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Iron(III) Chloride/Diorganyl Diselenides Promoted Regio- and Stereoselective Cyclization of *ortho*-Alkynylanilides: Synthesis of (*Z*)-4-(chalcogen)methylenebenzoxazines

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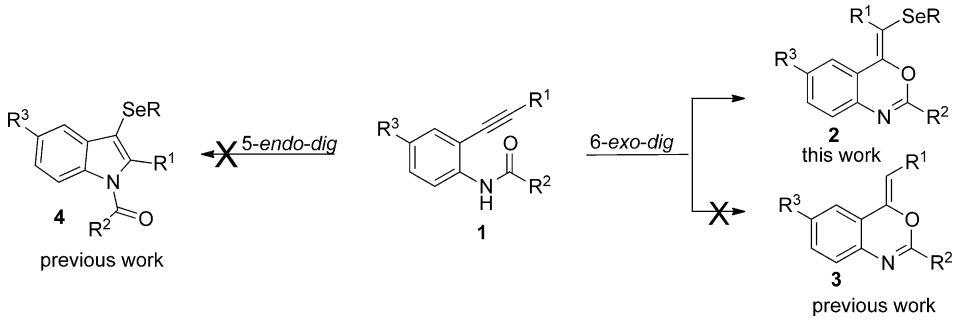
Abstract: Intramolecular 6-*exo-dig* cyclization of *ortho*-alkynylanilides has been employed in a regio- and stereoselective synthesis of (*Z*)-4-(chalcogen)-methylenebenzoxazines. Several reaction parameters were screened for the efficient cyclization of *ortho*-alkynylanilides. Among them, the reaction of *ortho*-alkynylanilides (0.25 mmol) with iron(III) chloride (3.0 equiv.) and diorganyl diselenides (0.75 equiv.) in dichloromethane as solvent gave the products in acceptable to good yields. The resulting products were then subjected to a nitrogen–oxygen exchange reaction with ammonium acetate to furnish quinazoline derivatives. The one-pot version of this cyclization, starting directly from 2-alkynylanilines, avoiding the previous preparation of *ortho*-alkynylanilides was also briefly studied.

Keywords: benzoxazines; diorganoyl diselenides; intramolecular 6-*exo-dig* cyclization; iron; quinazolines

Introduction

The development of efficient methods to allow the transformation of unsaturated substrates, having an internal nucleophile, in an appropriate distance, into heterocycles has been widely exploited. In this regard, transition metal-catalyzed cyclization[1] and electrophilic cyclization[2] have proven to be the most efficient approaches to the synthesis of heterocycles. Among the use of transition metals, not only palladium[3] but also gold,[4] copper,[5] rhodium,[6] platinum,[7] indium,[8] ruthenium[9] and iron salts[10] have been applied for the synthesis of heterocycles. From these metals, the application of iron salts has increased in the last few years due to the low cost, low toxicity, compatibility with solvents, air and with a wide range of functional groups.[10] Recently, a mixture of $FeCl_3$/PhSeSePh was found to be an alternative system to promote the cyclization of unsaturated substrates.[11] More recently, we have also demonstrated $FeCl_3$/PhSeSePh as an efficient system for the preparation of vinyl selenides,[12] organoselenoisoxazoles,[13] organoselenoisochromenones[14] and organoselenochromenones.[15] The cyclization of *ortho*-alkynylanilides is an appropriate way to produce nitrogen heterocycles, such as indoles and benzoxazines.[16] Despite the great progress made in indole synthesis,[17] only few general and efficient methods are available for the synthesis of oxazine derivatives.[18] An improved procedure for the cyclization of *ortho*-alkynylanilides was successfully applied by the Saito group.[19] This method involved a regio- and stereoselective 6-*exo-dig* cyclization of *N*-acyl-*ortho*-alkynylanilines producing 4-alkylidene-3,1-benzoxazines **3** (Scheme 1) by using $Pd(OAc)_2$ as catalyst and acetic acid as additive. In contrast, there are no examples for the formation of the corresponding *Z*-alkylidenebenzoxazines, where the two groups, R^1 and oxygen, are on opposite sides of the double bond (Scheme 1). The economic and environmental advantages of iron salts in association with the easy preparation of diorganyl diselenides,[20] led us to study whether iron(III) chloride and diorganyl dichalcogenides could be employed as cyclizing agent of *ortho*-alkynylanilides **1** to prepare *Z*-alkylidenebenzoxazine organoselenium derivatives **2** (Scheme 1).

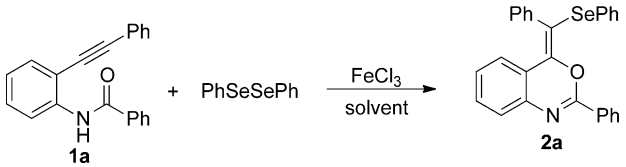


Scheme 1. General scheme.

