DOI: 10.1002/adsc.201100349

Iron-Facilitated Iodine-Mediated Electrophilic Annulation of *N,N*-Dimethyl-2-alkynylanilines with Disulfides or Diselenides

Hui-Ai Du,[a] Ri-Yuan Tang,[a,b] Chen-Liang Deng,[a] Yan Liu,[a] Jin-Heng Li,[b,*] and Xing-Guo Zhang[a,*]

[a] College of Chemistry and Materials Engineering, Wenzhou University, Wenzhou 325035, People's Republic of China
Fax: (+86)-577-8668-9372; phone: (+86)-577-8668-9615; e-mail: zxg@wzu.edu.cn
[b] State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha 410082, People's Republic of China
Fax: (+86)-731-8887-2531; phone: (+86)-731-8887-2576; e-mail: jhli@hunnu.edu.cn

Received: May 4, 2011; Revised: July 7, 2011; Published online: October 10, 2011

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adcs.201100349.

Abstract: An efficient synthesis of *N*-methyl-3-chalcogeno-indoles has been developed *via* iodine-mediated electrophilic annulation reactions of 2-alkynylaniline derivatives with disulfides or diselenides. In the presence of iodine and iron, a variety of 2-alkynylanilines selectively underwent the electrophilic annulation with numerous disulfides or diselenides leading to the corresponding 3-sulfenylindoles and 3-selenenylindoles in moderate to excellent yields. It is noteworthy that iron can promote the reaction.

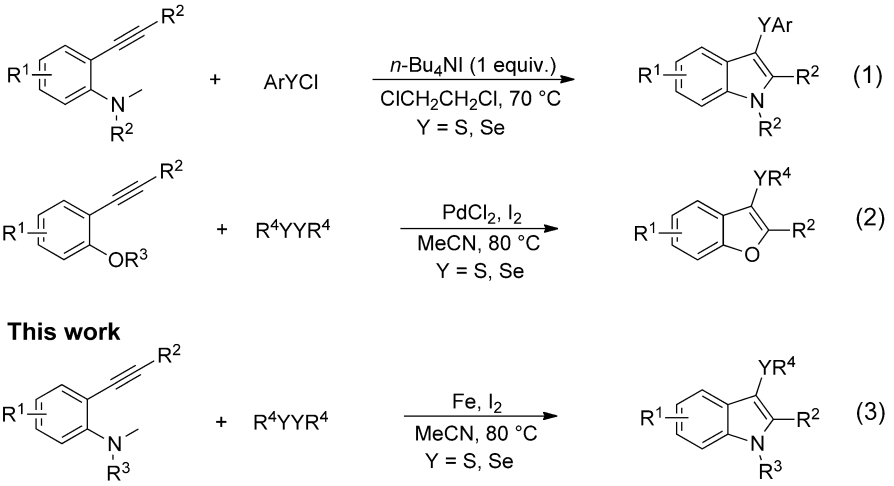
Keywords: 2-alkynylanilines; electrophilic annulation; iodine; iron; 3-selenenylindoles; 3-sulfenylindoles

Introduction

The indole moiety is presented in a wide range of biologically active compounds and natural products, as well as is useful building block in organic synthesis.[1] Among the indole derivatives, 3-sulfenylindoles are particularly attractive due to their potential use in therapeutic areas such as cancer,[2] HIV,[3] obesity[4]and heart disease.[5] Until now, a variety of efficient methods has been developed for the synthesis of 3-sulfenylindoles.[6,7] However, most have focused on the direct sulfenylations of indoles with different sulfenylating agents,[6] which is restricted with the functional groups compatibility and the use of foul smelling/harmful sulfenylating agents, associated with unnecessary economic wastes and environmental pollution. Recently, Larock and co-workers reported a novel synthetic approach to 3-chalcogen-substituted indoles by $(n\text{-Bu})_4$NI-induced electrophilic cyclization of *N,N*-dialkyl-2-alkynylanilines with arylsulfenyl chloride or phenylselenenyl chloride in moderate to excellent yields [Scheme 1, Eq. (1)].[8] However, this method was limited to the use of arylchalcogenyl chloride. Thus, the development of a general and simple route for synthesizing 3-chalcogen-substituted indoles using readily available aryl- and alkyl-chalcogen sources is interesting. Recently, we were interested to find that chalcogenyl iodides could be derived *in situ* from the reaction of disulfides or diselenides with I_2, which has been applied for the preparation of 3-chalcogenobenzo[*b*]furans [Eq. (2)].[9] With a continuing interest in the synthesis of chalcogen-containing heterocycles,[9,10] we decided to investigate the feasibility of the preparation of 3-chalcogen-substituted indoles using the generation of chalcogenyl iodides *in situ* and an annulation strategy. Here, we report a simple and efficient synthesis of 3-chalcogenoindoles by electrophilic annulation of *N,N*-dimethyl-2-alkynylanilines with chalcogenyl iodides derived from disulfides or diselenides with I_2 [Eq. (3)]. It is noteworthy that iron can facilitate the annulation.

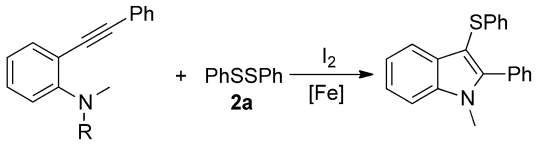
Results and Discussion

We began our study by examining the reaction between *N,N*-dimethyl-2-(phenylethynyl)aniline (**1a**) and 1,2-diphenyldisulfane (**2a**) to screen the optimal reaction conditions, and the results are summarized in Table 1. As expected, the reaction of *N,N*-dimethyl-2-(phenylethynyl)aniline (**1a**) with 1,2-diphenyldisulfane (**2a**) was carried out smoothly under the reported re-



Scheme 1. Routes to chalcogen-containing heterocycles.

Table 1. Screening for optimal reaction conditions.[a]



1 3

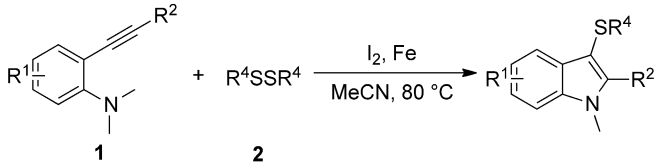
Entry	R	[Fe] (mol%)	Solvent	*T* [°C]	Yield [%][b]
1[c]	Me (**1a**)	–	MeCN	100	84
2	Me (**1a**)	–	MeCN	100	83
3	Me (**1a**)	Fe (20)	MeCN	100	95
4	Me (**1a**)	FeF_3 (20)	MeCN	100	92
5	Me (**1a**)	$FeCl_3$ (20)	MeCN	100	85
6	Me (**1a**)	$FeCl_2$ (20)	MeCN	100	86
7	Me (**1a**)	$FeBr_3$ (20)	MeCN	100	86
8[d]	Me (**1a**)	Fe (20)	MeCN	100	0
9	Me (**1a**)	Fe (10)	MeCN	100	96
10	Me (**1a**)	Fe (5)	MeCN	100	98
11	Me (**1a**)	Fe (5)	MeCN	80	98
12	Me (**1a**)	Fe (5)	MeCN	25	trace
13	Me (**1a**)	Fe (5)	CH_2ClCH_2Cl	80	50
14	Me (**1a**)	Fe (5)	toluene	80	82
15	Me (**1a**)	Fe (5)	DMSO	80	78
16	H (**1b**)	Fe (5)	MeCN	80	trace
17	Bn (**1c**)	Fe (5)	MeCN	80	mixture
18	Ac (**1d**)	Fe (5)	MeCN	80	63
19	Bz (**1e**)	Fe (5)	MeCN	80	46
20[e]	Me (**1a**)	Fe (5)	MeCN	80	96

