Parallel Solution-Phase Synthesis of 2-Alkylthio-5-arylidene-3,5-dihydro-4*H*-imidazol-4-one by One-Pot Three-Component Domino Reaction

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A practical protocol for the preparation of a parallel solution-phase library of 5-arylidene imidazolone is reported. Target compounds were obtained in good yield, stereoselectively, and purity by one-pot domino reaction from various thiohydantoines, arylaldimines, and halogenoalkanes. Purification of the final products by recrystallization with a mixture of pentane/ethanol allowed simple isolation of the 17 components of the array.

Introduction

The solution-phase parallel synthesis[1] methodology and related multiple synthesis technologies toward the preparation of small molecular weight compound libraries have been widely used in the lead generation and lead optimization stages. The solution-phase parallel synthesis is indeed a tool of choice for this purpose, because it avoids the need to re-optimize the chemistry to the solid or liquid phase prior to library generation. In medicinal chemistry, traditional structure–activity relationship evaluations involve the preparation of an advanced intermediate that can be analogued readily to introduce the molecular diversity necessary to prepare a collection, or a library, of structurally related compounds. In this context, the multicomponent reactions[2] (MCRs) constitute an attractive synthetic strategy for rapid and efficient library generation due to the fact that the products are formed in a single step and the diversity can be achieved simply by varying the reacting components. Usually, MCR transformation does not involve the simultaneous reaction of all reaction components; rather, they react in a sequence of steps that are programmed by the synthetic design. This involves an equilibrium-driven step(s), followed by a non-equilibrium process that pulls the process to product, which means that, overall, MCR processes can be kinetically quite slow.

The imidazolone core represents an interesting pharmacophore that displays a wide range of applications such as therapeutics[3] as well as fungicides and herbicides.[4] Among this class of compounds, the 2-alkylthio imidazolones presents interesting biological properties. As examples, the isatinylidene derivative **I** (Figure 1) exhibits immunosuppressive activity,[5] and the 5-alkylidene imidazolone **II** substituted with a (biphenyl)tetrazole (BPT) group at the C-2 position shows activities as angiotensine II receptor antagonists.[6] The S-glucosylated 5-arylidene imidazolones **III** have been also identified as antiviral agents for the herpes simplex virus[7] (HSV) and the human immunodeficiency virus (HIV).[8]

Due to the biological activity associated with the imidazolone moiety, we embarked on a project to investigate possible bioactive molecules based on 2-alkylthio-5-arylidene derivatives of the imidazolone core. Herein, we report a facile solution-phase parallel synthetic protocol to diversify the imidazolone scaffold in three different positions using an MCR methodology.

Results and Discussion

Synthetic approaches described in the literature toward 2-alkylthio-5-arylidene imidazolone structure involve: (i) condensation of an aryl/heteroaryl aldehyde with thiohydantoïne followed by regioselective S-alkylation[9] or (ii) reaction of vinyl isothiocyanate[10] (available from iminophosphorane and carbon disulfide) with a primary amine giving directly the 5-arylidene-2-thioxo imidazolone[11] structure which was converted into the S-alkyl derivative by the action of an excess of alkylating reagent.[12] An alternative and elegant approach has been developed using a dimethylamine substitution in *N*,*N*-(dimethylamino)methylidene derivatives of thiohydantoïne[13] with various indoles unsubstituted at the C-2 position.

In this context, the 2-alkylthio-5-arylidene imidazolone scaffold (Figure 2) can be built from arylaldehyde, halogenoalkane, and thiohydantoïne, which is easily available from glycinate and commercial isothiocyanate. In order to find a straightforward synthesis of the imidazolone moiety,[14] attention was turned to explore the preparation of this unit using a one-pot multicomponent protocol. Hence, it was pertinent to evaluate the accessibility of the 2-alkylthio-5-arylidene imidazolone scaffolds through solution-phase parallel synthesis employing a domino reaction. Domino

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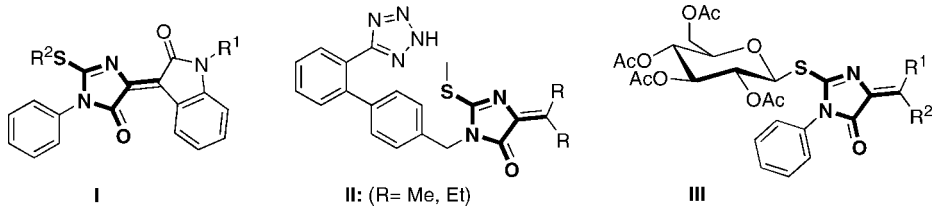


Figure 1. Some 5-ylidene-3,5-dihydro-4*H*-imidazol-4-one derivatives, which present pharmacological activities.

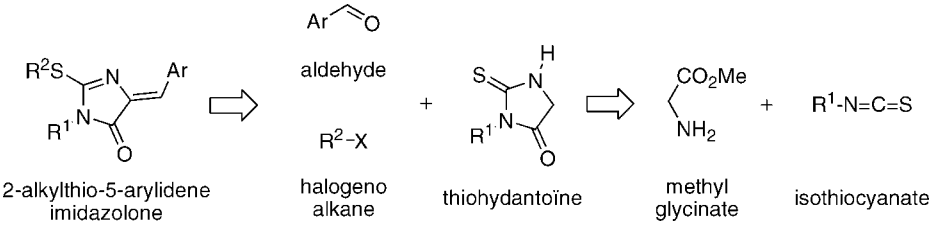
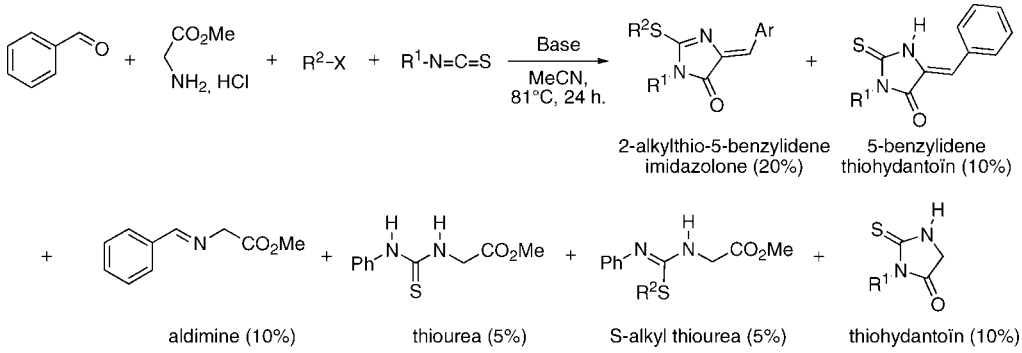


Figure 2. Components used for the synthesis of 2-alkylthio-5-arylidene-3,5-dihydro-4*H*-imidazol-4-ones.

Scheme 1. Possible Synthesis of 2-Alkylthio-5-arylidene-3,5-dihydro-4*H*-imidazol-4-ones by One-Pot Four-Component Reaction



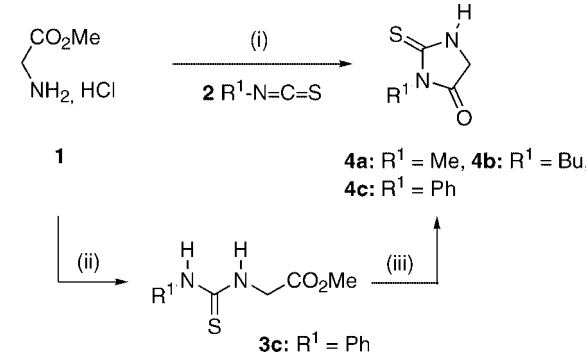
reactions describe closely coupled reactions where intermediates are inseparable, while, in sequential reactions, intermediates are separable.[15]

For the first time, we envisioned synthesizing the 2-alkylthio-5-arylidene imidazolone structures directly utilizing all commercially available starting materials by a one-pot four-component method in acetonitrile at 81 °C (Scheme 1). Unfortunately, we obtained the expected product (20%, after analysis of the crude reaction mixture by ^{1}H NMR) in a complex mixture, which did not allow its purification. To overcome this difficulty, we decided to reduce the number of components in our one-pot reaction. Thus, thiohydantoïn will be used as starting material in order to develop this time a three-component approach, to lead to the 2-alkylthio-5-aryliden-imidazolone scaffold.

