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Shao-Qin Ge [a], Yun-Yu Hua [a] & Min Xia [a]

[a] Department of Chemistry, Zhejiang Sci-Tech University, Hangzhou, China

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ACCELERATED AMINATION OF BAYLIS–HILLMAN ACETATES UNDER ULTRASOUND IRRADIATION

Shao-Qin Ge, Yun-Yu Hua, and Min Xia
Department of Chemistry, Zhejiang Sci-Tech University, Hangzhou, China

The amination of the Baylis–Hillman acetates with primary amines can be dramatically promoted with improved yields and shortened reaction time under ultrasound irradiation. The selected aromatic, heteroaromatic, and aliphatic amines were investigated as the effective candidates for the sonochemical transformation.

Keywords: Amination; Baylis–Hillman acetate; primary amine; sonication

The Baylis–Hillman reaction, one of the most significant C–C bond-forming reactions, affords a highly functionalized product with multiple reactive groups. Therefore, the Baylis–Hillman adducts and their derivatives are widely utilized as the useful bricks for building various novel or complicated structures.[1–6] The amination of Baylis–Hillman acetates is an essential starting step in the preparation of many cyclic frameworks with N atoms.[7–9] However, it always takes a prolonged time for such transformation at room temperature, especially in the cases which aromatic amines with electron-withdrawing substituents are involved.[10–12] Although Pathak and coworkers recently reported[13] that their aminations were completed in 3 h at room temperature for the anilines with either electron-withdrawing or electron-donating groups in reasonable to good yields, we could not repeat their results for the anilines with electron-withdrawing groups. We found the exact reaction time for them to afford the products in moderate yields was more than 12 h. When the aniline with a vicinal electron-withdrawing group was concerned, it was reported[14] that it took 7 days for the amination with 2-bromoaniline to be accomplished in moderate (56%) yield. Considering the power of the Baylis–Hillman derivatives with amino groups in the construction of many significant molecules, we still desired to develop a more efficient approach to their rapid and convenient access.

In recent years, ultrasound irradiation has been extensively applied in organic reactions because of its special sonochemical effect, which is primarily attributed to hot spots formed during acoustic cavitations.[15–19] In some cases, the thermal effect

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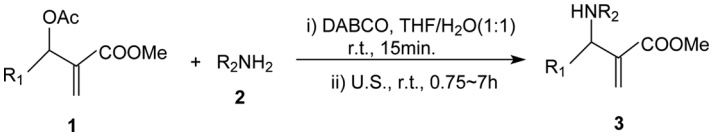
Address correspondence to Min Xia, Department of Chemistry, Zhejiang Sci-Tech University, Hangzhou 310018, China. E-mail: xiamin@zstu.edu.cn



Scheme 1. Ultrasound-promoted preparation of Baylis–Hillman amines.

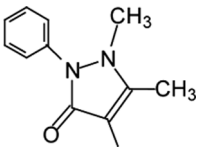
resulted from the classical heating, and ultrasound irradiation will lead to entirely different chemical outcomes. Generally, sonication increases reaction rates and yields without using harsh conditions. It is also observed that reactions under ultrasound irradiation are commonly easier to workup than those in conventional stirring methods. In continuation of our interest in the ultrasonic effect on organic reactions,[20] herein we describe our example for the observably accelerated amination of the Baylis–Hillman acetates with primary amines in enhanced yields under ultrasound irradiation (Scheme 1).

Since there is a successive S_{N2}–S_{N2} nucleophilic substitution in the process of introducing the amino groups at the secondary position of the Baylis–Hillman acetate, an additional base such as 1,4-diazabicyclo[2.2.2]octane (DABCO) should be used. We adopt a standard reaction condition for the amination of the Baylis–Hillman acetates: first treat the reaction mixture with DABCO in tetrahydrofuran (THF)/H_2O (1:1) for 15 min, at room temperature, either stirring the mixture or sonicating it under ultrasound irradiation with the corresponding amine. Both the acetates derived from aromatic and heteroaroamtic aldehydes and the primary amines of aromatic, heterocyclic, and aliphatic ones are screened as the candidates to carry out the nucleophilic substitution, and the results of the reaction in the two different methods are listed in Table 1. To our best knowledge, there has been no report in literature about the ultrasonic amination of the Baylis–Hillman acetates.