[a] *Reaction conditions:* **1** (0.2 mmol), **2a** (0.1 mmol), 1.1 equiv. of I_2, and [Fe] in solvent (2 mL) under an N_2 atmosphere for 3 h.
[b] Isolated yield.
[c] In the presence of $PdCl_2$ (10 mol%).
[d] In the absence of I_2 for 14 h.
[e] **1** (1 mmol) and **2a** (0.5 mmol) for 10 h.

action conditions ($PdCl_2$ combined with I_2),[9] providing the desired product **3** in 84% yield (entry 1). It was interesting to find that an identical yield was achieved in the presence of I_2 alone (entry 2). These promoted us to investigate other reaction conditions to obtain the best results (entries 3–20). After a series of trials, we found that the presence of iron salts affected the reaction to some extent (entries 3–7): while both Fe power and FeF_3 could enhance the yield of **3** to 95% and 92%, respectively, the other iron salts, $FeCl_3$, $FeCl_2$ and $FeBr_3$, affected the reaction slightly. Notably, I_2 played a key role in the reaction: without I_2 the reaction could not take place even in the presence of Fe (entry 8). We were interested to discover that the reaction gave the desired product **3** in quantitative yield when 5 mol% Fe combined with 1.1 equiv. I_2 was added (entry 10). Among the effects of both the reaction temperature and solvent examined, it turned out that the reaction in MeCN at 80 °C provided the best results (entries 11–15). In light of the above results, several N-substituents as the leaving group were evaluated in the presence of Fe and I_2 (entries 16–19). It was found that substrates **1b** and **1c**, with an N–H group or an N–Bn group instead of the N–Me group, were not suitable substrates for the annulation reaction (entries 16 and 17). Although N–Ac and N–Bz groups were suitable leaving groups, both were less active than the N–Me group in terms of yields (entries 18 and 19). For example, *N*-methyl-*N*-[2-(phenylethynyl)phenyl]acetamide (**1d**) was treated with 1,2-diphenyldisulfane (**2a**), I_2, and Fe to afford the desired product **3** in moderate yield (entry 18). To our delight, the optimal reaction conditions were compatible with a 1 mmol scale of substrate **1a** (entry 20).

With the optimal reaction conditions in hand, we explored the scope of both *N*,*N*-dimethyl-2-alkynylanilines and disulfides for the annulation reaction

Table 2. Electrophilic annulation reactions of 2-alkynylanilines (**1**) with disulfides (**2**) in the presence of I_2 and Fe.[a]



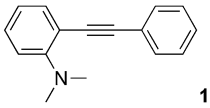
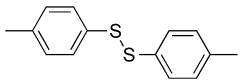
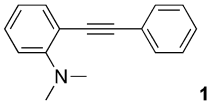
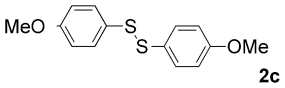
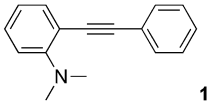
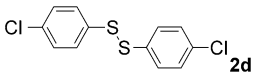
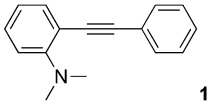
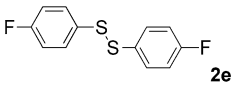
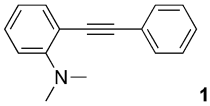
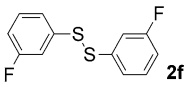
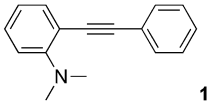
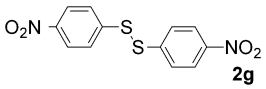
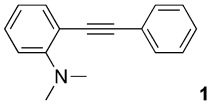
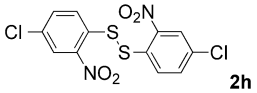
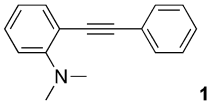
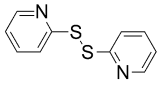
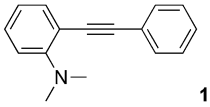
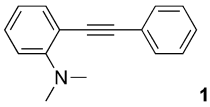
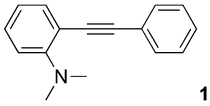
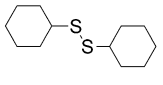
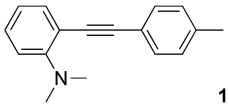
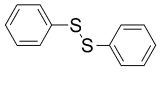
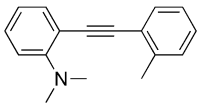
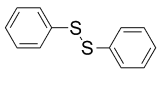
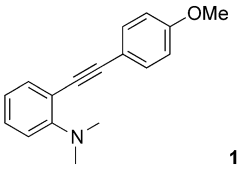
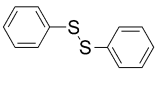
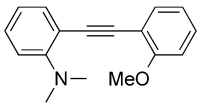
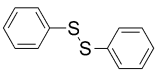
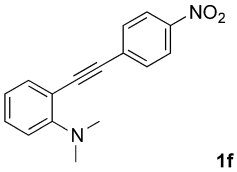
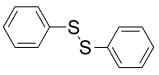
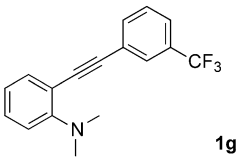
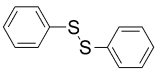
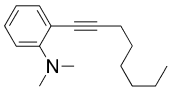
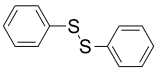
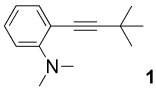
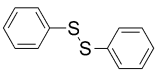
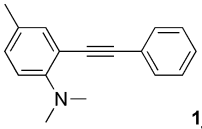
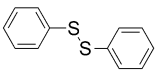
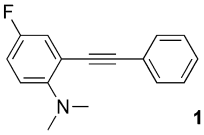
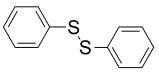
Entry	Amine **1**	Disulfide **2**	Yield [%][b] (Product)
1	 **1a**	 **2b**	81 (**4**)
2	 **1a**	 **2c**	92 (**5**)
3	 **1a**	 **2d**	98 (**6**)
4	 **1a**	 **2e**	92 (**7**)
5	 **1a**	 **2f**	99 (**8**)
6	 **1a**	 **2g**	80 (**9**)
7	 **1a**	 **2h**	83 (**10**)
8	 **1a**	 **2i**	81 (**11**)
9	 **1a**	 **2j**	95 (**12**)
10	 **1a**	 **2k**	92 (**13**)
11	 **1a**	 **2l**	97 (**14**)
12	 **1b**	 **2a**	99 (**15**)
13	 **1c**	 **2a**	67 (**16**)

Table 2. (Continued)

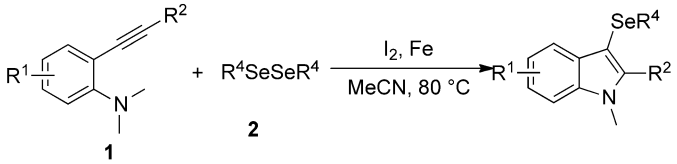
Entry	Amine **1**	Disulfide **2**	Yield [%][b] (Product)
14	 **1d**	 **2a**	95 (**17**)
15	 **1e**	 **2a**	87 (**18**)
16	 **1f**	 **2a**	67 (**19**)
17	 **1g**	 **2a**	92 (**20**)
18	 **1h**	 **2a**	83 (**21**)
19	 **1i**	 **2a**	53 (**22**)
20	 **1j**	 **2a**	61 (**23**)
21	 **1k**	 **2a**	90 (**24**)

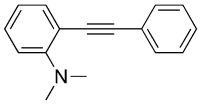
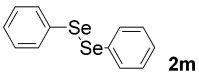
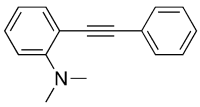
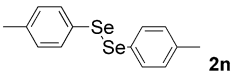
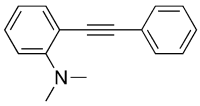
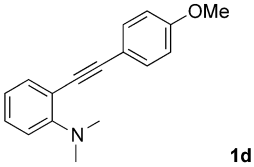
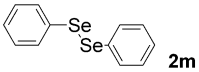
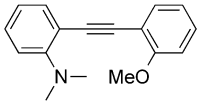
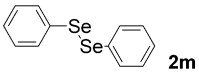
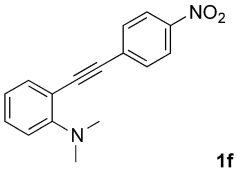
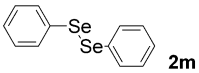
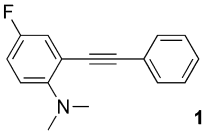
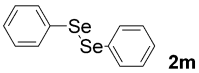
[a] *Reaction conditions:* **1** (0.2 mmol), **2** (0.1 mmol), I_2 (1.1 equiv.), Fe (5 mol%), and MeCN (2 mL) under N_2 at 80 °C for 3 h.

