Tetrahedron 65 (2009) 9244–9255

Contents lists available at ScienceDirect

Tetrahedron

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

Efficient synthesis of 3-substituted indoles through a domino gold(I) chloride catalyzed cycloisomerization/C3-functionalization of 2-(alkynyl)anilines

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ARTICLE INFO

Article history:
Received 5 July 2009
Received in revised form 2 September 2009
Accepted 3 September 2009
Available online 9 September 2009

ABSTRACT

An efficient synthesis of 3-substituted indoles by a sequential approach involving gold(I) chloride catalyzed cycloisomerization/bis-addition and conjugate addition of 2-(alkynyl)anilines has been accomplished. A variety of 2-(alkynyl)anilines, aldehydes, isatins and nitroolefins undergo this overall process in good to excellent yields. This methodology represents an effective alternative to the classical C3-functionalization of indoles.

1. Introduction

1.1. Natural occurrence and pharmacological activity of 3-substituted indoles

The 3-substituted indole nucleus is prevalent in numerous natural products and is extremely important in medicinal chemistry.[1] For example, two diastereoisomeric tris-indole alkaloids, occurring as enantiomeric pairs, designated as (±)–gelliusinus A and B **I** (Fig. 1) represent the major components of a deep water Caledonian sponge[2] and vibrindole A **II** is a metabolite of the marine bacterium, *Vibrio parahaemalyticus* is isolated from the toxic mucus of the boxfish *Ostracion cubicus*.[3] In animals, serotonin[4] **III** (5-hydroxytryptamine) is a crucial neurotransmitter in the central nervous system.[5]

1.2. Synthetic methods, applications and biological properties of bis(indolyl)methanes, di(indolyl)-indolin-2-ones and 2-indolyl-1-nitroalkanes

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.[6] They are known to promote beneficial oestrogen metabolism[7] 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

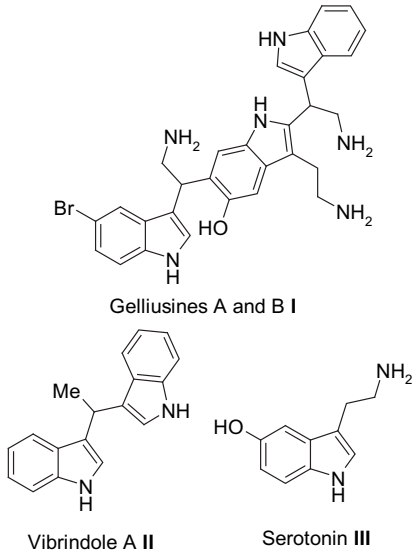

Figure 1. Representatives of 3-substituted indoles.

Lewis acids such as $LiClO_4$,[8] $InCl_3$,[9] I_2,[10] $CuBr_2$,[11] $[RE(PFO)_3]$,[12] $ZrCl_4$,[13] and Bronsted acids such as sulphamic acid,[14,15] PTSA,[16] $KHSO_4$.[17] All the synthetic avenues to bis(indolyl)methanes comprise reaction between pre-constructed indole skeletons with aldehydes (or their acetals), ketones, a-ketoacids, imines, iminium salts or nitrones.[18] On the other-hand 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.[19] These compounds have also been used as laxatives[20] and lead molecules for Ca^{2+} depletion mediated inhibition of translation initiation.[21] The

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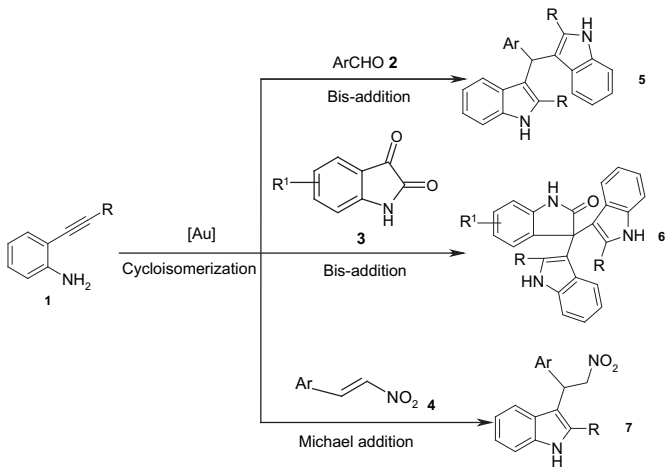
0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.09.019

3,3-di(indolyl)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.[22] Only a few methodologies have been accommodated for the synthesis of di(indolyl)indolin-2-ones.[20,23] 2-Indolyl-1-nitroalkanes have become important synthetic intermediates and can be readily converted into tryptamines by reduction reactions.[24] Various methods for the synthesis of 2-indolyl-1-nitroalkanes have been developed. For example, they can be prepared from indoles and nitroolefins by Michael addition reaction promoted by several catalysts[25] or through a microwave assisted reaction of indoles with nitroolefins,[26] and by the reaction of sulphonyl indoles with nitroalkanes in the presence of sodium hydride.[27]

1.3. Gold catalysts in sequential cycloisomerization/C3-functionalization process of 2-(alkynyl)anilines

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.[28] 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.[29] The unique reactivity of Au(I) and Au(III) with allenes and alkynes opened the doors to the discovery and invention of new reactions.[30] But, participation of Au(I) and Au(III) in intramolecular cyclization/C3-functionalization of *o*-ethynylanilines to 3-substituted indoles was less explored.[31] Recently Au(III) catalyzed sequential cycloisomerization/conjugate addition of *o*-ethynylanilines with α,β-enones[32] and Au(III) catalyzed bis-arylation were reported.[33] Stimulated by the growing interest in the development of gold catalysis,[34] and the ongoing exploration of the novel synthetic process of nitrogen containing heterocycles,[35] using gold(I) chloride,[35c,d] we found that AuCl effectively catalyses the sequential cycloisomerization/C3-functionalization of 2-ethynylanilines with a wide range of aldehydes, isatins[35c] and nitrostyrenes. Herein, we disclose the application of AuCl in the synthesis of some 3-substituted indoles using sequential cycloisomerization/C3-functionalization strategy (Scheme 1).[36]



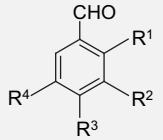
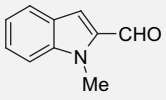
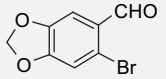
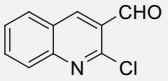
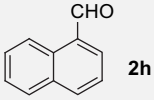
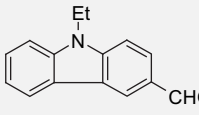
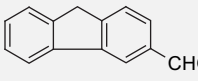
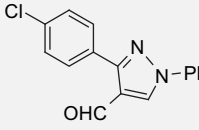
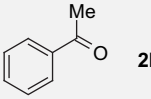
Scheme 1.

2. Results and discussion

2.1. Optimization of reaction conditions for the synthesis of bis(indolyl)methanes

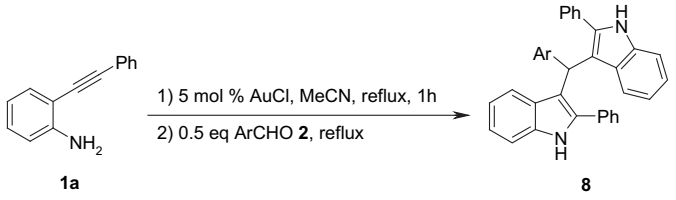
We initiated our studies by reacting *o*-(phenylethynyl) aniline (**1a**) and biphenyl-4-carbaldehyde (**2d**) with 5 mol % AuCl in acetonitrile at room temperature. Under this condition only the cycloisomerized product that, 2-phenyl indole was obtained as the sole product (85% isolated yield). Bis-addition, 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 (**8d**) 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 (**8d**) was formed, and 35% of the starting material, 2-(phenylethynyl)aniline (**1a**) 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. Needless to say, in the absence of catalyst, the cycloisomerization did not proceed at all. The possibility of participation of Au(III) as a catalytic species, (via. oxidation of Au(I) to Au(III)) was ruled out by performing the same reaction using 5 mol % of $AuCl_3$ in acetonitrile under reflux followed by the addition of aldehyde led to the formation of only 40% of the product (**8d**). This observation suggested that the catalytic activity of AuCl is

Table 1
Gold(I) catalyzed synthesis of bis(indolyl)methanes from 2-(phenylethynyl)aniline **1a** 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**	**8a**	2.0	76
2	R^1=Br, R^2=H, R^3=OMe, R^4=OMe **2b**	**8b**	2.0	79
3	R^1=H, R^2=H, R^3=COOH, R^4=H **2c**	**8c**	1.5	65
4	R^1=H, R^2=H, R^3=Ph, R^4=H **2d**	**8d**	1.5	80
5	 **2e**	**8e**	4.0	53
6	 **2f**	**8f**	1.0	85
7	 **2g**	**8g**	3.5	59
8	 **2h**	**8h**	0.5	83
9	 **2i**	**8i**	0.5	77
10	 **2j**	**8j**	0.5	76
11	 **2k**	**8k**	0.5	82
12	 **2l**	**8l**	1.5	—

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

superior to that of $AuCl_3$ in this domino process. 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).



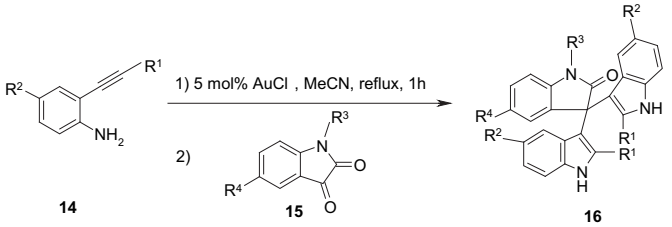
Scheme 2.

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.[8,37] 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 (**1a**) in the presence of AuCl in acetonitrile, it was found that only 3,3′-(biphenyl-4-ylmethylene)bis(2-phenyl-1*H*-indole) (**8d**) was obtained, while acetophenone did not give the corresponding product (**8l**). 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. Most of these aldehydes gave good yields of products. However the low yields in the case of (**8e**) and (**8g**) may be attributed to the lower reactivity of their corresponding aldehydes (**2e** and **2g**) towards bis-addition. The ^{1}H NMR spectra of compounds (**8a**–**8k**) 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.

A tentative mechanistic interpretation (Scheme 3) to explain the formation of the observed bis(indolyl)methanes (**8**) might reasonably assume a reaction path that implies an initial π-coordination of Lewis acidic AuCl with the alkyne residue (**1a**) to form a π-complex (**9**). Subsequent nucleophilic attack of the tethered amino group leads to ring closure to afford cyclized intermediate (**10**), followed by Proto-deauration affording indole (**11**) and AuCl. The later activates the carbonyl oxygen of the aldehyde and carries out an electrophilic addition reaction at C3 of the indole (**11**) giving intermediate (**12**). After loss of water, an azafulvene derivative (**13**) is generated, which reacts further with a second molecule of indole to form the bis(indolyl)methane (**8**).

2.2. Gold(I) catalyzed synthesis of di(indolyl)indolin-2-ones

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).[19] The results of which are summarized in Table 2.



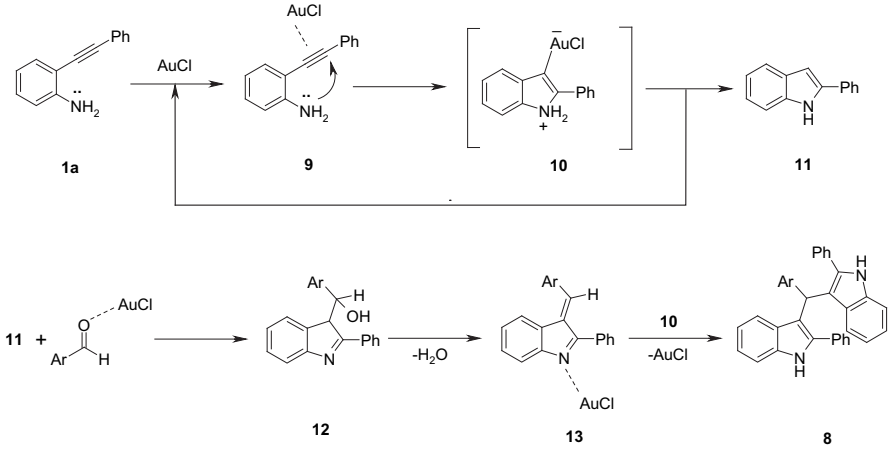
Scheme 4.

Table 2
Gold(I) catalyzed synthesis of di(indolyl)indolin-2-ones from 2-ethynylanilines **14** and isatin **15**[a]

Entry	R^1	R^2	R^3	R^4	Time (h)	Product[b]	Yield[c] (%)
1	Ph	H	H	H	1.0	**16a**	83
2	Ph	H	Me	H	0.5	**16b**	89
3	Ph	Cl	H	Me	1.5	**16c**	80
4	Ph	Me	H	H	0.5	**16d**	91
5	Ph	CN	H	H	3.0	**16e**	67
6	^{n}Bu	H	H	H	7.0	**16f**	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.

