Tetrahedron Letters 50 (2009) 644–647

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Gold(I) catalyzed sequential cycloisomerization/bis-addition of *o*-ethynylanilines: an efficient access to bis(indolyl)methanes and di(indolyl)indolin-2-ones

C. Praveen, Y. Wilson Sagayaraj, P. T. Perumal *

Organic Chemistry Division, Central Leather Research Institute, Adyar, Chennai 600 020, Tamil Nadu, India

ARTICLE INFO

Article history:
Received 8 October 2008
Revised 10 November 2008
Accepted 22 November 2008
Available online 27 November 2008

ABSTRACT

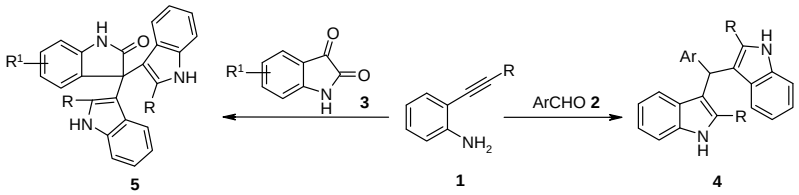
An efficient synthesis of bis(indolyl)methanes and di(indolyl)indolin-2-ones have been developed by a sequential approach involving gold(I) catalyzed cycloisomerization/bis-addition of *o*-ethynylanilines with various aldehydes and isatins respectively. This methodology opens clean and synthetically competitive alternative to the already established procedures of the synthesis of bis(indolyl)methanes and di(indolyl)indolin-2-ones.

Bis(indolyl)methanes constitute an important class of heterocyclic compounds that display diverse pharmacological activities and are useful in the treatment of fibromyalgia, chronic fatigue and irritable bowel syndrome.[1] They are known to promote beneficial estrogen metabolism[2] and induce apoptosis in human cancer cells. Thus the development of high-throughput methods for the synthesis of bis(indolyl)methanes remains a topic of paramount importance in view of their versatile biological and pharmacological properties. Bis(indolyl)methanes have been prepared mainly by the reaction of indole with carbonyl compounds in the presence of Lewis acids such as $LiClO_4$,[3] $InCl_3$,[4] I_2,[5] $CuBr_2$,[6] $[RE(PFO)_3]$,[7] $ZrCl_4$,[8] and Bronsted acids such as sulphamic acid,[9,10] PTSA,[11] $KHSO_4$.[12] All the synthetic avenues to bis(indolyl)methanes comprise reaction between pre-constructed indole skeletons with aldehydes (or their acetals), ketones, α-ketoacids, imines, iminium salts or nitrones.[13] On the otherhand 3,3-diaryloxindoles, a basic framework widely found in clinical drugs and biologically active substances have been shown to possess antiproliferative, antibacterial, antiprotozoal and antiinflammatory activities.[14] These compounds have also been used as laxatives[15] and lead molecules for Ca^{2+} depletion mediated inhibition of translation initiation.[16] The 3,3-di(indoly)indolin-2-ones can be formed by the reaction of isatin and indoles under acidic conditions for long reaction times or catalyzed by $KAl(SO_4)_2$ under microwave conditions.[17] Only a few methodologies has been accommodated for the synthesis of di(indolyl)indolin-2-ones.[15,18] As a result of the increased interest, new efficient methods are needed to synthesise these compounds and generate structurally diverse bis(indolyl)methanes and di(indolyl)indolin-2-ones with a variety of substituents. In recent years, intramolecular cyclization of *o*-ethynylanilines followed by C3 functionalization leading to 3-substituted indoles have been developed with remarkable improvements in terms of efficiency and scope of application.[19] However there is no report for the construction of bis(indolyl)methanes and di(indolyl)indolin-2-ones via one-pot cycloisomerization/bis-addition process. More recently it has been shown that the alkynophilic Lewis acidity of Au(I) and Au(III) present new opportunities for the cycloisomerization of wide array of alkynes-tethered nucleophiles.[20] The unique reactivity of Au(I) and Au(III) with allenes and alkynes opened the doors to the discovery and invention of new reactions.[21] But, participation of Au(I) and Au(III) in intramolecular cyclization/C3 functionalization of *o*-ethynylanilines to 3-substituted indoles were less explored.[22] In our ongoing efforts on intramolecular cyclization reactions[23] and stimulated by the growing interest in the development of gold catalysis,[24] we became interested in the development of gold-catalyzed synthesis of 3-substituted indoles. In particular we focussed our attention to the preparation of bis(indolyl)methanes and di(indolyl)indolin-2-ones through an integrated process involving two basic steps, cycloisomerization of *o*-ethynylanilines followed by bis-addition with aldehydes and isatins (Scheme 1).

