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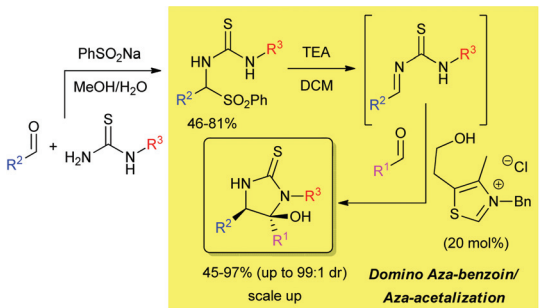
1

Synthesis of functionalized imidazolidine-2-thiones *via* NHC/base-promoted aza-benzoin/aza-acetalization domino reactions

Graziano Di Carmine, Daniele Ragno, Carmela De Risi,* Olga Bortolini, Pier Paolo Giovannini, Giancarlo Fantin and Alessandro Massi*

Benzylidene thioureas were generated *in situ* from α-sulfonylamines and used as novel umpolung acceptors in aza-benzoin/aza-acetalization domino reactions giving 5-hydroxy-imidazolidine-2-thiones.



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Organic & Biomolecular Chemistry

PAPER

Synthesis of functionalized imidazolidine-2-thiones *via* NHC/base-promoted aza-benzoin/aza-acetalization domino reactions†

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A strategy for the synthesis of biologically relevant 5-hydroxy-imidazolidine-2-thione derivatives is presented. A novel class of α-sulfonylamines have been suitably prepared (46–81% yield) as precursors of formal benzylidenethiourea acceptors; these are generated *in situ* and intercepted by N-heterocyclic carbene (NHC)-activated aldehydes affording open-chain aza-benzoin-type adducts, which in turn undergo an intramolecular aza-acetalization reaction in a one-pot fashion. A thiazolium salt/triethylamine couple proved to be the more effective system to trigger the domino sequence giving the target heterocycles in good yields (45–97%) and diastereoselectivities (up to 99 : 1 dr). The multigram scale synthesis and elaboration of a selected 5-hydroxy-imidazolidine-2-thione compound is also described.

Introduction

Since its application in the pioneering works of Wittig[1] and Seebach,[2] umpolung (polarity reversal) has gained well-established importance as an alternative strategy to conventional carbon–carbon and carbon–heteroatom bond-forming methodologies.[3] Within this realm, N-heterocyclic carbenes (NHCs) have been demonstrated to promote a variety of transformations in either chiral or achiral fashion.[4] In particular, NHCs offer a broad range of applications in the field of domino processes, which are powerful tools for the fast construction of complex (chiral) scaffolds with high chemical efficiency starting from simple substrates.[5]

Indeed, a wide range of functionalized carbo- and heterocyclic systems have been accessed by NHC-promoted oxidation/oxa-Michael addition,[6] aza-Michael/aldol,[7] Mannich/lactamization,[8] and Michael/Michael/esterification[9] reaction sequences, just to cite a few.

Typically, NHCs are employed in benzoin and Stetter reactions, where the acyl anion donor (usually an aldehyde) reacts with a carbonyl compound[10] and a Michael acceptor,[11] respectively.[12,13] Nevertheless, the use of unconventional reaction partners in umpolung processes has been attracting a great deal of attention in recent years.[14] In particular, non-activated C–C multiple bonds, arynes, and activated alkyl or aryl halides have been applied in hydroacylation[15] and nucleophilic substitution reactions.[16] The NHC-catalyzed umpolung of α,β-unsaturated esters,[17,18] enones,[19] and styrenes[20] has also been exploited as well as the addition of NHCs to alkyl halides,[21] iminium salts,[22] aldimines,[23] and isocyanides.[24] In addition, the capability of α-diketones to serve as valuable acyl anion donors in nucleophilic acylations under NHC catalysis has been recently demonstrated by our group.[25]

As a further extension of our interest in the development of NHC-catalyzed umpolung reactions, we herein introduce a novel class of acyl anion acceptors, namely benzylidenethioureas **I**, and we demonstrate their synthetic potential in domino processes by reporting on the synthesis of the 5-hydroxy-imidazolidine-2-thione scaffold **II** displaying two contiguous stereocenters and a challenging all-substituted carbon site (Scheme 1).[26,27]

Imidazolidine-2-thiones and the corresponding imidazole-2-thione analogs are special classes of biologically relevant thiourea derivatives[28] endowed with antithyroid,[29] antitumor,[30] antimicrobial,[31] and dopamine inhibition activities.[32] In spite of their relevance, the preparation of imidazole/imidazolidine-2-thiones is so far troublesome. Indeed, harsh reaction conditions are often required, and access to starting materials may be somewhat difficult. A typical method for the synthesis of imidazolidine-2-thiones is based on the addition of phenylisothiocyanate to α-aminoketones,[33] while the reaction of aminoacetaldehyde diethyl acetal with isothiocyanates,[34] cyclization of *N*,*N*′-disubstituted thioureas with carbonyl compounds,[35] and condensation of benzoin with either *N*-substituted or *N*,*N*′-disubstituted thioureas[36] have

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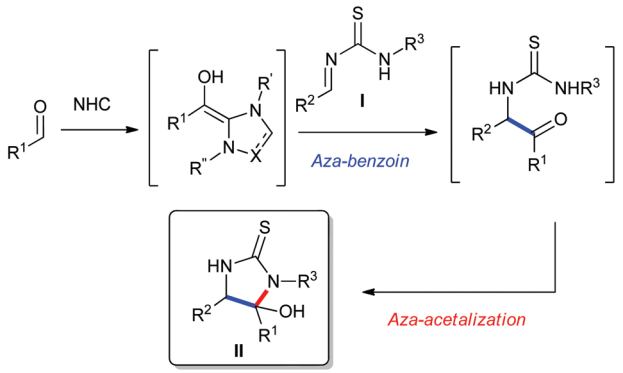
† Electronic supplementary information (ESI) available: Copies of NMR spectra, ROESY experiment for compound (±)-**5aam**. See DOI: 10.1039/c7ob02259j



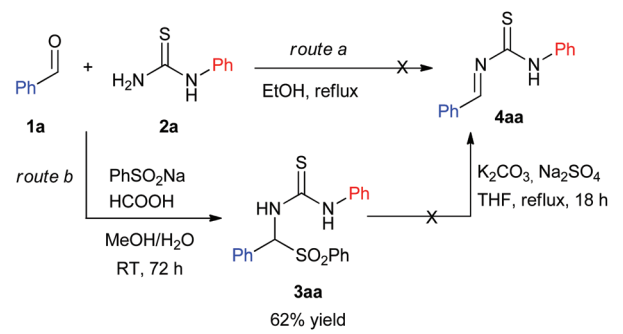
Scheme 1 Strategy for the synthesis of imidazolidine-2-thiones **II** *via* the domino reaction of aldehydes and benzylidenethioureas **I** under NHC catalysis.

been exploited to obtain imidazole-2-thione derivatives. Recently, the base-promoted metal-free hydroamination of propargylamines with isothiocyanates has been reported to achieve imidazole-2-thiones and spirocyclic imidazolidine-2-thiones.[37]

In our approach toward imidazolidine-2-thiones of type **II**, we envisaged that the acyl anion equivalent derived from a simple aldehyde and an NHC could promote an aza-benzoin reaction in the presence of the benzylidenethiourea acceptor **I**, with the resulting adduct then taking part in a one-pot domino sequence through an aza-acetalization step in a fully atom economical fashion (Scheme 1).

Results and discussion

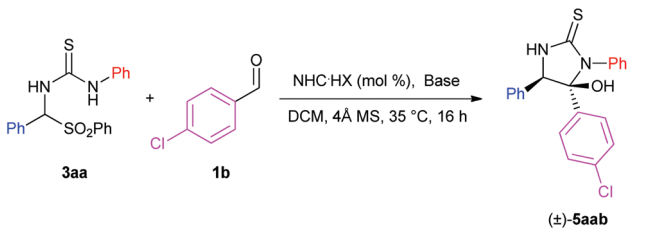
At the outset of our study, attempts to prepare the benzylidenethiourea **4aa** by condensation of benzaldehyde **1a** and *N*-phenylthiourea **2a** under literature conditions[38] were totally unsuccessful (Scheme 2, *route a*). Therefore, an optimization study was carried out by adopting the well-established procedure for the preparation of *N*-Boc imines.[39] Accordingly, coupling of **2a** and **1a** (2.0 equiv.) in the presence of sodium benzenesulfinate (2.5 equiv.) and formic acid (2.0 equiv.) in methanol/water (1 : 2 v/v) at room temperature for 72 h produced the expected α-sulfonylamine intermediate **3aa** in satisfactory 62% yield (*route b*). Disappointingly, when **3aa** was subjected to the subsequent elimination step (K_2CO_3, anhydrous Na_2SO_4, THF, reflux, 18 h), the only isolable products were **1a** and **2a** generated by hydrolysis of the target benzylidenethiourea **4aa**, which could be detected only in trace amounts by ^{1}H NMR analysis of the crude reaction mixture.



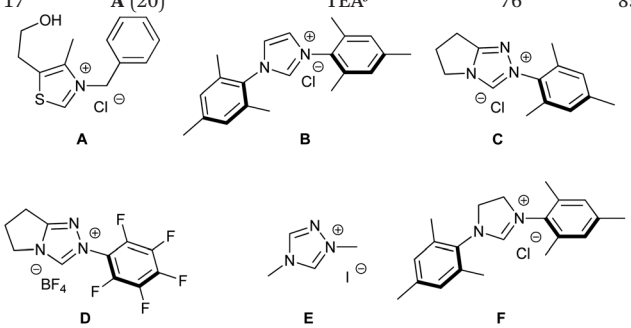
Scheme 2 Attempts to prepare the benzylidenethiourea **4aa**.

Therefore, in order to circumvent the troublesome isolation of **4aa**, we considered the opportunity to utilize the α-sulfonylamine precursor **3aa** in the planned domino sequence, expecting that the base used to generate the NHC active species could also promote the *in situ* formation of the actual imine acceptor **4aa** (Table 1).

Table 1 Optimization of the model domino process leading to imidazolidine-2-thione (±)-**5aab**[a]



Entry	NHC·HX (mol%)	Base	Yield[b] (%)	dr[c]
1	**A** (10)	TEA[d]	50	83/17
2	**B** (10)	TEA[d]	Trace[e]	—
3	**C** (10)	TEA[d]	0	—
4	**D** (10)	TEA[d]	0	—
5	**E** (10)	TEA[d]	0	—
6	**F** (10)	TEA[d]	11	81/19
7	**A** (10)	Cs_2CO_3[d]	Trace[e]	—
8	**A** (10)	DIPEA[d]	22	80/20
9	**A** (10)	DBU[d]	39	83/17
10[f]	**A** (10)	TEA[d]	0	—
11[g]	**A** (10)	TEA[d]	0	—
12[h]	**A** (10)	TEA[d]	Trace[e]	—
13	**A** (10)	TEA[i]	48	86/14
14	**A** (10)	TEA[j]	51	86/14
15[k]	**A** (10)	TEA[j]	42	85/15
16[l]	**A** (10)	TEA[j]	60	86/14
17[l]	**A** (20)	TEA[j]	76	85/15



[a] Typical reaction conditions: **3aa** (0.5 mmol), **1b** (0.55 mmol), pre-catalyst, base and 4 Å molecular sieves were reacted in DCM at 35 °C for 16 h. [b] Isolated yield. [c] Determined by ^{1}H NMR analysis. [d] 15 equiv. of base were used. [e] Detected by ^{1}H NMR analysis of the crude reaction mixture. [f] Reaction run in toluene. [g] Reaction run in DMSO. [h] Reaction run in THF. [i] 1.5 equiv. of TEA were used. [j] 3.0 equiv. of TEA were used. [k] Reaction run at 25 °C. [l] Reaction run at 30 °C.