[b] Isolated yield.

(Table 2). The results disclosed the broader generality of the reaction under the optimal reaction conditions, and various *N*,*N*-dimethyl-2-alkynylanilines **1** underwent the reaction with disulfides **2** in moderate to good yields. Initially, a number of disulfides **2b**–**2l** was investigated in the presence of I_2 and Fe (entries 1–11). The results demonstrated that diaryl disulfides, bearing either electron-rich or electron-deficient groups on the aryl ring, were successful for reacting with aniline **1a**, providing the corresponding products **4**–**10** in good to excellent yields (entries 1–7). For example, disulfides **2c** and **2g**, bearing a 4-methoxy group or 4-nitro group, reacted with substrate **1a**, Fe, and I_2 to give the corresponding products in 92% and 80% yields, respectively (entries 2 and 6). To our delight, heteroaryl disulfide **2i** was also a suitable substrate under the optimal conditions: the desired product **11** was obtained in 81% yield (entry 8). It was found that the optimal conditions were compatible with aliphatic disulfides (entries 9–11). 1,2-Dicyclohexyldisulfane (**2l**), for instance, underwent the reaction smoothly to afford the target product **14** in 97% yield (entry 11). Subsequently, a variety of *N*,*N*-dimethyl-2-alkynylanilines **1b**–**1k** was examined in the presence of I_2 and Fe (entries 12–21). Gratifyingly, a series of functional groups, including *p*-MeC_6H_4, *o*-MeC_6H_4, *p*-$MeOC_6H_4$, *o*-$MeOC_6H_4$, *p*-$NO_2C_6H_4$, *m*-$CF_3C_6H_4$, *n*-hexyl and *tert*-butyl, at the terminal

Table 3. Electrophilic annulation reactions of 2-alkynylanilines (**1**) with diselenides (**2**) in the presence of I_2 and Fe.[a]



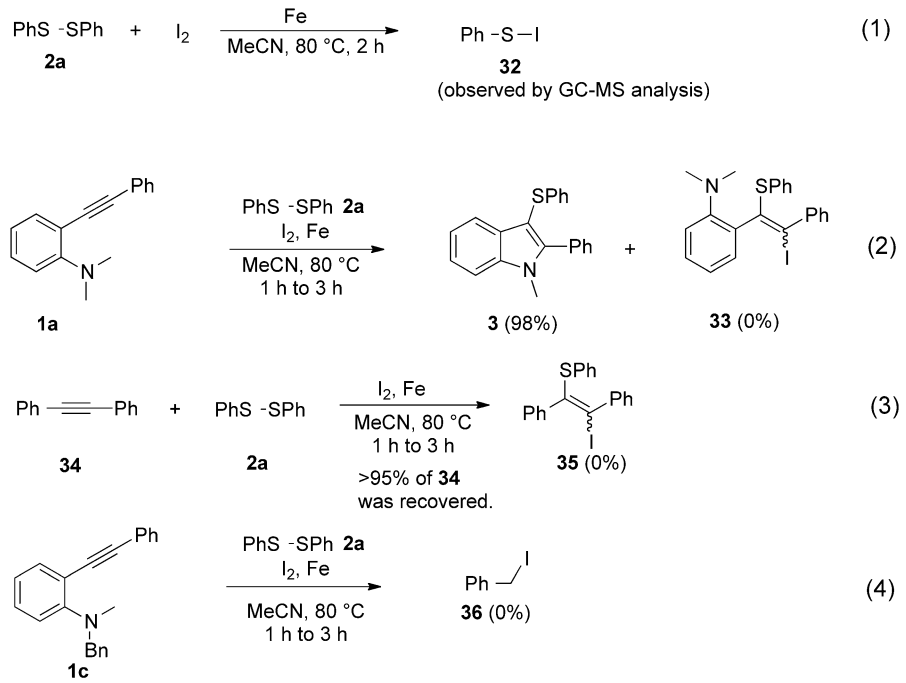
Entry	Amine **1**	Diselenide **2**	Yield [%][b] (Product)
1	 **1a**	 **2m**	92 (**25**)
2	 **1a**	 **2n**	84 (**26**)
3	 **1a**	 **2o**	93 (**27**)
4	 **1d**	 **2m**	90 (**28**)
5	 **1e**	 **2m**	80 (**29**)
6	 **1f**	 **2m**	32 (**30**)
7	 **1k**	 **2m**	82 (**31**)

[a] *Reaction conditions:* **1** (0.2 mmol), **2** (0.1 mmol), I_2 (1.1 equiv.), Fe (5 mol%), and MeCN (2 mL) under N_2 at 80 °C for 3 h.

[b] Isolated yield.

alkyne was well tolerated under the optimal conditions, and the steric hindrance disfavored the reaction in terms of yields. While substrate **1b**, bearing a *p*-methylphenyl group at the terminal alkyne, was reacted with disulfide **2a**, Fe, and I_2 to afford the corresponding product **15** in 99% yield (entry 12), substrate **1c** with a bulky *o*-methylphenyl group lowered the yield to 67% (entry 13). *N,N*-Dimethyl-2-(oct-1-yn-yl)aniline (**1h**) furnished the desired product **21** in 83% yield (entry 18); however, another bulky aliphatic alkyne **1i** gave the corresponding product **22** in only 53% yield (entry 19). Notably, substituents, such as Me or F, on the aryl ring of the aniline moiety were also consistent with the optimal conditions. Treatment of Me-substituted substrate **1j** with disulfide **2a**, I_2 and Fe afforded the cyclization product **23** in 61% yield (entry 20). Using F-substituted substrate **1k**, a good yield was obtained under the same conditions (entry 21). However, some substrates, including 2-ethynyl-*N,N*-dimethylaniline (**1l**), *N,N*-dimethyl-2-[(trimethylsilyl)ethynyl]aniline (**1m**) and 3-[2-(dimethylamino)phenyl]prop-2-yn-1-ol (**1n**), were not suitable substrates for the reaction.

Subsequently, the reactions between 2-alkynylanilines and diselenides were explored under the optimal conditions (Table 3). In the presence of Fe and I_2, ani-



Scheme 2. Control experiments.