Results and Discussion

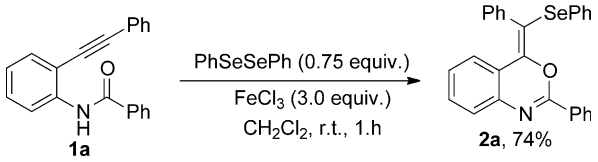
The required *ortho*-alkynylanilides **1** were obtained by Sonogashira cross-coupling of the corresponding 2-iodoanilines with terminal alkynes, followed by nitrogen acylation with acyl chlorides.[19] We started our research on the cyclization reaction by studying the most appropriate experimental conditions to deliver the desired products in high yields with a low rate of by-products. To this end, the reaction of *ortho*-alkynylanilide[19] **1a** with diphenyl diselenide and $FeCl_3$ was optimized in terms of relative rates of reagents, solvent, temperature and reaction time. We started our investigation by adding the *o*-alkynilanilide **1a** (0.25 mmol), at room temperature, under an argon atmosphere, to a solution of $FeCl_3$ (1.0 equiv.) and diphenyl diselenide (1.0 equiv.; which was prepared 10 min before use) in CH_2Cl_2 (5 mL). Using these conditions, the benzoxazine **2a** was obtained in 41% yield (Table 1, entry 1). Further loading of different amounts of iron(III) chloride and diphenyl diselenide proved that 3.0 equiv. and 0.75 equiv., respectively, are required to obtain a better yield and purity of product **2a**. Even though the use of iron(III) chloride (1.5 or 2.0 equiv.) with diphenyl diselenide (0.5 equiv.) afforded the benzoxazine **2a** in good yields, in such a case, due to the presence of an indole derivative, as by-product, the purification processes becomes more complex. The large amount of iron(III) chloride required in this cyclization proved to be necessary not only to activate the triple bond[21] but also to promote the selenium incorporation. In fact, when iron(III) chloride (1.0 equiv.) was used in the absence of diphenyl diselenide, the indole without the organoselenium moiety in the structure was obtained and the remainder of the starting material was recovered. Besides, when the *ortho*-alkynylanilide **1a** was previously treated with diphenyl diselenide, followed by addition of iron(III) chloride (1.0 equiv.) only a trace amount of the product was obtained and unreacted starting materials were recovered. We also observed that the inverse addition of a mixture of diphenyl diselenide (1.0 equiv.), iron(III) chloride (1.0 equiv) and CH_2Cl_2 to a solution of *ortho*-alkynylanilide **1a** in CH_2Cl_2 afforded only the starting materials. These results suggest that due to the strong affinity for nitrogen and oxygen atoms, as well as for the carbon-carbon triple bond, a portion of the iron(III) chloride was required to complex with these donor ligands, while other portion reacted with diphenyl diselenide to form the intermediate which promoted the cyclization and the incorporation of PhSe in the heterocycle. Additionally, the isolated yields obtained by using 0.75 equiv. of diphenyl diselenide (PhSeSePh) imply that two PhSe groups from the organoselenium reagents were transferred to the substrate. Among the solvents tested, dichloromethane proved to be the best choice, whereas

Table 1. Optimization of the cyclization conditions.[a]



Entry	$FeCl_3$ (equiv.)	PhSeSePh (equiv.)	Solvent	Time [h]	Yield [%][b]
1	1.0	1.0	CH_2Cl_2	1	41
2	1.0	0.5	CH_2Cl_2	1	59
3	1.2	0.5	CH_2Cl_2	1	59
4	1.5	0.5	CH_2Cl_2	1	79
5	1.5	1.0	CH_2Cl_2	1	61
6	2.0	0.5	CH_2Cl_2	1	88
7	2.0	0.5	DCE	1	87
8	2.0	0.5	$CHCl_3$	0.5	63
9	2.0	0.5	$MeNO_2$	4	74
10	2.0	0.5	MeOH	12	–
11	2.0	0.5	THF	12	–
12	3.0	0.75	CH_2Cl_2	1	74[c]
13	1.5	0.5	CH_2Cl_2	1	46[c,d]
14	3.0	0.75	CH_2Cl_2	2	48[c,e]

[a] The reactions were performed using the *N*-[2-(phenylethynyl)phenyl]benzamide (0.25 mmol) and diphenyl diselenide in solvent (5 mL).
[b] Yields were determined by GC analysis.
[c] Isolated yield after column chromatography.
[d] Reaction carried out at 40 °C.
[e] Reaction carried out at 0 °C.

