Tetrahedron 69 (2013) 481–486

Contents lists available at SciVerse ScienceDirect

Tetrahedron

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

# Vinyl selenones: annulation agents for the synthesis of six-membered benzo-1,4-heterocyclic compounds

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ARTICLE INFO

*Article history:*
Received 30 August 2012
Received in revised form 17 October 2012
Accepted 7 November 2012
Available online 14 November 2012

Dedicated to the memory of Professor Marcello Tiecco

*Keywords:*
Vinyl selenones
MIRC reaction
1,4-Benzodioxines
1,4-Benzothiines
1,4-Benzoxazines

ABSTRACT

A novel and general approach to six-membered bicyclic benzo fused 1,4-heterocycles is described. The addition–cyclization cascade of benzo 1,2-diols, 1,2-thiols and 2-(benzylamino)phenols with stable and easily available vinyl selenones affords differently substituted 2,3-dihydro-1,4-benzodioxines, benzodithiines and 3,4-dihydro-2*H*-1,4-benzoxazines in good yields. The same procedure has been extended to the synthesis of 1,2,3,4-tetrahydroquinoxalines. All of these heterocycles are present in a variety of biologically active compounds.

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## 1. Introduction

Development of new synthetic methods for the construction of six-membered bicyclic benzo fused 1,4-heterocycles is particularly important because these are the core structures in many natural products and biologically active medicinally significant compounds.[1]

Fig. 1 shows a variety of important pharmaceutical 1,4-benzodioxine derivatives such as piperoxan, an α-adrenergic blocking agent, fluparoxan, a potent antidepressant, and americanol A, that has interesting neurotrophic properties.[2] A simple 2,3-dihydro-1,4-benzodioxine is present in isovanillyl sweetening agents, that are 500 times sweeter than sucrose[2b,c] (Fig. 1). Furthermore, this nucleus exists in many natural products, such as silybin, isosilybin, haedoxan A, eusiderin, and so on.

In particular the six-membered bicyclic fused heterocycles containing nitrogen neighboring an aromatic ring, like the 3,4-dihydro-2*H*-1,4-benzoxazines, have received considerable attention due to their wide range of biological and therapeutic properties.[3] For example, in Fig. 2 are reported a precursor of a human URAT-1 (urate transporter-1) inhibitor,[3c] and another 1,4-benzoxazine that possesses peroxisome proliferator-activated receptor α (PPARα) and

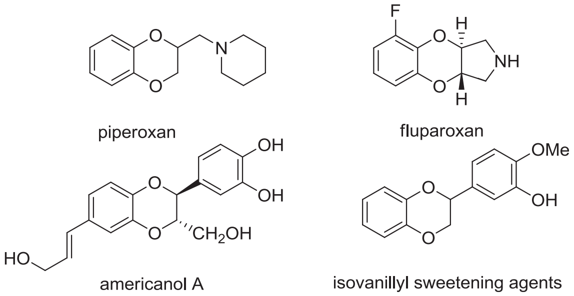

**Fig. 1.** Examples of biologically active 1,4-benzodioxine derivatives.

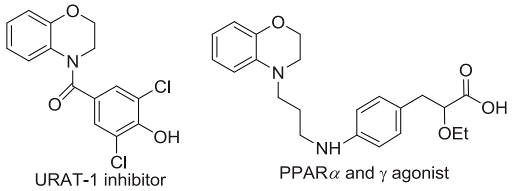

**Fig. 2.** Selected biologically active 3,4-dihydro-2*H*-1,4-benzoxazines.

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http://dx.doi.org/10.1016/j.tet.2012.11.036

PPARγ agonist activity, potentially used in the treatment of diabetes, hyperlipidemia, and other diabetic complications.[3b]

Considering their remarkable biological relevance, several methods for the synthesis of this type of benzo fused heterocycles have been developed in recent years.[2–6] However some of these procedures have limitations such as the availability of the starting materials, the high costs of the catalysts,[2,4a,b,6a] or the use of multistep sequences.[1,3b,d] Moreover, most of the methods reported target the synthesis of specific benzo fused compounds and lack generality. Thus it is important to develop general and straightforward approaches for their construction. Cascade or tandem reactions can be useful economical and environmentally friendly tools for the rapid assembly of heterocycles.[7] Previously[8] vinyl selenones were shown to be valuable and versatile substrates to realize these types of reactions. They were employed for the one-pot synthesis of cyclopropanes[8a] or aziridines[8b] through Michael initiated ring closure (MIRC) reactions. The vinyl selenone plays a dual role as activating group in the conjugate addition and as leaving group in the following cyclization. Very recently we also described a cascade reaction for the one-pot synthesis of enantiopure morpholines, thiomorpholines, and piperazines through an MIRC reaction starting from readily available enantiopure aminoalcohols/thiols/amines and vinyl selenones.[9]

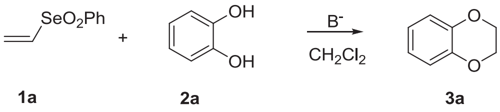
Herein we describe the simple and novel use of MIRC reactions to obtain, in one step and in good yields, six-membered 1,4-heterocycles fused to an aromatic group from commercially available benzene 1,2-diols, 1,2-thiols, 1,2-aminoalcohols or 1,2-diamines using vinyl selenones as Michael acceptors.