The starting thiohydantoïnes were easily prepared according to the route represented in Scheme 2. The compounds **4**(**a**,**b**) (**4a**: R^1 = Me, **4b**: R^1 = Bu) were readily available by addition of commercial isothiocyanates **2** (**2a**: methylisothiocyanate, **2b**: butylisothiocyanate) to methyl glycinate hydrochloride in basic medium (Et_3N) in refluxing diethyl ether after 14 h. For the 3-phenyl derivative **4c**, the reaction of phenylisothiocyanate **2c** with methyl glycinate hydrochloride in refluxing AcOEt produced quantitatively the stable methyl 3-thioureido acetate **3c**, and subsequent ring closure under thermal conditions (81 °C) led to **4c** in 98% yield (Table 1).

Aryl aldehydes should be good reagents for the multicomponent reaction that we wish to develop. However, the

Scheme 2. Preparation of the 2-Thioxo-imidazolidin-4-ones **4**(**a**–**c**)[a]



[a] Reagents and reaction conditions: (i) Et_3N 1 equiv, Et_2O, reflux, 14 h. (ii) Et_3N 1 equiv, AcOEt, reflux, 14 h. (iii) MeCN, 81 °C, 14 h.

condensation step to hydantoïn requires the presence of an organic base such as CH_3CO_2Na[9] and piperidine.[17] In order to be able to carry out the three-component reaction in avoiding these conditions, we planned to employ aryl aldimines in place of aryl aldehydes. Microwave-assisted organic synthesis[16] (MAOS) has been demonstrated to dramatically reduce reaction times and affect product ratios and yields. We thus decided to examine the preparation of aryl aldimines (Scheme 3) under microwave.[18] Reaction optimization for the synthesis of aryl aldimine **6** consisted of varying the reaction temperature, the power and reaction concentration (ratio aldehyde **5**/propylamine) under microwave, and the experiments revealed that the optimal reaction

Table 1. Results for the Preparation of the Starting 2-Thioxo-imidazolidin-4-ones **4**(**a**–**c**) and Aryl Aldimines **6**(**a**–**h**)

product	R^1	starting reagent **2** or **5**	yield (%)
3c	Ph	**2c**	98[b]
4a	Me	**2a**	95[a]
4b	Bu	**2b**	97[a]
4c	Ph	**2c**	97[a]
6a		**5a**	97[b]
6b		**5b**	95[b]
6c		**5c**	95[b]
6d		**5d**	91[b]
6e		**5e**	90[b]
6f		**5f**	99[b]
6g		**5g**	97[b]
6h		**5h**	97[b]

[a] Yield of isolated product. [b] Reactions conducted under microwave irradiations ($\mu\omega$) were realized in the Synthewave 402 oven (Merck Eurolab, Div. Prolabo, France).

conditions were obtained after 30 min with a stoiechiometry of 1:2 of aldehyde **5**/propylamine to produce the aldimine **6**.

Note that in this microwave flash heating process without solvent, there is no need to use a catalyst as is often used in the literature, and the optimal reaction temperature was at 60 °C. As can be seen from inspection of the data presented in Table 1, the aryl aldimines **6**(**a**–**h**) were prepared in good yields (90–97%). This study was realized with a variety of substituted aromatic aldehydes **6** carrying either an electron-donating or electron-withdrawing substituent for the introduction of diversity into the imidazolone scaffold in the MCR.

With the 2-thioxo-imidazolin-4-ones **4**(**a**–**c**) and aryl aldimines **6**(**a**–**h**) in hand, we designed an experimental strategy for the preparation of an array of trisubstituted imidazolone (Scheme 4) by using a carousel 6 place reaction station (from Radleys Discovery Technologies) which is particularly suitable for parallel synthesis. The six vials of the system were charged respectively with 5 mmol of N-substituted thiohydantoïne **4** with 0.5 equiv of potassium carbonate, then 5 mmol of aryl aldimine **6**, and finally 7.5 mmol of halogenoalkane **7**. The set of halogeno compounds represents the third point of the diversity in this collection by using commercial products (ethyl iodide **7a**, allyl bromide **7b**, propargyl bromide **7c**, benzyl chloride **7d**, and *para*-nitrobenzyl chloride **7e**). Owing to the lesser reactivity of the chloro and bromo derivatives **7**(**b**–**e**), 7.5 mmol of potassium iodide were added in the appropriate vial and the reagents were recovered with dry acetonitrile (10 mL). The six vials of the carousel 6 place reaction station were stirred at 60–70 °C (Table 2) for 14 h and then cooled at room temperature. After workup (elimination of the salts and solvent), all of the 2-alkylthio-5-arylidene-3,5-dihydro-4*H*-imidazol-4-one **8** in each vial were purified by recrystallization with a mixture of pentane/EtOH (1:1).

After drying under high vacuum (10^{-2} Torr), the purity of the products was controlled by ^{1}H NMR analysis (200 or 300 MHz). As illustrated in Figure 3, the versatility of the one-pot domino reaction was demonstrated through the three-component preparation of a small library of 2-alkylthio-5-arylidene-3,5-dihydro-4*H*-imidazol-4-ones **8**(**a**–**q**). In table *2*, it can be observed that the one-pot domino reaction gave yields ranging from 35 to 62% for the *N*-Me derivatives **8**, 40 to 60% for the *N*-Bu derivatives, and 56 to 71% for the *N*-phenyl compounds. It should be noted that no domino reaction was observed when arylaldimine **6e**, thiohydantoine **4a** (or **4b** or **4c**) and iodoethane **7a** were used.

The structural assignment of 2-alkylthio-5-arylidene-3,5-dihydro-4*H*-imidazol-4-one **8**(**a**–**q**) is based on spectroscopic data (^{1}H, ^{13}C NMR, HRMS). In all cases, compounds **8** were obtained in a stereospecific way and the geometry of the double bond was attributed as being Z by the shielding effect of the carbonyl group C-4 on the olefinic proton H-5 (**8a**–**q**: $\delta_{H\text{-}5}$ = 6.83–7.35 ppm).[20] The alkylation's step gave also regioselective S-alkylation with retention of the (5Z)-stereochemistry.