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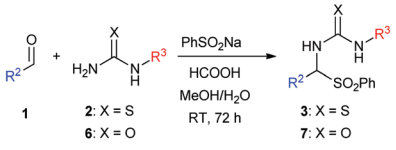
Hence, the model α-sulfonylamine **3aa** and 4-chlorobenzaldehyde **1b** (1.1 equiv.) were reacted in CH_2Cl_2 at 35 °C for 16 h in the presence of 4 Å molecular sieves using the thiazolium chloride **A** (10 mol%) as the pre-catalyst and triethylamine (15 equiv.) as the base.[13f] Under these conditions, the imidazolidine-2-thione **5aab** was formed in 50% isolated yield as an inseparable mixture of diastereoisomers in 83 : 17 ratio (entry 1). Encouraged by this result, pre-catalysts **B–F** were also tested under the same conditions, observing that only traces of **5aab** were produced with the imidazolium salt **B** (entry 2). On the other hand, triazolium pre-catalysts **C**, **D**, and **E** were completely ineffective (entries 3–5), while the imidazolinium salt **F** gave access to **5aab** in only poor yield (11%, entry 6). The screening of bases with the preferred **A** pre-catalyst in CH_2Cl_2 revealed that the inorganic base Cs_2CO_3 caused a severe loss of yield (entry 7); diisopropylethylamine and DBU were less effective than triethylamine (entries 8 and 9), with the stronger DBU base promoting the fast dehydration of **5aab** to the corresponding imidazole-2-thione derivative (*vide infra*). Examination of various solvents (toluene, DMSO, THF) indicated CH_2Cl_2 as the optimal reaction medium (entries 10–12). The use of lower amounts of triethylamine (3.0 and 1.5 equiv.) did not significantly affect the yield and slightly increased diastereoselectivity (entries 13 and 14). The study of the temperature effect showed a partial loss of efficiency at 25 °C (entry 15), while the yield of **5aab** raised to 60% when the domino sequence was performed at 30 °C (entry 16). A gratifying 76% yield was finally achieved at this temperature by increasing the catalyst loading to 20 mol% (entry 17).

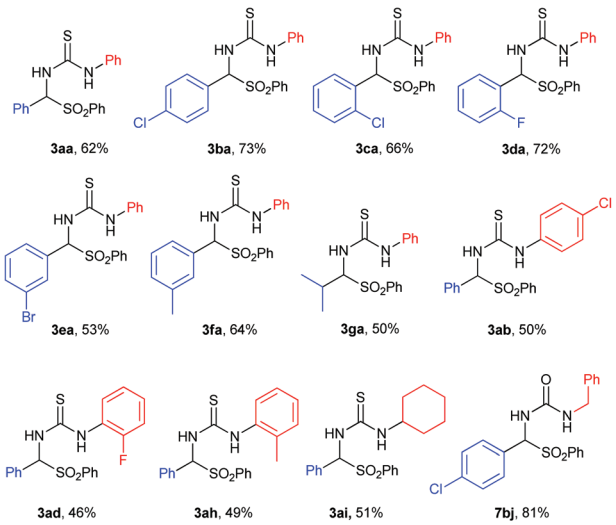
With the optimal conditions in hand, the generality of the disclosed strategy toward imidazolidine-2-thiones **5** was next investigated by first considering the scope of the synthesis of α-sulfonylamines **3** (Table 2). The reactivity of substituted aromatic aldehydes **1b–f** (**b**: 4-ClPh; **c**: 2-ClPh; **d**: 2-FPh; **e**: 3-BrPh; **f**: 3-MePh) with *N*-phenylthiourea **2a** was similar to that of benzaldehyde **1a**, with higher yields (66–73%) being obtained for substrates bearing a halogen in the *ortho*-position (**3ca**, **3da**) or the *para*-position (**3ba**) compared with the *meta*-substituted analog (**3ea**; 53%). Conversely, the presence of a methyl group in the *meta*-position (**3fa**) produced a yield (64%) comparable to that of benzaldehyde (**3aa**). Instead, a partial drop in yield was caused by the use of an aliphatic aldehyde **1g** (**g**: i-Pr; **3ga**: 50%). Besides, α-sulfonylamines **3ab**, **3ad**, **3ah**, and **3ai** were obtained by reacting benzaldehyde **1a** with thioureas **2b,d,h,i** displaying different *N*-substituents (**h**: 2-MePh; **i**: cyclohexyl), but in all cases the yields were inferior irrespective of the electronic nature of the substituent on the nitrogen atom. Finally, keeping in mind the possibility to extend the aza-benzoin/aza-acetalization sequence to benzylideneurea derivatives, the use of 3-benzylurea **6j** (**j**: Bn) was also attempted obtaining the *N*-substituted urea **7bj** in a remarkable 81% yield.

The optimal conditions of the domino sequence (Table 1, entry 17) were next applied to different combinations of substrates **1** and **3**/**7** (Table 3). This study commenced with the α-sulfonylamine **3aa** as the reacting partner of aldehyde donors **1** having different steric and/or electronic features. In the series of halogen-substituted benzaldehydes, both yields and diastereoselectivities were susceptible to either the nature or the position of the halogen atom. 2-Chlorobenzaldehyde **1c** and 2-fluorobenzaldehyde **1d** gave lower yields than 4-chlorobenzaldehyde **1b** and 3-chlorobenzaldehyde **1k** (**k**: 3-ClPh), plausibly due to steric effects (**5aac** and **5aad** *vs.* **5aab** and **5aak**). The best results in terms of diastereoselectivity were obtained for the compound **5aac**, with the presence of an *ortho*-located chlorine atom likely determining steric hindrance for the aza-acetalization step. This effect, however, was not observed in the case of the 2-fluoro-substituted analog **5aad** as a possible result of the smaller size of the fluorine atom. As expected, the electron-poor donors **1m** and **1n** (**m**: 4-pyridyl; **n**: 4-CNPh) leading to **5aam** and **5aan**, respectively, performed much better than the electron-neutral benzaldehyde **1a**, while the electron-rich donor **1l** (**l**: 4-OMePh) gave **5aal** in poor yield with high diastereoselectivity. A substantial maintenance of reaction efficiency was also observed for **5aag** starting from isobutyraldehyde **1g**, which is typically a poorly effective donor in many umpolung transformations.

As far as the variation of acceptors is concerned, fair to good yields were achieved for products **5** bearing electron-rich and halogen-substituted aromatic moieties as R^2 substituents

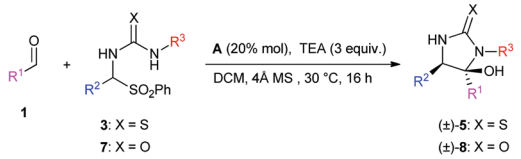
Table 2 Synthesis of α-sulfonylamines **3** and **7** (**a**: Ph; **b**: 4-ClPh; **c**: 2-ClPh; **d**: 2-FPh; **e**: 3-BrPh; **f**: 3-MePh; **g**: i-Pr; **h**: 2-MePh; **i**: cyclohexyl; **j**: Bn. Numbering: first letter R^2, second letter R^3)[a]

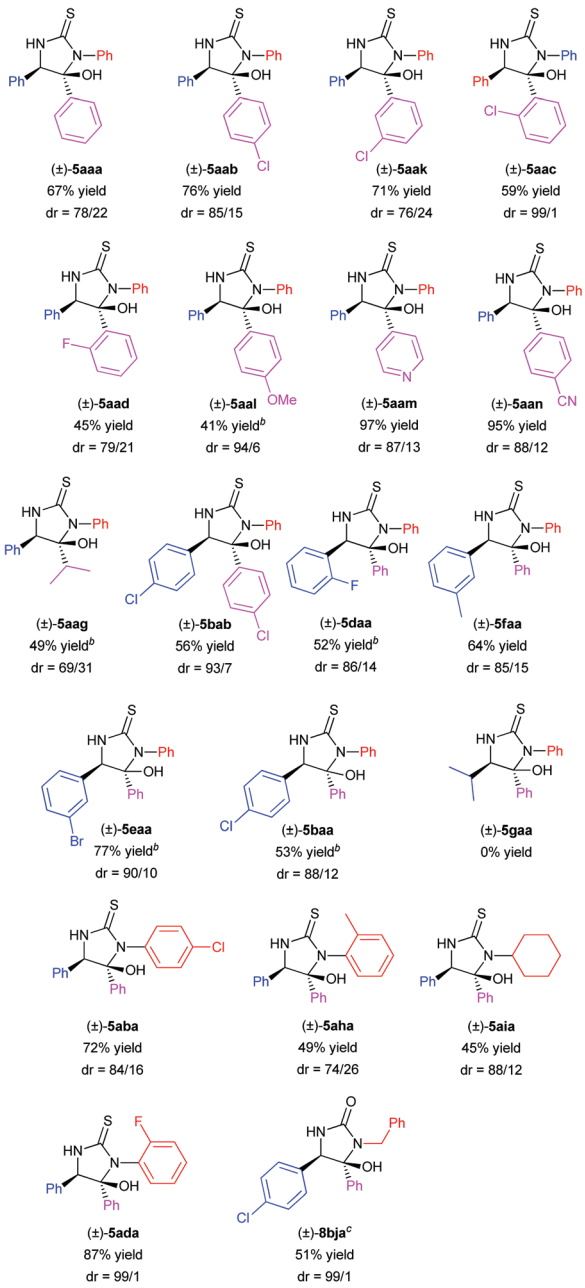




[a] Typical reaction conditions: **1** (20 mmol), **2** or **6** (10 mmol), benzenesulfinic acid sodium salt (25 mmol) and formic acid (55% w/w in water, 0.76 mL, 20 mmol) were reacted in H_2O (20 mL) and MeOH (10 mL) at RT for 72 h.

Table 3 Scope of the NHC-catalyzed/base promoted aza-benzoin/aza-acetalization domino reaction (**a**: Ph; **b**: 4-ClPh; **c**: 2-ClPh; **d**: 2-FPh; **e**: 3-BrPh; **f**: 3-MePh; **g**: i-Pr; **h**: 2-MePh; **i**: cyclohexyl; **j**: Bn; **k**: 3-ClPh; **l**: 4-OMePh; **m**: 4-pyridyl; **n**: 4-CNPh. Numbering: first letter R^2, second letter R^3, third letter R^1)[a]



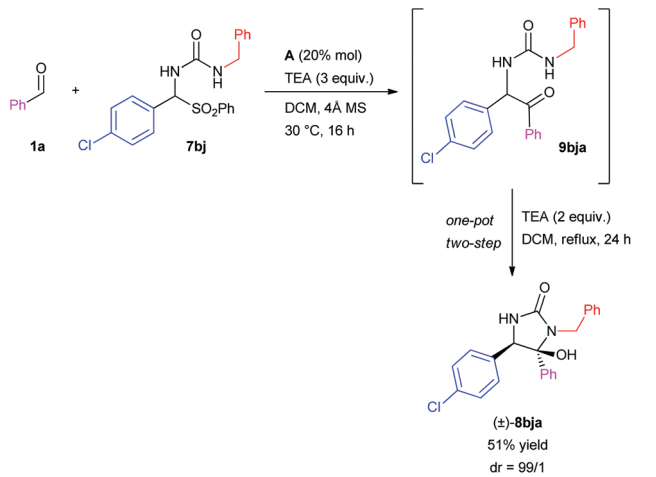


[a] Typical reaction conditions: **1** (1.2 mmol), **3** (1 mmol), **A** (0.2 mmol), 4 Å MS, TEA (3.0 mmol) were reacted in DCM (5 mL) and MeOH (10 mL) at 30 °C for 16 h. [b] Reaction run with 2.0 equiv. of **1**. [c] See the Experimental section.