## 2. Results and discussion

The vinyl selenones necessary for the present investigation were easily synthesized through oxidation of the corresponding vinyl selenides.[9] We began our investigation by examining the reaction of pyrocatechol **2a** with simple vinyl selenone **1a** (Scheme 1). As shown in Table 1, the choice of base was important, and the reaction did not take place in its absence (Table 1, entry 1). The reactions proceeded in good yields using sodium hydride and cesium carbonate (Table 1, entries 2 and 3), while using organic bases such as triethylamine, DBU (1,8-diazabicyclo[5,4,0]undec-7-ene), and DABCO (1,4-diazabicyclo [2.2.2]octane) (Table 1, entries 4–6) lower yields were obtained.

We then synthesized different 2,3-dihydro-1,4-benzodioxines **3a**–**e** employing vinyl selenones **1a**–**c** and the commercially available pyrocatechol **2a** and naphthalene-2,3-diol **2b**. The reaction conditions, the reaction products, and the yields are reported in Table 2 and the plausible mechanism is reported in Scheme 2.

On the basis of the accepted mechanism for Michael initiated ring closure (MIRC) reactions it can be proposed that the reactions of the selenones **1a**–**c** with the commercial benzene-1,2-diols **2a**,**b** in the presence of base initially gives the carbanions **4a**–**e**, which after a proton transfer form oxygen anions **5a**–**e**. The subsequent intramolecular displacement of the phenylselenonyl group affords the 2,3-dihydro-1,4-benzodioxines **3a**–**e** (Scheme 2). As showed in Table 2, starting from substituted vinyl selenones **1b**,**c** (Table 2, entries 3–5) sodium hydride was used as base to complete the reaction, in the case of selenone **1c** the solution in tetrahydrofuran was refluxed. Only 2,3-dihydro-1,4-benzodioxines **3a**–**c** were obtained using selenones **1a**,**b**, while starting from selenone **1c** the 2,3-dihydro-1,4-benzodioxines **3d**,**e** and the 2,2-disubstituted-1,3-benzodioxoles **7d**,**e** were isolated after column chromatography.



**Scheme 1.** Reaction of vinyl selenone with pyrocatechol.

**Table 1**
Optimization of the reaction conditions

| Entry | Base | equiv | Reaction conditions | Yield (%) |
|---|---|---|---|---|
| 1 | — | — | $CH_2Cl_2$, rt, 36 h | — |
| 2 | NaH | 1.2 | $CH_2Cl_2$, 0 °C to rt, $t$=5 h | 53 |
| 3 | $Cs_2CO_3$ | 1.2 | $CH_2Cl_2$, rt, $t$=24 h | 80 |
| 4 | $Et_3N$ | 2 | $CH_2Cl_2$, rt, $t$=18 h | 38 |
| 5 | DBU | 2 | $CH_2Cl_2$, rt, $t$=18 h | 40 |
| 6 | DABCO | 2 | $CH_2Cl_2$, rt, $t$=36 h | 35 |

As observed in previous works,[9,10] the oxygen anions **5d**,**e** behave as bases rather than as nucleophiles and give the alkenes **6d**,**e**, which were rapidly converted into the 1,3-benzodioxoles **7d**,**e** through purification by column chromatography on silica gel (Scheme 3).

A variety of naturally bioactive compounds such as piperine, sesamol, and justicidin are known to possess a 1,3-benzodioxole scaffold.[11]

Encouraged by these good results we carried out a similar MIRC procedure for the preparation of 2,3-dihydro-1,4-benzodithiines **9a**–**d**, using commercial available benzene-1,2-dithiols **8a**,**b** (Table 3). The one-pot Michael addition/cyclization sequence should proceed with the same mechanism illustrated in Scheme 2 for the synthesis of the 2,3-dihydro-1,4-benzodioxines. In the case of the sulfur nucleophile the base of choice was triethylamine. Different substituted 2,3-dihydro-1,4-benzodithiines can be obtained in moderate yields simply changing the selenones (entries 2 and 3, Table 3) or varying the substituents on the aromatic nucleus (entry 4, Table 3).

Finally we extended the method to the synthesis of nitrogen containing heterocycles. Starting from 2-(benzylamino)phenols **10a**–**c**, prepared using standard procedures,[12] we have synthesized 4-benzyl-3,4-dihydro-2*H*-benzo-1,4-oxazines **14a**–**c** (Table 4). As observed in previous work,[9] the initial formation of an oxygen anion, which effects the conjugate addition at the β-position of the selenone, followed by the intramolecular displacement of the phenylselenonyl group by the nitrogen atom is likely. As showed in Table 4, electron-rich substituents and electron-deficient substituents on the aryl ring (entries 2 and 3) were employed and the corresponding heterocycles **14a**–**c** were obtained in moderate to good yields. The possibility of removing the protecting group, according to the procedure reported in the literature,[13] increases the importance of the present method for the synthesis of 3,4-dihydro-2*H*-benzo-1,4-oxazines.