Table 1 shows that there is an obvious sonochemical effect in the amination of the Baylis–Hillman acetates under the ultrasound irradiation. Compared with conventional stirring at room temperature, the reaction time is dramatically cut down and the yield is remarkably increased with ultrasonic amination. More important, the thermal effect induced by the acoustic cavitations accelerates the reaction without the simultaneously promoting the generation of by-products. Instead, when the temperature of the reaction under the classical heating condition is elevated, the formation of many side products will make the separation of the desired compounds tedious, which eventually results in reduced yields. Apparently, the thermal effects of the classical heating and the ultrasound irradiation lead to somewhat different chemical outcomes.

We investigated both the electron effect and the space effect of the substituents on anilines in the amination reaction (entries 1–3, 5, 10, 19, and 20 and entries 4 and 6, respectively). It takes an extended reaction time for the anilines with the electron-withdrawing groups to afford the products in relatively poor yields. Amination of 4-nitroaniline, which contains a strong electron-withdrawing group, cannot be carried out in the DABCO/THF/H_2O system, even when the ultrasound irradiation is executed for a prolonged time (more than 12 h). It is possible that the nucleophilicity of the anilines is reduced because of the deactivation of the

Table 1. Amination of Baylis–Hillman acetates under ultrasound irradiation

				Classical reaction		Ultrasound reaction	
Entry	R_1	R_2	Product	Time (h)	Yield (%)	Time (h)	Yield (%)
1	C_6H_5	C_6H_5	**3a**	8	67	3	84
2	C_6H_5	4-$CH_3OC_6H_4$	**3b**	3	83	1	93
3	C_6H_5	4-$CH_3C_6H_4$	**3c**	5	80	1.5	88
4	C_6H_5	2-$CH_3C_6H_4$	**3d**	8	41	4.5	55
5	C_6H_5	4-ClC_6H_4	**3e**	12	55	5	63
6	C_6H_5	2,5-$(CH_3)_2C_6H_3$	**3f**	12	23	5	41
7	C_6H_5	$C_6H_5CH_2$	**3g**	5	50	2	70
8	C_6H_5	$(CH_3)_2CH$	**3h**	6	75	3	80
9	2-Pyridiyl	C_6H_5	**3i**	10	54	3.5	85
10	4-ClC_6H_4	C_6H_5	**3j**	10	66	3	87
11	2-ClC_6H_4	C_6H_5	**3k**	12	49	5	72
12	4-FC_6H_4	C_6H_5	**3l**	10	56	4	78
13	4-$F_3CC_6H_4$	C_6H_5	**3m**	10	63	4	81
14	4-BrC_6H_4	2-$H_2NC_6H_4$	**3n**	3	81	1.5	87
15	4-$CH_3C_6H_4$	4-$CH_3OC_6H_4$	**3o**	4	77	1	88
16	2,4-$Cl_2C_6H_3$		**3p**	6	72	2.5	84
17	2,4-$Cl_2C_6H_3$	3-ClC_6H_4	**3q**	12	31	7	55
18	2,4-$Cl_2C_6H_3$	2-Naphthyl	**3r**	12	25	5	33
19	4-ClC_6H_4	4-HOC_6H_4	**3s**	3	88	0.75	95
20	4-ClC_6H_4	4-$CH_3C_6H_4$	**3t**	5	75	2	91

electron-withdrawing groups present in the molecules, leading to the obstruction of the amination or even the failure of the reaction. Moreover, when there is an aniline with the substituent at the vicinal position of the amino group, it is envisaged that the amination involved is largely hindered, as demonstrated in entries 4 and 6. In addition, when aliphatic primary amines such as benzylamine and isopropylamine are tested, both of them exhibit the desired nucleophilicity in the amination, providing the corresponding Baylis–Hillman amines in good yields. Interestingly, it is also smooth for 4-amino antipyrine (entry 16) as a heterocyclic primary amine to carry out the substitution of the Baylis–Hillman acetates. Although 2-naphthylamine (entry 18) is not an active candidate, there is still an observable ultrasonic effect on its reaction with the corresponding acetate. In the case when double nucleophilic substituents such as hydroxyl and amino groups are present in the same molecule (entry 19), the substitution selectively occurs on the amino group.

