



A FeCl₃-promoted highly atropodiastereoselective cascade reaction: synthetic utility of radical cations in indolostilbene construction

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ABSTRACT

The FeCl₃-promoted oxidative cyclization/coupling of acetamidostilbenes possessing 3-methoxy, 4-methoxy and 3,5-methoxy substitutions (**21**), (**22**) and (**23**) is described. Only 3,5-substitution gave rise to novel indolostilbenes, each possessing two stereogenic axes (axially chiral but racemic dimers (**39**) and (**40**)). The 4-methoxy substituted acetamidostilbenes, by contrast, yielded the bisindoline dimer (**36**).

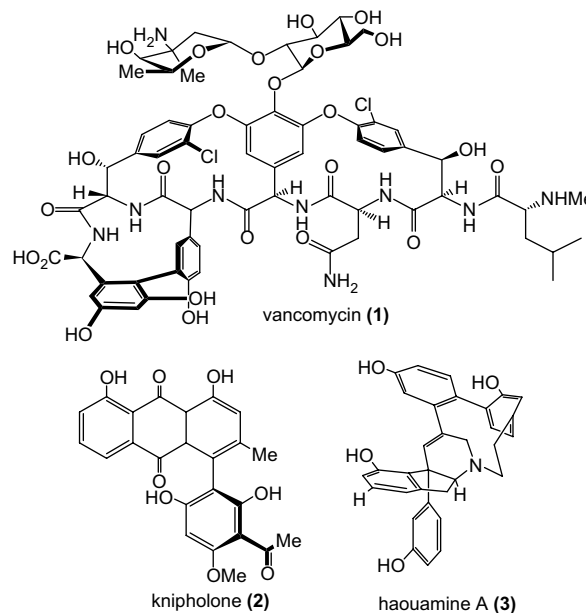
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1. Introduction

Axially chiral molecules are no longer regarded as exotic curiosities. Such molecules, possessing one or more stereogenic axes about which rotation is restricted, have become increasingly important since the configuration at a biaryl axis often plays a major role in the pharmacological characteristics of the compound.¹ Among the axially chiral molecules exhibiting remarkable properties are the antibiotic heptapeptide vancomycin (**1**)² and knipholone (**2**),² from the family of 1-phenylanthraquinones, which exhibit antimalarial and antitumour properties. Many invaluable reagents for asymmetric synthesis have exploited axial chirality.^{3,4}

Many approaches have been adopted for constructing the biaryl (or biheteroaryl) motif. These include the Ullman Coupling (Cu/DMF Δ),^{5–7} oxidative methods (Mn(acac)₃),^{8–10} palladium assisted aryl coupling [PdCl₂(PPh₃)₂]¹¹ and one-pot deiodination/aryl–aryl coupling (^tBuLi/CuCN).^{12–14} As an alternative to transition metal mediated approaches for direct aryl–aryl coupling, Carter¹⁵ has described a Diels–Alder cycloaddition/cycloreversion tactic involving a disubstituted alkynyl stannane and a functionalized cyclohexadiene. An even more spectacular [4+2]/[reverse 4+2] cycloaddition was accomplished by Baran¹⁶ in which a pyrone was appended to a benzene ring thus setting up an intramolecular

Diels–Alder reaction with a pendant ethynyl moiety. This tactic effectively installed not only the distorted biaryl system but also the azaparcyclophane ring system characteristic of (±)-haouamine A (**3**).



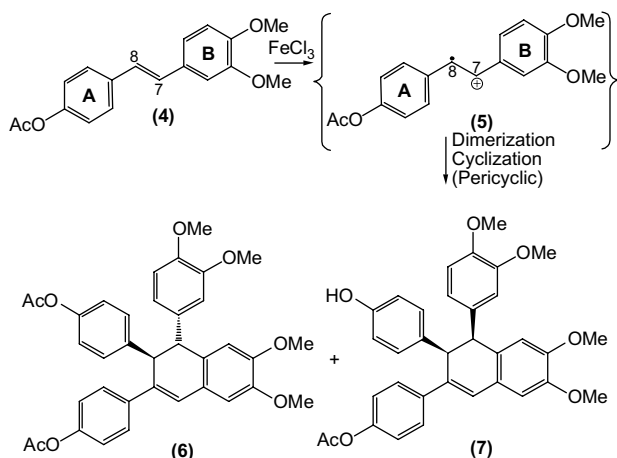
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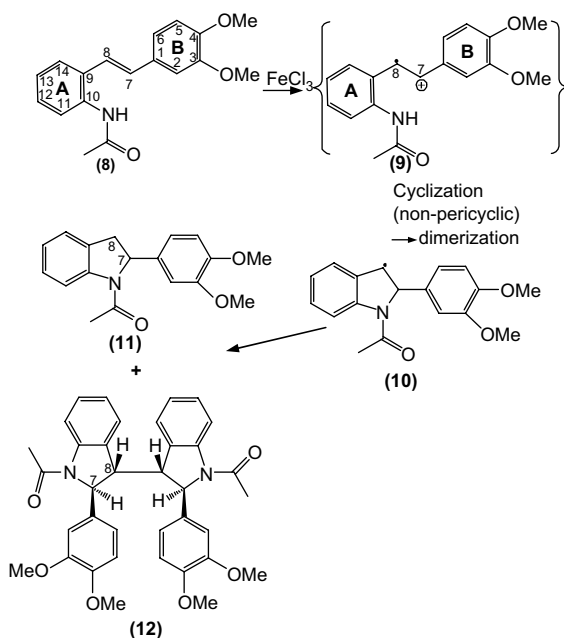
The above do not exhaust all creativity in this field since Jaisankar¹⁷ has reported a three-component route to chiral 3,3'-bipyrroles that employs diaryl acetylenes, 1,3-dicarbonyls and ammonium acetate.

We have previously described our investigation of radical cation mediated cascades culminating in the synthesis of dihydronaphthalenes¹⁸ (pericyclic) and a bisindoline¹⁹ (non-pericyclic). The mechanistic hypotheses then and now are worth considering. The dihydronaphthalene (**6**) and bisindoline (**12**) construction we previously described is predicated on the prior generation of stilbene radical cations (**5**) and (**9**) (Schemes 1 and 2) where the position of the positive charge is determined by the mesomeric stabilization made available by a *para* electron donating substituent. This requirement is met in the dihydronaphthalene (**6**) and bisindoline (**12**) syntheses described below (Schemes 1 and 2).^{18,19} The radical cations (**5**) (Scheme 1) and (**9**) (Scheme 2) are thus crucial intermediates.

In examining the bisindoline construction in Scheme 2, the following questions need to be addressed.

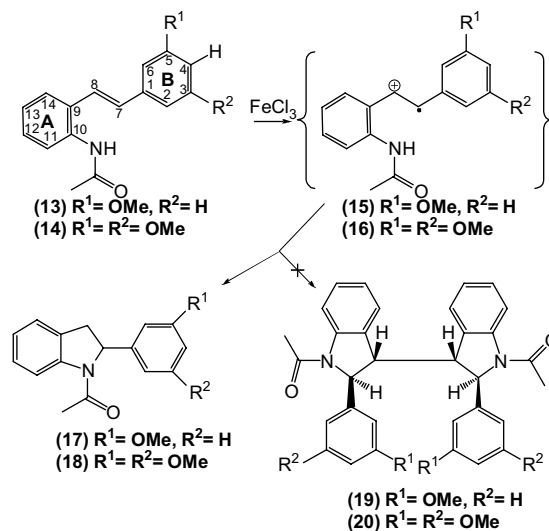


Scheme 1.



Scheme 2.

- (1) What would be the effect of subjecting an analogue of (**8**) lacking the 4-methoxy substituent (but retaining the 3-methoxy) in ring B (**9**) (Scheme 2) to the FeCl_3 oxidation conditions?
- (2) Would the 3-methoxy and 3,5-dimethoxy acetamidostilbene radical cations exhibit similar behaviour, e.g., inhibition of bisindoline formation, etc. (Scheme 3).



Scheme 3.

We would expect that in the absence of a *para* electron donating substituent in ring B (Scheme 2), a different radical cation would be generated. Under these conditions bisindoline formation should be extremely unlikely in contrast to indoline formation (Scheme 3).

Addressing these questions would lend further support to the radical cation hypothesis we have employed in previous reports. We would like to highlight the fact that cyclization of (**9**) (Scheme 2) produces an indolyl radical (**10**) from which (**11**) and (**12**) are generated. We have already described²⁰ the remarkable elevation in the yield of indoline (**11**) and suppression of bisindolisation by the simple expedient of the addition of benzophenone, which on a number of occasions was quantitatively recovered from the reaction mixture at the end of the reaction. We suggested that electron transfer from the benzophenone radical anion to the indoline radical was the key to understanding this transformation and lends considerable weight to the hypothesized intermediacy of radical cations (and radical cation-radical cation or in this case radical-radical dimerization).²⁰

In order to probe the relationship between the aryl substitution pattern and stilbene radical cation reactivity (Scheme 3) the following stilbenes (**21**), (**22**) and (**23**) (Fig. 1) were prepared as described in the next section.

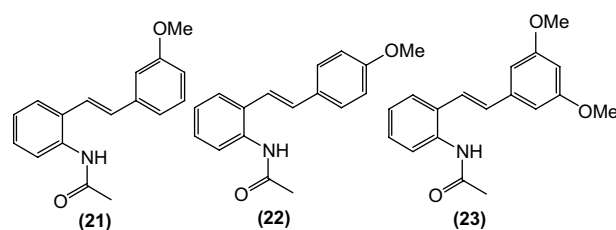
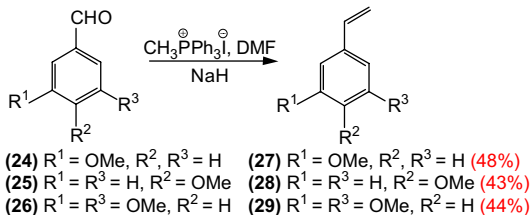


Figure 1.

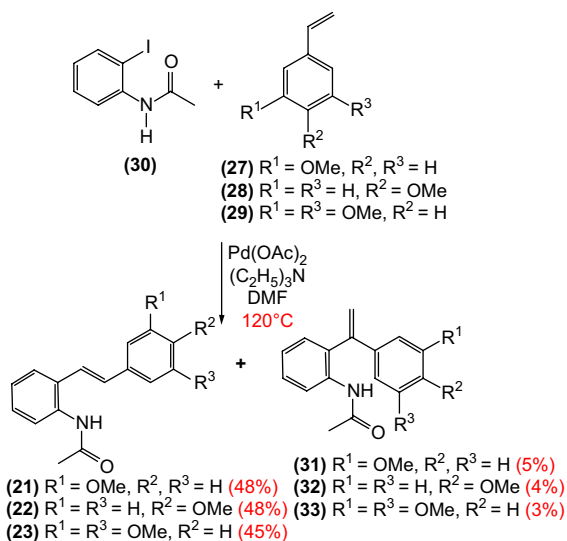
2. Results and discussion

The styrenes (**27**), (**28**) and (**29**) were readily obtained by Wittig methodology from the corresponding aldehydes (Scheme 4); the subsequent Heck coupling proceeded smoothly according to our usual protocol.^{18,19}



Scheme 4.