Conclusion

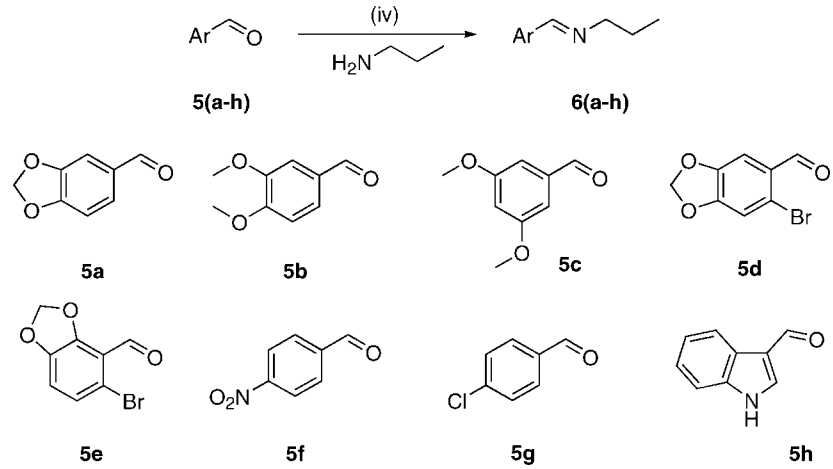
In summary, with this experiment we have showed that it is possible to develop a practical and straightforward parallel solution-phase synthesis of 2-alkylthio-5-arylidene-3,5-dihydro-4*H*-imidazol-4-one using a one-pot domino reaction. Our protocol for this three-component reaction demonstrates a wide applicability for the obtention of stereocontroled thioalkyl and aryl substituted imidazolones and in establishing fast and inexpensive purification methodologies. The yields are always coupled to a high purity of target products, and the precursors were easily prepared from commercially available starting products. Further studies of the biological activity for this library are currently ongoing.

Experimental Section

General Remarks. Melting points were determined on a Kofler melting point apparatus and were uncorrected. Thin-layer chromatography (TLC) was accomplished on 0.2-mm precoated plates of silica gel 60 F-254 (Merck), and visualization was performed with ultraviolet light (254 and 312 nm) or with a fluorescence indicator. For parallel synthesis, a carousel 6 place reaction station with a working volume of 30–150 mL (Radleys Discovery Technologies, Interchim, France) was used. ^{1}H NMR spectra were recorded on Bruker AC 300 P (300 MHz) and Bruker ARX 200 (200 MHz) spectrometers, and ^{13}C NMR spectra were obtained on a Bruker AC 300 P (75 MHz) spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Data are given in the following order: δ value, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), and number of protons; coupling constants *J* are given in Hertz. The mass spectra (HRMS) were taken on a Varian MAT 311 at an ionizing potential of 70 eV in the Centre Régional de Mesures Physiques de l'Ouest (CRMPO, Rennes). Acetonitrile was distilled over calcium chloride after standing overnight and stored over molecular sieves (3Å). Solvents were evaporated with a Buchi rotary evaporator. All reagents were purchased from Acros, Aldrich Chimie, and Fluka France and were used without further purification.

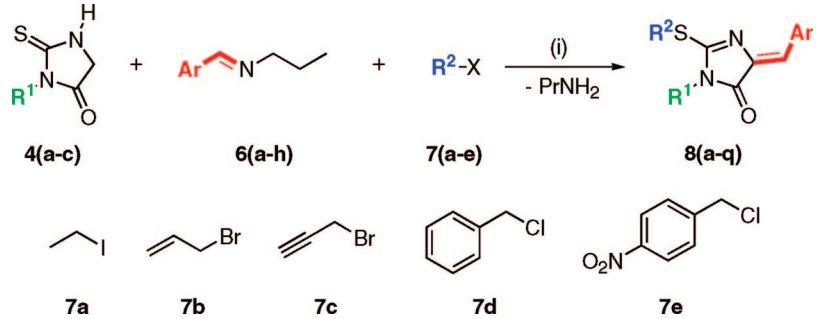
Standard Procedure for the Parallel Synthesis of 5-Arylidene-2-alkylthio-3,5-dihydro-4*H*-imidazol-4-one (8a–q) by One-Pot Three-Component Domino Reaction. In each vial of the carousel 6 place reaction station (Radleys Discovery Technologies), a mixture of 5 mmol of compound

Scheme 3. Preparation of Aryl Aldimines **6**(**a**–**h**) under Microwave Irradiations ($\mu\omega$) using Solventless Reaction Conditions[a]



[a] Reagent and reaction conditions: (iv) $Me(CH_2)_2NH_2$ 2 equiv, $\mu\omega$ (Synthewave 402 reactor), 60 °C, 30 min.

Scheme 4. Preparation of the 2-Alkylthio-5-arylidene-3,5-dihydro-4*H*-imidazol-4-one **8**(**a**–**q**) using Three-Component Reaction[a]



[a] Reagents and reaction conditions: (i) **4** 1 equiv, **6** 1 equiv, **7** 1.5 equiv, K_2CO_3 0.5 equiv, KI 1.5 equiv if X = CI, Br for **7**, MeCN, Δ from 60 to 70 °C, 14 h, then recristallyzation (1:6 w/v) in pentane/EtOH (1:1).

Table 2. Results for the Preparation of Compounds **8**(**a**–**q**) from Thiohydantoines **4**(**a**–**c**), Aryl Aldimines **6**(**a**–**h**), and Halogenoalkanes **7**(**a**–**e**) by Three-Component Tandem Reaction Using Parallel Solution-Phase Reaction Conditions

		starting reagents				
product	R^1	**4**	**6**	**7**	temp (°C)	yield (%)[a]
8a	Me	**4a**	**6a**	**7a**	60	62
8b	Me	**4a**	**6a**	**7b**[b]	65	40
8c	Me	**4a**	**6a**	**7c**[b]	70	56
8d	Me	**4a**	**6a**	**7d**[b]	60	50
8e	Bu	**4b**	**6a**	**7a**	60	57
8f	Bu	**4b**	**6a**	**7b**[b]	65	43
8g	Bu	**4b**	**6a**	**7c**[b]	70	44
8h	Bu	**4b**	**6a**	**7d**[b]	60	54
8i	Bu	**4b**	**6a**	**7e**	60	60
8j	Me	**4a**	**6b**	**7a**	60	35
8k	Bu	**4b**	**6b**	**7a**	60	43
8l	Me	**4a**	**6c**	**7a**	60	44
8m	Bu	**4b**	**6d**	**7a**	60	40
8n	Ph	**4c**	**6f**	**7a**	60	63
8o	Ph	**4c**	**6g**	**7a**	60	71
8p	Ph	**4c**	**6g**	**7e**[b]	60	56
8q	Ph	**4c**	**6h**	**7a**	60	37

[a] Isolated yield after recrystallization from pentane/EtOH (1:1). [b] KI (1.5 equiv) was added in the reaction mixture.

4 (**4a**: 650.1 mg or **4b**: 861.3 mg or **4c**: 961.2 mg), aldimine **6** (5 mmol), halogenoalkane R^2X **7** (7.5 mmol), and, eventually, potassium iodide (1.25 g, 7.5 mmol) if X = Cl, Br for **7**, in dry acetonitrile (10 mL) was stirred vigorously at the appropriate reaction temperature (60–70 °C) for 14 h. After heating, the carousel 6 place reaction station apparatus was allowed to cool down at room temperature, the solvent and the volatile components in each vial were eliminated by rotary evaporation under reduced pressure. The residue of each vial was dissolved in methylene chloride (20 mL), and the contents were filtered though a sintered glass disc; the solution was recovered, and the solvent was removed under reduced pressure. In each vial, the expected compound **8** was purified by recrystallization from a mixture of pentane/ethanol (1:1). The precipitated product **8** was filtered off and further dried under high vacuum (10^{-2} Torr) at 30 °C for 1 h, which gave the desired 5-arylidene-2-alkylthio-3,5-dihydro-4*H*-imidazol-4-one **8** as a powder. The pure compound **8** was characterized by ^1H, ^{13}C NMR, and HRMS.

