Lewis Acid Catalyzed Three-Component [3+2] Cycloaddition Reaction Using Pentafulvene as 2π Component: An Easy Way to Construct Pentaleno(1,2-*b*)indoles

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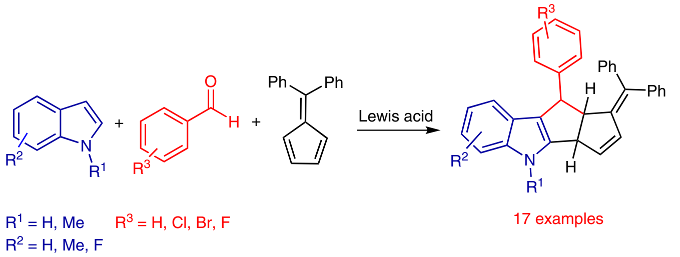

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Abstract A facile route toward the synthesis of pentaleno(1,2-*b*)indoles via multicomponent reaction of indole, aldehyde, and pentafulvene is realized. The reaction proceeds through Lewis acid catalyzed [3+2] cycloaddition of in situ generated indolylmethanol and pentafulvene. This methodology provides an easy access to biologically relevant indole derivatives.

Keywords fulvene, indole, cycloaddition, multicomponent reaction, cyclopentaleno indoles

Ring-fused indoles, ubiquitous to many structurally complex natural products and bioactives, have acquired considerable scientific attention over the years (Figure 1).[1,2] A number of synthetic procedures including Friedel–Crafts reactions,[3] transition-metal[4]/Lewis/Brønsted acid catalysis[5] and catalytic asymmetric synthetic strategies[5] have been developed for such fused indole scaffolds. The 3- or 2-indolylmethanols formed by the acid-catalyzed condensation of indole and aldehyde were utilized as the three-carbon synthons in a variety of [3+2], [3+3], and [4+3] intermolecular cycloaddition reactions providing fused indole derivatives.[6] In line with the report of Yonemitsu on the three-component reaction of indole, aldehydes, and meldrums acid, diverse indole scaffolds, in particular, 2,3-disubstituted/ring-fused indoles were synthesized.[7] Inspired by the report of Winne et al. on the [4+3] cycloaddition reaction of furfuryl cations to 1,3-diene, Wu and co-workers adopted a similar protocol for the gallium(III)-catalyzed regio- and diastereoselective three-component [4+3] cycloaddition reaction of in situ generated indolyl methanol to 1,3-diene toward the synthesis of cyclohepta[*b*]indoles (Figure 2, a).[8] Motivated by these results and our continuing interest in the chemistry of cross-conjugated trienes,[9] we were intrigued to study the reaction outcome by replacing the diene component of the reaction by replacing it with pentafulvene.

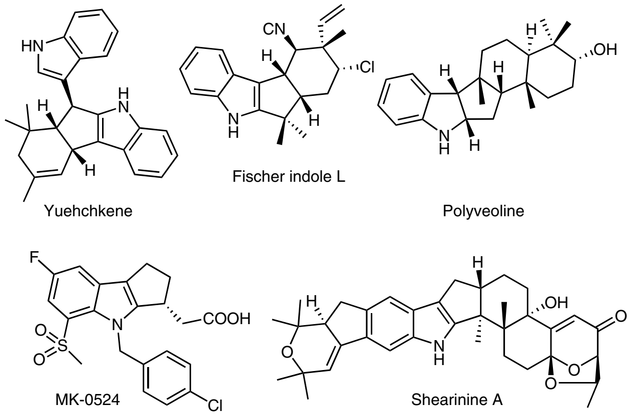


Figure 1 Biologically important fused indole derivatives[1]

Pentafulvenes have been utilized as a valuable synthons for the synthesis of many natural products and biologically active molecules[10] due to its ability to act as a 2π,[11] 4π[12], or 6π[13] component in diverse cycloaddition reactions. New endocyclic ring functionalization of fulvenes based on transition-metal or FLP system mediated reactions have also emerged.[14] Very recently, we have utilized pentafulvene as an unsymmetrical alkene for the Lewis acid catalyzed regioselective hydroheteroarylation reaction (Figure 2, b).[15] Herein we report a Lewis acid catalyzed three-component cycloaddition reaction involving indole, aldehyde, and pentafulvene in which one of the endocyclic double bonds of pentafulvene acts as a 2π component towards the synthesis of cyclopenta-annulated indole derivatives (Figure 2, c).