We initiated our studies by reacting *o*-(phenylethynyl) aniline **(6)** and biphenyl-4-carbaldehyde **(2d)** with 5 mol % AuCl in acetonitrile at room temperature. Under this condition only the cycloisomerized product that is, 2-phenyl indole was obtained as the sole product (85% isolated yield). Bis-addition, under these conditions proved to be ineffective, even when the reaction was carried out for 24 h. By elevating the temperature to 80 °C, we were able to obtain the bis-addition product **(7d)** in high yield in a short reaction time (Table 1, entry 4). When the same reaction was performed using 2 mol % of AuCl, only 40% of the product **(7d)** was formed, and 35% of the starting material, that is, 2-(phenyleth-

* Corresponding author. Tel.: +91 44 24911329; fax: +91 44 24911539.
E-mail address: ptperumal@gmail.com (P.T. Perumal).

0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.11.086

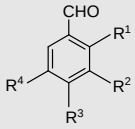
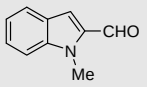
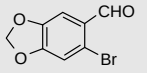
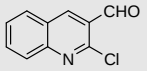
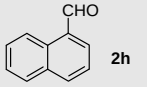
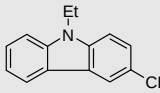
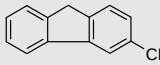
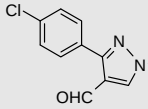
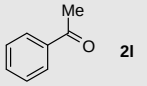


Scheme 1.

ynyl)aniline **(6)** was recovered. So we inferred that 2 mol % of AuCl was ineffective for the complete cycloisomerization of *o*-(phenylethynyl)aniline. Toluene, methanol and dichloromethane gave only 38%, 20%, and 50% of the product respectively. Based on these observations, we used a procedure, that utilizes 5 mol % of AuCl in acetonitrile under reflux, followed by the addition of 0.5 equiv of aldehyde, for the synthesis of bis(indolyl)methanes. (Scheme 2).[25]

Under these conditions, the reaction proceeded smoothly with a wide range of functionalized aldehydes, including those containing ether, phenol, carboxylic acid, polyaromatic and heteroaromatic groups. The results are summarized in Table 1. The results revealed that electron deficiency and the nature of the araldehyde had marked effect on this conversion. Aldehydes with electron withdrawing groups gave lower yields of the products (entry 3) than those with electron releasing counterparts (entries 1–2). This observation was in good agreement with other bis-addition protocols.[3,26] Moreover this method is chemoselective. For example, when a 1:1 mixture of biphenyl-4-carbaldehyde (**2d**) and acetophenone (**2l**) was allowed to react with 2-(phenylethynyl)aniline (**6**) and AuCl in acetonitrile, it was found that only 3,3′-(biphenyl-4-ylmethylene)bis(2-phenyl-1*H*-indole) (**7d**) was obtained, while acetophenone did not give the corresponding product (**7l**). On the basis of the above results we extended our methodology for the synthesis of bis(indolyl)methanes derived from aldehydes with structural diversity including polycyclic and heteroaromatic. All these aldehydes gave good yields of products **(7a–7k)**. However the low yields in the case of **(7e)** and **(7g)** may be attributed to the lower reactivity of their corresponding aldehydes (**2e** and **2g**) towards bis-addition. The ^{1}H NMR spectra of compounds (**7a–7k**) in DMSO-d_6 consisted of a characteristic singlet due to the methine proton (–C*H*-Ar) in the region of 5.8–6.7 ppm. Another characteristic feature of the ^{1}H NMR spectra was the appearance of a singlet at δ_H 11.3–11.5 ppm, which corresponds to two indole-N*H* protons. These observations confirm the formation of bis(indolyl)methanes.

