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Chelation-controlled asymmetric aminohalogenation reaction

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Abstract—The chelation-controlled asymmetric aminohalogenation of α,β-unsaturated 3-aryl-*N*-acyl-*N*-4-phenyl-2-oxazolidinones have been established by using palladium(II) acetate as the catalyst and as the chelation metal. The reaction is very convenient to perform by simply mixing the three reactants, cinnamates, *N*,*N*-dichloro-*p*-toluenesulfonamide and catalyst together with 4 Å molecular sieves at rt in any convenient vial of appropriate size without special protection from inert gases. Unlike the previous asymmetric aminohalogenation, the ionic liquid, [BMIM][NTf_2], was found to be superior to [BMIM][BF_4] as the reaction media. It was also found that palladium(II) acetate has to be used together with 1 equiv of MeCN to achieve the opposite chelation control. The resulting absolute stereochemistry of the product was unambiguously determined by X-ray structural analysis.

The aminohalogenation reaction is an important tool for functionalizing unsaturated carbon–carbon bonds, and has long been a challenging topic in modern organic and medicinal chemistry.[1–3] The resulting vicinal haloamines are versatile building blocks which can be further converted into other precursors, such as aziridines,[4] dehydroamino acids,[5] and many other important organic products.[1–3]

In the past few years, we[6] and others[7] have developed a series of catalytic aminohalogenation processes to approach the vicinal haloamine functionality. More importantly, we have established the first asymmetric aminohalogenation reaction by using an ionic liquid, [BMIM][BF_4], as the reaction medium in the presence of Cu(I)OTf as the catalyst (Scheme 1).[6g] The reaction is among the very rare cases in which common organic solvents failed to give any product, but ionic liquids proved to be efficient reaction media. The asymmetric induction was controlled by dipole–dipole interaction of the two carbonyl groups of the substrate for the formation of the most stable conformation (Scheme 1, **B**). The reaction is believed to go through the formation of aziridinium ion intermediate at the initial key step,[6,8] which is next subjected to regio- and stereoselective ring openings. The ionic liquid media[9,10,12,13] can accelerate the formation of this polar intermediate by solvation effect to make this species and the resulting chlorine anion more stable. At the same time, the polar ionic liquid can help the chlorine atom of $TsNCl_2$ to leave the nitrogen source.

During our continuing effort on this work, we anticipated that if suitable Lewis acid catalysts can be found, they can not only facilitate the reaction but also coordinate with the two carbonyl groups of the substrate to form a chelation complex prior to aminohalogenation; this would result in the opposite control of asymmetric induction. In this Letter, we would like to report our preliminary results of the asymmetric aminohalogenation with the opposite asymmetric control (Scheme 2). This will indeed be the second asymmetric aminohalogenation report to appear in the literature.

Initially, a series of typical Lewis acids, such as $ZnCl_2$, $TiCl_4$, Ti(OPr-*i*)$_4$, $AlCl_3$ and $SnCl_2$ were screened under the previous asymmetric aminohalogenation condition, but no satisfactory results were obtained in terms of chemical yields and diastereoselectivity. This work was put away for a while until recently when two findings were made in our laboratories: (1) $Pd(OAc)_2$ was found to be an efficient catalyst for the aminohalogenation reaction,[4c,11] for example, a nearly quantitative yield and complete regioselectivity were achieved when the reaction of styrene (1 equiv) with $TsNCl_2$ (1.5 equiv) was performed in DMF at rt in the presence of as low