(**5bab**, **5daa**, **5faa**, **5eaa**, **5baa**). No product formation was detected for the alkyl substituted derivative **5gaa**. *N*-Substituents other than phenyl did not suppress reactivity (**5aba**, **5aha**, **5aia**, **5ada**), with better results being observed in the presence of halogen-substituted aromatic residues (**5aba**, **5ada**), which likely make the aniline portion in the aza-benzoin adduct more acidic, thereby facilitating the aza-acetalization step. As a general consideration, a higher excess (2.0 equiv.) of the aldehyde donor **1** was required in some combinations (**5aal**, **5aag**, **5daa**, **5eaa**, **5baa**) to overcome competition in the domino sequence of the more reactive aldehyde eventually formed by *in situ* hydrolysis of the parent benzylidene-thiourea acceptor.

Interestingly, the synthesis of imidazolidine-2-one **8bja** required a slightly different procedure. Indeed, the reaction of urea **7bj** with benzaldehyde **1a** (2.0 equiv.) proceeded in a one-pot, two-step fashion contrarily to what was observed for the thiourea analogs **3**. As a matter of fact, under the optimized reaction conditions, the aza-benzoin adduct **9bja** was predominantly formed, as confirmed by ^{1}H NMR analysis of the crude reaction mixture (Scheme 3 and the ESI†). However, addition of further triethylamine base (2.0 equiv.) and heating at reflux for 24 h allowed producing the expected cyclization product **8bja** in 51% yield with very high diastereoselectivity (dr = 99/1). This result may depend on electronic effects caused by the presence of the oxygen atom, thus confirming the distinctive behavior of the thioureidic substrates **3** in the disclosed domino process.

Further studies demonstrated that the novel cyclization reaction could be run under optimized conditions on a large scale without losing reactivity or diastereoselectivity and with improved practicality. Indeed, the reaction of 2 grams (5.24 mmol) of α-sulfonylamine **3aa** with 4-chlorobenzaldehyde **1b** produced the expected compound **5aab** in 62% yield and 84/16 diastereomeric ratio after facile purification by recrystallization (Scheme 4).



Scheme 3 Synthesis of the imidazolidine-2-one (±)-**8bja**.

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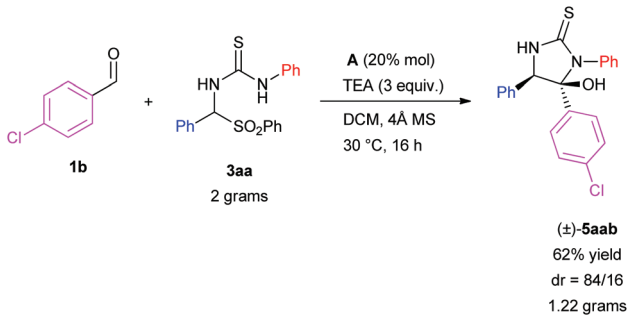


Scheme 4 Preparative scale synthesis of (±)-**5aab**.

The relative configuration of diastereomeric imidazolidine-2-thiones **5** was determined by HMQC and ROESY experiments using the pyridyl-substituted derivative **5aam** as the model substrate. As shown in Fig. 1, a correlation between δ 5.68 (H-4 imidazoline ring) and δ 7.80 (H-3′ pyridyl ring) was detected for the major diastereoisomer, thereby supporting a relative *syn* configuration of the phenyl and hydroxyl substituents at C4 and C5 of the imidazolidine-2-thione ring (see the ESI†). This assignment was corroborated by the concomitant lack of the above correlation for the minor diastereoisomer of **5aam** and was extended to all products **5** by analogy.

A mechanistic rationalization for the disclosed domino sequence is proposed as shown in Scheme 5. The attack of the Breslow intermediate **10** on the *in situ* generated imine **4** produces the alkoxide **12** *via* the intermediate **11** (*route a*). In the ensuing step, expulsion of NHC gives the aza-benzoin adduct **9**, which then takes part in the base-promoted aza-acetalization reaction leading to the imidazolidine-2-thione **5**. However, the direct intramolecular S_N2 reaction of anion **13** originating from the common intermediate **11** cannot be excluded (*route b*, dotted line).

Route a of our mechanistic proposal seemed to be sustained by the control experiment described in Scheme 6. Thus, benzoin **14** was converted into the ammonium salt **16** by standard chemistry; intermediate **16** was then treated with Edman's reagent under the basic conditions optimized for the domino sequence (TEA, DCM), affording the imidazolidine-2-thione **5aaa** in 77% yield. Given that the reaction between **16** and phenylisothiocyanate is expected to produce the adduct **9aaa**, one may conclude that the latter represents the actual precursor of the imidazolidine-2-thione **5aaa**. Hence, it

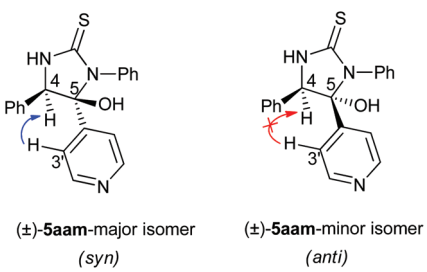
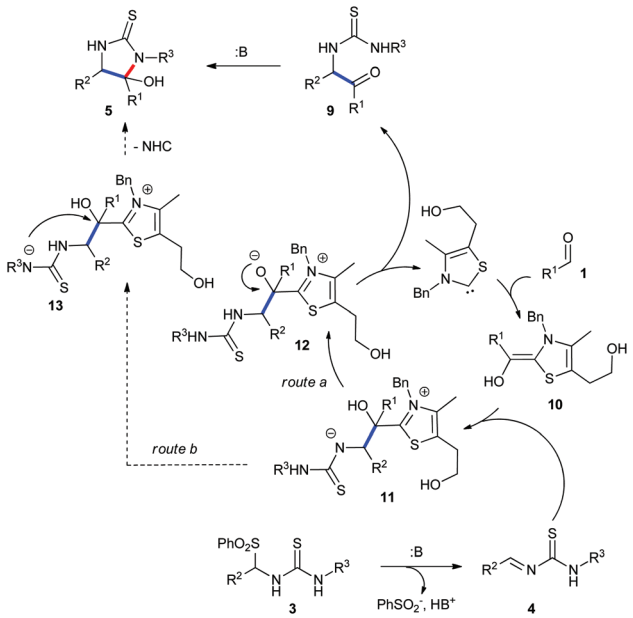
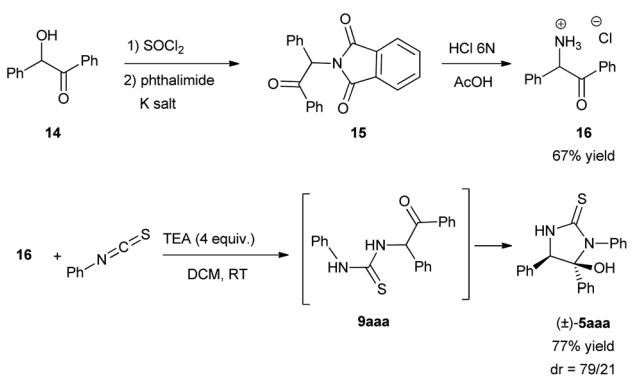


Fig. 1 Stereochemical assignment.



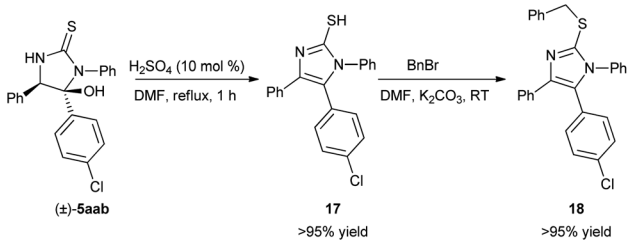
Scheme 5 Proposed mechanisms for the synthesis of imidazolidine-2-thiones **5**.



Scheme 6 Control experiment for mechanism elucidation.

appears more likely that the cyclization process toward **5** takes place after the release of the NHC in the catalytic cycle (*route a*; Scheme 5) rather than *via* an S_N2 mechanism (*route b*). This conclusion is further corroborated by analysis of the diastereoselectivity of compound **5aaa** that gave almost identical results irrespective of whether NHC catalysis was used or not for **5aaa** preparation.

Finally, bearing in mind the biological value of imidazole-2-thione derivatives,[29,31,32] we embarked on the synthetic elaboration of the imidazolidine-2-thione **5aab** previously prepared on the gram-scale (Scheme 7). Accordingly, sequential dehydration (H_2SO_4, DMF, reflux, 1 h) and alkylation (BnBr, K_2CO_3, DMF, RT) gave access to compound **18** in quantitative yield without the need for intermediate **17** purification. Importantly, *S*-alkyl-imidazoles of the type **18** have been recently reported with antioxidant, antibacterial, and antifungal activities[40] as well as with anti-hyperthyroid effects.[41]



Scheme 7 Synthetic elaboration of (±)-**5aab** toward biologically relevant *S*-alkyl-imidazole derivatives.

Conclusions

In summary, we have described an efficient methodology for the rapid assembly of the biologically relevant 5-hydroxy-imidazoline-2-thione scaffold, which relied on a domino sequence consisting of an aza-benzoin condensation and a subsequent aza-acetalization reaction promoted by a suitable thiazolium salt pre-catalyst under basic conditions. Crucial for the successful realization of the synthetic plan has been the design of a novel class of umpolung acceptors, namely benzylidenethioureas, which have been generated *in situ* from suitable α-sulfonylamine precursors. The robustness of the disclosed domino process has been demonstrated by the synthesis of a small collection of 5-hydroxy-imidazoline-2-thiones displaying three points of diversity, two contiguous stereocenters, and an all-substituted carbon center. The easy elaboration of these domino products into the corresponding imidazole-2-thione derivatives has also permitted the introduction of a further element of diversity at the sulphur atom. Efforts regarding the development of an asymmetric version of the disclosed domino sequence are currently underway in our laboratory.[42]

Experimental section

All commercially available reagents were used as received without further purification, unless otherwise stated. Catalysts **A–F** were purchased from Sigma-Aldrich. Liquid aldehydes and bases were freshly distilled before their utilization. All solvents were dried over standard drying agents. 4 Å MS were activated before use. Reactions were monitored by TLC on silica gel 60 F_{254} with detection by charring with phosphomolybdic acid. Flash column chromatography was performed on silica gel 60 (230–400 mesh). ^{1}H (300/400 MHz), ^{13}C (76/101 MHz), and ^{19}F (376 MHz) NMR spectra were recorded in the stated deuterated solvent at room temperature. Peak assignments were aided by ^{1}H–^{1}H COSY and gradient-HMQC experiments. For accurate mass measurements, the compounds were detected in positive ion mode by HPLC-Chip Q/TOF-MS (nanospray) analysis using a quadrupole, a hexapole, and a time-of-flight unit to produce spectra. IR spectra were recorded on a PerkinElmer FT-IR Paragon 500 system.

General procedure for the synthesis of α-sulfonylamines 3 and 7

To a vigorously stirred suspension of (thio)urea **2**/**6** (10.0 mmol), aldehyde **1** (20.0 mmol, 2.0 equiv.), benzenesulfinic acid sodium salt (25.0 mmol, 2.5 equiv.) in H_2O (20 mL) and MeOH (10 mL), and an aqueous solution of formic acid (55% w/w, 0.760 mL, 20 mmol, 2.0 equiv.) was added in one portion. The suspension was stirred at room temperature for 72 h; then the white fluffy precipitate was filtered and washed with a large amount of Et_2O until the elimination of unreacted aldehyde to afford the desired product **3** or **7** as a white amorphous solid.