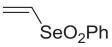
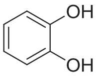
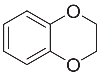
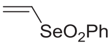
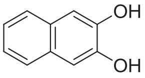
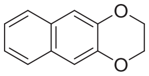
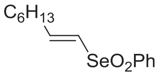
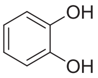
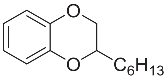
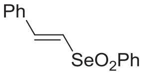
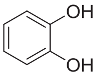
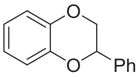
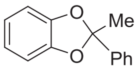
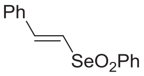
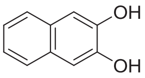
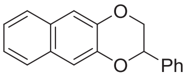
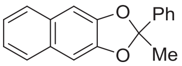
The reactivity of *N*,*N*′-1,2-phenylenebis(4-methyl benzenesulfonamide) **15** was also investigated. Using sodium hydride (1.2 equiv) as base, we have obtained 1,4-bis[(4-methylphenyl) sulfonyl]-1,2,3,4-tetrahydroquinoxaline **16** (58% yield) (Scheme 4).

This heterocyclic core is present in many bioactive compounds. Several 1,2,3,4-tetrahydroquinoxalines have found applications as prostaglandin D2 receptor antagonists, vasopresin V2 receptor antagonists, and potent cholesteryl ester transfer protein inhibitors.[14]

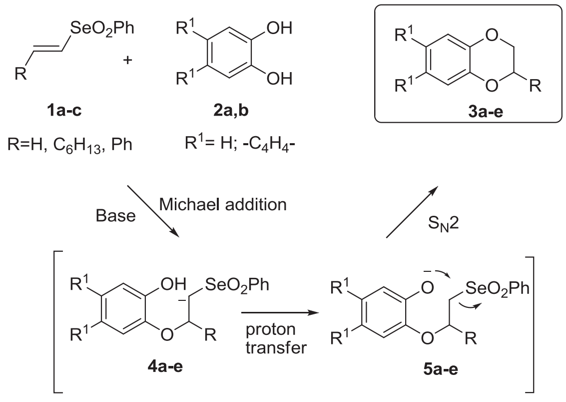
## 3. Conclusion

In the present investigation we have reported a novel and simple approach for the synthesis of benzo fused heterocyclic rings through an MIRC reaction from vinyl selenones and benzene 1,2-bis nucleophiles. Various biologically and pharmaceutically important nuclei such as 2,3-dihydro-1,4-benzodioxines,[2] 2,3-dihydro-1,4-benzodithiines, 4-benzyl-3,4-dihydro-2*H*-benzo-1,4-oxazines,[3] and 1,2,3,4-tetrahydroquinoxaline[14] were obtained in *one pot* and in good yields. The wide applicability of this method, the easy availability, and low cost of the starting materials confirm the potential of vinyl selenones as valuable substrates for cascade reactions. Further applications of this strategy for the synthesis of

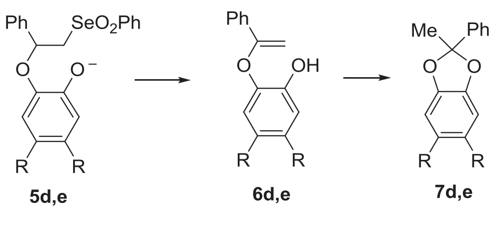
**Table 2**
Synthesis of 2,3-dihydro-1,4-benzodioxines

| Entry | Selenones **1a**–**c** | | Substrates **2a**–**b** | | $B^-$ | equiv | Reaction conditions | Products **5a**–**e**, **7d**–**e** | | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 |  | **1a** |  | **2a** | $Cs_2CO_3$ | 1.2 | $CH_2Cl_2$, 0 °C to rt, 24 h |  | **3a** | 80 |
| 2 |  | **1a** |  | **2b** | $Cs_2CO_3$ | 1.2 | $CH_2Cl_2$, 0 °C to rt, 36 h |  | **3b** | 73[a] |
| 3 |  | **1b** |  | **2a** | NaH | 1.2 | $CH_2Cl_2$, 0 °C to rt, 36 h |  | **3c** | 60 |
| 4 |  | **1c** |  | **2a** | NaH | 1.2 | THF, 0 °C to reflux, 72 h | <br> | **3d**<br>**7d** | 35<br>35 |
| 5 |  | **1c** |  | **2b** | NaH | 1.2 | THF, 0 °C to reflux, 72 h | <br> | **3e**<br>**7e** | 35<br>61 |

[a] Employing 1 equiv of NaH, the yields of the products **3a** and **3b** were 53% and 43%, respectively.