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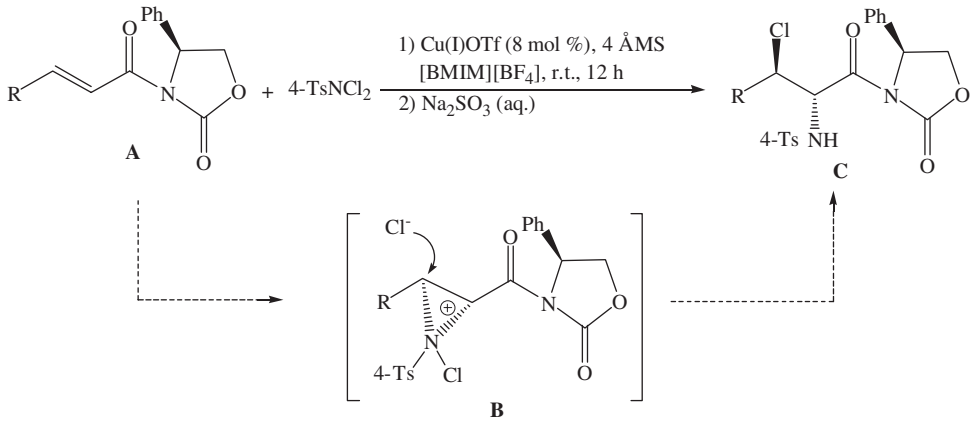
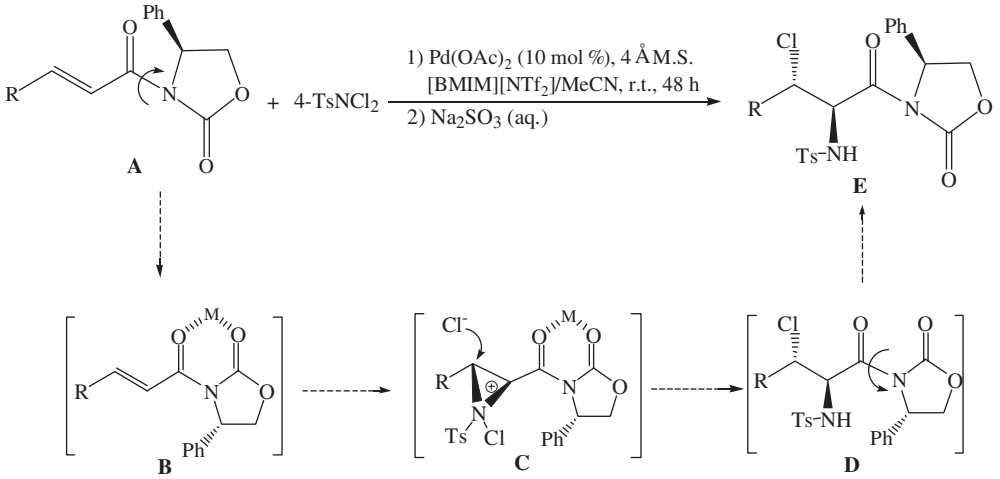


Scheme 1.



Scheme 2.

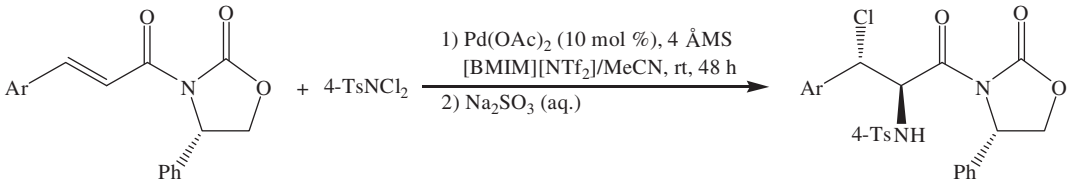
as $Pd(OAc)_2$ (2.0 mol %). (2) The ionic liquid, [BMIM]-[NTf_2] (1-*n*-butyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide), was found to be superior to [BMIM][BF_4] for the aminochlorination of α,β-unsaturated ketones.[6k] The combination of the above two findings played an important role for the present success.[14]

α,β-Unsaturated 3-phenyl-*N*-acyl-*N*-4-phenyl-2-oxazolidinone[15] was first subjected to the aminohalogenation reaction with 4-$TsNCl_2$ (1.5 equiv) in [BMIM][NTf_2] in the presence of $Pd(OAc)_2$ as the catalyst. However, after stirring for 48 h at room temperature, only a small amount of starting material was converted into the haloamine product. Adding another portion of 4-$TsNCl_2$ (1.5 equiv) did not show any significant improvement. Pleasingly, when 1 equiv of acetonitrile was added into the catalytic system, and at the same time, to keep excess nitrogen source ($TsNCl_2$, 3.0 equiv), the starting material of alkene was consumed within 24 h, and a single aminohalogenation product was isolated in a chemical yield of 54% and in excellent diastereoselectivity (>20:1).

