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# Acid-catalysed formation of tricyclic *N*,*S*-acetals in imidazolinone series based on the use of the unprecedented *N*-acyliminium ion cascade reaction involving transposition, heterocyclisation and π-cyclisation†

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***Received 10th July 2005, Accepted 5th September 2005***
***First published as an Advance Article on the web 4th October 2005***

4-Hydroxy-5,5-dimethylimidazolines tethered at *N*-1 to an aryl sulfide undergo an unprecedented acid-catalysed domino reaction, involving double methyl transposition, heterocyclisation, isomerisation of thiazetidinium ion and, finally, π-cyclisation. In this way a one-pot synthesis of original tricyclic *N*,*S*-acetals was developed. The same triheterocyclic products can be prepared also starting from the corresponding 5-hydroxy isomers (in this case the cascade of reactions does not involve methyl transposition).



## Introduction

Sequential processes that enable the easy access to complex structures from simple building blocks in a single preparative step are of high interest in organic synthesis, especially if they allow the generation of biologically active compounds.[1,2]

While the importance of *N*-acyliminium chemistry involving olefinic and aromatic cationic cyclisations has been widely demonstrated and reviewed extensively,[3] useful synthetic reactions of the construction of carbon–heteroatom bonds mediated by *N*-acyliminium ion species has been by far less explored, but constitutes a novel and powerful strategy to access new compounds as cyclic *N*,*O*-, *N*,*N*-, and *N*,*S*-acetals.[4]

Because we are interested in developing new reactions for accessing libraries of original *N*,*S*-heterocyclic systems containing imidazolinone and benzothiazine skeletons with promising pharmaceutical activities, we have continued to explore synthetic opportunities based on our recent reports dealing with intramolecular heteroamidoalkylation.[4j,l,m,5] Although the cationic cyclisation using a nitrogen and oxygen atom as internal nucleophile has been mentioned,[4] the intramolecular use of a sulfur nucleophile for trapping an *N*-acyliminium cation was unprecedented before our previous work.[5] The association of this process in tandem with *N*-acyliminium isomerisation–π-cationic cyclisation was reported, and led conveniently to substituted benzothiazoles and thiazines fused to an isoindolinone nucleus.[6,7] To the best of our knowledge the present application of this cascade process, which would produce the central six-membered and/or bridged ring systems as cyclic *N*,*S*-acetals (types **II**–**V**: Fig. 1) starting from hydroxyimidazolidinone of type **I**, represents a novel illustration of this chemistry. In fact, the selection of the functionality N–$CH_2$–S in an imidazolinone ring allows consideration of both endocyclic and/or exocyclic *N*-acyliminium intermediates, which, if containing a moderately activated aromatic ring and a sulfur atom, would acts as effective π-aromatic and/or sulfur nucleophile scavenger. Herein, we present the preliminary results of our finding on this combination of double transposition–heterocyclisation–

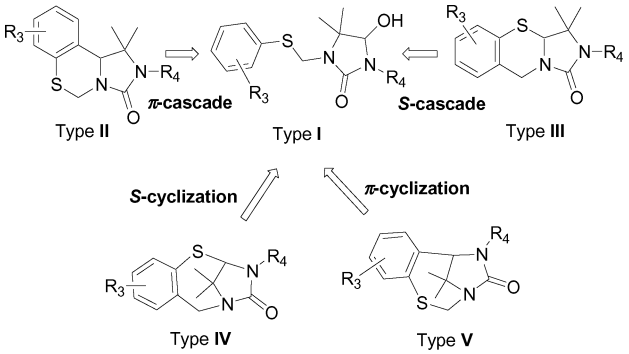



**Fig. 1** All plausible targets structures *via* the cascade *N*-acyliminium ion rearrangement–heterocyclisation–π-cationic cyclisation.