1-Phenyl-3-(phenyl(phenylsulfonyl)methyl)thiourea (3aa). White amorphous solid (2.37 g, 62%). ^{1}H NMR (300 MHz, acetone-d_6) δ 9.69 (s, 1H, NH(1)), 8.69 (d, J = 10.4 Hz, 1H, NH (3)), 8.01–7.93 (m, 2H, Ar), 7.77–7.66 (m, 1H, Ar), 7.64–7.54 (m, 4H, Ar), 7.47–7.38 (m, 5H, Ar), 7.33–7.21 (m, 3H, Ar, CH), 7.16–7.07 (m, 1H, Ar); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 181.3, 139.4, 137.3, 134.7, 130.8, 130.1, 130.0, 129.8, 129.7, 129.6, 129.0, 128.8, 128.7, 125.2, 124.7, 123.8, 76.2; HRMS (ESI) m/z calcd for $C_{20}H_{19}N_2O_2S_2$ $[M + H]^+$ 383.0882, found 383.0865; IR (neat) ν_{max}/cm^{-1} 3285, 3061, 2921, 1597, 1527, 1495, 1446, 1343, 1314, 1283, 1257, 1180, 1130, 1080, 1024, 971, 874, 848, 762.

1-((4-Chlorophenyl)(phenylsulfonyl)methyl)-3-phenylthiourea (3ba). White amorphous solid (3.04 g, 73%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.90 (s, 1H, NH(3)), 9.35 (d, J = 10.3 Hz, 1H, NH(1)), 7.95–7.87 (m, 2H, Ar), 7.78–7.70 (m, 1H, Ar), 7.66–7.57 (m, 3H, Ar), 7.56–7.51 (m, 4H, Ar), 7.35–7.20 (m, 3H, Ar), 7.17–7.03 (m, 2H, Ar, CH); ^{13}C{^{1}H} NMR (76 MHz, DMSO-d_6) δ 186.3, 144.3, 142.1, 139.9, 136.4, 135.5, 134.8, 133.8, 133.2, 130.2, 128.8, 80.5; HRMS (ESI) m/z calcd for $C_{20}H_{18}ClN_2O_2S_2$ $[M + H]^+$ 417.0493; found 417.0511; IR (neat) ν_{max}/cm^{-1} 3337, 3068, 2926, 1594, 1520, 1489, 1447, 1410, 1348, 1310, 1294, 1226, 1196, 1149, 1092, 1078, 1015, 999, 972, 938, 845, 828, 776, 749.

1-((2-Chlorophenyl)(phenylsulfonyl)methyl)-3-phenylthiourea (3ca). White amorphous solid (2.75 g, 66%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (s, 1H, NH(3)), 9.36 (d, J = 10.2 Hz, 1H, NH(1)), 7.90–7.81 (m, 2H, Ar), 7.81–7.73 (m, 1H, Ar), 7.73–7.57 (m, 4H, Ar), 7.57–7.45 (m, 3H, Ar), 7.38–7.33 (m, 2H, Ar), 7.31–7.22 (m, 2H, Ar, CH), 7.14–7.04 (m, 1H, CH, Ar); ^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ 181.3, 139.3, 137.3, 135.1, 131.8, 130.6, 130.1, 129.9, 129.4, 128.9, 128.1, 125.3, 124.7, 123.7, 72.5; HRMS (ESI) m/z calcd For $C_{20}H_{18}ClN_2O_2S_2$ $[M + H]^+$ 417.0493, found 417.0508; IR (neat) ν_{max}/cm^{-1} 3290, 3103, 3042, 2931, 1592, 1521, 1490, 1449, 1410, 1349, 1311, 1294, 1225, 1199, 1089, 1071, 1015, 991, 973, 846, 829, 774, 742.

1-((2-Fluorophenyl)(phenylsulfonyl)methyl)-3-phenylthiourea (3da). White amorphous solid (2.88 g, 72%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ 10.02 (s, 1H, NH(3)), 9.39 (d, J = 10.3 Hz, 1H, NH(1)), 7.88–7.81 (m, 2H, Ar), 7.79–7.71 (m, 1H, Ar), 7.67–7.58 (m, 3H, Ar), 7.57–7.44 (m, 2H, Ar), 7.39–7.35 (m, 1H, Ar), 7.33–7.26 (m, 3H, Ar, CH), 7.24–7.21 (m, 2H, Ar), 7.15–7.02 (m, 1H, Ar); ^{13}C{^{1}H} NMR (76 MHz, DMSO-d_6) δ 181.7, 162.6,

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159.3, 139.6, 137.2, 135.2, 132.7, 132.6, 131.0, 130.0, 129.8, 129.3, 129.1, 128.8, 125.5, 124.9, 124.1, 123.7, 118.9, 118.7, 116.5, 116.2, 70.5; ^{19}F-NMR (376 MHz, DMSO-d_6) δ −115.58, −118.07; HRMS (ESI) m/z calcd for $C_{20}H_{18}FN_2O_2S_2$ $[M + H]^+$ 401.0788, found 401.0779; IR (neat) ν_{max}/cm^{-1} 3284, 3102, 3043, 2934, 1615, 1585, 1558, 1525, 1495, 1446, 1344, 1315, 1283, 1240, 1132, 1080, 1025, 998, 975, 956, 912, 879, 812, 764, 753.

1-((3-Bromophenyl)(phenylsulfonyl)methyl)-3-phenylthiourea (3ea). White amorphous solid (2.44 g, 53%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.74 (s, 1H, NH(3)), 9.2 (d, J = 12.0 Hz, 1H, NH(1)), 7.98–7.86 (m, 2H, Ar), 7.80–7.72 (m, 2H, Ar), 7.69–7.60 (m, 3H, Ar), 7.59–7.51 (m, 1H, Ar), 7.48–7.41 (m, 1H, Ar), 7.34–7.22 (m, 4H, Ar), 7.17–7.01 (m, 2H, Ar, CH); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 181.2, 139.3, 137.0, 135.0, 133.4, 132.9, 132.2, 131.1, 129.7, 129.0, 128.8, 125.3, 123.8, 122.1, 75.4; HRMS (ESI) m/z calcd for $C_{20}H_{18}BrN_2O_2S_2$ $[M + H]^+$ 460.9988, found 461.0008; IR (neat) ν_{max}/cm^{-1} 3297, 3143, 3040, 2908, 1596, 1573, 1523, 1496, 1474, 1446, 1344, 1318, 1279, 1243, 1192, 1181, 1142, 1080, 1025, 998, 973, 903, 865, 843, 772, 748.

1-Phenyl-3-((phenylsulfonyl)(*m*-tolyl)methyl)thiourea (3fa). White amorphous solid (2.53 g, 64%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H, NH(1)), 9.22 (d, J = 10.4 Hz, 1H, NH (3)), 7.97–7.84 (m, 2H, Ar), 7.77–7.69 (m, 1H, Ar), 7.64–7.56 (m, 2H, Ar), 7.38–7.29 (m, 5H, Ar), 7.29–7.24 (m, 3H, Ar), 7.14–6.99 (m, 2H, Ar, CH), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 181.2, 139.3, 138.2, 137.3, 134.7, 130.6, 130.2, 129.6, 128.9, 128.8, 126.9, 125.2, 123.7, 76.1, 21.4; HRMS (ESI) m/z calcd for $C_{21}H_{21}N_2O_2S_2$ $[M + H]^+$ 397.1039, found 397.1056; IR (neat) ν_{max}/cm^{-1} 3295, 3075, 2916, 1584, 1515, 1447, 1343, 1284, 1255, 1179, 1136, 1080, 1025, 971, 854, 794, 760.

1-(2-Methyl-1-(phenylsulfonyl)propyl)-3-phenylthiourea (3ga). White amorphous solid (1.70 g, 50%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.81 (s, 1H, NH(3)), 8.38 (d, J = 10.5 Hz, 1H, NH (1)), 7.86–7.79 (m, 2H, Ar), 7.73–7.64 (m, 1H, Ar), 7.60–7.52 (m, 2H, Ar), 7.40–7.35 (m, 1H, Ar), 7.34–7.29 (m, 2H, Ar), 7.27–7.22 (m, 1H, Ar), 7.12–7.04 (m, 1H, Ar), 5.92 (d, J = 10.5 Hz, 1H, CH), 2.78–2.53 (ept, J = 6.8 Hz, 1H, CH_{ipr}), 1.09 (d, J = 6.8 Hz, 3H, CH_{3ipr}), 1.00 (d, J = 6.8 Hz, 3H, CH_{3ipr}); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 182.4, 139.4, 138.4, 134.4, 129.5, 129.3, 129.1, 128.8, 125.1, 124.8, 123.6, 123.4, 76.4, 40.6, 40.4, 40.1, 39.9, 39.7, 39.5, 39.3, 27.7, 20.8, 17.9; HRMS (ESI) m/z calcd for $C_{17}H_{21}N_2O_2S_2$ $[M + H]^+$ 349.1039, found 349.1055; IR (neat) ν_{max}/cm^{-1} 3286, 3075, 2964, 2901, 1593, 1519, 1495, 1448, 1311, 1283, 1229, 1179, 1083, 1059, 1026, 867, 829, 791, 768, 749, 727, 716.

1-(4-Chlorophenyl)-3-(phenyl(phenylsulfonyl)methyl)thiourea (3ab). White amorphous solid (2.08 g, 50%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.93 (s, 1H, NH(1)), 9.37 (d, J = 10.3 Hz, 1H, NH(3)), 7.94–7.81 (m, 2H, Ar), 7.79–7.68 (m, 1H, Ar), 7.69–7.56 (m, 2H, Ar), 7.56–7.50 (m, 2H, Ar), 7.50–7.41 (m, 3H, Ar), 7.38–7.26 (m, 4H, Ar), 7.07 (d, J = 10.3 Hz, 1H, CH); ^{13}C{^{1}H} NMR (76 MHz, DMSO-d_6) δ 181.9, 181.6, 138.9, 138.6, 137.5, 135.0, 130.9, 130.3, 130.0, 129.9, 129.2, 128.9, 125.5, 125.2, 125.0, 76.4; HRMS (ESI) m/z calcd for $C_{20}H_{18}ClN_2O_2S_2$ $[M + H]^+$ 417.0493, found 417.0512; IR (neat) ν_{max}/cm^{-1} 3288, 2918, 1583, 1523, 1490, 1447, 1403, 1331, 1307, 1283, 1233, 1179, 1130, 1079, 1015, 971, 878, 850, 829, 762.

1-(2-Fluorophenyl)-3-(phenyl(phenylsulfonyl)methyl)thiourea (3ad). White amorphous solid (1.84 g, 46%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.62 (d, J = 10.3 Hz, 1H, NH(3)), 9.55 (s, 1H, NH(1)), 7.94–7.84 (m, 2H, Ar), 7.79–7.70 (m, 1H, Ar), 7.64–7.56 (m, 3H, Ar), 7.56–7.43 (m, 5H, Ar), 7.25–7.14 (m, 2H, Ar, CH), 7.13–7.02 (m, 2H, Ar); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 182.4, 157.1, 154.6, 137.3, 134.8, 130.6, 130.5, 130.1, 130.0, 129.8, 129.7, 129.6, 129.0, 128.8, 127.9, 127.4 127.3, 127.1, 127.0, 124.7, 124.3 (2C), 116.0, 115.8, 76.5; ^{19}F NMR (376 MHz, DMSO-d_6) δ −124.19 to −124.25 (m, 1F, Ar); HRMS (ESI) m/z calcd for $C_{20}H_{18}FN_2O_2S_2$ $[M + H]^+$ 401.0788, found 401.0805; IR (neat) ν_{max}/cm^{-1} 3283, 3095, 2921, 1600, 1582, 1526, 1456, 1446, 1339, 1251, 1141, 1079, 1027, 886, 848, 812, 796, 753.

1-(Phenyl(phenylsulfonyl)methyl)-3-(*o*-tolyl)thiourea (3ah). White amorphous solid (1.94 g, 49%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.42 (d, J = 10.4 Hz, 1H, NH(1)), 9.30 (s, 1H, NH (3)), 7.98–7.89 (m, 2H, Ar), 7.78–7.68 (m, 1H, Ar), 7.66–7.53 (m, 4H, Ar), 7.51–7.43 (m, 3H, Ar), 7.20–7.11 (m, 2H, Ar), 7.07 (m, 3H, Ar, CH), 1.96 (s, 3H, CH_3); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 182.5, 137.7, 137.5, 134.7, 134.6, 130.8, 130.5, 130.0, 129.8, 129.6, 129.0, 128.7, 128.1, 126.8, 126.3, 124.7, 76.4, 18.1; HRMS (ESI) m/z calcd for $C_{21}H_{21}N_2O_2S_2$ $[M + H]^+$ 397.1039, found 397.1020; IR (neat) ν_{max}/cm^{-1} 3293, 3079, 2917, 1585, 1549, 1514, 1456, 1447, 1343, 1284, 1257, 1180, 1121, 1109, 1080, 1045, 1025, 998, 970, 882, 854, 795.

