



Synthesis of imidazoisindol-3-ones by a palladium-catalyzed intramolecular C–H insertion reaction

Srinivasa Reddy Dandepally, Alfred L. Williams *

Department of Pharmaceutical Sciences, Biomanufacturing Research Institute and Technology Enterprise (BRITE), North Carolina Central University, Durham, NC 27707, USA

ARTICLE INFO

Article history:

Received 22 November 2008

Revised 30 December 2008

Accepted 7 January 2009

Available online 13 January 2009

ABSTRACT

A simple protocol for the synthesis of various imidazoisindol-3-ones is described by employing a palladium-catalyzed intramolecular C–H insertion reaction of substituted 2-haloaryl imidazolin-2-ones.

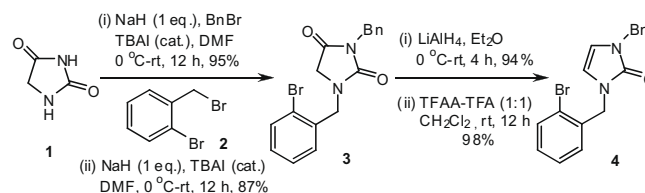
© 2009 Elsevier Ltd. All rights reserved.

Heterocyclic compounds are commonly used as scaffolds in designing biologically active compounds.¹ Imidazolone-based heterocyclic molecules play an important role in various biochemical processes, and their use as building blocks in developing new drugs such as COX-2 inhibitors,^{2a} anti-inflammatory,^{2b} anticancer,^{2c,d} cardioactive agents,^{2e} angiotensin II receptor antagonists,^{2f} and others^{2g-i} is well documented. Imidazoisindolones with phenolic subunits have been reported to exhibit high fluorescent properties.³ Recently, imidazoisindolone-based orally active drug candidates for the treatment of respiratory syncytial virus were explored.⁴

Transition metal-catalyzed C–H activation reactions have gained significant importance over the years.⁵ Functional group-directed C–H insertion reactions are widely used for the synthesis of various heterocyclic ring systems.⁶ Among these, palladium-catalyzed C-arylation reaction is a valuable synthetic tool for the formation of a wide variety of oxygen and nitrogen heterocycles.⁷ Palladium-catalyzed intermolecular C–H functionalization of imidazolin-2-one under ligand-less conditions has been published recently by Chen and co-workers.⁸ Herein, we report an intramolecular C–H insertion reaction of 2-haloaryl imidazolinones to synthesize aryl imidazoisindolones.⁹

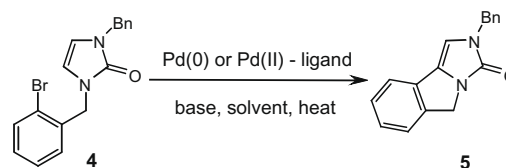
Although imidazolin-2-one is commercially available, we have prepared 2-bromobenzyl imidazolinone derivative **4** from commercially cheaply available hydantoin (**1**) in four steps rather than from the quite expensive imidazolin-2-one.¹⁰ Hydantoin (**1**) was first subjected to monobenylation¹¹ by treating with NaH, benzyl bromide, and a catalytic amount of tetrabutylammonium iodide (TBAI) in anhydrous DMF, and then reacted with 2-bromobenzyl bromide (**2**) under same conditions to furnish N,N-diarylated hydantoin **3**. Selective reduction of the amide carbonyl of **3** by LiAlH₄ (1 equiv) in Et₂O, and the subsequent elimination of aminol

by treating with a mixture of trifluoroacetic anhydride (TFAA)¹² and TFA in CH₂Cl₂ furnished 1-benzyl-3-(2-bromobenzyl)-1H-imidazol-2(3H)-one (**4**) (Scheme 1).



Scheme 1.

Our study began with the cyclization of 1-benzyl-3-(2-bromobenzyl)-1H-imidazol-2(3H)-one (**4**). In the very first attempt, **4** was treated with Pd(OAc)₂, PPh₃, and Cs₂CO₃ in anhydrous DMF at 80 °C. We were delighted to observe the complete consumption of **4** in 12 h to furnish 2-benzyl-2H-imidazo[5,1-a]isindol-3(5H)-one (**5**) in 66% yield (Scheme 2). In an attempt to improve the yield of **5**, we carried out a series of experiments with different palladium catalysts, ligands, and bases (Table 1). The best observed reaction conditions for C–H insertion reaction were Pd(OAc)₂ with bidentate ligand 1,2-bis(diphenylphosphino)ethane (dppe) (Table 1, entry 4) and Pd(PPh₃)₄ (Table 1, entry 8) with yields of 79%



Scheme 2.