The three styrenes (**27**), (**28**) and (**29**) were produced in yields of 48%, 43% and 44%, respectively. Heck reactions were performed by heating (120 °C) the corresponding styrenes with 2-iodophenyl-*N*-acetamide¹⁹ (**30**) with Pd(OAc)₂ in dry DMF for 48 h. The corresponding stilbenes (**21**), (**22**) and (**23**) were generated in yields exceeding 40% (Scheme 5).



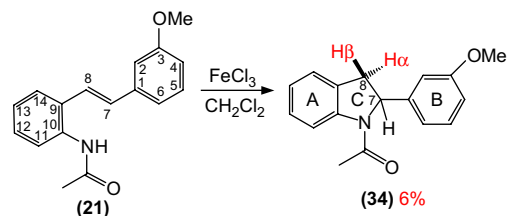
Scheme 5.

The geminally substituted olefins (**31**), (**32**) and (**33**) were obtained as minor products.

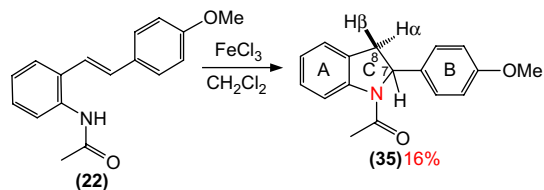
2.1. The Ferric chloride reactions—the moment of truth!

The acetamidostilbene (**21**) was subjected to 'anhydrous' FeCl₃[‡] (as opposed to the hydrated salt) oxidation (1:5 molar ratio). The only isolable product was the indoline (**34**) obtained in 6% yield (Scheme 6).

The influence of substitution pattern in the B-ring of the stilbene was dramatically revealed when the stilbene (**22**) was subjected to FeCl₃ oxidation. In contrast to the previously described chemistry (Scheme 6), the 4-methoxystilbene (**22**) gave rise to the bisindoline (**36**) in 24% yield in addition to indoline (**35**) in 16% yield (Scheme 7).



Scheme 6.



Scheme 7.

With respect to the bisindoline (**36**), spectroscopic agreement with its previously described analogue (**12**) (Scheme 2) was observed. Thus the H-7 resonated at δ 4.66 as a singlet as did H-8 (δ 3.48 and also a singlet). These features are consistent with the symmetrical structure and stereochemical assignments have been made by comparison with previously published determinations, both mechanistic¹⁹ and computational¹⁹ (AM 1).

We must now address a quite unexpected development made as a result of the FeCl₃ oxidation of the 3,5-dimethoxy acetamidostilbene (**23**), as fully described in the next section.

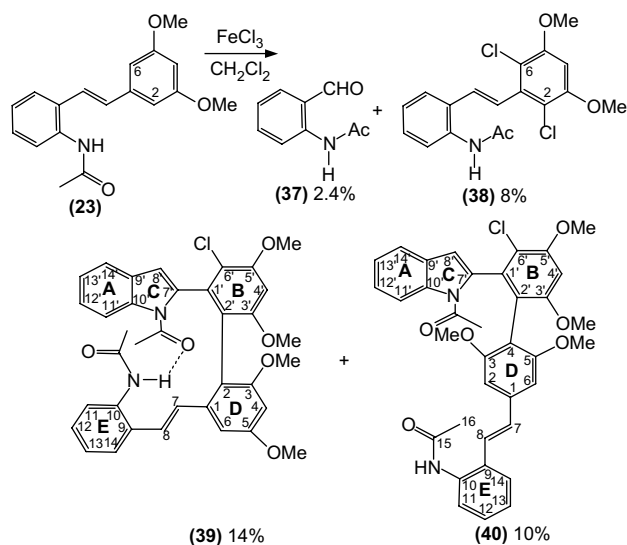
2.2. The unprecedented construction of the axially chiral (racemic) stilbenes incorporating an indole moiety

That 3,5-dimethoxy substitution should profoundly influence stilbene radical cation reactivity compared to 3,4-dimethoxy substitution was to be expected. What was not foreseen was the radical departure from the pattern observed for 3-methoxyacetamidostilbene (**21**) (Scheme 6).

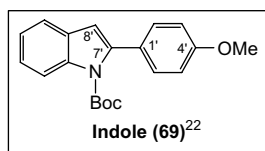
Subjection of (**23**) to our oxidative protocol produced *ortho*-acetamidobenzaldehyde (**37**), a dichlorostilbene monomer (**38**) and two dimers (**39**) and (**40**), each of the latter contained a clearly intact stilbene olefinic bond (Scheme 8). We suspect that oxidative cleavage of (**23**) (for example) leading to water-soluble products (e.g., carboxylic acids) is a major factor for the low yields in these and previously described reactions.[‡]

[‡] Strictly speaking 'anhydrous' FeCl₃ does absorb small amounts of water due to its hygroscopic character.

[‡] Oxidation of (**23**) would produce two aldehydes, however, the 3,5-dimethoxybenzaldehyde undergoes faster oxidation to the water soluble carboxylic acid (**50**) and (unlike (**37**)) is therefore not isolated. The electrochemical oxidative cleavage of alkenes has been described by Fry.³⁴



In examining **(39)** and **(40)**, two stereogenic axes (biaryl linkages) have been installed. This is a unique structural feature (when set in the context of an arrangement incorporating biphenyl, stilbene and indole moieties in the same molecule) although other oxidative methods for constructing the biaryl linkage are known.^{8–10,21}



2.3. Spectroscopic features

The comparison of the spectroscopic features of these two unprecedented structures with previously published indole (**69**)²² is instructive. The H-2, H-6 doublets (see **23**, Scheme 8 and indole (**69**)) are clearly absent in **(39)** and **(40)**. The corresponding carbons (C-2' and C-6') in **(39)**, at δ 120.6 and 115.7, are considerably more deshielded than the corresponding carbons of starting acetamidostilbene (**23**) (δ 105.0). The disruption of symmetry in ring B of **(39)** when compared to **(38)** should be duly noted along with the C-2' ¹³C chemical shift. Replacement of a chlorine in **(38)** with an aromatic ring (D) in **(39)** has resulted in a greater deshielding of the C-2' (δ 120.6) in **(39)** compared to 114.0 in **(38)**.

It should also be noticed that the carbons connected by the stereogenic axis between indole ring C and ring B (C-7' and C-1') (Scheme 8) are significantly more deshielded in **(39)** compared to the indole (**69**)²² probably reflecting the radical departure from coplanarity with respect to these rings (**39**) and the reduced sp^2 character (increased sp^3 character) of these carbons. The C-2' (δ 120.6) in **(39)** is noticeably more deshielded than the C-2 of the acetamidodichlorostilbene (**38**) in spite of the presence of an electron withdrawing chlorine. This is another indication of the profound effect of two new stereogenic axes in **(39)**.

Analogous arguments could be made regarding dimer (**40**) where the point of attachment of ring D to ring B is different. The H-4 doublet (δ 6.08) in **(39)** (ring D) is clearly absent in **(40)**. The C-4 in **(39)** (ring D) (δ 98.1) is found in **(40)** at δ 113.3. Once again we observe a phenomenon to which we have previously referred. It

Table 1
¹H NMR [400 MHz, δ_H (J, Hz)] and ¹³C NMR [100 Hz, δ_C] in CDCl₃

No.	(39)		(40)	
	[M ⁺ +Na]=648.1998 (calcd 648.1998)		[M ⁺ +H]=625.2111 (calcd 625.2105)	
	¹ H (J Hz)	¹³ C	¹ H (J Hz)	¹³ C
1	—	138.9	—	138.2
2	—	116.1	6.48 (s)	102.0
3	—	157.7	—	157.5
4	6.08 (s)	98.1	—	113.3
5	—	160.2	—	157.7
6	6.48 (s)	102.5	6.48 (s)	102.6
7	6.65 (d, 16.0)	131.1	6.77 (d, 16.0)	133.1
8	6.82 (d, 16.0)	128.0	6.96 (d, 16.0)	123.9
9	—	130.4	—	130.3
10	—	135.6	—	134.7
11	7.85 (d, 8.2)	124.9	7.76 (d, 7.8)	124.2
12	7.26 (t, 8.2)	128.5	7.25 (t, 7.8)	128.5
13	7.08 (t, 8.2)	125.0	7.13 (t, 7.8)	125.6
14	7.85 (d, 8.2)	127.3	7.37 (d, 7.8)	127.1
1'	—	134.4	—	134.7
2'	—	120.6	—	118.9
3'	—	156.4	—	155.3
4'	6.72 (s)	97.5	6.72 (s)	97.7
5'	—	155.5	—	158.3
6'	—	115.7	—	115.6
7'	—	136.4	—	135.7
8'	6.42 (s)	112.6	6.36 (s)	111.4
9'	—	129.0	—	129.1
10'	—	136.5	—	137.0
11'	8.03 (d, 8.2)	115.8	8.34 (d, 8.2)	117.0
12'	7.21 (t, 8.2)	124.8	7.22 (t, 8.2)	124.7
13'	7.16 (t, 8.2)	123.6	7.19 (t, 8.2)	123.2
14'	7.39 (d, 8.2)	120.4	7.39 (d, 8.2)	127.1
3-Ome	3.59 (s)	55.4	3.78 (s)	56.6
5-Ome	3.67 (s)	55.3	3.61 (s)	55.3
3'-Ome	3.85 (s)	56.4	4.00 (s)	56.5
5'-Ome	3.99 (s)	56.6	3.74 (s)	55.8
NH	8.86 (s)	—	—	—
NHC=O	—	169.7	—	168.8
NHCO-CH ₃	2.36 (s)	24.2	2.30 (s)	24.5
NC=O	—	172.3	—	171.4
NCO-CH ₃	1.88 (s)	26.3	2.14 (s)	25.2

must be borne in mind that sp^2 carbons have higher s character and are more electronegative than sp^3 carbons. The C-4 carbon that is now located at a stereogenic axis (C-4 \leftrightarrow C-2' in **(40)**) is now more deshielded than the corresponding C-4 in **(39)** because of increased steric hindrance (barriers to rotation), which results in reduced sp^2 (increased sp^3 or lower % of s character) on the carbon and concomitant greater deshielding.

We see this phenomenon in relation to the C-2 carbon in **(40)** (δ 102.0) (ring D). Note that the C-2 and C-6 carbons are close to being but not quite equivalent (Table 1). Once the C-2 carbon (ring D) is bound to C-2' of ring B as in **(39)** its chemical shift changes to δ 116.0. These observations confirm the location of the stereogenic axes C-7' \leftrightarrow C-1'-C-2' \leftrightarrow C-2 (**39**) and C-7' \leftrightarrow C-1'-C-2' \leftrightarrow C-4 (**40**). These connectivities are confirmed by HSQC and HMBC correlations. Stereochemical relationship in **(39)** and **(40)** were established by computational calculations (PM6²³/MOPAC2007²⁴) and NOESY correlations (Figs. 2 and 3). One critical observation is NH signal in **(39)** at δ 8.86. The 3-dimensional arrangement corresponding to conformational isomer **(39)** incorporating H-bonding (missing in **40**) has been determined. This data have enabled us to confirm the structures of both atropodiastereoisomers **(39)** and **(40)** demonstrating the remarkable atropodiastereoselective nature of this stilbene radical cation mediated transformation. The 14-membered pseudo-macrocytic structure **(39)**, made possible by intramolecular H bonding, is unique (in the stilbenoid-indole field).