The next optimization was to increase the reaction temperature to 40 and 60 °C, respectively, but there was no improvement in both yield and diastereoselectivity. Even though the reaction time was shortened under higher temperature, the complex products were obtained, which made the purification very difficult. Increasing the amount of acetonitrile led to a diminished yield. Obviously, the increased loading of MeCN caused the polarity of the reaction media to become less polar, which is unfavorable for the formation of aziridinium intermediate. However, MeCN can be reduced to 20 mol % without much loss of diastereoselectivity and chemical yield, but 1 equiv of acetonitrile was needed to achieve the optimized outcomes.

As shown in Table 1, the substituents on the aromatic ring showed notable effects on chemical yields and diastereoselectivities. These results indicated that the chelation-controlled aziridinium ion intermediate behaved differently from the previous non-chelation-controlled ones. As compared with our first asymmetric aminohalogenation, a similar range of yields and diastereoselectivities were observed for all cases in this new system except for case 1 in Table 1 in which the diastereoselectivity was improved substantially from 3:1 to >20:1. At this moment, it is not clear about how much non-chelated starting material remained, which is partially responsible for the formation of minor isomers.

Table 1. Results of asymmetric aminochlorination reactions in [BMIM][NTf_2][16]



Entry	Ar	Yield[a] (%)	Diastereoselectivity[b]
1	4-H–C_6H_5	54	>20:1[c]
2	2-F–C_6H_4	51	6.8:1.0
3	2-Cl–C_6H_4	58	3.6:1.0
4	4-Cl–C_6H_4	62	3.2:1.0
5	2,4-Cl–C_6H_3	60	2.6:1.0
6	2-Br–C_6H_4	69	1.9:1.0
7	4-Br–C_6H_4	58	2.4:1.0
8	2-Me–C_6H_4	64	3.6:1.0
9	4-MeO–C_6H_4	60	2.9:1.0
10	3-CF_3–C_6H_4	34	2.9:1.0

[a] The combined yields of two diastereomers separated by column chromatography.
[b] Determined after column chromatography.
[c] It means only one diastereomer was observed as revealed by crude ^{1}H NMR analysis.

When an electron-withdrawing group was present on the aromatic ring of the substrate (Table 1, entries 10), poor chemical yields were obtained (34%). However, in the previous asymmetric aminohalogenation, the substrates with electron-donating groups on their aromatic rings (Table 1, entries 8–9) failed to give any product. However, they worked well under this new condition.

The absolute structure was unambiguously confirmed by X-ray structural analysis for product **6** of Table 1 (Fig. 1). This structure revealed that the stereoselectivity of the resulting product is *anti*, and the resulting chirality of α,β-positions as '2*S*,3*R*' which is opposite to the previously observed chirality of '2*R*,3*S*'. These results confirmed what we exactly designed at the beginning of this project.

The mechanism of this asymmetric reaction process is shown in Scheme 2. The nitrogen electrophile approaches the C=C bond for the less hindered side of the chiral auxiliary. The palladium metal acts as the coordination center, and is responsible for the formation of a chelation complex. At this stage, the state of the palladium center was not clear. It seems that ligands such as acetonitrile or triphenyl phosphine can help to stabilize the chelation palladium complex. We have observed that with the addition of 0.2 equiv triphenyl phosphine, similar chemical yields and diastereoselectivities can be obtained. Further study of this reaction will be conducted in our laboratories in due course.

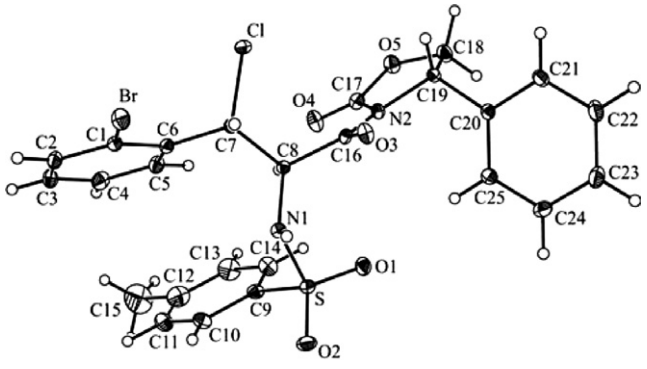


Figure 1. X-ray structure of the product (Table 1, entry 6).