* Corresponding author. Tel.: +1 919 530 6706; fax: +1 919 530 6600.

E-mail address: awilliams@ncu.edu (A.L. Williams).

Table 1
Optimization of reaction conditions^a

Entry	Catalyst	Ligand	Base	Time (h)	Yield ^b (%)
1	Pd(OAc) ₂	PPh ₃	Cs ₂ CO ₃	10	66
2	Pd(OAc) ₂	PPh ₃	K ₂ CO ₃	10	60
3	Pd(OAc) ₂	dppp	Cs ₂ CO ₃	3	53
4	Pd(OAc) ₂	dppe	Cs ₂ CO ₃	3	80
5	Pd(OAc) ₂	dppb	Cs ₂ CO ₃	3	72
6	Pd(OAc) ₂	(±)BINAP	Cs ₂ CO ₃	24	40 ^c
7	Pd(OAc) ₂	Xantophos	Cs ₂ CO ₃	24	40 ^c
8	Pd(PPh ₃) ₄	—	Cs ₂ CO ₃	12	79
9	Pd(OAc) ₂	—	NaOAc·3H ₂ O	24	—
10	Pd(OAc) ₂	—	NaOAc	24	—

^a Conditions: Pd catalyst (10 mol %), ligand (20 mol %), base (1.5 equiv), DMF (entries 1–8), DMSO (entries 9 and 10), 80 °C.

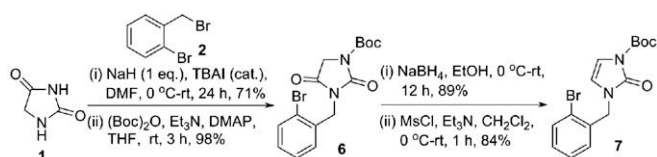
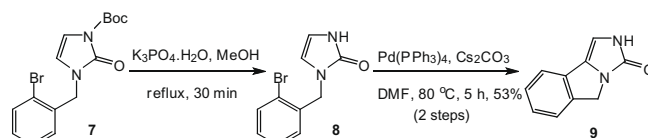
^b Isolated yield.

^c Conversion based on TLC.

and 80%, respectively. Attempted C–H insertion of **4** under ligand-less conditions⁸ using Pd(OAc)₂ and NaOAc in DMSO gave multiple products (Table 1, entries 9 and 10).

2-Benzyl-2*H*-imidazo[5,1-*a*]isoindol-3(5*H*)-one (**5**) was characterized by NMR spectroscopy (¹H and ¹³C) and MS. But to our surprise, **5** decomposed in CDCl₃ within an hour resulting in multiple spots. The compound **5** is quite stable in CD₃OD for several days when stored in the freezer, and somewhat stable in acetone-*d*₆, as we noticed approximately 15% decomposition in 24 h at room temperature.

Owing to the unusual decomposition of **5**, we first sought to replace the benzyl protecting group with a Boc group. Thus, the 2-bromobenzyl group was first introduced onto hydantoin (**1**) by reacting with 2-bromobenzyl bromide (**2**) and NaH, and then transformed it to the Boc protected 2-bromobenzyl derivative **6**. Selective reduction of the amide carbonyl with NaBH₄ in EtOH and elimination of the resulted aminol by MsCl and excess of Et₃N in CH₂Cl₂ afforded the *tert*-butyl 3-(2-bromobenzyl)-2-oxo-2,3-dihydro-1*H*-imidazole-1-carboxylate (**7**) (Scheme 3). When

**Scheme 3.****Scheme 4.**

compound **7** was allowed to react, only a 26% yield of cyclized product **7a** was obtained.¹³

We next decided to attempt the C–H insertion reaction while retaining the free hydrogen on the imidazolin-2-one. Recently, we have developed a mild and efficient method for the *N*-Boc deprotection under basic conditions in boiling MeOH.¹⁴ The *N*-Boc moiety on **7** was cleaved under mild basic conditions using K₃PO₄·H₂O in refluxing MeOH within a short reaction time of 30 min to afford 1-(2-bromobenzyl)-1*H*-imidazol-2(3*H*)-one (**8**) (Scheme 4). With suitable reaction conditions in hand, we examined the palladium-catalyzed intramolecular C–H insertion reaction on **8**. When **8** was treated with 20 mol % of Pd(PPh₃)₄ and Cs₂CO₃ in DMF, we obtained 2*H*-imidazo[5,1-*a*]isoindol-3(5*H*)-one (**9**) in 53% yield for 2 steps (Scheme 4).¹⁵

