JOC Article
pubs.acs.org/joc

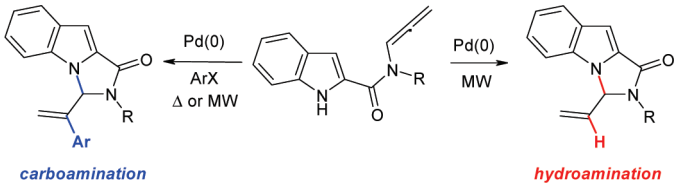
Tunable Pd-Catalyzed Cyclization of Indole-2-carboxylic Acid Allenamides: Carboamination vs Microwave-Assisted Hydroamination

Egle M. Beccalli,[‡] Alice Bernasconi,[‡] Elena Borsini,[‡] Gianluigi Broggini,*[,§] Micol Rigamonti,[§] and Gaetano Zecchi[§]

[‡]*DISMAB, Sezione di Chimica Organica "A. Marchesini", Università di Milano, via Venezian 21, 20133 Milano, Italy, and* [§]*Dipartimento di Scienze Chimiche e Ambientali, Università dell'Insubria, via Valleggio 11, 22100 Como, Italy*

gianluigi.broggini@uninsubria.it

Received July 30, 2010



A variety of 3-vinyl-substituted imidazo[1,5-*a*]indole derivatives were synthesized by intramolecular Pd-catalyzed cyclization of the title allenamides through either a domino carbopalladation/*exo*-cyclization process or a novel hydroamination reaction that proceeds smoothly under microwave irradiation. Both the observed pathways involve a π-allyl-palladium(II) complex arising from insertion of the allene group into a palladium(II) species, the latter being formed in situ by the intervention of an aryl iodide or of the N−H group. In both cases, the role of nucleophile is covered by the indole nitrogen.

Introduction

For a long time, the reactions of allenes have attracted much attention due to the peculiar chemical properties associated with their cumulated double bonds.[1] In particular, during the past decades, an increasing interest has been placed on transition metal-catalyzed cyclization of functionalized allenes as a powerful one-step method to prepare carbo- and heterocycles endowed with highly substituted olefin groups,[2] which can be useful intermediates for natural and pharmaceutical product synthesis.[3] Palladium catalysts often have been employed for cyclization reactions of allenes bearing a nucleophilic functionality, leading to *exo*- or *endo*-olefin-containing cyclic compounds (Figure 1, paths a and b).[4,5] In this context, among the different kinds of

(1) (a) Krause, N.; Hashmi, A. S. K. *Modern Allene Chemistry*; Wiley-VCH: Weinheim, Germany, 2004. (b) Alcaide, B.; Almendros, P.; Aragoncillo, C. *Chem. Soc. Rev.* **2010**, *39*, 783. (c) Back, T. G. *Tetrahedron* **2001**, *57*, 5263.

(2) (a) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067. (b) Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12. (c) Ma, S. *Chem. Rev.* **2005**, *105*, 2829. (d) Ma, S. *Acc. Chem. Res.* **2009**, *42*, 1679. (e) Jeganmohan, M.; Cheng, C.-H. *Chem. Commun.* **2008**, 3101. (f) Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, *3*, 387. (g) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590.

(3) (a) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196. (b) Hattori, G.; Yoshida, A.; Miyake, Y.; Nishibayashi, Y. *J. Org. Chem.* **2009**, *74*, 7603. (c) Fukamizu, K.; Miyake, Y.; Nishibayashi, Y. *J. Am. Chem. Soc.* **2008**, *130*, 10498. (d) Yang, Q.; Jiang, X.; Ma, S. *Chem.—Eur. J.* **2007**, *13*, 9310. (e) Klein, A.; Miesch, M. *Tetrahedron Lett.* **2003**, *44*, 4483. (f) Winter, H.; Maeda, Y.; Mitsuya, H.; Zemlicka, J. *J. Med. Chem.* **1996**, *39*, 3300. (g) Bouyssi, D.; Gore, J.; Balme, G.; Louis, D.; Wallach, J. *Tetrahedron Lett.* **1993**, *34*, 3129.

(4) For examples of Pd-catalyzed *exo*-cyclizations of allenes, see: (a) Franzen, J.; Backvall, J.-E. *J. Am. Chem. Soc.* **2003**, *125*, 6056. (b) Walkup, R. D.; Park, G. *Tetrahedron Lett.* **1987**, *28*, 1023. (c) Walkup, R. D.; Mosher, M. D. *Tetrahedron* **1993**, *49*, 9285. (d) Walkup, R. D.; Mosher, M. D. *Tetrahedron Lett.* **1994**, *35*, 8545. (e) Lathbury, D.; Vernon, P.; Gallagher, T. *Tetrahedron Lett.* **1986**, *27*, 6009. (f) Gallagher, T.; Davies, I. W.; Jones, S. W.; Lathbury, D. *J. Chem. Soc., Perkin Trans. 1* **1992**, 433. (g) Kimura, M.; Saeki, N.; Uchida, S.; Harayama, H.; Tanaka, S.; Fugami, H.; Tamaru, Y. *Tetrahedron Lett.* **1993**, *34*, 7611. (h) Kimura, M.; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1995**, *60*, 3764. (i) Ma, S.; Zhao, S. *J. Am. Chem. Soc.* **1999**, *121*, 7943. (j) Kang, S.-K.; Baik, T.-G.; Hur, Y. *Tetrahedron* **1999**, *55*, 6863. (k) Rutjes, F. P. J. T.; Tjen, K. C. M. F.; Wolf, L. B.; Karstens, W. F. J.; Schoemaker, H. E.; Hiemstra, H. *Org. Lett.* **1999**, *1*, 717. (l) Ohno, H.; Anzai, M.; Toda, A.; Ohishi, S.; Fujii, N.; Tanaka, T.; Takemoto, Y.; Ibuka, T. *J. Org. Chem.* **2001**, *66*, 4904.

(5) For examples of Pd-catalyzed *endo*-cyclizations of allenes, see: (a) Ma, S.; Gao, W. *J. Org. Chem.* **2002**, *67*, 6104. (b) Ma, S.; Yu, Z. *Angew. Chem., Int. Ed.* **2002**, *41*, 1775. (c) Ma, S.; Gu, Z.; Yu, Z. *J. Org. Chem.* **2005**, *70*, 6291. (d) Ma, S.; Yu, Z. *Org. Lett.* **2003**, *5*, 1507. (e) Ma, S.; Yu, Z.; Gu, Z. *Chem.—Eur. J.* **2005**, *11*, 2351. (f) Tsukamoto, H.; Kondo, Y. *Org. Lett.* **2008**, *10*, 2633. (g) Hamaguchi, A.; Kosaka, S.; Ohno, H.; Fujii, N.; Tanaka, T. *Chem.—Eur. J.* **2007**, *13*, 1692. (h) Karstens, W. F. J.; Klomp, D.; Rutjes, F. P. J. T.; Hiemstra, H. *Tetrahedron* **2001**, *57*, 5123. (i) Yu, F.; Lian, X.; Ma, S. *Org. Lett.* **2007**, *9*, 1703.

DOI: 10.1021/jo101501u Published on Web 09/23/2010

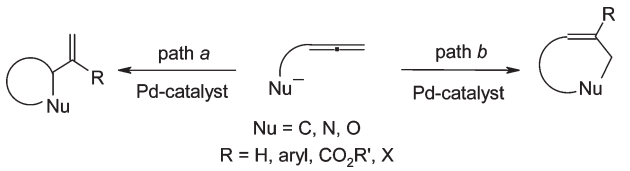


FIGURE 1. Pd-catalyzed *exo*- and *endo*-cyclization of nucleophilic substituted allenes.

1,2-diene derivatives, allenamides have been shown to be versatile and effective building blocks for generating nitrogen-containing heterocycles.[6]

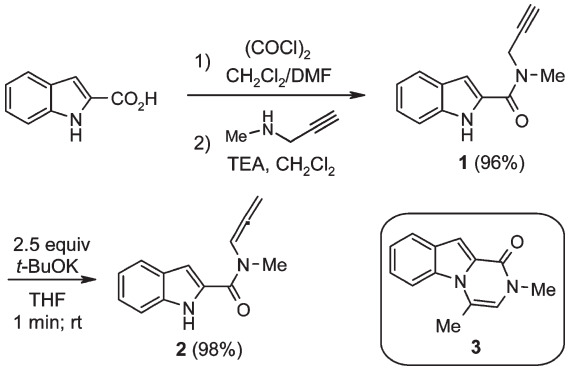
On the basis of our late interest toward the syntheses of five-membered heterocycles starting from allenes,[6f,g,7] as well as of our ongoing efforts directed to the development of intramolecular palladium-catalyzed procedures,[8] we have recently reported the domino carbopalladation/5-*exo*-allylic amination of α-aminoacid allenamides as a fruitful route to imidazolidinone derivatives.[9]

Herein, we describe new results concerning the Pd-catalyzed intramolecular carboamination and hydroamination of indolyl allenamides leading to vinyl-substituted imidazo-[1,5-*a*]indole derivatives, where a pivotal role in determining the feasibility of the hydroamination process was covered by the microwave assistance.

Results and Discussion

The paradigmatic allene **2** suitable to our study was synthesized in near quantitative yields from indole-2-carboxylic acid through conversion into the propargylamide **1** and following prototropic isomerization promoted by *t*-BuOK (Scheme 1). It is crucial for the formation of the allene **2** to avoid an exposure to the base longer than 1 min, in order to prevent the nucleophilic attack of the nitrogen atom to the central carbon of the 1,2-diene moiety giving the pyrazino[1,2-*a*]indole **3**.

SCHEME 1. Preparation of the Indole Allenamide 2



Carboamination Reactions. At first, we examined the possibility of cyclizing compound **2** by exploiting the known electrophilic reactivity of a π-allyl-palladium complex such as **4**, easily accessible by carbopalladation of the allene moiety.[10] In the present case, the second step of the domino process could have been accomplished by either the nitrogen atom or the C-3 of the indole ring. Under the best conditions typically used to promote this kind of reaction (1.5 equiv of PhI, 5 mol % of $Pd(PPh_3)_4$, 4.0 equiv of K_2CO_3), the cyclization really took place giving the α-styryl imidazo-[1,5-*a*]indole derivative **5a** (Scheme 2, path A). Among the array of solvents tested to optimize the reaction (DMF, DMA, MeCN, dioxane), acetonitrile was proven as the most effective. The formation of **5a** constitutes an overall carbopalladation/5-*exo*-allylic amination process, which is doubly selective since the π-allyl-palladium complex **4** is trapped exclusively on its internal carbon atom by the only indole nitrogen. The scope of this reaction was then explored with different aryl iodides, thus providing the expected products **5b**−**e**.