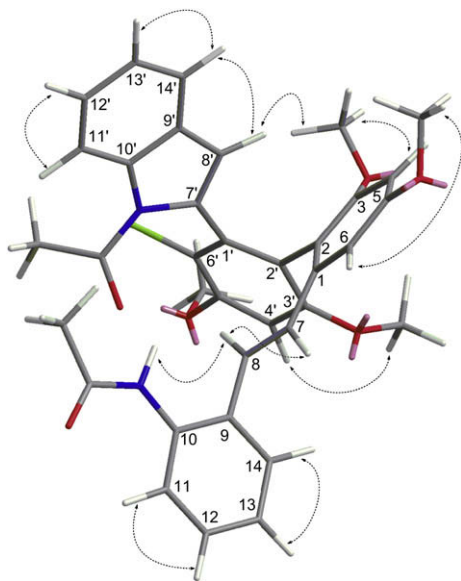


Figure 2. Selected NOESY correlations chloroindolostilbene (**39**).

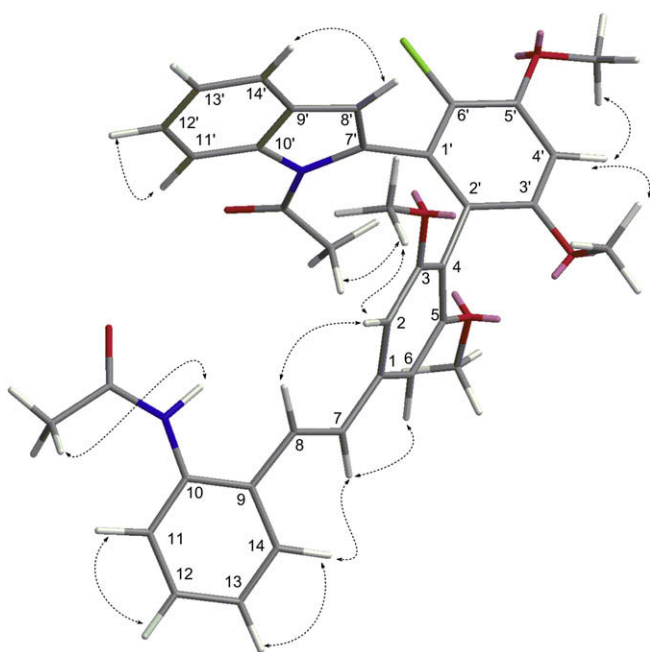


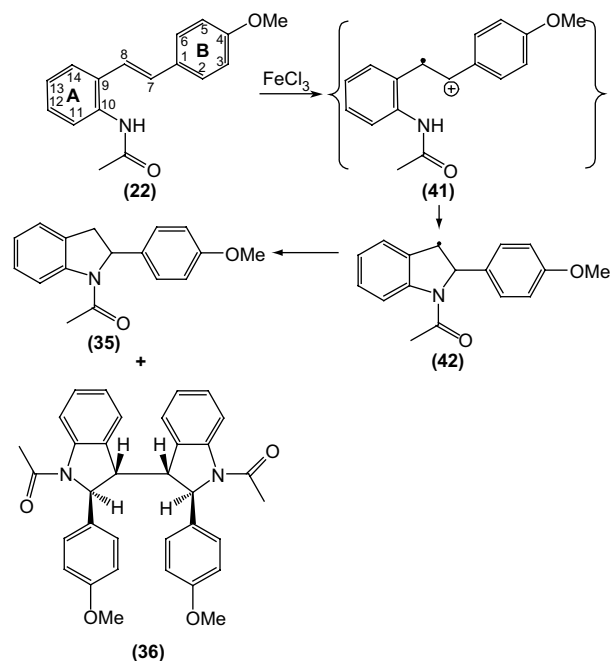
Figure 3. Selected NOESY correlations chloroindolostilbene (**40**).

whose site-specificity is explainable based on frontier orbital considerations.²⁵

The remarkable regioselectivity of our FeCl₃, 3,4-dimethoxy-12-acetoxystilbene dimerizations seem to us to require a radical cation–radical cation union.¹⁸

The classic synthesis of usnic acid by Barton²⁶ exploited the one-electron oxidant [K₃Fe(CN)₆] and was rationalized as proceeding via the generation and coupling of delocalized phenoxy radicals (the heterodimerization of resonance contributors).²⁷ A more recent demonstration of single electron transfer was described by Baran²⁷ in his direct indole and pyrrole coupling using copper(II) 2-ethylhexanoate. Mechanistically, Baran favours a radical–radical (or radical anion–radical) dimerization assisted by chelation to the copper reagent.²⁷ Chelation could play a vital role in our FeCl₃ oxidative couplings.

Steckhan²⁸ in 1978 described extensive spectroelectrochemical studies in the stilbene field. The anodic oxidation of 4,4'-dimethoxystilbene²⁶ gave rise to tetrahydronaphthalene and tetrahydrofuran dimers. His detailed experiments (including kinetic evaluations) pointed to two pathways: radical cation–radical cation and radical cation–neutral molecule, with the former predominating in the absence of methanol.²⁸ Further examples of stilbene radical dimerization may be seen in the work of Niwa²⁹ and Lin.^{30–32} Nelson's³¹ comprehensive discussion on the possible resonance forms for 4-methoxytriphenylaminium³³ cation radicals and the subsequent dimerization is worthy of careful study.



Scheme 9.

It is noteworthy that the bisindoline (**36**) (Scheme 9) is now the major product in contrast to our experience with the dimerization of 3,4-dimethoxystilbene (**8**) (Scheme 2).¹⁹

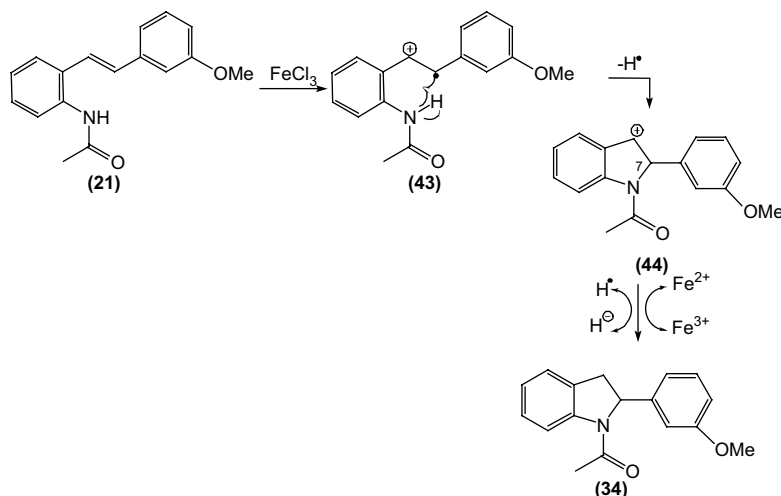
With 3-methoxyacetamidostilbene (**21**), the pathway to the indoline is as shown in Scheme 10.

As previously described (Scheme 8), the 3,5-dimethoxy derivative produced the aldehyde (**37**), dichlorostilbene (**38**) and the unprecedented indolostilbene dimers (**39**) and (**40**). The low yield of the *ortho*-acetamidobenzaldehyde (**37**) suggested to us the minor pathway for its formation as described in Scheme 11.³⁴

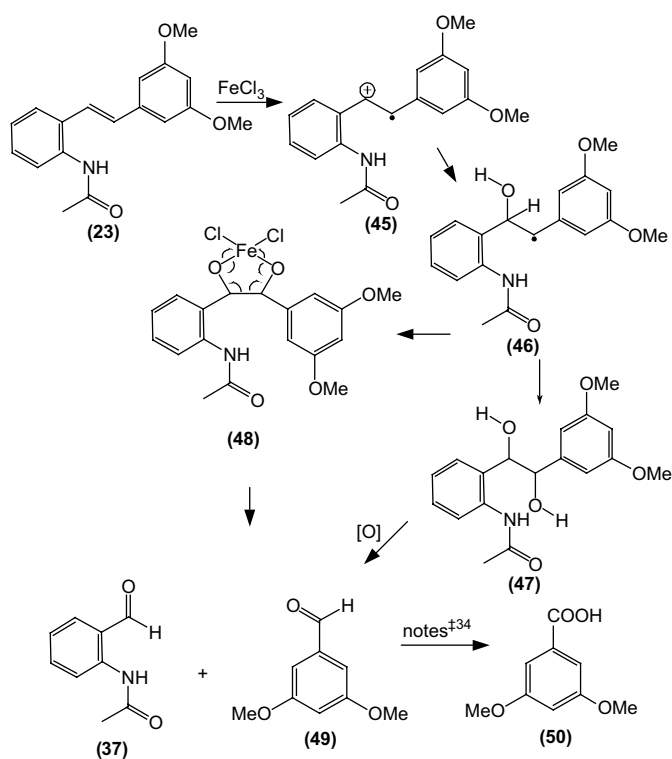
2.4. Mechanistic considerations

The cyclization and dimerization pathways of the stilbene (**22**), incorporating the 4-methoxy substituent, must follow a mechanistic pathway similar to that we previously reported¹⁹ for the 3,4-dimethoxyacetamido stilbene (**8**).

This study like its predecessors (the construction of catechol substituted bisindolines¹⁹ and the benzophenone radical anion phenomenon²⁰), fully vindicates radical cation–radical cation dimerization as a reasonable mechanistic interpretation. Although it is often said that radical coupling²⁰ (or for that matter radical cation coupling) is not a common reaction²⁵ because of the low concentration of the reactive intermediate, the phenomenon is not unknown.²⁵ Radical–radical coupling has been observed for the benzyl and α -nitromethyl radicals



Scheme 10.



Scheme 11.

An alternative pathway that involves the oxygen diradical leading to the dioxetane (52) is shown in Scheme 12.³⁵

The dichlorostilbene monomer (38) could be explained as the product of an electrophilic substitution either via an intermolecular pathway (Scheme 13) or the intramolecular alternative (the azaquinodimethide (55) intermediate) (Scheme 14). Alternatively a radical cation pathway (Scheme 15) may be proposed. Chlorination at C-4 in (23) appears to be prohibited for steric reasons.

Schemes 13 and 14 depict an electrophilic chlorination mechanism. An alternative mechanism that depends on prior generation of the radical cation (45) and clearly implies the presence of chloro radicals ($\cdot\text{Cl}$) is shown in Scheme 15.