As an extension of this methodology, we decided to elaborate this for differentially substituted 2-haloaryl imidazolone derivatives. Accordingly, we have prepared 2-iodobenzyl imidazolone derivative **10** (Table 2, entry 2) by adopting the same reaction sequence from hydantoin (**1**) and 2-iodobenzyl bromide. *N*-Boc moiety in **10** was deprotected with K₃PO₄·H₂O in refluxing MeOH, and the resulted compound was then treated with 20 mol % of Pd(PPh₃)₄ and Cs₂CO₃ in DMF to give 2*H*-imidazo[5,1-*a*]isoindol-3(5*H*)-one (**9**) in an improved yield of 84% (Table 2, entry 2). Replacement of bromine with iodine increased the reaction rate and the yield of C–H insertion product.

Our next objective was to study the scope of this protocol for differentially substituted 2-bromoaryl imidazolone derivatives. Hence, we have prepared various substituted 2-bromoaryl-imidazolone derivatives with both electron-deficient aryl bromides and electron-rich aryl bromides by employing the appropriate synthetic sequences. Palladium-catalyzed intramolecular C–H insertion reactions of the substituted 2-bromoaryl-imidazolone derivatives were carried out and they produced various imidazoisoindol-3-ones (Table 2).¹⁶ The reaction tolerated a variety of different aryl substitution. As shown in Table 2, the nature as well as the position of the substituents on the aromatic ring affects the yields of the reaction. Substitution with electron-

Table 2

Entry	Substrate ^a	C–H insertion reaction time (h)	Product	Yield ^b (%)
1		5		53
2		1		84

Table 2 (continued)

Entry	Substrate ^a	C–H insertion reaction time (h)	Product	Yield ^b (%)
3		5		69
4		4		90
5		3		60
6		4		55
7		7		44
8		7		28

^a Conditions: Boc deprotection: K₃PO₄·H₂O (20 mol %), MeOH, reflux, 30 min. C–H insertion: Pd(PPh₃)₄ (20 mol %), Cs₂CO₃ (1.5 equiv), DMF, 80 °C.

^b Isolated yields after 2 steps (Boc deprotection and C–H insertion).

donating groups resulted in lower yields (Table 2, entries 7 and 8). The lower yields appear to be attributed to the decomposition of the cyclized products **20** and **22** during the work-up and/or purification step. Analysis of the reaction by LC/MS showed that, after 7 h, the starting materials were all consumed to give the products **20** and **22**, and there was no detection of any bromo-reduced by-products.¹⁷

In conclusion, we have developed an efficient methodology for the synthesis of various imidazoisoindol-3-ones by palladium-catalyzed intramolecular C–H insertion reaction. The synthetic utility of this method for the construction of imidazoisoquinolone, aryl imidazoazipinone ring systems, and their application toward natural product synthesis is under investigation, and the results will be published in due course.

Acknowledgments

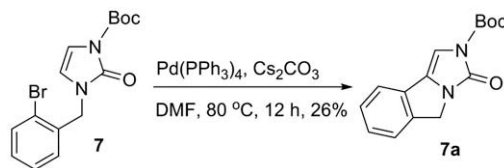
We gratefully acknowledge The Golden LEAF Foundation, Rocky Mount, NC, for the financial support. We thank Dr. Li-An Yeh, Director, BRITE, for the encouragement, and Dr. Sabapathy Sankar, Lab Supervisor for NMR facility, Department of Chemistry, NC State University, for NMR discussions. We also thank the Department of Chemistry at NC Central University for using their NMR facility.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.01.019.

