0107.

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