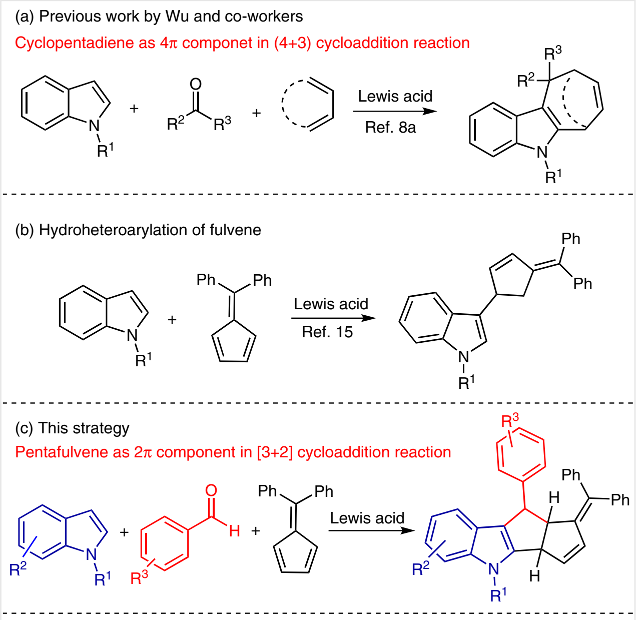
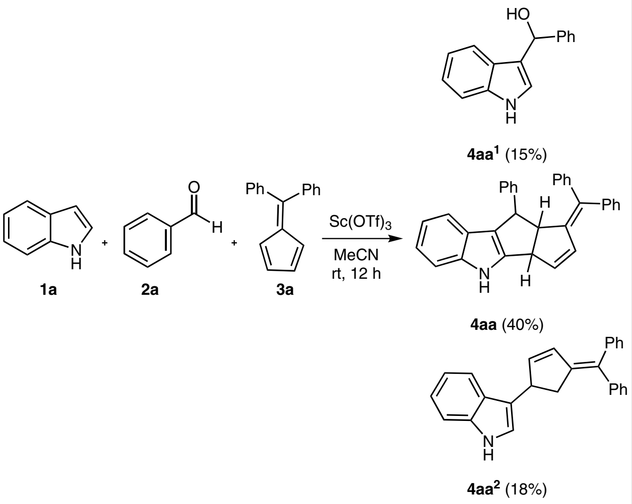


Figure 2 New strategy toward the synthesis of cyclopentaleno[1,2-*b*]indoles

Anticipating a three-component cycloaddition reaction, we initiated our experiments by treating an equimolar mixture of indole **1a**, aldehyde **2a**, and diphenylfulvene **3a** in MeCN at room temperature in the presence of catalytic amount of Sc(OTf)$_3$ for 12 hours (Scheme 1). Interestingly, the reaction afforded the [3+2] cycloadduct **4aa** in 40% yield (instead of the established [3+4] cycloaddition product for other dienes (Figure 2, a) along with minor amounts of hydroheteroarylated product (**4aa²**) and indolyl methanol (**4aa¹**). The structural assignment of the fused indole scaffold **4aa** was done with the aid of various spectroscopic techniques such as ^{1}H NMR and ^{13}C NMR spectroscopy and HRMS. Furthermore, the stereochemistry of compound **4ad** was unambiguously confirmed by single-crystal X-ray analysis (Figure 3).



Scheme 1 Multicomponent reaction of indole, aldehyde, and diphenyl fulvene

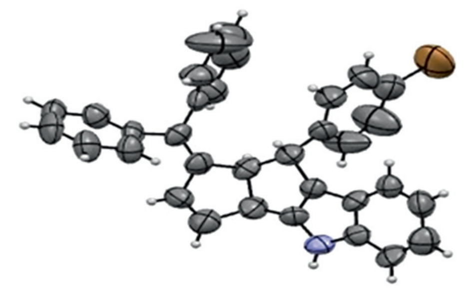


Figure 3 Single-crystal X-ray structure of **4ad** (CCDC 1488241)[16]