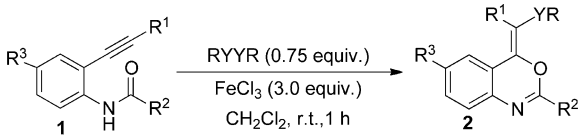


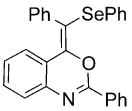
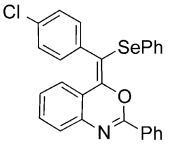
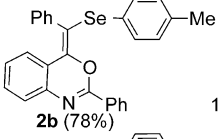
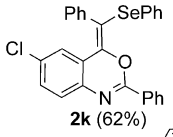
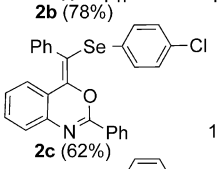
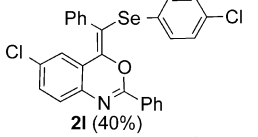
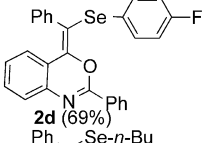
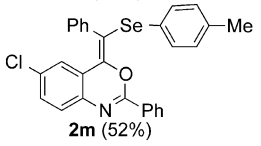
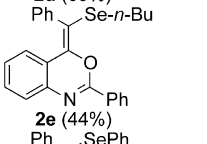
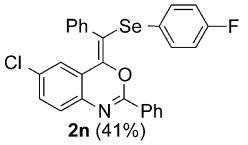
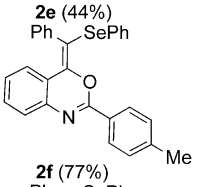
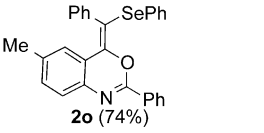
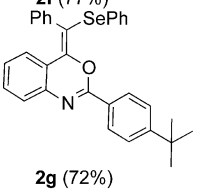
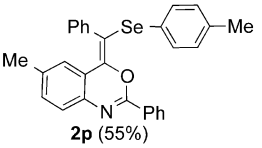
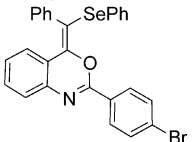
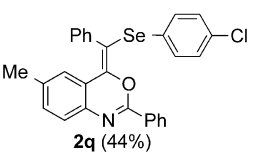
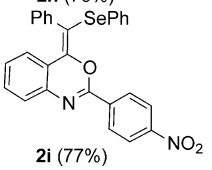
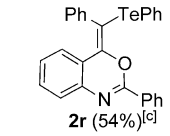
Scheme 2. Preparation of organoselenobenzoxazine **2a**.

the other solvents, such as methanol, tetrahydrofuran and chloroform were inferior (Table 1, entries 7–11). With regard to temperature, the use of room temperature was more beneficial than a lower temperature or reflux (Table 1, entries 13 and 14). Finally, at various interval times during the optimization reactions, samples of the reaction mixture were analyzed by TLC, which showed that 1 h was the reaction time necessary for the complete consumption of the starting material. Under the optimized condition: *ortho*-alkynylanilide **1a** (0.25 mmol), $FeCl_3$ (3.0 equiv.), diphenyl diselenide (0.75 equiv.) in CH_2Cl_2 (5 mL) as solvent at room temperature for 1 h, organoselenobenzoxazine **2a** was formed in 74% isolated yield (Scheme 2) with the complete absence of hydrogenated benzoxazine **3** and indole **4** (Scheme 1).

The optimized conditions were then applied to other *ortho*-alkynylanilidea **1** and the results are presented in Table 2. We started by examining the influence of diorganyl diselenides in the cyclization reaction (Table 2, entries 1–5). The nature of the functional groups on the aromatic ring of the diorganyl diselenides seems to have influence on the course of the reaction. In fact, better yields were obtained with diorganyl diselenides having neutral or electron-donating groups in comparison to those having electron-withdrawing groups (Table 2, entries 1–4). The reactivity of an alkyl diselenide was also investigated. In this case, when dibutyl diselenide was employed as organoselenium source, the yield of the corresponding product **2e** decreased to 44% (Table 2, entry 5). This low yield can be attributed to losses *via syn* elimination of selenoxide formed during purification by column chromatography. Next, we studied the influence of the R^2 substituent directly bonded to the carbonyl group of *ortho*-alkynylanilides **1** (Table 2, entries 6–9). Thus, the addition of some groups in the aromatic ring R^2, such as Me, *t*-Bu, Br and NO_2, had no influence on the course of the cyclization whereby the benzoxazines **2f–i** were obtained in similar yields. Substrates bearing both electron-withdrawing and electron-donating substituents at the 4-position reacted to give the desired biaryl products in moderate yields (Table 2, entries 10–17). The cyclization was not limited only to diorganyl diselenides. Treatment of the *ortho*-alkynylanilide **1** with diphenyl ditelluride, using the optimized conditions, resulted in the formation of benzoxazine organotelluro derivative **2r** in 54% yield (Table 2, entry 18). In this case, the product