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,

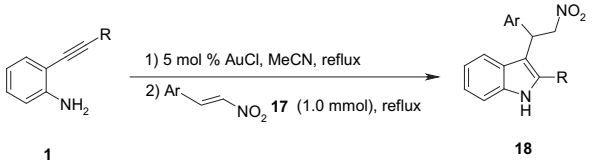


Scheme 3.

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 (**14**) 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 (**16a–16f**) was ascertained by the appearance of a low intense peak in the ^{13}C NMR spectrum at δ_C 52.2–59.7 ppm, 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.

2.3. Gold(I) catalyzed synthesis of 2-indolyl-1-nitroalkanes

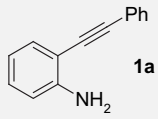
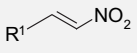
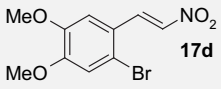
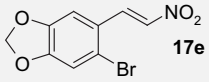
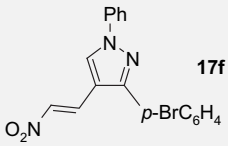
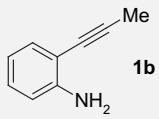
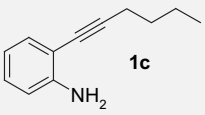
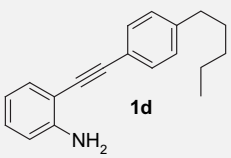
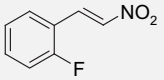
Since we had already established that 5 mol % of AuCl in acetonitrile under refluxing condition, is optimal for the cycloisomerization of 2-(alkynyl)anilines, we followed the same reaction condition for the cycloisomerization/Michel addition process. To begin our study, we carried out the reaction between 2-(phenylethynyl)aniline **1a** and nitrostyrene **17a** with 5 mol % AuCl in acetonitrile under refluxing condition. To our delight the reaction proceeded well and gave the desired 2-indolyl-1-nitroalkane **18a** in excellent yield (Scheme 5, Table 3, entry 1). A controlled experiment in which 2-phenyl indole was exposed to nitrostyrene **17a** in the absence of AuCl does not lead to any 3-alkylated product at all. This finding suggested that AuCl is indeed required for the Michael addition step. One-pot synthesis coupled with the excellent yield of the product, encouraged us to extend this methodology to a range of 2-(alkynyl)anilines and nitroolefins (Table 3, entries 1–12). The results revealed that the groups attached to the nitroolefin have a marked effect on the yield of the product. The presence of electron withdrawing group on the nitroolefin gave good yield of the product (Table 3, entry 3)



1 18

Scheme 5.

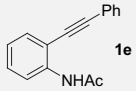
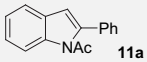
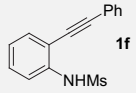
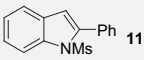
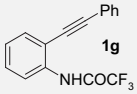
Table 3
Gold(I) catalyzed synthesis of 2-(indolyl)-1-nitroalkanes **18** from 2-(alkynyl)aniline **1** and nitroolefin **17**

Entry	2-(Alkynyl)aniline **1**	Nitroolefin **17**	2-(Indolyl)-1-nitroalkane **18**[a]	Time (h)	Yield[b] (%)
					
	Ph, **1a**, NH_2	R^1, NO_2			
1		R^1=Ph **17a**	**18a**	3.0	85
2		R^1=*p*-MeC_6H_4 **17b**	**18b**	3.0	79
3		R^1=*p*-ClC_6H_4 **17c**	**18c**	3.0	88
4			**18d**	5.0	69
		MeO, MeO, NO_2, **17d**, Br			
5			**18e**	5.0	72
		O, O, NO_2, **17e**, Br			
6			**18f**	4.5	77
		Ph, N, N, **17f**, O_2N, *p*-BrC_6H_4			
7		**17a**	**18g**	0.5	93
	Me, **1b**, NH_2				
8		**17a**	**18h**	1.0	87
	1c, NH_2				
9		**17b**	**18i**	1.0	80
10			**18j**	6.0	63
	1d, NH_2	NO_2, **17g**, F			

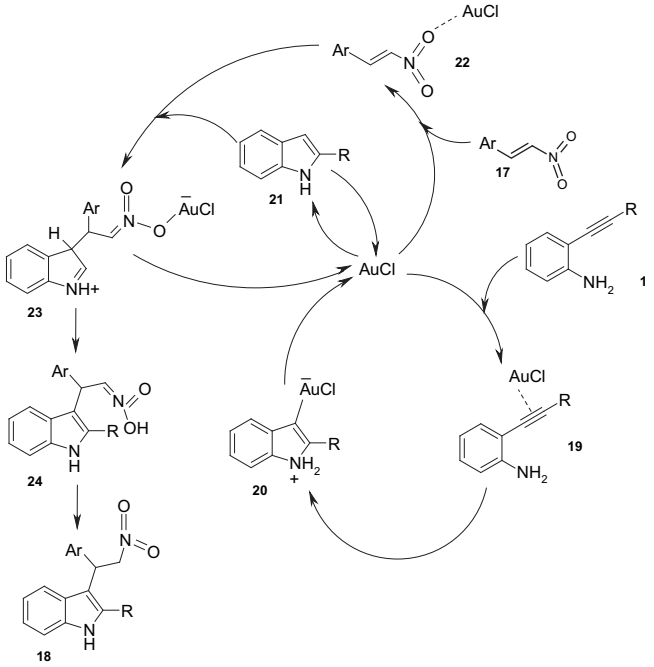
[a] Isolated yield.
[b] The products were characterized by IR, ^1H NMR, ^{13}C NMR and mass spectroscopy.

and the presence of electron releasing group, gave slightly lower yields (Table 3, entries 1, 2 and entries 4–6). Similarly, the triple bond of 2-(alkynyl)anilines, possessing methyl or *n*-butyl group afforded product with good yield (Table 3, entries 7 and 8). This observation may be reasoned due to the better electrophilic activation of the in situ formed 2-methylindole and 2-^{n}butylindole towards nitroolefins. In addition, electron withdrawing substituent at the amino group of the 2-(alkynyl)anilines underwent only cycloisomerization and did not gave the Michael addition product. The reaction of *N*-substituted(alkynyl)anilines such as **1e** and **1f** with nitrostyrene **17a** gave only the cycloisomerized product **11a** and **11b** (Table 4, entries 1 and 2). This could be attributed due to the electron withdrawing nature of Ac and Ms groups, which deactivates the formed indole nucleus. On the other hand alkyne **1g** possessing $-C(O)CF_3$, a very strong electron withdrawing group completely failed to undergo cycloisomerization (Table 4, entry 3). This observation was in sharp contrast to the other cycloisomerization protocols,[38] wherein, the presence of an acidic proton (in the form of amide instead of amine) is essential for effective cycloisomerization (Scheme 5).

Table 4
Gold(I) catalyzed cycloisomerization of *N*-substituted 2-(alkynyl)anilines **1**

Entry	2-(alkynyl)aniline **1**	Indole derivative **2**[b]	Time (h)	Yield[c] (%)
1[a]	 **1e**	 **11a**	2.5	78
2[a]	 **1f**	 **11b**	3.0	69
3	 **1g**	—	6.0	—

[a] Michael addition was checked using nitroolefin **17a**.
[b] The products were characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectra.
[c] Isolated yield.



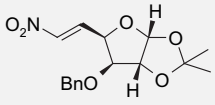
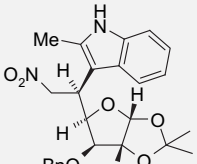
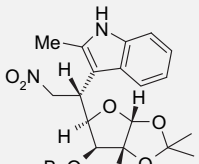
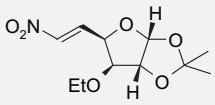
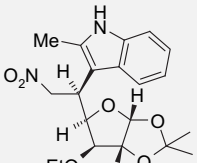
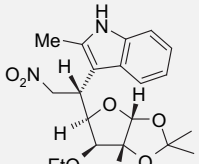
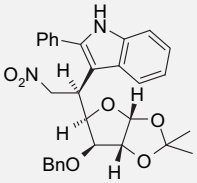
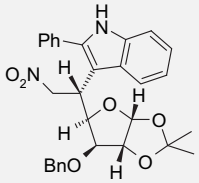
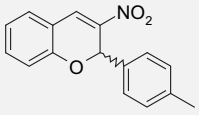
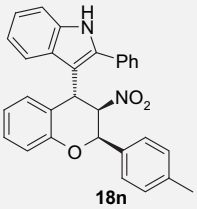
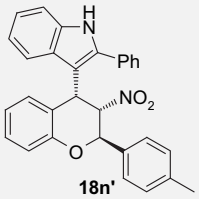
Scheme 6.

A mechanistic rationale portraying the probable sequence of events is given in Scheme 6. Initial coordination of the π-acidic AuCl with the alkynylaniline **1** forms π-complex **19**. Subsequent nucleophilic attack of the tethered amino group would leads to ring closure to afford the cyclized intermediate **20**, followed by protodeauration affording indole **21** and AuCl. The later again enters the catalytic loop by interacting with the nitro oxygen of the nitroolefin **17** to form **22**, which undergo a conjugate addition with the electron rich β-position of the indole **21** giving intermediate **23**. After proton transposition, **24** is generated, which rearranges to form the Michael adduct **18** and AuCl.

2.4. Gold(I) catalyzed synthesis of 2-indolyl-1-nitroalkanes from chiral Michael acceptors

On the basis of the above results, coupled with the fact that indoles and carbohydrates[39] are often associated with important biological properties, we then intended to examine the fate of sugar derived chiral Michael acceptors.[40] However these Michael acceptors, towards conjugate addition required longer reaction time (Table 5, entries 1–3). This may be due to the poor electrophilicity of the β-carbon atom of these nitroolefins, making them less reactive towards Michael addition. Crude ^{1}H NMR analysis revealed that in all cases, D-*gluco* isomer was formed as the major product (**18k**–**18m**) and L-*ido* isomer was formed as the minor product (**18k′**–**18m′**). To extend the scope of this methodology, nitrochromene[41] **17j** was subjected to our reaction conditions, since the resultant 2*H*-benzopyran derivatives possess important medicinal properties.[42] In this case the products were obtained in excellent diastereoselectivity (**18n** and **18n′**). The relative stereochemistry of the substituents in **18n** was unambiguously assigned on the basis of 1-D NOE experiment. The assignment of relative stereochemistry at C5 in compounds **18l** and **18l′** became difficult, since the coupling constant values in both diastereoisomers are very close. Inorder to eliminate the CH_2 coupling in C5–H, and to establish the actual stereochemistry, we intended to convert $-CH_2NO_2$ group to nitrile oxide and carry out a sequential [3+2] cycloaddition with diethylacetylene dicarboxylate to form the isoxazole ring.[43] The cycloaddition reaction of **18l** and **18l′** was separately carried out with ethylchloroformate, triethylamine and DMAP in dichloromethane at room temperature (Scheme 7). The ^{1}H NMR data of the obtained isoxazole **20a** (from **18l**) and **20b** (from **18l′**) turned out to be informative, it is known that for a given C5-epimeric pair derived from D-*gluco*furanose, the $J_{4,5}$ in the L-*ido* isomer is consistently larger than that of the corresponding D-*gluco* isomer.[44] The higher value of $J_{4,5}$ observed in isoxazole **20b** (10.7 Hz) as compared to isoxazole **20a** (9.9 Hz) indicated, the L-*ido* configuration for **20b** and the D-*gluco* configuration for **20a**. This assignment was further supported by comparing the chemical shifts of H3 in **20a** and **20b** is reported to be diagnostic such that, in the L-*ido* isomer, it is significantly upfield ($\delta \sim 3.6$) as compared to that in the D-*gluco* isomer ($\delta \sim 4.0$).[44] In **20b** H3 appeared upfield $\delta \sim 3.37$ as compared to **20a** at $\delta \sim 4.20$. From the above facts we were assigned the stereochemistry of the major diastereoisomers **18k**–**18m** and minor diastereoisomers **18k′**–**18m′** as D-*gluco* and L-*ido*, respectively. In the ^{1}H NMR spectrum of compound **18n**, a doublet at 5.06 ppm, triplet at 5.41 ppm and singlet at 5.68 ppm were assigned to Ha, Hb and Hc protons, respectively. These assignments of protons were confirmed by HMBC spectrum. In HMBC spectrum, the indole NH makes HMBC correlation with carbon at 111.7, 127.3 and 137.1 ppm and a proton signal at 5.06 ppm makes the HMBC correlation with the above same carbons and additionally two more correlation with carbon at 75.2 ppm (O–CH) and 89.5 ppm ($CH–NO_2$). From this we have assigned the signal at 5.06 ppm to Ha. The proton Ha (5.06 ppm) couples with proton at 5.41 ppm and the proton was assigned as Hb. From these facts signal at 5.68 ppm to Hc. The

Table 5
Gold(I) catalyzed sequential cycloisomerization/Michael addition of 2-(alkynyl)anilines with chiral Michael acceptors[a]

Entry	2-(Alkynyl)aniline **1**	Nitroolefin **3**	Nitroadduct **4**	Yield[b,c] (%)	(dr)[d]
1	**1b**	 **17h**	 D-gluco **18k**  L-ido **18k'**	84	88:12 **18k**/**18k'**
2	**1b**	 **17i**	 D-gluco **18l**  L-ido **18l'**	82	90:10 **18l**/**18k'**
3	**1a**	**17h**	 D-gluco **18m**  L-ido **18m'**	85	98:2 **18m**/**18m'**
4	**1a**	 **17j**	 **18n**  **18n'**	92	99:1 **18n**/**18n'**

[a] All reactions were carried out for 12 h under reflux in acetonitrile.
[b] All products were characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectroscopy.
[c] Isolated yield.
[d] Diastereoisomeric ratio was determined on the basis of crude ^{1}H NMR analysis.

stereochemistry of the diastereoisomers was confirmed by 1-D NOE experiment. In 1-D NOE measurement, selective irradiation of Ha proton effected enhancement of the signal of Hb is 3.4%. Irradiation of Hb effected enhancement of the signal of Ha (4.9%) and Hc (11.2%). Irradiation of Hc effected enhancement of the signal of Hb is 9.6%. These facts shows that the proton Hb *cis* to Hc and *trans* to Ha (Fig. 2).