It seems that the acetates originating from the aromatic aldehydes with different substituents have a small influence on the generation of compounds **3** (entries 1 and 10–13 and entries 3 and 20); this may be attributed to the sp^3 carbon at the secondary position of the Baylis–Hillman acetate. Also, the acetate derived from the heteroaromatic aldehyde such as 2-pyridiylaldehyde was tested to be a potent candidate for the amination, providing good yields. It is notable in each case of

the amination of the different acetates that the ultrasonic irradiation reduces reaction time and enhances yield more than the same reaction using the classical stirring method.

In conclusion, herein we describe our efficient amination of the Baylis–Hillman acetates under both conventional stirring and ultrasound irradiation conditions. For the various primary amines and acetates, the ultrasonic amination generally affords improved yields and reduced reaction time without the formation of the side products. The results in our reactions largely expand the substrate scope in the formation of Baylis–Hillman amines than that in previous literature. The ultrasonically accelerated preparation of the Baylis–Hillman derivatives containing amino groups is a promising methodology for the convenient approach to significant molecules with N atoms.

EXPERIMENTAL

All the compounds used are analytical reagents, and some chemicals are further purified by recrystallization or distillation. The ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained on a Bruker Avance II DMX400 spectrometer using $CDCl_3$ as the solvent. Fourier transform–infrared (FT-IR) spectra were performed as liquid films or KBr pellets on a Nicolet Avatar spectrophotometer. Ultrasound irradiation was performed in a KQ250E ultrasound cleaner, whose frequency is 40 KHz and output power is 250 W. The temperature of the water bath is controlled by addition or removal of water.

General Procedure for the Amination of Baylis–Hillman Acetates Under Classical Stirring

At room temperature, DABCO (1.5 mmol) was added to the solution of the Baylis–Hillman acetate **1** (1.0 mmol) in THF/H_2O (1:1) (5 mL). The resulting mixture was stirred for 15 min, and then the corresponding amine (1.2 mmol) was added. The solution was stirred at room temperature for the appropriate time (indicated by thin-layer chromatography, TLC). When the reaction is over, water was poured into the solution and EtOAc (2×10 mL) was used to extract the mixture. The combined organic layers were washed by brine and dried over anhydrous Na_2SO_4. After the solvent was removed on a rotating evaporator, the residue was purified using silica-gel column chromatography with petroleum ether/ethyl acetate as the eluent to give a yellowish oil or solid.

General Procedure for the Amination of Baylis–Hillman Acetates Under Ultrasound Irradiation

At room temperature, DABCO (1.5 mmol) was added to the solution of the Baylis–Hillman acetate **1** (1.0 mmol) in THF/H_2O (1:1) (5 mL). The resulting mixture was stirred for 15 min, and then the corresponding amine (1.2 mmol) was added. The solution was irradiated at 25–30 °C for the appropriate time (indicated by TLC). The temperature of the water bath was controlled by the addition or removal of water. When the reaction was over, water was poured into the solution and EtOAc

(2×10 mL) was used to extract the mixture. The combined organic layers were washed by brine and dried over anhydrous Na_2SO_4. After the solvent was removed on a rotating evaporator, the residue was purified using silica-gel column chromatography with petroleum ether/ethyl acetate as the eluent to give a yellowish oil or solid.