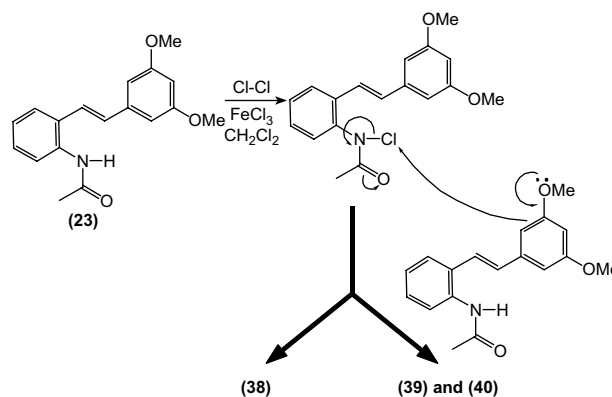
In the anodic chlorination of aromatics (30% CH_2Cl_2 -MeCN containing 0.1 M Et_4NClO_4 and 2,6-lutidine), CH_2Cl_2 is thought to be the source of chlorine.³⁶ This possibility cannot be ruled out although given the number of potential sites for chlorination in our molecules as opposed to those studied by Kam³⁶ it would appear to be less likely. For alternative chlorination pathways see Schemes 13–15.

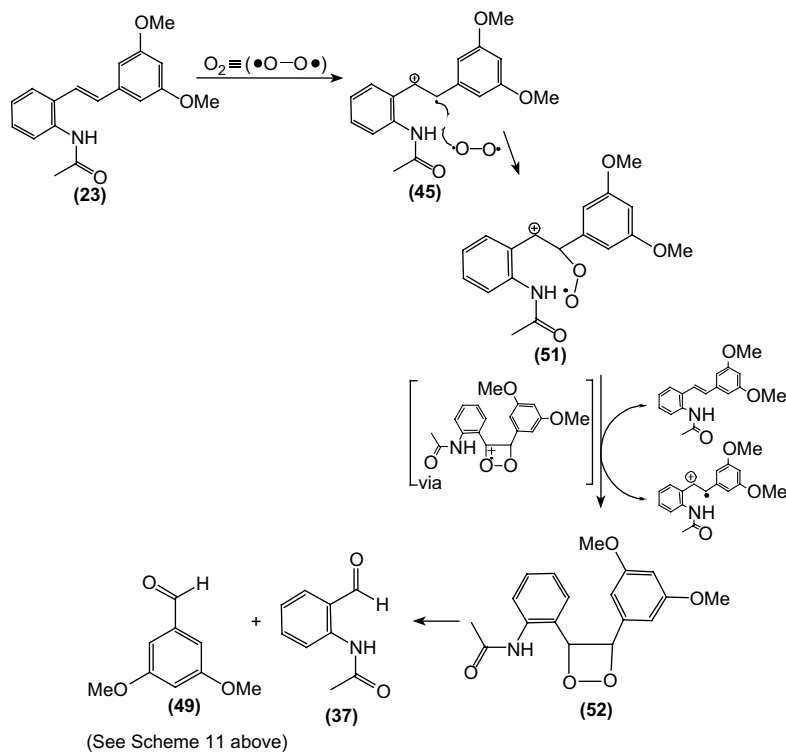
By contrast, Tanemura³⁷ has described halogenation of aromatics by means of FeCl_3 (10 mmol %) in CH_3CN at 100 °C. On balance, an electrophilic chlorination pathway is to be preferred all be it slightly favour electrophilic over free radical chlorination or some combination of the two e.g.[§] (and Scheme 15). The regio-specificity of our chlorinations would appear to favour an electrophilic pathway.

2.5. Pathways leading to indolostilbene dimers (39) and (40)—stereochemical considerations

In accordance with our previous discussion, oxidation of stilbene (23) generates the radical cation (45) from which the indole (58) is obtained (Scheme 16). We note at this point (to which we will return, see Scheme 16) that in contrast to our experience with the 3-methoxyacetamidostilbene (21) (Scheme 10), the 3,5-

[§] By analogy with *N*-chlorosuccinimide promoted electrophilic chlorination, N-H to N-Cl conversion (free radical) would produce the *N*-chloroacetamidostilbene. The electrophilic N-Cl would then be attacked by a second stilbene molecule.

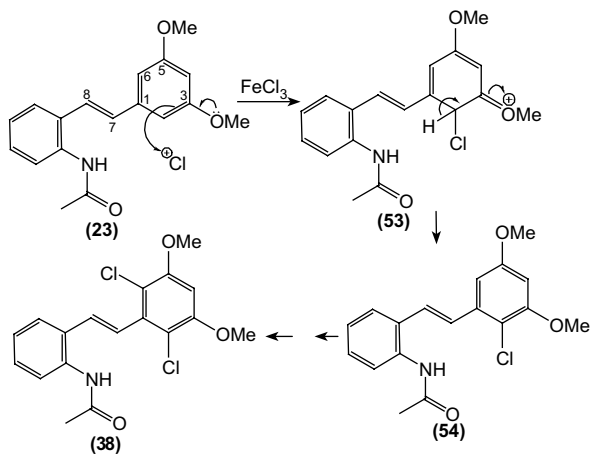




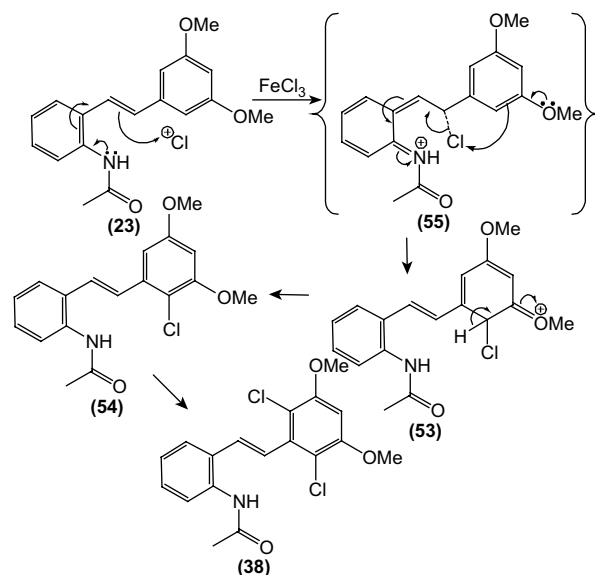
Scheme 12.

dimethoxy analogue appears to undergo the deprotonation necessary for indole (**58**) formation, as opposed to the indoline. This allows us to suggest another way of visualizing the chlorination step. In this alternative, electrophilic chlorination proceeds in contrast to the reactions in Schemes 13–15, via the indolenium species (**59**), Scheme 16. Compound (**61**) is of course a racemate (assuming restricted rotation).

The next scheme (Scheme 17) describes the pathway leading from (**61**) to the indolostilbene. The alignment of the acetamidostilbene (**23**) with the chlorophenylindole (**61**) is guided, it would seem, by hydrogen bonding. Removal of an electron from the olefinic bond of (**23**) produces the radical cation (**62**), which attacks the chlorophenylindole (**61**) as shown. Removal of an electron from the methoxy lone pair sets up the *para*–*para* (or *ortho*–*ortho*)



Scheme 13.

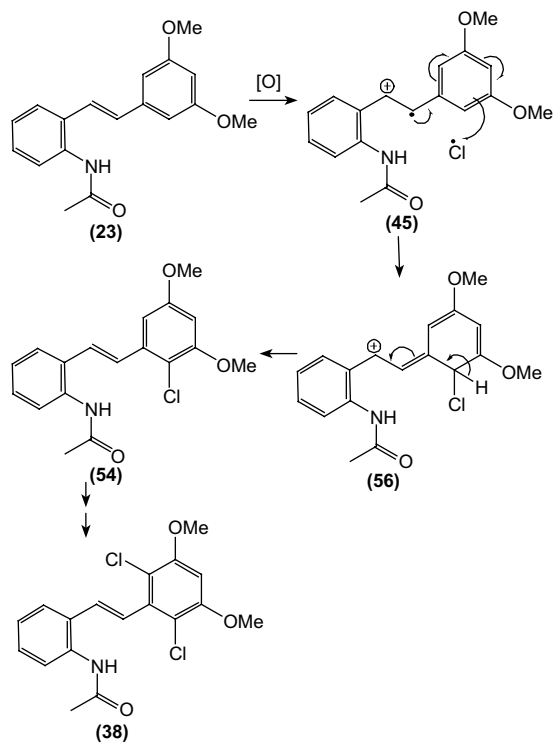


Scheme 14. Indirect pathway (intramolecular).

oxidative coupling. This accounts for the installation of the stereogenic axes between rings B and D.

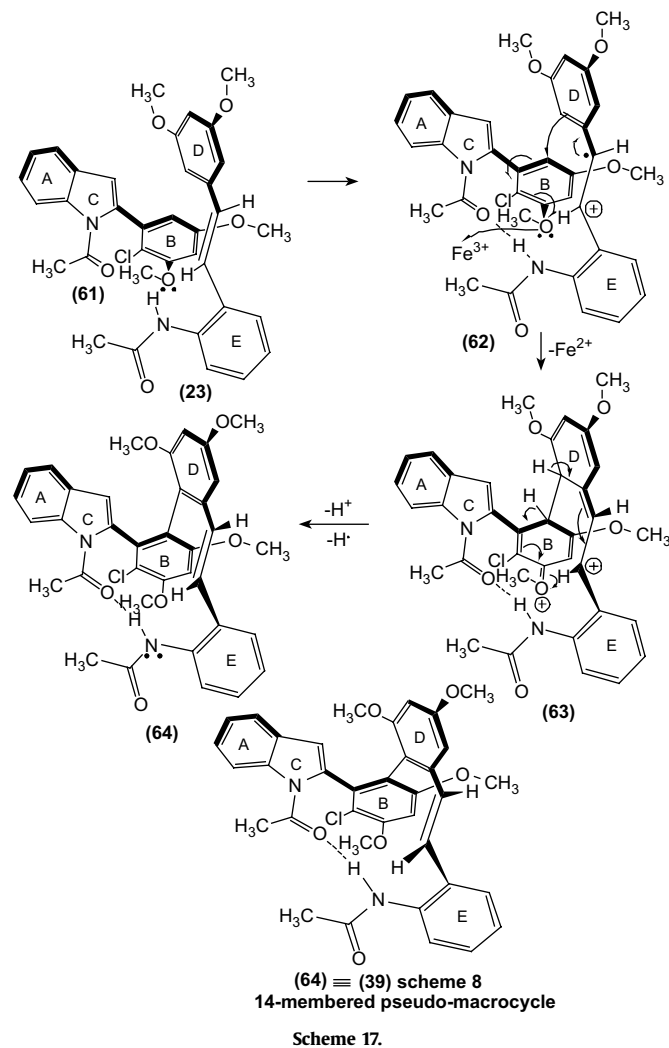
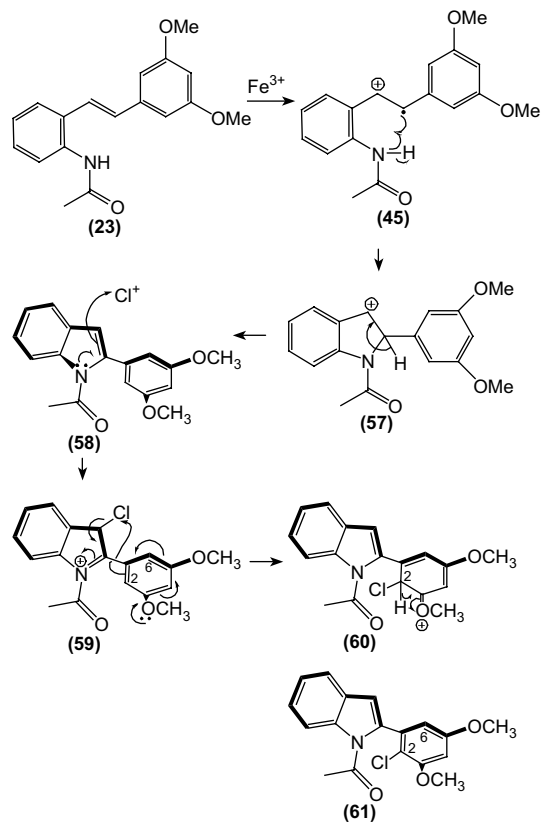
The H-bonded conformational isomer (one of the most stable arrangements but see Fig. 5) (heat of formation of $-134.29 \text{ kcal mol}^{-1}$) with a 2.02 \AA hydrogen bond length (Fig. 4) is in effect a pseudo-macrocycle.