3. Conclusion

In conclusion Au(I) catalyzed synthesis of some 3-substituted indole derivatives via sequential cycloisomerization/bis and conjugate addition of 2-(alkynyl)anilines with varies electrophiles has been achieved. Further studies concerning both the mechanism and possible synthetic applications of this protocol are currently being carried out.

4. Experimental section

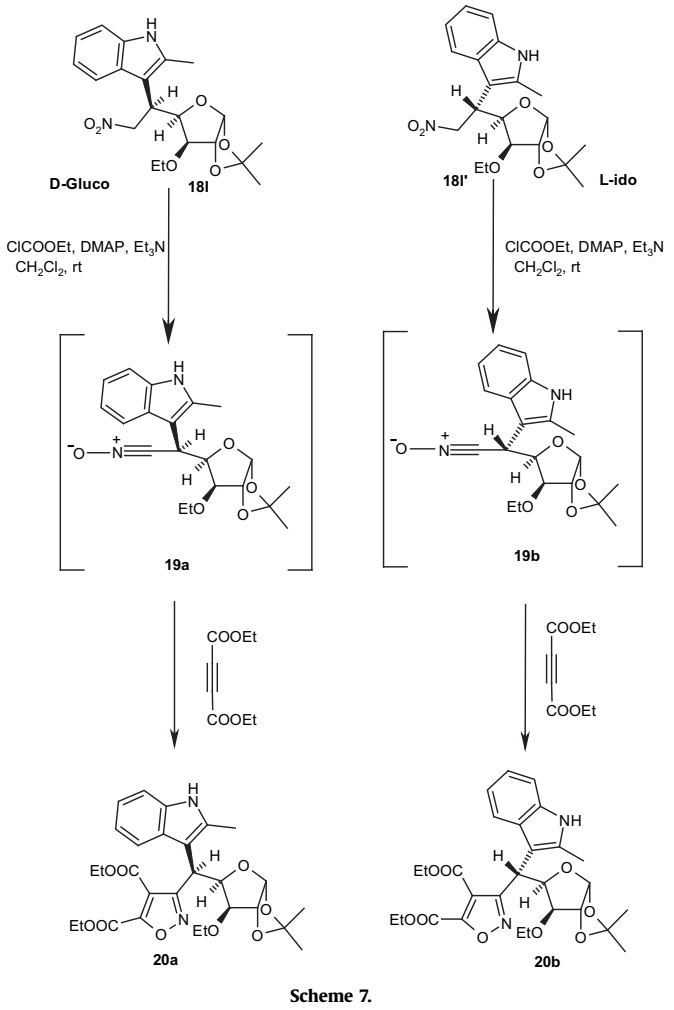
4.1. General

Melting points were determined in capillary tubes and are uncorrected. Infrared (IR) spectra were recorded on a Perkin–Elmer FTIR spectrophotometer. ^{1}H NMR (500 MHz) and ^{13}C (75 MHz and 125 MHz) spectra were recorded in $CDCl_3$, DMSO-d_6 and acetone-d_6 solution with TMS as internal standard on a JEOL spectrometer and BRUKER spectrophotometer, respectively. Mass spectra were recorded using a Thermo Finnigan LCQ Advantage MAX 6000 ESI mass spectrometer. Elemental analyses were recorded using a Thermo Finnigan FLASH EA 1112CHN analyzer. Column chromatography was performed on silica gel (100–200 mesh, SRL. India). Analytical TLC was performed on pre-coated aluminium sheets of silica gel $60F_{254}$ of 0.2 mm thickness (Merck, Germany).

4.2. Typical procedure for the preparation of bis(indolyl)-methanes and di(indolyl)indolin-2-ones

To a solution of *o*-ethynylaniline (1.0 mmol) in acetonitrile (1 mL) was added AuCl (5 mol %) in acetonitrile (1 mL) and refluxed for 1 h. To this reaction mixture, aldehyde or isatin (0.5 mmol) was added and refluxed for the specified time (see Tables 1 and 2). After completion of the reaction as indicated by TLC (petroleum ether/ethyl acetate), the reaction mixture was concentrated under reduced pressure and purified by column chromatography on silica gel using petroleum ether/ethyl acetate to afford pure product of bis(indolyl)methanes or di(indolyl)indolin-2-ones.

*4.2.1. 4-[Bis(2-phenyl-1H-indol-3-yl)methyl]-2-bromo-6-methoxyphenol (**8a**).* 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}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 3.47 (s, 3H, –OC*H*$_3$), 5.87 (s, 1H, –C*H*–Ar), 6.66–6.71 (m, 3H, Ar–H), 6.78 (s, 1H,



Scheme 7.

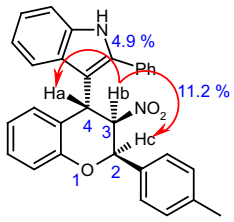


Figure 2. NOEs observed for Michael adduct 18n.

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, –O*H*), 11.3 (s, 2H, –N*H*). ^{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. 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, 4.45; N, 4.81.

*4.2.2. 3,3′-[(2-Bromo-4,5-dimethoxyphenyl)methylene]bis(2-phenyl-1H-indole) (**8b**).* Colourless solid; mp 240–242 °C; R_f=0.17 (AcOEt/petroleum ether 20%). IR (KBr): 3391, 1602, 1492, 1454, 1377, 1305, 1274, 1149, 744, 699 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 3.30 (s, 3H, –OC*H*$_3$), 3.73 (s, 3H, –OC*H*$_3$), 6.06 (s, 1H, –C*H*–Ar), 6.60–6.80 (m, 3H, Ar–H), 6.97 (t, 2H, *J*=7.6 Hz, Ar–H), 7.07 (d, 4H, *J*=6.1 Hz, Ar–H), 7.18–7.24 (m, 8H, Ar–H), 7.31 (d, 3H, *J*=7.6 Hz, Ar–H), 11.21 (s, 2H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 43.9, 60.8, 61.0, 116.5, 119.8, 120.6, 121.3, 123.9, 124.9, 126.0, 132.3, 133.2 (2C), 133.5, 138.1, 141.0, 141.2, 152.9, 153.3. MS(EI): *m*/*z*=612 [M^+], 614 [M^{+2}]. Anal. Calcd for $C_{37}H_{29}BrN_2O_2$: C, 72.43; H, 4.76; N, 4.57. Found: C, 72.52; H, 4.71; N, 4.69.

*4.2.3. 4-[Bis(2-phenyl-1H-indol-3-yl)methyl]benzoic acid (**8c**).* Colourless solid; mp 292–294 °C; R_f=0.19 (AcOEt/petroleum ether 40%). IR (KBr): 3401, 3055, 2923, 2560, 1666, 1606, 1457, 1426, 1294, 743, 696 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 5.96 (s, 1H, –C*H*–Ar), 6.66 (t, 2H, *J*=8.4 Hz, Ar–H), 6.85 (d, 2H, *J*=8.4 Hz, Ar–H), 6.98 (t, 2H, *J*=8.4 Hz, Ar–H), 7.18–7.25 (m, 14H, Ar–H), 7.35 (d, 2H, *J*=8.4 Hz, Ar–H), 7.80 (s, 1H, –N*H*), 7.82 (s, 1H, –N*H*), 11.36 (s, 1H, –COO*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 39.7, 111.4, 113.3, 118.6, 120.5, 121.0, 127.3, 127.9, 128.0, 128.3, 128.5, 128.8, 129.4, 132.5, 135.6, 136.2, 150.8, 167.31. MS(EI): *m*/*z*=519 [M^++H^+]. Anal. Calcd for $C_{36}H_{26}N_2O_2$: C, 83.37; H, 5.05; N, 5.40. Found: C, 83.45; H, 4.99; N, 5.44.

*4.2.4. 3,3′-(Biphenyl-4-ylmethylene)bis(2-phenyl-1H-indole) (**8d**).* Yellow solid; mp 258–260 °C; R_f=0.43 (AcOEt/petroleum ether 50%). IR (KBr): 3398, 1601, 1450, 1306, 1011, 735 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 6.01 (s, 1H, –C*H*–Ar), 6.67 (t, 2H, *J*=7.6 Hz, Ar–H), 6.99 (t, 4H, *J*=7.6 Hz, Ar–H), 7.18–7.22 (m, 8H, Ar–H), 7.27–7.33 (m, 5H, Ar–H), 7.36–7.41 (m, 4H, Ar–H), 7.58 (d, 2H, *J*=8.4 Hz, Ar–H), 7.65 (d, 2H, *J*=7.6 Hz, Ar–H), 11.35 (s, 2H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 38.6, 111.2, 114.6, 118.4, 120.7, 120.8, 126.3, 127.1, 128.0 (2C), 128.2, 128.7, 129.2, 132.6, 135.3, 136.2, 137.3, 139.6, 144.7. MS(EI): *m*/*z*=550 [M^+]. Anal. Calcd for $C_{41}H_{30}N_2$: C, 89.42; H, 5.49; N, 5.09. Found: C, 89.55; H, 5.45; N, 4.99.

*4.2.5. 3,3′-[(1-Methyl-1H-indol-2-yl)methylene]bis(2-phenyl-1H-indole) (**8e**).* Brown solid; mp 258–260 °C; R_f=0.45 (AcOEt/petroleum ether 40%). IR (KBr): 3439, 3393, 1454, 1306, 744, 696 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 3.14 (s, 3H, –NC*H*$_3$), 5.98 (s, 1H, –C*H*–Ar), 6.10 (s, 1H, Indolyl-H), 6.62 (t, 2H, *J*=7.6 Hz, Ar–H), 6.95–7.04 (m, 4H, Ar–H), 7.18–7.28 (m, 13H, Ar–H), 7.37 (d, 2H, *J*=8.4 Hz, Ar–H), 7.43 (d, 1H, *J*=7.6 Hz, Ar–H), 11.3 (s, 2H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 29.1, 33.5, 101.5, 109.2, 111.2, 118.7, 118.9, 119.7, 119.8, 120.4, 121.0, 126.8, 127.2, 127.8, 128.0, 128.2, 132.4, 134.8, 136.0, 137.3, 143.5. MS(EI): *m*/*z*=528 [M^++H^+]. Anal. Calcd for $C_{38}H_{29}N_3$: C, 86.50; H, 5.54; N, 7.96. Found: C, 86.46; H, 5.59; N, 7.95.

*4.2.6. 3,3′-[(6-Bromo-1,3-benzodioxol-5-yl)methylene]bis(2-phenyl-1H-indole) (**8f**).* Pale yellow solid; mp 222–224 °C; R_f=0.26 (AcOEt/petroleum ether 20%). IR (KBr): 3386, 1474, 1234, 1036, 752 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 6.61 (s, 2H, –OC*H*$_2$O–), 6.79 (s, 1H, –C*H*–Ar), 6.85 (s, 1H, Ar–H), 6.99–7.05 (m, 6H, Ar–H), 7.13 (s, 1H, Ar–H), 7.20–7.34 (m, 12H, Ar–H), 11.26 (s, 2H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 26.3, 40.6, 101.8, 110.7, 111.3, 112.7, 114.6, 118.8, 119.6, 120.9, 127.3, 127.9, 128.1, 128.2, 132.7, 136.0, 137.2, 146.6, 146.8. MS(EI): *m*/*z*=596 [M^+], 598 [M^{+2}]. Anal. Calcd for $C_{36}H_{25}BrN_2O_2$: C, 72.37; H, 4.22; N, 4.69. Found: C, 72.49; H, 4.33; N, 4.75.