In summary, the chelation-controlled asymmetric aminohalogenation has been achieved under a new combinational condition consisting of $Pd(OAc)_2$ catalyst, [BMIM][NTf_2], and MeCN. The reaction can be conveniently carried out in a one-pot operation without the use of inert gas protection. Moderate to good chemical yields and excellent diastereoselectivity have been obtained. The absolute configuration of the resulting products was ambiguously determined by X-ray structural analysis.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 648718. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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References and notes

1. Kemp, J. E. G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, pp 471–513, and references cited therein.

2. (a) Griffith, D. A.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1991**, *113*, 5863; (b) Barton, D. H. R.; Britten-Kelly, M. R.; Ferreira, D. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1090; (c) Driguez, H.; Vermes, J.-P.; Lessard, J. *Can. J. Chem.* **1978**, *56*, 119; (d) Lessard, J.; Driguez, H.; Vermes, J.-P. *Tetrahedron Lett.* **1970**, *11*, 4887.
3. (a) Daniher, F. A.; Butler, P. E. *J. Org. Chem.* **1968**, *33*, 4336; (b) Daniher, F. A.; Butler, P. E. *J. Org. Chem.* **1968**, *33*, 2637; (c) Daniher, F. A.; Melchior, M. T.; Butler, P. E. *Chem. Commun.* **1968**, 931; (d) Seden, T. P.; Tuner, R. W. *J. Chem. Soc. (C)* **1968**, 876; (e) Klepacz, A.; Zwierzak, A. *Tetrahedron Lett.* **2001**, *42*, 4539.
4. (a) Chen, D.; Kim, S. H.; Hodges, B.; Li, G. *ARKIVOC* **2003**, *xii*, 56; (b) Chen, D.; Timmons, C.; Guo, L.; Xu, X.; Li, G. *Synthesis* **2004**, 2479; (c) Han, J.; Li, Y.; Zhi, S.; Pan, Y.; Timmons, C.; Li, G. *Tetrahedron Lett.* **2006**, *47*, 7225.
5. Chen, D.; Guo, L.; Liu, J.; Kirtane, S.; Cannon, J. F.; Li, G. *Org. Lett.* **2005**, *7*, 921.
6. (a) Li, G.; Wei, H.-X.; Kim, S. H.; Neighbors, M. *Org. Lett.* **1999**, *1*, 395; (b) Li, G.; Wei, H.-X.; Kim, S. H. *Org. Lett.* **2000**, *2*, 2249; (c) Wei, H.-X.; Kim, S. H.; Li, G. *Tetrahedron* **2001**, *57*, 3869; (d) Li, G.; Wei, H.-X.; Kim, S. H. *Tetrahedron* **2001**, *57*, 8407; (e) Chen, D.; Timmons, C.; Chao, S.; Li, G. *Eur. J. Org. Chem.* **2004**, 3097; (f) Kotti, S. R. S. S.; Xu, X.; Wang, Y.-N.; Headley, A. D.; Li, G. *Tetrahedron Lett.* **2004**, *45*, 7209; (g) Xu, X.; Kotti, S. R. S. S.; Liu, J.; Cannon, J. F.; Headley, A. D.; Li, G. *Org. Lett.* **2004**, *6*, 4881; (h) Li, Q.; Shi, M.; Timmons, C.; Li, G. *Org. Lett.* **2006**, *8*, 625; (i) Han, J.; Zhi, S.; Wang, L.; Pan, Y.; Li, G. *Eur. J. Org. Chem.* **2007**, 1332; (j) Liu, J.; Wang, Y.-N.; Li, G. *Eur. J. Org. Chem.* **2006**, 3112; (k) Wang, Y.-N.; Ni, B.; Headley, A. D.; Li, G. *Adv. Synth. Catal.* **2007**, *349*, 319.