**Scheme 2.** Proposed mechanism for the synthesis of 2,3-dihydro-1,4-benzodioxines.



**Scheme 3.** Synthesis of acetals **7d**,**e**.

more complex benzo fused heterocycles are currently underway in our laboratory.

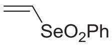
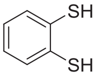
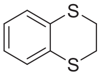
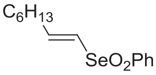
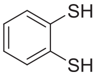
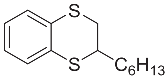
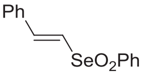
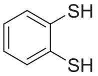
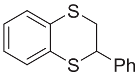
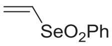
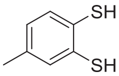
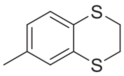
## 4. Experimental section

### 4.1. General

All new compounds were characterized by GC–MS, $^1H$ and $^{13}C$ NMR spectra. $^1H$ and $^{13}C$ NMR spectra were recorded at 400 and 100.62 MHz, respectively, on a Bruker DRX 400 instrument. The chemical shifts ($\delta$) are referred to internal standard TMS ($^1H$ NMR) and the residual signals of the solvent ($CDCl_3$—77.0 ppm for $^{13}C$ NMR). *J* values are given in hertz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; m, multiplet; br, broad signal. GC analyses and MS spectra were carried out with an HP 6890 gas chromatograph (25 m dimethyl silicone capillary column) equipped with an HP 5973 Mass Selective Detector at an ionizing voltage of 70 eV. For the ions containing selenium, only the peaks arising from the selenium-80 isotope are given. FTIR spectra were recorded with a Jasco model 410 spectrometer equipped with a diffuse reflectance accessory. Elemental analyses were carried out on a Carlo Erba 1106 Elemental Analyzer. The melting points are uncorrected. Thin layer chromatography (TLC) was performed on silica gel 60 $F_{254}$ (Merck). Purification of reaction products was carried out by chromatography on silica gel Merck 60 (70–230 mesh).

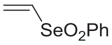
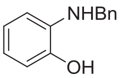
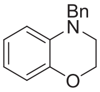
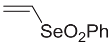
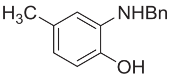
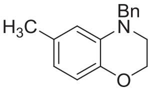
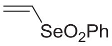
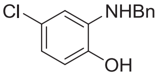
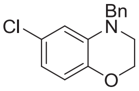
The vinyl selenones **1a**–**c** were prepared according to the procedure reported in the literature.[8,9] Benzo-1,2-diols **2a**,**b**, benzo-1,2-thiols **8a**,**b** are commercially available. The 2-(benzylamino)phenols

**Table 3**
Synthesis of 2,3-dihydro-1,4-benzodithiines

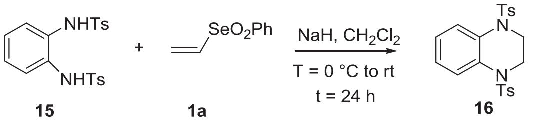
| Entry | Selenones **1a**–**c** | | Substrates **8a**,**b** | | Base | Equiv | Reaction conditions | Products **9a**–**d** | | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 |  | **1a** |  | **8a** | $Et_3N$ | 3.0 | $CH_2Cl_2$, rt, 48 h |  | **9a** | 85[a] |
| 2 |  | **1b** |  | **8a** | $Et_3N$ | 5.0 | $CH_2Cl_2$, rt, 72 h |  | **9b** | 63 |
| 3 |  | **1c** |  | **8a** | $Et_3N$ | 5.0 | THF reflux, 48 h |  | **9c** | 58 |
| 4 |  | **1a** |  | **8b** | $Et_3N$ | 3 | $CH_2Cl_2$, rt, 48 h |  | **9d** | 57 |

[a] Employing 1 equiv of $Cs_2CO_3$, the yield of the product **9a** was 67%.

**Table 4**
Synthesis of 4-benzyl-3,4-dihydro-2*H*-benzo-1,4-oxazines

| Entry | Selenone **1a** | | Substrates **10a**–**c** | | $B^-$ | equiv | Reaction conditions | Products **14a**–**c** | | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 |  | **1a** |  | **10a** | NaH | 1.2 | $CH_2Cl_2$, 0 °C to rt, 48 h |  | **14a** | 68[a] |
| 2 |  | **1a** |  | **10b** | NaH | 1.2 | $CH_2Cl_2$, 0 °C to rt, 48 h |  | **14b** | 70 |
| 3 |  | **1a** |  | **10c** | NaH | 1.2 | $CH_2Cl_2$, 0 °C to rt, 48 h |  | **14c** | 60 |

[a] Employing 1 equiv of $Cs_2CO_3$ the product **14a** was obtained with 50% yield.