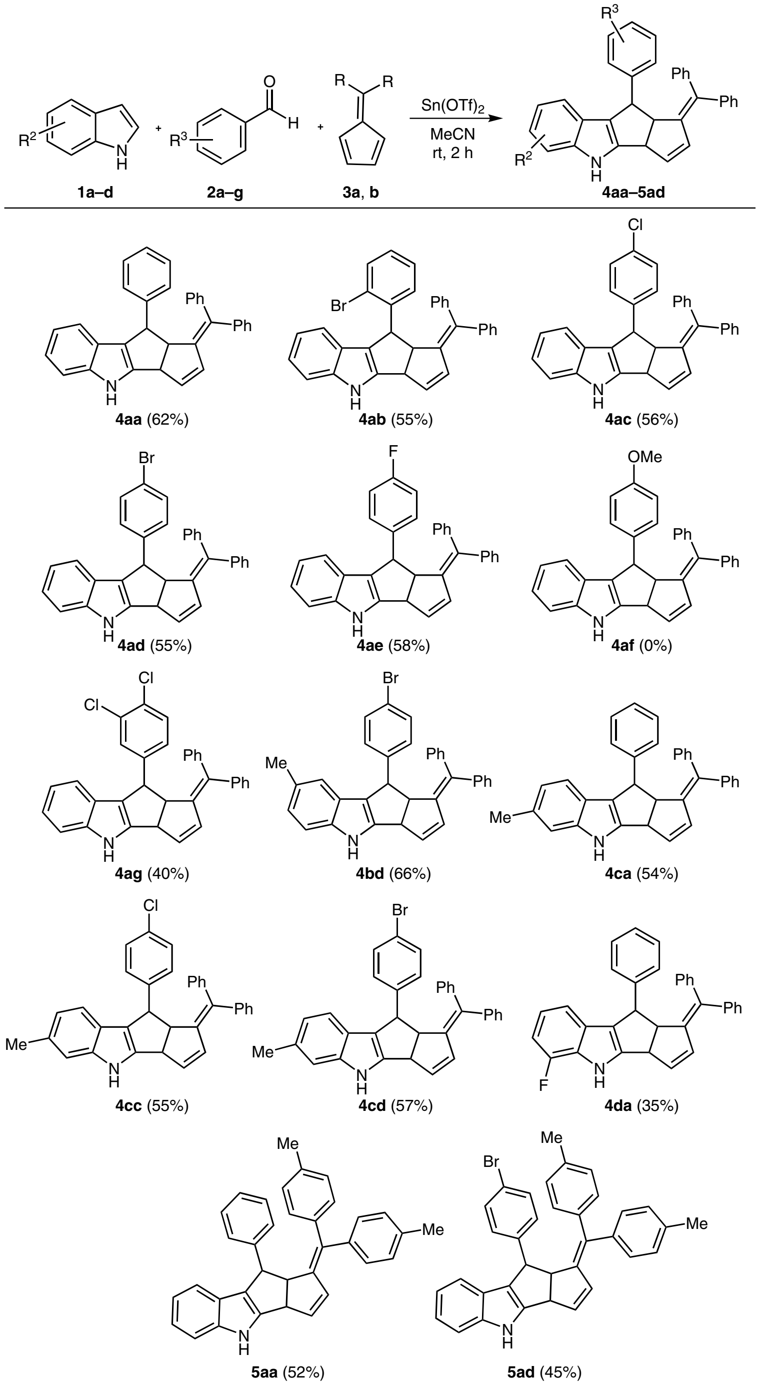
We then turned our attention to optimize the reaction conditions with **1a**, **2a**, and **3a** as substrates. Lewis acids such as Sc(OTf)$_3$, Cu(OTf)$_2$, Fe(OTf)$_3$, BF$_3$·OEt$_2$, and Sn(OTf)$_2$ were able to furnish the desired product **4aa** along with **4aa¹** and **4aa²**. The expected cycloaddition product **4aa** was not observed with Yb(OTf)$_3$, Zn(OTf)$_2$, and La(OTf)$_3$, and in these cases the reaction was found to halt at the stage of the intermediate indolyl methanol **4aa¹**. However, the AgOTf-catalyzed reaction was found to furnish the hydroheteroarylated product **4aa²** in addition to **4aa¹**. To determine the

Table 1 Optimization studies

Entry	Catalyst	Solvent	Yield (%)		
			4aa	**4aa¹**	**4aa²**
1[a]	Sc(OTf)$_3$	MeCN	40	15	18
2[a]	Cu(OTf)$_2$	MeCN	45	12	20
3[a]	La(OTf)$_3$	MeCN	–	45	–
4[a]	Yb(OTf)$_3$	MeCN	–	43	–
5[a]	Zn(OTf)$_2$	MeCN	–	52	-
6[a]	Ag(OTf)	MeCN	–	32	23
7[a]	Fe(OTf)$_3$	MeCN	35	18	22
8[a]	AlCl$_3$	MeCN	43	–	15
9[a]	BF$_3$·OEt$_2$	MeCN	45	14	18
10[a]	Sn(OTf)$_2$	MeCN	52	12	8
11[a]	TfOH	MeCN	10	–	15
12[b]	Sn(OTf)$_2$	CH$_2$Cl$_2$	35	–	14
13[b]	Sn(OTf)$_2$	DCE	35	–	8
14[b]	Sn(OTf)$_2$	THF	–	35	–
15[b]	Sn(OTf)$_2$	toluene	–	33	25
16[b]	Sn(OTf)$_2$	DMF	–	31	32
17[b,c]	Sn(OTf)$_2$	MeCN	62	trace	trace