Despite the well-established palladium-catalyzed carbonylations[11] and their applications on allene derivatives,[12] the rarity of this kind of carboamination reactions on allenes in carbonylative conditions[13] prompted us to perform the domino heterocyclization of **2** in the presence of carbon monoxide. By using the same catalyst, base, and solvent, the allenamide **2** reacted with iodobenzene in CO atmosphere (1 atm) to give compound **7a**, even if in modest yield

(6) (a) Wei, L.-L.; Xiong, H.; Hsung, R. P. *Acc. Chem. Res.* **2003**, *36*, 773. (b) Berry, C. R.; Hsung, R. P. *Tetrahedron* **2004**, *60*, 7629. (c) Shen, L.; Hsung, R. P. *Org. Lett.* **2005**, *7*, 775. (d) Hyland, C. J. T.; Hegedus, L. S. *J. Org. Chem.* **2006**, *71*, 8658. (e) Gonzalez-Gomez, A.; Dominguez, G.; Pérez-Castells, J. *Eur. J. Org. Chem.* **2009**, 5057. (f) Broggini, G.; Galli, S.; Rigamonti, M.; Sottocornola, S.; Zecchi, G. *Tetrahedron Lett.* **2009**, *50*, 1447. (g) Manzo, A. M.; Perboni, A. D.; Broggini, G.; Rigamonti, M. *Tetrahedron Lett.* **2009**, *50*, 4696. (h) Chen, G.; Fu, C.; Ma, S. *Org. Lett.* **2009**, *11*, 2900. (i) Lohse, A. G.; Hsung, R. P. *Org. Lett.* **2009**, *11*, 3430. (j) Hayashi, R.; Feltenberger, J. B.; Hsung, R. P. *Org. Lett.* **2010**, *12*, 1152.

(7) (a) Broggini, G.; Bruché, L.; Zecchi, G.; Pilati, T. *J. Chem. Soc., Perkin Trans. 1* **1990**, 533. (b) Broggini, G.; Molteni, G.; Zecchi, G. *J. Org. Chem.* **1994**, *59*, 8271. (c) Broggini, G.; Zecchi, G. *Gazz. Chim. Ital.* **1996**, *126*, 479. (d) Broggini, G.; Molteni, G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1685.

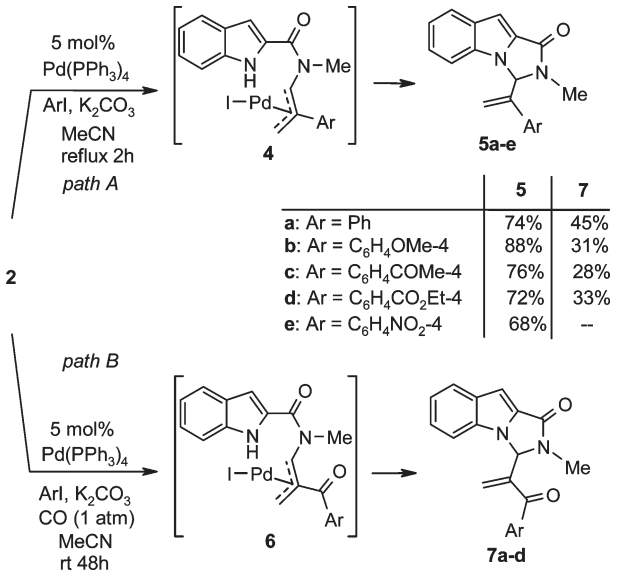
(8) (a) Abbiati, G.; Beccalli, E. M.; Broggini, G.; Zoni, C. *J. Org. Chem.* **2003**, *68*, 7625. (b) Abbiati, G.; Beccalli, E. M.; Broggini, G.; Martinelli, M.; Paladino, G. *Synlett* **2006**, 73. (c) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Masciocchi, N.; Sottocornola, S. *Org. Lett.* **2006**, *8*, 4521. (d) Beccalli, E. M.; Borsini, E.; Broggini, G.; Rigamonti, M.; Sottocornola, S. *Synlett* **2008**, 1053. (e) Beccalli, E. M.; Borsini, E.; Broggini, G.; Palmisano, G.; Sottocornola, S. *J. Org. Chem.* **2008**, *73*, 4746. (f) Basolo, L.; Beccalli, E. M.; Borsini, E.; Broggini, G. *Tetrahedron* **2009**, *65*, 3486. (g) Beccalli, E. M.; Borsini, E.; Brenna, S.; Galli, S.; Rigamonti, M.; Broggini, G. *Chem.—Eur. J.* **2010**, *16*, 1670.

(9) Beccalli, E. M.; Broggini, G.; Clerici, F.; Galli, S.; Kammerer, C.; Rigamonti, M.; Sottocornola, S. *Org. Lett.* **2009**, *11*, 1563.

(10) For recent examples of Pd-catalyzed carboalkylations of allenes, see: (a) Jiang, X.; Yang, Q.; Yu, Y.; Fu, C.; Ma, S. *Chem.—Eur. J.* **2009**, *15*, 7283. (b) Kammerer, C.; Prestat, G.; Madec, D.; Poli, G. *Chem.—Eur. J.* **2009**, *15*, 4224. (c) Ohno, H.; Miyamura, K.; Mizutani, T.; Kadoh, Y.; Takeoka, Y.; Hamaguchi, H.; Tanaka, T. *Chem.—Eur. J.* **2005**, *11*, 3728. (d) Ohno, H.; Miyamura, K.; Takeoka, Y.; Tanaka, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 2647. For recent examples of Pd-catalyzed carboaminations of allenes, see: (e) Cheng, X.; Ma, S. *Chem. Commun.* **2009**, 4263. (f) Okano, A.; Mizutani, T.; Oishi, S.; Tanaka, T.; Ohno, H.; Fujii, N. *Chem. Commun.* **2008**, 3534. (g) Cheng, X.; Ma, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 4581. (h) Ma, S.; Yu, F.; Li, J.; Gao, W. *Chem.—Eur. J.* **2007**, *13*, 247. (i) Yang, Q.; Jiang, X.; Ma, S. *Chem.—Eur. J.* **2007**, *13*, 9310. For recent examples of Pd-catalyzed carboalkoxylations of allenes, see: (j) Li, W.; Shi, M. *Eur. J. Org. Chem.* **2009**, 270. (k) Shin, C.; Oh, Y.; Cha, J. H.; Pae, A. N.; Choo, H.; Cho, Y. S. *Tetrahedron* **2007**, *63*, 2182. (l) Alcaide, B.; Almendros, P.; Martínez del Campo, T.; Rodríguez-Acebes, R. *Adv. Synth. Catal.* **2007**, *349*, 749. (m) Alcaide, B.; Almendros, P.; Rodríguez-Acebes, R. *J. Org. Chem.* **2006**, *71*, 2346. (n) Ma, S.; Zheng, Z.; Jiang, X. *Org. Lett.* **2007**, *9*, 529. (o) Ma, S.; Yu, Z. *Angew. Chem., Int. Ed.* **2003**, *42*, 1955.

(11) (a) Kollár, L. *Modern Carbonylation Methods*; Wiley-VCH: Weinheim, Germany, 2008. (b) Brennführer, A.; Neumann, H.; Beller, M. *ChemCatChem.* **2009**, *1*, 28. (c) Muzart, J. *Tetrahedron* **2005**, *61*, 9423. (d) Kadnikov, D. V.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 9423. (e) Grigg, R.; Rasparini, M.; MacLachlan, W. *Chem. Commun.* **2000**, 2241. (f) Grigg, R.; Liu, A.; Shaw, D.; Suganthan, S.; Woodall, D. E.; Yoganathan, G. *Tetrahedron Lett.* **2000**, *41*, 7125. (g) Grigg, R.; MacLachlan, W. S.; MacPherson, D. T.; Sridharan, V.; Suganthan, S.; Thornton-Pett, M.; Zhang, J. *Tetrahedron* **2000**, *56*, 6585. (h) Xiao, W.-J.; Alper, H. *J. Org. Chem.* **1999**, *64*, 9646. (i) Xiao, W.-J.; Vasapollo, G.; Alper, H. *J. Org. Chem.* **1998**, *63*, 2609. (j) Okuro, K.; Alper, H. *J. Org. Chem.* **1997**, *62*, 1566. (k) Imada, Y.; Vasapollo, G.; Alper, H. *J. Org. Chem.* **1996**, *61*, 7982. (l) Darcel, C.; Bruneau, C.; Dixneuf, P. H. *Synlett* **1996**, 218. (m) Piotti, M. E.; Alper, H. *J. Org. Chem.* **1994**, *59*, 1956.

SCHEME 2. Pd-Catalyzed Carboamination and Carbonylative Amination of Allenamide 2

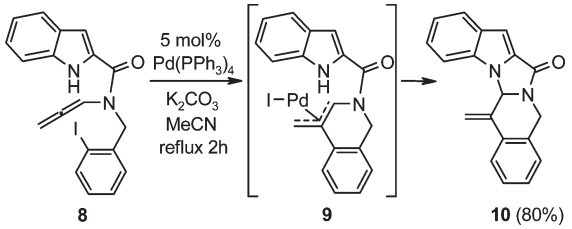


	5	7
a: Ar = Ph	74%	45%
b: Ar = C_6H_4OMe-4	88%	31%
c: Ar = C_6H_4COMe-4	76%	28%
d: Ar = $C_6H_4CO_2Et$-4	72%	33%
e: Ar = $C_6H_4NO_2$-4	68%	--

due to the presence of degradation products, having the imidazo[1,5-*a*]indole skeleton bearing an enone moiety (Scheme 2, path B). This reaction gave the best results working at room temperature for a prolonged time; in fact, by refluxing the mixture for 24 h an increased amount of carboamination product **5a** was formed. The reaction of compound **2** with 4-nitroiodobenzene under the same conditions at room temperature took place with formation of the carboamination compound **5e**, and no carbonylation product was detected. A reasonable step sequence leading to the products **7a**−**d** involves (i) carbonylation of the first-formed PhPd(II)I species to give the PhCOPdI complex and (ii) addition of the latter to the central carbon of the 1,2-diene group to form the aroyl intermediate **6**, which then undergoes the 5-*exo*-allylic cyclization to **7**.

The further stage of our investigation was directed to realize a totally intramolecular version of the domino allene carboamination described above, a kind of process that finds

SCHEME 3. Pd-Catalyzed Heteroyclization of Allenamide 8



rare precedents in the literature.[14] To this end, we synthesized the *o*-iodoaryl-substituted allenamide **8** from the corresponding propargylamide and reacted it with $Pd(PPh_3)_4$ and K_2CO_3 in acetonitrile. Actually, the reaction gave the pentacyclic imidazolinone derivative **10**, which can be ascribed to intramolecular carbopalladation of the allene group to form the π-allyl-palladium complex **9** and subsequent intramolecular amination by the indole nitrogen (Scheme 3).

Once again, acetonitrile was essential as the solvent to maximize the yield of the domino carboamination product **10**. In fact, the utilization of DMF provided, beside traces of the pentacyclic compounds **10** and **12**, a high amount of the pyrazine derivative **11** (Scheme 4, path a). The latter product can be justified by the direct nucleophilic attack of the nitrogen atom on the 1,2-diene central carbon, similarly to what has occurred in the conversion of **2** to **3**. The iodo derivative **11** was proven to be the precursor of **12** by an independent intramolecular Heck reaction carried out on the pyrazine double bond following the ligand-free "Jeffery conditions" (Scheme 4, path b).[15] The pentacyclic system **12** was also obtained directly starting from the allene **8** in the same conditions of path b, which are able to promote both the amination and the Heck reaction steps (Scheme 4, path c).