1-Cyclohexyl-3-(phenyl(phenylsulfonyl)methyl)thiourea (3ai). White amorphous solid (1.98 g, 51%). ^{1}H NMR (300 MHz, acetone-d_6) δ 8.16 (d, J = 10.5 Hz, 1H, NH(3)), 7.97–7.86 (m, 2H, Ar, NH(1)), 7.75–7.65 (m, 1H, Ar), 7.62–7.57 (m, 1H, Ar), 7.55–7.49 (m, 3H, Ar), 7.46–7.38 (m, 4H, Ar), 7.26 (d, J = 10.5 Hz, 1H, CH), 4.12–3.81 (m, 1H), 1.91–1.70 (m, 2H), 1.70–1.59 (m, 2H) 1.49–1.40 (m, 1H), 1.38–1.03 (m, 5H); ^{13}C{^{1}H} NMR (101 MHz, acetone-d_6) δ 181.8, 138.0, 133.8, 131.2, 129.5, 129.3 (2C), 128.9, 128.4, 76.0, 52.7, 32.4, 32.1, 31.9, 25.3, 24.8, 24.4, 24.3; HRMS (ESI) m/z calcd for $C_{20}H_{25}N_2O_2S_2$ $[M + H]^+$ 389.1352, found 389.1378; IR (neat) ν_{max}/cm^{-1} 3282, 3065, 2930, 2853, 1618, 1586, 1524, 1497, 1447, 1368, 1310, 1256, 1230, 1162, 1081, 1027, 998, 974, 891, 846, 805, 760.

1-Benzyl-3-((4-chlorophenyl)(phenylsulfonyl)methyl)urea (7bj). White amorphous solid (3.35 g, 81%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.89–7.80 (m, 3H), 7.80–7.69 (m, 1H), 7.65–7.54 (m, 2H), 7.53–7.47 (m, 4H), 7.31–7.12 (m, 4H), 7.02–6.93 (m, 1H), 6.47–6.39 (m, 1H), 6.32–6.23 (m, 1H), 4.09 (dd, J = 15.4, 6.2 Hz, 1H, CH_2), 4.00 (dd, J = 15.4, 6.2 Hz, 1H, CH_2); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 156.0, 140.4, 137.6, 134.4, 131.7, 129.7, 129.6, 129.4, 128.7, 128.6, 127.2, 127.1, 73.6, 43.1; HRMS (ESI) m/z calcd for $C_{21}H_{20}ClN_2O_3S$ $[M + H]^+$ 415.0878, found 415.0861; IR (neat) ν_{max}/cm^{-1} 3380, 2979, 1715, 1589, 1493, 1367, 1165, 1054, 1027, 1015, 982, 971, 941, 849, 796, 747.

General procedure for the synthesis of 5-hydroxy-imidazolidine-2-thiones 5

To a vigorously stirred suspension of **3** (1.00 mmol), pre-catalyst **A** (54 mg, 0.20 mmol), and 4 Å MS (25 mg) in anhydrous

DCM (5 mL), aldehyde **1** (1.20 mmol) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (balloon) three times. At this point, TEA (417 μL, 3.00 mmol) was added in one portion and the suspension was stirred at 30 °C for 16 h, filtered over a pad of Celite, diluted with brine (10 mL), and extracted with EtOAc (2 × 40 mL). The combined organic phases were dried (Na_2SO_4), concentrated, and purified by column chromatography on silica gel (cyclohexane/EtOAc/TEA) to afford the desired product **5**. The diastereoisomeric ratio was determined by ^{1}H-NMR. Reactions for the preparation of compounds **5aal**, **5aag**, **5daa**, **5eaa**, and **5baa** were performed using 2.00 mmol of aldehyde **1**.

(±)-5-Hydroxy-1,4,5-triphenylimidazolidine-2-thione (5aaa). *Method A*: General procedure. Column chromatography with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5aaa** as white amorphous solid (231 mg, 67%, dr 78/22). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.26 (s, 0.78H, NH_{maj}), 11.15 (s, 0.22H, NH_{min}), 10.28 (s, 0.22H, OH_{min}), 9.53 (s, 0.78H, OH_{maj}), 8.05–8.03 (m, 0.44H, Ar_{min}), 7.99–7.96 (m, 1.56H, Ar_{maj}), 7.89–7.87 (m, 2H, Ar), 7.57–7.54 (m, 0.44H, Ar_{min}), 7.46–7.44 (m, 1.56H, Ar), 7.42–7.33 (m, 5.44H, Ar), 7.37–7.10 (m, 1.56H, Ar_{maj}), 7.21–7.16 (m, 0.44H, Ar_{min}), 7.15–6.94 (m, 1.56H, Ar_{maj}), 5.75 (s, 0.22H, H-4_{min}), 5.68 (s, 0.78H, H-4_{maj}); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 184.5, 141.6, 139.6, 130.1, 129.9, 128.6, 128.5 (2C), 128.4, 128.2, 127.7, 126.9, 99.8 (C-4_{min}), 97.2 (C-5_{maj}), 73.5 (C-4_{min}), 72.5 (C-4_{maj}); HRMS (ESI) *m*/*z* calcd for $C_{21}H_{19}N_2OS$ $[M + H]^+$ 347.1213, found 347.1237; IR (neat) ν_{max}/cm^{-1} 3349, 3178, 2243, 1700, 1596, 1494, 1450, 1395, 1360, 1254, 1229, 1174, 1132, 1103, 1076, 1047, 1022, 989, 916, 893, 852, 821, 792, 747, 693.

Method B: Mechanistic study. To a vigorously stirred suspension of crude **16** (247 mg, 1.00 mmol) in DCM (5 mL), TEA (417 μL, 3.00 mmol) was added in one portion. The mixture was stirred for 30 min at room temperature, then phenyl isothiocyanate (110 μL, 1.00 mmol) was added in one portion. The mixture was stirred for additional 16 h at room temperature, then concentrated, diluted with brine (10 mL), and extracted with EtOAc (2 × 40 mL). The combined organic phases were dried (Na_2SO_4), concentrated, and purified by column chromatography on silica gel with cyclohexane/EtOAc/TEA 7 : 3 : 0.5 to afford the desired products **5aaa** (265 mg, 77%, dr 79/21).

(±)-5-(4-Chlorophenyl)-5-hydroxy-1,4-diphenylimidazolidine-2-thione (5aab). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5aab** as a white amorphous solid (290 mg, 76%, dr 85/15). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.31 (s, 0.85H, NH_{maj}), 11.21 (s, 0.15H, NH_{min}), 10.43 (s, 0.15H, OH_{min}), 9.70 (s, 0.85H, OH_{maj}), 8.05–8.00 (m, 0.30H, Ar_{min}), 7.98–7.93 (m, 1.70H, Ar_{maj}), 7.85–7.80 (m, 1.70H, Ar_{maj}), 7.54–7.51 (m, 0.30H, Ar_{min}), 7.48–7.23 (m, 8H, Ar), 7.21–7.04 (m, 2H, Ar), 5.73 (s, 0.15H, H-4_{min}), 5.65 (s, 0.85H, H-4_{maj}); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 185.2, 151.1, 151.0, 150.1, 141.0, 140.1, 139.9, 138.7, 138.5, 135.8, 134.9, 134.3, 130.9, 130.7, 130.6, 130.5, 130.4, 130.2, 130.0, 129.4 (2C), 129.3, 129.2 (2C), 129.1, 128.9, 128.4, 128.3, 127.7 (2C), 126.5, 124.8, 123.7, 99.9 (C-5_{min}), 97.4 (C-5_{maj}), 74.0 (C-4_{min}), 73.1 (C-4_{maj}); HRMS (ESI) *m*/*z* calcd for $C_{21}H_{18}ClN_2OS$ $[M + H]^+$ 381.0823, found 381.0846; IR (neat) ν_{max}/cm^{-1} 3155, 3059, 1697, 1598, 1564, 1494, 1450, 1389, 1290, 1235, 1134, 1047, 1002, 917, 843, 814, 780, 751.

(±)-5-(3-Chlorophenyl)-5-hydroxy-1,4-diphenylimidazolidine-2-thione (5aak). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5aak** as a white amorphous solid (270 mg, 71%, dr 76/24). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.38 (s, 0.76H, NH_{maj}), 11.28 (s, 0.24H, NH_{min}), 10.55 (s, 0.24H, OH_{min}), 9.80 (s, 0.76H, OH_{maj}), 8.07–8.03 (m, 0.76H, Ar_{maj}), 8.01–7.95 (m, 0.24H, Ar_{min}), 7.79–7.77 (m, 1.52H, Ar_{maj}), 7.59–7.58 (m, 0.24H, Ar_{min}), 7.46–7.41 (m, 0.76H, Ar_{min}), 7.44–7.30 (m, 7.6H, Ar), 7.29–7.25 (m, 2.28H, Ar), 7.24–7.09 (m, 0. 24H, Ar_{min}), 7.12–6.91 (m, 0.24H, Ar_{min}), 5.74 (s, 0.24H, H-4_{min}), 5.69 (s, 0.76H, H-4_{maj}); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 184.5, 150.3, 144.0, 141.4, 139.4, 138.0, 135.7, 135.5, 134.2, 130.1, 130.0, 129.9, 129.8, 129.1, 128.8, 128.7, 128.6 (2C), 128.5, 128.4, 128.2, 128.1, 127.5, 127.1 (2C), 126.9, 126.7, 99.0 (C-5_{min}), 96.6 (C-5_{maj}), 73.4 (C-4_{min}), 72.4 (C-4_{maj}); HRMS (ESI) *m*/*z* calcd for $C_{21}H_{18}ClN_2OS$ $[M + H]^+$ 381.0823, found 381.0847; IR (neat) ν_{max}/cm^{-1} 3198, 1689, 1597, 1576, 1495, 1451, 1399, 1354, 1227, 1199, 1189, 1044, 997, 892, 831, 794, 752.

(±)-5-(2-Chlorophenyl)-5-hydroxy-1,4-diphenylimidazolidine-2-thione (5aac). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5aac** as a white amorphous solid (224 mg, 59%, dr 99/1). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.34 (s, 1H, NH), 9.85 (s, 1H, OH), 8.24–8.19 (m, 2H, Ar), 7.44–7.42 (m, 3H, Ar), 7.34–7.29 (m, 3H, Ar), 7.25–7.21 (m, 3H, Ar), 7.21–7.14 (m, 2H, Ar), 7.07–7.02 (m, 1H, Ar), 6.23 (s, 1H, H-4); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 183.9, 139.1, 137.9, 136.2, 135.5, 132.7, 131.9, 131.3 (2C), 130.6, 129.5, 128.7, 128.5, 128.2, 127.1, 126.8, 123.9, 123.6, 123.4, 95.5, 68.1. HRMS (ESI) *m*/*z* calcd for $C_{21}H_{18}ClN_2OS$ $[M + H]^+$ 381.0823, found 381.0839; IR (neat) ν_{max}/cm^{-1} 3156, 1704, 1597, 1554, 1540, 1495, 1450, 1393, 1292, 1233, 1209, 1035, 1002, 843, 812, 782, 753.