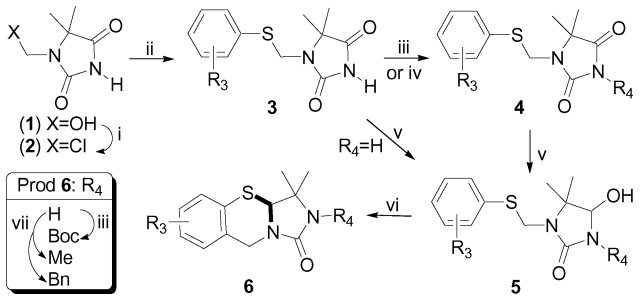
π-cationic cyclisation, a new mechanistic pathway to access cyclic thiolactams. A cascade reaction is proposed, relying on chemical and spectroscopic considerations, including X-ray crystallography.

## Results and discussion

The synthesis of the required hydroxyimidazolidinones of type **I** (**5**) was accomplished in a four/five-step sequence as outlined in Scheme 1. The commercially available 1-hydroxymethyl derivative **1** was chlorinated quantitatively with thionyl chloride and the resulting halide **2** was *S*-alkylated with slight excess of aryl mercaptan in alkaline medium (41 to 86%).[8] Regioselective reduction of the resulting imide (**3a**: $R_3$ = H), chosen as a model substrate, was performed with a large excess of $NaBH_4$ (6 mole equiv.) in analogy to reports by Hough *et al.*[9] To avoid the poor solubility of the imide **3a**, in addition to the laborious work-up encountered during this process, we have anticipated that the conversion of **3a** to the *N*-Boc protected imide **4a** could offer a better result by increasing the solubility of hydroxyimidazolidinone substrate. So, treatment of **4a**, obtained by standard *N*-protection with the tandem $Boc_2O$–DMAP (quantitative yield),[10] under our reduction protocol (conditions (v)) gave 5-hydroxyimidazolidinone **5a** ($R_3$ = H, $R_4$ = Boc) in 89% yield.

† Electronic supplementary information (ESI) available: detailed spectroscopic ($^1$H and $^{13}$C NMR and DEPT) data of all compounds in Schemes 1 and 2. See DOI: 10.1039/b508214e

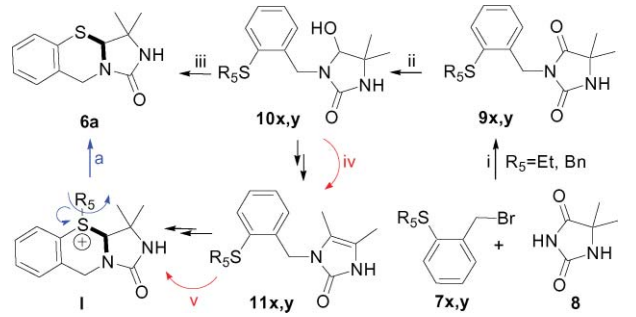
DOI:10.1039/b508214e



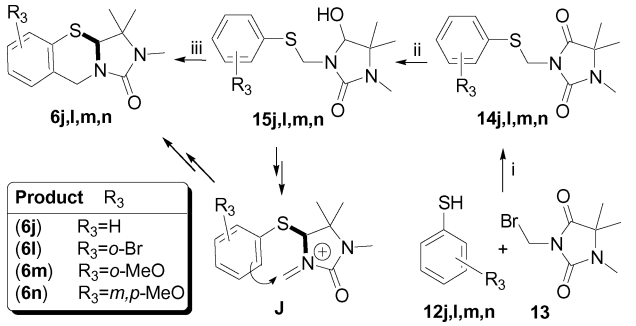
**Scheme 1** Reagents and conditions: (i) $SOCl_2$ (3.0 mole equiv.), $CH_2Cl_2$, 0 to 20 °C, 12 h, 100%; (ii) Ar–SH (1.2 mole equiv.), MeONa (1.2 mole equiv.), DMF, 20 °C, 12 to 24 h, 41 to 86%; (iii) $Boc_2O$, $DMAP_{cat}$, $CH_3CN$ or THF, 20 °C, 12 to 24 h, 54 to 100%; (iv) $R_4$–X (1.2 mole equiv.), $K_2CO_3$ (1.2 mole equiv.), 18-C-6 (1% molar), KI (0.1 mole equiv.), toluene, reflux, 24 h, 91% ($R_4$ = Me) and 97% ($R_4$ = Bn); (v) $NaBH_4$ (6 mole equiv.), EtOH, 20 °C, 12 to 48 h, 70 to 100%; (vi) TFA (1.5 mL for 1 mmol of 5-hydroxyimidazolidinone **5**), 24 h, 21 to 92%; (vii) $R_4$–X (1.2 mole equiv.), NaH (1.2 mole equiv.), THF, 20 °C, 60 h, 62% ($R_4$ = Me) and 58% ($R_4$ = Bn).