Hydroamination Reactions. The results described above provide an efficient and general entry to imidazo[1,5-*a*]indoles bearing in the 3-position a vinyl pendant that in turn happens to be α-substituted (eventually involving a further fused-ring). However, we envisaged the possibility to synthesize more simple substrates having in the 3-position an unsubstituted vinyl pendant, which are products of a hydroamination process. Although transition metal-catalyzed hydroamination reactions of allenes are an attractive atom-economical route to achieve nitrogen-containing heterocycles,[16] the examples of the Pd-catalyzed processes remain scarcely reported in the literature.[17] In the search for new conditions to this purpose, we investigated the behavior of the indolyl allenamide **2** under microwave irradiation.[18,19] We found that the microwave activation is able to provide a 5-*exo*-allylic hydroamination in the presence solely of

(12) (a) Kato, K.; Mochida, T.; Takayama, H.; Kimura, M.; Moriyama, H.; Takeshita, A.; Kanno, Y.; Inouye, Y.; Akita, H. *Tetrahedron Lett*. **2009**, *50*, 4744. (b) Kodama, S.; Nishinaka, E.; Nomoto, A.; Sonoda, M.; Ogawa, A. *Tetrahedron Lett*. **2007**, *48*, 6312. (c) Orito, K.; Miyazawa, M.; Nakamura, T.; Horibata, A.; Ushito, H.; Nagasaki, H.; Yuguchi, M.; Yamashita, S.; Yamazaki, T.; Tokuda, M. *J. Org. Chem*. **2006**, *71*, 5951. (d) Tang, S.; Yu, Q.-F.; Peng, P.; Li, J.-H.; Zhong, P.; Tang, R.-Y. *Org. Lett*. **2007**, *9*, 3413. (e) Acs, P.; Müller, E.; Rangits, G.; Lóránd, T.; Kollár, L. *Tetrahedron* **2006**, *62*, 12051. (f) Szolcsányi, P.; Gracza, T.; Spánik, I. *Tetrahedron Lett*. **2008**, *49*, 1357. (g) Gabriele, B.; Salerno, G.; Veltri, L.; Mancuso, R.; Li, Z.; Crispini, A.; Bellusci, A. *J. Org. Chem*. **2006**, *71*, 7895. (h) Liu, C.; Widenhoefer, R. A. *Chem.—Eur. J*. **2006**, *12*, 2371. (i) Gabriele, B.; Plastina, P.; Salerno, G.; Mancuso, R.; Costa, M. *Org. Lett*. **2007**, *9*, 3319. (j) Trzeciak, A. M.; Ziólowski, J. J. *Coord. Chem. Rev*. **2005**, *249*, 2308. (k) Gabriele, B.; Salerno, G.; Fazio, A.; Veltri, L. *Adv. Synth. Catal*. **2006**, *348*, 2212. (l) Gabriele, B.; Mancuso, R.; Salerno, G.; Costa, M. *Adv. Synth. Catal*. **2006**, *348*, 1101. (m) Cao, H.; Xiao, W.-J.; Alper, H. *Adv. Synth. Catal*. **2006**, *348*, 1807. (n) Kato, K.; Nouchi, H.; Ishikura, K.; Takaishi, S.; Motodate, S.; Tanaka, H.; Okudaira, K.; Mochida, T.; Nishigaki, R.; Shigenobu, K.; Akita, H. *Tetrahedron* **2006**, *62*, 2545. (o) Ma, W.; Li, X.; Yang, J.; Liu, Z.; Chen, B.; Pan, X. *Synthesis* **2006**, 2489.

(13) (a) Kang, S.-K.; Kim, K.-J. *Org. Lett*. **2001**, *3*, 511. (b) See ref 9.

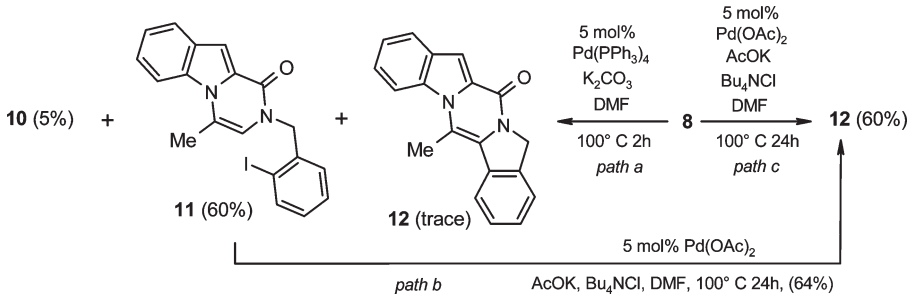
(14) (a) Grigg, R.; Koppen, I.; Rasparini, M.; Sridharan, V. *Chem. Commun*. **2001**, 964. (b) Hiroi, K.; Hiratsuka, Y.; Watanabe, K.; Abe, I.; Kato, F.; Hiroi, M. *Synlett* **2001**, 263. (c) Hiroi, K.; Hiratsuka, Y.; Watanabe, K.; Abe, I.; Kato, F.; Hiroi, M. *Tetrahedron: Asymmetry* **2002**, *13*, 1351. (d) Inuki, S.; Oishi, S.; Fujii, N.; Ohno, H. *Org. Lett*. **2008**, *10*, 5239. (e) See ref 9.

(15) (a) Jeffery, T.; Galland, J.-C. *Tetrahedron Lett*. **1994**, *35*, 4103. (b) Jeffery, T. *Tetrahedron* **1996**, *52*, 10113. (c) Jeffery, T.; David, M. *Tetrahedron Lett*. **1998**, *39*, 5751.

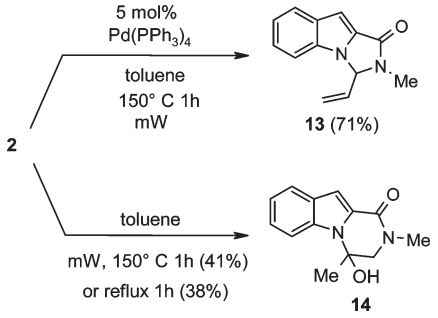
(16) For some recent examples, see: (a) LaLonde, R. L.; Sherry, B. D.; Kang, E. J.; Toste, F. D. *J. Am. Chem. Soc*. **2007**, *129*, 2452. (b) Tobisch, S. *Chem.—Eur. J*. **2008**, *14*, 8590. (c) Kinder, R. E.; Zhang, Z.; Widenhoefer, R. A. *Org. Lett*. **2008**, *10*, 3157. (d) Zeng, X.; Soleilhavoup, M.; Bertrand, G. *Org. Lett*. **2009**, *11*, 3166. (e) Li, H.; Widenhoefer, R. A. *Org. Lett*. **2009**, *11*, 2671. (f) Nishina, N.; Yamamoto, Y. *Tetrahedron* **2009**, *65*, 1799. (g) Toups, K. L.; Widenhoefer, R. A. *Chem. Commun*. **2010**, *46*, 1712. (h) LaLonde, R. L.; Wang, Z. J.; Mba, M.; Lackner, A. D.; Toste, F. D. *Angew. Chem., Int. Ed*. **2010**, *49*, 598.

(17) (a) Qiu, S.; Wei, Y.; Liu, G. *Chem.—Eur. J*. **2009**, *15*, 2751. (b) Meguro, M.; Yamamoto, Y. *Tetrahedron Lett*. **1998**, *39*, 5421. (c) Al-Masum, M.; Meguro, M.; Yamamoto, Y. *Tetrahedron Lett*. **1997**, *38*, 6071. (d) Besson, L.; Gorè, J.; Cazes, B. *Tetrahedron Lett*. **1995**, *36*, 3857.

SCHEME 4. Competitive Cyclizations of Allenamide 8



SCHEME 5. Intramolecular Cyclizations of Allenamide 2 under Microwave Irradiation



$Pd(PPh_3)_4$ as catalyst, affording the desired vinyl derivative **13** (Scheme 5). Both palladium catalyst and microvawe irradiation are necessary to promote the 5-*exo*-allylic hydroamination of indole allenamide **2**. In fact, heating **2** in the absence of microwave activation, only a tarry mixture due to degradation processes was obtained. Conversely, the lack of the palladium catalyst afforded the formation of the hydroxy-substituted pyrazino[1,2-*a*]indole **14** (41%). This latter arises from **3** by a formal addition of water and, however, the use of microwave activation is not essential, being achievable in 38% yield also by heating a solution of **2** in toluene.

Gratifyingly, a similar trend of reactivity was observed in analogous preparative reactions carried out on several indole allenamides variously substituted on the phenyl ring as well as on the amide nitrogen. Actually, the substrates **15a**−**i** afforded the vinyl compounds **16a**−**i** in satisfactory to high yields (Table 1).

In view of its novelty, the observed hydroamination reaction of the allenamides **2** and **15a**−**i** deserves a mechanistic picture. Similarly to what was previously reported for different NH groups (i.e., amines, amides, and pyrrole), an initial coordination of the Pd(0) catalyst with the indole nitrogen can give the Pd(II)−hydride complex **A** (Figure 2).[20]

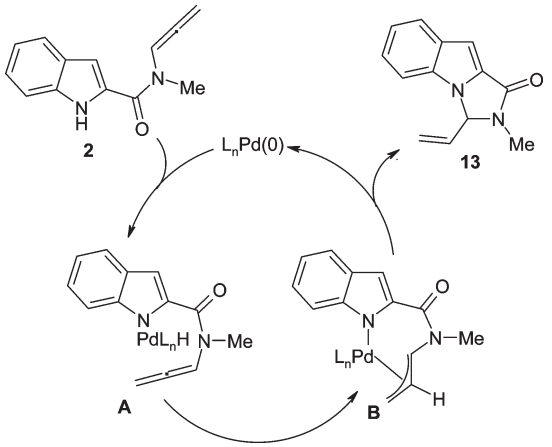


FIGURE 2. Proposed mechanistic cycle.

Such an intermediate would be susceptible to insertion of the allene group into the Pd−H bond to generate the π-allyl-Pd(II) complex **B**, which in turn would undergo the intramolecular formation of the new carbon−nitrogen bond and the subsequent reductive elimination of a Pd(0) species. As a support for the proposed mechanism, we found that the deuterated hydroamination product **18** was formed in the cyclization of the deuterium-substituted allene **17**, prepared by treatment of a solution of **2** in $CDCl_3$ with D_2O (Scheme 6).