*4.2.7. 3-[Bis(2-phenyl-1H-indol-3-yl)methyl]-2-chloroquinoline (**8g**).* Yellow solid; mp 232–234 °C; R_f=0.21 (AcOEt/petroleum ether 40%). IR (KBr): 3408, 1655, 1025, 750 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 6.23 (s, 1H, –C*H*–Ar), 6.63 (t, 2H, *J*=7.6 Hz, Ar–H), 6.98 (t, 2H, *J*=8.4 Hz, Ar–H), 7.16–7.23 (m, 12H, Ar–H), 7.37 (d, 2H, *J*=8.4 Hz, Ar–H), 7.52 (t, 1H, *J*=8.4 Hz, Ar–H), 7.72 (t, 1H, *J*=8.4 Hz, Ar–H), 7.81 (d, 1H, *J*=7.6 Hz, Ar–H), 7.86 (d, 1H, *J*=8.4 Hz, Ar–H), 8.17 (s, 1H, Quinolinyl-H), 11.42 (s, 2H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 39.5, 111.5, 118.9, 119.5, 121.0, 126.6, 127.2 (2C), 127.3 (2C), 127.9 (2C), 128.1 (2C), 130.2, 132.6, 136.1, 136.8, 138.4, 145.7, 150.6. MS(EI): *m*/*z*=560 [M^++H^+], 562 [M^{+2}+H^+]. Anal. Calcd for $C_{38}H_{26}ClN_3$: C, 81.49; H, 4.68; N, 7.50. Found: C, 81.61; H, 4.75; N, 7.60.

*4.2.8. 3,3′-(1-Naphthylmethylene)bis(phenyl-1H-indole) (**8h**).* Pale yellow solid; mp 282–284 °C; R_f=0.20 (AcOEt/petroleum ether 20%). IR (KBr): 3394, 1451, 1306, 739 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6)

δ_H 6.49 (s, 1H, –C*H*–Ar), 6.56–6.57 (m, 2H, Ar–H), 6.90–7.03 (m, 2H, Ar–H), 7.10–7.13 (m, 11H, Ar–H), 7.30 (t, 5H, *J*=7.6 Hz, Ar–H), 7.44 (t, 1H, *J*=7.6 Hz, Ar–H), 7.50 (d, 1H, *J*=9.15 Hz, Ar–H), 7.53 (d, 1H, *J*=6.8 Hz, Ar–H), 7.84 (t, 2H, *J*=8.4 Hz, Ar–H), 11.34 (s, 2H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 37.5, 111.2, 118.5, 120.1, 120.7, 123.1, 125.0, 122.2, 125.7, 126.7, 127.2 (2C), 127.8, 128.1, 128.5, 131.0, 132.6, 133.4, 134.7, 136.1, 140.9. MS(EI): *m*/*z*=524 [M^+]. Anal. Calcd for $C_{39}H_{28}N_2$: C, 89.28; H, 5.38; N, 5.34. Found: C, 89.41; H, 5.47; N, 5.48.

*4.2.9. 3-[Bis(2-phenyl-1H-indol-3-yl)methyl]-9-ethyl-9H-carbazole (**8i**).* Pale yellow solid; mp 278–280 °C; R_f=0.23 (AcOEt/petroleum ether 20%). IR (KBr): 3401, 1483, 1457, 1340, 1233, 743 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 1.26 (t, 3H, *J*=7.6 Hz, –NCH$_2$C*H*$_3$), 4.33 (q, 2H, *J*=6.8 Hz, –NC*H*$_2$CH$_3$), 6.17 (s, 1H, –C*H*–Ar), 6.58 (t, 2H, *J*=8.4 Hz, Ar–H), 6.88 (d, 2H, *J*=7.6 Hz, Ar–H), 6.94–7.00 (m, 3H, Ar–H), 7.15–7.16 (m, 6H, Ar–H), 7.27 (d, 1H, *J*=7.6 Hz, Ar–H), 7.31–7.37 (m, 7H, Ar–H), 7.44 (d, 1H, *J*=8.4 Hz, Ar–H), 7.48 (d, 1H, *J*=7.6 Hz, Ar–H), 7.79 (d, 1H, *J*=7.6 Hz, Ar–H), 7.85 (s, 1H, carbazolyl-H), 11.33 (s, 2H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 13.7, 37.0, 39.4, 108.5, 108.9, 111.3, 115.1, 118.4, 119.8, 120.2, 120.8, 122.0, 122.1, 125.5, 126.8, 127.1, 128.0, 128.2, 128.4, 132.8, 135.1, 136.1, 136.3, 138.1, 139.8. MS(EI): *m*/*z*=591 [M^+]. Anal. Calcd for $C_{43}H_{33}N_3$: C, 87.28; H, 5.62; N, 7.10. Found: C, 87.41; H, 5.70; N, 7.17.

*4.2.10. 3,3′-(9H-Fluoren-3-ylmethylene)bis(2-phenyl-1H-indole) (**8j**).* Colourless solid; mp 244–246 °C; R_f=0.27 (AcOEt/petroleum ether 20%). IR (KBr): 3394, 1454, 1306, 741 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 3.75 (s, 2H, –C*H*$_2$–), 6.03 (s, 1H, –C*H*–Ar), 6.64 (t, 2H, *J*=7.6 Hz, Ar–H), 6.98 (d, 4H, *J*=7.6 Hz, Ar–H), 7.17–7.24 (m, 8H, Ar–H), 7.31–7.37 (m, 8H, Ar–H), 7.47 (d, 1H, *J*=7.6 Hz, Ar–H), 7.74 (d, 1H, *J*=7.6 Hz, Ar–H), 7.79 (d, 1H, *J*=7.6 Hz, Ar–H), 11.35 (s, 2H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 36.2, 40.08, 114.3, 114.4, 118.5, 119.7, 120.8, 120.9, 125.0, 125.2 (2C), 126.4, 126.6, 127.1, 127.4, 128.0 (2C), 128.2, 132.7, 135.3, 136.3, 139.0, 141.1, 143.0, 144.6. MS(EI): *m*/*z*=562 [M^+]. Anal. Calcd for $C_{42}H_{30}N_2$: C, 89.65; H, 5.37; N, 4.98. Found: C, 89.75; H, 5.30; N, 5.08.

*4.2.11. 4-[Bis(2-phenyl-1H-indol-3-yl)methyl]-3-(4-chlorophenyl)-1-phenyl-1H-pyrazole (**8k**).* Pink solid; mp 270–272 °C; R_f=0.21 (AcOEt/petroleum ether 20%). IR (KBr): 3413, 1598, 1499, 1449, 1212, 1092, 746, 697 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 5.94 (s, 1H, –C*H*–Ar), 6.71 (t, 2H, *J*=7.6 Hz, Ar–H), 6.97 (t, 2H, *J*=8.4 Hz, Ar–H), 7.05 (d, 2H, *J*=8.4 Hz, Ar–H), 7.15–7.25 (m, 15H, Ar–H), 7.30 (d, 2H, *J*=8.4 Hz, Ar–H), 7.39 (t, 2H, *J*=8.4 Hz, Ar–H), 7.66 (d, 2H, *J*=7.6 Hz, Ar–H), 7.83 (s, 1H, Pyrazolyl-H), 11.25 (s, 2H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 31.25, 111.2, 113.6, 118.1, 118.6, 120.0, 120.8, 126.17 (2C), 127.2, 127.6, 127.7, 127.9, 128.0, 128.4, 129.4, 131.9 (2C), 132.6, 135.1, 136.1, 139.2, 148.9. MS(EI): *m*/*z*=650 [M^+], 652 [M^{+2}]. Anal. Calcd for $C_{44}H_{31}ClN_4$: C, 81.15; H, 4.80; N, 8.60. Found: C, 80.97; H, 4.75; N, 9.79.

*4.2.12. 3,3-Bis(2-phenyl-1H-indol-3-yl)indolin-2-one (**16a**).* Red solid; mp 240–242 °C; R_f=0.69 (AcOEt/petroleum ether 50%). IR (KBr): 3376, 1719, 1613, 1454, 1328, 746, 700 cm^{-1}. ^{1}H NMR (500 MHz, Acetone-d_6) δ_H 6.65 (t, 2H, *J*=6.6 Hz, Ar–H), 6.71 (t, 1H, *J*=8.4 Hz, Ar–H), 6.85 (t, 1H, *J*=6.9 Hz, Ar–H), 6.92–6.98 (m, 4H, Ar–H), 7.00 (t, 2H, *J*=7.6 Hz, Ar–H), 7.06 (t, 2H, *J*=7.6 Hz, Ar–H), 7.16–7.21 (m, 6H, Ar–H), 7.25 (t, 4H, *J*=8.4 Hz, Ar–H), 9.36 (s, 1H, –N*H*–CO–), 9.78 (s, 1H, –N*H*), 10.11 (s, 1H, –N*H*). ^{13}C NMR (75 MHz, Acetone-d_6) δ_C 54.2, 109.9, 111.2, 111.6, 112.3, 113.1, 113.4, 119.1, 119.4, 121.7, 122.3, 122.9, 123.8, 125.4, 126.7, 126.9, 127.5, 127.9, 128.2, 128.6, 129.1, 129.9, 130.1, 134.8, 135.4, 135.9, 136.6, 138.8, 139.1, 141.9, 178.7. MS(EI): *m*/*z*=1053 [dimer+Na^+]. Anal. Calcd for $C_{36}H_{25}N_3O$: C, 83.86; H, 4.89; N, 8.15. Found: C, 83.97; H, 4.85; N, 8.09.

*4.2.13. 1-Methyl-3,3-bis(2-phenyl-1H-indol-3-yl)indolin-2-one (**16b**).* Brown solid; mp 294–296 °C; R_f=0.40 (AcOEt/petroleum ether 25%). IR (KBr): 3411, 3319, 1698, 1605, 1489, 1454, 1351, 741, 696 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 2.83 (s, 3H, –NC*H*$_3$), 6.58 (t, 1H, *J*=6.8 Hz, Ar–H), 6.64 (t, 2H, *J*=6.8 Hz, Ar–H), 6.81 (t, 1H, *J*=7.6 Hz, Ar–H), 6.89–7.09 (m, 11H, Ar–H), 7.23–7.33 (m, 7H, Ar–H), 10.75 (s, 1H, –N*H*), 11.02 (s, 1H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 25.9, 52.2, 108.0, 110.2, 110.9, 111.3, 117.8, 118.3, 119.6, 120.4, 121.5, 121.8, 124.8, 125.7, 126.6, 127.1 (2C), 127.4 (2C), 127.7, 128.5 (2C), 128.6, 133.2, 134.0, 134.4, 134.5, 135.3, 135.4, 141.9, 175.5. MS(EI): *m*/*z*=552 [M^++Na^+]. Anal. Calcd for $C_{37}H_{27}N_3O$: C, 83.91; H, 5.14; N, 7.93. Found: C, 84.01; H, 5.25; N, 7.85.

*4.2.14. 5-Methyl-3,3-bis(5-chloro-2-phenyl-1H-indol-3-yl)indolin-2-one (**16c**).* Pink solid; mp 279–281 °C; R_f=0.46 (AcOEt/petroleum ether 50%). IR (KBr): 768, 1311, 1464, 1711, 2924, 3419 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 2.04 (s, 3H, –C*H*$_3$), 6.89–7.10 (m, 19H, Ar–H), 10.49 (s, 1H, –N*H*–CO–), 11.14 (s, 1H, –N*H*), 11.21 (s, 1H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 31.5, 58.0, 114.2, 115.3, 116.2, 117.3, 125.1, 125.4, 125.8, 126.0, 128.1, 129.0, 131.6, 132.0, 132.3, 132.5, 133.5 (2C), 133.6 (2C), 133.7, 134.2, 135.2, 138.4, 138.5, 138.9, 139.0, 139.1, 142.6, 143.9, 183.0. MS(EI): *m*/*z*=1217 [dimer+Na^+], 1219 [dimer+M^{+2}+Na^+], 1221 [dimer+M^{+4}+Na^+]. Anal. Calcd for $C_{37}H_{25}ClN_3O$: C, 74.25; H, 4.21; N, 7.02. Found: C, 74.11; H, 4.25; N, 7.15.