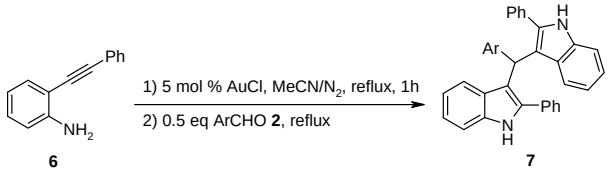
Table 1
Gold(I) catalyzed synthesis of bis(indolyl)methanes from 2-(phenylethynyl)aniline **6** and aldehyde **2**

Entry	ArCHO **2**		Product[a]	Time (h)	Yield[b]
					
1	R^1 = H, R^2 = OMe, R^3 = OH, R^4 = Br	2a	**7a**	2.0	76
2	R^1 = Br, R^2 = H, R^3 = OMe, R^4 = OMe	2b	**7b**	2.0	79
3	R^1 = H, R^2 = H, R^3 = COOH, R^4 = H	2c	**7c**	1.5	65
4	R^1 = H, R^2 = H, R^3 = Ph, R^4 = H	2d	**7d**	1.5	80
5		**2e**	**7e**	4.0	53
6		**2f**	**7f**	1.0	85
7		**2g**	**7g**	3.5	59
8		**2h**	**7h**	0.5	83
9		**2i**	**7i**	0.5	77
10		**2j**	**7j**	0.5	76
11		**2k**	**7k**	0.5	82
12		**2l**	**7l**	1.5	—

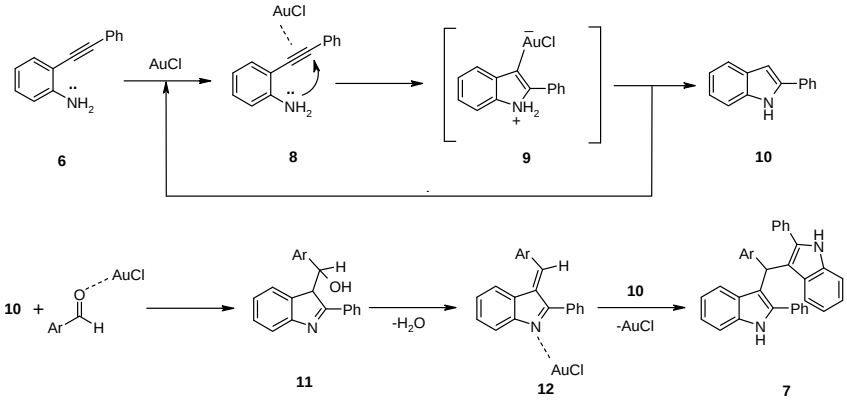
[a] Isolated yield.
[b] The products were characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectra.

With an efficient protocol for the gold catalyzed synthesis of bis(indolyl)methanes in hand, we next set out to apply the same reaction conditions for the synthesis of di(indolyl)indolin-2-ones from various 2-ethynylanilines and isatins (Scheme 4).[27] The results of which are summarized in Table 2.

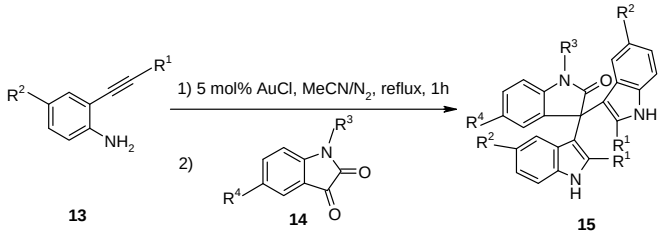
The substituents on the aniline moiety play a significant role in the cycloisomerization/bis-addition process. The presence of electron-releasing group, such as methyl in *para* position to the amino group enhances the product formation as indicated by a short reaction time and higher yield (entry 4). Similarly, for a strong electron-withdrawing group, such as cyano, para to amino group,



Scheme 2.



Scheme 3.



Scheme 4.