References and notes

- Pozharskii, A. F.; Soldatenkov, A. T.; Katritzky, A. R. *Heterocycles in Life and Society*; John Wiley and Sons Ltd: New York, 1997.
- (a) Hassanein, H. H.; Khalifa, M. M.; El-Samalaty, O. N.; El-Rahim, M. A.; Taha, R. A.; Magda Ismail, M. F. *Arch. Pharm. Res.* **2008**, *31*, 562–568; (b) Sheppeck, J. E., II; Glimore, J. L.; Tebben, A.; Xue, C.-B.; Liu, R.-Q.; Decicco, C. P.; Duan, J. J. W. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2769–2774; (c) Xue, N.; Yang, X.; Wu, R.; Chen, J.; He, Q.; Yang, B.; Lu, X.; Hu, Y. *Bioorg. Med. Chem.* **2008**, *16*, 2550–2557; (d) Lai, Z.; Yang, T.; Kim, Y. B.; Sielecki, T. M.; Diamond, M. A.; Strack, P.; Rolfe, M.; Caligiuri, M.; Benfield, P. A.; Auger, K. R.; Copleland, R. A. *PNAS* **2002**, *99*, 14734–14739; (e) Schnettler, R. A.; Dage, R. C.; Grisar, J. M. *J. Med. Chem.* **1982**, *25*, 1477–1481; (f) Bernhart, C. A.; Perreaut, P. M.; Ferrari, B. P.; Muneaux, Y. A.; Assens, J.-L. A.; Clement, J.; Haudricourt, F.; Muneaux, C. F.; Taillades, J. E.; Vignal, M.-A.; Gougat, J.; Guiraudou, P. R.; Lacour, C. A.; Roccon, A.; Cazaubon, C. F.; Brelriere, J.-C.; Le Fur, G.; Nisato, D. *J. Med. Chem.* **1993**, *36*, 3371–3380; (g) Naylor, E. M.; Parmee, E. R.; Colandrea, V. J.; Perkins, L.; Brockunier, L.; Candelore, M. R.; Cascieri, M. A.; Colwell, L. F., Jr.; Deng, L.; Feeney, W. P.; Forrest, M. J.; Hom, G. J.; MacIntyre, D. E.; Strader, C. D.; Tota, L.; Wang, P.-R.; Wyvratt, M. J.; Fisher, M. H.; Weber, A. E. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 755–758; (h) Reitz, D. B.; Garland, D. J.; Norton, M. B.; Collins, J. T.; Reinhard, E. J.; Manning, R. E.; Olins, G. M.; Chen, S. T.; Palomo, M. A.; McMahon, E. G. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 1055–1060; (i) Carling, R. W.; Moore, K. W.; Moyes, C. R.; Jones, E. A.; Bonner, K.; Emms, F.; Marwood, R.; Patel, S.; Patel, S.; Fletcher, A. E.; Beer, M.; Sohal, B.; Pike, A.; Leeson, P. D. *J. Med. Chem.* **1999**, *42*, 2706–2715.
- Das, S.; Frohlich, R.; Pramanik, A. *Org. Lett.* **2006**, *8*, 4263–4266.
- (a) Bond, S.; Draffin, A.; Lambert, J.; Lim, C.-Y.; Lin, B.; Luttick, A.; Mitchell, J.; Morton, C.; Nearn, R.; Sanford, V.; Tucker, S. *Antiviral Res.* **2007**, *74*, A30; (b) Luttick, A.; Lin, B.; Morton, C.; Tucker, S.; Bond, S.; Draffin, A.; Lambert, J.; Lim, C.-Y.; Mitchell, J.; Sanford, V.; Ryan, J.; Kerr, A.; Iswaran, J.; Suzich, J.; McCarthy, M. *Antiviral Res.* **2007**, *74*, A55.
- For reviews on transition metal-catalyzed C–H functionalization: (a) Dick, A. R.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 2439–2463; (b) Yu, J.-Q.; Giri, R.; Chen, X. *Org. Biomol. Chem.* **2006**, *4*, 4041–4047; (c) Daugulis, O.; Zaitsev, V. G.; Shabashov, D.; Pham, Q.-N.; Lazareva, A. *Synlett* **2006**, 3382–3388; (d) Goj, L. A.; Gunnoe, T. B. *Curr. Org. Chem.* **2005**, *9*, 671–685; (e) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731–1769; (f) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1698–1712.
- For examples: (a) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972–4973; (b) Chen, X.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 12634–12635; (c) Beck, E. M.; Grimster, N. P.; Hatley, R.; Gaunt, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 2528–2529; (d) Bressy, C.; Alberico, D.; Lautens, M. J. *Am. Chem. Soc.* **2005**, *127*, 13148–13149; (e) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 13154–13155; (f) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 8050–8057; (g) Rieth, R. D.; Mankad, N. P.; Calimano, E.; Sadighi, J. P. *Org. Lett.* **2004**, *6*, 3981–3983; (h) Wiedemann, S. H.; Lewis, J. C.; Ellman, J. A.; Bergman, R. G. *J. Am. Chem. Soc.* **2006**, *128*, 2452–2462; (i) Chotana, G. A.; Rak, M. A.; Smith, M. R., III. *J. Am. Chem. Soc.* **2005**, *127*, 10539–10544.
- (a) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174–238. and references cited therein; (b) Seregin, I. Y.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173–1193; (c) Wolfe, J. P.; Thomas, J. S. *Curr. Org. Chem.* **2005**, *9*, 625–655; (d) Miura, M.; Satoh, T. *Top. Organomet. Chem.* **2005**, *14*, 55–83.
- Lu, J.; Tan, X.; Chen, C. *J. Am. Chem. Soc.* **2007**, *129*, 7768–7769.
- For intramolecular C-arylation of imidazole and pyrrole see: Arai, N.; Takahashi, M.; Mitani, M.; Mori, A. *Synlett* **2006**, 3170–3172.
- The price of imidazolin-2-one for 1 g: \$950 from a leading chemical supplier, Focus Synthesis LLC, San Diego, CA, USA.
- Martinez, A.; Alonso, M.; Castro, A.; Dorronsoro, I.; Gelpi, J. L.; Luque, F. J.; Perez, C.; Moreno, F. *J. Med. Chem.* **2005**, *48*, 7103–7112.
- Liao, Z. K.; Kohn, H. *J. Org. Chem.* **1984**, *49*, 4745–4752.
- Reaction conditions for the cyclization of compound **7**. The low yield is attributed to the decomposition of the product **7a**. Similar to compound **5**, fast decomposition of **7a** was observed in CDCl₃. The structure of **7a** was confirmed by ¹H NMR spectroscopy.