(*5Z*)-5-[(1,3-Benzodioxol-5-yl)methylene]-3-methyl-2-ethylthio-3,5-dihydro-4*H*-imidazol-4-one (8a). Reaction temperature: 60 °C. Yield = 62%. Orange powder, mp = 152–154 °C. ^1H NMR ($CDCl_3$) δ = 1.55 (t, 3H, J = 7.4Hz, SCH_2CH_3), 3.17 (s, 3H, NCH_3), 3.40 (q, 2H, J = 7.4Hz, SCH_2CH_3), 6.00 (s, 2H, OCH_2O), 6.82 (d, 1H, J = 8.1 Hz, H-5, Ar), 6.83 (s, 1H, =CH), 7.37 (dd, 1H, J = 8.1, 1.03 Hz, H-6, Ar), 8.05 (s, 1H, H-2, Ar). ^{13}C NMR ($CDCl_3$) δ = 14.7 (SCH_2CH_3), 25.6 (SCH_2CH_3), 26.9 (NCH_3), 101.8 (OCH_2O), 108.8 (C-5, Ar), 111.2 (C-2, Ar), 124.0 (=CH), 128.4 (C-6, Ar), 129.5 (C-1, Ar), 137.5 (C-5, N–C=C), 148.3 (C-4, Ar), 149.5 (C-3, Ar), 164.1 (C-2, S–C=N), 170.3 (C-4, C=O). HRMS, m/z = 290.0730 found (calculated for $C_{14}H_{14}N_2O_3S$, $M^{+\bullet}$ requires 290.0725).

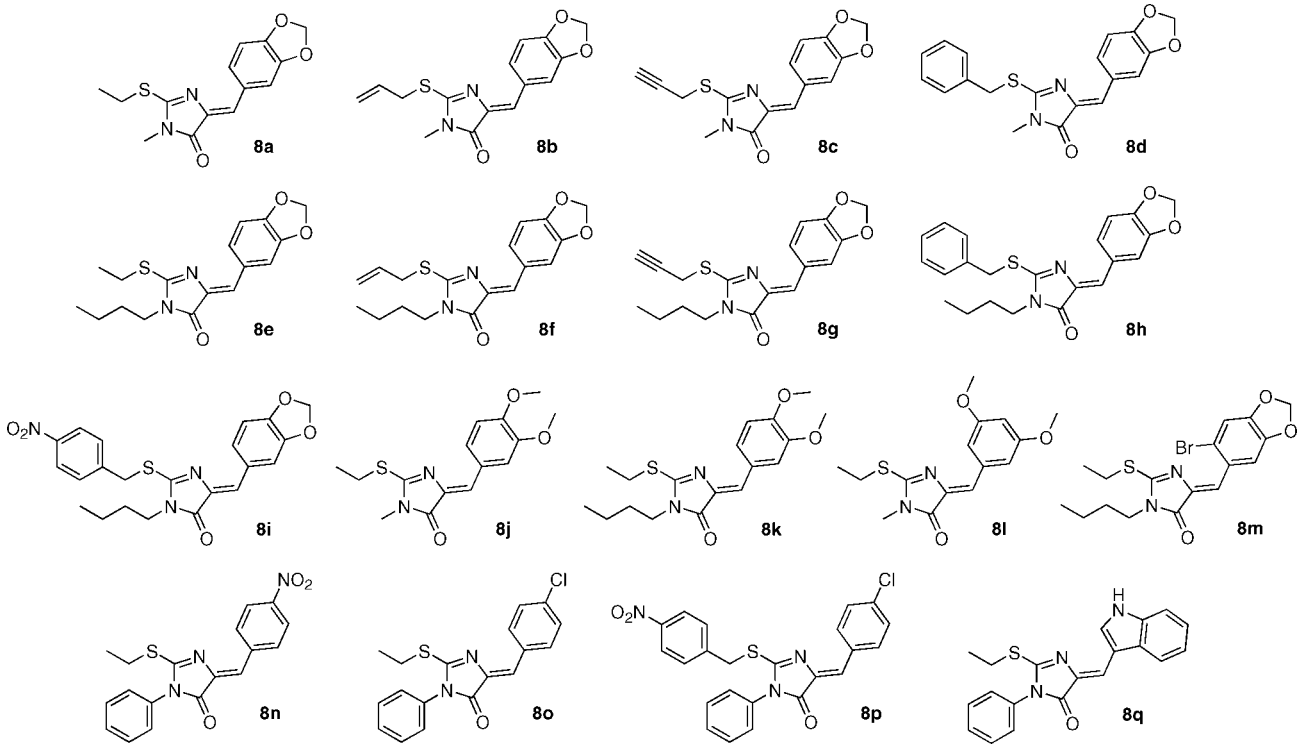


Figure 3. Library products **8**(**a**–**q**) obtained by parallel three-component domino reaction.

(5*Z*)-5-[(1,3-Benzodioxol-5-yl)methylene]-3-methyl-2-(prop-2-enyl)thio-3,5-dihydro-4*H*-imidazol-4-one (8b). Reaction temperature: 65 °C. Yield = 40%. Yellow powder, mp = 154–156 °C. ^{1}H NMR ($CDCl_3$) δ = 3.17 (s, 3H, NC*H*$_3$), 4.02 (d, 2H, J = 7 Hz, SC*H*$_2$), 5.15 (d, 1H, J = 10 Hz, SCH$_2$CH=C*H*$_2$), 5.40 (d, 1H, J = 17 Hz, SCH$_2$CH=C*H*$_2$), 6.00 (s, 2H, OC*H*$_2$O), 6.10 (m, 1H, SCH$_2$C*H*=CH$_2$), 6.82 (d, 1H, J = 8.1 Hz, H-5, Ar), 6.83 (s, 1H, =C*H*), 7.37 (dd, 1H, J = 8.1, 1.05 Hz, H-6, Ar), 8.05 (s, 1H, H-2, Ar). ^{13}C NMR ($CDCl_3$) δ = 26.5 (N*C*H$_3$), 33;3 (S*C*H$_2$CHCH$_2$), 101.8 (O*C*H$_2$O), 108.5 (C-5, Ar), 110.8 (C-2, Ar), 119.5 (CH=*C*H$_2$), 124.1 (=*C*H), 128.0 (C-6, Ar), 129.0 (C-1, Ar), 132.0 (*C*H=CH$_2$), 136.9 (C-5, N–*C*=C), 148.0 (C-4, Ar), 149.2 (C-3, Ar), 163.0 (C-2, S–*C*=N), 169.9 (C-4, C=O). HRMS, *m/z* = 302.0723 found (calculated for $C_{15}H_{14}N_2O_3S$, $M^{+\bullet}$ requires 302.0725).

(5*Z*)-5-[(1,3-Benzodioxol-5-yl)methylene]-3-methyl-2-(prop-2-ynyl)thio-3,5-dihydro-4*H*-imidazol-4-one (8c). Reaction temperature: 70 °C. Yield = 56%. Yellow powder, mp = 199–200 °C. ^{1}H NMR ($CDCl_3$) δ = 2.37 (t, 1H, J = 2.7 Hz, SCH$_2$C≡C*H*), 3.17 (s, 3H, NC*H*$_3$), 4.08 (d, 2H, J = 2.7 Hz, SC*H*$_2$), 6.00 (s, 2H, OC*H*$_2$O), 6.82 (d, 1H, J = 8.1 Hz, H-5, Ar), 6.83 (s, 1H, =C*H*), 7.37 (dd, 1H, J = 8.1, 1.05 Hz, H-6, Ar), 8.05 (s, 1H, H-2, Ar). ^{13}C NMR ($CDCl_3$) δ = 19.2 (S*C*H$_2$), 26.5 (N*C*H$_3$), 72.4 (SCH$_2$C≡*C*H), 77.7 (SCH$_2$*C*≡CH), 101.5 (O*C*H$_2$O), 108.5 (C-5, Ar), 110.9 (C-2, Ar), 124.9 (=*C*H), 128.3 (C-6, Ar), 128.8 (C-1, Ar), 136.6 (C-5, N-*C*=C), 148.0 (C-4, Ar), 149.4 (C-3, Ar), 161.7 (C-2, S–*C*=N), 169.7 (C-4, C=O). HRMS, *m/z* = 300.0555 found (calculated for $C_{15}H_{12}N_2O_3S$, $M^{+\cdot}$ requires 300.0569).