7. For the recent excellent work on aminohalogenation by several other groups, see: (a) Qi, X.; Lee, S. H.; Kwon, J. Y.; Kim, Y.; Kim, S. J.; Lee, Y. S.; Yoon, J. *J. Org. Chem.* **2003**, *68*, 9140; (b) Thakur, V. V.; Talluri, S. K.; Sudalai, A. *Org. Lett.* **2003**, *5*, 861; (c) Śliwińska, A.; Zwierzak, A. *Tetrahedron* **2003**, *59*, 5927; (d) Manzoni, M. R.; Zabawa, T. P.; Kasi, D.; Chemler, S. R. *Organometallics* **2004**, *23*, 5618; (e) Minakata, S.; Yoneda, Y.; Oderaotoshi, Y.; Komatsu, M. *Org. Lett.* **2006**, *8*, 967; (f) Danielec, H.; Klugge, J.; Schlummer, B.; Bach, T. *Synthesis* **2006**, 551; (g) Yeung, Y.-Y.; Gao, X.; Corey, E. J. *J. Am. Chem. Soc.* **2006**, *128*, 9644.
8. (a) Li, G.; Wei, H.-X.; Kim, S. H.; Carducci, M. D. *Angew. Chem., Int. Ed.* **2001**, *40*, 4277; (b) Wei, H.-X.; Kim, S. H.; Li, G. *J. Org. Chem.* **2002**, *67*, 4777; (c) Brooker-Milburn, K. I.; Guly, D. J.; Cox, B.; Procopiou, P. A. *Org. Lett.* **2003**, *5*, 3313; (d) Muniz, K.; Nieger, M. *Synlett* **2003**, 211; (e) Chen, D.; Timmons, C.; Wei, H.-X.; Li, G. *J. Org. Chem.* **2003**, *68*, 5742; (f) Timmons, C.; Chen, D.; Xu, X.; Li, G. *Eur. J. Org. Chem.* **2003**, 3850; (g) Pei, W.; Wei, H.-X.; Headley, A. D.; Li, G. *J. Org. Chem.* **2003**, *68*, 8404.
9. (a) Sheldon, R. *Chem. Commun.* **2001**, 2399; (b) Earle, M. J.; McCormac, P. B.; Seddon, K. R. *Green Chem.* **1999**, 23; (c) Jaeger, D. A.; Tucker, C. E. *Tetrahedron Lett.* **1989**, *30*, 1785; (d) Howarth, J.; Hanlon, K.; Fayne, D.; McCormac, P. *Tetrahedron Lett.* **1997**, *38*, 3097; (e) Park, S.; Kazlauskas, R. *J. Org. Chem.* **2001**, *66*, 8395; (f) Wu, J. X.; Beck, B.; Ren, R. X. *Tetrahedron Lett.* **2002**, *43*, 387.
10. (a) Kabalka, G. W.; Venkataiah, B.; Dong, G. *Tetrahedron Lett.* **2003**, *44*, 4673; (b) Kotti, S. R. S. S.; Xu, X.; Li, G.; Headley, A. D. *Tetrahedron Lett.* **2004**, *45*, 1427.
11. For a comprehensive review on palladium chemistry, see: Hegedus, L. S. In *Organometallics in Synthesis: A Manual*; Schlosser, M., Ed., 2nd ed.; John Wiley & Sons, Ltd., 2002; pp 1123–1217, and references cited therein.
12. (a) Jaeger, D. A.; Tucker, C. E. *Tetrahedron Lett.* **1989**, *30*, 1785; (b) Earle, M. J.; McCormac, P. B.; Seddon, K. R. *Green Chem.* **1999**, 23; (c) Sheldon, R. *Chem. Commun.* **2001**, 2399; (d) Park, S.; Kazlauskas, R. *J. Org. Chem.* **2001**, *66*, 8395; (e) Wu, J. X.; Beck, B.; Ren, R. X. *Tetrahedron Lett.* **2002**, *43*, 387.
13. Lucas, P.; El Mehdi, N.; Anh Ho, H.; Bélanger, D.; Breau, L. *Synthesis* **2000**, *9*, 1253.
14. For an opposite control of asymmetric aldol reaction using similar chiral auxiliary, see: Evans, D. A.; Downey, C. W.; Shaw, J. T.; Tedrow, J. S. *Org. Lett.* **2002**, *4*, 1127.
15. (a) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc* **1981**, *103*, 2127; (b) Evans, D. A.; Rieger, D. L.; Bilodeau, M. T.; Urpi, F. *J. Am. Chem. Soc.* **1991**, *113*, 1047; (c) Evans, D. A.; Nelson, J. V.; Taber, T. *Top. Stereochem.* **1982**, *13*, 15.