Table 2. *ortho*-Alkynylanilide cyclization by the combination $FeCl_3$/ArYYAr.[a]

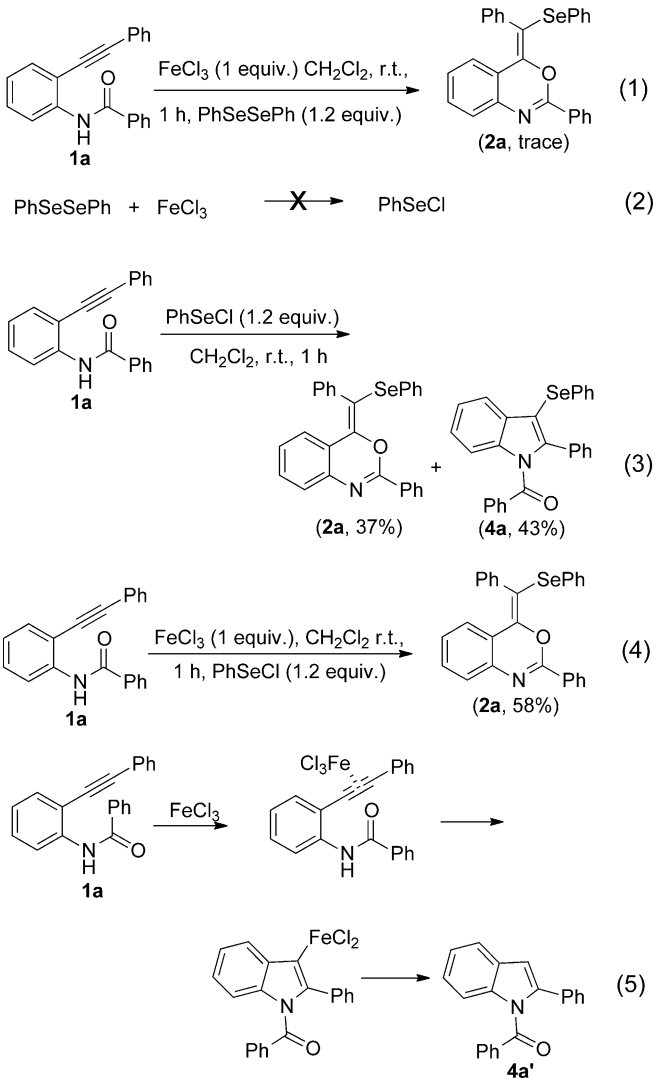


Entry	Product (yield)[b]	Entry	Product (yield)[b]
1	 **2a** (74%)	10	 **2j** (54%)
2	 **2b** (78%)	11	 **2k** (62%)
3	 **2c** (62%)	12	 **2l** (40%)
4	 **2d** (69%)	13	 **2m** (52%)
5	 **2e** (44%)	14	 **2n** (41%)
6	 **2f** (77%)	15	 **2o** (74%)
7	 **2g** (72%)	16	 **2p** (55%)
8	 **2h** (76%)	17	 **2q** (44%)
9	 **2i** (77%)	18	 **2r** (54%)[c]

[a] The reaction was performed in the presence of **1** (0.25 mmol), diorganyl dichalcogenides (0.75 equiv.), $FeCl_3$ (3.0 equiv.), CH_2Cl_2 (5 mL) as solvent, under an argon atmosphere, at room temperature for 1 h.

[b] Yields for isolated products.

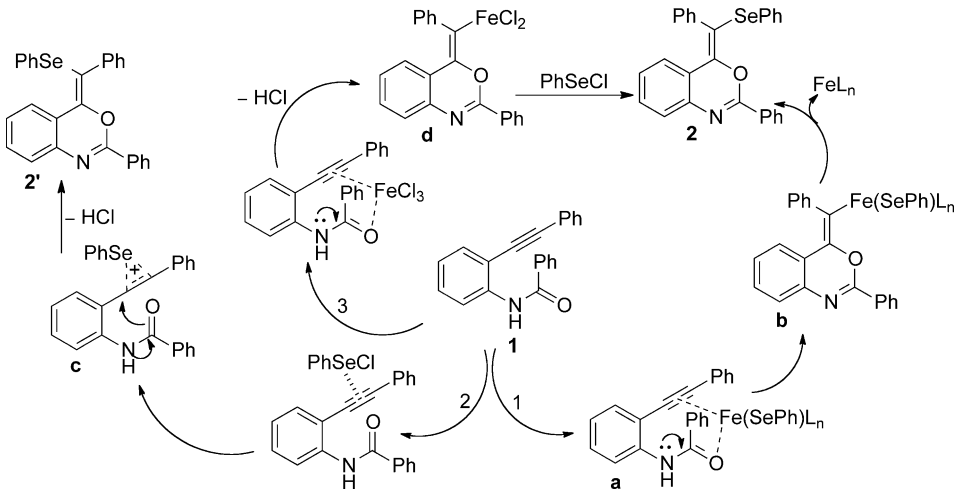
[c] Yields determined by gas chromatography.