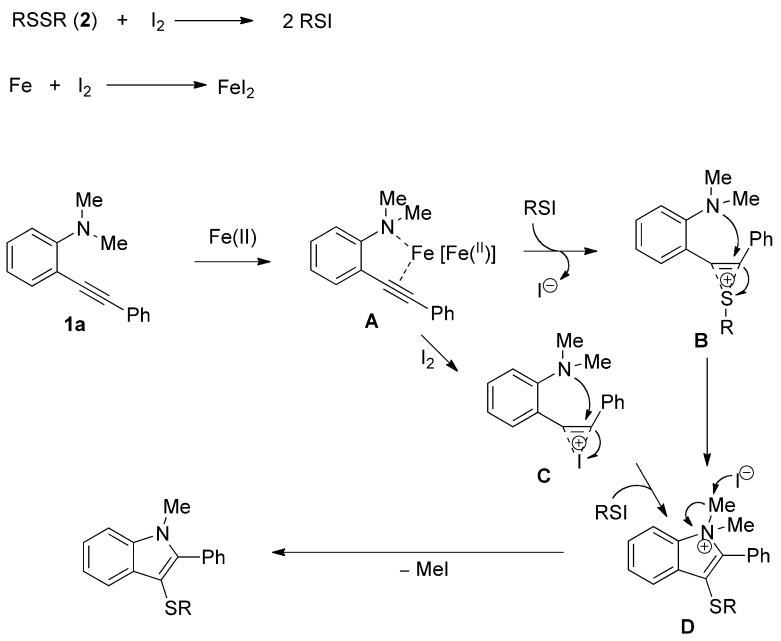
line **1a** was treated with diaryl diselenides **2m** or **2n** to smoothly give the corresponding products **25** and **26** in 92% and 84% yields, respectively (entries 1 and 2). Gratifyingly, an excellent yield was still achieved from the reaction of substrate **1a** with aliphatic diselenide **2o** (entry 3). Encouraged by these results, several anilines **1d–1f** and **1k** were examined in the presence of 1,2-diphenyl diselenide (**2m**), I_2 and Fe (entries 4–7). The results showed that substrates **1d** and **1e** with electron-rich aryl groups at the terminal alkyne displayed higher activity leading to the desired products **28** and **29** in good yields. However, aniline **1f** with an electron-deficient group gave a low yield (32% yield, entry 6). To our delight, F-substituted substrate **1k** successfully underwent the annulation reaction with 1,2-diphenyldiselenide (**2m**), I_2 and Fe, furnishing the target product **31** in good yield (entry 7).

To elucidate the mechanism, some control experiments were carried out (Scheme 2). The reaction between disulfide **2a** and I_2 was carried out, and PhSI was observed by GC-MS analysis [Eq. (1)]. It is noteworthy that no addition products **33** or **35** were obtained using *N,N*-dimethyl-2-(phenylethynyl)aniline (**1a**) or 1,2-diphenylethyne (**34**) substrates in the presence of disulfide **2a**, Fe and I_2 [Eq. (2) and Eq. (3)]. Although a mixture of products were observed by GC-MS analysis, (iodomethyl)benzene (**36**) was not detected [Eq. (4)]. However, the reaction could not take place under the standard conditions, suggesting that the reaction does not proceed through an iodocyclization process.

Consequently, possible mechanisms are proposed as outlined in Scheme 3 on the basis of the reported mechanisms[8,9] and the present results. The reaction could be conducted in the presence of I_2 alone (entry 1 in Table 1, and did not proceed through an iodocyclization process (Scheme 2). These results imply that the reaction of disulfide **2** with I_2 may take place to yield the active RSI *in situ*.[11] Initially, complexation of Fe or Fe(II) with both an alkyne and a nitrogen afforded intermediate **A**, followed by the electrophilic addition of RSI to the C≡C triple bond in intermediate **A** which gives intermediate **B**. Intermediate **B** undergoes the annulation reaction leading to intermediate **D**. A methyl group is removed from intermediate **D** with the aid of an I^- nucleophile to furnish the product. We deduce that the Fe catalyst may activate the substrates by complexation with the carbon-carbon triple bond (intermediate **A**). Although we did not observe the addition products [Eq. (2) and Eg. (3) in Scheme 2], we cannot rule out the second pathway: the electrophilic addition of I_2 to the C≡C triple bond in intermediate **A** gives intermediate **C**, followed by addition of PhSI and cyclization with nitrogen resulting in intermediate **D**.

Conclusions

In summary, we have developed a new, practical Fe-promoted electrophilic annulation method for the synthesis of 3-chalcogenoindoles. In the presence of I_2 and Fe, a variety of 2-alkynylanilines selectively un-



Scheme 3. Possible mechanism.

derwent the electrophilic annulation with numerous disulfides or diselenides leading to the corresponding 3-sulfenylindoles and 3-selenenylindoles in moderate to excellent yields. The key to the reaction is the generation of RYI (Y = S, Se) *in situ* from the reaction of RYYR with I_2.

Experimental Section

Typical Experimental Procedure for the Electrophilic Tandem Cyclization

To a Schlenk tube were added 2-alkynylaniline derivative **1** (0.2 mmol), disulfide or diselenide **2** (0.1 mmol), I_2 (1.1 equiv.), Fe (5 mol%) and MeCN (2 mL). Then the tube was recharged with nitrogen and stirred at 80 °C until complete consumption of starting material as monitored by TLC or GC-MS analysis. After the reaction was finished, the reaction mixture was filtered through glass filter and washed with ethyl acetate. The solution was washed with saturated aqueous $Na_2S_2O_3$ and extracted with diethyl ether. The combined organic layers were dried with anhydrous Na_2SO_4 and concentrated under vacuum. The resulting residue was purified by column chromatography on silica gel (hexane/ethyl acetate) to afford the desired product.

1-Methyl-2-phenyl-3-(phenylthio)-1*H*-indole (3):[8a] Yellow solid, mp 94.4–95.8 °C (uncorrected) (lit. 98–100 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, J = 7.8 Hz, 1H), 7.50–7.48 (m, 6H), 7.39–7.36 (m, 1H), 7.29–7.26 (m, 1H), 7.20–7.17 (m, 2H), 7.13–7.08 (m, 3H), 3.78 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.8, 140.0, 137.6, 130.6, 130.5, 129.7, 128.7, 128.6, 128.2, 125.5, 124.4, 122.8, 120.9, 119.8, 109.8, 99.6, 31.7; IR (KBr): ν = 1476, 1265, 800, 739, 700 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 315 (M^+, 100), 316 (25), 300 (13), 283 (12), 223 (25).

1-Methyl-2-phenyl-3-(*p*-tolylthio)-1*H*-indole (4):[8a] Yellow solid, mp 106.1–106.8 °C (uncorrected) (lit. 106–108 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64 (d, J = 7.5 Hz, 1H), 7.45–7.39 (m, 6H), 7.30 (t, J = 7.5 Hz, 1H), 7.18 (t, J = 7.5 Hz, 1H), 6.94 (s, 4H), 3.71 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.7, 137.6, 136.3, 134.1, 130.6, 130.5, 129.8, 129.4, 128.6, 128.2, 125.8, 122.7, 120.8, 119.8, 109.8, 100.1, 31.7, 20.8; IR (KBr): ν = 1465, 1265, 801, 741, 700 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 329 (M^+, 100), 330 (25), 314 (15), 297 (15), 223 (18).

3-(4-Methoxyphenylthio)-1-methyl-2-phenyl-1*H*-indole (5):[12] Pale yellow solid, mp 122.2–124.0 °C (uncorrected). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67 (d, J = 8.0 Hz, 1H), 7.44–7.37 (m, 6H), 7.29 (t, J = 7.5 Hz, 1H), 7.19–7.18 (m, 1H), 7.00 (d, J = 8.5 Hz, 2H), 6.68 (d, J = 9.0 Hz, 2H), 3.68 (s, 3H), 3.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.4, 145.4, 137.5, 130.6 (2C), 130.4, 129.7, 128.6, 128.2, 127.9, 122.6, 120.8, 119.7, 114.4; 109.7, 101.2, 55.2, 31.6; IR (KBr): ν = 1490, 1265, 1238, 741, 700 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 345 (M^+, 100), 346 (26), 330 (31), 313 (11), 223 (14).