[a] All reactions were carried out with 2 mol% catalyst, 1 equiv of **1a**, 1 equiv of **2a**, 1 equiv of **3a** in 2 mL of solvent at r.t. for 4 h.
[b] Equivalents of **2a** and **3a** increased to 1.5 equiv in 2 mL of toluene at r.t. for 2 h.
[c] Trace amount of the byproduct alcohol was observed.

effect of Brønsted acid on the present reaction, a reaction was performed with catalytic amounts of HOTf, from which the product **4aa** was obtained in poor yield. We then checked the feasibility of various solvents for the exclusive formation of the cycloaddition product. The use of solvents such as toluene, CH_2Cl_2, DCE, and THF was less effective in delivering the expected product. Finally, MeCN turned out as the best reaction medium for the present multicomponent reaction. The use of $Sn(OTf)_2$ as Lewis acid in MeCN (2 mL) decreased the reaction time to two hours with a better yield of cycloaddition product **4aa** (62%).[16,17] In addition, the yield of the reaction was found to improve with the in-



Scheme 2 Scope of the reaction with various indoles and aldehydes. All reactions were carried out with 2 mol% catalyst, indole (1 equiv), aldehyde (1.5 equiv), pentafulvene (1.5 equiv) in 2 mL of toluene at r.t. for 2 h.

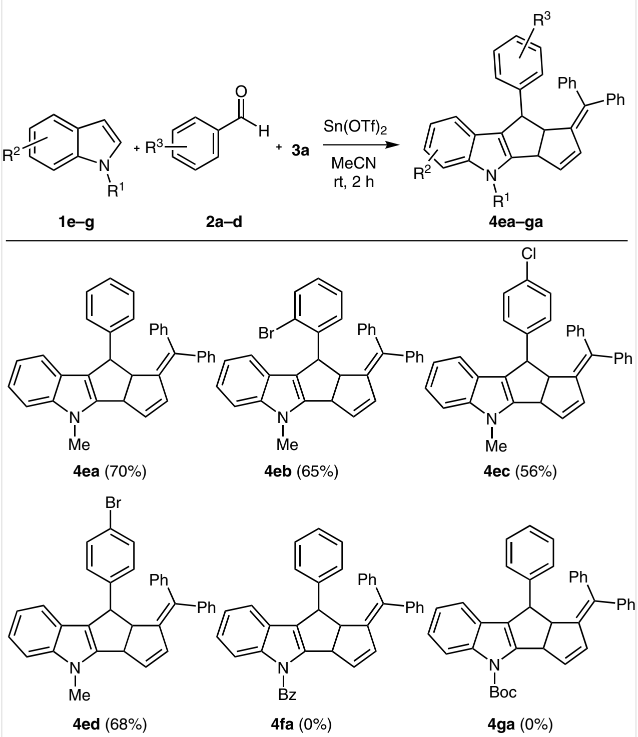
crease in the equivalents of fulvene and aldehyde (Table 1, entry 17). From the detailed optimization, the standard conditions for the reaction was found to be a combination of indole (1 equiv), aldehyde (1.5 equiv), fulvene (1.5 equiv), and $Sn(OTf)_2$ (2 mol %) affording [3+2] cycloaddition product **4aa** in 62% yield in MeCN within two hours.

Under the optimal reaction conditions, the scope of the reaction was explored with various aldehydes and ketones. Aromatic aldehydes bearing electron-withdrawing groups (R^3 = Cl, Br, F) were tolerated well under the reaction conditions, and afforded the cycloaddition products **4aa–ag** in moderate to good yields. However, aldehydes with electron-rich substituents (R^3 = 2,4-OMe, Me) were unable to take part in the cycloaddition reaction.

In addition, aliphatic aldehydes and ketones also failed to undergo multicomponent [3+2] cycloaddition reaction resulting in a complex reaction mixture. Pentafulvenes with alkyl, dialkyl, and unsymmetrical substituents at the exocyclic position did not afford the expected products **4aa**, instead hydroarylated and polymerized products were formed as evident from ^{1}H NMR analysis of the reaction mixture. The scope of the reaction was then explored with 6,6′-diaryl pentafulvene **3b** (derived from 4,4′-dimethylbenzophenone), which afforded the product **5aa–ad** in moderate yields. Further reactions were performed to extend the scope of reaction to indole substrates bearing electron-donating and electron-withdrawing substituents; all of which afforded the corresponding products in good yields (Scheme 2).