Table 2
Gold(I) catalyzed synthesis of di(indolyl)indolin-2-ones from 2-ethynyl anilines **13** and isatin **14**[a]

Entry	R^1	R^2	R^3	R^4	Time (h)	Product[b]	Yield[c] (%)
1	Ph	H	H	H	1.0	**15a**	83
2	Ph	H	Me	H	0.5	**15b**	89
3	Ph	Cl	H	Me	1.5	**15c**	80
4	Ph	Me	H	H	0.5	**15d**	91
5	Ph	CN	H	H	3.0	**15e**	67
6	^{n}Bu	H	H	H	7.0	**15f**	70

[a] All reactions were carried out using 0.5 equiv of isatin.
[b] All the products were characterized by IR, NMR and mass spectroscopies.
[c] Isolated yield.

required a longer reaction time and gave a lower yield (entry 5). The nature of groups on the triple bond of the 2-ethynylanilines viz R^1, also affects the product yield. Compound (**13**) with a phenyl group on the alkyne, underwent the cycloisomerization/bis-addition process smoothly in a short reaction time, and the total conversions were high (entries 1–5). However *n*-butyl on the alkyne residue afforded a product with low yield and required a longer reaction time (entry 6). The formation of di(indolyl)indolin-2-ones (**15a**–**15f**) was ascertained by the appearance of a low intensity ^{13}C peak at δ_C 52.2–59.7 ppm, which indicates the presence of a quaternary carbon. Moreover, no quaternary carbon signal appeared in the ^{13}C NMR 135 DEPT spectra. Furthermore, all compounds exhibited a ^{13}C peak at δ_C 175–183 ppm supporting the presence of an amide carbon.

In summary, an efficient and one-pot synthesis of structurally diverse bis(indolyl)methanes and di(indolyl)indolin-2-ones via Au(I) catalyzed cycloisomerization/bis-addition of *o*-ethynylanilines with aldehydes and isatins has been developed. This methodology affords the products in good yields and could be extended to a wide range of aldehydes/isatins. Significantly this procedure affords indoles with a free –NH group without requiring the use of nitrogen protecting group. One-pot synthesis, functional group compatibility and no additional solvent extraction steps are the noteworthy advantages of this method. Further studies to delineate the scope and limitations of the present methodology are underway.

Acknowledgement

The authors thank the Council of Scientific and Industrial Research, New Delhi, India for the research fellowship.