3-(4-Chlorophenylthio)-1-methyl-2-phenyl-1*H*-indole (6): Yellow solid, mp 119.1–120.2 °C (uncorrected). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.61 (d, J = 8.0 Hz, 1H), 7.46–7.43 (m, 4H), 7.39–7.37 (m, 2H), 7.35–7.32 (m, 1H), 7.21 (t, J = 7.5 Hz, 1H), 7.09 (d, J = 9.0 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 3.74 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 146.0, 138.6, 137.6, 130.9, 130.5, 130.3, 130.1, 128.9, 128.7, 128.3, 126.8, 122.9, 121.1, 119.6, 109.9, 99.2, 31.7; IR (KBr): ν = 1473, 1265, 800, 740, 700 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 351 (M^+, 37)/349 (M^+, 100), 351 (37), 350 (24), 317 (12), 223 (25); HR-MS (EI): m/z = 349.0689, calcd. for $C_{21}H_{16}ClNS$ (M^+): 349.0686.

3-(4-Fluorophenylthio)-1-methyl-2-phenyl-1*H*-indole (7): Yellow solid, mp 111.8–112.3 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63 (d, J = 7.8 Hz, 1H), 7.45–7.31 (m, 7H), 7.22–7.17 (m, 1H), 7.01–6.97 (m, 2H), 6.84–6.79 (m, 2H), 3.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.6 (d, $J_{C,F}$ = 242.0 Hz, 1C), 145.7, 137.5, 134.8 , 130.5, 130.3, 129.5, 128.8, 128.2, 127.4 (d, $J_{C,F}$ = 7.6 Hz, 1C), 122.8, 121.0, 119.5, 115.6 (d, $J_{C,F}$ = 21.9 Hz, 1C), 109.9, 100.0, 31.6; IR (KBr): ν = 1487, 1266, 800, 742, 702 cm^{-1}; LR-MS (EI, 70 eV) m/z (%) = 333 (M^+, 100), 334 (24), 318 (14), 301 (14), 223 (20); HR-MS (EI): m/z = 333.0987, calcd. for $C_{21}H_{16}FNS$ (M^+): 333.0982.

3-(3-Fluorophenylthio)-1-methyl-2-phenyl-1*H*-indole (8): Yellow solid, mp 68.8–69.6 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, J = 8.1 Hz, 1H), 7.44–7.32 (m, 7H), 7.23–7.17 (m, 1H), 7.11–7.03 (m, 1H), 6.83 (d, J = 8.1, 1H), 6.71–6.66 (m, 2H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.1 (d, $J_{C,F}$ = 147.8 Hz, 1C), 146.1, 142.8 (d, $J_{C,F}$ = 3.8 Hz, 1C), 137.6, 130.5, 130.2, 129.8 (d, $J_{C,F}$ = 5.3 Hz, 1C), 129.4, 128.8, 128.3, 122.9, 121.1, 120.9 (d, $J_{C,F}$ = 1.5 Hz, 1C), 119.5, 112.1 (d, $J_{C,F}$ = 14.3 Hz, 1C), 111.3 (d, $J_{C,F}$ = 12.8 Hz, 1C), 109.9, 98.5, 31.7; IR (KBr): ν = 1467, 1265, 879, 742, 704 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 333 (M^+, 100), 334 (26), 301 (11), 238 (11), 223 (24); HR-MS (EI): m/z = 333.0987, calcd. for $C_{21}H_{17}FNS$ (M^+): 333.0982.

1-Methyl-3-(4-nitrophenylthio)-2-phenyl-1*H*-indole (9):[8a] Yellow solid, mp 161.6–162.3 °C (uncorrected) (lit. 162–164 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.97 (d, J = 8.5, 2H), 7.56 (d, J = 8.0 Hz, 1H), 7.49–7.45 (m, 4H), 7.38–7.35 (m, 3H), 7.24–7.21 (m, 1H), 7.09 (d, J = 9.0 Hz, 2H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.4, 146.4, 144.8, 137.7, 130.3, 129.9, 129.1, 129.0, 128.4, 124.8, 123.8, 123.3, 121.4, 119.2, 110.2, 97.0, 31.8; IR (KBr): ν = 1507, 1331, 1266, 740, 701 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 360 (M^+, 100), 361 (25), 281 (11), 238 (10), 223 (23).

3-(4-Chloro-2-nitrophenylthio)-1-methyl-2-phenyl-1*H*-indole (10): Yellow solid, mp 206.8–207.8 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.24 (s, 1H), 7.53–7.36 (m, 8H), 7.27–7.20 (m, 2H), 7.00–6.94 (m, 1H), 3.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.9, 144.8, 139.6, 137.8, 133.4, 130.3, 129.9, 129.7, 129.2, 128.9 (2C), 128.5, 125.6, 123.3, 121.5, 119.3, 110.2, 97.9, 31.8; IR (KBr): ν = 1335, 1266, 766, 743, 699 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 396 (M^+, 3)/394 (M^+, 7), 329 (4), 223 (20), 222 (100), 207 (5); HR-MS (EI): m/z = 394.0538, calcd. for $C_{21}H_{15}ClN_2O_2S$ (M^+): 394.0537.

1-Methyl-2-phenyl-3-(pyridin-2-ylthio)-1*H*-indole (11): Pale solid, mp 140.6–141.3 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.36–8.34 (m, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.45–7.41 (m, 6H), 7.35–7.29 (m, 2H), 7.23–7.20 (m, 1H), 6.89–6.85 (m, 1H), 6.72 (d, J = 8.1 Hz, 1H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.1, 149.2, 146.0, 137.7, 136.3, 130.2, 129.4, 128.9, 128.7, 128.1, 122.9, 121.0, 119.6, 119.4, 118.9, 109.9, 98.4, 31.7; IR (KBr): ν = 1446, 1415, 1265, 741, 701 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 317 (M^++1, 24), 316 (M^+, 100), 315 (41), 283 (50), 223 (64); HR-MS (EI): m/z = 316.1033, calcd. for $C_{20}H_{16}N_2S$ (M^+): 316.1034.

1-Methyl-3-(methylthio)-2-phenyl-1*H*-indole (12): Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90 (d, J = 7.8 Hz, 1H), 7.57–7.51 (m, 5H), 7.42–7.37 (m, 1H), 7.34–7.31 (m, 2H), 3.69 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.0, 137.2, 131.1, 130.8, 129.5, 128.5, 128.3, 122.4, 120.4, 119.4, 109.7, 104.9, 31.3, 20.1; IR (KBr): ν = 1464, 1265, 800, 741, 700 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 253 (M^+, 100), 254 (19), 238 (77), 223 (25), 222 (19); HR-MS (EI): m/z = 253.0917, calcd. for $C_{16}H_{15}NS$ (M^+): 253.0920.

3-(Ethylthio)-1-methyl-2-phenyl-1*H*-indole (13): Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, J = 4.5 Hz, 1H), 7.44–7.35 (m, 5H), 7.29 (d, J = 4.8 Hz, 1H), 7.23–7.20 (m, 1H), 7.17–7.14 (m, 1H), 3.56 (s, 3H), 2.52–2.47 (m, 2H), 0.95 (t, J = 4.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.9, 137.2, 131.2, 130.9, 130.3, 128.4, 128.1, 122.4, 120.4, 119.6, 109.6, 103.0, 31.4, 30.5, 15.0; IR (KBr): ν = 1465, 1266, 800, 742, 701 cm^{-1}; LR-MS (EI, 70 eV): m/z = (%): 267 (M^+, 94), 239 (21), 238 (100), 223 (80), 222 (22); HR-MS (EI): m/z = 267.1075, calcd. for $C_{17}H_{17}NS$ (M^+): 267.1076.

3-(Cyclohexylthio)-1-methyl-2-phenyl-1*H*-indole (14): Yellow solid, mp 105.6–106.3 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90 (d, J = 8.1 Hz, 1H), 7.56–7.49 (m, 5H), 7.41–7.35 (m, 1H), 7.32–7.29 (m, 2H), 3.69 (s, 3H), 2.81–2.78 (m, 1H), 1.82–1.79 (m, 2H), 1.67–1.52 (m, 2H), 1.51–1.45 (m, 1H), 1.32–1.17 (m, 1H), 1.14–1.12 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.3, 137.1, 131.3, 131.1, 130.8, 128.3, 128.0, 122.3, 120.3, 119.9, 109.5, 102.4, 48.0, 33.4, 31.4, 25.9, 25.7; IR (KBr): ν = 1464, 1265, 800, 740, 699 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 321 (M^+, 44), 240 (21), 239 (100), 238 (21), 223 (26); HR-MS (EI): m/z = 321.1548, calcd. for $C_{21}H_{23}NS$ (M^+): 321.1546.