Spectral Data

Compound 3a. Yellowish liquid; IR (liquid film): 694, 750, 958, 1069, 1100, 1154, 1194, 1286, 1315, 1436, 1452, 1503, 1597, 1717, 2951, 3028, 3052, 3401; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.69 (s, 3H), 3.99 (s, br, 1H, NH), 5.41 (s, 1H), 5.98 (s, 1H), 6.39 (s, 1H), 6.57 (d, 2H, $J = 8.0$ Hz), 6.72 (t, 1H, $J = 7.2$ Hz), 7.16 (t, 2H, $J = 7.6$ Hz), 7.28 (m, 1H), 7.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.79, 58.77, 113.27, 117.75, 126.10, 127.40, 127.68, 128.61, 129.01, 139.70, 140.36, 146.41, 166.49.

Compound 3b. Yellowish liquid; IR (liquid film): 701, 776, 819, 1036, 1089, 1117, 1154, 1244, 1439, 1512, 1629, 1717, 2832, 2951, 3030, 3396; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.68 (s, 3H), 3.71 (s, 3H), 3.97 (s, br, 1H, NH), 5.33 (s, 1H), 5.97 (s, 1H), 6.38 (s, 1H), 6.53 (d, 2H, $J = 8.4$ Hz), 6.75 (d, 2H, $J = 8.0$ Hz), 7.30 (m, 1H), 7.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.08, 55.69, 59.79, 114.73, 126.31, 126.32, 127.61, 127.84, 128.79, 140.18, 140.78, 140.89, 152.37, 166.83.

Compound 3c. Yellowish liquid; IR (liquid film): 700, 807, 952, 1091, 1126, 1154, 1194, 1285, 1438, 1519, 1617, 1717, 2918, 2950, 3028, 3400; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.22 (s, 3H), 3.69 (s, 3H), 3.87 (s, br, 1H, NH), 5.37 (s, 1H), 5.97 (s, 1H), 6.38 (s, 1H), 6.49 (d, 2H, $J = 7.6$ Hz), 6.96 (d, 2H, $J = 8.0$ Hz), 7.29 (m, 1H), 7.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.47, 49.98, 57.28, 111.64, 124.28, 125.20, 125.61, 125.84, 126.80, 127.73, 138.07, 138.74, 142.37, 164.75.

Compound 3d. Yellowish liquid; IR (liquid film): 700, 748, 957, 1052, 1072, 1123, 1155, 1195, 1284, 1442, 1506, 1605, 1719, 2951, 3030, 3429; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.14 (s, 3H), 3.71 (s, 3H), 3.80 (s, br, 1H, NH), 5.47 (s, 1H), 5.92 (s, 1H), 6.38 (s, 1H), 6.50 (d, 1H, $J = 8.4$ Hz), 6.67 (t, 1H, $J = 7.6$ Hz), 7.07 (t, 2H, $J = 7.2$ Hz), 7.28 (m, 1H), 7.38 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 17.61, 51.94, 58.83, 111.05, 117.56, 122.21, 126.18, 127.04, 127.52, 127.82, 128.82, 130.11, 140.11, 140.79, 144.59, 166.71.

Compound 3e. Yellowish liquid; IR (liquid film): 502, 701, 764, 816, 960, 1007, 1122, 1155, 1287, 1438, 1452, 1496, 1599, 1716, 2951, 3030, 3402; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.61 (s, 3H), 4.21 (s, br, 1H, NH), 5.36 (s, 1H), 5.90 (s, 1H), 6.37 (s, 1H), 6.48 (m, 2H), 7.07 (dd, 2H, $J_1 = 2.8$ Hz, $J_2 = 8.8$ Hz), 7.33 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.07, 59.05, 114.58, 122.51, 126.40, 127.52, 128.02, 128.88, 129.05, 139.72, 140.19, 145.23, 166.59.

Compound 3f. Yellowish liquid; IR (liquid film): 700, 748, 797, 913, 1072, 1127, 1155, 1285, 1438, 1519, 1582, 1615, 1724, 2921, 2951, 3028, 3434; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.10 (s, 3H), 2.25 (s, 3H), 3.71 (s, 3H), 3.98 (s, br, 1H, NH), 5.46 (s, 1H), 5.94 (s, 1H), 6.31 (s, 1H), 6.39 (s, 1H), 6.49 (d, 1H, $J = 7.6$ Hz), 6.94

(d, 1H, $J = 7.6$ Hz), 7.30 (m, 1H), 7.37 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 17.20, 21.60, 51.95, 58.78, 111.72, 118.16, 119.16, 126.15, 127.51, 127.79, 128.81, 129.95, 136.68, 140.04, 140.93, 144.47, 166.76.