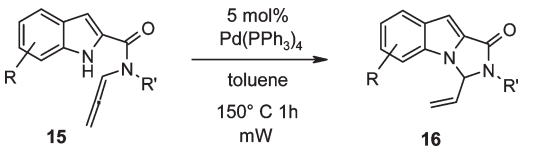
On comparing the carboamination and hydroamination pathways going from **2** to **5a**−**e** and **13** respectively, one can note that both of them involve the attack of the indole nitrogen to the inner carbon of a π-allyl-Pd(II) unity. However, the origin of the latter species is different in the two cases. In the first case, the π-allyl-Pd(II) intermediate is

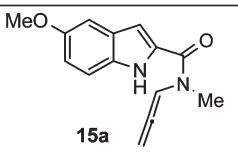
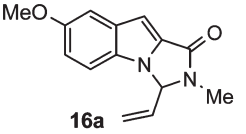
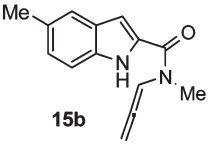
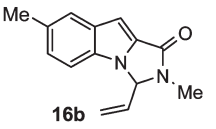
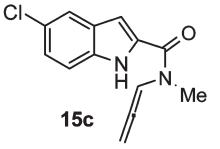
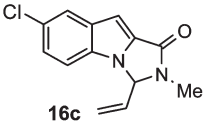
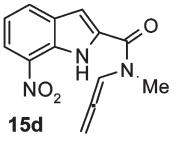
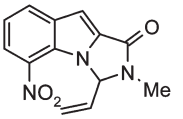
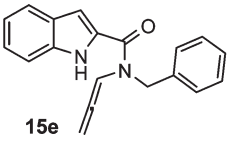
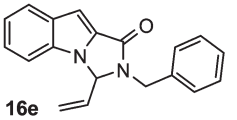
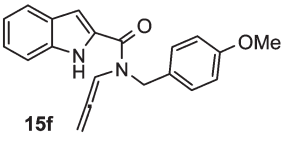
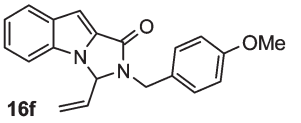
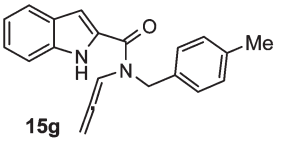
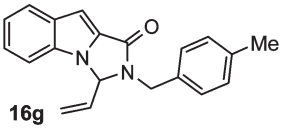
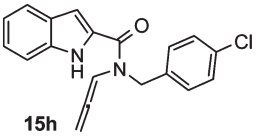
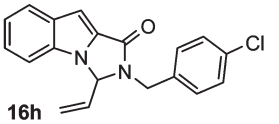
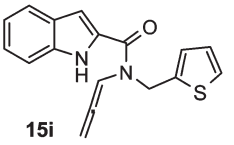
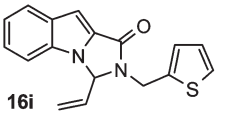
(18) For recent reviews and books on microwave-assisted organic synthesis, see: (a) Kappe, O. C. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250. (b) Loupy, A. *Microwaves in Organic Synthesis*, 2nd ed.; Wiley-VCH: Weinheim, Germany, 2006. (c) Polshettiwar, V.; Varma, R. S. *Acc. Chem. Res.* **2008**, *41*, 629. (d) Pineiro, M.; Pinho e Melo, T. M. V. D. *Eur. J. Org. Chem.* **2009**, 5287. (e) Caddick, S.; Fitzmaurice, R. *Tetrahedron* **2009**, *65*, 3325.

(19) For recent reviews on Pd-catalyzed reactions by microwave activation, see: (a) Appukkuttan, P.; Van der Eycken, E. *Eur. J. Org. Chem.* **2008**, 1133. (b) Barge, A.; Tagliapietra, S.; Tei, L.; Cintas, P.; Cravotto, G. *Curr. Org. Chem.* **2008**, *12*, 1588. For recent examples of Pd-catalyzed reactions by microwave activation, see: (c) Tsukamoto, H.; Matsumoto, T.; Kondo, Y. *J. Am. Chem. Soc.* **2008**, *130*, 388. (d) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Synthesis* **2008**, 136. (e) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Paladino, G.; Rossi, E. *Synthesis* **2006**, 2404. (f) Andaloussi, M.; Lindh, J.; Saevmarker, J.; Sjoeberg, P. J. R.; Larhed, M. *Chem.—Eur. J.* **2009**, *15*, 13069. (g) Roberts, B.; Liptrot, D.; Alcaraz, L. *Org. Lett.* **2010**, *12*, 1264. (h) Reichelt, A.; Falsey, J. R.; Rzasa, R. M.; Thiel, O. R.; Achmatowicz, M. M.; Larsen, R. D.; Zhang, D. *Org. Lett.* **2010**, *12*, 792.

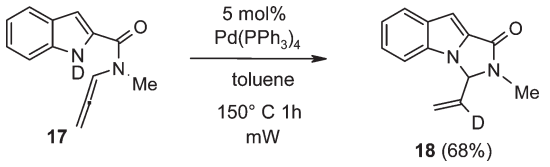
(20) (a) Tsuji, J. In *Palladium Reagents and Catalysts—New Perspectives for the 21st Century*; John Wiley & Sons, Ltd: Hoboken, NJ, 2004; pp 527, 538, 569, and 605. (b) Muller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675. (c) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, *28*, 199. (d) Seligson, A. L.; Cowan, R. L.; Trogler, W. C. *Inorg. Chem.* **1991**, *30*, 3371. (e) Fafard, C. M.; Adhikari, D.; Foxman, B. M.; Mindiola, D. J.; Ozerov, O. V. *J. Am. Chem. Soc.* **2007**, *129*, 10318. (f) Ozerov, O. V.; Guo, C.; Fan, L.; Foxman, B. M. *Organometallics* **2004**, *23*, 5573. (g) Fan, L.; Foxman, B. M.; Ozerov, O. V. *Organometallics* **2004**, *23*, 326. (h) Macchioni, A.; Romani, A.; Zuccaccia, C.; Guglielmetti, G.; Querci, C. *Organometallics* **2003**, *22*, 1526. (i) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Paladino, G. *Tetrahedron* **2005**, *61*, 1077. (j) Nakamura, I.; Itagaki, H.; Yamamoto, Y. *J. Org. Chem.* **1998**, *63*, 6458. (k) Shi, M.; Chen, Y.; Xu, B. *Org. Lett.* **2003**, *5*, 1225. (l) Radhakrishnan, U.; Al-Masum, M.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 1037. (m) Cheng, X.; Hii, K. K. *Tetrahedron* **2001**, *57*, 5445.

TABLE 1. Scope of the Reaction



Entry	Substrate	Product	Yield (%)
1	 15a	 16a	67
2	 15b	 16b	78
3	 15c	 16c	85
4	 15d	 16d	58
5	 15e	 16e	63
6	 15f	 16f	89
7	 15g	 16g	69
8	 15h	 16h	85
9	 15i	 16i	72

SCHEME 6. Pd-Catalyzed Hydroamination of Deuterated Indole Allenamides



due to a rather common reaction between the allene function and the first-formed PhPd(II)I, while in the second case the Pd(0)-catalyst acts at the indole NH group and the subsequent hydride transfer on the allene function generates the π-allyl-Pd(II) intermediate.

Conclusions

In summary, we have developed effective Pd-catalyzed protocols for the intramolecular carboamination or hydroamination reactions of indole allenamides that proceeded differently giving either α-styryl or simply vinyl imidazo[1,5-*a*]indoles. Two remarkable features are worth showing: (i) the nucleophilic activity of the indole nitrogen in the well-established carboamination reactions and (ii) the feasibility of the unusual Pd-catalyzed hydroamination of allenes in mild conditions under microwaves irradiation. We are currently working toward the development of a more general scope of the microwave-assisted hydroamination of allenes.

Experimental Section

General. Melting points are uncorrected. IR spectra were recorded on a FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts (δ) are given as ppm relative to the residual solvent peak (chloroform-d_1 7.25 ppm/77 ppm). Mass spectra were determined with an HPLC-MS apparatus. Elemental analyses were executed on CHN apparatus analyzer. Column chromatography was performed on silica gel 60 (mesh size 63−200 μm). The microwave reactions were performed in a standard CEM Discover instrument with temperature control, using the instrument's in-built IR sensor.

General Procedure for the Preparation of Propargylamides. A solution of indole-2-carboxylic acid (6.20 mmol), DMF (0.3 mL), and oxalyl chloride (18.60 mmol) in anhydrous CH_2Cl_2 (40 mL) was stirred at rt for 1 h and refluxed for 1 h. The solvent was evaporated under reduced pressure, the crude residue was diluted with CH_2Cl_2 (40 mL), and a solution of propargylamine (8.24 mmol) and triethylamine (8.24 mmol) in CH_2Cl_2 was added at 0 °C. The solution was stirred at rt for 1 h, the organic phase was washed with 1 M HCl and dried over Na_2SO_4, then the solvent was evaporated under reduced pressure. The resulting crude mixture was purified by flash chromatography to afford the desired product (eluent: light petroleum/AcOEt 7:3).

***N*-Methyl-*N*-propargyl-1*H*-indole-2-carboxamide (1):** yield 96%, white solid, mp 145 °C (*i*-Pr_2O); IR 3308, 3230, 2116, 1661 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (1H, s), 3.23 (3H, s), 4.49 (2H, s), 7.00 (1H, s), 7.15 (1H, dd, J = 8.0 Hz, 7.1 Hz), 7.30 (1H, dd, J = 8.2 Hz, 7.1 Hz), 7.46 (1H, d, J = 8.2 Hz), 7.69 (1H, d, J = 8.0 Hz), 9.56 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.8 (q), 40.3 (t), 73.2 (d), 78.5 (s), 106.4 (d), 112.3 (d), 120.7 (d), 122.3 (d), 124.8 (d), 127.8 (s), 129.0 (s), 136.3 (s), 163.6 (s); MS m/z 212 (M^+). Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.41; H, 5.82; N, 13.34.

***N*-(2-Iodobenzyl)-*N*-propargyl-1*H*-indole-2-carboxamide:** yield 84%, white solid, mp 173 °C (*i*-Pr_2O); IR 3310, 3227, 2123, 1670 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (1H, s), 4.44 (2H, s), 5.03 (2H, s), 7.07−7.14 (2H, m), 7.27−7.46 (5H, m), 7.63−7.69 (1H, m), 7.95−7.97 (1H, m), 9.62 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 38.3 (t), 49.7 (t), 73.2 (d), 78.0 (s), 87.1 (s), 104.9 (d), 111.1 (d), 119.8 (d), 120.7 (d), 121.7 (d), 127.4 (d), 128.6 (d), 129.5 (d), 131.3 (s) 138.5 (s), 139.1 (d), 139.8 (s), 146.1 (s), 162.3 (s); MS m/z 414 (M^+). Anal. Calcd for $C_{19}H_{15}IN_2O$: C, 55.09; H, 3.65; N, 6.76. Found: C, 55.15; H, 3.42; N, 6.55.

***N*-Methyl-*N*-propargyl-5-methoxy-1*H*-indole-2-carboxamide:** yield 94%, white solid, mp 143 °C (*i*-Pr_2O); IR 3305, 3224, 2114, 1658 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (1H, s), 3.20 (3H, s), 3.85 (3H, s), 4.48 (2H, s), 6.91 (1H, s), 6.96 (1H, d, J = 8.9 Hz), 7.08 (1H, s), 7.37 (1H, d, J = 8.9 Hz), 9.95 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 38.7 (q), 45.8 (t), 55.7 (q), 74.5 (d), 78.6 (s), 102.3 (d), 105.7 (d), 112.9 (d), 116.0 (d), 127.9 (s), 129.3 (s), 131.4 (s), 154.5 (s), 163.2 (s); MS m/z 242 (M^+). Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.22; H, 5.98; N, 11.69.

***N*-Methyl-*N*-propargyl-5-methyl-1*H*-indole-2-carboxamide:** yield 65%, white solid, mp 136 °C (*i*-Pr_2O); IR 3312, 3220, 2118, 1664 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (1H, s), 2.47 (3H, s), 3.41 (3H, s), 4.50 (2H, s), 6.93 (1H, s), 7.14 (1H, d, J = 8.4 Hz), 7.39 (1H, d, J = 8.4 Hz), 7.46 (1H, s), 10.09 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5 (q), 39.4 (q), 46.1 (t), 73.6 (d), 78.6 (s), 105.6 (d), 111.7 (d), 121.3 (d), 126.5 (d), 127.9 (s), 128.9 (s), 129.7 (s), 134.5 (s), 163.3 (s); MS m/z 226 (M^+). Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.56; H, 6.12; N, 12.45.