Scheme 3. Mechanism investigations.

2r was obtained as a mixture containing hydrogenenated oxazine and diphenyl ditelluride. Therefore, the purification to high purity from the mixture was impossible. This result represents an additional attractive feature of our methodology since the higher reactivity of the organotellurium moiety offers the possibility for developing more complex heterocyclic compounds.[22] Concerning the use of disulfides instead of diselenides or ditellurides, we found some limitations in this methodology. For example, reaction of diphenyl disulfide under the optimized conditions resulted in the formation of a trace amount of product together with unreacted starting material.

Concerning the mechanism pathway, the main question is whether the cyclization may occur *via* an electrophilic cyclization involving the PhSeCl (obtained *in situ* by reaction of diphenyl diselenides and $FeCl_3$) or *via* an iron selenolate complex.[23] To obtain further insight in order to rationalize the factors which could govern the mechanism aspect of this cyclization reaction, we performed some control experiments as follows: (a) when diphenyl diselenide was added to a solution of *ortho*-alkynylanilide **1a** and $FeCl_3$ in CH_2Cl_2 the reaction gave only traces of product [Scheme 3, Eq. (1)]. From this result we conclude that the mechanism by which $FeCl_3$ promotes the cyclization to form a cyclized Csp^2–Fe intermediate **d** (Scheme 4) that could react with diphenyl diselenide to give the product is improbable; (b) when diphenyl diselenide was reacted with $FeCl_3$ in CH_2Cl_2, in the absence of substrate **1a**, no PhSeCl was detectable [Scheme 3, Eq. (2)]. These results provide the first evidence to discard the electrophilic cyclization pathway promoted by PhSeCl. However, when PhSeCl, previously prepared by reaction of diphenyl diselenide with thionyl chloride,[24] was added to a solution of **1a** in CH_2Cl_2, a 37% yield of the desired product **2a** and



Scheme 4. Proposed mechanism for the synthesis of organoselenobenzoxazines.

a 43% yield of the indole derivative were obtained [Scheme 3, Eq. (3)]. When the solution of *ortho*-alkynylanilide **1a**, $FeCl_3$ in CH_2Cl_2 was reacted for 1 h at room temperature and then PhSeCl was added, a mixture of product **2a** with both hydrogenated oxazine **3** and indole **4** was obtained [Scheme 3, Eq. (4)]. The reaction of *ortho*-alkynilanilide **1a**, with iron(III) chloride (1.0 equiv.) in the absence of diphenyl diselenide gave a trace of the indole **4a′**. In this case, the iron(III) chloride acts as a Lewis acid to activate the triple bond to the nitrogen nucleophilic attack giving the indole [Scheme 3, Eq. (5)]. Finally, the radical pathway was not discarded; however, when the reaction of **1a** with diphenyl diselenide was carried out in the presence of TEMPO, a radical inhibitor, **2a** was obtained in 70% yield. This result indicates that the pathway does not follow the typical radical addition, where the radical source is PhSe•. All results together showed that the oxazine **2a** formation is dependent on the iron selenolate complex previously formed. With this information in hand, we assume that: (i) the iron selenolate species[21] coordinates to the carbon-carbon bond to generate an intermediate **a**,[25] which activates the carbon-carbon bond towards oxygen attack, (ii) the *anti* attack of the oxygen atom on the activated intermediate produces the oxazine-iron species **b**, which suffers a reductive elimination to give the desired cyclized product **2** (Scheme 4, pathway 1). In addition, the Z stereochemistry obtained for benzoxazines **2** is the second piece of evidence to discard the electrophilic pathway 2 (Scheme 4). In this case, the coordination of the electrophilic source, PhSeCl, to the carbon-carbon triple bond could give the intermediate **c**, (ii) the nucleophilic anti attack of the oxygen atom on the activated triple bond could produce the *E*-alkylidenebenzoxazines **2′** which have the two groups, PhSe and oxygen, in opposite sides of the double bond (Scheme 4, pathway 2). In addition, analyzing the results, a non-dominant pathway 3, Scheme 4, where $FeCl_3$ promotes the cyclization of *ortho*-alkynylanilide to form the intermediate **d**, which reacts with electrophilic PhSeCl to give the oxazine **2** cannot be excluded. As depicted in the study for optimization of the conditions, amounts of indole derivative **4** were obtained as a result of a 5-*endo* cyclization, however, after the determination of the best conditions, only 6-*exo* products were obtained, which were determined by NMR and confirmed by X-ray diffraction analysis (Figure 1).[26]