Compound 3g. Yellowish liquid; IR (liquid film): 700, 743, 957, 1103, 1149, 1193, 1283, 1438, 1453, 1494, 1626, 1720, 2950, 3028, 3061, 3335; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.93 (s, br, 1H, NH), 3.65 (s, 3H), 3.70 (d, 2H, $J = 8.0$ Hz), 4.71 (s, 1H), 6.02 (s, 1H), 6.37 (s, 1H), 7.23 (t, 2H, $J = 7.2$ Hz), 7.31 (m, 6H), 7.39 (d, 2H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.78, 51.88, 62.15, 125.69, 127.06, 127.41, 127.75, 128.23, 128.47, 140.25, 141.53, 141.90, 166.89.

Compound 3h. Colorless liquid; IR (liquid film): 702, 762, 957, 1086, 1144, 1195, 1269, 1323, 1364, 1438, 1494, 1627, 1721, 2868, 2962, 3028, 3330; ^{1}H NMR (400 MHz, $CDCl_3$) δ1.06 (dd, 6H, $J_1 = 6.4$ Hz, $J_2 = 8.4$ Hz), 1.57 (s, br, 1H, NH), 2.72 (m, 1H), 3.67 (s, 3H), 4.80 (s, 1H), 5.92 (s, 1H), 6.32 (s, 1H), 7.22 (t, 1H, $J = 7.2$ Hz), 7.33 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.95, 23.23, 46.03, 51.75, 60.02, 125.42, 127.14, 127.53, 128.37, 142.03, 142.51, 166.97.

Compound 3i. Yellowish liquid; IR (liquid film): 693, 750, 813, 996, 1115, 1153, 1286, 1322, 1437, 1511, 1603, 1715, 2951, 3013, 3051, 3393; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.73 (s, 3H), 5.23 (s, br, 1H, NH), 5.63 (s, 1H), 6.01 (s, 1H), 6.34 (s, 1H), 6.64 (d, 2H, $J = 8.0$ Hz), 6.70 (t, 1H, $J = 7.2$ Hz), 7.18 (m, 3H), 7.48 (d, 1H, $J = 8.0$ Hz), 7.63 (m, 1H), 8.57 (d, 1H, $J = 4.8$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.01, 58.61, 113.50, 117.72, 122.63, 122.76, 126.82, 129.29, 136.85, 139.63, 146.30, 149.39, 159.00, 166.91.

Compound 3j. Yellowish liquid; IR (liquid film): 692, 751, 817, 1015, 1093, 1155, 1286, 1436, 1503, 1602, 1716, 2951, 3019, 3052, 3401; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.71 (s, 3H), 4.24 (s, br, 1H, NH), 5.38 (s, 1H), 5.96 (s, 1H), 6.40 (s, 1H), 6.57 (d, 2H, $J = 8.0$ Hz), 6.74 (t, 1H, $J = 7.2$ Hz), 7.16 (t, 2H, $J = 7.6$ Hz), 7.31 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.65, 57.99, 113.11, 117.79, 126.34, 128.47, 128.51, 128.82, 133.18, 138.63, 139.18, 146.07, 166.00.

Compound 3k. Yellowish liquid; IR (liquid film): 692, 751, 1037, 1099, 1155, 1268, 1437, 1503, 1601, 1720, 2951, 3019, 3053, 3401; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.73 (s, 3H), 3.92 (s, br, 1H, NH), 5.80 (s, 1H), 5.84 (s, 1H), 6.43 (s, 1H), 6.57 (d, 2H, $J = 7.2$ Hz), 6.73 (m, 1H), 7.15 (t, 1H, $J = 7.2$ Hz), 7.24 (m, 2H), 7.40 (d, 2H, $J = 2.4$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.18, 55.39, 113.40, 118.15, 127.11, 127.76, 128.34, 129.04, 129.23, 130.05, 134.09, 137.75, 139.42, 146.40, 166.55.