(5*Z*)-5-[(1,3-Benzodioxol-5-yl)methylene]-3-methyl-2-phenylmethylthio-3,5-dihydro-4*H*-imidazol-4-one (8d). Reaction temperature: 60 °C. Yield = 50%. Yellow powder, mp = 210–212 °C. ^{1}H NMR ($CDCl_3$) δ = 3.17 (s, 3H, NC*H*$_3$), 4.56 (s, 2H, SC*H*$_2$), 6.00 (s, 2H, OC*H*$_2$O), 6.91 (d, 1H, J = 8.1 Hz, H-5, Ar), 6.83 (s, 1H, =C*H*), 7.20–7.50 (m, 5H, Ar), 7.37 (dd, 1H, J = 8.1, 1.5 Hz, H-6, Ar), 8.05 (s, 1H, H-2, Ar). ^{13}C NMR ($CDCl_3$) δ = 26.9 (N*C*H$_3$), 35.2 (S*C*H$_2$), 101.9 (O*C*H$_2$O), 108.9 (C-5, Ar), 111.3 (C-2, Ar), 124.5 (=CH), 128.3 (C-6, Ar), 128.5 (C-4′, Ar), 129.2 (C-3′, C-5′, Ar), 129.4 (C-1, Ar), 129.6 (C-2′, C-6′, Ar), 136.4 (C-1′, Ar), 137.4 (C-5, N-*C*=C), 148.4 (C-4, Ar), 149.6 (C-3, Ar), 163.7 (C-2, S–*C*=N), 170.2 (C-4, C=O). HRMS, *m/z* = 352.0873 found (calculated for $C_{19}H_{16}N_2O_3S$, $M^{+\bullet}$ requires 352.0882).

(5*Z*)-5-[(1,3-Benzodioxol-5-yl)methylene]-3-butyl-2-ethylthio-3,5-dihydro-4*H*-imidazol-4-one (8e). Reaction temperature: 60 °C. Yield = 57%. Yellow powder, mp = 106–108 °C. ^{1}H NMR ($CDCl_3$) δ = 0.91 (t, 3H, J = 7.2 Hz, N(CH$_2$)$_3$C*H*$_3$), 1.35 (sext, 2H, J = 7.4 Hz, N(CH$_2$)$_2$C*H*$_2$CH$_3$), 1.50 (t, 3H, J = 7.4 Hz, SCH$_2$C*H*$_3$), 1.61 (qt, 2H, J = 7.4 Hz, NCH$_2$C*H*$_2$CH$_2$CH$_3$), 3.35 (q, 2H, J = 7.4 Hz, SC*H*$_2$CH$_3$), 3.60 (t, 2H, J = 7.4 Hz, NC*H*$_2$(CH$_2$)$_2$CH$_3$), 6.00 (s, 2H, OC*H*$_2$O), 6.82 (d, 1H, J = 8.1 Hz, H-5, Ar), 6.84 (s, 1H, =CH), 7.37 (dd, 1H, J = 8.1, 1.05 Hz, H-6, Ar), 8.05 (s, 1H, H-2, Ar). ^{13}C NMR ($CDCl_3$) δ = 13.6 (NCH$_2$CH$_2$CH$_2$*C*H$_3$), 14.2 (SCH$_2$*C*H$_3$), 19.9 (NCH$_2$CH$_2$*C*H$_2$CH$_3$), 25.3 (S*C*H$_2$CH$_3$), 30.9 (NCH$_2$*C*H$_2$CH$_2$CH$_3$), 40.6 (N*C*H$_2$CH$_2$CH$_2$CH$_3$), 101.4 (O*C*H$_2$O), 108.5 (C-5, Ar), 110,8 (C-2, Ar), 123.5 (=*C*H), 127.9 (C-6, Ar), 129.2 (C-1, Ar), 137.2 (C-5, N–*C*=C), 147.9 (C-4), 149.0 (C-3, Ar), 163.6 (C-2, S–*C*=N), 169.9 (C-4, C=O). HRMS, *m/z* = 332.1189 found (calculated for $C_{17}H_{20}N_2O_3S$, $M^{+\bullet}$ requires 332.1195).

(5*Z*)-5-[(1,3-Benzodioxol-5-yl)methylene]-3-butyl-2-(prop-2-enyl)thio-3,5-dihydro-4*H*-imidazol-4-one (8f). Reaction temperature: 65 °C. Yield = 43%. Yellow powder, mp = 82–84 °C. ^{1}H NMR ($CDCl_3$) δ = 0.91 (t, 3H, J = 7.2 Hz,

N(CH$_2$)$_3$C***H*$_3$**), 1.35 (sext, 2H, J = 7.4 Hz, N(CH$_2$)$_2$C***H*$_2$**CH$_3$), 1.61 (qt, 2H, J = 7.4 Hz, NCH$_2$C***H*$_2$**CH$_2$CH$_3$), 3.60 (t, 2H, J = 7.4 Hz, NC***H*$_2$**(CH$_2$)$_2$CH$_3$), 4.02 (d, 2H, J = 7.1 Hz, SC***H*$_2$**CH=CH$_2$), 5.25 (d, 1H, J = 10 Hz, SCH$_2$CH=C***H*$_2$**), 5.40 (d, 1H, J = 17 Hz, SCH$_2$CH=C***H*$_2$**), 6.00 (s, 2H, OC***H*$_2$O), 6.10 (m, 1H, SCH$_2$C***H***=CH$_2$), 6.82 (d, 1H, J = 8.1 Hz, H-5, Ar), 6.84 (s, 1H, =C***H***), 7.37 (dd, 1H, J = 8.1, 1.05 Hz, H-6, Ar), 8.05 (s, 1H, H-2, Ar). ^{13}C NMR (CDCl$_3$) δ = 13.7 (NCH$_2$CH$_2$CH$_2$***C***H$_3$), 20.0 (NCH$_2$CH$_2$***C***H$_2$CH$_3$), 31.0 (NCH$_2$***C***H$_2$CH$_2$CH$_3$), 33.4 (S***C***H$_2$CHCH$_2$), 40.7 (N***C***H$_2$CH$_2$CH$_2$CH$_3$), 101.4 (O***C***H$_2$O), 108.5 (C-5, Ar), 110.8 (C-2, Ar), 119.5 (CH=***C***H$_2$), 123.8 (=***C***H), 128.0 (C-6, Ar), 129.0 (C-1, Ar), 132.1 (CH$_2$***C***H=CH$_2$), 137.0 (C-5, N–***C***=C), 148.0 (C-4, Ar), 149.1 (C-3, Ar), 163,0 (C-2, S–***C***=N), 169.9 (C-4, C=O). HRMS, *m/z* = 344.1188 found (calculated for C$_{18}$H$_{20}$N$_2$O$_3$S, M$^{+\bullet}$ requires 344.1195).