- Dandepally, S. R.; Williams, A. L. *Tetrahedron Lett.* **2009**, *50*, 1071–1074.
- Representative procedure for Boc deprotection and C–H insertion reaction:** Step 1: To a solution of *tert*-butyl 3-(2-bromobenzyl)-2-oxo-2,3-dihydro-1H-imidazole-1-carboxylate (**7**) (0.2 g, 0.566 mmol) in MeOH (4 mL) was added K₃PO₄·H₂O (0.026 g, 0.113 mmol) and heated at reflux for 30 min. Reaction mixture was filtered through a pad of Celite and the filtrate was evaporated under vacuo to give a crude 1-(2-bromobenzyl)-1H-imidazol-2(3H)-one (**8**), which was carried forward without further purification. Step 2: After dissolving **8** in anhydrous DMF (4 mL) were added Pd(PPh₃)₄ (0.131 g, 0.113 mmol) and Cs₂CO₃ (0.277 g, 0.849 mmol), and heated at 80 °C under nitrogen atmosphere for 5 h. After completion of the reaction, solvent was removed under vacuo and the crude mixture was purified by flash silica gel column chromatography by eluting with MeOH–CH₂Cl₂ (1:19) to furnish a pure colorless solid, 2H-imidazo[5,1-a]isoindol-3(5H)-one (**9**) (0.052 g, 53% for 2 steps).
- Spectroscopic data of the final imidazoisoindol-3-ones:** 2-Benzyl-2H-imidazo[5,1-a]isoindol-3(5H)-one (**5**): Colorless syrup. ¹H NMR (300 MHz, CD₃OD) δ (ppm) 4.83 (s, 2H), 4.88 (s, 2H), 6.73 (s, 1H), 7.27–7.34 (m, 7H), 7.49 (t, 2H, *J* = 7.8 Hz). ¹³C NMR (75 MHz, CD₃OD) δ (ppm) 49.4 (2C), 104.3, 122.0, 126.0, 129.4, 129.6, 129.7, 130.2, 130.7, 131.8, 139.5, 142.4. APCI/ESI-MS: *m/z* 263 [M+H]⁺. 2H-imidazo[5,1-a]isoindol-3(5H)-one (**9**): White solid, mp: 224–226 °C. ¹H NMR (300 MHz, CD₃OD) δ (ppm) 4.78 (s, 2H), 6.67 (s, 1H), 7.29 (dt, 1H, *J* = 1.2, 7.5 Hz), 7.37 (t, 1H, *J* = 7.5 Hz), 7.47 (d, 1H, *J* = 7.5 Hz), 7.53 (d, 1H, *J* = 7.5 Hz). ¹³C NMR (75 MHz, CD₃OD) δ (ppm) 48.1, 100.6, 121.0, 125.1, 128.3, 129.3, 131.1, 141.8. APCI/ESI-MS: *m/z* 173 [M+H]⁺. 