Compound 3l. Yellowish liquid; IR (liquid film): 693, 751, 821, 1101, 1157, 1224, 1287, 1437, 1506, 1603, 1717, 2952, 3019, 3052, 3400; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.70 (s, 3H), 4.17 (s, br, 1H, NH), 5.39 (s, 1H), 5.96 (s, 1H), 6.39 (s, 1H), 6.57 (d, 2H, $J = 7.6$ Hz), 6.73 (t, 1H, $J = 7.6$ Hz), 7.02 (t, 1H, $J = 8.4$ Hz), 7.23 (m, 2H), 7.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.14, 51.90, 55.75, 59.55, 114.76, 125.97, 127.46, 129.42, 137.47, 137.78, 140.33, 140.85, 152.37, 166.78.

Compound 3m. Yellowish liquid; IR (liquid film): 694, 751, 850, 1018, 1067, 1124, 1164, 1326, 1504, 1603, 1717, 2954, 3019, 3056, 3400; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.72 (s, 3H), 4.42 (s, br, 1H, NH), 5.47 (s, 1H), 6.00 (s, 1H), 6.44

(s, 1H), 6.60 (d, 2H, $J = 8.0$ Hz), 6.77 (d, 1H, $J = 7.2$ Hz), 7.17 (dd, 2H, $J_1 = 7.2$ Hz, $J_2 = 8.0$ Hz), 7.51 (d, 2H, $J = 8.0$ Hz), 7.59 (d, 2H, $J = 8.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.13, 58.93, 113.88, 118.73, 122.67, 125.37, 125.69, 125.72, 125.76, 125.80, 127.34, 127.83, 129.30, 129.86, 130.19, 139.40, 166.27.

Compound 3n. Yellowish liquid; IR (liquid film): 742, 817, 1011, 1072, 1153, 1195, 1273, 1438, 1486, 1505, 1596, 1627, 1716, 2848, 2949, 3032, 3352; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.46 (s, br, 3H, -NH- and -NH_2), 3.71 (s, 3H), 5.37 (s, 1H), 5.89 (s, 1H), 6.73 (s, 1H), 6.49 (d, 1H, $J = 7.2$ Hz), 6.73 (m, 3H), 7.28 (d, $J = 7.6$ Hz, 2H), 7.44 (d, $J = 7.6$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.05, 58.35, 113.73, 116.87, 119.59, 120.58, 121.71, 126.56, 129.34, 131.84, 134.58, 135.75, 139.85, 139.92, 166.51.

Compound 3o. Yellowish liquid; IR (liquid film): 817, 1037, 1086, 1154, 1248, 1512, 1718, 2951, 2999, 3393; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.33 (s, 3H), 3.69 (s, 3H), 3.72 (s, 3H), 4.00 (s, br, 1H, NH), 5.29 (s, 1H), 5.97 (s, 1H), 6.36 (s, 1H), 6.53 (d, 2H, $J = 8.8$ Hz), 6.75 (d, 2H, $J = 8.8$ Hz), 7.13 (d, 2H, $J = 7.6$ Hz), 7.25 (d, 2H, $J = 8.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.14, 51.90, 55.75, 59.55, 114.76, 125.97, 127.46, 129.42, 137.47, 137.78, 140.33, 140.85, 152.37, 166.78.

Compound 3p. Yellowish liquid; IR (liquid film): 732, 763, 1138, 1194, 1270, 1438, 1497, 1594, 1667, 1721, 2951, 2990, 3068, 3296; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.15 (s, 3H), 2.83 (s, 3H), 3.75 (s, 3H), 5.29 (s, br, 1H, NH), 5.75 (s, 1H), 5.80 (s, 1H), 6.39 (s, 1H), 7.23 (d, 2H, $J = 5.2$ Hz), 7.38 (s, 1H), 7.42 (m, 4H), 7.53 (d, 1H, $J = 7.6$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.08, 37.60, 52.17, 57.27, 119.46, 123.04, 126.12, 127.10, 127.41, 129.10, 129.51, 129.54, 133.84, 134.42, 135.13, 137.05, 140.43, 140.83, 162.10, 166.37.