Scheme 3 delineates the scope of the reaction with respect to the substituents on the indole nitrogen. The reactions with *N*-methyl indole delivered the expected fused indole derivatives **4ea** in good yield (70%) compared to the unprotected indoles. On the other hand, electron-deficient N-protecting groups (Boc, Bz, Ts) failed to afford the desired cyclopentalenoindole derivatives.

A mechanistic proposal for the Lewis acid catalyzed three-component reaction on the basis of our experimental results and previous reports is shown in Scheme 4.[8] The process involves an intial Lewis acid catalyzed formation of carbocation intermediate **A** or the vinyliminium intermediate **B** from indole **1** and aldehyde **2** which can undergo either a concerted or a stepwise reaction to realize the cycloadduct. The initial [2+2] cycloaddition of the intermediate **A**/**B** with the pentafulvene **3** is followed by a ring expansion, by 1,2-migration analogous to the mechanism proposed for [3+2] cycloaddition reported by Moody et al. furnishing cyclopentalenoindoles **III** in a concerted manner.[6a] The stepwise pathway involves endocyclic functionalization of fulvene **3**, with the indole core **A**/**B** to deliver the intermediate **C** in a regioselective manner and followed by proton loss to yield cyclopentalenoindole **III** from the intermediate **D**.[6b]



Scheme 3 Scope of the reaction with various N-substituted indoles. All reactions were carried out with 2 mol% catalyst, indole (1 equiv), aldehyde (1.5 equiv), pentafulvene (1.5 equiv) in 2 mL of toluene at r.t. for 2 h.

In conclusion, we have developed a Lewis acid mediated three-component reaction for the synthesis of fused polycyclic indole skeleton in which fulvene acts as a 2π cycloaddition partner. This Schlenk-free strategy tolerates a variety of aryl aldehydes and indoles to furnish various pentaleno[1,2-*b*]indoles. Studies on the scope of the reaction with pentafulvenes other than diphenylfulvenes and various 3π components are currently under way.

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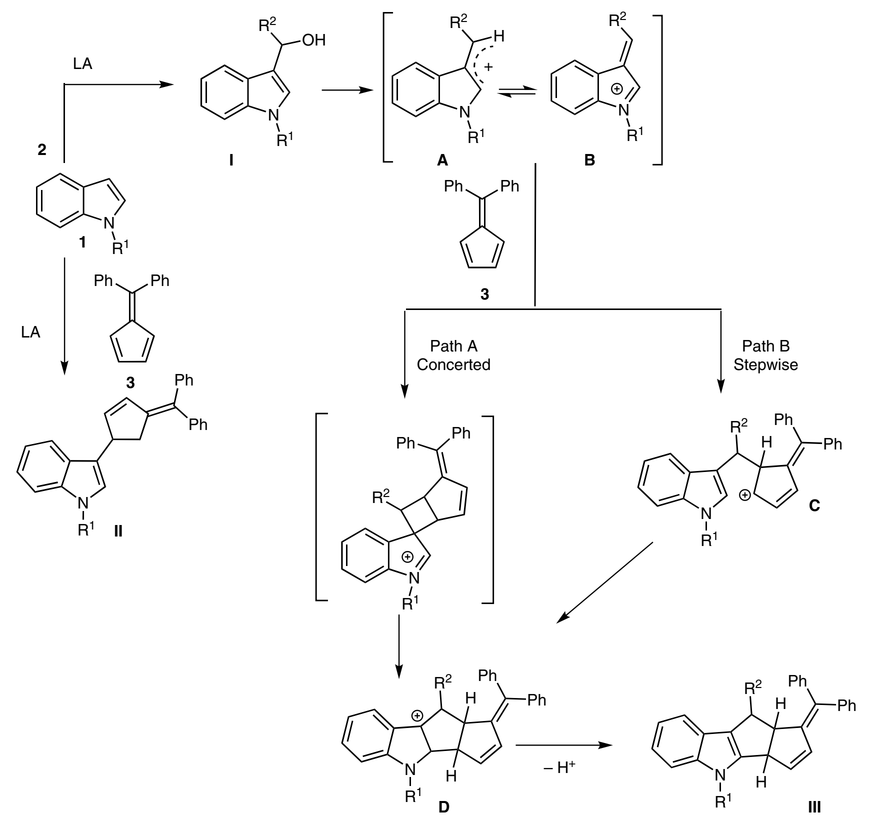
Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588696.



Scheme 4 Plausible reaction pathways

References and Notes

(1) (a) Kaushik, N. K.; Kaushik, N.; Attri, P.; Kumar, N.; Kim, C. H.; Verma, A. K.; Choi, E. H. *Molecules* **2013**, *18*, 6620. (b) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2011**, *111*, 215. (c) Kochanowska-Karamyan, A. J.; Hamann, M. T. *Chem. Rev.* **2010**, *110*, 4489. (d) Bandini, M.; Eichholzer, A. *Angew. Chem. Int. Ed.* **2009**, *48*, 9608. (e) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875. (f) Somei, M.; Yamada, F. *Nat. Prod. Rep.* **2005**, *22*, 73.