An alternative arrangement that has a different stilbene double bond orientation and a H-bond length of 2.20 \AA is the conformational isomer (Fig. 5) that has a lower heat of formation ($-139.28 \text{ kcal mol}^{-1}$). 3D-representation of these conformations

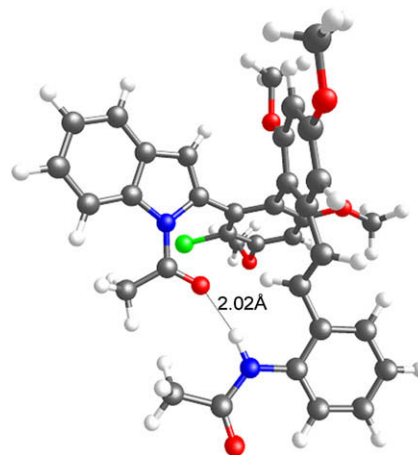


was obtained by PM6²³/MOPAC2007²⁴ determinations and is provided in Figures 4 and 5.

The formation of the second dimer (**40**) is the result of an analogous radical cation mediated *ortho-para* coupling (Scheme 18).



Intramolecular hydrogen bonding is clearly impossible in this case. The PM6²³/MOPAC2007²⁴ determined heat of formation (the lowest) is $-123.41 \text{ kcal mol}^{-1}$ (Fig. 6). PM6²³/MOPAC2007²⁴ calculations indicate the most stable conformational isomers.



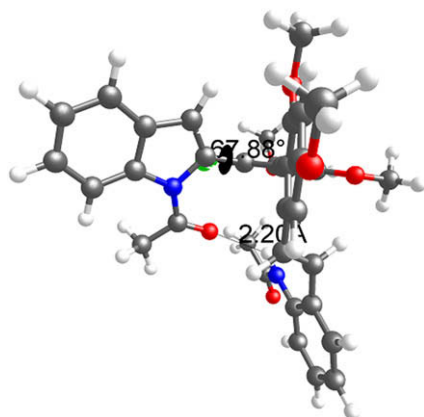
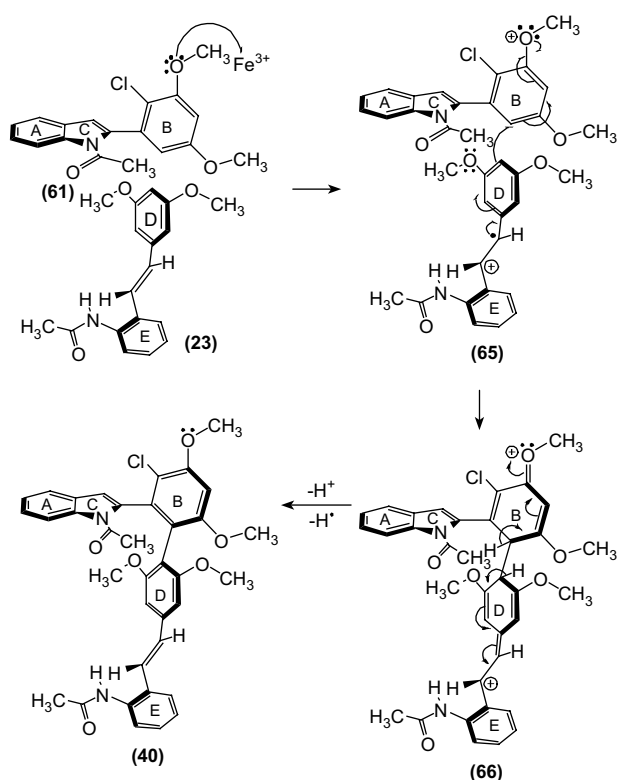
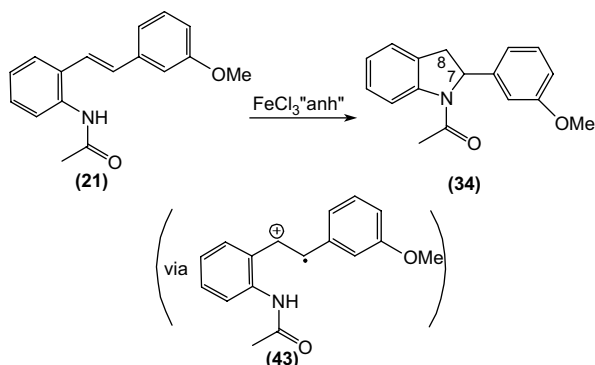


Figure 5.

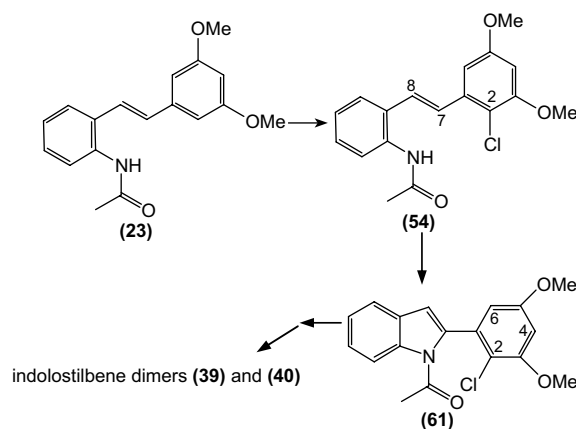


Scheme 18.

We can now return to the problem of indole formation. We observed that the 3-methoxyacetamidostilbene (**21**) did not produce indole but indoline (**34**) on FeCl_3 oxidation (see Scheme 6).



By contrast, 3,5-substitution produces the indole (**61**).



This difference in behaviour may be explained by a ‘charge-radical inversion’. In this process electrophilic chlorination produces stilbene (**54**) and cyclization proceeds to produce chlorodimethoxystilbene (**61**). The 2-chloro substituent in (**54**) (Scheme 19) provides some degree of stabilization for the C-7 carbenium ion through delocalization of Cl lone pairs. This is an alternative interpretation—see our previous hypothesis in Scheme 16.

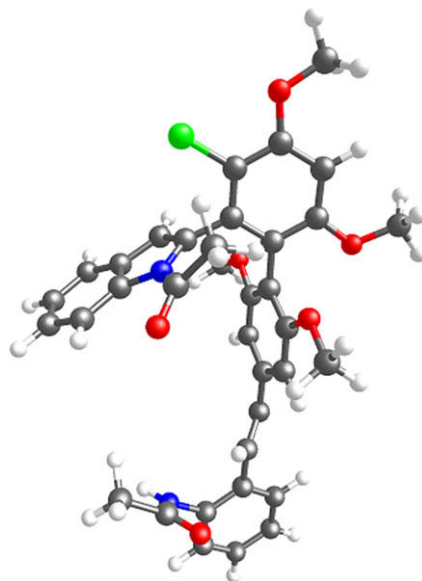
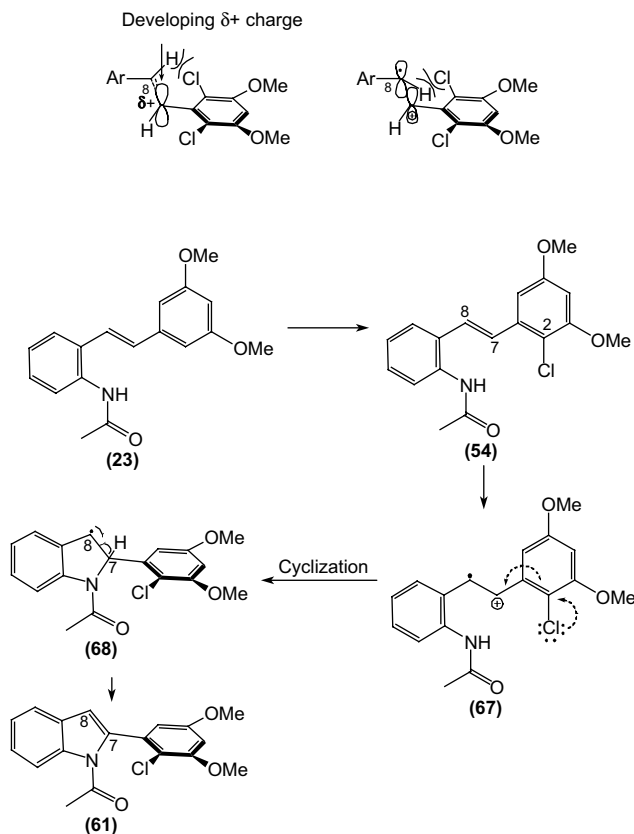


Figure 6.

The indolyl radical (**68**) unlike its analogue (**42**) (Schemes 7 and 9) undergoes rapid loss of H^+ *en route* to indole formation. The orientation of the chlorophenyl ring and the substitution pattern sufficiently modifies indolyl radical (**68**) behaviour given, we presume, a more product-like transition state (early indole double bond formation) between C-7 and C-8. The chlorophenyl ring's orientation and the electron withdrawing Cl substituent may also contribute to inhibition of the bisindoline formation we observed in Scheme 9. With regard to the failure of dichloro derivatives of (**54**) to cyclize (see (**38**), Scheme 14), effective delocalization and hence stabilization of the δ^+ (p-orbital) with respect to a planar dichlorophenyl ring is rendered difficult because of steric inhibition involving the Cl group. In addition, the inductive withdrawal of electrons by the two chlorines may render oxidative radical cation formation more difficult.



Scheme 19.

3. Conclusions

This study culminates in the syntheses of a new class of axially chiral (racemic) indolostilbenes by a FeCl_3 -promoted radical cation mediated cascade reaction. Further developments in this field will be reported in due course.