(±)-5-(2-Fluorophenyl)-5-hydroxy-1,4-diphenylimidazolidine-2-thione (5aad). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5aad** as a white amorphous solid (164 mg, 45%, dr 79/21). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.30 (s, 0.79H, NH_{maj}), 11.19 (s, 0.21H, NH_{min}), 10.54 (s, 0.21H, OH_{min}), 9.83 (s, 0.79H, OH_{maj}), 8.16–8.14 (m, 0.42H, Ar_{min}), 8.07–8.05 (m, 1.79H, Ar), 7.98–7.93 (m, 1.21H, Ar), 7.59–7.56 (m, 1.79H, Ar), 7.48–7.46 (m, 2.79H, Ar), 7.34–7.31 (m, 3H, Ar), 7.26–7.14 (m, 2.58H, Ar) 7.03–7.01 (m, 0.42H, Ar_{min}), 5.98 (s, 0.79H, H-4_{maj}), 5.90 (s, 0.21, H-4_{min}); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 182.3, 159.9, 157.5, 137.7, 129.9, 129.8, 129.1, 128.3, 127.8, 127.1 (2C), 126.9 (2C), 126.5, 126.0, 125.7, 122.8, 115.2, 115.0, 93.1, 71.8 (C-4_{min}), 68.3 (C-4_{maj}); ^{19}F NMR (376 MHz, pyridine-d_5) δ −107.44 (s, br, 0.21 F, F_{min}), −111.61 to −111.68 (m, 0.79 F, F_{maj}); HRMS (ESI) *m*/*z* calcd for $C_{21}H_{18}FN_2OS$ $[M + H]^+$ 365.1118, found 365.1131; IR (neat) ν_{max}/cm^{-1} 3147, 1617, 1587, 1551, 1538, 1492, 1453, 1406, 1360, 1307, 1255, 1232, 1128, 1108, 1044, 1021, 1002, 970, 826, 782, 758, 680.

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(±)-5-Hydroxy-5-(4-methoxyphenyl)-1,4-diphenylimidazolidine-2-thione (5aal). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5aal** as a white amorphous solid slightly contaminated by uncharacterized by-products (154 mg, 41%, dr 94/6). ^{1}H NMR (400 MHz, pyridine-d_5, selected data) δ 11.21 (s, 0.94H, NH_{maj}), 11.10 (s, 0.06H, NH_{min}), 9.83 (s, 0.06H, OH_{min}), 9.43 (s, 0.94H, OH_{maj}), 8.08–8.04 (m, 0.12H, Ar_{min}), 8.02–7.98 (m, 1.88H, Ar_{maj}), 7.90–7.86 (m, 0.12H, Ar_{min}), 7.85–7.81 (m, 1.88H, Ar_{maj}), 7.52–7.48 (m, 2H, Ar), 7.39–7.22 (m, 6H), 7.09–7.03 (m, 1H, Ar), 7.00–6.96 (m, 1H, Ar), 5.70 (s, 0.94H, H-4_{maj}), 5.66 (s, 0.06H, H-4_{min}), 3.62 (s, 0.18H, CH_{3min}), 3.57 (s, 2.82H, CH_{3maj}); ^{13}C{^{1}H} NMR (101 MHz, pyridine-d_5) δ 184.1, 159.5, 139.4, 135.4, 133.0, 129.7, 129.2, 128.4, 128.2, 128.1, 126.6, 113.5, 96.9, 72.2, 54.8; IR (neat) ν_{max}/cm^{-1} 3155, 2837, 2250, 1669, 1611, 1596, 1538, 1514, 1492, 1450, 1396, 1362, 1304, 1229, 1206, 1173, 1135, 1107, 1034, 1016, 981, 968, 916, 893, 840, 817, 795, 784, 753, 728, 701.

(±)-5-Hydroxy-1,4-diphenyl-5-(pyridin-4-yl)imidazolidine-2-thione (5aam). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 6 : 4 : 0.5 afforded **5aam** as a white amorphous solid (337 mg, 97%, dr 87/13). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.44 (s, 0.87H, NH_{maj}), 11.39 (s, 0.13H, NH_{min}), 9.84 (s, 1H, OH), 8.79–8.74 (m, 1.74H, Ar_{maj}), 8.48–8.47 (m, 0.26H, Ar_{min}), 8.03–8.01 (m, 0.26H, Ar_{min}), 7.98–7.95 (m, 1.74H, Ar_{maj}), 7.81–7.79 (m, 1.74H, Ar_{maj}), 7.51–7.33 (m, 7.26H, Ar), 7.29–7.07 (m, 3H, Ar), 5.77 (s, 0.13H, H-4_{min}), 5.68 (s, 0.87H, H-4_{maj}); ^{13}C{^{1}H} NMR (101 MHz, pyridine-d_5) δ 184.6, 150.4, 150.2, 150.0, 149.7, 149.6, 139.2, 135.9, 135.6, 135.4, 135.1, 130.0, 129.7, 129.5, 128.9, 128.8, 128.7 (2C), 128.6 (2C), 128.5, 127.6, 127.2, 125.9, 123.9, 123.6, 123.4, 123.0, 96.2, 72.1; HRMS (ESI) m/z calcd for $C_{20}H_{18}N_3OS$ $[M + H]^+$ 348.1165, found 348.1144; IR (neat) ν_{max}/cm^{-1} 3155, 3063, 1604, 1564, 1495, 1449, 1389, 1527, 1235, 1134, 1048, 1003, 917, 843, 812, 779, 751, 692.

(±)-4-(4-Hydroxy-3,5-diphenyl-2-thioxoimidazolidine-4-yl)benzonitrile (5aan). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5aan** as a white amorphous solid (352 mg, 95%, dr 88/12). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.45 (s, 0.88H, NH_{maj}), 11.34 (s, 0.12H, NH_{min}), 10.73 (s, br, 0.12H, OH_{min}), 9.99 (s, 0.88H, OH_{maj}), 8.06–8.00 (m, 0.24H, Ar_{min}), 7.99–7.93 (m, 3.76H, Ar), 7.71–7.66 (m, 2H, Ar), 7.47–7.40 (m, 2H, Ar), 7.39–7.30 (m, 2H, Ar), 7.29–7.24 (m, 2H, Ar), 7.19–7.07 (m, 2H, Ar), 5.75 (s, 0.12H, H-4_{min}), 5.66 (s, 0.88H, H-4_{maj}); ^{13}C{^{1}H} NMR (101 MHz, pyridine-d_5) δ 184.6, 150.2, 150.1, 146.5, 139.3, 138.1, 137.8, 135.1, 132.4, 131.5, 130.0, 129.7, 129.5, 129.4, 129.1, 128.9, 128.8, 128.7 (2C), 128.6, 128.4, 127.5, 127.2, 125.9, 120.4, 119.2, 112.4, 110.0, 96.8 (C-5_{min}), 96.6 (C-5_{maj}), 73.4 (C-4_{min}), 72.3 (C-4_{maj}); HRMS (ESI) m/z calcd for $C_{22}H_{18}N_3OS$ $[M + H]^+$ 372.1165, found 372.1150; IR (neat) ν_{max}/cm^{-1} 3317, 3197, 2243, 1596, 1585, 1495, 1452, 1395, 1350, 1231, 1204, 1173, 1131, 1102, 1089, 1049, 990, 892, 852, 820, 748, 699.

(±)-5-Hydroxy-5-isopropyl-1,4-diphenylimidazolidine-2-thione (5aag). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5aag** as a white amorphous solid contaminated by uncharacterized by-products (153 mg, 49%, dr 69/31). ^{1}H NMR (400 MHz, pyridine-d_5, selected data) δ 11.24 (s, 0.31H, NH_{min}), 10.78 (s, 0.69H, NH_{maj}), 10.24 (s, 0.31H, OH_{min}), 9.51 (s, 0.69H, OH_{maj}), 7.97–7.95 (m, 1.28H, Ar_{maj}), 7.91–7.87 (m, 0.69H, Ar_{maj}), 7.78–7.74 (m, 1.28H, Ar_{maj}), 7.44–7.40 (m, 1.69H, Ar), 7.37–7.31 (m, 3.94H, Ar), 7.08–7.03 (m, 1H, Ar), 5.68 (s, 0.31H, H-4_{min}), 5.40 (s, 0.69H, H-4_{maj}), 2.30 (ep, J = 6.9 Hz, 1H, CH_{ipr}), 1.23 (d, J = 6.9 Hz, 3H, CH_{3ipr}), 1.21 (d, J = 6.9 Hz, 3H, CH_{3ipr}); ^{13}C{^{1}H} NMR (101 MHz, pyridine-d_5) δ 181.8, 137.3, 137.1, 134.0, 129.9, 128.4, 128.2, 128.0, 127.6, 127.2, 126.9, 126.7, 126.6, 126.2, 125.4, 97.5 (C-5_{maj}), 95.7 (C-5_{min}), 71.0 (C-4_{min}), 61.6 (C-4_{maj}), 34.7 (CH_{ipr}), 16.1 (CH_{3ipr}), 15.2 (CH_{3ipr}); IR (neat) ν_{max}/cm^{-1} 3156, 2968, 1699, 1596, 1494, 1450, 1409, 1304, 1230, 1131, 1026, 968, 825, 752.

(±)-4,5-Bis(4-chlorophenyl)-5-hydroxy-1-phenylimidazolidine-2-thione (5bab). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5bab** as a white amorphous solid (230 mg, 56%, dr 93/7). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.29 (s, 0.93H, NH_{maj}), 11.18 (s, 0.07H, NH_{min}), 10.41 (s, 0.07H, OH_{min}), 9.74 (s, 0.93H, OH_{maj}), 8.01–7.99 (m, 0.14H, Ar_{min}), 7.95–7.90 (m, 1.86H, Ar_{maj}), 7.86–7.80 (m, 1.86H, Ar_{maj}), 7.57–7.52 (m, 0.14H, Ar_{min}), 7.45–7.41 (m, 2H, Ar), 7.40–7.36 (m, 1H, Ar), 7.36–7.12 (m, 5H, Ar), 7.14–7.03 (m, 1H), 5.73 (s, 0.07H, H-4_{min}), 5.63 (s, 0.93H, H-4_{maj}); ^{13}C{^{1}H} NMR (101 MHz, pyridine-d_5) δ 183.2, 138.6, 137.8, 132.9, 132.8, 132.7, 128.5, 128.4, 128.3, 127.3, 127.2, 127.1, 125.7, 95.1, 70.3; HRMS (ESI) m/z calcd for $C_{21}H_{16}Cl_2N_2OS$ $[M + H]^+$ 414.0360, found 414.0378; IR (neat) ν_{max}/cm^{-1} 3156, 2948, 1594, 1553, 1499, 1454, 1385, 1348, 1308, 1285, 1228, 1207, 1176, 1127, 1089, 1038, 1015, 998, 971, 897, 825, 801, 748, 695.

(±)-4-(2-Fluorophenyl)-5-hydroxy-1,5-diphenylimidazolidine-2-thione (5daa). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5daa** as a white amorphous solid (189 mg, 52%, dr 86/14). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.15 (s, 0.86H, NH_{maj}), 11.12 (s, 0.14H, NH_{min}), 10.46 (s, br, 0.14H, OH_{min}), 9.53 (s, 0.86H, OH_{maj}), 8.11–8.07 (m, 0.28H, Ar_{min}), 8.03–7.98 (m, 0.86H, Ar_{maj}), 7.97–7.94 (m, 1.86H, Ar), 7.93–7.87 (m, 1.72, Ar_{maj}), 7.72–7.67 (m, 0.28H, Ar_{min}), 7.39–7.31 (m, 1.86H, Ar), 7.30–7.24 (m, 1.86H, Ar), 7.20–7.15 (m, 1.86H, Ar), 7.14–6.98 (m, 3.42H, Ar), 6.10 (s, 0.14H, H-4_{min}), 6.05 (s, 0.86H, H-4_{maj}); ^{13}C{^{1}H} NMR (101 MHz, pyridine-d_5) δ 183.1 (C-2_{min}), 182.8 (C-2_{maj}), 161.3, 158.8, 140.7, 137.8, 137.6, 136.9, 128.8, 128.7 (2C), 128.6, 128.5, 128.0, 127.7, 127.2 (2C), 127.0, 126.9 (2C), 126.6, 126.0, 125.9, 125.8, 125.6, 125.4, 122.8 (2C), 114.2, 113.9, 113.7, 98.0 (C-5_{min}), 95.3 (C-5_{maj}), 65.8 (C-4_{min}), 64.9 (C-4_{maj}); ^{19}F NMR (376 MHz, pyridine-d_5) δ −116.25 to −116.31 (m, 0.14 F, Ar_{min}), −116.41 to −116.47 (m, 0.86 F, Ar_{maj}); HRMS (ESI) m/z calcd for $C_{21}H_{18}FN_2OS$ $[M + H]^+$ 365.1118, found 365.1102; IR (neat) ν_{max}/cm^{-1} 3158, 2809, 1618, 1587, 1552, 1489, 1451, 1407, 1356, 1307, 1239, 1220, 1132, 1082, 1020, 998, 970, 951, 901, 834, 825, 817, 786, 740, 696.