1-Methyl-3-(phenylthio)-2-*p*-tolyl-1*H*-indole (15): Yellow solid, mp 112,6–113.8 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.61 (d, J = 7.8 Hz, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.32–7.27 (m, 2H), 7.23–7.19 (m, 3H), 7.17–7.08 (m, 3H), 7.04–6.97 (m, 3H), 3.70 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.1, 140.1, 138.8, 137.6, 130.5, 129.8, 129.1, 128.6, 127.5, 125.4, 124.3, 122.7, 120.9, 119.7, 109.8, 99.2, 31.8, 21.5; IR (KBr): ν = 1476, 1266, 825, 741, 704 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 329 (M^+, 100), 330 (25), 314 (11), 297 (12), 237 (21); HR-MS (EI): m/z = 329.1238, calcd. for $C_{22}H_{19}NS$ (M^+): 329.1233.

1-Methyl-3-(phenylthio)-2-*o*-tolyl-1*H*-indole (16): Yellow solid, mp 99.4–100.8 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, J = 8.7 Hz, 1H), 7.43 (d, J = 8.1 Hz, 1H), 7.38–7.31 (m, 3H), 7.29–7.18 (m, 3H), 7.13–7.08 (m, 2H), 7.03–6.97 (m, 3H), 3.55 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.6, 139.5, 138.3, 137.3, 131.1, 130.4, 130.0, 129.5, 129.3, 128.5, 125.7, 125.6, 124.3, 122.4, 120.7, 119.7, 109.7, 99.8, 30.9, 19.8; IR (KBr): ν = 1463, 1265, 739, 703, 690 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 329 (M^+, 100), 330 (25), 314 (25), 237 (27), 236 (12); HR-MS (EI): m/z = 329.1238, calcd. for $C_{22}H_{19}NS$ (M^+): 329.1233.

2-(4-Methoxyphenyl)-1-methyl-3-(phenylthio)-1*H*-indole (17):[8a] Yellow solid, mp 136.4–137.3 °C (uncorrected) (lit. 136–138 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, J = 7.8 Hz, 1H), 7.41 (d, J = 8.1 Hz, 1H), 7.34–7.28 (m, 3H), 7.22–7.10 (m, 3H), 7.05–7.01 (m, 3H), 6.96 (d, J = 8.4 Hz, 2H), 3.82 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9, 145.9, 140.1, 137.5, 131.8, 129.8, 128.6, 125.4, 124.3, 122.6 (2C), 120.8, 119.6, 113.8, 109.7, 99.1, 55.2, 31.6; IR (KBr): ν = 1265, 1249, 740, 703, 691 cm^{-1}; LR-MS (EI, 70 eV): m/z (%) = 345 (M^+, 100), 346 (25), 330 (12), 268 (9), 237 (15).

2-(2-Methoxyphenyl)-1-methyl-3-(phenylthio)-1*H*-indole (18):[8a] Pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ =

7.68 (d, $J=7.8$ Hz, 1H), 7.48–7.46 (m, 2H), 7.37–7.30 (m, 2H), 7.27–7.18 (m, 1H), 7.17–7.00 (m, 7H), 3.73 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=157.8$, 143.5, 140.0, 137.3, 132.9, 130.8, 129.6, 128.4, 125.6, 124.1, 122.3, 120.4(2C), 119.6, 119.5, 110.9, 109.6, 99.6, 55.3, 31.2; IR (KBr): $\nu=1464$, 1265, 1248, 739, 703 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 345 (M^+, 100), 346 (25), 236 (21), 234 (14), 221 (14).

1-Methyl-2-(4-nitrophenyl)-3-(phenylthio)-1*H*-indole (19): Yellow solid, mp 166.3–167.5 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=8.28$ (d, $J=8.4$ Hz, 2H), 7.67 (d, $J=8.0$ Hz, 1H), 7.59 (d, $J=8.4$ Hz, 2H), 7.46 (d, $J=8.1$ Hz, 1H), 7.38 (d, $J=7.2$ Hz, 1H), 7.25–7.22 (m, 1H), 7.17–7.12 (m, 2H), 7.06–7.00 (m, 3H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=147.6$, 142.8, 139.1, 138.0, 136.9, 131.5, 129.6, 128.8, 125.4, 124.8, 123.8, 123.5, 121.4, 120.1, 110.1, 101.6, 32.0; IR (KBr): $\nu=1465$, 1339, 1266, 742, 704 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 360 (M^+, 100), 361 (24), 330 (11), 237 (10), 222 (11); HR-MS (EI): *m/z* = 360.0930, calcd. for $C_{21}H_{16}N_2O_2S$ (M^+): 360.0927.

1-Methyl-3-(phenylthio)-2-[3-(trifluoromethyl)phenyl]-1*H*-indole (20): Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$ 7.69–7.65 (m, 3H), 7.60–7.52 (m, 2H), 7.44 (d, $J=8.1$ Hz, 1H), 7.37–7.32 (m, 1H), 7.24–7.19 (m, 1H), 7.16–7.11 (m, 2H), 7.04–7.02 (m, 3H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=143.8$, 139.5, 137.7, 133.9, 131.3, 130. 7 (q, $J_{C,F}=$ 32.3 Hz), 129.7, 128.8, 128.7, 127.4 (q, $J_{C,F}=3.8$ Hz), 125.8, 125.4 (q, $J_{C,F}=3.8$ Hz), 124.7, 122.8, 122.3 (q, $J_{C,F}=$ 258.8 Hz), 120.0, 110.0, 101.0, 31.7; IR (KBr): $\nu=1323$, 1266, 1124, 740, 702 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 384 (M^++1, 24), 383 (M^+, 100), 368 (13), 351 (11), 291 (16); HR-MS (EI): *m/z* = 383.0955, calcd. for $C_{22}H_{16}F_3NS$ (M^+): 383.0950.

2-Hexyl-1-methyl-3-(phenylthio)-1*H*-indole (21): Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.60$ (d, $J=7.8$ Hz, 1H), 7.38 (d, $J=8.1$ Hz, 1H), 7.30–7.25 (m, 1H), 7.20–7.14 (m, 3H), 7.07 (d, $J=7.6$ Hz, 3H), 3.81 (s, 3H), 2.97 (t, $J=$ 7.8 Hz, 2H), 1.63–1.53 (m, 2H), 1.30 (m, 6H), 0.88 (t, $J=$ 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=147.0$, 139.9, 137.2, 129.7, 128.5, 125.3, 124.3, 121.7, 120.4, 119.0, 109.1, 97.7, 31.5, 30.3, 29.9, 29.0, 24.9, 22.5, 14.0; IR (KBr): $\nu=$ 1466, 1439, 1265, 739, 704 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 323 (M^+, 67), 252 (32), 220 (25), 214 (32), 144 (100); HR-MS (EI): *m/z* = 323.1704, calcd. for $C_{21}H_{25}NS$ (M^+): 323.1702.

2-*tert*-Butyl-1-methyl-3-(phenylthio)-1*H*-indole (22): White solid, mp 153.5–154.3 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.61$ (d, $J=7.8$ Hz, 1H), 7.33 (d, $J=$ 8.1 Hz, 1H), 7.27–7.22 (m, 1H), 7.16–7.02 (m, 3H), 7.00–6.95 (m, 3H), 7.05–6.95 (m, 3H), 3.99 (s, 3H), 1.64 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=151.0$, 141.0, 138.1, 130.8, 128.6, 124.8, 123.9, 122.4, 120.5, 119.5, 108.8, 97.5, 35.1, 34.1, 31.4; IR (KBr): $\nu=1467$, 1266, 740, 703, 690 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 295 (M^+, 93), 280 (46), 171 (100), 170 (21), 149 (34); HR-MS (EI): *m/z* = 295.1392, calcd. for $C_{19}H_{21}NS$ (M^+): 295.1389.