References and notes

1. (a) Bradfield, C. A.; Bjeldanes, L. F. *J. Toxicol. Environ. Health* **1987**, *21*, 311; (b) Dashwood, R. H.; Uyetake, L.; Fong, A. T.; Hendricks, J. D.; Bailey, G. S. *Food Chem. Toxicol.* **1987**, *27*, 385.
2. Zeligs, M. A. *J. Med. Food* **1998**, *1*, 67.
3. Yadav, J. S.; Reddy, B. V. S.; Murthy, Ch. V. S. R.; Mahesh Kumar, G.; Madan, Ch. *Synthesis* **2001**, 783.
4. Babu, G.; Sridhar, N.; Perumal, P. T. *Synth. Commun.* **2000**, *30*, 1609.
5. Bandgar, B. P.; Shaikh, K. A. *Tetrahedron Lett.* **2003**, *44*, 1959.
6. Mo, L.-P.; Ma, Z.-C.; Zhang, Z.-H. *Synth. Commun.* **2005**, *35*, 1997.
7. Wang, L.; Han, J.; Tian, H.; Sheng, J.; Fan, Z.; Tang, X. *Synlett* **2005**, 337.
8. Zhang, Z.-H.; Yin, L.; Wang, Y.-M. *Synthesis* **2005**, 1949.
9. (a) Singh, P. R.; Singh, D. U.; Samant, S. D. *Synth. Commun.* **2005**, *35*, 2133; (b) Li, W.-J.; Lin, X.-F.; Wang, J.; Li, G.-L.; Wang, Y.-G. *Synth. Commun.* **2005**, *35*, 2765.
10. Li, J.-T.; Dai, H.-G.; Xu, W.-Z.; Li, T.-S. *Ultrason. Sonochem.* **2006**, *13*, 24.
11. Raju, B. C.; Rao, J. M. *Ind. J. Chem.* **2008**, 623.
12. Nagarajan, R.; Perumal, P. T. *Chem. Lett.* **2004**, *3*, 288.
13. Chakrabarty, M.; Basak, R.; Harigaya, Y. *Heterocycles* **2001**, *55*, 2431.
14. (a) Joshi, K. C.; Pathak, V. N.; Jain, S. K. *Pharmazie* **1980**, *35*, 677; (b) Boltov, V. V.; Drugovina, V. V.; Yakovleva, L. V.; Bereznyakova, A. I. *Khim. -Farm. Zh.* **1982**, *16*, 58; c William, C.E. US Patent 3,558,653, 1971.; (d) Pajouhesh, H.; Parsons, R.; Popp, F. D. *J. Pharm. Sci.* **1983**, *72*, 318.
15. Garrido, F.; Ibanez, J.; Gonalons, E.; Giraldez, A. *Eur. J. Med. Chem.* **2004**, *47*, 1882.
16. Natarajan, A.; Fan, Y.-H.; Chen, H.; Guo, Y.; Iyasere, J.; Harbinski, F.; Christ, W. J.; Aktas, H.; Halperin, J. A. *J. Med. Chem.* **2004**, *47*, 1884.
17. (a) Bergman, J.; Eklund, N. *Tetrahedron* **1980**, *36*, 1445; (b) Azizian, J.; Mohammadi, A. A.; Karimi, A. R.; Mohammadizadeh, M. R. *J. Chem. Res. Synop.* **2004**, *6*, 424.
18. (a) Hewawasam, P.; Gribkoff, V. K.; Pendri, Y.; Dworetzky, S. I.; Meanwell, N. a.; Martinez, E.; Boissard, C. G.; Post-Munson, D. J.; Trojnacki, J. T.; Yeleswaram, K.; Pajor, L. M.; Knipe, J.; Gao, Q.; Perrone, R.; Starrett, J. E., Jr. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1023; (b) Nicolaou, K. C.; Bella, M.; Chen, D. Y.-K.; Huang, X.; Ling, T.; Snyder, S. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 3495; (c) Klumpp, A. A.; Yeung, K. Y.; Surya Prakash, G. K.; Olah, G. A. *J. Org. Chem.* **1998**, *63*, 4481; (d) Kobayashi, M.; Aoki, S.; Gato, K.; Matsunami, K.; Kurosu, M.; Kitagawa, I. *Chem. Pharm. Bull.* **1994**, *42*, 2449.
19. (a) Yue, D.; Yao, T.; Larock, R. *J. Org. Chem.* **2006**, *71*, 62; (b) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Parisi, L. M. *J. Org. Chem.* **2005**, *70*, 6213; (c) Battistuzzi, G.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Parisi, L. M. *Org. Lett.* **2002**, *4*, 1355; (d) Barluenga, J.; Trincado, M.; Rubio, E.; Gonzalez, J. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 2406; (e) Cacchi, S.; Fabrizi, S.; Pace, P. *J. Org. Chem.* **1998**, *63*, 1001; (f) Amjad, M.; Knight, D. W. *Tetrahedron Lett.* **2004**, *45*, 539; (g) Sakai, N.; Annaka, K.; Konakahara, T. *Tetrahedron Lett.* **2006**, *47*, 631; (h) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F. *Synlett* **2000**, 647; (i) Collini, M. D.; Ellingboe, J. W. *Tetrahedron Lett.* **1997**, *46*, 7963; (j) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F. *Synlett* **2000**, 394; (k) Takeda, A.; Kamijo, S.; Yamamoto, Y. *J. Am. Chem. Soc.*

2000, *122*, 5662; (l) Saulnier, M. G.; Frennesson, D. B.; Deshpande, M. S.; Vyas, D. M. *Tetrahedron Lett.* **1995**, *36*, 7841; (m) Iritani, K.; Matsubara, S.; Utimoto, K. *Tetrahedron Lett.* **1988**, *29*, 1799; (n) Yasuhara, A.; Kaneko, T.; Sakamoto, T. *Heterocycles* **1998**, *43*, 2741; (o) Ambrogio, I.; Arcadi, A.; Cacchi, S.; Fabrio, G.; Marinelli, F. *Synlett* **2007**, 1775; (p) Wang, M.-Z.; Wong, M.-K.; Che, C.-M. *Chem. Eur. J.* **2008**, *14*, 8353.