4. Experimental

4.1. Phase I: preparation of 2-iodophenyl-*N*-acetamide

Iodoaniline (2.5014 g, 0.0114 mol) was dissolved in 20 mL dry dimethylformamide (DMF) and reacted with 0.550 g (0.01375 mol) sodium hydride (NaH) and acetic anhydride (5.435 mL). The mixture was stirred overnight at room temperature under nitrogen. After 24 h, saturated ammonium chloride (aqueous) was added to the reaction mixture followed by extraction with ethyl acetate (3 × 50 mL). The combined ethyl acetate extracts were then washed six times with distilled water to remove DMF. The mixture was then dried over anhydrous sodium sulfate. The crude product, obtained after concentration under reduced pressure, was purified by column chromatography (hexane/ethyl acetate, 4:6) to give 70% yield (2.083 g) of 2-iodophenyl-*N*-acetamide **30** (CAS No. 19591-17-4) as light brown crystals.¹⁹

4.1.1. 2-Iodophenyl-*N*-acetamide **30**¹⁹

MS m/z : 261 [M^+]; UV (MeOH) λ_{max} nm: 223; IR ν_{max} cm^{-1} : 3270, 1660. ^1H NMR (400 MHz, CDCl_3) δ ppm: 8.18 (d, $J=8.0$ Hz, H-14, 1H), 7.75 (d, $J=8.0$ Hz, H-11, 1H), 7.39 (br s, NH, 1H), 7.32 (d, $J=7.3$ Hz, H-13, 1H), 6.82 (d, $J=7.3$ Hz, H-12, 1H), 2.22 (s, CH_3 , 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm: 168.2 (C-15), 138.7 (C-14), 138.1 (C-10), 129.1 (C-12), 126.0 (C-13), 122.2 (C-11), 90.2 (C-9), 24.7 (C-16).

4.2. Phase II: preparation of protected styrenes

4.2.1. Preparation of 3-methoxystyrene **27**

Methyltriphenylphosphonium iodide (9.72 g, 0.0240 mol) was stirred in dry DMF (20 mL) at 0 °C for 0.5 h in a two-necked round bottomed flask. Sodium hydride (3.30 g, 0.1375 mol) and 3-methoxybenzaldehyde **24** (3.0 mL, 0.025 mol) were then added. The temperature was maintained between 0 and 4 °C under nitrogen for 4 h. The mixture was allowed to stir at room temperature overnight. When the product was obtained (based on the TLC), an aqueous solution of NH_4Cl (25 mL) was added. The mixture was transferred to a separating funnel and extracted with ethyl acetate (3 × 25 mL). The organic layer was then washed with distilled water and dried over anhydrous sodium sulfate. The crude extract was purified by column chromatography (hexane/ethyl acetate, 99.6:0.4) to yield 3-methoxystyrene **27**³⁸ as a light yellowish oil (1.4405 g, 43% yield).

4.2.1.1. 3-Methoxystyrene **27**³⁸. MS m/z : 134 [M^+]; UV (MeOH) λ_{max} nm: 266, 221; IR ν_{max} cm^{-1} : 1603, 1517. ^1H NMR (400 MHz, CDCl_3) δ ppm: 7.23 (t, $J=8.0$ Hz, H-5, 1H), 6.99 (d, $J=8.0$ Hz, H-6, 1H), 6.93 (t, $J=2.0$ Hz, H-2, 1H), 6.79 (dd, $J=2.4, 8.0$ Hz, H-4, 1H), 6.67 (dd, $J=11.0, 17.6$ Hz, H-7, 1H), 5.73 (d, $J=17.6$ Hz, H-8a, 1H), 5.24 (d, $J=11.0$ Hz, H-8b, 1H), 3.81 (s, OCH_3 , 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm: 159.7 (C-3), 139.0 (C-1), 136.8 (C-7), 129.5 (C-5), 118.9 (C-6), 114.1 (C-8), 113.4 (C-4), 111.5 (C-2), 55.2 (OCH_3).

4.2.2. Preparation of 4-methoxystyrene **28**

Methyltriphenylphosphonium iodide (8.8409 g, 0.02186 mol) was stirred in dry DMF (20 mL) at 0 °C for 0.5 h in a two-necked round bottomed flask. Sodium hydride (3.3349 g, 0.14 mol) and 4-methoxybenzaldehyde **25** (2.75 mL, 0.02263 mol) were then added. The temperature was maintained between 0 and 4 °C under nitrogen for 4 h. The mixture was allowed to stir at room temperature overnight. When starting material was consumed (based on the TLC), an aqueous solution of NH_4Cl (25 mL) was added. The mixture was transferred to a separating funnel and extracted with ethyl acetate (3 × 25 mL). The organic layer was then washed with distilled water and dried over anhydrous sodium sulfate. The crude extract was purified by column chromatography (hexane/ethyl acetate, 99:1) to yield 4-methoxystyrene **28**^{38,39} (1.456 g, 48% yield) in the form of a light yellowish oil.

4.2.2.1. 4-Methoxystyrene **28**^{38,39}. MS m/z : 134 [M^+]; UV (MeOH) λ_{max} nm: 266, 221; IR ν_{max} cm^{-1} : 1603, 1516. ^1H NMR (400 MHz, CDCl_3) δ ppm: 7.34 (d, $J=8.8$ Hz, H-2, H-6, 1H), 6.86 (d, $J=8.8$ Hz, H-3, H-5, 1H), 6.66 (dd, $J=10.7, 17.6$ Hz, H-7, 1H), 5.61 (dd, $J=1.0, 17.6$ Hz, H-8a, 1H), 5.12 (dd, $J=1.0, 10.7$ Hz, H-8b, 1H), 3.82 (s, OCH_3 , 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm: 159.3 (C-4), 136.2 (C-7), 130.4 (C-1), 127.4 (C-2, C-6), 113.9 (C-8), 111.5 (C-3, C-5), 55.2 (OCH_3).

4.2.3. Preparation of 3,5-dimethoxystyrene **29**

Methyltriphenylphosphonium iodide (2.4264 g, 0.006 mol) was stirred in dry DMF (20 mL) at 0 °C for 0.5 h in a two-necked round bottomed flask. Potassium *tert*-butoxide (0.6917 g, 0.006 mol) and 3,5-dimethoxybenzaldehyde **26** (1.000 g, 0.006 mol) were then added. The temperature was maintained between 0 and 4 °C under nitrogen for 4 h. Then the mixture was allowed to stir at room temperature overnight. When starting material was consumed (based on the TLC), an aqueous solution of NH_4Cl (25 mL) was added. The mixture was transferred to a separating funnel and extracted with ethyl acetate (3 × 25 mL). The organic layer was then washed with distilled water and dried over anhydrous sodium sulfate. The crude extract was purified by column chromatography (hexane/ethyl acetate, 90:10), which afforded **29**⁴⁰ (0.443 g, 44% yield) in the form of a light yellowish oil.

4.2.3.1. *3,5-Dimethoxystyrene* **29**⁴⁰. MS m/z : 164 [M⁺]; UV (MeOH) λ_{\max} nm: 266, 221; IR ν_{\max} cm⁻¹: 1603, 1516. ¹H NMR (400 MHz, CDCl₃) δ ppm: 6.68 (dd, $J=10.8, 17.6$ Hz, H-7, 1H), 6.61 (d, $J=2.0$ Hz, H-2, H-6, 2H), 6.43 (d, $J=2.0$ Hz, H-4, 1H), 5.77 (d, $J=17.6$ Hz, H-8a, 1H), 5.28 (d, $J=10.8$ Hz, H-8b, 1H), 3.82 (s, 2×OCH₃, 6H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 160.8 (C-3, C-5), 139.4 (C-1), 136.7 (C-7), 114.0 (C-8), 104.1 (C-2, C-6), 99.8 (C-4), 55.0 (2×OCH₃).

4.3. Phase III: synthesis of stilbenes

4.3.1. Synthesis of 3-methoxystilbene (21)

2-Iodophenyl-*N*-acetamide **30** (1.2046 g, 4.62 mmol) was dissolved in 10 mL dry DMF in a clean dry two-necked round bottomed flask. The solution was heated to 120 °C and stirred under nitrogen. Palladium(II) acetate (0.023 g, 0.1025 mmol) was added to the solution followed by triethylamine (2.6 mL, 0.187 mmol) and 3-methoxystyrene **27** (0.6216 g, 4.64 mmol). The mixture was refluxed under nitrogen for 48 h. After this period, the reaction mixture was filtered and saturated aqueous sodium chloride (25 mL) added. The mixture was then extracted with ethyl acetate (3×25 mL) and the combined extracts were dried over anhydrous sodium sulfate. Finally the crude extract was purified by column chromatography (hexane/ethyl acetate, 50:50) to give 3-methoxystilbene **21** (0.5923 g, 48%) as amorphous white solid and its isomer **31** (62 mg, 5%) as a brownish oil.

4.3.1.1. *3-Methoxystilbene* (**21**). HRESIMS m/z : 268.1334 ([M+H]⁺; calcd for C₁₇H₁₈NO₂, 268.1338); UV (MeOH) λ_{\max} nm: 300, 240, 203; IR ν_{\max} cm⁻¹: 3040, 1650, 1219, 773. ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.76 (d, $J=8.0$ Hz, H-11, 1H), 7.50 (d, $J=8.0$ Hz, H-14, 1H), 7.27 (t, $J=8.0$ Hz, H-12, 1H), 7.25 (t, $J=8.0$ Hz, H-5, 1H), 7.16 (t, $J=8.0$ Hz, H-13, 1H), 7.10 (d, $J=16.1$ Hz, H-8, 1H), 7.07 (d, $J=4.0$ Hz, H-6, 1H), 7.01 (t, $J=4.0$ Hz, H-2, 1H), 6.93 (d, $J=16.1$ Hz, H-7, 1H), 6.83 (dd, $J=2.4, 8.0$ Hz, H-4, 1H), 3.82 (s, OCH₃, 3H), 2.18 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 168.6 (C-15), 159.9 (C-3), 138.4 (C-1), 134.6 (C-10), 132.4 (C-7), 130.2 (C-9), 129.7 (C-5), 128.4 (C-12), 126.9 (C-14), 125.6 (C-13), 124.3 (C-11), 123.8 (C-8), 119.3 (C-6), 113.4 (C-4), 112.3 (C-2), 55.3 (OCH₃), 24.3 (C-16).

4.3.1.2. *N*-[2-[1-(3-Methoxyphenyl)vinyl]phenyl]acetamide (**31**). HRESIMS m/z : 268.1324 ([M+H]⁺; calcd for C₁₇H₁₈NO₂, 268.1338); UV (MeOH) λ_{\max} nm: 290, 250, 210; IR ν_{\max} cm⁻¹: 3291, 1673, 1041, 752. ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.09 (d, $J=8.0$ Hz, H-11, 1H), 7.33 (t, $J=8.0$ Hz, H-12, 1H), 7.25 (d, $J=8.0$ Hz, H-14, 1H), 7.23 (t, $J=8.0$ Hz, H-5, 1H), 7.13 (t, $J=8.0$ Hz, H-13, 1H), 6.88 (d, $J=8.0$ Hz, H-6, 1H), 6.84 (d, $J=8.0$ Hz, H-4, 1H), 6.81 (br s, H-2, 1H), 5.83 (s, H-8a, 1H), 5.34 (s, H-8b, 1H), 3.73 (s, OCH₃, 3H), 1.78 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 168.2 (C-15), 159.9 (C-3), 146.2 (C-7), 140.9 (C-1), 135.1 (C-10), 132.0 (C-9), 130.3 (C-14), 129.9 (C-5), 128.8 (C-12), 124.4 (C-13), 122.0 (C-11), 119.0 (C-6), 117.6 (C-8), 113.9 (C-4), 112.2 (C-2), 55.3 (OCH₃), 24.3 (C-16).