***N*-Methyl-*N*-propargyl-5-chloro-1*H*-indole-2-carboxamide:** yield 65%, white solid, mp 152 °C (*i*-Pr_2O); IR 3307, 3235, 2120, 1673 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (1H, s), 3.43 (3H, s), 4.48 (2H, s), 6.92 (1H, s), 7.24 (1H, d, J = 8.7 Hz), 7.40 (1H, d, J = 8.7 Hz), 7.64 (1H, s), 10.03 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.4 (q), 47.8 (t), 72.8 (d), 78.3 (s), 105.5 (d), 111.7 (d), 121.3 (d), 126.5 (d), 127.9 (s), 128.9 (s), 129.7 (s), 134.5 (s), 163.3 (s); MS m/z 246 (M^+). Anal. Calcd for $C_{13}H_{11}ClN_2O$: C, 63.29; H, 4.49; N, 11.36. Found: C, 63.01; H, 4.62; N, 11.58.

***N*-Methyl-*N*-propargyl-7-nitro-1*H*-indole-2-carboxamide:** yield 74%, white solid, mp 161 °C (*i*-Pr_2O); IR 3315, 3216, 2112, 1664 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (1H, s), 3.12 (3H, s), 4.45 (2H, s), 7.10 (1H, s), 7.27 (1H, dd, J = 7.8 Hz, 7.9 Hz), 8.02 (1H, d, J = 7.8 Hz), 8.25 (1H, d, J = 7.9 Hz), 10.50 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 38.7 (q), 45.8 (t), 72.4 (d), 78.1 (s), 106.5 (d), 120.0 (d), 121.6 (d), 128.8 (s), 130.3 (d), 131.3 (s), 131.6 (s), 133.3 (s), 161.8 (s); MS m/z 257 (M^+). Anal. Calcd for $C_{13}H_{11}N_3O_3$: C, 60.70; H, 4.30; N, 16.33. Found: C, 60.92; H, 4.12; N, 16.21.

***N*-Benzyl-*N*-propargyl-1*H*-indole-2-carboxamide:** yield 59%, white solid, mp 163 °C (*i*-Pr_2O); IR 3313, 3220, 2116, 1668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.37 (1H, s), 4.39 (2H, s), 5.05 (2H, s), 7.09−7.14 (1H, m), 7.15−7.45 (8H, m), 7.63−7.66 (1H, m), 9.35 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.9 (t), 52.8 (t), 74.1 (d), 78.6 (s), 105.7 (d), 111.7 (d), 120.6 (d), 122.2 (d), 122.4 (d), 124.6 (d), 127.7 (s), 127.8 (d), 128.6 (s), 128.8 (d), 135.8 (s), 136.0 (s), 159.0 (s); MS m/z 288 (M^+). Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 79.22; H, 5.41; N, 9.65.

***N*-(4-Methoxybenzyl)-*N*-propargyl-1*H*-indole-2-carboxamide:** yield 98%, white solid, mp 138 °C (*i*-Pr_2O); IR 3321, 3218, 2108, 1667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (1H, s), 3.83 (3H, s), 4.37 (2H, s), 5.00 (2H, s), 6.91−6.94 (2H, m), 7.11−7.15 (1H, m), 7.27−7.33 (4H, m), 7.44−46 (1H, m), 7.63−7.65 (1H, m), 9.53 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.9 (t), 53.4 (t), 55.3 (q), 73.4 (d), 78.7 (s), 105.7 (d), 106.5 (d), 111.8 (d), 114.3 (d), 120.6 (d), 122.2 (d), 124.7 (d), 127.7 (s), 127.9 (s), 128.7 (s), 135.9 (s), 159.3 (s), 163.3 (s); MS m/z 318 (M^+). Anal. Calcd for

$C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.38; H, 5.85; N, 8.92.

***N*-(4-Methylbenzyl)-*N*-propargyl-1*H*-indole-2-carboxamide:** yield 98%, white solid, mp 138 °C (*i*-Pr_2O); IR 3309, 3222, 2120, 1670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.38 (4H, s), 4.36 (2H, s), 5.01 (2H, s), 7.11−7.65 (9H, m), 9.26 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (q), 33.9 (t), 49.1 (t), 72.8 (d), 78.7 (s), 105.7 (d), 106.5 (d), 111.8 (d), 120.6 (d), 122.1 (d), 124.7 (d), 127.6 (s), 128.6 (s), 129.6 (d), 132.9 (s), 135.9 (s), 137.6 (s), 163.4 (s); MS *m*/*z* 302 (M^+). Anal. Calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.52; H, 5.87; N, 9.21.

***N*-(4-Chlorobenzyl)-*N*-propargyl-1*H*-indole-2-carboxamide:** yield 58%, white solid, mp 166 °C (*i*-Pr_2O); IR 3320, 3210, 2109, 1657 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.41 (1H, s), 4.42 (2H, s), 5.02 (2H, s), 7.12−7.65 (9H, m), 10.06 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.1 (t), 50.3 (t), 73.3 (d), 78.5 (s), 105.8 (d), 105.9 (d), 112.0 (d), 120.6 (d), 122.1 (d), 124.8 (d), 127.5 (s), 128.3 (s), 129.1 (d), 133.7 (s), 134.7 (s), 136.2 (s), 163.6 (s); MS *m*/*z* 322 (M^+). Anal. Calcd for $C_{19}H_{15}ClN_2O$: C, 70.70; H, 4.68; N, 8.68. Found: C, 70.88; H, 4.53; N, 8.49.

***N*-Propargyl-*N*-(thiophen-2-ylmethyl)-1*H*-indole-2-carboxamide:** yield 51%, white solid, mp 121 °C (*i*-Pr_2O); IR 3312, 3220, 2114, 1676 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.44 (1H, s), 4.46 (2H, s), 5.15 (2H, s), 7.00−7.03 (1H, m), 7.09−7.17 (3H, m), 7.27−7.32 (2H, m), 7.48 (1H, d, *J* = 8.3 Hz), 7.68 (1H, d, *J* = 8.0 Hz), 9.87 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.6 (t), 44.4 (t), 73.2 (d), 78.6 (s), 105.8 (d), 112.0 (d), 122.2 (d), 124.8 (d), 126.1 (d), 126.9 (d), 127.0 (d), 127.1 (d), 127.6 (s), 128.4 (s), 136.1 (s), 138.4 (s), 163.2 (s); MS *m*/*z* 294 (M^+). Anal. Calcd for $C_{17}H_{14}N_2OS$: C, 69.36; H, 4.79; N, 9.52. Found: C, 69.55; H, 4.91; N, 9.63.

Synthesis of Allenamides 2, 8, and 15a−i. A solution of propargylamide (1 mmol) in THF (10 mL) was treated with *t*-BuOK (2.5 mmol). The resulting solution was stirred at rt for 1 min, then filtered on silica gel (AcOEt). The solvent was evaporated under reduced pressure and the residue was used without further purification for the next step.

***N*-Methyl-*N*-(propa-1,2-dienyl)-1*H*-indole-2-carboxamide (2):** yield 98%, white solid, mp 143 °C (*i*-Pr_2O); IR 3306, 1940, 1668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.34 (3H, s), 4.49 (2H, d, *J* = 6.6 Hz), 7.00 (1H, s), 7.17 (1H, dd, *J* = 8.2 Hz, 7.0 Hz), 7.27−7.72 (1H, m), 7.28 (1H, dd, *J* = 8.8 Hz, 7.0 Hz), 7.44 (1H, d, *J* = 8.2 Hz), 7.68 (1H, d, *J* = 8.8 Hz), 9.07 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.7 (q), 87.6 (t), 102.7 (d), 107.9 (d), 112.0 (d), 120.9 (d), 122.4 (d), 125.2 (d), 127.9 (s), 129.1 (s), 136.1 (s), 161.7 (s), 202.4 (s); MS *m*/*z* 212 (M^+). Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.43; H, 5.79; N, 13.11.

***N*-(2-Iodobenzyl)-*N*-(propa-1,2-dienyl)-1*H*-indole-2-carboxamide (8):** yield 98%, white solid, mp 171 °C (*i*-Pr_2O); IR 3296, 1949, 1650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.96 (2H, s), 5.29 (2H, d, *J* = 6.2 Hz), 7.12−7.34 (6H, m), 7.40 (1H, s), 7.45−7.67 (2H, m), 7.87−7.96 (1H, m), 9.02 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.7 (t), 85.2 (t), 96.1 (s), 110.0 (d), 111.1 (d), 114.9 (d), 119.8 (d), 120.7 (d), 121.7 (d), 127.4 (d), 128.3 (d), 128.5 (d), 131.3 (s), 138.5 (s), 139.1 (d), 139.8 (s), 151.3 (s), 162.8 (s), 204.5 (s); MS *m*/*z* 414 (M^+). Anal. Calcd for $C_{19}H_{15}IN_2O$: C, 55.09; H, 3.65; N, 6.76. Found: C, 54.88; H, 3.76; N, 6.77.

***N*-Methyl-*N*-(propa-1,2-dienyl)-5-methoxy-1*H*-indole-2-carboxamide (15a):** yield 85%, white solid, mp 143 °C (*i*-Pr_2O); IR 3310, 1935, 1672 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.35 (3H, s), 3.86 (3H, s), 5.50 (2H, d, *J* = 6.3 Hz), 6.92 (1H, s), 6.99 (1H, d, *J* = 8.9 Hz), 7.08 (1H, s), 7.36 (1H, d, *J* = 8.9 Hz), 7.57−7.88 (1H, m), 9.22 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.2 (q), 55.7 (q), 87.4 (t), 102.3 (d), 102.6 (d), 106.9 (d), 112.8 (d), 116.3 (d), 127.9 (s), 129.3 (s), 131.6 (s), 154.6 (s), 161.6 (s), 201.9 (s); MS *m*/*z* 242 (M^+). Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.34; H, 5.89; N, 11.49.

***N*-Methyl-*N*-(propa-1,2-dienyl)-5-methyl-1*H*-indole-2-carboxamide (15b):** yield 88%. white solid. mp 135 °C (*i*-Pr_2O); IR 3301, 1944, 1660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.46 (3H, s), 3.36 (3H, s), 5.51 (2H, d, *J* = 6.3 Hz), 6.92 (1H, s), 7.13 (1H, d, *J* = 8.4 Hz), 7.36 (1H, d, *J* = 8.4 Hz), 7.45 (1H, s), 7.50−7.79 (1H, m), 9.80 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4 (q), 30.3 (q), 87.3 (t), 106.8 (d), 111.6 (d), 121.4 (d), 121.9 (d), 126.8 (d), 127.8 (s), 128.9 (s), 129.9 (s), 134.6 (s), 162.0 (s), 202.5 (s); MS *m*/*z* 226 (M^+). Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.14; H, 6.35; N, 12.22.

***N*-Methyl-*N*-(propa-1,2-dienyl)-5-chloro-1*H*-indole-2-carboxamide (15c):** yield 85%, white solid, mp 145 °C (*i*-Pr_2O); IR 3313, 1937, 1655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.31 (3H, s), 5.52 (2H, d, *J* = 6.3 Hz), 6.92 (1H, s), 7.25 (1H, d, *J* = 8.8 Hz), 7.39 (1H, d, *J* = 8.8 Hz), 7.64 (1H, s), 7.23−7.82 (1H, m), 10.16 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.8 (q), 87.5 (t), 106.6 (d), 113.1 (d), 121.2 (d), 121.8 (d), 125.3 (d), 126.2 (s), 128.4 (s), 130.1 (s), 134.5 (s), 161.4 (s), 201.8 (s); MS *m*/*z* 246 (M^+). Anal. Calcd for $C_{13}H_{11}ClN_2O$: C, 63.29; H, 4.49; N, 11.36. Found: C, 63.44; H, 4.23; N, 11.23.