*4.2.15. 3,3-Bis(5-methyl-2-phenyl-1H-indol-3-yl)indolin-2-one (**16d**).* Brown solid; mp 270–272 °C; R_f=0.38 (AcOEt/petroleum ether 50%). IR (KBr): 1105, 1250, 1601, 1706, 1712, 3377, 3409, 3473 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 2.03 (s, 3H, –C*H*$_3$), 2.13 (s, 3H, –C*H*$_3$), 6.80–7.33 (m, 20H, Ar–H), 10.40 (s, 1H, –N*H*–CO–), 10.51 (s, 1H, –N*H*), 10.83 (s, 1H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 21.2, 22.0, 53.4, 109.4, 110.3, 110.5, 110.9, 111.6, 112.6, 120.6, 121.4, 121.7, 122.4, 123.2, 125.1, 125.9, 126.0, 126.4, 126.5, 126.7, 127.5, 127.6, 128.1 (2C), 128.7, 128.9, 129.3, 134.1, 134.4, 134.8, 135.3, 138.8, 141.4, 177.8. MS(EI): *m*/*z*=1109 [dimer+Na^+]. Anal. Calcd for $C_{38}H_{29}N_3O$: C, 83.95; H, 5.38; N, 7.73. Found: C, 84.05; H, 5.29; N, 7.81.

*4.2.16. 3,3-Bis(5-cyano-2-phenyl-1H-indol-3-yl)indolin-2-one (**16e**).* Colourless solid; mp 320–322 °C; R_f=0.41 (AcOEt/petroleum ether 50%). IR (KBr): 1200, 1307, 1464, 1717, 2266, 3346, 3404, 3481 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 6.63–7.63 (m, 20H, Ar–H), 10.69 (s, 1H, –N*H*–CO–), 11.56 (s, 1H, –N*H*), 11.76 (s, 1H, –N*H*). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 59.7, 100.5, 100.6, 109.5, 110.8, 111.7, 112.0, 112.3, 120.6, 120.8, 121.8, 123.4, 123.5, 123.6, 125.6, 125.8, 126.3, 126.4, 126.8, 127.2, 127.4, 127.9, 128.4, 128.5, 128.6, 132.1, 132.4, 133.9, 137.2, 138.0, 140.9, 177.4. MS(EI): *m*/*z*=1153 [dimer+Na^+]. Anal. Calcd for $C_{38}H_{23}N_5O$: C, 80.69; H, 4.10; N, 12.38. Found: C, 80.55; H, 4.15; N, 12.25.

*4.2.17. 3,3-Bis(2-butyl-1H-indol-3-yl)indolin-2-one (**16f**).* Brown solid; mp 199–201 °C; R_f=0.50 (AcOEt/petroleum ether 25%). IR (KBr): 749, 1459, 1713, 2925, 3385 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 0.59 (t, 3H, *J*=6.8 Hz, –C*H*$_3$), 0.67 (t, 3H, *J*=6.8 Hz, –C*H*$_3$), 0.91–1.42 (m, 8H, –C*H*$_2$–C*H*$_2$–C*H*$_3$), 2.29–2.35 (m, 4H, Ar–C*H*$_2$–), 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 (75 MHz, DMSO-d_6) δ_C 13.4, 13.5, 22.0, 22.1, 26.4, 26.5, 30.8, 31.3, 52.6, 109.1, 110.1, 110.2, 110.5, 117.3, 117.4, 119.4, 119.7, 120.0, 120.4, 120.9, 125.1, 127.1, 127.5, 127.6, 135.1, 135.2, 135.3, 135.6, 135.8, 137.9, 141.0, 179.0. 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, 7.10; N, 8.72.

4.3. Typical procedure for the preparation of 2-indolyl-1-nitroalkanes

To a solution of *o*-ethynylaniline (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 nitrostyrene (1.0 mmol) was added and refluxed for the specified time (Table 3 and 5). 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 the pure product.

*4.3.1. 3-(2-Nitro-1-phenylethyl)-2-phenyl-1H-indole (**18a**).* Pale yellow solid; mp 148–149 °C; R_f=0.34 (EtOAc/petroleum ether 20%). IR (KBr): 3396, 3056, 1549, 1490, 1453, 1428, 1376, 1308, 746, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 5.13 (dd, 1H, *J*=8.4, 12.2 Hz, –C*H*$_2$NO$_2$), 5.18 (dd, 1H, *J*=7.6, 12.2 Hz, –C*H*$_2$NO$_2$), 5.32 (t, 1H, *J*=8.4 Hz, –C*H*–CH$_2$NO$_2$), 7.11 (t, 1H, *J*=7.6 Hz, Ar–H), 7.22 (t, 2H, *J*=8.4 Hz, Ar–H), 7.30 (t, 2H, *J*=8.4 Hz, Ar–H), 7.34 (d, 2H, *J*=7.6 Hz, Ar–H), 7.39 (d, 1H, *J*=8.4 Hz, Ar–H), 7.42–7.46 (m, 5H, Ar–H), 7.53 (d, 1H, *J*=8.4 Hz, Ar–H), 8.16 (s, 1H, –N*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 30.9, 85.9, 111.1, 112.3, 120.0, 121.0, 122.0, 123.4, 125.7, 127.0, 127.9, 128.4, 128.5, 129.0, 129.1, 132.1, 136.1, 136.2. MS(EI): *m*/*z*=342 [M^+]. Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.01; H, 5.49; N, 8.30.

*4.3.2. 3-[1-(4-Chlorophenyl)-2-nitroethyl]-2-phenyl-1H-indole (**18b**).* Yellow solid; mp 116–118 °C; R_f=0.32 (EtOAc/petroleum ether 20%). IR (KBr): 3410, 1548, 1490, 1450, 1380, 1207, 1013, 809, 739, 699 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 5.09 (dd, 1H, *J*=8.4, 12.2 Hz, –C*H*$_2$NO$_2$), 5.16 (dd, 1H, *J*=7.6, 12.2 Hz, –C*H*$_2$NO$_2$), 5.27 (t, 1H, *J*=7.6 Hz, –C*H*–CH$_2$NO$_2$), 7.12 (t, 1H, *J*=7.6 Hz, Ar–H), 7.21–7.25 (m, 5H, Ar–H), 8.22 (s, 1H, –N*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 40.3, 78.8, 109.1, 111.5, 119.7, 120.4, 122.6, 126.8, 128.7, 128.8, 129.0, 132.0, 133.1, 136.0, 137.0, 138.4. MS(EI): *m*/*z*=376 [M^+], 378 [M^{+2}]. Anal. Calcd for $C_{22}H_{17}ClN_2O_2$: C, 70.12; H, 4.55; N, 7.43. Found: C, 70.00; H, 4.45; N, 7.59.

*4.3.3. 3-[1-(4-Methylphenyl)-2-nitroethyl]-2-phenyl-1H-indole (**18c**).* Yellow solid; mp 158–160 °C; R_f=0.31 (EtOAc/petroleum ether 20%). IR (KBr): 3414, 2921, 1545, 1511, 1451, 1376, 1305, 817, 765, 746 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 2.30 (s, 3H, –C*H*$_3$), 5.11 (dd, 1H, *J*=8.4, 12.2 Hz, –C*H*$_2$NO$_2$), 5.16 (dd, 1H, *J*=7.6, 12.2 Hz, –C*H*$_2$NO$_2$), 5.27 (t, 1H, *J*=7.6 Hz, –C*H*–CH$_2$NO$_2$), 7.11 (t, 1H, *J*=8.4 Hz, Ar–H), 7.21 (t, 1H, *J*=8.4 Hz, Ar–H), 7.39 (d, 1H, *J*=8.4 Hz, Ar–H), 7.42–7.45 (m, 4H, Ar–H), 7.53 (d, 1H, *J*=7.6 Hz, Ar–H), 7.46 (s, 1H, –N*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 31.8, 40.3, 79.3, 108.7, 111.0, 119.0, 119.9, 121.7, 127.1, 127.4, 129.9, 135.8, 136.6, 137.0, 138.1. MS(EI): *m*/*z*=356 [M^+]. Anal. Calcd for $C_{23}H_{20}N_2O_2$: C, 77.51; H, 5.66; N, 7.86. Found: C, 77.40; H, 5.50; N, 7.77.

*4.3.4. 3-[1-(6-Bromo-1,3-benzodioxol-5-yl)-2-nitroethyl]-2-phenyl-1H-indole (**18d**).* Colourless solid; mp 188–190 °C; R_f=0.35 (EtOAc/petroleum ether 25%). IR (KBr): 3406, 1549, 1473, 1377, 1236, 1034, 925, 742 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 4.94 (dd, 1H, *J*=6.1, 13.0 Hz, –C*H*$_2$NO$_2$), 5.23 (dd, 1H, *J*=10.7, 12.9 Hz, –C*H*$_2$NO$_2$), 5.55 (dd, 1H, *J*=5.3, 10.7 Hz, –C*H*–CH$_2$NO$_2$), 5.92 (d, 2H, *J*=11.4 Hz, –OC*H*$_2$O–), 7.05 (s, 1H, Ar–H), 7.09 (s, 1H, Ar–H), 7.18–7.24 (m, 2H, Ar–H), 7.35 (d, 2H, *J*=6.1 Hz, Ar–H), 7.39–7.46 (m, 4H, Ar–H), 7.73 (d, 1H, *J*=7.6 Hz, Ar–H), 8.22 (s, 1H, –N*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 41.5, 76.7, 101.8, 108.2, 109.8, 111.6, 113.3, 114.3, 119.8, 120.6, 122.5, 127.3, 128.6, 128.7, 128.9, 131.7, 132.0, 136.0, 137.6, 147.7, 147.8. MS (EI): *m*/*z*=465 [M^+], 467 [M^{+2}]. Anal. Calcd for $C_{23}H_{17}BrN_2O_4$: C, 59.37; H, 3.68; N, 6.02. Found: C, 59.50; H, 3.75; N, 5.99.

*4.3.5. 3-[1-(2-Bromo-4,5-dimethoxyphenyl)-2-nitroethyl]-2-phenyl-1H-indole (**18e**).* Pale yellow solid; mp 149–151 °C; R_f=0.40 (EtOAc/petroleum ether 40%). ^1H NMR (500 MHz, $CDCl_3$) δ_H 3.55 (s, 3H, –OC*H*$_3$), 3.85 (s, 3H, –OC*H*$_3$), 4.96 (dd, 1H, *J*=6.1, 13.0 Hz, –C*H*$_2$NO$_2$), 5.23 (dd, 1H, *J*=10.7, 13.0 Hz, –C*H*$_2$NO$_2$), 5.57 (dd, 1H, *J*=6.1, 10.7 Hz, –C*H*–CH$_2$NO$_2$), 7.06 (s, 1H, Ar–H), 7.16–7.23 (m, 3H, Ar–H), 7.35 (d, 2H, *J*=6.9 Hz, Ar–H), 7.38–7.45 (m, 4H, Ar–H), 7.77 (d, 1H, *J*=8.4 Hz, Ar–H), 8.31 (s, 1H, –N*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 41.3, 55.8, 56.1, 76.8, 108.1, 111.7, 112.7, 113.7, 116.0, 119.6, 120.4, 122.4, 127.3, 128.5, 128.6, 128.9, 130.4, 132.0, 136.0, 137.7, 148.6, 148.7. MS(EI): *m*/*z*=481 [M^++H^+], 483 [M^{+2}+H^+]. Anal. Calcd for $C_{24}H_{21}BrN_2O_4$: C, 59.89; H, 4.40; N, 5.82. Found: C, 59.80; H, 4.44; N, 5.82.

*4.3.6. 3-(4-Bromophenyl)-4-[1-(2-phenyl-1H-indol-3-yl)-2-nitroethyl]-1-phenyl-1H-pyrazole (**18f**).* Yellow solid; mp 174–176 °C; R_f=0.35 (EtOAc/petroleum ether 35%). ^1H NMR (500 MHz, $CDCl_3$) δ_H 4.93 (dd, 1H, *J*=6.8, 12.2 Hz, –C*H*$_2$NO$_2$), 5.10 (dd, 1H, *J*=9.2, 12.2 Hz, –C*H*$_2$NO$_2$), 5.52 (t, 1H, *J*=8.4 Hz, –C*H*–CH$_2$NO$_2$), 7.17 (t, 1H, *J*=6.9 Hz, Ar–H), 7.22–7.29 (m, 2H, Ar–H), 7.33–7.35 (m, 4H, Ar–H), 7.37–7.45 (m, 8H, Ar–H), 7.59 (d, 2H, *J*=7.6 Hz, Ar–H), 7.65 (d, 1H, *J*=8.4 Hz, Ar–H), 7.89 (s, 1H, Pyrazolyl-H), 8.22 (s, 1H, –N*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 32.5, 78.2, 108.7, 111.7, 119.1, 119.3, 119.5, 120.4, 122.4, 122.6, 126.4, 126.7, 127.1, 128.7 (2C), 128.9, 129.4, 129.5, 131.7, 131.9, 136.0, 136.9, 139.6, 150.2. MS(EI): *m*/*z*=563 [M^++H^+], 565 [M^++H^+]. Anal. Calcd for $C_{31}H_{23}N_4O_2$: C, 66.08; H, 4.11; N, 9.94. Found: C, 65.96; H, 4.15; N, 10.01.