**Scheme 4.** Synthesis of 1,4-bis[(4-methylphenyl) sulfonyl]-1,2,3,4-tetrahydroquinoxaline **16**.

**10a**–**c**[12] and *N*,*N*′-1,2-phenylenebis(4-methyl benzenesulfonamide) **15**[15] were prepared according to the procedure described in the literature. Physical and spectral data of *o*-(benzylamino)phenol **10a**,[16] 2-benzylamino-4-chlorophenol **10c**,[12] and the *N*,*N*′-1,2-phenylenebis(4-methyl benzenesulfonamide) **15**[15] are identical to those reported in the literature. Physical and spectral data of the 2-(benzylamino)-4-methylphenol **10b** are reported below.

*2-(Benzylamino)-4-methylphenol (**10b**): colorless solid*; mp 106–109 °C [lit.[17] mp 110–111 °C]; $^1H$ NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.42–7.30 (m, 5H, Ar–H), 6.65–6.46 (m, 3H, Ar–H), 4.38–4.36 (m, 4H, $CH_2Ph$, OH, NH), 2.26 (s, 3H). Anal. Calcd for $C_{14}H_{15}NO$: C, 78.48; H, 7.09; N, 6.57. Found: C, 78.16; H, 6.93; N, 6.36.

## 4.2. General procedure for the synthesis of 2,3-dihydro-1,4-benzodioxines, 5a–e and 2-methyl-2-phenyl-1,3-benzodioxoles, 5d,e

A stirred solution of benzene-1,2-diols **2a**,**b** (0.5 mmol) in $CH_2Cl_2$ (3 mL) or THF was treated under argon with $Cs_2CO_3$ (0.6 mmol) at room temperature in the case of simple selenone **1a** or NaH (0.6 mmol) at 0 °C to room temperature in the cases of substituted selenones **1b**,**c**. After 10 min a solution of vinyl selenones **1a**–**c** (0.5 mmol) was added and the reaction mixture was stirred for the times and at the temperature indicated in Table 2. The progress of the reactions was monitored by TLC. The reaction mixtures were poured into aqueous ammonium chloride solution and extracted with $CH_2Cl_2$, washed with water and brine, dried over $Na_2SO_4$, filtered, and evaporated under vacuum. Reaction products **3a**–**e** and **7d**,**e** were obtained in a pure form after column chromatography of the residue on silica gel. Physical and spectral data of the 2,3-dihydro-1,4-benzodioxine (**3a**),[4b] 2,3-dihydronaphtho[2,3-*b*][1,4]dioxine (**3b**),[4c] 2-phenyl-2,3-dihydro-1,4-benzodioxine (**3d**),[2b] and 2-methyl-2-phenyl-1,3-benzodioxole (**7d**)[11] are identical to those reported in the literature. Physical and spectral data of the 2,3-dihydro-1,4-benzodioxines **3c**,**e** and the acetal **7e** are reported below.

*4.2.1. 2-Hexyl-2,3-dihydro-1,4-benzodioxine (**3c**).* Purification by column chromatography (EE/EP from 2:98 to 10:90). Yield 60%; oil; $^1H$ NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=6.90–6.82 (m, 4H, Ar–H), 4.25 (dd, $^2J$(H,H)=11.2 Hz, $^3J$(H,H)=2.1 Hz, 1H, $CH_2O$), 4.16–4.09 (m, 1H, CHO), 3.90 (dd, $^2J$(H,H)=11.2 Hz, $^3J$(H,H)=7.8 Hz, 1H, $CH_2O$), 1.77–1.23 (m, 10H, $5CH_2$), 0.92 (t, $^3J$(H,H)=6.6 Hz, 3H, $CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$, 25 °C): $\delta$=143.5 (C*ipso*), 143.3 (C*ipso*), 121.4 (CH, Ar), 121.1 (CH, Ar), 117.3 (CH, Ar), 116.9 (CH, Ar), 73.0 (CHO), 68.1 ($CH_2O$), 31.6, 31.0, 29.1, 24.9, 22.5 ($5CH_2$), 14.0 ($CH_3$); MS (70 eV, EI): *m*/*z* (rel int.): 220 (100) [$M^+$], 135 (32), 121 (66), 110 (97), 81

(23), 69 (54), 55 (33). FTIR (KBr): $\nu_{max}$, cm$^{-1}$ 2959, 2930, 2869, 1591, 1461, 1283, 1055, 747. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.21; H, 9.01.