1,5-Dimethyl-2-phenyl-3-(phenylthio)-1*H*-indole (23): White solid, mp 110.0–110.4 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.43$–7.39 (m, 6H), 7.31 (d, $J=$ 8.1 Hz, 1H), 7.21–7.11 (m, 3H), 7.05–6.99 (m, 3H), 3.70 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=152.1$, 146.0, 140.3, 136.0, 130.9, 130.6, 130.5, 130.0, 128.7, 128.2, 125.3, 124.4, 124.3, 119.3, 109.6, 98.6, 31.8, 21.5; IR (KBr): $\nu=1265$, 793, 774, 740, 701 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 329 (M^+, 100), 330 (25), 297 (14), 237 (25), 236 (15); HR-MS (EI): *m/z* = 329.1238, calcd. for $C_{22}H_{19}NS$ (M^+): 329.1233.

5-Fluoro-1-methyl-2-phenyl-3-(phenylselanyl)-1*H*-indole (24): Yellow solid, mp 112.0–113.2 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.50$–7.45 (m, 5H), 7.37–7.36 (m, 2H), 7.20–7.17 (m, 2H), 7.11–7.07 (m, 4H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=158.7$ (d, $J_{C,F}=$ 141.0 Hz, 1C), 147.4, 139.5, 134.0, 130.5 (d, $J_{C,F}=5.3$ Hz, 1C), 130.1, 128.9, 128.7, 128.3, 125.4, 124.5, 111.1 (d, $J_{C,F}=$ 15.0 Hz, 1C), 110.7 (d, $J_{C,F}=6.0$ Hz, 1C), 104.7 (d, $J_{C,F}=$ 14.3 Hz, 1C), 99.6, 99.5, 31.9; IR (KBr): $\nu=1474$, 1266, 776, 741, 701 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 333 (M^+, 100), 334 (26), 241 (26), 98 (17), 43 (19); HR-MS (EI): *m/z* = 333.0987, calcd. for $C_{21}H_{16}FNS$ (M^+): 333.0982.

1-Methyl-2-phenyl-3-(phenylselanyl)-1*H*-indole (25):[8a] Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.68$ (d, $J=$ 7.8 Hz, 1H), 7.44–7.34 (m, 9H), 7.24–7.09 (m, 4H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=145.9$, 137.7, 134.6, 131.2, 130.8, 130.6, 128.8, 128.6, 128.4, 128.1, 125.2, 122.7, 120.8, 120.7, 109.7, 96.4, 31.7; IR (KBr): $\nu=1474$, 1464, 733, 699, 690 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 363 (M^+, 28), 329 (35), 283 (100), 279 (22), 204 (24).

1-Methyl-2-phenyl-3-(*p*-tolylselanyl)-1*H*-indole (26): Yellow solid, mp 110.2–110.6 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.67$ (d, $J=7.8$ Hz, 1H), 7.45–7.37 (m, 6H), 7.31–7.26 (m, 1H), 7.24–7.19 (m, 1H), 7.06 (d, $J=$ 8.1 Hz, 2H), 6.92 (d, $J=7.8$ Hz, 2H), 3.72 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=145.7$, 137.7, 135.0, 131.3, 130.8, 130.7, 130.6, 129.7, 128.6, 128.1, 127.7, 122.6, 120.8, 120.7, 109.7, 96.8, 31.8, 20.9; IR (KBr): $\nu=1465$, 1266, 800, 741, 702 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 377 (M^+, 21), 375 (12), 298 (24), 297 (100), 141 (10); HR-MS (EI): *m/z* = 377.0678, calcd. for $C_{22}H_{19}NSe$ (M^+): 377.0677.

1-Methyl-3-(methylselanyl)-2-phenyl-1*H*-indole (27): Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.86$ (d, $J=$ 8.1 Hz, 1H), 7.56–7.50 (m, 5H), 7.42–7.31 (m, 3H), 3.71 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=144.2$, 137.4, 131.6, 130.9, 130.3, 128.5, 128.1, 122.4, 120.4, 120.3, 109.6, 98.3, 31.5, 9.1; IR (KBr): $\nu=1465$, 1266, 896, 741, 703 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 301 (M^+, 100), 299 (48), 286 (77), 271 (53), 206 (63); HR-MS (EI): *m/z* = 301.0367, calcd. for $C_{16}H_{15}NSe$ (M^+): 301.0364.

2-(4-Methoxyphenyl)-1-methyl-3-(phenylselanyl)-1*H*-indole (28): Yellow solid, mp 123.8–124.4 °C (uncorrected). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.67$ (d, $J=7.8$ Hz, 1H), 7.43 (d, $J=8.1$ Hz, 1H), 7.35–7.31 (m, 3H), 7.26–7.07 (m, 6H), 6.98 (d, $J=8.4$ Hz, 2H), 3.86 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=159.8$, 145.9, 137.7, 134.7, 132.0, 130.7, 128.8, 128.3, 125.2, 123.4, 122.5, 120.8, 120.5, 113.6, 109.7, 96.1, 55.3, 31.7; IR (KBr): $\nu=1326$, 1266, 896, 742, 704 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 393 (M^+, 20), 391 (11), 314 (26), 313 (100), 270 (7); HRMS (EI): *m/z* = 393.0628, calcd. for $C_{22}H_{19}NOSe$ (M^+): 393.0626.

2-(2-Methoxyphenyl)-1-methyl-3-(phenylselanyl)-1*H*-indole (29): Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$ 7.70 (d, $J=7.8$ Hz, 1H), 7.45 (d, $J=7.8$ Hz, 2H), 7.34–7.19 (m, 5H), 7.13–7.00 (m, 5H), 3.73 (s, 3H), 3.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=157.9$, 143.4, 137.5, 134.7, 133.1, 130.7, 130.5, 128.6 (2C), 128.4, 125.0, 122.2, 120.5,

120.4, 120.3, 110.8, 109.5, 96.5, 55.3, 31.2; IR (KBr): ν = 1265, 1247, 739, 704, 690 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 393 (M^+, 33), 314 (24), 313 (100), 234 (21), 220 (19); HR-MS (EI): *m/z* = 393.0628, calcd. for $C_{22}H_{19}NOSe$ (M^+): 393.0626.

1-Methyl-2-(4-nitrophenyl)-3-(phenylselanyl)-1*H*-indole (30): Yellow solid, mp 137.7–138.7 °C (uncorrected). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.29 (d, *J* = 9.0 Hz, 2H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.46–7.36 (m, 1H), 7.26–7.21 (m, 1H), 7.13–7.09 (m, 5H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.7, 142.9, 138.2, 137.8, 133.9, 131.7, 130.6, 129.1, 128.4, 125.7, 123.7, 123.3, 121.4, 121.1, 109.9, 98.4, 32.0; IR (KBr): ν = 1465, 1339, 1266, 741, 704 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 408 (M^+, 29), 329 (25), 328 (100), 282 (31), 267 (24); HR-MS (EI): *m/z* = 408.0374, calcd. for $C_{21}H_{16}N_2O_2Se$ (M^+): 408.0372.