*4.3.7. 2-Methyl-3-(2-nitro-1-phenylethyl)-1H-indole (**18g**).* Orange solid; mp 79–81 °C; R_f=0.45 (EtOAc/petroleum ether 20%). IR (KBr): 3387, 3055, 3025, 1550, 1454, 1370, 770 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 2.35 (s, 3H, –C*H*$_3$), 5.12 (dd, 1H, *J*=6.9, 10.7 Hz, –C*H*CH$_2$NO$_2$), 5.18–5.25 (m, 2H, –C*H*$_2$NO$_2$), 7.04 (t, 1H, *J*=7.6 Hz, Ar–H), 7.12 (t, 1H, *J*=6.9 Hz, Ar–H), 7.22–7.26 (m, 2H, Ar–H), 7.29–7.34 (m, 4H, Ar–H), 7.39 (d, 1H, *J*=8.4 Hz, Ar–H), 7.88 (s, 1H, –N*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 12.1, 40.6, 79.5, 108.8, 110.8, 118.6, 118.7, 119.8, 121.3, 126.9, 127.3, 128.9, 133.0, 135.5, 139.6. MS(EI): *m*/*z*=280 [M^+]. Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.78; H, 5.80; N, 10.01.

*4.3.8. 2-Butyl-3-(2-nitro-1-phenylethyl)-1H-indole (**18h**).* Brown oil; R_f=0.55 (EtOAc/petroleum ether 20%). IR (CH_2Cl_2): 3406, 1552, 1461, 1376, 742, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 0.91 (t, 3H, *J*=6.9 Hz, –C*H*$_3$), 1.35–1.38 (m, 2H, –C*H*$_2$–CH$_3$), 1.59 (q, 2H, *J*=7.6 Hz, –C*H*$_2$–CH$_2$–CH$_3$), 2.72–2.77 (m, 2H, –C*H*$_2$–CH$_2$–CH$_2$–CH$_3$), 5.10 (dd, 1H, *J*=7.6, 11.4 Hz, –C*H*$_2$NO$_2$), 5.20 (t, 1H, *J*=7.6 Hz, –C*H*–CH$_2$NO$_2$), 5.26 (dd, 1H, *J*=6.9, 11.4 Hz, –C*H*$_2$NO$_2$), 7.09 (t, 1H, *J*=6.9 Hz, Ar–H), 7.12 (t, 1H, *J*=7.6 Hz, Ar–H), 7.22 (t, 1H, *J*=6.9 Hz, Ar–H), 7.27–7.33 (m, 5H, Ar–H), 7.37 (d, 1H, *J*=7.6 Hz, Ar–H), 7.92 (s, 1H, –N*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 13.8, 22.5, 25.9, 31.8, 40.3, 78.8, 108.5, 110.7, 118.8, 119.7, 121.3, 126.7, 127.0, 127.3, 128.7, 135.5, 137.6, 139.6. MS(EI): *m*/*z*=322 [M^++H^+]. Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.55; H, 6.85; N, 8.72.

*4.3.9. 2-Butyl-3-[1-(4-methylphenyl)-2-nitroethyl]-1H-indole (**18i**).* Pink solid; mp 86–88 °C; R_f=0.60 (EtOAc/petroleum ether 10%). IR (KBr): 3400, 2918, 1614, 1550, 1460, 1428, 1378, 1242, 1019, 817 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 0.94 (t, 3H, *J*=7.6 Hz, –(CH$_2$)$_3$C*H*$_3$); 1.35–1.40 (m, 2H, –(CH$_2$)$_2$–C*H*$_2$–CH$_3$), 1.59 (pentet, 2H, *J*=6.9 Hz, –CH$_2$–C*H*$_2$–CH$_2$–CH$_3$), 2.32 (s, 3H, Ar–CH$_3$), 2.70–2.76 (m, 2H, –C*H*$_2$–(CH$_2$)$_2$CH$_3$), 5.10 (dd, 1H, *J*=8.4, 11.4 Hz, –C*H*$_2$NO$_2$), 5.19 (t, 1H, *J*=8.4 Hz, –C*H*–CH$_2$NO$_2$), 5.25 (dd, 1H, *J*=6.9, 11.4 Hz, –CH$_2$NO$_2$), 7.05 (t, 1H, *J*=8.4 Hz, Ar–H), 7.11–7.15 (m, 3H, Ar–H), 7.23 (d, 2H, *J*=7.6 Hz, Ar–H), 7.28 (d, 1H, *J*=8.4 Hz, Ar–H), 7.41 (d, 1H, *J*=8.4 Hz, Ar–H), 7.93 (s, 1H, –NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 13.8, 21.0, 22.5, 25.9, 31.9, 40.1, 79.0, 108.6, 110.8, 118.9, 119.6, 121.3, 126.7, 127.2, 129.4, 135.5, 136.6 (2C), 137.6. MS(EI): *m*/*z*=336 [M^++H^+]. Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33. Found: C, 75.05; H, 7.25; N, 8.25.

*4.3.10. 2-(4-Pentylphenyl)-3-[1-(2-fluorophenyl)-2-nitroethyl]-1H-indole (**18j**).* Brown solid; mp 56–58 °C; R_f=0.25 (EtOAc/petroleum

ether 20%). IR (KBr): 3410, 2929, 1553, 1488, 1455, 1376, 1223, 745 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 0.91 (t, 3H, J=6.9 Hz, –C*H*$_3$), 1.36–1.37 (m, 4H, –(CH$_2$)$_2$–(C*H*$_2$)$_2$–CH$_3$), 1.66 (pentet, 2H, J=7.6 Hz, –CH$_2$–C*H*$_2$–(CH$_2$)$_2$–CH$_3$), 2.66 (t, 2H, J=7.6 Hz, –C*H*$_2$–(CH$_2$)$_3$–CH$_3$), 5.16 (d, 2H, J=7.6 Hz, –C*H*$_2$NO$_2$), 5.56 (t, 1H, J=8.4 Hz, –C*H*–CH$_2$NO$_2$), 7.02–7.07 (m, 2H, Ar–H), 7.12 (t, 1H, J=7.6 Hz, Ar–H), 7.21 (t, 2H, J=6.9 Hz, Ar–H), 7.25–7.27 (m, 2H, Ar–H), 7.33 (d, 2H, J=8.4 Hz, Ar–H), 7.36–7.38 (m, 2H, Ar–H), 7.57 (d, 1H, J=8.4 Hz, Ar–H), 8.14 (s, 1H, –N*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 14.0, 22.5, 30.9, 31.5, 35.6, 35.7, 77.3 (J_{C-F}=3.0 Hz), 107.7, 111.3, 115.8 (J_{C-F}=18.0 Hz), 119.6, 120.2, 122.3, 124.3 (J_{C-F}=3.0 Hz), 126.5 (J_{C-F}=11.0 Hz), 127.2, 128.6, 128.9, 129.1 (J_{C-F}=7.0 Hz), 129.3, 129.5 (2C), 135.8, 137.4, 143.6, 160.5 (J_{C-F}=196.0 Hz). MS(EI): m/z=430 [M^++H^+]. Anal. Calcd for $C_{27}H_{27}FN_2O_2$: C, 75.33; H, 6.32; N, 6.51. Found: C, 75.25; H, 6.30; N, 6.55.

*4.3.11. 1-Acetyl-2-phenyl-1H-indole (**11a**).* Colourless solid; mp 80–82 °C; R_f=0.25 (EtOAc/petroleum ether 10%). IR (KBr): 3065, 1690, 1559, 1367, 761 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 2.07 (s, 3H, –CO–C*H*$_3$), 6.62 (s, 1H, Indolyl-H), 7.28 (t, 1H, J=7.6 Hz, Ar–H), 7.35 (t, 1H, J=7.6 Hz, Ar–H), 7.43–7.47 (m, 5H, Ar–H), 7.56 (d, 1H, J=7.6 Hz, Ar–H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 27.9, 111.5, 116.0, 120.3, 123.6, 125.1, 128.6, 128.7, 128.9, 129.0, 134.1, 137.7, 139.7, 171.4. MS(EI): m/z=235 [M^+]. Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.75; H, 5.45; N, 6.00.

*4.3.12. 1-(Methylsulphonyl)-2-phenyl-1H-indole (**11b**).* Colourless solid; mp 116–118 °C; R_f=0.35 (EtOAc/petroleum ether 20%). IR (KBr): 1654, 1559, 1446, 1367, 1171, 769 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 2.73 (s, 3H, –SO$_2$–C*H*$_3$), 6.71 (s, 1H, Indolyl-H), 7.33–7.43 (m, 5H, Ar–H), 7.54–7.60 (m, 3H, Ar–H), 8.13 (d, 1H, J=8.4 Hz, Ar–H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 39.6, 113.1, 115.8, 121.0, 124.6, 125.1, 127.7, 128.9, 130.1, 130.3, 132.0, 138.0, 141.9. MS(EI): m/z=271 [M^+]. Anal. Calcd for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; N, 5.16. Found: C, 66.35; H, 4.80; N, 5.21.

*4.3.13. 3-{(1R)-1-[(5R,6S)-6-Benzyloxy-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl]-2-nitroethyl}-2-methyl-1H-indole (**18k**).* Yellow solid; $[\alpha]_D^{28}$ −84.66 (0.2, $CHCl_3$); mp 207–209 °C; R_f=0.45 (AcOEt/Petroleum ether 40%). IR (KBr): 3372, 2937, 2346, 1553, 1350, 751 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ_H 1.21 (s, 3H, –C–C*H*$_3$), 1.31 (s, 3H, –C–C*H*$_3$), 2.24 (s, 3H, Indole-C*H*$_3$), 4.02 (d, 1H, J=3.0 Hz, C3–*H*), 4.04–4.09 (m, 1H, C5–*H*), 4.59 (d, 1H, J=11.4 Hz, –OC*H*HPh), 4.64–4.67 (m, 2H, C4–*H*, –CH*H*NO2), 4.77 (d, 1H, J=11.4 Hz, –OCH*H*Ph), 4.84 (d, 1H, J=4.2 Hz, C2–*H*), 5.01 (t, 1H, J=11.4 Hz, –C*H*HNO$_2$), 5.76 (d, 1H, J=3.8 Hz, C1–*H*), 6.89 (t, 1H, J=6.9 Hz, Ar–H), 6.97 (t, 1H, J=7.6 Hz, Ar–H), 7.24 (d, 1H, J=8.4 Hz, Ar–H), 7.32 (t, 1H, J=6.8 Hz, Ar–H), 7.38 (t, 2H, J=8.0 Hz, Ar–H), 7.45 (d, 2H, J=6.9 Hz, Ar–H), 7.59 (d, 1H, J=6.5 Hz, Ar–H), 10.85 (s, 1H, –NH). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C 11.9, 26.7, 27.1, 35.7, 71.0, 76.6, 78.8, 79.7, 80.8, 81.7, 104.4, 106.2, 111.2, 111.3, 118.3, 118.9, 120.5, 128.4, 128.6, 128.9, 134.2, 135.8, 138.2. MS(EI): m/z=454 [M^++H^+]. Anal. Calcd for $C_{25}H_{28}N_2O_6$: C, 66.36; H, 6.24; N, 6.19%. Found: C, 66.45; H, 6.20; N, 6.16%.

*4.3.14. 3-{(1S)-1-[(5R,6S)-6-Benzyloxy-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl]-2-nitroethyl}-2-methyl-1H-indole (**18k′**).* Viscous liquid; $[\alpha]_D^{28}$ 45.73 (0.2, $CHCl_3$); R_f=0.47 (AcOEt/Petroleum ether 40%). IR (CH_2Cl_2): 3405, 2950, 2349, 1559, 1353, 761 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 1.28 (s, 3H, –C–C*H*$_3$), 1.42 (s, 3H, –C–C*H*$_3$), 2.26 (s, 3H, indole-C*H*$_3$), 3.92 (d, 1H, J=3.1 Hz, C3–*H*), 4.27–4.31 (m, 1H, C5–*H*), 4.40 (dd, 1H, J=3.8, 12.2 Hz, –CH*H*NO$_2$), 4.52 (d, 1H, J=11.5 Hz, –OC*H*HPh), 4.66 (dd, 1H, J=3.0, 9.9 Hz, C4–*H*), 4.71 (d, 1H, J=3.8 Hz, C2–*H*), 4.78–4.84 (m, 2H, –OCH*H*Ph, –C*H*HNO$_2$), 5.88 (d, 1H, J=3.8 Hz, C1–*H*), 6.97 (t, 1H, J=9.9 Hz, Ar–H), 7.04 (t, 1H, J=7.6 Hz, Ar–H), 7.34–7.50 (m, 6H, Ar–H), 7.94 (s, 1H, –NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 11.8, 26.4, 26.8, 31.0, 35.6, 71.4, 75.5, 79.3, 80.7, 81.6, 104.4, 106.0, 110.0, 111.9, 117.7, 119.4, 121.0, 128.2, 128.5, 128.8, 134.0, 135.6, 136.8. MS(EI): m/z=454 [M^++H^+]. Anal. Calcd for $C_{25}H_{28}N_2O_6$: C, 66.36; H, 6.24; N, 6.19%. Found: C, 66.29; H, 6.27; N, 6.25%.