***N*-Methyl-*N*-(propa-1,2-dienyl)-7-nitro-1*H*-indole-2-carboxamide (15d):** yield 80%, white solid, mp 128 °C (*i*-Pr_2O); IR 3302, 1945, 1667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.27 (3H, s), 5.51 (2H, d, *J* = 6.3 Hz), 6.97 (1H, s), 7.27 (1H, dd, *J* = 7.4 Hz, 7.8 Hz), 7.32−7.47 (1H, m), 8.02 (1H, d, *J* = 7.8 Hz), 8.25 (1H, d, *J* = 7.4 Hz), 10.50 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.3 (q), 87.6 (t), 107.6 (d), 119.9 (d), 121.7 (d), 122.1 (d), 128.9 (s), 130.3 (d), 131.1 (s), 131.6 (s), 133.3 (s), 160.1 (s), 202.0 (s); MS *m*/*z* 257 (M^+). Anal. Calcd for $C_{13}H_{11}N_3O_3$: C, 60.70; H, 4.30; N, 16.33. Found: C, 60.51; H, 4.54; N, 16.42.

***N*-Benzyl-*N*-(propa-1,2-dienyl)-1*H*-indole-2-carboxamide (15e):** yield 69%, white solid, mp 145 °C (*i*-Pr_2O); IR 3298, 1953, 1669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.01 (2H, s), 5.36 (2H, s), 7.11−7.68 (11H, m), 9.34 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.8 (t), 87.5 (t), 102.6 (d), 107.5 (d), 111.7 (d), 120.7 (d), 122.3 (d), 125.0 (d), 127.2 (d), 127.6 (d), 127.8 (s), 128.4 (s), 128.6 (d), 136.0 (s), 137.2 (s), 161.6 (s), 202.8 (s); MS *m*/*z* 288 (M^+). Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 78.98; H, 5.62; N, 9.88.

***N*-(4-Methoxybenzyl)-*N*-(propa-1,2-dienyl)-1*H*-indole-2-carboxamide (15f):** yield 84%, white solid, mp 136 °C (*i*-Pr_2O); IR 3310, 1954, 1670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.81 (3H, s), 4.90 (2H, s), 5.39 (2H, s), 6.88−7.43 (10H, m), 9.41 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.4 (t), 55.3 (q), 87.4 (t), 102.1 (d), 108.2 (d), 111.8 (d), 114.0 (d), 120.7 (d), 122.3 (d), 125.0 (d), 127.6 (s), 128.7 (s), 129.2 (s), 130.0 (d), 136.0 (s), 158.8 (s), 161.5 (s), 202.4 (s); MS *m*/*z* 318 (M^+). Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.51; H, 5.62; N, 8.72.

***N*-(4-Methylbenzyl)-*N*-(propa-1,2-dienyl)-1*H*-indole-2-carboxamide (15g):** yield 92%, white solid, mp 155 °C (*i*-Pr_2O); IR 3310, 1933, 1655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.36 (3H, s), 4.90 (2H, s), 5.38 (2H, s), 7.03−7.77 (10H, m), 9.62 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4 (q), 43.2 (t), 87.2 (t), 102.3 (d), 108.0 (d), 111.7 (d), 114.1 (d), 120.9 (d), 122.5 (d), 125.3 (d), 127.3 (s), 128.6 (d), 131.4 (s), 133.0 (s), 136.1 (s), 136.9 (s), 161.7 (s), 202.6 (s); MS *m*/*z* 302 (M^+). Anal. Calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.55; H, 5.81; N, 9.31.

***N*-(4-Chlorobenzyl)-*N*-(propa-1,2-dienyl)-1*H*-indole-2-carboxamide (15h):** yield 92%, white solid, mp 167 °C (*i*-Pr_2O); IR 3295, 1938, 1652 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.96 (2H, s), 5.37 (2H, d, *J* = 5.9 Hz), 6.85−7.64 (10H, m), 9.28 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.6 (t), 87.7 (t), 101.9 (d), 108.0 (d), 111.8 (d), 120.8 (d), 122.3 (d), 125.1 (d), 127.5 (d), 127.5 (s), 128.8 (d), 129.9 (s), 133.1 (s), 135.7 (s),

136.1 (s), 161.6 (s), 202.1 (s); MS *m*/*z* 322 (M^+). Anal. Calcd for $C_{19}H_{15}ClN_2O$: C, 70.70; H, 4.68; N, 8.68. Found: C, 70.65; H, 4.81; N, 8.94.

***N*-(Propa-1,2-dienyl)-*N*-(thiophen-2-ylmethyl)-1*H*-indole-2-carboxamide (15i):** yield 95%, white solid, mp 166 °C (*i*-Pr_2O); IR 3321, 1952, 1654 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.10 (2H, s), 5.54 (2H, d, J = 5.3 Hz), 6.95−7.45 (1H, m), 6.96−6.99 (1H, m), 7.06−7.17 (3H, m), 7.24−7.27 (1H, m), 7.31 (1H, dd, J = 7.6 Hz, 7.7 Hz), 7.43 (1H, d, J = 8.3 Hz), 7.67 (1H, d, J = 8.0 Hz), 9.47 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.5 (t), 88.1 (t), 101.8 (d), 107.7 (d), 111.8 (d), 120.8 (d), 122.3 (d), 125.1 (d), 125.5 (d), 126.5 (d), 127.5 (d), 128.5 (s), 130.3 (s), 136.1 (s), 139.8 (s), 161.2 (s), 201.9 (s); MS *m*/*z* 294 (M^+). Anal. Calcd for $C_{17}H_{14}N_2OS$: C, 69.36; H, 4.79; N, 9.52. Found: C, 69.21; H, 4.85; N, 9.44.

Synthesis of Imidazo[1,5-*a*]indoles Derivatives 5a−e. K_2CO_3 (4 mmol), aryl iodide (1.5 mmol), and $Pd(PPh_3)_4$ (5 mol %) were added to a solution of allenamide (1 mmol) in acetonitrile (10 mL). The resulting solution was heated at reflux for 2 h. The solvent was evaporated under reduced pressure, then the resulting crude mixture was diluted with brine and extracted with AcOEt (3 × 20 mL). The organic phase was dried over Na_2SO_4 and the product was purified by flash chromatography.

2-Methyl-3-(1-phenylvinyl)-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (5a): yield 74%, white solid, mp 178 °C (*i*-Pr_2O); IR 1670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.99 (3H, s), 5.82 (1H, s), 5.86 (1H, s), 6.01 (1H, s), 6.73 (2H, d, J = 7.4 Hz), 6.90 (1H, s), 7.10 (2H, dd, J = 7.7 Hz, 7.2 Hz), 7.16−7.19 (2H, m), 7.24−7.27 (1H, m), 7.34 (1H, d, J = 8.2 Hz), 7.76 (1H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.1 (q), 77.5 (d), 98.3 (d), 110.5 (d), 121.3 (d), 123.6 (t), 123.8 (d), 124.2 (d), 127.1 (d), 128.8 (d), 128.9 (d), 132.0 (s), 132.1 (s), 133.2 (s), 135.9 (s), 144.2 (s), 161.0 (s); MS *m*/*z* 288 (M^+). Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.71. Found: C, 79.33; H, 5.45; N, 9.50.

3-(1-(4-Methoxyphenyl)vinyl)-2-methyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (5b): yield 88%, white solid, mp 140 °C (*i*-Pr_2O); IR 1666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.99 (3H, s), 3.68 (3H, s), 5.77 (1H, s), 5.80 (1H, s), 6.03 (1H, s), 6.62−6.79 (4H, m), 6.91 (1H, s), 7.17 (1H, dd, J = 8.0 Hz, 7.6 Hz), 7.25 (1H, dd, J = 8.2 Hz, 7.6 Hz), 7.35 (1H, d, J = 8.2 Hz), 7.74 (1H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8 (q), 55.1 (q), 77.4 (d), 97.9 (d), 110.3 (d), 114.0 (d), 121.0 (d), 122.3 (t), 123.6 (d), 123.9 (d), 127.8 (s), 128.0 (d), 128.6 (s), 131.8 (s), 133.0 (s), 143.3 (s), 159.8 (s), 160.8 (s); MS *m*/*z* 318 (M^+). Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.17; H, 5.98; N, 9.01.

3-(1-(4-Acetylphenyl)vinyl)-2-methyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (5c): yield 76%, yellow oil; IR 1652 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.44 (3H, s), 2.97 (3H, s), 5.88 (1H, s), 5.97 (1H, s), 5.99 (1H, s), 6.76 (2H, d, J = 8.6 Hz), 6.88 (1H, s), 7.16 (1H, dd, J = 6.9 Hz, 8.1 Hz), 7.23 (1H, dd, J = 6.9 Hz, 8.2 Hz), 7.29 (1H, d, J = 8.2 Hz), 7.71 (1H, d, J = 8.1 Hz), 7.71 (2H, d, J = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5 (q), 26.9 (q), 76.8 (d), 98.3 (d), 110.1 (d), 121.3 (d), 123.7 (d), 124.2 (d), 124.9 (t), 127.1 (d), 128.5 (d), 131.5 (s), 131.8 (s), 132.9 (s), 136.8 (s), 140.2 (s), 143.1 (s), 160.7 (s), 197.4 (s); MS *m*/*z* 330 (M^+). Anal. Calcd for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.49; N, 8.48. Found: C, 76.55; H, 5.16; N, 8.52.

2-Methyl-3-(1-(4-ethoxycarbonylphenyl)vinyl)-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (5d): yield 72%, yellow oil; IR 1659 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (3H, t, J = 7.1 Hz), 2.97 (3H, s), 4.27 (2H, q, J = 7.1 Hz), 5.85 (1H, s), 5.92 (1H, s), 5.95 (1H, s), 6.75 (2H, d, J = 8.5 Hz), 6.87 (1H, s), 7.16 (1H, dd, J = 6.9 Hz, 8.0 Hz), 7.23 (1H, dd, J = 6.9 Hz, 8.2 Hz), 7.29 (1H, d, J = 8.2 Hz), 7.71 (1H, d, J = 8.0 Hz), 7.76 (2H, d, J = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2 (q), 26.8 (q), 61.0 (t), 76.9 (d), 98.2 (d), 110.1 (d), 121.2 (d), 123.6 (d), 124.2 (d), 124.7 (t), 126.9 (d), 129.7 (d), 130.5 (s), 131.6 (s), 131.8 (s), 132.9 (s), 140.0 (s), 143.2 (s), 160.6 (s), 165.9 (s); MS *m*/*z* 360 (M^+). Anal. Calcd for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.14; H, 5.71; N, 7.89.