(5*Z*)-5-[(1,3-Benzodioxol-5-yl)methylene]-3-butyl-2-(prop-2-ynyl)thio-3,5-dihydro-4*H*-imidazol-4-one (8g). Reaction temperature: 70 °C. Yield = 44%. Yellow powder, mp = 118–120 °C. ^{1}H NMR (CDCl$_3$) δ = 0.91 (t, 3H, J = 7.2 Hz, N(CH$_2$)$_3$C***H*$_3$**), 1.35 (sext, 2H, J = 7.4 Hz, N(CH$_2$)$_2$-C***H*$_2$**CH$_3$), 1.61 (qt, 2H, J = 7.4 Hz, NCH$_2$C***H*$_2$**CH$_2$CH$_3$), 2.37 (t, 1H, J = 2.7 Hz, SCH$_2$C≡C***H***), 3.60 (t, 2H, J = 7.4 Hz, NC***H*$_2$**(CH$_2$)$_2$CH$_3$), 4.15 (d, 2H, J = 2.6 Hz, SC***H*$_2$**CCH), 6.01 (s, 2H, OC***H*$_2$O), 6.82 (d, 1H, J = 8.1 Hz, H-5, Ar), 6.83 (s, 1H, =C***H***), 7.37 (dd, 1H, J = 8.1, 1.05 Hz, H-6, Ar), 8.05 (s, 1H, H-2, Ar). ^{13}C NMR (CDCl$_3$) δ = 13.6 (NCH$_2$CH$_2$CH$_2$***C***H$_3$), 19.3 (SCH$_2$), 19.9 (NCH$_2$CH$_2$***C***H$_2$CH$_3$), 31.0 (NCH$_2$***C***H$_2$CH$_2$CH$_3$), 40.7 (N***C***H$_2$CH$_2$CH$_2$CH$_3$), 72.3 (SCH$_2$C≡***C***H), 77.5 (SCH$_2$***C***≡CH), 101.8 (O***C***H$_2$O), 108.8 (C-5, Ar), 111.2 (C-2, Ar), 124.7 (=***C***H), 128.2 (C-6, Ar), 128.9 (C-1, Ar), 136.8 (C-5, N–***C***=C), 148.0 (C-4, Ar), 149.3 (C-3, Ar), 161.7 (C-2, S–***C***=N), 169.8 (C-4, C=O). HRMS, *m/z* = 342.1025 found (calculated for C$_{18}$H$_{18}$N$_2$O$_3$S, M$^{+\bullet}$ requires 342.1038).

(5*Z*)-5-[(1,3-Benzodioxol-5-yl)methylene]-3-butyl-2-phenylmethylthio-3,5-dihydro-4*H*-imidazol-4-one (8h). Reaction temperature: 60 °C. Yield = 54%. Yellow powder, mp = 150–152 °C. ^{1}H NMR (CDCl$_3$) δ = 0,91 (t, 3H, J = 7.2 Hz, N(CH$_2$)$_3$C***H*$_3$**), 1.35 (sext, 2H, J = 7.4 Hz, N(CH$_2$)$_2$-C***H*$_2$**CH$_3$), 1.61 (qt, 2H, J = 7.4 Hz, NCH$_2$C***H*$_2$**CH$_2$CH$_3$), 3.60 (t, 2H, J = 7.4 Hz, NC***H*$_2$**(CH$_2$)$_2$CH$_3$), 4.56 (s, 2H, SC***H*$_2$**), 6.00 (s, 2H, OC***H*$_2$O), 6.82 (d, 1H, J = 8.1 Hz, H-5, Ar), 6.83 (s, 1H, =C***H***), 7.20–7.50 (m, 5H, Ar), 7,37 (dd, 1H, J = 8.1, 1.05 Hz, H-6, Ar), 8.05 (s, 1H, H-2, Ar). ^{13}C NMR (CDCl$_3$) δ = 13.6 (NCH$_2$CH$_2$CH$_2$***C***H$_3$), 20.0 (NCH$_2$CH$_2$-***C***H$_2$CH$_3$), 31.0 (NCH$_2$***C***H$_2$CH$_2$CH$_3$), 35.1 (S***C***H$_2$), 40.7 (N***C***H$_2$CH$_2$CH$_2$CH$_3$), 101.5 (O***C***H$_2$O), 108.5 (C-5, Ar), 110.8 (C-2, Ar), 124.0 (=***C***H), 127.9 (C-6, Ar), 128.5 (C-4′, Ar), 129.2 (C-3′, C-5′, Ar), 129.4 (C-1, Ar), 129.6 (C-2′, C-6′, Ar), 136.0 (C-1′, Ar), 137.1 (C-5, N–***C***=C), 148.1 (C-4, Ar), 149.2 (C-3, Ar), 163.2 (C-2, S–***C***=N), 169.9 (C-4, C=O). HRMS, *m/z* = 394.1334 found (calculated for C$_{22}$H$_{22}$N$_2$O$_3$S, M$^{+\bullet}$ requires 394.1351).

(5*Z*)-5-[(1,3-Benzodioxol-5-yl)methylene]-3-butyl-2-(4-nitrophenylmethyl)thio-3,5-dihydro-4*H*-imidazol-4-one (8i). Reaction temperature: 60 °C. Yield = 60%. Yellow powder, mp = 143–145 °C. ^{1}H NMR (CDCl$_3$) δ = 0.95 (t, 3H, J = 7.3 Hz, N(CH$_2$)$_3$C***H*$_3$**), 1.36 (sext, 2H, J = 7.6 Hz, N(CH$_2$)$_2$-C***H*$_2$**CH$_3$), 1.64 (qt, 2H, J = 7.8 Hz, NCH$_2$C***H*$_2$**CH$_2$CH$_3$), 3.58 (t, 2H, J = 7.4 Hz, NC***H*$_2$**(CH$_2$)$_2$CH$_3$), 4.62 (s, 2H, SC***H*$_2$**), 6.05 (s, 2H, OC***H*$_2$O), 6.85 (d, 1H, J = 8.1 Hz, H-5, Ar), 6.90 (s, 1H, =C***H***), 7.33 (d, 1H, J = 8 Hz, H-6, Ar), 7.69 (d, 2H, J = 8.6 Hz, ArNO$_2$), 8.00 (s, 1H, H-2, Ar), 8.23 (d, 2H, ArNO$_2$). ^{13}C NMR (CDCl$_3$) δ = 13.6 (NCH$_2$CH$_2$-CH$_2$***C***H$_3$), 20.0 (NCH$_2$CH$_2$***C***H$_2$CH$_3$), 31.0 (NCH$_2$***C***H$_2$CH$_2$-CH$_3$), 33.9 (SC***H*$_2$**), 40.8 (N***C***H$_2$CH$_2$CH$_2$CH$_3$), 101.6 (OC***H*$_2$O), 108.5 (C-5, Ar), 110.6 (C-2, Ar), 124.0 (C-3′, C-5′, Ar-NO$_2$), 124.7 (C-6, Ar), 128.1 (=***C***H), 128.8 (C-1, Ar), 129,9 (C-2′, C-6′, Ar), 136.7 (C-5, N–***C***=C), 144.2 (C-4′, ArNO$_2$), 148.1 (C-4, Ar), 149.4 (C-3, Ar), 162.0 (C-2, S–***C***=N), 169.6 (C-4, C=O). HRMS, *m/z* = 439.4850 found (calculated for C$_{22}$H$_{21}$N$_3$O$_5$S, M$^{+\bullet}$ requires 439.4842).