We next turned our attention to the preparation of oxazines **2** starting directly from 2-alkynylanilines **5** avoiding the previous prepartion of *ortho*-alkynylanilide **1**. In view of this, aniline **5** was reacted with acid chloride (1.0 equiv.) in CH_2Cl_2 (5 mL) for 4 h. Then, a solution of diphenyl diselenide and $FeCl_3$ in CH_2Cl_2 was subsequently added. The resulting solution was stirred for 1 h at room temperature. This one-pot procedure furnished oxazines **2a**, **2i** and **2m** in moderate yields (Scheme 5).

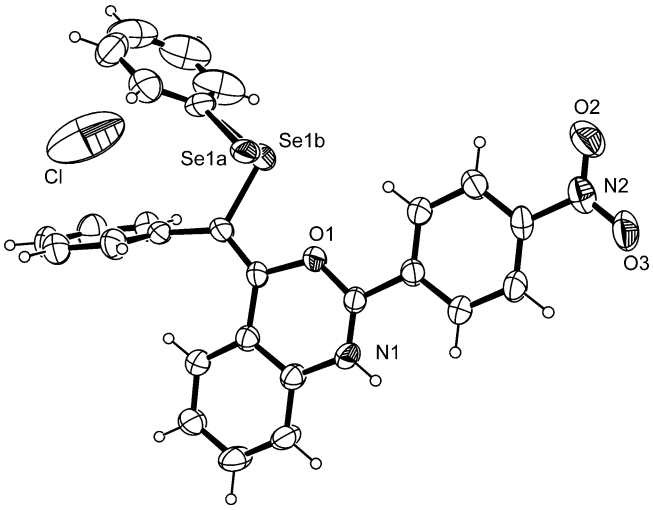
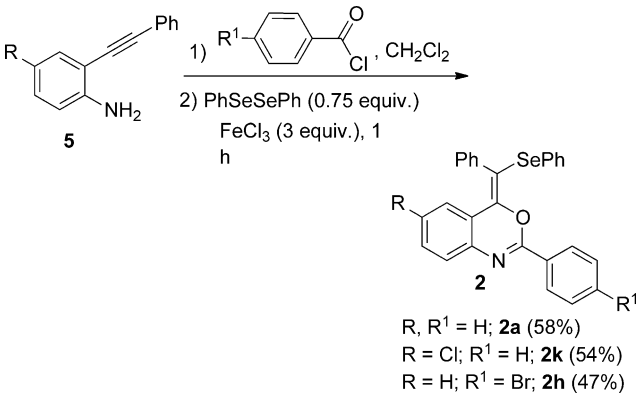


Figure 1. ORTEP view of the compound **2i**.

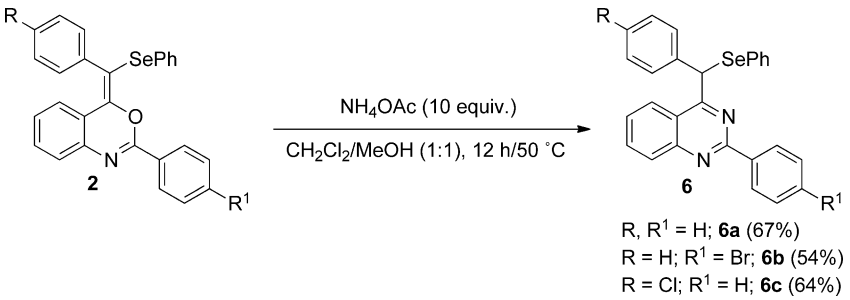


Scheme 5. Preparation of oxazines **2**.

As a result of the importance of quinazolines in the field of pharmacologically active molecules, the development of synthetic approaches using mild reaction conditions remains an attractive area for research. One method of synthesizing quinazolines consists of the reaction of oxazines with a nitrogen nucleophilic source.[16,27] In this context, we evaluated the use of oxazine **2** as substrate in the reaction with NH_4OAc. A brief optimization of the conditions for this reaction revealed that the use of an excess of NH_4OAc (10 equiv.) afforded the quinazoline **6a** in 67% yield. Furthermore, under these experimental conditions, quinazolines **6b** and **6c** were also obtained in 54% and 64% yields, respectively (Scheme 6).[28]

Conclusions

In conclusion, we have found that the mixture of $FeCl_3$ and diorganyl dichalcogenides is a valuable



Scheme 6. Preparation of quinazolines **6a–c**.