Compound 3q. Yellowish solid; mp 85–87 °C; IR (KBr): 682, 766, 818, 868, 990, 1046, 1088, 1143, 1195, 1276, 1385, 1438, 1483, 1598, 1719, 2952, 3023, 3089, 3393; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.74 (s, 3H), 4.24 (s, br, 1H, NH), 5.76 (d, 2H, $J = 9.2$ Hz), 6.39 (dd, 1H, $J_1 = 2.0$ Hz, $J_2 = 8.4$ Hz), 6.44 (s, 1H), 6.52 (t, 1H, $J = 2.0$ Hz), 6.68 (dd, 1H, $J_1 = 1.2$ Hz, $J_2 = 7.6$ Hz), 7.04 (t, 1H, $J = 8.0$ Hz), 7.21 (dd, 1H, $J_1 = 2.0$ Hz, $J_2 = 8.4$ Hz), 7.32 (d, 1H, $J = 7.6$ Hz), 7.43 (d, 1H, $J = 2.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.29, 55.07, 111.47, 113.18, 118.30, 127.47, 128.15, 129.15, 129.96, 130.30, 134.37, 134.71, 135.00, 136.04, 138.71, 147.38, 166.17.

Compound 3r. Red liquid; IR (liquid film): 423, 456, 570, 738, 769, 818, 866, 964, 1049, 1107, 1143, 1196, 1286, 1346, 1385, 1408, 1437, 1470, 1525, 1582, 1630, 1716, 2858, 2951, 3010, 3061, 3424; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.75 (s, 3H), 5.03 (s, br, 1H, NH), 5.85 (s, 1H), 5.98 (s, 1H), 6.40 (t, 1H, $J = 4.4$ Hz), 6.46 (s, 1H), 7.18 (dd, 1H, $J_1 = 2.0$ Hz, $J_2 = 8.4$ Hz), 7.25 (m, 2H), 7.43 (m, 4H), 7.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.31, 55.42, 105.96, 118.39, 119.79, 123.38, 125.03, 125.87, 126.49, 127.51, 128.42, 128.83, 129.37, 129.93, 134.25, 134.31, 134.81, 136.31, 138.71, 141.13, 166.49.

Compound 3s. Yellowish liquid; IR (liquid film): 731, 820, 1015, 1089, 1114, 1156, 1238, 1438, 1514, 1628, 1713, 2952, 3030, 3397; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.70 (s, 3H), 3.84 (s, br, 1H, NH), 5.28 (s, 1H), 5.93 (s, 1H), 6.38 (s, 1H), 6.47 (d, 2H, $J = 8.8$ Hz), 6.66 (d, 2H, $J = 8.8$ Hz), 7.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ: 52.13, 59.30, 115.13, 116.12, 126.89, 128.88, 133.50, 139.29, 140.00, 140.39, 148.41, 166.76.

Compound 3t. Yellowish liquid; IR (liquid film): 511, 644, 733, 807, 887, 959, 1015, 1090, 1127, 1154, 1194, 1286, 1406, 1437, 1489, 1519, 1617, 1717, 2866, 2919, 2951, 3022, 3401; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.22 (s, 3H), 3.69 (s, 3H), 4.05 (s, br, 1H, NH), 5.34 (s, 1H), 5.94 (s, 1H), 6.38 (s, 1H), 6.48 (d, 2H, $J = 8.4$ Hz), 6.96 (d, 2H, $J = 8.4$ Hz), 7.28 (d, 4H, $J = 9.2$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.43, 52.00, 58.75, 113.74, 126.68, 127.51, 128.91, 129.75, 133.55, 139.31, 139.91, 144.12, 166.51.

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