(5*Z*)-5-(3,4-Dimethoxybenzylidene)-3-methyl-2-ethylthio-3,5-dihydro-4*H*-imidazol-4-one (8j). Reaction temperature: 60 °C. Yield = 35%. Yellow powder, mp = 171–173 °C. ^{1}H NMR (CDCl$_3$) δ = 1.55 (t, 3H, J = 7.4 Hz, SCH$_2$C***H*$_3$**), 3.12 (s, 3H, NC***H*$_3$**), 3.32 (q, 2H, J = 7.3 Hz, SC***H*$_2$**CH$_3$), 3.92 (br s, 3H, OC***H*$_3$**), 3.93 (br s, 3H, OC***H*$_3$**), 6.87 (d, 1H, J = 8.4 Hz, H-5, Ar), 6.89 (s, 1H, =C***H***), 7.37 (d, 1H, J = 7 Hz, H-6, Ar), 8.28 (s, 1H, H-2, Ar). ^{13}C NMR (CDCl$_3$) δ = 14.6 (SCH$_2$***C***H$_3$), 25.0 (N***C***H$_3$), 26.5 (S***C***H$_2$CH$_3$), 55.5 (O***C***H$_3$), 55.9 (O***C***H$_3$), 110.7 (C-5, Ar), 113.4 (C-2, Ar), 123.8 (=***C***H), 126.5 (C-6, Ar), 127.8 (C-1, Ar), 136.9 (C-5, N–***C***=C), 148.8 (C-4, Ar), 150.6 (C-3, Ar), 163.2 (C-2, S–***C***=N), 169.8 (C-4, C=O). HRMS, *m/z* = 306.1023 found (calculated for C$_{15}$H$_{18}$N$_2$O$_3$S, M$^{+\bullet}$ requires 306.1038).

(5*Z*)-5-(3,4-Dimethoxybenzylidene)-3-butyl-2-ethylthio-3,5-dihydro-4*H*-imidazol-4-one (8k). Reaction temperature: 60 °C. Yield = 43%. Yellow powder, mp = 114–116 °C. ^{1}H NMR (CDCl$_3$) δ = 0.94 (t, 3H, J = 7.2 Hz, N(CH$_2$)$_3$C***H*$_3$**), 1.36 (sext, 2H, J = 7.4 Hz, N(CH$_2$)$_2$C***H*$_2$**CH$_3$), 1.52 (t, 3H, J = 7.4 Hz, SCH$_2$C***H*$_3$**), 1.62 (qt, 2H, J = 7.4 Hz, NCH$_2$C***H*$_2$**CH$_2$CH$_3$), 3.34 (q, 2H, J = 7.4 Hz, SC***H*$_2$**CH$_3$), 3.57 (t, 2H, J = 7.4 Hz, NC***H*$_2$**(CH$_2$)$_2$CH$_3$), 3.93 (s, 3H, OC***H*$_3$**), 3.94 (s, 3H, OC***H*$_3$**), 6.88 (d, 1H, J = 8.1 Hz, H-5, Ar), 6.90 (s, 1H, =C***H***), 7.39 (dd, 1H, J = 8.1, 1.05 Hz, H-6, Ar), 8.30 (s, 1H, H-2, Ar). ^{13}C NMR (CDCl$_3$) δ = 13.7 (NCH$_2$CH$_2$CH$_2$***C***H$_3$), 14.6 (SCH$_2$***C***H$_3$), 20.0 (NCH$_2$CH$_2$***C***H$_2$CH$_3$), 25.1 (S***C***H$_2$CH$_3$), 30.9 (NCH$_2$ ***C***H$_2$CH$_2$CH$_3$), 40.6 (N***C***H$_2$CH$_2$CH$_2$CH$_3$), 55.5 (O***C***H$_3$), 55.9 (O***C***H$_3$), 110.7 (C-5, Ar), 113.4 (C-2, Ar), 123.8 (=***C***H), 126;5 (C-6, Ar), 127.8 (C-1, Ar), 137.0 (C-5, N–***C***=C), 148.8 (C-4, Ar), 150.6 (C-3, Ar), 163.2 (C-2, S–***C***=N), 169.9 (C-4, C=O). HRMS, *m/z* = 348.1511 found (calculated for C$_{18}$H$_{24}$N$_2$O$_3$S, M$^{+\bullet}$ requires 348.1508).

(5*Z*)-5-(3,5-Dimethoxybenzylidene)-3-methyl-2-ethylthio-3,5-dihydro-4*H*-imidazol-4-one (8l). Reaction temperature: 60 °C. Yield = 44%. Yellow powder, mp = 141–143 °C. ^{1}H NMR (CDCl$_3$) δ = 1.53 (t, 3H, J = 7.4 Hz, SCH$_2$C***H*$_3$**), 3.14 (s, 3H, C***H*$_3$**), 3.34 (q, 2H, J = 7.1 Hz, SC***H*$_2$**CH$_3$), 3.83 (s, 6H, OC***H*$_3$**), 6.49 (s, 1H, H-4, Ar), 6.85 (s, 1H, =C***H***), 7.40 (s, 2H, H-2, H-6, Ar). ^{13}C NMR (CDCl$_3$) δ = 14.6 (SCH$_2$***C***H$_3$), 25.2 (N***C***H$_3$), 26;5 (S***C***H$_2$CH$_3$), 55.1 (O***C***H$_3$), 103.0 (C-4, Ar), 109.3 (C-2, Ar), 123.5 (=***C***H), 136.2 (C-1, Ar), 138.8(C-5, N–***C***=C), 160.6 (C-3, Ar), 165.0

(C-2, S–*C*═N), 169.8 (C-4, C═O). HRMS, *m/z* = 306.1033 found (calculated for $C_{15}H_{18}N_2O_3S$, $M^{+\bullet}$ requires 306.1038).

(5*Z*)-5-[(6-Bromo-1,3-benzodioxol-5-yl)methylene]-3-butyl-2-ethylthio-3,5-dihydro-4*H*-imidazol-4-one (8m). Reaction temperature: 60 °C. Yield = 40%. Yellow powder, mp = 134–136 °C. ^{1}H NMR ($CDCl_3$) δ = 0.94 (t, 3H, *J* = 7.5 Hz, $N(CH_2)_3CH_3$), 1.35 (sext, 2H, *J* = 7.5 Hz, $N(CH_2)_2CH_2CH_3$), 1.49 (t, 3H, *J* = 7.9 Hz, SCH_2CH_3), 1.63 (qt, 2H, *J* = 7.3 Hz, $NCH_2CH_2CH_2CH_3$), 3.33 (q, 2H, *J* = 7.9 Hz, SCH_2CH_3), 3.57 (t, 2H, *J* = 7.5 Hz, $NCH_2(CH_2)_2CH_3$), 6.02 (s, 2H, OCH_2O), 7;07 (s, 1H, C-5, Ar), 7.28 (s,1H, ═C*H*), 8.51 (s, 1H, C-2, Ar). ^{13}C NMR ($CDCl_3$) δ = 13.6 ($NCH_2CH_2CH_2CH_3$), 14.2 (SCH_2CH_3), 18.3 ($NCH_2CH_2CH_2CH_3$), 25.3 (SCH_2CH_3), 29.7 ($NCH_2CH_2CH_2CH_3$), 40.6 ($NCH_2CH_2CH_2CH_3$), 102.0 (OCH_2O), 111.6 (C-5, Ar), 113.1 (C-2, Ar), 119.6 (C-6, Ar), 121.0 (═*C*H), 127.7 (C-1, Ar), 138.4 (C-5, N–*C*═C), 147.3 (C-4, Ar), 149.2 (C-3, Ar), 165.1 (C-2, S–*C*═N), 169.7 (C-4, C═O). HRMS, *m/z* = 410.0309 found (calculated for $C_{17}H_{19}BrN_2O_3S$, $M^{+\bullet}$ requires 410.0300).