5-Fluoro-1-methyl-2-phenyl-3-(phenylselanyl)-1*H*-indole (31): Yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.44 (m, 3H), 7.39–7.32 (m, 4H), 7.12–7.09 (m, 6H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8 (d, $J_{C,F}$ = 141.0 Hz, 1C), 147.4, 134.3, 134.2, 131.4, 131.0, 130.7, 128.9 (2C), 128.6, 128.5, 128.2, 125.5, 111.0 (d, $J_{C,F}$ = 16.5 Hz, 1C), 110.5 (d, $J_{C,F}$ = 6.0 Hz, 1C), 105.7 (d, $J_{C,F}$ = 14.3 Hz, 1C), 32.0; IR (KBr): ν = 1474, 1022, 794, 775, 698 cm^{-1}; LR-MS (EI, 70 eV): *m/z* (%) = 381 (M^+, 26), 379 (13), 301 (100), 302 (23), 285 (12); HR-MS (EI): *m/z* = 381.0429, calcd. for $C_{21}H_{16}FNSe$ (M^+): 381.0427.

Acknowledgements

We thank the Natural Science Foundation of China (Nos. 20872112 and 21002070), and Zhejiang Provincial Natural Science Foundation of China (Nos. Y4100307 and Y4080169) for financial support.

References

[1] For selected recent reviews, see a) J.-R. Weng, C.-H. Tsai, S. K. Kulp, C.-S. Chen, *Cancer Lett.* **2008**, *262*, 153; b) G. C. Rieck, A. N. Fiander, *Mol. Nutr. Food Res.* **2008**, *52*, 105; c) A. Brancale, R. Silvestri, *Med. Res. Rev.* **2007**, *27*, 209.

[2] G. La Regina, M. C. Edler, A. Brancale, S. Kandil, A. Coluccia, F. Piscitelli, E. Hamel, G. De Martino, R. Matesanz, J. F. Díaz, A. I. Scovassi, E. Prosperi, A. Lavecchia, E. Novellino, M. Artico, R. Silvestri, *J. Med. Chem.* **2007**, *50*, 2865.

[3] a) R. Ragno, A. Coluccia, G. La Regina, G. De Martino, F. Piscitelli, A. Lavecchia, E. Novellino, A. Bergamini, C. Ciaprini, A. Sinistro, G. Maga, E. Crespan, M. Artico, R. Silvestri, *J. Med. Chem.* **2006**, *49*, 3172; b) T. M. Williams, T. M. Ciccarone, W. S. Saari, J. S. Wai, W. J. Greenlee, S. K. Balani, M. E. Goldman, J. M. Hoffman Jr, W. C. Lumma Jr, J. R. Huff, C. S. Rooney, P. E. Sanderson, A. D. Theoharides, *PCT Int. Appl.* WO 9419321, **1994**; c) R. Silvestri, M. Artico, B. Bruno, S. Massa, E. Novellino, G. Greco, M. E. Marongiu, A. Pani, A. De Montis, P. La Colla, *Antiviral Chem. Chemother.* **1998**, *9*, 139; d) R. Ragno, A. Coluccia, La G. Regina, G. De Matrino, F. Piscitelli, A. Lavecchia, E. Novellino, A. Bergamini, C. Ciapini, A. Sinistro, G. Maga, E. Crespan, M. Artico, R. Silvestri, *J. Med. Chem.* **2006**, *49*, 3172; e) G. De Martino, G. La Regina, A. Coluccia, E. Edler, M. Artico, R. Silvestri, *J. Med. Chem.* **2004**, *47*, 6120.

[4] a) V. S. N. Ramakrishna, V. S. Shirsath, R. S. Kambhampati, S. Vishwakarma, N. V. Kandikere, S. Kota, V. Jasti, *PCT Int. Appl.* WO 2007020653, **2007**; b) J. P. Berger, T. W. Doebber, M. Leibowitz, D. E. Moller, R. T. Mosley, R. L. Tolman, J. Ventre, B. B. Zhang, G. Zhou, *PCT Int. Appl.* WO 0130343, **2001**; c) V. S. N. Ramakrishna, V. S. Shirsath, R. S. Kambhampai, S. Vishwakarma, N. V. Kandikere, S. Kota, V. Jasti, *PCT Int. Appl.* WO 2007020653, **2007**.

[5] C. D. Funk, *Nat. Rev. Drug Discovery* **2005**, *4*, 664.

[6] For selected papers on the synthesis of 3-sulfenylindoles *via* direct sulfenylation of indoles: a) K. M. Schlosser, A. P. Krasutsky, H. W. Hamilton, J. E. Reed, K. Sexton, *Org. Lett.* **2004**, *6*, 819; b) J. A. Campbell, C. A. Broka, L. Gong, K. A. Walker, J.-H. Wang, *Tetrahedron Lett.* **2004**, *45*, 4073; c) J. S. Yadav, B. V. S. Reddy, Y. J. Reddy, *Tetrahedron Lett.* **2007**, *48*, 7034; d) Y. Maeda, M. Koyabu, T. Nishimura, S. Uemura, *J. Org. Chem.* **2004**, *69*, 7688; e) J. G. Atkinson, P. Hamel, Y. Girard, *Synthesis* **1988**, 480; f) P. F. Ranken, B. G. McKinnie, *J. Org. Chem.* **1989**, *54*, 2985; g) M. Matsugi, K. Murata, K. Gotanda, H. Nambu, G. Anilkumar, K. Matsumoto, Y. Kita, *J. Org. Chem.* **2001**, *66*, 2434; h) M. Tudge, M. Tamiya, C. Savarin, G. R. Humphrey, *Org. Lett.* **2006**, *8*, 565; i) A. Pezzella, A. Palma, A. Iadonisi, A. Napolitano, M. d'Ischia, *Tetrahedron Lett.* **2007**, *48*, 3883; j) J. S. Yadav, B. V. S. Reddy, A. D. Krishna, C. S. Reddy, A. V. Narsaiah, *Synthesis* **2005**, 961; k) G. Wu, Q. Liu, Y. Shen, W. Wu, L. Wu, *Tetrahedron Lett.* **2005**, *46*, 5831.

[7] For selected papers on the synthesis of 3-sulfenylindoles *via* the other methods, see: a) H. Shirani, B. Stensland, J. Bergman, T. Janosik, *Synlett* **2006**, 2459; b) P. Barraja, P. Diana, A. Carbone, G. Cirrincione, *Tetrahedron* **2008**, *64*, 11625.

[8] a) Y. Chen, C.-H. Cho, F. Shi, R. C. Larock, *J. Org. Chem.* **2009**, *74*, 6802; b) Y. Chen, C.-H. Cho, F. Shi, R. C. Larock, *Org. Lett.* **2009**, *11*, 173.

[9] H.-A. Du, X.-G. Zhang, R.-Y. Tang, J.-H. Li, *J. Org. Chem.* **2009**, *74*, 7844.

[10] For papers on the use of disulfides from our group, see: a) R.-Y. Tang, P. Zhong, Q.-L. Lin, *J. Fluorine Chem.* **2006**, *127*, 948; b) R.-Y. Tang, P. Zhong, Q.-L. Lin, *Synlett* **2007**, 85; c) Z.-L. Wang, R.-Y. Tang, P.-S. Luo, C.-L. Deng, P. Zhong, J.-H. Li, *Tetrahedron* **2008**, *64*, 10670; d) P.-S. Luo, M. Yu, R.-Y. Tang, P. Zhong, J.-H. Li, *Tetrahedron Lett.* **2009**, *50*, 1066; e) P.-S. Luo, F. Wang, J.-H. Li, R.-Y. Tang, P. Zhong, *Synthesis* **2009**, 921; f) Y.-J. Guo, R.-Y. Tang, J.-H. Li, P. Zhong, X.-G. Zhang, *Adv. Synth. Catal.* **2009**, *351*, 2615; g) X.-L. Fang, R.-Y. Tang, P. Zhong, J.-H. Li, *Synthesis* **2009**, 4183.

[11] K. Goto, G. Yamamoto, B. Tan, R. Okazaki, *Tetrahedron Lett.* **2001**, *42*, 4875.

[12] P. Barraja, P. Diana, A. Carbone, G. Cirrincione, *Tetrahedron* **2008**, *64*, 11625.