2-Methyl-3-(1-(4-nitrophenyl)vinyl)-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (5e): yield 68%, white solid, mp 190 °C (*i*-Pr_2O); IR 1654 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.03 (3H, s), 5.94 (1H, s), 6.07 (1H, s), 6.09 (1H, s), 6.84 (2H, d, J = 8.7 Hz), 6.89 (1H, s), 7.18 (1H, dd, J = 8.0 Hz, 7.1 Hz), 7.27 (1H, dd, J = 8.2 Hz, 7.1 Hz), 7.33 (1H, d, J = 8.1 Hz), 7.73 (1H, d, J = 8.0 Hz), 7.93 (2H, d, J = 8.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.9 (q), 76.9 (d), 98.6 (d), 109.9 (d), 121.4 (d), 123.7 (d), 123.9 (d), 124.5 (d), 125.9 (t), 127.9 (d), 131.3 (s), 131.9 (s), 132.8 (s), 142.0 (s), 142.5 (s), 147.8 (s), 160.6 (s); MS *m*/*z* 333 (M^+). Anal. Calcd for $C_{19}H_{15}N_3O_3$: C, 68.46; H, 4.54; N, 12.61. Found: C, 68.12; H, 4.65; N, 12.50.

Synthesis of Imidazo[1,5-*a*]indoles Derivatives 7a−d. $Pd(PPh_3)_4$ (8%), aryl iodide (1.5 mmol), and K_2CO_3 (4 mmol) were added to a solution of **2** (1 mmol) in acetonitrile (10 mL) under CO atmosphere (balloon). The resulting suspension was stirred at rt for 48 h. The solvent was evaporated under reduced pressure, then the crude mixture was diluted with brine and extracted with AcOEt (3 × 20 mL). The organic phase was dried over Na_2SO_4 and the product was purified by flash chromatography.

2-Methyl-3-(3-oxo-3-phenylprop-1-en-2-yl)-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (7a): yield 45%, white solid, mp 133 °C (*i*-Pr_2O); IR 1730, 1640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.10 (3H, s), 5.88 (1H, s), 6.10 (1H, s), 6.57 (1H, s), 6.97 (1H, s), 7.10−7.27 (3H, m), 7.45−7.51 (2H, m), 7.60−7.64 (1H, m), 7.74−7.81 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.5 (q), 70.5 (d), 98.3 (d), 110.3 (d), 121.1 (d), 123.7 (d), 124.2 (d), 128.7 (d), 129.6 (d), 131.2 (t), 131.7 (s), 132.0 (s), 132.5 (s), 133.5 (d), 136.1 (s), 142.0 (s), 160.7 (s), 195.3 (s); MS *m*/*z* 316 (M^+). Anal. Calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.85. Found: C, 75.87; H, 5.22; N, 8.72.

3-(3-(4-Methoxyphenyl)-3-oxoprop-1-en-2-yl)-2-methyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (7b): yield 31%, white solid, mp 163 °C (*i*-Pr_2O); IR 1724, 1633 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.10 (3H, s), 3.89 (3H, s), 5.78 (1H, s), 6.03 (1H, s), 6.56 (1H, s), 6.96 (2H, d, J = 9.0 Hz), 6.97 (1H, s), 7.17−7.23 (3H, m), 7.76 (1H, d, J = 7.8 Hz), 7.84 (2H, d, J = 9.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.5 (q), 55.6 (q), 70.8 (d), 98.3 (d), 110.0 (s), 110.4 (d), 114.0 (d), 121.1 (d), 123.7 (d), 124.1 (d), 128.6 (s), 129.2 (t), 131.9 (s), 132.2 (d), 132.5 (s), 142.2 (s), 164.1 (s), 193.7 (s), 206.9 (s); MS *m*/*z* 346 (M^+). Anal. Calcd for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.09. Found: C, 72.67; H, 5.34; N, 8.18.

3-(3-(4-Acetylphenyl)-3-oxoprop-1-en-2-yl)-2-methyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (7c): yield 28%, white solid, mp 145 °C (*i*-Pr_2O); IR 1738, 1636 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.66 (3H, s), 3.12 (3H, s), 5.96 (1H, s), 6.12 (1H, s), 6.60 (1H, s), 6.99 (1H, s), 7.18−7.27 (3H, m), 7.77 (1H, d, J = 8.0 Hz), 7.85 (2H, d, J = 8.4 Hz), 8.04 (2H, d, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8 (q), 27.5 (q), 70.4 (d), 98.5 (d), 110.1 (d), 121.2 (d), 123.8 (d), 124.3 (d), 128.5 (d), 129.7 (d), 131.6 (s), 132.0 (t), 132.4 (s), 135.0 (s), 139.6 (s), 140.4 (s), 142.1 (s), 160.6 (s), 194.7 (s), 197.1 (s); MS *m*/*z* 358 (M^+). Anal. Calcd for $C_{22}H_{18}N_2O_3$: C, 73.73; H, 5.06; N, 7.82. Found: C, 73.84; H, 4.95; N, 7.92.

3-[3-(4-Ethoxycarbonylphenyl)-3-oxoprop-1-en-2-yl]-2-methyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (7d): yield 33%, white solid, mp 121 °C (*i*-Pr_2O); IR 1732, 1655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (3H, t, J = 7.1 Hz), 3.03 (3H, s), 4.30 (2H, q, J = 7.1 Hz), 5.90 (1H, s), 5.99 (1H, s), 6.12 (1H, s), 6.80 (2H, d, J = 8.4 Hz), 6.91 (1H, s), 7.18 (1H, dd, J = 7.0 Hz, 8.0 Hz), 7.27 (1H, dd, J = 7.0 Hz, 8.1 Hz), 7.35 (1H, d, J = 8.0 Hz), 7.74 (1H, d, J = 8.1 Hz), 7.79 (2H, d, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2 (q), 26.9 (q), 61.0 (t), 77.1 (d), 98.4 (d), 110.1 (d), 121.2 (d), 123.7 (d), 124.2 (d), 124.5 (t), 126.9 (d), 129.7 (s), 129.8 (d), 130.6 (s), 131.6 (s), 131.9 (s), 132.9 (s), 140.0 (s), 143.4 (s),

160.7 (s), 165.9 (s); MS *m*/*z* 388 (M^+). Anal. Calcd for $C_{23}H_{20}N_2O_4$: C, 71.12; H, 5.19; N, 7.21. Found: C, 71.05; H, 5.32; N, 7.32.

Synthesis of 6-Methylene-6,11-dihydro-5a*H*-indolo[1′,2′:3,4]-imidazo[1,2-*b*]isoquinolin-13-one (10). K_2CO_3 (4 mmol) and $Pd(PPh_3)_4$ (5 mol %) were added to a solution of **8** (1 mmol) in acetonitrile (10 mL). The resulting solution was heated at reflux for 2 h. The solvent was evaporated under reduced pressure, then the resulting crude mixture was diluted with brine and extracted with AcOEt (3 × 20 mL). The organic phase was dried over Na_2SO_4 and the product was purified by flash chromatography. Yield 80%, white solid, mp 179 °C (*i*-Pr_2O); IR 1652 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.65 (1H, d, J = 17.6 Hz), 5.24 (1H, s), 5.37 (1H, d, J = 17.6 Hz), 5.61 (1H, s), 6.00 (1H, s), 7.02 (1H, s), 7.22−7.30 (2H, m), 7.33−7.44 (3H, m), 7.47 (1H, d, J = 8.3 Hz), 7.62 (1H, d, J = 7.6 Hz), 7.80 (1H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.7 (t), 69.4 (d), 98.8 (d), 110.9 (t), 111.0 (d), 121.2 (d), 123.7 (d), 124.4 (d), 126.1 (d), 126.6 (d), 127.8 (d), 129.4 (d), 130.9 (s), 131.1 (s), 131.8 (s), 132.3 (s), 134.3 (s), 139.2 (s), 159.3 (s); MS *m*/*z* 286 (M^+). Anal. Calcd for $C_{19}H_{14}N_2O$: C, 79.70; H, 4.93; N, 9.78. Found: C, 79.55; H, 5.09; N, 9.89.

Synthesis of 2-(2-Iodobenzyl)-4-methylpyrazino[1,2-*a*]indol-1(2*H*)-one (11) (path a). K_2CO_3 (4 mmol) and $Pd(PPh_3)_4$ (5 mol %) were added to a solution of **8** (1 mmol) in DMF (10 mL). The resulting solution was heated at 100 °C for 2 h. The solvent was evaporated under reduced pressure, then the resulting crude mixture was diluted with brine and extracted with Et_2O (3 × 20 mL). The organic phase was dried over Na_2SO_4, then the solvent was evaporated under reduced pressure and the product was purified by flash chromatography. Yield 60%, white solid, mp 184 °C (*i*-Pr_2O); IR 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.68 (3H, s), 5.13 (2H, s), 6.02 (1H, s), 6.99 (1H, d, J = 7.9 Hz), 7.15 (1H, d, J = 7.6 Hz), 7.27−7.37 (3H, m), 7.56 (1H, s), 7.83−7.88 (2H, m), 7.98 (1H, d, J = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.3 (q), 54.0 (t), 98.4 (s), 104.9 (d), 112.0 (d), 113.9 (d), 119.0 (s), 122.2 (d), 122.8 (d), 124.1 (d), 128.5 (s), 128.6 (s), 128.7 (d), 128.8 (d), 129.5 (d), 134.0 (s), 138.7 (s), 139.7 (d), 156.6 (s); MS *m*/*z* 414 (M^+). Anal. Calcd for $C_{19}H_{15}IN_2O$: C, 55.09; H, 3.65; N, 6.76. Found: C, 55.17; H, 3.52; N, 6.72.

Synthesis of 6-Methyl-11*H*-isoindolo[2′,1′:4,5]pyrazino[1,2-*a*]-indol-13-one (12) (path b). AcOK (1 mmol), TBAC (1 mmol), and $Pd(OAc)_2$ (5 mol %) were added to a solution of **11** (1 mmol) in DMF (10 mL). The resulting solution was heated at 100 °C for 24 h. The solvent was evaporated under reduced pressure, then the resulting crude mixture was diluted with brine and extracted with Et_2O (3 × 20 mL). The organic phase was dried over Na_2SO_4 and the product was purified by flash chromatography. Yield 64%, white solid, mp 181 °C (*i*-Pr_2O); IR 1642 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.18 (3H, s), 5.14 (2H, s), 7.27−7.52 (6H, m), 7.83 (2H, d, J = 7.8 Hz), 8.14 (1H, d, J = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 16.1 (q), 53.4 (t), 102.2 (s), 114.1 (s), 114.9 (d), 115.6 (d), 119.8 (d), 123.5 (d), 124.3 (d), 126.2 (d), 126.6 (d), 127.2 (s), 127.7 (d), 129.9 (d), 136.7 (s), 143.2 (s), 143.4 (s), 144.5 (s), 151.4 (s); MS *m*/*z* 286 (M^+). Anal. Calcd for $C_{19}H_{14}N_2O$: C, 79.70; H, 4.93; N, 9.78. Found: C, 79.82; H, 4.79; N, 9.65.

Synthesis of 6-Methyl-11*H*-isoindolo[2′,1′:4,5]pyrazino[1,2-*a*]indol-13-one (12) (path c). AcOK (1 mmol), TBAC (1 mmol), and $Pd(OAc)_2$ (5 mol %) were added to a solution of **8** (1 mmol) in DMF (10 mL). The resulting solution was heated at 100 °C for 24 h. The solvent was evaporated under reduced pressure, then the resulting crude mixture was diluted with brine and extracted with Et_2O (3 × 20 mL). The organic phase was dried over Na_2SO_4 and the product was purified by flash chromatography. Yield 60%.