(2) (a) Cheng, K. F.; Wong, T. T.; Chan, K. P.; Kong, Y. C. *Eur. J. Med. Chem.* **1992**, *27*, 121. (b) Kong, Y.-C.; Cheng, K.-F.; Cambie, R. C.; Waterman, P. G. *J. Chem. Soc., Chem. Commun.* **1986**, 47. (c) Ngantchou, I.; Nyasse, B.; Denier, C.; Blonski, C.; Hannaert, V.; Schneider, B. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 3495. (d) Hocquemiller, R.; Dubois, G.; Leboeuf, M.; Cave, M.; Kunesch, N. *Tetrahedron Lett.* **1981**, *22*, 5057. (e) Kim, H.; Lantvit, D.; Hwang, C. H.; David, J. K.; Swanson, S. M.; Franzblau, S. G.; Orjala, J. *Bioorg. Med. Chem.* **2012**, *20*, 5290. (f) Park, A.; Moore, R. E.; Patterson, G. M. L. *Tetrahedron Lett.* **1922**, *20*, 3257. (g) Sturino, C. F.; O'Neill, G.; Lachance, N.; Boyd, M.; Berthelette, C.; Labelle, M.; Li, L.; Roy, B.; Scheigetz, J.; Tsou, N. *J. Med. Chem.* **2007**, *50*, 794.

(3) (a) Dange, N. S.; Hong, B.-C.; Leeb, G. H. *RSC Adv.* **2014**, *4*, 59706. (b) Richter, J. M.; Ishihara, Y.; Masuda, T.; Whitefield, B. W.; Llamas, T.; Pohjakallio, A.; Baran, P. S. *J. Am. Chem. Soc.* **2008**, *130*, 17938.

(4) (a) Zi, W.; Wu, H.; Toste, F. D. *J. Am. Chem. Soc.* **2015**, *137*, 3225. (b) Dhiman, S.; Ramasastry, S. S. V. *Chem. Commun.* **2015**, *51*, 557. (c) Ferrer, C.; Amijs, C. H. M.; Echavarren, A. M.; Xiong, H.; Xu, H.; Liao, S.; Xie, Z.; Tang, Y. *J. Am. Chem. Soc.* **2013**, *135*, 7851. (d) Xia, G.; Han, X.; Lu, X. *Org. Lett.* **2014**, *16*, 2058. (e) Ferreira, E. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2003**, *125*, 9578. (f) Saito, K.; Sogou, H.; Suga, T.; Kusama, H.; Iwasawa, N. *J. Am. Chem. Soc.* **2011**, *133*, 689. (g) Lian, Y.; Davies, H. M. L. *J. Am. Chem. Soc.* **2010**, *132*, 440. (h) Tseng, N.-W.; Lautens, M. *J. Org. Chem.* **2009**, *74*, 1809.

(5) (a) Yokosaka, T.; Nakayama, H.; Nemoto, T.; Hamada, Y. *Org. Lett.* **2013**, *15*, 2979. (b) Barluenga, J.; Tudela, E.; Ballesteros, A.; Tomás, M. *J. Am. Chem. Soc.* **2009**, *131*, 2096. (c) Spangler, J. E.; Davies, H. M. L. *J. Am. Chem. Soc.* **2013**, *135*, 6802. (d) Venkatesh, C.; Singh, P. P.; Ila, H.; Junjappa, H. *Eur. J. Org. Chem.* **2006**, 5378. (e) Li, H.; Hughes, R. P.; Wu, J. *J. Am. Chem. Soc.* **2014**, *136*, 6288.

(6) (a) Harrison, C.-A.; Leineweber, R.; Moody, C. J.; Williams, M. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1127. (b) McNulty, J.; Mcleod, D. *Synlett* **2011**, 717.