4.3.2. Synthesis of 4-methoxystilbene (22)

2-Iodophenyl-*N*-acetamide **30** (0.747 g, 2.86 mmol) was dissolved in 10 mL dry DMF in a clean dry two-necked round bottomed flask. The solution was heated to 120 °C and allowed to stir under nitrogen. Palladium(II) acetate (0.0138 g, 0.06147 mmol) was added to the solution followed by triethylamine (1.7 mL, 0.122 mmol) and 4-methoxystyrene **28** (0.4015 g, 3.00 mmol). The mixture was refluxed under nitrogen for 48 h. After this period, the reaction mixture was then filtered and an aqueous sodium chloride solution (25 mL) was added. The mixture was then extracted with ethyl acetate (3×25 mL) and the combined extracts were dried over anhydrous sodium sulfate. Finally the crude extract was purified by column chromatography (hexane/ethyl acetate, 50:50) to give

a 48% yield of 3-methoxystilbene **22** (0.3649 g) as amorphous white solid and 4% of its isomer **32** (30 mg) as brownish oil.

4.3.2.1. *4-Methoxystilbene* (**22**). HRESIMS m/z : 268.1335 ([M+H]⁺; calcd for C₁₇H₁₈NO₂, 268.1338); UV (MeOH) λ_{\max} nm: 306, 220, 200; IR ν_{\max} cm⁻¹: 3007, 1737, 1662, 1034, 770. ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.72 (d, $J=8.0$ Hz, H-11, 1H), 7.49 (d, $J=8.0$ Hz, H-14, 1H), 7.48 (br s, NH, 1H), 7.42 (d, $J=9.0$ Hz, H-2, H-6, 2H), 7.22 (t, $J=8.0$ Hz, H-12, 1H), 7.14 (t, $J=8.0$ Hz, H-13, 1H), 6.98 (d, $J=16.1$ Hz, H-7, 1H), 6.91 (d, $J=16.1$ Hz, H-8, 1H), 6.89 (d, $J=9.0$ Hz, H-3, H-5, 2H), 3.82 (s, OCH₃, 3H), 2.16 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 168.8 (C-15), 159.5 (C-4), 134.4 (C-10), 131.6 (C-7), 130.7 (C-9), 129.8 (C-1), 127.9 (C-2, C-6), 127.8 (C-12), 126.4 (C-14), 125.5 (C-13), 124.4 (C-11), 121.2 (C-8), 114.1 (C-3, C-5), 55.3 (OCH₃), 24.1 (C-16).

4.3.2.2. *N*-[2-[1-(4-Methoxyphenyl)vinyl]phenyl]acetamide (**32**). HRESIMS m/z : 268.1324 ([M+H]⁺; calcd for C₁₇H₁₈NO₂, 268.1338); UV (MeOH) λ_{\max} nm: 302, 270, 202; IR ν_{\max} cm⁻¹: 3300, 2841, 1737, 1673, 1032, 753. ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.17 (d, $J=8.0$ Hz, H-11, 1H), 7.36 (t, $J=8.0$ Hz, H-12, 1H), 7.27 (d, $J=8.0$ Hz, H-14, 1H), 7.26 (d, $J=9.0$ Hz, H-2, H-6, 2H), 7.15 (t, $J=8.0$ Hz, H-13, 1H), 7.09 (br s, NH, 1H), 6.86 (d, $J=9.0$ Hz, H-3, H-5, 2H), 5.78 (s, H-8a, 1H), 5.25 (s, H-8b, 1H), 3.80 (s, OCH₃, 3H), 1.84 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 168.3 (C-15), 160.0 (C-4), 145.6 (C-7), 135.3 (C-10), 132.1 (C-9), 131.8 (C-1), 130.3 (C-14), 128.7 (C-12), 127.9 (C-2, C-6), 124.3 (C-13), 124.3 (C-13), 121.7 (C-11), 115.4 (C-8), 114.2 (C-3, C-5), 55.4 (OCH₃), 24.5 (C-16).

4.3.3. Synthesis of 3,5-dimethoxystilbene (23)

2-Iodophenyl-*N*-acetamide **30** (1.02511 g, 3.93 mmol) was dissolved in 10 mL dry DMF in a clean dry two-necked round bottomed flask. The solution was heated to 120 °C and allowed to stir under nitrogen. Palladium acetate (16.5 mg, 0.0735 mmol) was added to the solution followed by triethylamine (1.938 mL, 0.139 mmol) and 3,5-dimethoxystyrene **29** (0.7817 g, 4.77 mmol). The mixture was refluxed under nitrogen for 48 h. After this period, the reaction mixture was then filtered and an aqueous solution of sodium chloride (25 mL) was added. The mixture was then extracted with ethyl acetate (3×25 mL) and the combined extracts were dried over anhydrous sodium sulfate. Finally the crude extract was purified by column chromatography (hexane/ethyl acetate, 40:60) to give 45% yield of 3,5-dimethoxystilbene **23** (0.52 g) as amorphous white solid and 3% of its isomer **33** (35 mg) as a brownish oil.

4.3.3.1. *3,5-Dimethoxystilbene* (**23**). HRESIMS m/z : 298.1430 ([M+H]⁺; calcd for C₁₈H₂₀NO₃, 298.1443); UV (MeOH) λ_{\max} nm: 305, 215; IR ν_{\max} cm⁻¹: 3262, 1654, 1153, 773. ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.77 (d, $J=8.0$ Hz, H-11, 1H), 7.49 (d, $J=8.0$ Hz, H-14, 1H), 7.27 (t, $J=8.0$ Hz, H-12, 1H), 7.20 (br s, NH, 1H), 7.15 (t, $J=8.0$ Hz, H-13, 1H), 7.08 (d, $J=16.1$ Hz, H-8, 1H), 6.88 (d, $J=16.1$ Hz, H-7, 1H), 6.63 (d, $J=2.2$ Hz, H-2, H-6, 2H), 6.41 (t, $J=2.2$ Hz, H-4, 1H), 3.82 (s, 2×OCH₃, 6H), 2.19 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 168.8 (C-15), 161.1 (C-3, C-5), 139.1 (C-1), 134.7 (C-10), 132.4 (C-7), 130.3 (C-9), 128.4 (C-12), 126.9 (C-14), 125.7 (C-13), 124.4 (C-11), 124.2 (C-8), 105.0 (C-2, C-6), 100.1 (C-4), 55.4 (C-3, C-5), 24.3 (C-16).

4.3.3.2. *N*-[2-[1-(3,5-Dimethoxyphenyl)vinyl]phenyl]acetamide (**33**). HRESIMS m/z : 298.1426 ([M+H]⁺; calcd for C₁₈H₂₀NO₃, 298.1443); UV (MeOH) λ_{\max} nm: 303, 210; IR ν_{\max} cm⁻¹: 3009, 1677, 1156, 752. ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.08 (d, $J=8.0$ Hz, H-11, 1H), 7.33 (t, $J=8.0$ Hz, H-12, 1H), 7.32 (d, $J=8.0$ Hz, H-14, 1H), 7.12 (t, $J=8.0$ Hz, H-13, 1H), 6.99 (br s, NH, 1H), 6.41 (d, $J=2.4$ Hz, H-2, H-4, H-6, 3H), 5.81 (s, H-8a, 1H), 5.33 (s, H-8b, 1H), 3.71 (s, 2×OCH₃, 6H), 1.82 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 168.1 (C-15), 161.0 (C-3, C-5), 146.3 (C-7), 141.6 (C-1), 135.1 (C-10), 131.8 (C-9), 130.1 (C-14),

128.7 (C-12), 124.3 (C-13), 122.0 (C-11), 117.6 (C-8), 104.7 (C-2, C-6), 100.2 (C-4), 55.3 (2×OCH₃), 24.2 (C-16).

4.4. Phase IV: ferric chloride oxidative coupling and cyclization

Acetamidostilbene **23** (0.2775 g, 0.9343 mmol) was dissolved in 10 mL dichloromethane. 'Anhydrous' FeCl₃ (0.7578 g, 4.672 mmol) was then added to the mixture under nitrogen. The mixture was stirred for 7 h at room temperature and monitored by TLC. After the consumption of the starting material, the reaction mixture was diluted with an aqueous ammonium chloride solution and extracted with ethyl acetate (3×25 mL). The combined ethyl acetate extracts were dried over anhydrous sodium sulfate. The crude product was finally purified by column chromatography (hexane/ethyl acetate; 80:20, 70:40; toluene/ethyl acetate; 80:20 and 70:30), which afforded four compounds, **37**,⁴¹ **38**, **39** and **40** in 2.4% (12 mg), 8% (18 mg), 14% (18 mg) and 10% (13 mg) yields, respectively.

The reaction described above was repeated on stilbenes **21** (0.0978 g, 36.629 mmol) and **22** (0.1089 g, 40.787 mmol). To each of these stilbenes in 10 mL dichloromethane, anhydrous FeCl₃ (0.2348 g, 1.4475 mmol and 0.3116 g, 1.921 mmol) was added, respectively, which resulted in the formation of indoline **34** (6 mg, 6%, hexane/ethyl acetate, 80:20), indoline **35** (18 mg, 16%, hexane/ethyl acetate, 85:15) and bisindoline **36** (13 mg, 24%, hexane/ethyl acetate, 80:20), respectively.

4.4.1. 1-[2-(3-Methoxyphenyl)-2,3-dihydro-1H-indol-1-yl]-1-ethanone (**34**)

HRESIMS *m/z*: 268.1325 ([M+H]⁺; calcd for C₁₇H₁₈NO₂, 268.1338); UV (MeOH) λ_{max} nm: 280, 252, 239, 213; IR ν_{max} cm⁻¹: 3001, 1662, 1049, 752. ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.30 (d, *J*=8.0 Hz, H-11, 1H), 7.25 (t, *J*=8.0 Hz, H-12, 1H), 7.22 (d, *J*=8.0 Hz, H-4, 1H), 7.12 (d, *J*=8.0 Hz, H-14, 1H), 7.04 (t, *J*=8.0 Hz, H-13, 1H), 6.78 (d, *J*=8.0 Hz, H-6, 1H), 6.75 (t, *J*=8.0 Hz, H-5, 1H), 6.70 (s, H-2, 1H), 5.34 (d, *J*=9.0 Hz, H-7, 1H), 3.80 (dd, *J*=16.0, 9.0 Hz, H-8β, 1H), 3.67 (s, OCH₃, 3H), 2.98 (dd, *J*=16.0, 2.0 Hz, H-8α, 1H), 2.05 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 169.7 (C-15), 160.2 (C-3), 144.8 (C-10), 143.3 (C-1), 130.4 (C-4), 129.2 (C-9), 127.8 (C-12), 124.9 (C-14), 124.1 (C-13), 117.3 (C-5), 117.0 (C-11), 112.7 (C-6), 111.0 (C-2), 63.5 (C-7), 55.2 (OCH₃), 38.9 (C-8), 24.2 (C-16).