Synthesis of Vinyl Imidazo[1,5-*a*]indoles 13 and 16a−h. A mixture of allenamide (1 mmol) and $Pd(PPh_3)_4$ (0.08 mmol) in toluene (10 mL) was heated at 150 °C for 1 h under microwave irradiation, then filtered on a Celite layer. The solvent was evaporated under reduced pressure and the crude residue was purified by flash chromatography.

2-Methyl-3-vinyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (13): yield 71%, colorless oil; IR 1645 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.07 (3H, s), 5.30−5.77 (3H, m), 5.88−5.96 (1H, m), 6.92 (1H, s), 7.10 (1H, dd, J = 7.8 Hz, 7.0 Hz), 7.25−7.32 (2H, m), 7.75 (1H, d, J = 8.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8 (q), 75.2 (d), 97.9 (d), 110.1 (d), 121.0 (d), 123.6 (d), 123.8 (d), 124.4 (t), 131.4 (s), 131.9 (s), 133.0 (s), 133.5 (d), 160.5 (s); MS *m*/*z* 212 (M^+). Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20. Found: C, 73.50; H, 5.85; N, 13.41.

7-Methoxy-2-methyl-3-vinyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (16a): yield 67%, white solid, mp 138 °C (*i*-Pr_2O); IR 1638 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.03 (3H, s), 3.83 (3H, s), 5.59−5.73 (3H, m), 5.85−5.89 (1H, m), 6.80 (1H, s), 6.91 (1H, dd, J = 8.9 Hz, 2.3 Hz), 7.13 (1H, d, J = 2.3 Hz), 7.16 (1H, d, J = 8.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7 (q), 55.7 (q), 75.1 (d), 97.3 (d), 103.9 (d), 110.8 (d), 115.1 (d), 124.3 (t), 128.4 (s), 131.9 (s), 132.3 (s), 133.6 (d), 154.8 (s), 160.5 (s); MS *m*/*z* 242 (M^+). Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.29; H, 5.99; N, 11.45.

2,7-Dimethyl-3-vinyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (16b): yield 78%, white solid, mp 122 °C (*i*-Pr_2O); IR 1655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.44 (3H, s), 3.04 (3H, s), 5.60−5.74 (3H, m), 5.85−5.91 (1H, m), 6.82 (1H, s), 7.09 (1H, d, J = 8.5 Hz), 7.17 (1H, d, J = 8.5 Hz), 7.51 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4 (q), 26.7 (q), 75.1 (d), 97.2 (d), 109.7 (d), 122.9 (d), 124.2 (t), 125.6 (d), 130.3 (s), 131.5 (s), 132.2 (s), 133.2 (s), 133.6 (d), 160.6 (s); MS *m*/*z* 226 (M^+). Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.17; H, 6.45; N, 12.50.

7-Chloro-2-methyl-3-vinyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (16c): yield 85%, white solid, mp 144 °C (*i*-Pr_2O); IR 1632 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.04 (3H, s), 5.60−5.93 (4H, m), 6.79 (1H, s), 7.17 (2H, s), 7.67 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8 (q), 75.1 (d), 97.2 (d), 111.0 (d), 122.6 (d), 124.3 (d), 124.8 (t), 126.6 (s), 131.2 (s), 132.6 (s), 132.7 (s), 133.1 (d), 160.0 (s); MS *m*/*z* 246 (M^+). Anal. Calcd for $C_{13}H_{11}ClN_2O$: C, 63.29; H, 4.49; N, 11.36. Found: C, 63.41; H, 4.34; N, 11.22.

2-Methyl-5-nitro-3-vinyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (16d): yield 58%, white solid, mp 170 °C (*i*-Pr_2O); IR 1652 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.12 (3H, s), 5.37−5.45 (1H, m), 5.51−5.61 (2H, m), 6.37 (1H, d, J = 7.6 Hz), 7.09 (1H, s), 7.27 (1H, dd, J = 7.9 Hz, 8.0 Hz), 8.06 (1H, d, J = 7.9 Hz), 8.11 (1H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.0 (q), 76.8 (d), 99.3 (d), 120.3 (d), 121.6 (d), 124.1 (t), 125.1 (s), 130.7 (d), 133.3 (d), 135.1 (s), 135.2 (s), 136.1 (s), 158.9 (s); MS *m*/*z* 257 (M^+). Anal. Calcd for $C_{13}H_{11}N_3O_3$: C, 60.70; H, 4.31; N, 16.33. Found: C, 60.58; H, 4.44; N, 16.52.

2-Benzyl-3-vinyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (16e): yield 63%, white solid, mp 111 °C (*i*-Pr_2O); IR 1648 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.14 (1H, d, J = 15.2 Hz), 5.35 (1H, d, J = 15.2 Hz), 5.64−5.77 (4H, m), 6.98 (1H, s), 7.17−7.36 (8H, m), 7.75 (1H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.6 (t), 72.9 (d), 98.2 (d), 110.1 (d), 121.0 (d), 123.6 (d), 123.9 (d), 124.5 (t), 128.0 (d), 128.3 (d), 128.9 (d), 131.1 (s), 131.9 (s), 133.0 (s), 133.4 (d), 136.2 (s), 160.3 (s); MS *m*/*z* 288 (M^+). Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 79.26; H, 5.48; N, 9.54.

2-(4-Methoxybenzyl)-3-vinyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (16f): yield 89%, white solid, mp 113 °C (*i*-Pr_2O); IR 1659 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.79 (3H, s) 4.08 (1H, d, J = 15.0 Hz), 5.27 (1H, d, J = 15.0 Hz), 5.64−5.73 (4H, m), 6.87−6.89 (2H, m), 6.96 (1H, s), 7.14−7.18 (1H, m), 7.22−7.26 (4H, m), 7.74 (1H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.1 (t), 55.3 (q), 72.8 (d), 98.1 (d), 110.1 (d), 114.3 (d), 121.0 (d), 123.5 (d), 123.9 (d), 124.5 (t), 128.3 (s), 129.7 d), 131.3 (s), 131.8 (s), 133.0 (s), 133.4 (d), 159.3 (s), 160.3 (s); MS *m*/*z* 318 (M^+). Anal. Calcd for

$C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.38; H, 5.61; N, 8.92.

2-(4-Methylbenzyl)-3-vinyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (16g): yield 69%, white solid, mp 138 °C (*i*-Pr_2O); IR 1648 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.36 (3H, s), 4.10 (1H, d, J = 15.1 Hz), 5.32 (1H, d, J = 15.1 Hz), 5.63−5.82 (4H, m), 6.98 (1H, s), 7.15−7.27 (7H, m), 7.74−7.77 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (q), 43.4 (t), 72.8 (d), 98.1 (d), 110.1 (d), 121.0 (d), 123.5 (d), 123.9 (d), 124.5 (t), 128.3 (d), 129.7 (d), 131.2 (s), 131.9 (s), 133.0 (s), 133.2 (s), 133.4 (d), 137.7 (s), 160.3 (s); MS m/z 302 (M^+). Anal. Calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.58; H, 5.88; N, 9.18.

2-(4-Chlororbenzyl)-3-vinyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (16h): yield 85%,. white solid, mp 131 °C (*i*-Pr_2O); IR 1650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.16 (1H, d, J = 15.4 Hz), 5.24 (1H, d, J = 15.4 Hz), 5.63−5.82 (4H, m), 6.98 (1H, s), 7.16−7.20 (1H, m), 7.24−7.27 (4H, m), 7.30−7.35 (2H, m), 7.75 (1H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.0 (t), 73.0 (d), 98.4 (d), 110.1 (d), 121.1 (d), 123.6 (d), 124.1 (d), 124.7 (t), 129.1 (d), 129.7 (d), 130.8 (s), 131.8 (s), 133.1 (s), 133.3 (d), 133.9 (s), 134.8 (s), 160.3 (s); MS m/z 322 (M^+). Anal. Calcd for $C_{19}H_{15}ClN_2O$: C, 70.70; H, 4.68; N, 8.68. Found: C, 70.88; H, 4.51; N, 8.55.

2-(Tiophen-2-ylmethyl)-3-vinyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-one (16i): yield 72%, white solid, mp 112 °C (*i*-Pr_2O); IR 1656 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.38 (1H, d, J = 15.7 Hz), 5.40 (1H, d, J = 15.7 Hz), 5.67−5.90 (1H, d, J = 16.4 Hz), 6.97−6.99 (2H, m), 7.04−7.05 (1H, m), 7.15−7.19 (1H, m), 7.23−7.27 (3H, m), 7.74 (1H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 38.0 (t), 72.8 (d), 98.4 (d), 110.1 (d), 121.1 (d), 123.6 (d), 124.0 (d), 124.9 (t), 126.0 (d), 127.1 (d), 127.3 (d), 130.9 (s), 131.8 (s), 133.1 (s), 133.2 (d), 138.5 (s), 159.9 (s); MS m/z 294 (M^+). Anal. Calcd for $C_{17}H_{14}N_2OS$: C, 69.36; H, 4.79; N, 9.52. Found: C, 69.21; H, 4.92; N, 9.54.

3-(1-Deuteriumvinyl)-2-methyl-2,3-dihydro-1*H*-imidazo[1,5-*a*]-indol-1-one (18): yield 68%, colorless oil; IR 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.07 (3H, s), 5.70−5.75 (2H, m), 5.89−5.92 (1H, m), 6.90 (1H, s), 7.19−7.30 (3H, m), 7.73−7.76 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8 (q), 75.1 (d), 97.9 (d), 110.3 (d), 121.0 (d), 123.2 (s), 123.6 (d), 123.8 (d), 124.3 (t), 131.7 (s), 132.9 (s), 133.5 (s), 158.5 (s); MS m/z 213 (M^+). Anal. Calcd for $C_{13}H_{11}DN_2O$: C, 73.22; H, 6.14; N, 13.14. Found: C, 73.34; H, 6.05; N, 13.01.

Synthesis of 4-Hydroxy-2,4-dimethyl-3,4-dihydropyrazino-[1,2-*a*]indol-1(2*H*)-one (14). A mixture of allenamide **2** (1 mmol) in toluene (10 mL) was heated at 150 °C for 1 h under microwave irradiation, or refluxed for 24 h, then filtered on a Celite layer. The solvent was evaporated under reduced pressure and the crude residue was purified by flash chromatography. Yield 41%, white solid, mp 134 °C (*i*-Pr_2O); IR 3313, 1652 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.78 (3H, s), 2.93 (3H, s), 3.49 (1H, d, J = 12.6 Hz), 3.67 (1H, d, J = 12.6 Hz), 4.92 (1H, br s), 7.03 (1H, s), 7.10 (1H, dd, J = 8.5 Hz, 7.4 Hz), 7.22 (1H, dd, J = 7.9 Hz, 7.4 Hz), 7.52 (1H, d, J = 7.9 Hz), 7.83 (1H, d, J = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7 (q), 34.1 (q), 60.7 (t), 82.9 (s), 108.0 (d), 113.3 (d), 120.9 (d), 122.6 (d), 124.7 (d), 128.1 (s), 128.2 (s), 135.8 (s), 160.1 (s); MS m/z 230 (M^+). Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.66; H, 6.32; N, 11.97.

Acknowledgment. We acknowledge MIUR for financial support (PRIN 2008KRBX3B) and the Ph.D. fellowship to M.R. (Progetto Giovani 2006). We are also grateful to the Centro Interuniversitario sulle Reazioni Pericicliche.

Supporting Information Available: ^1H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.