(±)-5-Hydroxy-1,5-diphenyl-4-(*m*-tolyl)imidazolidine-2-thione (5faa). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5faa** as a white amorphous

solid (230 mg, 64%, dr 85/15). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.19 (s, 0.85H, NH_{maj}), 11.09 (s, 0.15H, NH_{min}), 10.19 (s, br, 0.15H, OH_{min}), 9.46 (s, 0.85H, OH_{maj}), 8.06–8.02 (m, 0.30H, Ar_{min}), 8.01–7.96 (m, 1.70H, Ar_{maj}), 7.93–7.87 (m, 1.70H, Ar_{maj}), 7.68–7.63 (m, 0.30H, Ar_{min}), 7.39–7.33 (m, 2H, Ar), 7.32–7.23 (m, 2H, Ar), 7.19–6.96 (m, 5.85, Ar), 8.06–8.02 (m, 0.30H, Ar_{min}), 6.95–6.90 (m, 0.15, Ar_{min}), 5.75 (s, 0.15H, H-4_{min}), 5.67 (s, 0.85H, H-4_{maj}), 2.23 (s, 0.45H, CH_{3min}), 2.08 (s, 2.55H, CH_{3maj}); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 184.1 (C-2_{min}), 184.1 (C-2_{maj}), 141.5, 139.2, 138.9, 138.8, 137.6, 137.3, 135.6, 129.8, 129.6, 129.4, 129.3, 129.2 (2C), 129.1, 129.0, 128.9, 128.8, 128.4, 128.2, 127.9, 127.8, 127.5, 127.3, 126.8, 126.6 (2C), 125.5, 125.3, 125.2, 124.5, 123.9, 123.8, 123.6, 123.3, 123.1, 122.8, 99.6 (C-5_{min}), 96.9 (C-5_{maj}), 73.1 (C-4_{min}), 72.1 (C-4_{maj}), 21.0 (C–CH_{3min}), 20.9 (C–CH_{3maj}); HRMS (ESI) m/z calcd for $C_{22}H_{21}N_2OS$ $[M + H]^+$ 361.1369, found 361.1342; IR (neat) ν_{max}/cm^{-1} 3177, 3035, 1596, 1548, 1538, 1492, 1426, 1348, 1305, 1241, 1197, 1140, 1041, 1022, 969, 875, 823, 798, 753, 715, 698.

(±)-4-(3-Bromophenyl)-5-hydroxy-1,5-diphenylimidazolidine-2-thione (5eaa). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5eaa** as a white amorphous solid (326 mg, 77%, dr 90/10). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.21 (s, 0.90H, NH_{maj}), 11.11 (s, 0.10H, NH_{min}), 9.69 (s, br, 1H, OH), 8.02–7. 92 (m, 2H, Ar), 7.91–7.86 (m, 2H, Ar) 7.83–7.79 (m, 1H, Ar), 7.54–7.46 (m, 1H, Ar), 7.39–7.33 (m, 1H, Ar), 7.29–7.22 (m, 1H, Ar), 7.20–7.10 (m, 4H, Ar), 7.09–7.02 (m, 2H, Ar), 5.75 (s, 0.10H, H-4_{min}), 5.68 (s, 0.90H, H-4_{maj}); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 183.0, 139.8, 137.9, 136.8, 130.0, 129.8, 128.8, 128.4, 127.2, 127.0 (2C), 126.6, 125.8, 125.6, 121.1, 95.6, 70.4; HRMS (ESI) m/z calcd for $C_{21}H_{18}BrN_2OS$ $[M + H]^+$ 425.0318, found 425.0336; IR (neat) ν_{max}/cm^{-1} 3145, 2785, 1595, 1596, 1549, 1538, 1496, 1475, 1427, 1409, 1344, 1305, 1268, 1236, 1201, 1134, 1040, 996, 948, 849, 826, 773, 761, 733, 697.

(±)-4-(4-Chlorophenyl)-5-hydroxy-1,5-diphenylimidazolidine-2-thione (5baa). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5baa** as a white amorphous solid (201 mg, 53%, dr 88/12). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.22 (s, 0.88H, NH_{maj}), 11.18 (s, 0.12H, NH_{min}), 10.41 (s, br, 0.12H, OH_{min}), 9.55 (s, 0.88H, OH_{maj}), 8.04–7.98 (m, 0.24H, Ar_{min}) 7.97–7.92 (m, 1.76H, Ar_{maj}), 7.90–7.81 (m, 2H, Ar), 7.41–7.31 (m, 5H, Ar), 7.30–7.17 (m, 3.76H, Ar), 7.13–6.98 (m, 1.24H, Ar), 5.74 (s, 0.12H, H-4_{min}), 5.65 (s, 0.88H, H-4_{maj}); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 183.1, 139.9, 137.9, 133.1, 132.6, 128.5, 128.4, 127.2, 127.0 (2C), 126.6, 125.5, 95.5, 70.4; HRMS (ESI) m/z calcd for $C_{21}H_{18}ClN_2OS$ $[M + H]^+$ 381.0823, found 381.0805; IR (neat) ν_{max}/cm^{-1} 3164, 1594, 1549, 1538, 1493, 1452, 1413, 1392, 1351, 1305, 1231, 1208, 1128, 1091, 1018, 998, 968, 941, 898, 849, 824, 811, 773, 760, 738, 701.

(±)-1-(4-Chlorophenyl)-5-hydroxy-4,5-diphenylimidazolidine-2-thione (5aba). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5aba** as a white amorphous solid (274 mg, 72%, dr 84/16). ^{1}H-NMR (400 MHz, pyridine-d_5) δ 11.41 (s, 0.84H, NH_{maj}), 10.95 (s, 0.16H, NH_{min}), 10.31 (s, br, 0.16H, OH_{min}), 9.56 (s, 0.84H, OH_{maj}), 8.01–7.98 (m, 0.32H, Ar_{min}), 7.95–7.90 (m, 1.84H, Ar), 7.89–7.83 (m, 1.68H, Ar_{maj}), 7.48–7.23 (m, 7.68H, Ar) 7.19–6.97 (m, 2.48H, Ar), 5.74 (s, 0.16H, H-4_{min}), 5.68 (s, 0.84, H-4_{min}); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 183.9, 141.0, 138.0, 131.9, 131.1, 130.8, 128.4 (2C), 128.2, 128.1, 127.8, 127.5, 127.3, 99.4 (C-5_{min}), 96.8 (C-5_{maj}), 73.1 (C-4_{min}), 72.2 (C-4_{maj}); HRMS (ESI) m/z calcd for $C_{21}H_{18}ClN_2OS$ $[M + H]^+$ 381.0823, found 381.0841; IR (neat) ν_{max}/cm^{-1} 3156, 2896, 1595, 1550, 1494, 1452, 1392, 1352, 1305, 1232, 1208, 1175, 1128, 1091, 1040, 1019, 1003, 969, 941, 898, 850, 811, 773, 761, 739, 699.

(±)-5-Hydroxy-4,5-diphenyl-1-(*o*-tolyl)imidazolidine-2-thione (5aha). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 8 : 2 : 0.5 afforded **5aha** as a white amorphous solid (176 mg, 49%, dr 74/26). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.12 (s, 0.74H, NH_{maj}), 10.95 (s, 0.26H, NH_{min}), 9.60 (s, br, 0.26H, OH_{min}), 9.33 (s, 0.74H, OH_{maj}), 8.14–8.09 (m, 0.52H, Ar_{min}), 7.91–7.95 (m, 1.48H, Ar_{maj}), 7.65–7.60 (m, 0.52H, Ar_{min}), 7.52–7.46 (m, 1.48H, Ar_{maj}), 7.35–7.22 (m, 6H, Ar), 7.15–6.92 (m, 3.74H, Ar), 6.89–6.73 (m, 0.26H, Ar_{min}), 6.10 (s, 0.74H, H-4_{maj}), 5.60 (s, 0.26H, H-4_{min}); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 183.2, 144.9, 141.0, 139.7, 138.5, 137.8, 137.0, 135.4, 131.1, 131.0, 130.7, 129.3, 129.2, 129.0, 128.6 (2C), 128.5, 128.2, 128.1, 127.9 (2C), 127.6, 127.0, 125.9, 125.7, 125.5, 110.2, 97.7 (C-5_{min}), 96.8 (C-5_{maj}), 71.8 (C-4_{min}), 70.6 (C-4_{maj}), 19.7 (C–CH_{3min}), 19.6 (C–CH_{3maj}); HRMS (ESI) m/z calcd for $C_{22}H_{21}N_2OS$ $[M + H]^+$ 361.1369, found 361.1384; IR (neat) ν_{max}/cm^{-1} 3154, 3061, 2250, 1682, 1602, 1538, 1494, 1449, 1397, 1300, 1235, 1203, 1136, 1072, 1052, 1027, 1002, 968, 940, 886, 824, 784, 746, 720, 698.

(±)-1-Cyclohexyl-5-hydroxy-4,5-diphenylimidazolidine-2-thione (5aia). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 9 : 1 : 0.5 afforded **5aia** as a white amorphous solid (158 mg, 45%, dr 88/12). ^{1}H-NMR (400 MHz, pyridine-d_5) δ 10.45 (s, 0.88H, NH_{maj}), 10.20 (s, 0.12H, NH_{min}), 9.40 (s, br, 0.12H, OH_{min}), 8.61 (s, 0.88H, OH_{maj}), 7.93–7.89 (m, 2H, Ar), 7.55–7.41 (m, 3H, Ar), 7.36–7.25 (m, 3H, Ar), 7.20–7.15 (m, 1H, Ar), 7.14–7.06 (m, 1H, Ar), 5.62 (s, 0.12H, H-4_{min}), 5.40 (s, 0.88H, H-4_{maj}), 4.28 (s, br, 0.12H, Ali_{min}), 4.01 (s, br, 0.88H, Ali_{maj}), 3.08 (s, br, 0.12H, Ali_{min}), 2.96 (s, br, 0.88H, Ali_{maj}), 2.74 (s, br, 1H, Ali), 2.18–2.06 (m, 1.76H, Ali_{maj}), 2.03–1.95 (m, 0.24H, Ali_{min}), 1.67–1.46 (m, 2H, Ali), 1.15–0.88 (m, 4H, Ali); $^{13}C\{^1H\}$ NMR (101 MHz, pyridine-d_5) δ 183.4, 142.7, 135.6, 128.5, 128.2, 128.0, 127.9 (2C), 127.8, 127.5, 127.3, 99.3 (C-5_{min}), 96.9 (C-5_{maj}), 72.4 (C-4_{min}), 71.4 (C-4_{maj}), 57.2, 56.7, 31.2, 30.7, 26.4, 25.4; HRMS (ESI) m/z calcd for $C_{21}H_{25}N_2OS$ $[M + H]^+$ 353.1682, found 353.1699; IR (neat) ν_{max}/cm^{-1} 3198, 2936, 2851, 1684, 1539, 1485, 1450, 1404, 1349, 1304, 1259, 1234, 1208, 1175, 1110, 1070, 1010, 968, 908, 894, 826, 790, 701.