Analogous procedures (**3** → **4** → **5**) were used successfully to afford elegantly **5c**–**i** ($R_4$ = Boc), with other substituents on different positions of the aromatic ring (see Table 1). In addition, to measure the effect of the $R_4$ group, on both reduction and cyclisation steps and to establish the generality and versatility of our proposed cascade process, the $N_3$-alkylated imides **4j**,**k** were elaborated successfully with high yields (91 and 97% yields, respectively) under PTC conditions.[4j] Their reduction led to corresponding 5-hydroxyimidazolidinones **5j** and **5k** in 89 and 84% yields, respectively. On the other hand, 4-hydroxyimidazolidinones **10x** ($R_5$ = Et) and **10y** ($R_5$ = Bn) were easily obtained in two steps from bromides **7x** and **7y**,[6] by *N*-alkylation (63% and 73% yields, respectively (see Scheme 2)) and a sodium borohydride regioselective reduction (94 and 84% yields, respectively). Similarly, as shown in Scheme 3, 4-hydroxyimidazolidinones **15j**,**l**–**n** were obtained in two steps and very good yields by *S*-alkylation of halide **13**[11] and sodium borohydride reduction.

In the outset of our investigations, the 5-hydroxyimidazolidinone **5a**, as an *N*-acyliminium generator model, was subjected to different acid conditions (entries 1–4). The obtained results allowed us to select neat trifluoroacetic acid (TFA) in precise proportion to substrate (1.5 mL for 1 mmol of **5**) as the best cyclisation protocol (conditions **D** in Table 1).



**Scheme 2** Reagents and conditions: (i) **7x**,**y** (see ref. 6) (1.2 mole equiv.), $K_2CO_3$ (1.2 mole equiv.), 18-C-6 (1% molar), KI (0.1 mole equiv.), toluene, reflux, 48 h, 63% ($R_5$ = Et) and 73% ($R_5$ = Bn); (ii) $NaBH_4$ (6 mole equiv.), EtOH, 20 °C, 24 h, 94% ($R_5$ = Et) and 84% ($R_5$ = Bn); (iii) TFA (1.5 mL for 1 mmol of 4-hydroxyimidazolidinones **10**), 24 h, 67 and 52%, respectively; (iv) $PTSA_{cat}$, toluene, reflux, 48 h, 58%. (v) neat TFA, reflux, 48 h, 67%.



**Scheme 3** Reagents and conditions: (i) **13** (1.0 mole equiv.) Ar–SH (1.2 mole equiv.), MeONa (1.2 mole equiv.), DMF, 20 °C, 12 to 24 h, 66 to 85% ($R_3$ = H (**12j**), $R_3$ = *o*–Br (**12l**), $R_3$ = *o*-MeO (**12m**), $R_3$ = *m*,*p*-MeO (**12n**)); (ii) $NaBH_4$ (6 mole equiv.), EtOH, 20 °C, 12 to 48 h, 69 to 95%; (vi) $PTSA_{cat}$, toluene, reflux, 48 h, 58%. (vii) neat TFA, reflux, 48 h, 67%; (iii) TFA (1.5 mL for 1 mmol of 4-hydroxyimidazolidinones **15**), 24 h, 44 to 100%.