20. (a) Gorin, D. J.; Toste, D. *Nature* **2007**, *446*, 395; (b) Widenhoefer, R. A.; Han, X. *Eur. J. Org. Chem.* **2006**, 4555; (c) Ferrer, C.; Amijis, C. H. M.; Echavarren, A. M. *Chem. Eur. J.* **2007**, *13*, 1358.
21. (a) Xiao, F.; Chen, Y.; Liu, Y.; Wang, J. *Tetrahedron* **2008**, *64*, 2755; (b) Morita, N.; Krause, N. *Org. Lett.* **2004**, *6*, 4121; (c) Nair, V.; Abhilash, K. G.; Vidya, N. *Org. Lett.* **2005**, *7*, 5857; (d) Hoffman-Roder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537; (e) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *J. Am. Chem. Soc.* **2000**, *122*, 11533; (f) Liu, Y.; Liu, M.; Guo, S.; Tu, H.; Zhou, Y.; Gao, H. *Org. Lett.* **2006**, *8*, 3445; (g) Srome, A. W.; Rubina, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2005**, *127*, 10500; (h) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285; (i) Kenndy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4526; (j) Hashmi, A. S. K.; Weyrauch, J. P.; Frey, W.; Bats, J. W. *Org. Lett.* **2004**, *6*, 4391; (k) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Org. Lett.* **2001**, *3*, 3769; (l) Asao, N.; Nogami, T.; Lee, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 10921; (m) Nair, V.; Vidya, N.; Abhilash, K. G. *Synthesis* **2006**, 3647.
22. (a) Nakamura, I.; Yamagishi, U.; Song, D.; Konta, S.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 2284; (b) Alfonsi, M.; Arcadi, A.; Aschi, M.; Bianchi, G.; Marinelli, F. *J. Org. Chem.* **2005**, *70*, 2265; (c) Arcadi, A.; Bianchi, G.; Marinelli, F. *Synthesis* **2004**, 610; (d) Miyazaki, Y.; Kobayashi, S. *J. Comb. Chem.* **2008**, *10*, 355; (e) Tois, J.; Franmen, R.; Koskinen, A. *Tetrahedron* **2003**, *59*, 5395; 23 Praveen, C.; Kumar, K. H.; Muralidharan, D.; Perumal, P. T. *Tetrahedron* **2008**, *64*, 2369.
24. (a) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896; (b) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180; (c) Sun, X.; Sun, W.; Fan, R.; Wu, J. *Adv. Synth. Catal.* **2007**, *349*, 2151; (d) Amijs, C. H. M.; Ferrer, C.; Echaverren, A. M. *Chem. Commun.* **2007**, 698; (e) Shi, Y.; Peterson, S. M.; Haberaecker, W. W., III; Blum, S. A. *J. Am. Chem. Soc.* **2008**, *130*, 2168; (f) Mizushima, E.; Sato, K.; Hayashi, T.; Tanaka, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 4563; (g) Nair, V.; Vidya, N.; Abhilash, K. G. *Tetrahedron Lett.* **2006**, *47*, 2871; (h) Marchal, E.; Uriac, P.; Legouin, B.; Toupet, L.; Weghe, P. V. d. *Tetrahedron* **2007**, *63*, 9979; (i) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 11806.