(7) (a) Shiri, M. *Chem. Rev.* **2012**, *112*, 3508. (b) Cioc, R. C.; Ruijter, E.; Orru, R. A. *Green Chem.* **2014**, *16*, 2958. (c) Rotstein, B. H.; Zaretsky, S.; Rai, V.; Yudin, A. K. *Chem. Rev.* **2014**, *114*, 8323. (d) Toure, B. B.; Hall, D. G. *Chem. Rev.* **2009**, *109*, 4439. (e) Oikawa, Y.; Hirasawa, H.; Yonemitsu, O. *Tetrahedron Lett.* **1978**, *20*, 1759. (f) Oikawa, Y.; Hirasawa, H.; Yonemitsu, O. *Chem. Pharm. Bull.* **1982**, *30*, 3092. (g) Palframan, M. J.; Pattenden, G. *Chem. Commun.* **2014**, *50*, 7223; and references cited therein. (h) Lebee, C.; Kataja, A. O.; Blanchard, F.; Masson,

G. *Chem. Eur. J.* **2015**, *21*, 8399. (i) Hao, W. J.; Wang, S. Y.; Ji, S. J. *ACS Catal.* **2013**, *3*, 2501. (j) Harmata, M. *Chem. Commun.* **2010**, *46*, 8904. (k) Gong, W.; Liu, Y.; Zhang, J.; Jiao, Y.; Li, X. J. *Chem. Asian J.* **2013**, *8*, 546. (l) Cao, K.-S.; Bian, H. X.; Zheng, W.-H. *Org. Biomol. Chem.* **2015**, *13*, 6449.

(8) (a) Han, X.; Li, H.; Hughes, R. P.; Wu, J. *Angew. Chem. Int. Ed.* **2012**, *51*, 10390. (b) Winne, J. M.; Catak, S.; Waroquier, M.; Speybroeck, V. V. *Angew. Chem. Int. Ed.* **2011**, *50*, 11990. (c) Laplace, D. R.; Verbraeken, B.; Hecke, K. V.; Winne, J. M. *Chem. Eur. J.* **2014**, *20*, 253.

(9) (a) Sarath Chand, S.; Jijy, E.; Prakash, P.; Szymoniak, J.; Preethanuj, P.; Dhanya, B. P.; Radhakrishnan, K. V. *Org. Lett.* **2013**, *15*, 3338. (b) Sarath Chand, S.; Saranya, S.; Preethanuj, P.; Dhanya, B. P.; Jijy, E.; Prakash, P.; Sasidhar, B. S.; Szymoniak, J.; Santhini, P. V.; Radhakrishnan, K. V. *Org. Biomol. Chem.* **2014**, *12*, 3045. (c) Sarath Chand, S.; Sasidhar, B. S.; Prakash, P.; Sasikumar, P.; Preethanuj, P.; Jaroschik, F.; Harakat, D.; Vasse, J.-L.; Radhakrishnan, K. V. *RSC Adv.* **2015**, *5*, 38075.

(10) (a) Little, R. D.; Carroll, G. L. *Tetrahedron Lett.* **1981**, *22*, 4389. (b) Little, R. D.; Miller, G. W.; Venegas, M. G.; Carroll, G. L.; Bukhari, A.; Patton, L.; Stone, K. *Tetrahedron* **1981**, *33*, 4371. (c) Lei, B.; Fallis, A. G. *J. Am. Chem. Soc.* **1990**, *112*, 4609. (d) Goering, B. K.; Li, J.; Ganem, B. *Tetrahedron Lett.* **1995**, *36*, 8905. (e) Ebner, C.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2015**, *54*, 11227.

(11) (a) Arai, K. *Synthesis* **1989**, 501. (b) Nair, V.; Anilkumar, G.; Radhakrishnan, K. V.; Nandakumar, M. V.; Kumar, S. *Tetrahedron* **1997**, *53*, 15903. (c) Nair, V.; Kumar, S.; Williard, P. G. *Tetrahedron Lett.* **1995**, *36*, 1605. (d) Nair, V.; Anilkumar, G.; Radhakrishnan, K. V.; Sheela, K. C.; Rath, N. P. *Tetrahedron* **1997**, *53*, 17361. (e) Nair, V.; Nandakumar, M. V.; Maliakal, D.; Mathen, J. S.; Rath, N. P. *Tetrahedron* **2000**, *56*, 8001. (f) Nair, V.; Mathew, B.; Menon, R. S.; Mathew, S.; Vairamani, M.; Prabhakar, S. *Tetrahedron* **2002**, *58*, 3235. (g) Hong, B.-C.; Shri, Y.-J.; Liao, J.-H. *Org. Lett.* **2002**, *4*, 663. (h) Boger, D. L.; Huter, O.; Mbiya, K.; Zhang, M. *J. Am. Chem. Soc.* **1995**, *117*, 11839.