7-Fluoro-2H-imidazo[5,1-a]isoindol-3(5H)-one (**12**): Light yellow solid, mp: 241–243 °C. ¹H NMR (300 MHz, CD₃OD+CDCl₃) δ (ppm) 4.80 (s, 2H), 6.60 (s, 1H), 7.11 (dt, 1H, *J* = 2.4, 8.4 Hz), 7.24 (dd, 1H, *J* = 2.7, 8.4 Hz), 7.51 (dd, 1H, *J* = 4.8, 8.4 Hz). ¹³C NMR (75 MHz, CD₃OD+CDCl₃) δ (ppm) 47.9 (d), 100.0 (d), 112.4 (d), 116.3 (d), 122.1 (d), 127.2 (d), 143.7 (d), 161.6, 164.9. APCI/ESI-MS: *m/z* 191 [M+H]⁺. 7-Chloro-2H-imidazo[5,1-a]isoindol-3(5H)-one (**14**): Light yellow solid, mp: 226–228 °C. ¹H NMR (300 MHz, CD₃OD) δ (ppm) 4.81 (s, 2H), 6.66 (s, 1H), 7.37 (dt, 1H, *J* = 1.8, 8.1 Hz), 7.47–7.51 (m, 2H). ¹³C NMR (75 MHz, CD₃OD) δ (ppm) 47.7, 101.0, 121.9, 125.3, 129.4, 133.8, 143.3. APCI/ESI-MS: *m/z* 207 [M+H]⁺. 7-Nitro-2H-imidazo[5,1-a]isoindol-3(5H)-one (**16**): Brown solid, mp > 300 °C. ¹H NMR (300 MHz, DMSO-*d*₆) δ (ppm) 4.87 (s, 2H), 7.07 (d, 1H, *J* = 2.4 Hz), 7.73 (d, 1H, *J* = 8.7 Hz), 8.27 (dd, 1H, *J* = 2.4, 8.7 Hz), 8.36 (s, 1H), 10.50 (br s, 1H, NH). ¹³C NMR (75 MHz, DMSO-*d*₆) δ (ppm) 46.7, 104.3, 119.8, 120.0, 124.3, 136.5, 142.0. APCI/ESI-MS: *m/z* 218 [M+H]⁺. 8-Methyl-2H-imidazo[5,1-a]isoindol-3(5H)-one (**18**): Light yellow solid, mp: 226–228 °C. ¹H NMR (300 MHz, CD₃OD) δ (ppm) 2.39 (s, 3H), 4.73 (s, 2H), 6.59 (s, 1H), 7.11 (d, 1H, *J* = 8.1 Hz), 7.30–7.34 (m, 2H). ¹³C NMR (75 MHz, CD₃OD+CDCl₃) δ (ppm) 21.6, 47.7, 100.1, 121.3, 124.5, 129.1, 130.8, 131.0, 138.5, 139.2, 152.5. APCI/ESI-MS: *m/z* 178 [M+H]⁺. 7,8-Dimethoxy-2H-imidazo[5,1-a]isoindol-3(5H)-one (**20**): White solid, mp: 234–236 °C. ¹H NMR (300 MHz, CD₃OD) δ (ppm) 3.86 (s, 6H), 4.70 (s, 2H), 6.54 (s, 1H), 7.12 (s, 1H), 7.15 (s, 1H). ¹³C NMR (75 MHz, CDCl₃+CD₃OD) δ (ppm) 46.9, 56.0 (2C), 97.3, 102.8, 106.8, 122.3, 129.9, 132.6, 148.9, 149.4. APCI/ESI-MS: *m/z* 233 [M+H]⁺. 6H-[1,3]Dioxolo[4,5-*ff*]imidazo[5,1-a]isoindol-7(9H)-one (**22**): Brown solid, mp > 300 °C. ¹H NMR (300 MHz, CD₃OD+CDCl₃) δ (ppm) 4.68 (s, 2H), 6.01 (s, 2H), 6.51 (s, 1H), 6.96 (s, 1H), 6.99 (s, 1H). ¹³C NMR (75 MHz, CD₃OD+CDCl₃) δ (ppm) 47.9, 98.9, 101.4, 103.0, 105.6, 124.6, 135.2, 149.6. APCI/ESI-MS: *m/z* 217 [M+H]⁺.
- See [Supplementary data](#) for the LC/MS analysis data.