4.4.2. 1-[2-(4-Methoxyphenyl)-2,3-dihydro-1H-indol-1-yl]-1-ethanone (**35**)

HRESIMS *m/z*: 268.1330 ([M+H]⁺; calcd for C₁₇H₁₈NO₂, 268.1338); UV (MeOH) λ_{max} nm: 281, 252, 238, 213; IR ν_{max} cm⁻¹: 3002, 1663, 1049, 752. ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.28 (d, *J*=8.0 Hz, H-11, 1H), 7.25 (t, *J*=8.0 Hz, H-12, 1H), 7.10 (d, *J*=8.0 Hz, H-14, 1H), 7.05 (d, *J*=8.0 Hz, H-2, H-6, 2H), 7.03 (t, *J*=8.0 Hz, H-13, 1H), 6.80 (d, *J*=8.0 Hz, H-3, H-5, 2H), 5.30 (d, *J*=10.0 Hz, H-7, 1H), 3.75 (dd, *J*=16.0, 10.0 Hz, H-8β, 1H), 3.74 (s, OCH₃, 3H), 2.92 (dd, *J*=16.0, 2.0 Hz, H-8α, 1H), 2.02 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 169.7 (C-15), 159.2 (C-4), 143.4 (C-10), 135.3 (C-1), 129.3 (C-9), 127.8 (C-12), 126.2 (C-2, C-6), 125.0 (C-14), 124.1 (C-13), 117.1 (C-11), 114.5 (C-3, C-5), 63.2 (C-7), 55.4 (OCH₃), 39.1 (C-8), 24.2 (C-16).

4.4.3. Bis-1-[2-(4-methoxyphenyl)-2,3-dihydro-1H-indol-1-yl]-1-ethanone (**36**)

HRESIMS *m/z*: 533.2430 ([M+H]⁺; calcd for C₃₄H₃₃N₂O₄, 533.2440); UV (MeOH) λ_{max} nm: 282, 252, 239, 214; IR ν_{max} cm⁻¹: 1668, 1049, 752. ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.45 (d, *J*=8.0 Hz, H-11, H-11', 2H), 7.46 (t, *J*=8.0 Hz, H-12, H-12', 2H), 7.27 (d, *J*=8.0 Hz, H-14, H-14', 2H), 7.25 (t, *J*=8.0 Hz, H-13, H-13', 2H), 6.66 (d, *J*=9.0 Hz, H-3, H-3', H-5, H-5', 4H), 6.43 (d, *J*=9.0 Hz, H-2, H-2',

H-6, H-6', 4H), 4.66 (s, H-7, H-7', 2H), 3.69 (s, 2×OCH₃, 6H), 3.48 (s, H-8, H-8', 2H), 1.87 (s, 2×CH₃, 6H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 169.8 (C-15, C-15'), 159.1 (C-4, C-4'), 143.9 (C-10, C-10'), 133.9 (C-1, C-1'), 130.1 (C-9, C-9'), 129.4 (C-12, C-12'), 125.7 (C-2, C-2', C-6, C-6'), 125.3 (C-14, C-14'), 125.0 (C-13, C-13'), 117.7 (C-11, C-11'), 114.5 (C-3, C-3', C-5, C-5'), 64.2 (C-7, C-7'), 56.8 (C-8, C-8'), 55.3 (OCH₃), 23.7 (C-16, C-16').

4.4.4. *N*-(2-Formylphenyl)acetamide (**37**)⁴¹

MS *m/z*: 163 [M⁺]; UV (MeOH) λ_{max} nm: 223; IR ν_{max} cm⁻¹: 3270, 1660. ¹H NMR (400 MHz, CDCl₃) δ ppm: 11.11 (s, N-H, 1H), 9.90 (s, H-17, 1H), 8.71 (d, *J*=8.7 Hz, H-11, 1H), 7.65 (dd, *J*=1.8, 7.8 Hz, H-14, 1H), 7.60 (t, *J*=8.7 Hz, H-12, 1H), 7.21 (t, *J*=7.8 Hz, H-13, 1H), 2.24 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 195.7 (C-17), 169.8 (C-15), 141.0 (C-10), 136.3 (C-12), 136.2 (C-14), 123.0 (C-13), 121.6 (C-9), 119.9 (C-11), 25.5 (C-16).

4.4.5. *N*-{2-[(*E*)-2-(2,6-Dichloro-3,5-dimethoxyphenyl)-ethenyl]phenyl}acetamide (**38**)

HRESIMS *m/z*: 388.0463 ([M+Na]⁺; calcd for C₁₈H₁₇NO₃NaCl₂, 388.0483); UV (MeOH) λ_{max} nm: 223; IR ν_{max} cm⁻¹: 3475, 1738, 1213, 802, 747. ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.97 (d, *J*=8.0 Hz, H-11, 1H), 7.52 (d, *J*=8.0 Hz, H-14, 1H), 7.31 (t, *J*=8.0 Hz, H-12, 1H), 7.17 (t, *J*=8.0 Hz, H-13, 1H), 7.09 (d, *J*=17.0 Hz, H-8, 1H), 6.87 (d, *J*=17.0 Hz, H-7, 1H), 6.52 (s, H-4, 1H), 3.92 (s, 2×OCH₃, 6H), 2.18 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 168.6 (C-15), 154.7 (C-3, C-5), 136.1 (C-1), 135.2 (C-10), 132.9 (C-8), 129.2 (C-9), 129.0 (C-12), 127.4 (C-7, C-14), 125.2 (C-13), 123.1 (C-11), 114.0 (C-2, C-6), 96.4 (C-4), 56.7 (2×OCH₃), 24.3 (C-16).

4.4.6. *N*-(2-[(*E*)-2-[2'-(1-Acetyl-1H-indol-2-yl)-3'chloro-4,4',6,6'-tetramethoxy[1,1'-biphenyl]-2-yl]ethenyl]phenyl)acetamide (**39**)

HRESIMS *m/z*: 648.1998 ([M+Na]⁺; calcd for C₃₆H₃₃ClN₂NaO₆, 648.1998); UV (MeOH) λ_{max} nm: 302, 270, 202; IR ν_{max} cm⁻¹: 3378, 2969, 1738, 1218, 775. ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.86 (s, NH, 1H), 8.03 (d, *J*=8.2 Hz, H-11', 1H), 7.85 (d, *J*=8.2 Hz, H-11, H-14, 2H), 7.39 (d, *J*=8.2 Hz, H-14', 1H), 7.26 (t, *J*=8.2 Hz, H-12, 1H), 7.21 (t, *J*=8.2 Hz, H-12', 1H), 7.16 (t, *J*=8.2 Hz, H-13', 1H), 7.08 (t, *J*=8.2 Hz, H-13, 1H), 6.82 (d, *J*=16.0 Hz, H-8, 1H), 6.72 (s, H-4', 1H), 6.65 (d, *J*=16.0 Hz, H-7, 1H), 6.48 (s, H-6, 1H), 6.42 (s, H-8', 1H), 6.08 (s, H-4, 1H), 3.99 (s, 5'-OCH₃, 3H), 3.85 (s, 3'-OCH₃, 3H), 3.67 (s, 5-OCH₃, 3H), 3.59 (s, 3-OCH₃, 3H), 2.36 (s, CH₃, 3H), 1.88 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 172.3 (C-15'), 169.7 (C-15), 160.2 (C-5), 157.7 (C-3), 156.4 (C-3'), 155.5 (C-5'), 138.9 (C-1), 136.5 (C-10'), 136.4 (C-7'), 135.6 (C-10), 134.4 (C-1'), 131.1 (C-7), 130.4 (C-9), 129.0 (C-9'), 128.5 (C-12), 128.0 (C-8), 127.3 (C-14), 125.0 (C-13), 124.9 (C-11), 124.8 (C-12'), 123.6 (C-13'), 120.6 (C-2'), 120.4 (C-14'), 116.1 (C-2), 115.8 (C-11'), 115.7 (C-6'), 112.6 (C-8'), 102.5 (C-6), 98.1 (C-4), 97.5 (C-4'), 56.6 (5'-OCH₃), 56.4 (3'-OCH₃), 55.4 (3-OCH₃), 55.3 (5-OCH₃), 26.3 (C-16'), 24.2 (C-16).

4.4.7. *N*-(2-[(*E*)-2-[2'-(1-Acetyl-1H-indol-2-yl)-3'chloro-2,4',6,6'-tetramethoxy[1,1'-biphenyl]-4-yl]ethenyl]phenyl)acetamide (**40**)

HRESIMS *m/z*: 625.2111 ([M+H]⁺; calcd for C₃₆H₃₄ClN₂O₆, 625.2105); UV (MeOH) λ_{max} nm: 298, 240, 202; IR ν_{max} cm⁻¹: 3675, 3016, 2970, 1738, 1217, 772. ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.34 (d, *J*=8.2 Hz, H-11', 1H), 7.76 (d, *J*=7.8 Hz, H-11, 1H), 7.39 (d, *J*=8.2 Hz, H-14', 1H), 7.37 (d, *J*=7.8 Hz, H-14, 1H), 7.25 (t, *J*=7.8 Hz, H-12, 1H), 7.22 (t, *J*=8.2 Hz, H-12', 1H), 7.19 (t, *J*=8.2 Hz, H-13', 1H), 7.13 (t, *J*=7.8 Hz, H-13, 1H), 6.96 (d, *J*=16.0 Hz, H-8, 1H), 6.77 (d, *J*=16.0 Hz, H-7, 1H), 6.72 (s, H-4', 1H), 6.48 (s, H-2, H-6, 2H), 6.36 (s, H-8', 1H), 4.00 (s, 3'-OCH₃, 3H), 3.78 (s, 3-OCH₃, 3H), 3.74 (s, 5'-OCH₃, 3H), 3.61 (s, 5-OCH₃, 3H), 2.30 (s, CH₃, 3H), 2.14 (s, CH₃, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm: 171.4 (C-15'), 168.8 (C-15), 158.3 (C-5'), 157.7 (C-5), 157.5 (C-3), 155.3 (C-3'), 138.2 (C-1), 137.0 (C-10'), 135.7 (C-7'), 134.7 (C-10), 134.7 (C-1'), 133.1 (C-7), 130.3 (C-9), 129.1

(C-9'), 128.5 (C-12), 127.1 (C-14), 125.6 (C-13), 124.7 (C-12'), 124.2 (C-11), 123.9 (C-8), 123.2 (C-13'), 120.2 (C-14'), 118.9 (C-2'), 117.0 (C-11'), 115.6 (C-6'), 113.3 (C-4), 111.4 (C-8'), 102.6 (C-6), 102.0 (C-2), 97.7 (C-4'), 56.6 (3-OCH₃), 56.5 (3'-OCH₃), 55.8 (5'-OCH₃), 55.3 (5-OCH₃), 25.2 (C-16'), 24.5 (C-16).

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