*4.3.15. 3-{(1R)-1-[(5R,6S)-6-Ethoxy-2,2-dimethyltetrahydrofuro[2,3-d]-[1,3]dioxol-5-yl]-2-nitroethyl}-2-methyl-1H-indole (**18l**).* Yellow solid; $[\alpha]_D^{30}$ −129.60 (0.60, $CHCl_3$); mp 160–162 °C; R_f=0.50 (AcOEt/Petroleum ether 40%). IR (KBr): 3378, 2957, 2343, 1576, 1350, 759 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ_H 1.17–1.19 (m, 6H, –C–C*H*$_3$, –OCH$_2$C*H*$_3$), 1.28 (s, 3H, –C–C*H*$_3$), 2.25 (s, 3H, indole-C*H*$_3$), 3.45–3.51 (m, 1H, –OCH*H*CH$_3$), 3.70–3.75 (m, 1H, –OC*H*HCH$_3$), 3.88 (d, 1H, J=3.1 Hz, C3–*H*), 3.97–4.01 (m, 1H, C5–*H*), 4.60 (dd, 1H, J=10.7, 3.1 Hz, C4–*H*), 4.68 (d, 1H, J=3.8 Hz, C2–*H*), 4.79 (dd, 1H, J=12.2, 4.6 Hz, –CH*H*NO$_2$), 5.01 (t, 1H, J=11.4 Hz, –C*H*HNO$_2$), 5.72 (d, 1H, J=3.8 Hz, C1–*H*), 6.90 (t, 1H, J=7.6 Hz, Ar–H), 6.97 (t, 1H, J=7.6 Hz, Ar–H), 7.23 (d, 1H, J=8.4 Hz, Ar–H), 7.56 (d, 1H, J=7.6 Hz, Ar–H), 10.84 (s, 1H, –NH). ^{13}C NMR (125 MHz, DMSO-d_6) δ_C 15.7, 26.7, 27.1, 35.9, 65.0, 76.9, 79.1, 81.4, 81.8, 104.4, 106.6, 111.1, 111.4, 118.3, 118.9, 120.5, 134.1, 135.9. MS(EI): m/z=391 [M^++H^+]. Anal. Calcd for $C_{20}H_{26}N_2O_6$: C, 61.53; H, 6.71; N, 7.17%. Found: C, 61.65; H, 6.75; N, 7.06%.

*4.3.16. 3-{(1S)-1-[(5R,6S)-6-Ethoxy-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl]-2-nitroethyl}-2-methyl-1H-indole (**18l′**).* Viscous liquid; $[\alpha]_D^{28}$ 62.34 (0.48, $CHCl_3$); R_f=0.52 (AcOEt/Petroleum ether 40%). IR (CH_2Cl_2): 3416, 2950, 2349, 1559, 1353, 761 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 1.28 (t, 3H, J=6.9 Hz, –OCH$_2$C*H*$_3$), 1.30 (s, 3H, –C–C*H*$_3$), 1.51 (s, 3H, –C–C*H*$_3$), 2.38 (s, 3H, indole-C*H*$_3$), 3.09–3.16 (m, 1H, –OCH*H*CH$_3$), 3.36 (d, 1H, J=3.1 Hz, C3–*H*), 3.42–3.48 (m, 1H, –OC*H*HCH$_3$), 4.27–4.32 (m, 1H, C5–*H*), 4.49 (d, 1H, J=3.8 Hz, C2–*H*), 4.83 (d, 1H, J=8.4 Hz, C4–*H*), 4.95–5.03 (m, 2H, –C*H*$_2$NO$_2$), 5.98 (d, 1H, J=3.8 Hz, C1–*H*), 7.05–7.11 (m, 2H, Ar–H), 7.23 (d, 1H, J=6.9 Hz, Ar–H), 7.51 (d, 1H, J=7.6 Hz, Ar–H), 7.94 (s, 1H, –NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 15.3, 26.3, 26.9, 35.4, 65.4, 77.6, 79.2, 81.7, 81.8, 105.2, 105.7, 110.9, 111.8, 118.3, 119.8, 121.2, 134.2, 135.7. MS(EI): m/z=391 [M^++H^+]. Anal. Calcd for $C_{20}H_{26}N_2O_6$: C, 61.53; H, 6.71; N, 7.17%. Found: C, 61.45; H, 6.65; N, 7.26%.

*4.3.17. 3-{(1R)-1-[(5R,6S)-6-Benzyloxy-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl]-2-nitroethyl}-2-phenyl-1H-indole (**18m**).* Colourless solid; $[\alpha]_D^{29}$ 102.46 (0.54, $CHCl_3$); mp 240–242 °C; R_f=0.55 (AcOEt/Petroleum ether 40%). IR (KBr): 3398, 2965, 2385, 1575, 1352, 756 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 1.28 (s, 3H, –C–C*H*$_3$), 1.33 (s, 3H, –C–C*H*$_3$), 3.83 (d, 1H, J=3.1 Hz, C3–*H*), 4.38–4.43 (m, 2H, C2–*H*, –OC*H*HPh), 4.52–4.57 (m, 1H, C5–*H*), 4.60–4.66 (m, 3H, C4–*H*, –CH*H*NO$_2$, –OCH*H*Ph), 4.79 (t, 1H, J=11.4 Hz, –C*H*HNO$_2$), 5.81 (d, 1H, J=3.8 Hz, C1–*H*), 6.98 (t, 1H, J=6.9 Hz, Ar–H), 7.07 (t, 1H, J=7.6 Hz, Ar–H), 7.26–7.36 (m, 9H, Ar–H), 7.51 (d, 1H, J=7.6 Hz, Ar–H), 7.55 (d, 2H, J=6.9 Hz, Ar–H), 9.41 (s, 1H, –NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 25.9, 26.4, 34.7, 70.3, 76.1, 78.7, 80.2, 80.9, 103.7, 106.6, 110.7, 111.5, 118.2, 118.8, 121.0, 126.2, 127.2, 127.4, 127.9, 128.1, 128.7, 132.5, 136.1, 137.2, 137.4. MS(EI): m/z=515 [M^++H^+]. Anal. Calcd for $C_{30}H_{30}N_2O_6$: C, 70.02; H, 5.88; N, 5.44%. Found: C, 70.65; H, 5.75; N, 5.36%.

*4.3.18. 3(S)-(3(R)-Nitro-2(R)-p-tolyl-chroman-4-yl)-2-phenyl-1H-indole (**18n**).* Yellow solid; $[\alpha]_D^{28}$ 19.08 (1.0, $CHCl_3$); mp 128–130 °C; R_f=0.55 (AcOEt/Petroleum ether 20%). ^1H NMR (500 MHz, $CDCl_3$) δ_H 2.32 (s, 3H, indole-C*H*$_3$), 5.06 (d, 1H, J=3.8 Hz, H_a), 5.41 (t, 1H, J=3.8 Hz, H_b), 5.68 (br s, 1H, H_c), 6.09 (t, 1H, J=7.7 Hz, Ar–H), 6.97–6.99 (m, 1H, Ar–H), 7.07 (d, 1H, J=7.7 Hz, Ar–H), 7.12–7.20 (m, 7H, Ar–H), 7.26 (t, 1H, J=6.9 Hz, Ar–H), 7.38–7.45 (m, 6H, Ar–H), 8.28 (s, 1H, –NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 21.3, 35.9, 75.2, 90.1, 111.4, 111.7, 116.9, 119.6, 120.6, 121.4, 122.3, 122.7, 125.9, 128.5, 128.7, 128.8, 128.4, 128.6, 128.9, 134.2, 135.8, 138.2. MS(EI): m/z=461 [M^++H^+].

Anal. Calcd for $C_{30}H_{24}N_2O_3$: C, 78.24; H, 5.25; N, 6.08%. Found: C, 78.45; H, 5.15; N, 6.00%.

*4.3.19. 3-[(6-Ethoxy-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-(2-methyl-1H-indol-3-yl)-methyl]-isoxazole-4,5-dicarboxylic acid diethyl ester (**20a**).* Viscous liquid; $[\alpha]_D^{30}$ 139.34 (0.54, $CHCl_3$); R_f=0.47 (AcOEt/Petroleum ether 40%). IR (KBr): 3476, 2931, 2345, 1727, 1556, 1349, 751 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 1.01 (t, 3H, *J*=6.9 Hz, –$COOCH_2CH_3$), 1.12 (t, 3H, *J*=7.6 Hz, –$COOCH_2CH_3$), 1.27 (s, 3H, –C–CH_3), 1.33 (t, 3H, *J*=7.6 Hz, –OCH_2CH_3), 1.41 (s, 3H, –C–CH_3), 2.42 (s, 3H, indole-CH_3), 3.16–3.19 (m, 1H, –OCHHCH_3), 3.57–3.61 (m, 1H, –OCHHCH_3), 4.05–4.08 (m, 2H, –$COOCH_2CH_3$), 4.20 (d, 1H, *J*=3.1 Hz, C3–*H*), 4.36 (q, 2H, *J*=7.6 Hz, –$COOCH_2CH_3$), 4.59 (d, 1H, *J*=3.8 Hz, C2–*H*), 4.98 (d, 1H, *J*=9.9 Hz, C5–*H*), 5.26 (dd, 1H, *J*=9.9, 3.1 Hz, C4–*H*), 5.88 (d, 1H, *J*=3.8 Hz, C1–*H*), 6.95 (t, 1H, *J*=6.9 Hz, Ar–H), 7.00 (t, 1H, *J*=8.4 Hz, Ar–H), 7.16 (d, 1H, *J*=6.9 Hz, Ar–H), 7.62 (d, 1H, *J*=8.4 Hz, Ar–H), 7.83 (s, 1H, –NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 13.9, 14.0, 14.9, 26.5, 27.1, 29.8, 34.2, 61.7, 62.8, 65.9, 80.8, 82.3, 82.9, 104.9, 110.3, 111.6, 118.7, 119.4, 120.8, 123.5, 127.6, 133.4, 135.4, 155.6, 156.7, 160.5, 162.9. MS(EI): *m*/*z*=543 [M^++H^+]. Anal. Calcd for $C_{28}H_{34}N_2O_9$: C, 61.98; H, 6.32; N, 5.16%. Found: C, 61.90; H, 6.35; N, 5.31%.

*4.3.20. 3-[(6-Ethoxy-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-(2-methyl-1H-indol-3-yl)-methyl]-isoxazole-4,5-dicarboxylic acid diethyl ester (**20b**).* Yellow solid; $[\alpha]_D^{29}$ 618.70 (0.22, $CHCl_3$); mp 188–190 °C; R_f=0.50 (AcOEt/Petroleum ether 40%). IR (KBr): 3472, 2927, 2331, 1723, 1553, 1347, 751 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ_H 1.05 (t, 3H, *J*=6.9 Hz, –$COOCH_2CH_3$), 1.23 (t, 3H, *J*=7.6 Hz, –$COOCH_2CH_3$), 1.29 (s, 3H, –C–CH_3), 1.32 (t, 3H, *J*=7.6 Hz, –OCH_2CH_3), 1.56 (s, 3H, –C–CH_3), 2.49 (s, 3H, indole-CH_3), 2.98–3.01 (m, 1H, –OCHHCH_3), 3.32–3.36 (m, 1H, –OCHHCH_3), 3.37 (d, 1H, *J*=3.1 Hz, C3–*H*), 4.20 (q, 2H, *J*=7.6 Hz, –$COOCH_2CH_3$), 4.35 (q, 2H, *J*=6.9 Hz, –$COOCH_2CH_3$), 4.45 (d, 1H, *J*=3.8 Hz, C2–*H*), 5.17 (d, 1H, *J*=10.7 Hz, C5–*H*), 5.45 (dd, 1H, *J*=10.7, 3.1 Hz, C4–*H*), 5.94 (d, 1H, *J*=3.8 Hz, C1–*H*), 7.03–7.09 (m, 1H, Ar–H), 7.22 (d, 1H, *J*=6.9 Hz, Ar–H), 7.84 (d, 1H, *J*=7.6 Hz, Ar–H), 7.86 (s, 1H, –NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 13.9, 14.0, 15.2, 26.7, 27.1, 29.8, 33.4, 61.6, 62.6, 65.2, 80.1, 81.7, 81.8, 105.5, 106.8, 110.2, 111.9, 115.3, 119.6, 119.9, 121.2, 127.6, 133.2, 135.3, 159.8, 160.9, 163.4, 163.7. MS(EI): *m*/*z*=543 [M^++H^+]. Anal. Calcd for $C_{28}H_{34}N_2O_9$: C, 61.98; H, 6.32; N, 5.16%. Found: C, 61.72; H, 6.31; N, 5.32%.