16. *Experimental section*: All reactions were performed in oven-dried vials. Flash chromatography was performed using silica gel (Merck 60, 230–400 mesh). Ionic liquid, [BMIM][NTf_2], was readily prepared by reacting 1-methylimidazole with *n*-butyl bromide,[12] followed by the anion metathesis using *N*-lithiotrifluoromethanesulfonimide in acetone solution. The resulting ionic liquid, [BMIM][NTf_2], was carefully dried by heating at 60 °C in vacuum, and then confirmed by ^{1}H NMR analysis.[13] *Typical experimental procedure*: Into an oven-dried vial were loaded α,β-unsaturated 3-phenyl-*N*-acyl-*N*-4-phenyl-2-oxazolidinone (88 mg, 0.3 mmol, 1.0 equiv), 4 Å molecular sieves (100 mg), 4-$TsNCl_2$ (108 mg, 0.45 mmol, 1.5 equiv), [BMIM][NTf_2] (600 mg), palladium(II) acetate (6.7 mg, 10 mol %), and acetonitrile (16 μL, 0.3 mmol, 1.0 equiv). The resulting mixture was stirred at room temperature for 24 h, and then another portion of 4-$TsNCl_2$ (108 mg, 0.45 mmol, 1.5 equiv) was added. The reaction was stirred at room temperature for a further 24 h, and finally quenched with saturated aqueous solution of Na_2SO_3. The product was extracted with ethyl acetate (5 mL × 3) and the combined organic phases were washed with brine and dried over anhydrous Na_2SO_4. The crude product was subjected to flash column chromatography (EtOAc/hexane, v/v = 1/3) to yield 80 mg of the products as white solids (54%). *Analytical data*: Compound **1** (Table 1, entry 1) isolated as a white solid (80 mg, 54% yield); ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.45$–7.43 (d, $J = 8.5$ Hz, 2H), 7.40–7.32 (m, 3H), 7.26–7.21 (m, 3H), 7.16–7.12 (m, 4H), 7.07–7.05 (d, $J = 8.5$ Hz, 2H), 6.07 (s, 1H), 5.48–5.46 (d, $J = 10.0$ Hz, 1H), 5.42–5.40 (dd, $J = 4.0$, 9.0 Hz, 1H), 4.80–4.78 (d, $J = 9.0$ Hz, 1H), 4.67–4.63 (t, 1H), 4.26–4.24 (dd, $J = 4.0$, 9.0 Hz, 1H), 2.39 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 170.5$, 153.4, 143.5, 137.8, 136.2, 135.4, 129.5, 129.2, 128.8, 128.7, 128.6, 128.4, 127.9, 127.5, 125.6, 70.4, 61.4, 58.0, 21.6 ppm. Compound **2** (Table 1, entry 2) isolated as a white solid (79 mg, 51% yield); ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.52$–7.51 (d, $J = 8.0$ Hz, 2H), 7.39–7.33 (m, 4H), 7.26–7.22 (m, 1H), 7.20–7.19 (m, 2H), 7.09–7.08 (d, $J = 8.0$ Hz, 2H), 7.00–6.97 (m, 1H), 6.96–6.92 (m, 1H), 6.03 (s,1H), 5.38–5.36 (dd, $J = 3.5$, 8.5 Hz, 1H), 5.32–5.31 (d, $J = 8.0$ Hz, 2H), 4.72–4.68 (t, 1H), 4.29–4.26 (dd, $J = 4.0$, 9.0 Hz, 1H), 2.39 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 169.6$, 160.7, 158.7, 153.3, 143.6, 137.6, 135.7, 130.6, 130.5, 129.6, 129.5, 129.2, 128.8, 127.4, 125.6, 124.6, 124.5, 123.3, 123.2, 115.2, 115.0, 70.6, 58.0, 53.2, 21.6 ppm. Compound **3** (Table 1, entry 3) isolated as a white solid (92 mg, 58% yield); ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.52$–7.51 (d, $J = 8.0$ Hz, 2H), 7.41–7.35 (m, 4H), 7.28–7.26 (m, 1H), 7.23–7.16 (m, 3H), 7.10–7.05