(5*Z*)-2-(Ethylthio)-5-(4-nitrobenzylidene)-3-phenyl-3,5-dihydro-4*H*-imidazol-4-one (8n). Reaction temperature: 60 °C. Yield = 63%. Yellow powder, mp = 219–221 °C. ^{1}H NMR ($CDCl_3$) δ = 1.53 (t, 3H, *J* = 7.4 Hz, SCH_2CH_3), 3.38 (q, 2H, *J* = 7.4 Hz, SCH_2), 7.00 (s, 1H, C═C*H*), 7.35 (d, 2H, *J* = 6.6 Hz, H-2, Ph), 7.45–7.57 (m, 3H, H-3, H-4, Ph), 8.29 (d, 2H, *J* = 8.7 Hz, H-3′, H-5′, Ar), 8.35 (d, 2H, *J* = 9.0 Hz, H-2′, H-6′, Ar). ^{13}C NMR ($CDCl_3$) δ = 14.1 (SCH_2CH_3), 25.8 (SCH_2), 120.0 (═*C*H), 123.8 (C-3′, C-5′, Ar), 127.3 (C-2, C-6, Ph), 129.4 (C-4, Ph), 129.6 (C-3, C-5, Ph), 132.0 (C-2′, C-6′ Ar), 132.1 (C-1, Ph), 140.7 (C-5, N–*C*═C), 140.9 (C-1′, Ar), 147.5 (C-4′, Ar), 168.0 (C-2, S–*C*═N), 168.5 (C-4, C═O). HRMS, *m/z* = 353.0825 found (calculated for $C_{18}H_{15}N_3O_3S$, M^+ requires 353.0834).

(5*Z*)-5-(4-Chlorobenzylidene)-2-(ethylthio)-3-phenyl-3,5-dihydro-4*H*-imidazol-4-one (8o). Reaction temperature: 60 °C. Yield = 56%. Yellowish powder, mp = 150–152 °C. ^{1}H NMR ($CDCl_3$) δ = 1.51 (t, 3H, *J* = 7.5 Hz, SCH_2CH_3), 3.35 (q, 2H, *J* = 7.4 Hz, SCH_2), 6.98 (s, 1H, C═C*H*), 7.35 (dt, 2H, *J* = 6.6, 1.3 Hz, H-2, H-6, Ph), 7.42 (d, 2H, *J* = 8.7 Hz, H-3′, H-5′, Ar), 7.46–7.56 (m, 3H, H-3, H-4, H-5, Ph), 8.16 (d, 2H, *J* = 8.7 Hz, H-2′, H-6′, Ar). ^{13}C NMR ($CDCl_3$) δ = 14.1 (SCH_2CH_3), 25.6 (SCH_2), 122.5 (═*C*H), 127.3 (C-2, C-6, Ph), 129.0 (C-3, C-5, Ph), 129.2 (C-4, Ph), 129.5 (C-3′, C-5′, Ar), 132.4 (C-1, Ph), 133.0 (C-2′, C-6′, Ar), 133.1 (C-4′), 135.7 (C-1′), 138.4 (C-5, N–*C*═C), 165.1 (C-2, S–C═N), 168.9 (C-4, C═O). HRMS, *m/z* = 342.0563 found (calculated for $C_{18}H_{15}ClN_2OS$, M^+ requires 342.0594).

(5*Z*)-5-(4-Nitrobenzylidene)-2-(4-nitrophenylmethylthio)-3-phenyl-3,5-dihydro-4*H*-imidazol-4-one (8p). Reaction temperature: 60 °C. Yield = 56%. Light yellow powder, mp = 185–187 °C. ^{1}H NMR ($CDCl_3$, TMS): δ = 4.63 (s, 2H, SCH_2), 7.03 (s, 1H, ═C*H*), 7.33 (d, 2H, *J* = 6.3 Hz, H-2, H-6, Ph), 7.43 (d, 2H, *J* = 8.4 Hz, H-3′, H-5′, Ar), 7.46–7.55 (m, 3H, H-3, H-4, Ph), 7.65 (d, 2H, *J* = 8.4 Hz, H-2, H-6, $C_4H_4NO_2$), 8.12 (d, 2H, *J* = 8.4 Hz, H-2′, H-6′, Ar), 8.21 (d, 2H, *J* = 8.7 Hz, H-3, H-5′, $C_4H_4NO_2$). ^{13}C NMR ($CDCl_3$, TMS): δ = 34.26 (SCH_2), 123.7 (═*C*H), 124.0 (C-3, $C_4H_4NO_2$), 127.2 (C-2, Ph), 129.0 (C-3, Ph), 129.4 (C-4, Ph), 129.7 (C-3′), 130.0 (C-2, $C_4H_4NO_2$), 132.1 (C-1, Ph), 132.7 (C-4′), 133.0 (C-2′), 136.2 (C-1′), 138.0 (C-5, N–*C*═C), 143.8 (C-1 $C_4H_4NO_2$), 147.5 (C-4 $C_4H_4NO_2$), 163.7 (C-2, S–*C*═N), 168.6 (C-4, C═O). HRMS, *m/z* = 449.0587 found (calculated for $C_{23}H_{16}ClN_3O_3S$, M^+ requires 449.0601).

(5*Z*)-2-(Ethylthio)-5-[(1*H*-indolo-3-yl)methylene]-3-phenyl-3,5-dihydro-4*H*-imidazol-4-one (8q). Reaction temperature: 60 °C. Yield = 37%. Orange powder, mp = 199–201 °C. ^{1}H NMR (DMSO-d_6, TMS) δ = 1.45 (t, 3H, *J* = 7.2 Hz, SCH_2CH_3), 3.34 (q, 2H, *J* = 7.4 Hz, SCH_2), 7.21 (qt, 2H, *J* = 7.7 Hz, H-5′, H-6′, Ar), 7.35 (s, 1H, ═C*H*), 7.40 (d, 2H, *J* = 7.2 Hz, H-2, Ph), 7.44–7.58 (m, 4H, H-7′, H-3, Ph, H-4 Ph), 8.32 (d, 1H, *J* = 7.2 Hz, H-4′, Ar), 8.46 (d, 1H, *J* = 2.1 Hz, H-2′, Ar), 11.98 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, TMS): δ = 14.8 (SCH_2CH_3), 25.3 (SCH_2), 112.0 (C-3′, Ar), 112.7 (C-7′, Ar), 118.8 (C-4′, Ar), 120.5 (C-5′, Ar), 121.2 (C-6′, Ar), 123.1 (C═*C*H), 127.1 (C-3a′, Ar), 128.1 (C-2, Ph), 129.3 (C-4, Ph), 129.8 (C-3, Ph), 133.3 (C-7a′, Ar), 133.4 (C-2′, Ar), 133.6 (C-1, Ph), 137.0 (C-5, N–*C*═C), 159.1 (C-5, S–*C*═N), 168.0 (C-4, C═O). HRMS, *m/z* = 347.1078 found (calculated for $C_{20}H_{17}N_3OS$, M^+ requires 347.1092).

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Supporting Information Available. Details of experimental procedures and analytical data (^{1}H, ^{13}C NMR, and HRMS) for starting products **4**(**a**–**c**), aldimines **6**(**a**–**h**), and analytical data (^{1}H and ^{13}C NMR) for library members **8**(**a**–**q**). This material is available free of charge via the Internet at http://pubs.acs.org.

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