combination as a cyclization promoter of *ortho*-alkynylanilides to prepare benzoxazine derivatives. The results obtained demonstrate that: (a) the optimized reaction conditions were compatible with a large variety of functional groups, including electron-rich and electron-poor substrates; (b) the cyclization was stereoselective, affording exclusively the *Z*-alkylidenebenzoxazines; (c) the cyclization was also regioselective giving only the 6-*exo*-*dig*-cyclized products; (d) *Z*-alkylidenebenzoxazines proved to be potential substrates for quinazoline derivatives. In addition, a one-pot version for this cyclization, starting directly from 2-alkynylanilines, avoiding the previous preparation of *ortho*-alkynilanilides gave the benzoxazine derivatives in moderate yields. Finally, different from the bad reputation that organoselenium compounds have gained, with respect to bad smell, instability and high toxicity, the compounds prepared in this study were stable and odourless. Besides, they are currently under pharmacological and toxicological investigations showing positive preliminary results.

Experimental Section

General Procedure for Iron-Promoted Cyclization of *N*-Acyl-*ortho*-alkynylanilines and Diorganoyl Dichalcogenides

To a Schlenk tube, under argon atmosphere, containing a mixture of $FeCl_3$ (3 equiv.) in dry CH_2Cl_2 (4 mL) was added the appropriate diorganoyl dichalcogenide (0.75 equiv.). The resulting solution was stirred for 10 min at room temperature. After this the appropriate *N*-acyl-*ortho*-alkynylaniline (0.25 mmol) in CH_2Cl_2 (1 mL) was added and resulting solution was stirred at room temperature for 1 hour. After this the solution was diluted with dichloromethane (10 mL), and washed with saturated aqueous NaCl (3×10 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using *n*-hexane/CH_2Cl_2 60/40 v/v as the eluent.

General One-Pot Procedure for Iron-Promoted Cyclization of *N*-Acyl-*ortho*-alkynylanilines and Diorganoyl Dichalcogenides

In a Schlenk tube, under argon atmosphere, a mixture of the benzoyl chloride (1.01 equiv.), the appropriate 2-alkynylaniline (0.25 mmol) in dry CH_2Cl_2 (5 mL) was stirred for 4–6 h at room temperature. Then, diphenyl diselenide (0.75 equiv.) and $FeCl_3$ (3 equiv.) were subsequently additioned. The resulting solution was stirred for 1 hour at room temperature. After this the solution was diluted with dichloromethane (10 mL), and washed with saturated aqueous NaCl (3×10 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using *n*-hexane/CH_2Cl_2 60/40 v/v as the eluent.

(*Z*)-2-Phenyl-4-[phenyl(phenylselanyl)methylene]-4*H*-benzo[*d*][1,3]oxazine (2a): Yellow solid; mp 139–141 °C; yield: 0.084 g (74%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.38–8.33 (m, 2H), 7.56–7.45 (m, 3H), 7.39–7.04 (m, 12H), 6.81–6.73 (m, 1H), 6.54–6.49 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 155.7, 140.4, 140.3, 136.8, 135.5, 131.8, 131.2, 130.6, 130.1, 129.7, 128.6, 128.5, 128.4, 128.2, 127.6, 127.5, 126.6, 126.2, 125.6, 121.3, 111.8; MS (relative intensity): *m*/*z* = 453 (23), 296 (100), 267 (25), 165 (28), 77 (12); anal. calcd. for $C_{27}H_{19}NOSe$: C 71.68, H 4.23, N, 3.10; found: C 71.75, H 4.30, N 3.16.

(*Z*)-2-Phenyl-4-[phenyl(*para*-tolylphenylseleno)methylene]-4*H*-benzo[*d*][1,3]oxazine (2b): Yellow solid; mp 182–184 °C; yield: 0.091 g (78%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.39–8.33 (m, 2H), 7.53–7.43 (m, 3H), 7.32–7.08 (m, 9H), 6.87–6.71 (m, 3H), 6.51–6.46 (m, 1H), 2.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 155.7, 140.3, 140.0, 137.6, 136.8, 135.7, 131.8, 131.2, 130.6, 130.1 129.6, 129.3, 128.5, 128.4, 128.2, 127.5, 126.6, 126.2, 125.5, 124.3, 121.3, 112.4, 21.1; MS (relative intensity): *m*/*z* = 467 (6), 296 (100), 266 (25), 218 (11), 165 (24), 77 (25); HR-MS: *m*/*z* = 468.0895, calcd. for $C_{28}H_{21}NOSe$ ($M+H^+$): 468.0866.