(±)-1-(2-Fluorophenyl)-5-hydroxy-4,5-diphenylimidazolidine-2-thione (5ada). Column chromatography on silica gel with cyclohexane/EtOAc/TEA = 7 : 3 : 0.5 afforded **5ada** as a white amorphous solid (317 mg, 87%, dr 99/1). ^{1}H NMR (400 MHz, pyridine-d_5) δ 11.41 (s, 1H, NH), 9.56 (s, br, 1H, OH), 8.05–7.95 (m, 2H, Ar), 7.48–7.22 (m, 8H, Ar), 7.20–6.99 (m, 3H, Ar), 6.98–6.84 (m, 1H, Ar), 5.81 (s, 1H, H-4); $^{13}C\{^1H\}$ NMR

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(101 MHz, pyridine-d_5) δ 184.1, 160.9, 158.4, 140.6, 137.8, 130.5, 129.4, 129.2, 128.5 (2C), 128.3, 128.2, 128.1 (2C), 127.9, 127.8, 127.7, 127.5, 127.4, 127.1, 125.6, 124.1, 123.8, 116.2, 116.0, 96.9, 72.5; ^{19}F NMR (376 MHz, pyridine-d_5) δ −114.11 (s, 1F, Ar); HRMS (ESI) *m*/*z* calcd for $C_{21}H_{18}FN_2OS$ $[M + H]^+$ 365.1118, found 365.1101; IR (neat) ν_{max}/cm^{-1} 3146, 3064, 1682, 1587, 1538, 1504, 1450, 1396, 1359, 1304, 1238, 1108, 1041, 1024, 968, 942, 898, 824, 784, 747, 727, 699.

(±)-1-Benzyl-4-(4-chlorophenyl)-5-hydroxy-5-phenylimidazolidine-2-one (8bja). *Method A*: To a vigorously stirred suspension of **7bj** (415 mg, 1.00 mmol), pre-catalyst **A** (54 mg, 0.20 mmol) and 4 Å MS (25 mg) in anhydrous DCM (5 mL), benzaldehyde **1a** (203 μL, 2.00 mmol) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (balloon) three times. At this point, TEA (417 μL, 3.0 mmol) was added in one portion and the suspension was stirred at 30 °C for 16 h. After this time, another portion of TEA was added (278 μL, 2.00 mmol) and the mixture was refluxed for 1 day. The mixture was cooled to room temperature, filtered over a pad of Celite, diluted with brine (10 mL), and extracted with EtOAc (2 × 40 mL). The combined organic phases were dried (Na_2SO_4), concentrated, and purified by column chromatography on silica gel with cyclohexane/EtOAc/TEA 7 : 3 : 0.5 to afford the desired product **8bja** as a white amorphous solid (193 mg, 51%, dr 99/1). ^{1}H NMR (400 MHz, pyridine-d_5) δ 8.64 (s, 1H, OH), 7.79–7.72 (m, 2H, Ar), 7.49–7.43 (m, 2H, Ar), 7.42–7.25 (m, 9H, Ar, NH), 7.21–7.16 (m, 2H, Ar), 5.31 (s, 1H, CH), 4.83 (d, *J* = 15.4 Hz, 1H, CH_2), 4.45 (d, *J* = 15.4 Hz, 1H, CH_2); ^{13}C{^{1}H} NMR (101 MHz, pyridine-d_5) δ 162.1, 141.7, 140.1, 136.0, 133.2, 131.0, 129.6, 128.9, 128.6, 128.2, 128.1, 128.0 (2C), 127.6, 126.6, 92.4, 67.5, 44.3; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{20}ClN_2O_2$ $[M + H]^+$ 379.1208, found 379.1224; IR (neat) ν_{max}/cm^{-1} 3041, 2922, 2809, 1672, 1597, 1496, 1452, 1406, 1146, 1028, 768, 982, 969, 912, 894, 841, 820, 795, 783, 762, 729, 700, 696.

Method B: To a vigorously stirred suspension of **7bj** (415 mg, 1.00 mmol), pre-catalyst **A** (54 mg, 0.20 mmol) and 4 Å MS (25 mg) in anhydrous DCM (5 mL), benzaldehyde **1a** (203 μL, 2.00 mmol) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (balloon) three times. At this point, TEA (417 μL, 3.0 mmol) was added in one portion and the suspension was stirred at 30 °C for 16 h, filtered over a pad of Celite, diluted with brine (10 mL), and extracted with EtOAc (2 × 40 mL). The combined organic phases were dried (Na_2SO_4) and concentrated to give a crude mixture containing **9bja** and **8bja** as determined by ^{1}H-NMR. Selected data of **9bja**: ^{1}H NMR (300 MHz, pyridine-d_5) δ 8.30 (d, *J* = 6.6 Hz, 2H, Ar), 7.82 (d, *J* = 6.6 Hz, 2H, Ar), 6.55 (s, 1H, CH), 5.06–5.01 (d, *J* = 15 Hz, 0.25H, CH_{min}), 4.79–4.53 (m, 1.5H, CH_{2maj}), 4.49–4.44 (d, *J* = 15 Hz, 0.25H, CH_{min}); ^{13}C{^{1}H} NMR (101 MHz, pyridine-d$_5$) δ 197.3, 158.2, 141.0, 136.0, 130.2, 130.0, 129.7, 129.4, 129.2, 128.6 (2C), 128.0, 127.7, 127.5, 126.9, 126.6, 59.2, 44.1.

Multigram scale synthesis of (±)-5aab

To a vigorously stirred suspension of **3aa** (2.00 g, 5.24 mmol), pre-catalyst **A** (0.27 g, 1.05 mmol) and 4 Å MS (125 mg) in anhydrous DCM (25 mL), 4-chlorobenzaldehyde **1b** (0.87 g, 6.20 mmol) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (balloon) three times. At this point, TEA (2.10 mL, 15.6 mmol) was added in one portion and the suspension was stirred at 30 °C for 16 h, filtered over a pad of Celite, concentrated, diluted with saturated solution of Na_2CO_3 (30 mL), and extracted with EtOAc (2 × 100 mL). The collected organic phases were dried (Na_2SO_4), concentrated, and crystallized from hot toluene to afford the desired product **5aab** (1.22 g, 62%, dr 84 : 16) as a white amorphous solid.

2-Oxo-1,2-diphenylethanaminium chloride (16)

To a cooled (0 °C), stirred mixture of benzoin **14** (2.00 g, 9.43 mmol) in anhydrous DCM (25 mL), $SOCl_2$ (2.70 mL, 37.0 mmol) and 3 drops of DMF were added under a N_2 atmosphere. The mixture was stirred at 0 °C for 1 h, then warmed to room temperature, stirred for an additional 4 h, concentrated, diluted with EtOAc (25 mL), and washed with water (10 mL). The organic phase was dried (Na_2SO_4) and concentrated to afford the desired 2-chloro-1,2-diphenylethanone product[43] (1.60 g), which was used in the next step without further purifications. Selected data: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.17 Hz, 2H, Ar), 7.53–7.31 (m, 8H, Ar), 6.32 (s, 1H, CH).

To a stirred mixture of the above crude 2-chloro-1,2-diphenylethan-1-one (1.60 g, ~6.96 mmol) in anhydrous DCM (10 mL), phthalimide potassium salt (1.55 g, 8.32 mmol) was added in one portion. The mixture was stirred at room temperature for 18 h, then concentrated, diluted with brine (20 mL), and extracted with Et_2O (2 × 60 mL). The combined organic phases were dried (Na_2SO_4) and concentrated to afford **15** as a white solid (2.2 g), which was used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89–7.78 (m, 4H, Ar), 7.72–7.67 (m, 2H, Ar), 7.52–7.45 (m, 4H, Ar), 7.39–7.30 (m, 4H, Ar), 6.78 (s, 1H, CH).

A stirred solution of crude **15** (2.20 g, ~6.45 mmol) in acetic acid (10 mL) and HCl 6 N (10 mL) was refluxed for 3 days, then cooled to room temperature, and filtered. The filtrate was concentrated to give **16** as a white amorphous solid (1.56 g, 67% overall yield). This compound was used in the coupling with Edman's reagent without further purification. ^{1}H NMR (300 MHz, D_2O) δ 7.81–7.75 (m, 2H, Ar), 7.62–7.56 (m, 1H, Ar), 7.55–7.36 (m, 2H, Ar), 7.33–7.21 (m, 5H, Ar), 6.09 (s, 1H, CH); ^{13}C{^{1}H} NMR (101 MHz, D_2O) δ 194.3, 172.1, 134.9, 132.2, 131.6, 131.2, 130.3, 129.8, 129.0, 128.9, 128.5, 59.5.

5-(4-Chlorophenyl)-1,4-diphenyl-1,3-dihydro-2*H*-imidazole-2-thione (17)

To a stirred solution of (±)-**5aab** (191 mg, 0.50 mmol) in DMF (5 mL), concentrated sulfuric acid (3 μl) was added in one portion. The solution was stirred under reflux for 1 hour, then cooled to room temperature, diluted with brine (10 mL), and extracted with Et_2O (2 × 20 mL). The combined organic phases were dried (Na_2SO_4) and concentrated to give **17** (181 mg, >95%) at least 95% pure as judged by ^{1}H NMR analysis. ^{1}H

NMR (400 MHz, $CDCl_3$) δ 11.84 (s, br, 1H, SH), 7.42–7.33 (m, 4H, Ar), 7.30–7.20 (m, 6H, Ar), 7.18–7.13 (m, 2H, Ar), 6.98–6.93 (m, 2H, Ar); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 161.9, 135.3, 134.2, 131.2, 128.6, 128.4 (2C), 128.2, 128.0, 127.0, 126.7, 126.2, 125.9; HRMS (ESI) *m*/*z* calcd for $C_{21}H_{16}ClN_2S$ $[M + H]^+$ 363.0717, found 363.0737; IR (neat) ν_{max}/cm^{-1} 3036, 2902, 2730, 1667, 1597, 1489, 1447, 1374, 1263, 1342, 1089, 1017, 966, 915, 863, 781, 764, 736, 745, 702.

2-(Benzylthio)-5-(4-chlorophenyl)-1,4-diphenyl-1*H*-imidazole (18)

To a stirred solution of **17** (73 mg, 0.20 mmol) and benzyl bromide (25 μL, 0.21 mmol) in DMF (2 mL), cesium carbonate (78 mg, 0.24 mmol) was added in one portion. The suspension was stirred until the consumption of the starting **17** (24 h monitoring by TLC), then diluted with brine (5 mL), and extracted with Et_2O (2 × 10 mL). The combined organic phases were dried (Na_2SO_4), concentrated and purified by column chromatography on silica gel with cyclohexane/EtOAc 8 : 2 to afford **18** as a white amorphous solid (91 mg, >95%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.60–7.52 (m, 2H, Ar), 7.34–7.19 (m, 11H, Ar), 7.19–7.13 (m, 2H, Ar), 7.02–6.95 (m, 2H, Ar), 6.94–6.87 (m, 2H, Ar), 4.40 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 143.2, 139.1, 137.4, 135.6, 134.0, 133.8, 131.8, 129.7, 129.2, 129.0, 128.8, 128.7 (2C), 128.4, 128.3, 128.0, 127.4, 127.2, 126.9, 38.3; HRMS (ESI) *m*/*z* calcd for $C_{28}H_{22}ClN_2S$ $[M + H]^+$ 453.1187; found 453.1206; IR (neat) ν_{max}/cm^{-1} 3029, 2932, 2849, 1596, 1495, 1479, 1449, 1428, 1397, 1367, 1321, 1297, 1275, 1230, 1175, 1091, 1071, 1016, 960, 917, 832, 779, 769, 747, 692.

Conflicts of interest

There are no conflicts to declare.

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