*4.2.2. 2-Phenyl-2,3-dihydronaphtho[2,3-b][1,4]dioxine* (***3e***). Purification by flash column chromatography on silica gel (from EP to EE/EP 3:97). Yield 35%; colorless solid; mp 77–80 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.72–7.70 (m, 2H, Ar–H), 7.53–7.24 (m, 9H, Ar–H), 5.29 (dd, $^3J$(H,H)=9.0 Hz, $^3J$(H,H)=2.4 Hz, 1H, CHO), 4.47 (dd, $^2J$(H,H)=11.5 Hz, $^3J$ (H,H)=2.4 Hz, 1H, $CH_2O$), 4.18 (dd, $^2J$(H,H)=11.5 Hz, $^3J$(H,H)=9.0 Hz, 1H, $CH_2O$); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta$=144.2 (C*ipso*), 143.9 (C*ipso*), 136.4 (C*ipso*), 130.3 (2 C*ipso*), 128.9 (CH), 128.8 (2CH, Ar), 126.6 (2CH, Ar), 126.5 (CH, Ar), 126.4 (CH, Ar), 124.3 (CH, Ar), 124.2 (CH, Ar), 112.8 (CH, Ar), 112.4 (CH, Ar), 75.3 (CHO), 69.4 ($CH_2O$); MS (70 eV, EI): *m*/*z* (rel int.): 262 (28) [M$^+$], 171 (100), 102 (27), 77 (11). FTIR (KBr): $\nu_{max}$, cm$^{-1}$ 3059, 2930, 1509, 1471, 1439, 1271, 1239, 1169, 1021, 747, 699. Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.21; H, 5.15.

*4.2.3. 2-Methyl-2-phenylnaphtho[2,3-d][1,3]dioxole* (***7e***). Purification by flash column chromatography on silica gel (from EP to EE/EP 3:97). Yield 61%; oil; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.67–7.62 (m, 4H, Ar–H), 7.43–7.35 (m, 3H, Ar–H), 7.32–7.30 (m, 2H, Ar–H), 7.13–7.12 (m, 2H, Ar–H), 2.07 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta$=147.6 (2C*ipso*), 141.3 (C*ipso*), 130.4 (2C*ipso*, Ar), 128.9 (CH, Ar), 128.4 (2CH, Ar), 126.8 (2CH, Ar), 124.9 (2CH, Ar), 124.1 (2CH, Ar), 116.7 (Cquat), 103.8 (2CH, Ar), 27.0 ($CH_3$). MS (70 eV, El): *m*/*z* (rel int.): 262 (40) [M$^+$], 247 (21), 160 (100), 103 (57), 77 (27). FTIR (KBr): $\nu_{max}$, cm$^{-1}$ 3047, 2926, 1653, 1559, 1465, 1250, 1193, 926, 862, 751, 702. Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.21; H, 5.15.

### 4.3. General procedure for the synthesis of 2,3-dihydro-1,4-benzodithiines, 9a–d

A stirred solution of benzene-1,2-dithiols **8a**,**b** (0.5 mmol) in $CH_2Cl_2$ (3 mL) was treated with $Et_3N$ (1.5 mmol) at room temperature under argon. After 10 min, a solution of vinyl selenones **1a**–**c** (0.6 mmol) in $CH_2Cl_2$ (3 mL) or THF was stirred for the times indicated in Table 3. The progress of the reactions was monitored by TLC. The reaction mixtures were poured into aqueous ammonium chloride solution and extracted with $CH_2Cl_2$, washed with water and brine, dried over $Na_2SO_4$, filtered, and evaporated under vacuum. Reaction products **9a**–**d** were obtained in a pure form and in satisfactory yields after column chromatography of the residue on silica gel. Physical and spectral data of the 2,3-dihydro-1,4-benzodithiine, **9a** are identical to those reported in literature.[5a] Physical and spectral data of the 2,3-dihydro-1,4-benzodithiines **9b**–**d** are reported below.

*4.3.1. 2-Hexyl-2,3-dihydro-1,4-benzodithiine* (***9b***). Purification by column chromatography on silica gel (from EP to EtOAc/EP 3:97). Yield 63%; oil; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.20–7.16 (m, 2H, Ar–H), 7.05–6.98 (m, 2H, Ar–H), 3.52–3.45 (m, 1H, CHS), 3.24 (dd, $^2J$(H,H)=13.0 Hz, $^3J$(H,H)=3.2 Hz, 1H, $CH_2S$), 3.0 (dd, $^2J$(H,H)=13.0 Hz, $^3J$(H,H)=8.3 Hz, 1H, $CH_2S$), 1.76 (q, *J*=7.0 Hz, 2H, $CH_2$), 1.58–1.30 (m, 8H, 4×$CH_2$), 0.89 (t, 3H, *J*=7.0 Hz, $CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta$=131.9 (C*ipso*), 131.2 (C*ipso*), 128.6 (CH, Ar), 128.5 (CH, Ar), 125.3 (CH, Ar), 124.8 (CH, Ar–H), 43.4 (CHS), 35.7 ($CH_2S$), 34.4 ($CH_2$), 31.6 ($CH_2$), 29.7 ($CH_2$), 26.7 ($CH_2$), 22.6 ($CH_2$), 14.1 ($CH_3$); MS (70 eV, EI): *m*/*z* (rel int.): 252 (50), 167 (44), 153 (43), 142 (30), 140 (12), 135 (10), 134 (100). FTIR (KBr): $\nu_{max}$, cm$^{-1}$ 3050, 2968, 2845, 1650, 1453, 761. Anal. Calcd for $C_{14}H_{20}S_2$: C, 66.61; H, 7.99. Found: C, 66.31; H, 7.29.