(*Z*)-4-[(*para*-Chlorophenylseleno)(phenyl)methylene]-2-phenyl-4*H*-benzo[*d*][1,3]oxazine (2c): Yellow solid; mp 216–218 °C; yield: 0.076 g (62%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.37–8.32 (m, 2H), 7.53–6.99 (m, 14H), 6.82–6.74 (m, 1H), 6.54–6.49 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 155.6, 140.7, 140.3, 136.8, 134.0, 132.8, 131.9, 131.1, 130.6, 129.9, 128.7, 128.6, 128.5, 128.2, 127.8, 126.7, 126.3, 125.6, 121.1, 111.3, 106.9; MS (relative intensity): *m*/*z* = 487 (10), 296 (100), 207 (69), 165 (39), 77 (29); anal. calcd. for

$C_{27}H_{18}ClNOSe$: C 66.61, H 3.73, N 2.88; found: C 66.80, H 3.78, N 2.92.

(*Z*)-4-[(*para*-Fluorophenylseleno)(phenyl)methylene]-2-phenyl-4*H*-benzo[*d*][1,3]oxazine (2d): Yellow solid; mp 147–149 °C; yield: 0.081 g (69%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.39–8.34 (m, 2H), 7.54–7.47 (m, 3H), 7.35–7.03 (m, 10H), 6.81–6.66 (m, 3H), 6.53–6.46 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 162.6, 155.4, 140.1, 139.6, 138.2, 136.3, 131.8, 131.2, 130.6, 129.6, 128.6, 128.4, 128.1, 127.9, 127.6, 125.4, 122.4; MS (relative intensity): *m*/*z* = 471 (12), 296 (100), 267 (32), 207 (48), 165 (37), 105 (13), 73 (30); anal. calcd. for $C_{28}H_{21}FNOSe$: C 68.94, H 3.86, N 2.98; found: C 69.05, H 3.90, N 3.03.

(*Z*)-4-[Butylseleno(phenyl)methylene]-2-phenyl-4*H*-benzo[*d*][1,3]oxazine (2e): Yellow solid; mp 61–63 °C; yield: 0.048 g (44%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.49–8.44 (m, 1H), 7.67–7.62 (m, 2H), 7.54–7.22 (m, 11H), 2.36 (t, *J* = 7.2 Hz, 2H), 1.52 (quint, *J* = 7.2 Hz, 2H), 1.24 (sext, *J* = 7.2 Hz, 2H), 0.77 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 156.0, 141.7, 141.3, 138.4, 131.5, 130.3, 129.9, 129.2, 128.2, 128.1, 127.9, 127.5, 127.1, 126.3, 125.6, 122.2, 110.6, 32.2, 27.1, 22.8, 13.5; MS (relative intensity): *m*/*z* = 433 (38), 375 (37), 295 (100), 267 (40), 207 (30), 165 (89), 77 (27); HR-MS: *m*/*z* = 434.1025, calcd. for $C_{25}H_{23}NOSe$: 434.1023 ($M + H^+$).

(*Z*)-4-[Phenyl(phenylseleno)methylene]-2-*para*-tolyl-4*H*-benzo[*d*][1,3]oxazine (2f): Yellow solid; mp 105–107 °C; yield: 0.089 g (77%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.26–8.22 (m, 2H), 7.36–6.98 (m, 14H), 7.78–6.71 (m, 1H), 6.53–6.48 (m, 1H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 155.8, 142.3, 140.4, 136.8, 135.4, 130.6, 129.6, 129.1, 128.9, 128.5, 128.4, 128.3, 128.1, 127.5, 127.4, 126.3, 126.0, 125.6, 121.1, 111.5, 96.3, 21.6; MS (relative intensity): *m*/*z* = 467 (6), 310 (43), 281 (34), 207 (100), 165 (28), 73 (62); anal. calcd. for $C_{28}H_{21}NOSe$: C 72.10, H 4.54, N 3.00; found: C 72.26, H 4.61, N 3.07.

(*Z*)-2-(*para-tert*-Butylphenyl)-4-[phenyl(phenylseleno)-methylene]-4*H*-benzo[*d*][1,3]oxazine (2g): Yellow solid; mp 133–135 °C; yield: 0.091 g (72%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.31–8.26 (m, 2H), 7.54–7.49 (m, 2H), 7.36–7.03 (m, 12H), 6.79–6.70 (m, 1H), 6.53–6.49 (m, 1H), 1.36 (s, 9H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 155.9, 155.4, 140.7, 137.2, 135.4, 131.6, 130.7, 129.7, 129.0, 128.5, 128.4, 128.1, 127.9, 127.5, 126.3, 126.2, 125.7, 125.4, 125.2, 121.3, 111.6, 35.0, 31.2; MS (relative intensity): *m*/*z* = 509 (21), 352 (100), 296 (42), 207 (68), 165 (92), 57 (61); anal. calcd. for $C_{31}H_{27}NOSe$: C 73.22, H 5.35, N 2.75; found: C 73.41, H 5.41, N 2.80.

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[28] For the mechanism of the quinazoline **6a–c** preparation see Scheme 1 of the Supporting Information.