Acknowledgements

The authors thank the Council of Scientific and Industrial Research, New Delhi, for the financial support.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.09.019.

References and notes

1. For reviews, see: (a) Sundberg, R. J. *Prog. Heterocycl. Chem.* **1989**, *1*, 111; (b) Saxton, J. E. *Nat. Prod. Rep.* **1986**, *3*, 357; **1987**, *4*, 591; **1989**, *6*, 1; (c) Ezquerra, J.; Pedregal, C.; Lamas, C. *J. Org. Chem.* **1996**, *61*, 5804; (d) Lobo, A. M.; Prabhakar, S. *J. Heterocycl. Chem.* **2002**, *39*, 429; (e) Gribble, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045; (f) Xiong, W. N.; Yang, C. G.; Jiang, B. *Bioorg. Med. Chem.* **2001**, *9*, 1773; (g) Tokuyama, H.; Fukuyama, T. *Kagaku Kogyo* **2001**, *52*, 416; (h) Toyota, M.; Ihara, M. *Nat. Prod. Rep.* **1998**, *15*, 327.
2. Bifulco, G.; Bruno, I.; Riccio, R.; Lavayre, J.; Bourdy, G. *J. Nat. Prod.* **1995**, *58*, 1254.
3. Bell, R.; Carmeli, S.; Sar, N. *J. Nat. Prod.* **1994**, *57*, 1587.
4. Johnson, S.; Wilderson, J. E. R.; Wenninger, M. R.; Mitchell, G. S. *J. Appl. Physiol.* **2001**, *91*, 2703.
5. (a) Monckton, J. E.; McCormick, D. A. *J. Neurophysiol.* **2002**, *87*, 2124; (b) Vacker, C.-M.; Fettier, P.; Creminon, C.; Calas, A.; Hardin-Pouzet, H. *J. Neurosci.* **2002**, *22*, 1513.
6. (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.
7. Zeligs, M. A. *J. Med. Food* **1998**, *1*, 67.
8. Yadav, J. S.; Reddy, B. V. S.; Murthy, Ch. V. S. R.; Mahesh Kumar, G.; Madan, Ch. *Synthesis* **2001**, 783.
9. Babu, G.; Sridhar, N.; Perumal, P. T. *Synth. Commun.* **2000**, *30*, 1609.
10. Bandgar, B. P.; Shaikh, K. A. *Tetrahedron Lett.* **2003**, *44*, 1959.
11. Mo, L.-P.; Ma, Z.-C.; Zhang, Z.-H. *Synth. Commun.* **2005**, *35*, 1997.
12. Wang, L.; Han, J.; Tian, H.; Sheng, J.; Fan, Z.; Tang, X. *Synlett* **2005**, 337.
13. Zhang, Z.-H.; Yin, L.; Wang, Y.-M. *Synthesis* **2005**, 1949.
14. (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.
15. Li, J.-T.; Dai, H.-G.; Xu, W.-Z.; Li, T.-S. *Ultrason. Sonochem.* **2006**, *13*, 24.
16. Raju, B. C.; Rao, J. M. *Indian J. Chem., Sect. B* **2008**, *47B*, 623.
17. Nagarajan, R.; Perumal, P. T. *Chem. Lett.* **2004**, *3*, 288.
18. Chakrabarty, M.; Basak, R.; Harigaya, Y. *Heterocycles* **2001**, *55*, 2431.
19. (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. U.S. Patent 3,558,653, 1971; (d) Pajouhesh, H.; Parsons, R.; Popp, F. D. *J. Pharm. Sci.* **1983**, *72*, 318.
20. Garrido, F.; Ibanez, J.; Gonalons, E.; Giraldez, A. *Eur. J. Med. Chem.* **2004**, *47*, 1882.
21. 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.
22. (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.
23. (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.
24. (a) Kusurkar, R. S.; Alkobati, N. A. H.; Gokule, A. S.; Puranik, V. G. *Tetrahedron* **2008**, *64*, 1654; (b) Ram, S.; Ehrenkaufer, R. E. *Tetrahedron Lett.* **1984**, *25*, 3415; (c) Osby, J. O.; Ganem, B. *Tetrahedron Lett.* **1985**, *26*, 6413.
25. (a) Herrera, R. P.; Sgarzani, V.; Bernardi, L.; Ricci, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 6576; (b) Ballini, R.; Clemente, R. R.; Palmieri, A.; Petrini, M. *Adv. Synth. Catal.* **2006**, *348*, 191; (c) An, L.-T.; Zou, J.-P.; Zhang, L.-L.; Zhang, Y. *Tetrahedron Lett.* **2007**, *48*, 4297; (d) Lin, C.; Hsu, J.; Sastry, M. N. V.; Fang, H.; Tu, Z.; Liu, J.-T.; Ching-Fa, Y. *Tetrahedron* **2005**, *61*, 11751; (e) Kumar, R. S.; Perumal, P. T. *J. Heterocycl. Chem.* **2006**, *43*, 1383; (f) Damodiran, M.; Kumar, R. S.; Sivakumar, P. M.; Doble, M.; Perumal, P. T. *J. Chem. Sci.* **2009**, *121*, 65.
26. Bartoli, G.; Bosco, M.; Giuli, S.; Giuliani, A.; Lucarelli, L.; Marcantoni, E.; Sambri, L.; Torregiani, E. *J. Org. Chem.* **2005**, *70*, 1941.
27. Palmieri, A.; Petrini, M.; Torregiani, E. *Tetrahedron Lett.* **2007**, *48*, 5653.
28. (a) Yue, D.; Yao, T.; Larock, R. *J. Org. Chem.* **2006**, *71*, 62; (b) Battistuzzi, G.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Parisi, L. M. *Org. Lett.* **2002**, *4*, 1355; (c) Barluenga, J.; Trincado, M.; Rubio, E.; Gonzalez, J. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 2406; (d) Cacchi, S.; Fabrizi, S.; Pace, P. *J. Org. Chem.* **1998**, *63*, 1001; (e) Sakai, N.; Annaka, K.; Konakahara, T. *Tetrahedron Lett.* **2006**, *47*, 631; (f) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F. *Synlett* **2000**, 647; (g) Collini, M. D.; Ellingboe, J. W. *Tetrahedron Lett.* **1997**, *46*, 7963; (h) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F. *Synlett* **2000**, 394; (i) Takeda, A.; Kamijo, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 5662; (j) Saulnier, M. G.; Frennesson, D. B.; Deshpande, M. S.; Vyas, D. M. *Tetrahedron Lett.* **1995**, *36*, 7841; (k) Iritani, K.; Matsubara, S.; Utimoto, K. *Tetrahedron Lett.* **1988**, *29*, 1799; (l) Yasuhara, A.; Kaneko, T.; Sakamoto, T. *Heterocycles* **1998**, *43*, 2741; (m) Wang, M.-Z.; Wong, M.-K.; Che, C.-M. *Chem.—Eur. J.* **2008**, *14*, 8353.
29. (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.
30. (a) Xiao, F.; Chen, Y.; Liu, Y.; Wang, J. *Tetrahedron* **2008**, *64*, 2755; (b) Morita, N.; Krause, N. *Org. Lett.* **2004**, *6*, 4121; (c) Hoffman-Roder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537; (d) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *J. Am. Chem. Soc.* **2000**, *122*, 11533; (e) Liu, Y.; Liu, M.; Guo, S.; Tu, H.; Zhou, Y.; Gao, H. *Org. Lett.* **2006**, *8*, 3445; (f) Srome, A. W.; Rubina, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2005**, *127*, 10500; (g) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285; (h) Kenndy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4526; (i) Hashmi, A. S. K.; Weyrauch, J. P.; Frey, W.; Bats, J. W. *Org. Lett.* **2004**, *6*, 4391; (j) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Org. Lett.* **2001**, *3*, 3769; (k) Asao, N.; Nogami, T.; Lee, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 10921.
31. (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.
32. (a) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Parisi, L. M. *J. Org. Chem.* **2005**, *70*, 6213; (b) Ambrogio, I.; Arcadi, A.; Cacchi, S.; Fabrio, G.; Marinelli, F. *Synlett* **2007**, 1775.
33. (a) Nair, V.; Abhilash, K. G.; Vidya, N. *Org. Lett.* **2005**, *7*, 5857; (b) Nair, V.; Vidya, N.; Abhilash, K. G. *Synthesis* **2006**, 3647; (c) Nair, V.; Vidya, N.; Abhilash, K. G. *Tetrahedron Lett.* **2006**, *47*, 2871.

34. (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) Marchal, E.; Uriac, P.; Legouin, B.; Toupet, L.; Weghe, P. V. d. *Tetrahedron* **2007**, *63*, 9979; (h) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 11806.
35. (a) Karthikeyan, K.; Perumal, P. T.; Etti, S.; Shanmugam, G. *Tetrahedron* **2007**, *63*, 10581; (b) Praveen, C.; Kumar, K. H.; Muralidharan, D.; Perumal, P. T. *Tetrahedron* **2008**, *64*, 2369; (c) Praveen, C.; Sagayaraj, Y. W.; Perumal, P. T. *Tetrahedron Lett.* **2009**, *50*, 644; (d) Praveen, C.; Kiruthiga, P.; Perumal, P. T. *Synlett* **2009**, 1990.
36. Part of this work has been communicated previously: Ref. 35c.
37. Yadav, J. S.; Reddy, B. V. S.; Sunitha, S. *Adv. Synth. Catal.* **2003**, 345.
38. (a) Hiroya, K.; Itoh, S.; Sakamoto, T. *Tetrahedron* **2005**, *61*, 10958; (b) Amjad, M.; Knight, D. W. *Tetrahedron Lett.* **2004**, *45*, 539; (c) Hiroya, K.; Itoh, S.; Sakamoto, T. *J. Org. Chem.* **2004**, *69*, 1126; (d) Hiroya, K.; Itoh, S.; Ozawa, M.; Kanamori, Y.; Sakamoto, T. *Tetrahedron Lett.* **2002**, *43*, 1277; (e) Yasuhara, A.; Kanamori, Y.; Kaneko, M.; Numata, A.; Kondo, Y.; Sakamoto, T. *J. Chem. Soc., Perkin Trans. 1* **1999**, 529; (f) Nishikawa, T.; Ishikawa, M.; Isobe, M. *Synlett* **1999**, 123; (g) Xu, L.; Lewis, I. R.; Davidsen, S. K.; Summers, J. B. *Tetrahedron Lett.* **1998**, *39*, 5159; (h) Dai, W.-M.; Guo, D.-S.; Sun, L.-P. *Tetrahedron Lett.* **2001**, *42*, 5275.
39. (a) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683; (b) Rudd, P. M.; Elliott, T.; Cresswell, P.; Wilson, I. A.; Dwek, R. A. *Science* **2001**, *291*, 2370; (c) *Glycoscience: Chemistry and Chemical Biology*; Fraser Reid, B., Tatsuta, K., Thiem, J., Eds.; Springer: Heidelberg, 2001; (d) Varki, A. *Glycobiology* **1993**, *3*, 97; (e) Hotha, S.; Kashyap, S. *J. Am. Chem. Soc.* **2006**, *128*, 9620; (f) *Carbohydrate Based Drug Discovery*; Wong, C.-H., Ed.; Wiley-VCH: Weinheim, 2003; (g) deRaat, A.; Ekhart, C. W.; Ebner, M.; Stutz, A. E. *Top. Curr. Chem.* **1997**, *187*, 157; (h) Platt, F. M.; Butters, T. D. *Trends Glycosci. Glycotechnol.* **1995**, *7*, 495.
40. Torii, S.; Inokuchi, T.; Oi, R.; Kondo, K.; Kobayashi, T. *J. Org. Chem.* **1986**, *51*, 254.
41. Yan, M.-C.; Jang, Y.-J.; Yao, C.-F. *Tetrahedron Lett.* **2001**, *42*, 2717.
42. (a) Rao, T. S.; Singh, A. K.; Trivedi, G. K. *Heterocycles* **1984**, *22*, 1943; (b) Deshpande, S.; Mathur, H. H.; Trivedi, G. K. *Synthesis* **1986**, 486; (c) Booth, H.; Huckle, D.; Lockhart, I. M. *J. Chem. Soc., Perkin Trans. 2* **1973**, 227.
43. Mukaiyama, T.; Hoshino, T. *J. Am. Chem. Soc.* **1960**, *82*, 5339.
44. (a) Patil, N. T.; Tilekar, J. N.; Dhavale, D. D. *J. Org. Chem.* **2001**, *66*, 1065; (b) Cornia, M.; Casiraghi, G. *Tetrahedron* **1989**, *45*, 2869.