*4.3.2. 2-Phenyl-2,3-dihydro-1,4-benzodithiine* (***9c***). Purification by column chromatography on silica gel (from EP to EtOAc/EP 3:97). Yield 58%; oil; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.43–7.31 (m, 5H, Ar–H), 7.28–7.25 (m, 1H, Ar–H), 7.22–7.18 (m, 1H, Ar–H), 7.07–7.03 (m, 2H, Ar–H), 4.64 (dd, $^3J$(H,H)=10.1 Hz, $^3J$(H,H)=3.4 Hz, 1H, CHS), 3.44 (dd, $^2J$(H,H)=13.0 Hz, $^3J$(H,H)=10.1 Hz, 1H, $CH_2S$), 3.35 (dd, $^2J$(H,H)=13.0 Hz, $^3J$(H,H)=3.4 Hz, 1H, $CH_2S$); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta$=140.1 (C*ipso*), 133.2 (C*ipso*), 130.6 (C*ipso*), 128.9 (2CH, Ar), 128.6 (CH, Ar), 128.2 (CH, Ar), 128.1 (CH, Ar), 127.6 (2CH, Ar), 125.3 (CH, Ar), 125.1 (CH, Ar), 48.1 (CHS), 35.6 ($CH_2S$); MS (70 eV, EI): *m*/*z* (rel int.): 244 (50) [M$^+$], 229 (100), 167 (35), 152 (10), 103 (20). FTIR (KBr): $\nu_{max}$, cm$^{-1}$ 3055, 2917, 1558, 1489, 1453, 1422, 744, 697. Anal. Calcd for $C_{14}H_{12}S_2$: C, 66.81; H, 4.95. Found: C, 66.37; H, 4.62.

*4.3.3. 6-Methyl-2,3-dihydro-1,4-benzodithiine* (***9d***). Purification by column chromatography (from EP to EtOAc/EP 1:99). Yield 57%; oil; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.07 (d, $^3J$(H,H)=8.0 Hz, 1H, Ar–H), 7.03–7.0 (m, 1H, Ar–H), 6.86–6.83 (m, 1H, ArH), 3.28–3.26 (m, 4H, 2$CH_2S$), 2.26 (s, 3H, $CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta$=137.6 (C*ipso*), 136.7 (C*ipso*), 131.3 (C*ipso*), 129.2 (CH, Ar), 128.7 (CH, Ar), 126.3 (CH, ArH), 29.4 (2$CH_2S$), 21.0 ($CH_3$); MS (70 eV, EI): *m*/*z* (rel int.): 182 (11) [M$^+$], 167 (100), 153 (45), 134 (7), 121 (14). FTIR (KBr): $\nu_{max}$, cm$^{-1}$ 3044, 2916, 1653, 1583, 1457, 815, 735, 687. Anal. Calcd for $C_9H_{10}S_2$: C, 59.29; H, 5.53. Found: C, 59.10; H, 5,45.

### 4.4. General procedure for the synthesis of 4-benzyl-3,4-dihydro-2*H*-1,4-benzoxazines, 14a–c and 1,4-bis[(4-methylphenyl)sulfonyl]-1,2,3,4-tetrahydroquinoxaline, 16

A stirred solution of 2-(benzylamino)phenols **10a**–**c** (0.5 mmol) or *N*,*N*′-1,2-phenylenebis(4-methylbenzenesulfonamide) **15** (0.5 mmol) in $CH_2Cl_2$ (3 mL) was treated with NaH (0.6 mmol) at 0 °C under argon. After 10 min, a solution of vinyl selenone **1a** (0.5 mmol) in $CH_2Cl_2$ (3 mL) was added and the reaction mixture was allowed to warm at room temperature and stirred for the times indicated in Table 4 and in Scheme 4. The progress of the reactions was monitored by TLC. The reaction mixtures were poured into aqueous ammonium chloride solution and extracted with $CH_2Cl_2$, washed with water and brine, dried over $Na_2SO_4$, filtered, and evaporated under vacuum. Reaction products **14a**–**c** and **16** were obtained in a pure form after column chromatography of the residue on silica gel. Physical and spectral data of the 4-benzyl-3,4-dihydro-2*H*-1,4-benzoxazine **14a** are identical to those reported in the literature.[6a] Physical and spectral data of the 6-substituted-4-benzyl-3,4-dihydro-2*H*-1,4-benzoxazines **14b**,**c** and 1,4-bis[(4-methylphenyl)sulfonyl]-1,2,3,4-tetrahydroquinoxaline **16** are reported below.