(12) (a) Lonergan, D. G.; Deslongchamps, G. *Tetrahedron* **1998**, *54*, 14041. (b) Warrener, R. N.; Butler, D. N. *Aldrichimica Acta* **1997**, *30*, 119. (c) Radhakrishnan, K. V.; Nandakumar, M. V.; Rath, N. P. *Synlett* **1997**, 767. (d) Nzabamwita, G.; Kolani, B.; Jousseaume, B. *Tetrahedron Lett.* **1989**, *30*, 2207. (e) Manikandan, S.; Shanmugasundaram, M.; Raghunathan, R. *Tetrahedron* **2002**, *58*, 597. (f) Bhojgude, S. S.; Kaicharla, T.; Bhunia, A.; Biju, A. T. *Org. Lett.* **2012**, *14*, 4098.

(13) (a) Dunn, L. C.; Chang, Y.-M.; Houk, K. N. *J. Am. Chem. Soc.* **1976**, *98*, 7095. (b) Yujiro, H.; Hiroaki, G.; Masakazu, H.; Kuppusamy, S.; Indresh, K.; Hayato, I.; Kohzo, K.; Hiroharu, Y.; Seiji, T.; Tadafumi, U. *J. Am. Chem. Soc.* **2011**, *133*, 20175. (c) Radhakrishnan, K. V.; Krishnan, K. S.; Bhadbhade, M. M.; Bhosekar, G. V. *Tetrahedron Lett.* **2005**, *46*, 4785. (d) Krishnan, K. S.; Sajisha, V. S.; Anas, S.; Suresh, C. H.; Bhadbhade, M. M.; Bhosekar, G. V.; Radhakrishnan, K. V. *Tetrahedron* **2006**, *62*, 5952. (e) Hong, B.-C.; Sun, H.-I.; Chen, Z.-Y. *Chem. Commun* **1999**, 2125. (f) Hong, B.-C.; Shr, Y.-J.; Wu, J.-L.; Gupta, A. K.; Lin, K. J. *Org. Lett.* **2002**, *4*, 2249.

(14) (a) Joseph, J.; Jaroschik, F.; Radhakrishnan, K. V.; Vasse, J.-L.; Szymoniak, J. *Chem. Commun.* **2013**, *49*, 4549. (b) Joseph, J.; Jaroschik, F.; Harakat, D.; Radhakrishnan, K. V.; Vasse, J.-L.; Szymoniak, J. *Chem. Eur. J.* **2014**, *20*, 5433. (c) Tamke, S.; Daniliuc, C.-G.; Paradies, J. *Org. Biomol. Chem.* **2014**, *12*, 9139. (d) Barluenga, J.; Martinez, S.; Suarez-Sobrino, A. L.; Tomas, M. *J. Am. Chem. Soc.* **2002**, *124*, 5948.

(15) Sarath Chand, S.; Greeshma, G.; Santhini, P. V.; Preethanuj, P.; Jubi, J.; Harakat, D.; Jaroschik, F.; Radhakrishnan, K. V. *Org. Lett.* **2016**, *18*, 9646.

(16) **Typical Experimental Procedure for 4aa**

A mixture of indole **1a** (50 mg, 0.427 mmol), pentafulvene **3a** (147 mg, 0.640 mmol), aldehyde **2a** (70 mg, 0.640 mmol), and $Sn(OTf)_2$ (4 mg, 0.008 mmol) were weighed in to a reaction tube and dry MeCN (2 mL) was added and allowed to stir at r.t. for 2 h. The solvent was evaporated in vacuo and the residue on silica gel (100–200 mesh) column chromatography with mixture of hexane–EtOAc yielded the products.

(17) **Spectral Data of Compound 4aa**

Yield 115 mg, 62%; off-white solid, mp 155–160 °C; $R_f = 0.43$ (hexane–EtOAc = 9:1). IR (neat) ν_{max} = 3402, 3056, 3026, 2923, 1710, 1603, 1489, 1449, 1361, 1224, 1060, 1028, 750, 701 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ = 7.84 (s, 1 H), 7.27–7.7.25 (m, 3 H), 7.23–7.21 (m, 1 H), 7.19–7.17 (m, 2 H), 7.14–7.13 (m, 5 H), 7.05–7.01 (m, 2 H), 7.00–6.97 (m, 3 H), 6.89 (t, J = 8 Hz, 1 H), 6.50–6.48 (m, 2 H), 6.44–6.43 (m, 1 H), 6.33 (d, J = 8.5 Hz, 1 H), 4.74–4.66 (m, 2 H), 4.20 (s, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.0, 146.3, 143.6, 143.4, 142.9, 141.4, 136.8, 135.1, 134.8, 130.2, 129.7, 128.6, 127.9, 127.7, 126.9, 126.8, 126.7, 125.3, 124.3, 122.3, 121.1, 119.7, 118.9, 111.4, 61.5, 51.6, 50.8. ESI-HRMS: *m/z* calcd for $C_{23}H_{25}N$ $[M + H]^+$: 436.20652; found: 436.20610.