25. *General procedure for the synthesis of bis(indolyl)methanes* **7a–7k**. *Representative procedure for 4-[bis(2-phenyl-1H-indol-3-yl)methyl]-2-bromo-6-methoxyphenol* **7a** (Table 1, entry 1): To a solution of o-(phenylethynyl)aniline (1.0 mmol) in acetonitrile (1 mL) under N_2 was added AuCl (5 mol %) in acetonitrile (1 mL) and refluxed for 1 h. To this reaction mixture 3-bromo-4-hydroxy-5-methoxybenzaldehyde (0.5 mmol) was added and the mixture was refluxed for the specified time (Table 1). After completion of the reaction as indicated by TLC, the reaction mixture was concentrated under reduced pressure and purified by column chromatography over silica gel (100–200 mesh) to afford pure product **7a** (76%) as a brown solid; mp 228–230 °C; R_f = 0.62 (AcOEt/petroleum ether 40%). IR (KBr): 3480, 3387, 1493, 1453, 1414, 1274, 1227, 1042, 746, 698 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ_H 3.47 (s, 3H, $-OCH_3$), 5.87 (s, 1H, –CH-Ar), 6.66–6.71 (m, 3H, Ar-H), 6.78 (s, 1H, Ar-H), 6.91 (d, 2H, J = 7.6 Hz, Ar-H), 6.98 (t, 2H, J = 7.6 Hz, Ar-H), 7.19–7.21 (m, 6H, Ar-H), 7.28–7.29 (m, 4H, Ar-H), 7.34 (d, 2H, J = 8.4 Hz, Ar-H), 9.30 (s, 1H, –OH), 11.3 (s, 2H, –NH). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 56.1, 64.8, 109.0, 111.3, 112.1, 113.8, 118.6, 120.5, 120.9, 124.1, 127.2, 128.0, 128.2, 132.7, 135.3, 136.1, 137.4, 141.9, 148.4 (2C). MS (EI): m/z = 597 [M+], 599[M+2]. Anal. Calcd for $C_{36}H_{27}BrN_2O_2$: C, 72.14; H, 4.54; N, 4.67. Found: C, 72.22; H, 4.50; N, 4.71.
26. Yadav, J. S.; Reddy, B. V. S.; Sunitha, S. *Adv. Synth. Catal.* **2003**, 345.
27. *General procedure for the synthesis of di(indolyl)indolin-2-ones* **15a–15f**. *Representative procedure for 3,3-Bis(2-butyl-1H-indol-3-yl)indolin-2-one* **15f** (Table 2, entry 6): To a solution of *o*-hexynylaniline (1.0 mmol) in acetonitrile (1 mL) under N_2 was added AuCl (5 mol %) in acetonitrile (1 mL) and stirred the mixture under reflux for 1 h. To this reaction mixture 0.5 mmol of isatin was added and the mixture was refluxed for the specified time (Table 2). After completion of the reaction as indicated by TLC, the reaction mixture was concentrated under reduced pressure and purified by column chromatography over silica gel (100–200 mesh) to afford pure product **15f** (70%) as a brown solid; mp 199–201 °C; R_f = 0.50 (AcOEt/petroleum ether 25%). IR (KBr): 749, 1459, 1713, 2925, 3385 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ_H 0.59 (t, 3H, J = 6.8 Hz, $-CH_3$), 0.67 (t, 3H, J = 6.8 Hz, $-CH_3$), 0.91–1.42 (m, 8H, $-CH_2-CH_2-CH_3$), 2.29–2.35 (m, 4H, Ar-CH_2–), 6.39 (d, 1H, J = 7.6 Hz, Ar-H), 6.50 (t, 1H, J = 6.9 Hz, Ar-H), 6.58 (t, 1H, J = 7.6 Hz, Ar-H), 6.79–6.90 (m, 5H, Ar-H), 7.12–7.18 (m, 4H, Ar-H), 10.47 (s, 1H, –N*H*–CO–), 10.70 (s, 1H, –N*H*), 10.75 (s, 1H, –N*H*). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C 13.9, 14.0, 22.6 (2C), 26.9, 27.0, 31.4, 31.8, 53.1, 109.6, 109.7, 110.6, 110.7, 111.0, 117.9, 118.0, 120.0, 120.2, 120.5, 120.9, 121.5, 125.6, 127.6, 128.0, 128.1, 135.7, 135.8, 136.2, 136.3, 138.5, 141.5, 179.6. MS (EI): m/z = 973 [dimer+Na^+]. Anal. Calcd for $C_{32}H_{33}N_3O$: C, 80.81; H, 6.99; N, 8.83. Found: C, 80.97; H, 7.05; N, 8.76.