*4.4.1. 4-Benzyl-6-methyl-3,4-dihydro-2H-1,4-benzoxazine* (***14b***). Purification by flash column chromatography on silica gel (EE/EP 15:85). Yield 70%; oil; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.39–7.28 (m, 5H), 6.74 (d, $^3J$=8.0 Hz, 1H, Ar–H), 6.54 (d, $^4J$=2.0 Hz, 1H, Ar–H), 6.47 (dd, $^4J$=8.0 Hz, $^3J$=2.0 Hz, 1H, Ar–H), 4.46 (s, 2H, $NCH_2$), 4.27–4.24 (m, 2H, $CH_2O$), 3.36–3.34 (m, 2H, $CH_2N$), 2.23 (s, 3H, $CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta$=141.7 (C*ipso*), 138.1 (C*ipso*), 135.3 (C*ipso*), 130.9 (C*ipso*), 128.6 (2CH, Ar), 127.1 (2CH, Ar), 127.0 (CH, Ar), 118.1 (CH, Ar), 116.0 (CH, Ar), 113.9 (CH, Ar), 64.5 ($CH_2O$), 54.8 ($PhCH_2N$), 47.2 ($CH_2N$), 21.1 ($CH_3$). MS (70 eV, EI): *m*/*z* (rel int.): 239 (100) [M$^+$], 148 (67), 120 (31), 91 (96), 77 (20), 65 (29). FTIR (KBr): $\nu_{max}$, cm$^{-1}$ 3030, 2868, 1610, 1512, 1451, 1341, 1306, 1213, 1050, 799, 696. Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.12; H, 7.01; N, 5.76.

*4.4.2. 4-Benzyl-6-chloro-3,4-dihydro-2H-1,4-benzoxazine* (***14c***). Purification by flash column chromatography on silica gel (EE/EP 15:85). Yield 60%; oil; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.39–7.28

(m, 5H, Ar–H), 6.74 (d, $^3J$=8.4 Hz, 1H, Ar–H), 6.66 (d, $^4J$=2.3 Hz, 1H, Ar–H), 6.59 (dd, $^4J$=2.3 Hz, $^3J$=8.4 Hz, 1H, Ar–H), 4.45 (s, 2H, $NCH_2$), 4.27–4.24 (m, 2H, $CH_2O$), 3.40–3.35 (m, 2H, $CH_2N$); $^{13}C$ NMR (100 MHz, $CDCl_3$, 25 °C): $\delta$=142.4 (C*ipso*), 137.2 (C*ipso*), 136.4 (C*ipso*), 128.7 (2CH, Ar), 127.3 (CH, Ar), 127.0 (2CH, Ar), 126.4 (C*ipso*), 117.0 (2CH, Ar), 111.9 (CH, Ar), 64.4 ($CH_2O$), 54.6 ($NCH_2Ph$), 46.8 ($CH_2N$). MS (70 eV, EI): *m*/*z* (rel int.): 261 (10) [$M^+$+2], 259 (28) [$M^+$], 168 (7), 91 (100), 65 (10). FTIR (KBr): $\nu_{max}$, $cm^{-1}$ 3075, 2976, 2843, 1600, 1501, 1453, 1313, 1228, 1199, 915, 904, 838, 807, 761, 736, 700. Anal. Calcd for $C_{15}H_{14}ClNO$: C, 69.36; H, 5.43; N, 5.39. Found: C, 69.19; H, 5.18; N, 5.07.

*4.4.3. 1,4-Bis[(4-methylphenyl)sulfonyl]-1,2,3,4-tetrahydroquinoxaline (**16**).* Purification by column chromatography (MeOH/$CH_2Cl_2$ 3:97). Yield 58%; colorless solid; mp 165–168 °C [lit.[18] mp 162 °C]; $^1H$ NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.86–7.81 (m, 2H, Ar–H), 7.42 (d, *J*=8 Hz, 4H, Ar–H), 7.22 (d, *J*=8 Hz, 4H, Ar–H), 7.16–7.11 (m, 2H, Ar–H), 3.51 (s, 4H, $2CH_2$), 2.42 (s, 6H, $2CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$, 25 °C): $\delta$=144.3 (2C*ipso*), 135.6 (2C*ipso*), 129.8 (4CH, Ar), 128.2 (2C*ipso*), 127.0 (4CH, Ar), 124.9 (2CH, Ar–H), 123.6 (2CH, Ar–H), 43.3 ($2CH_2$), 21.5 ($2CH_3$). MS (70 eV, EI): *m*/*z* (rel int.). Anal. Calcd for $C_{22}H_{22}N_2O_4S_2$: C, 59.71; H, 5.01; N, 6.33. Found: C, 59.59; H, 4.91; N, 6.06.

## Acknowledgements

Financial support from M.I.U.R. (Ministero Italiano Università e Ricerca), National Projects PRIN2007, University of Perugia and Consorzio CINMPIS and Fondazione Cassa di Risparmio: Project ‘Processi ecosostenibili per la produzione e l’analisi di molecole di interesse farmaceutico’ 2012.0114.021, is gratefully acknowledged.

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