(m, 3H), 6.06 (s, 1H), 5.56–5.55 (d, $J = 7.0$ Hz, 1H), 5.40–5.35 (m, 2H), 4.70–4.66 (t, 1H), 4.29–4.26 (dd, $J = 4.0$, 9.0 Hz, 1H), 2.39 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 169.7$, 153.3, 143.6, 137.6, 135.7, 133.9, 133.3, 129.9, 129.7, 129.5, 129.3, 129.2, 129.0, 128.9, 128.8, 127.8, 127.5, 127.3, 125.7, 125.6, 70.5, 58.1, 57.6, 56.1, 21.6 ppm. Compound **4** (Table 1, entry 4) isolated as a white solid (99 mg, 62% yield); ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.42$–7.37 (m, 4H), 7.35–7.31 (m, 3H), 7.09–7.07 (d, $J = 8.0$ Hz, 2H), 7.00–6.96 (m, 4H), 6.00 (s, 1H), 5.73–5.71 (d, $J = 10.5$ Hz, 1H), 5.51–5.48 (dd, $J = 4.5$, 9.0 Hz, 1H), 4.75–4.72 (t, 1H), 4.64–4.62 (d, $J = 9.5$ Hz, 1H), 4.30–4.27 (dd, $J = 4.5$, 9.0 Hz, 1H), 2.44 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 171.0$, 153.6, 143.9, 137.8, 135.0, 134.7, 129.4, 129.3, 129.2, 128.8, 128.4, 127.5, 125.6, 70.4, 59.9, 58.0, 57.1, 21.6 ppm. Compound **5** (Table 1, entry 5) isolated as white solids (102 mg, 60% yield); ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.47$–7.45 (d, $J = 8.5$ Hz, 2H), 7.42–7.34 (m, 3H), 7.30–7.23 (m, 4H), 7.12–7.10 (d, $J = 8.0$ Hz, 2H), 6.92–6.90 (m, 1H), 6.04 (s, 1H), 5.46–5.44 (dd, $J = 4.5$, 8.5 Hz, 1H), 5.39 (s, 2H), 4.75–4.72 (t, 1H), 4.33–4.29 (dd, $J = 4.5$, 9.0 Hz, 1H), 2.43 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 170.1$, 153.5, 144.0, 137.5, 135.4, 135.3, 133.9, 133.0, 130.4, 129.5, 129.3, 128.9, 128.7, 127.6, 127.4, 125.7, 70.5, 58.1, 57.8, 55.1, 21.6 ppm. Compound **6** (Table 1, entry 6) isolated as white solids (119 mg, 69% yield); ^{1}H NMR ($CDCl_3$, 500 MHz):$\delta = 7.52$–7.51 (d, $J = 8.5$ Hz, 2H), 7.46–7.44 (m, 1H), 7.40–7.35 (m, 4H), 7.23–7.22 (m, 2H), 7.11–7.08 (m, 4H), 6.08 (s, 1H), 5.54–5.53 (d, $J = 7.0$ Hz, 1H), 5.41–5.38 (dd, $J = 4.5$, 9.0 Hz, 2H), 4.70–4.66 (t, 1H), 4.28–4.25 (dd, $J = 4.5$, 9.0 Hz, 1H), 2.39 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 169.9$, 153.3, 143.6, 137.6, 135.7, 132.5, 130.2, 129.8, 129.5, 129.2, 128.8, 127.9, 127.5, 125.7, 70.5, 58.7, 58.1, 57.7, 21.6 ppm. Compound **7** (Table 1, entry 7) isolated as white solids (101 mg, 58% yield); ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.42$–7.31 (m, 7H), 7.15–7.13 (d, $J = 8.5$ Hz, 2H), 7.10–7.09 (d, $J = 8.5$ Hz, 2H), 6.91–6.89 (d, $J = 8.5$ Hz, 2H), 5.99 (s, 1H), 5.76–5.74 (d, $J = 10.5$ Hz, 1H), 5.51–5.48 (dd, $J = 4.5$, 9.0 Hz, 1H), 4.75–4.72 (t, 1H), 4.62–4.60 (d, $J = 9.5$ Hz, 2H), 4.30–4.27 (dd, $J = 4.5$, 9.0 Hz, 1H), 2.45 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 171.2$, 153.6, 143.9, 137.8, 135.5, 134.9, 131.3, 129.4, 129.3, 128.8, 127.5, 125.6, 123.0, 70.4, 59.9, 58.0, 57.3, 21.7 ppm. Compound **8** (Table 1, entry 8) isolated as a white solid (99 mg, 64% yield); ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.53$–7.51 (d, $J = 8.0$ Hz, 2H), 7.38–7.34 (m, 3H), 7.23–7.07 (m, 7H), 6.99–6.96 (t, 1H), 6.20 (s, 1H), 5.45 (s, 1H), 5.34–5.32 (dd, $J = 3.5$, 8.5 Hz, 1H), 5.22 (s, 1H), 4.54–4.50 (t, 1H), 4.20–4.18 (dd, $J = 3.5$, 8.5 Hz, 1H), 2.40 (s, 3H), 2.32 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 170.0$, 153.1, 143.7, 137.8, 136.3, 135.6, 134.3, 130.6, 129.6, 129.2, 128.7, 128.6, 127.5, 126.2, 125.5, 70.4, 58.9, 58.0, 55.9, 21.6, 19.2 ppm. Compound **9** (Table 1, entry 9) isolated as white solids (95 mg, 60% yield); ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.53$–7.52 (m, 2H), 7.42–7.34 (m, 3H), 7.29–7.27 (m, 2H), 7.13–7.11 (d, $J = 8.0$ Hz, 2H), 7.02–6.99 (m, 2H), 6.71–6.68 (m, 2H), 6.10–6.08 (d, $J = 8.0$ Hz, 1H), 5.85–5.83 (d, $J = 9.0$ Hz, 1H), 5.41–5.39 (dd, $J = 4.0$, 8.5 Hz, 1H), 4.77–4.74 (t, 1H), 4.72–4.68 (t, 1H), 4.25–4.22 (dd, $J = 4.0$, 8.5 Hz, 1H), 3.75 (s, 3H), 2.35 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 167.1$, 159.5, 153.4, 143.2, 137.8, 137.2, 129.3, 129.2, 128.9, 128.5, 128.3, 127.2, 125.7, 114.0, 70.4,60.2, 57.8, 55.2, 54.8, 21.4 ppm. Compound **10** (Table 1, entry 10) isolated as a white solid (59 mg, 34% yield); ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.47$–7.46 (d, $J = 8.0$ Hz, 1H), 7.41–7.38 (m, 5H), 7.36–7.32 (m, 2H), 7.30–7.24 (m, 3H), 7.05–7.03 (d, $J = 8.0$ Hz, 1H), 6.03 (s, 1H), 5.64–5.62 (d, $J = 11.0$ Hz, 1H), 5.47–5.45 (dd, $J = 4.0$, 8.5 Hz, 1H), 4.78–4.76 (d, $J = 9.5$ Hz, 1H), 4.73–4.69 (t, 1H), 4.30–4.27 (dd, $J = 4.0$, 8.5 Hz, 1H), 2.37 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 170.5$, 153.5, 143.9, 137.7, 137.6, 135.0, 131.5, 130.8, 130.6, 129.5, 129.3, 129.0, 128.9, 127.4, 125.6, 125.5, 124.8, 124.7, 70.5, 60.3, 58.0, 57.4, 21.5 ppm.