In these acid conditions, the cyclised product, identified as the unexpected imidazolo[1,3]benzothiazine **6a**, was isolated as a crystalline material in 56% yield. From this result, its seems that the reaction did not occur by direct cyclisation but by a cascade process in one-pot procedure. This tricyclic product was obtained also in 92% of yield from **5b** ($R_3$ = $R_4$ = H) under the same conditions. These preliminary attempts revealed also that

**Table 1** Cascade *N*-acyliminium isomerisation–π-cyclisation[a]

| Entry | Reactant[b] | $R_3$ | $R_4$ | Method | Product[b] ($R_4$) | Yield (%)[c] |
|---|---|---|---|---|---|---|
| 1 | **5a** | H | Boc | **A** | **6a** (H) | [d] |
| 2 | **5a** | H | Boc | **B** | **6a** (H) | [d] |
| 3 | **5a** | H | Boc | **C** | **6a** (H) | [e] |
| 4 | **5a** | H | Boc | **D** | **6a** (H) | 56 |
| 5 | **5a** | H | H | **D** | **6a** (H) | 92 |
| 6 | **5c** | *o*.Br | Boc | **D** | **6c** (H) | 21 |
| 7 | **5d** | *o*-MeO | Boc | **D** | **6d** (H) | 29 |
| 8 | **5e**[f] | *m*-MeO | Boc | **D** | **6e** (H) | 77 |
| 9 | **5f** | *p*-MeO | Boc | **D** | **6f** (H) | [d] |
| 10 | **5g** | *p*-Cl | Boc | **D** | **6g** (H) | [d] |
| 11 | **5h** | *β*-Naphth | Boc | **D** | **6h** (H) | 61 |
| 12 | **5i** | *m*,*p*-MeO | Boc | **D** | **6i** (H) | 55 |
| 13 | **5j** | H | Me | **D** | **6j** (Me) | 87 |
| 14 | **5k** | H | Bn | **D** | **6k** (Bn) | 95 |

[a] Reagents and conditions: Method **A**: $PTSA_{cat}$, toluene, reflux, 24 h; Method **B**: $BF_3.Et_2O$ (2.0 mole equiv.), $CH_2Cl_2$, 20 °C, 24 h; Method **C**: TFA (2.0 mole equiv.), $CH_2Cl_2$, 20 °C, 24 h; Method **D**: (see conditions (vi) in Scheme 1) TFA, 24 h. [b] The substrates **5a** and **5c**–**i** have group $R_4$ = Boc. Importantly, it should be noted that the Boc group is lost during the cyclisation process and consequently when $R_4$ = Boc in substrate **5** it becomes H in product **6** after the cyclisation reaction. [c] Chromatographically pure compounds. [d] Only the thiophenol was isolated. [e] The unprotected starting material as 5-hydroxyimidazolidinone (**5b**) was recovered and was accompanied with the disulfur namely, 4-phenylthio-1-phenylthiomethyl-5,5-dimethylimidazolidin-2-one. [f] In the case of the *m*-methoxy derivative **6e** (entry 8), the reaction was performed with total regioselectivity in favor of the 2-position of the benzene ring.

only the thiophenol (entries 1, 2) or the 4-phenylthio-1-phenylthiomethyl-5,5-dimethylimidazolidin-2-one (entry 3) resulting from the cleavage of the thioether linkage, followed by its attack or not of the iminium intermediate, were isolated in protocols **A**, **B** and **C**, respectively.

Having established the capacity of 5-hydroxyimidazolidinones **5a**,**b** to provide a cascade process in forming unusual six-membered *N*,*S*-heterocyclic complex systems, we sought to determine if this novel mechanistic paradigm might be extended to other aromatic substituents. Significant structural variation in the π-aromatic system can also be realized. Importantly, the reaction appears quite tolerant with respect to the substituent at the benzene ring *o*-, *m*- and *m*,*p*-positions (entries 6–8, 11, 12). While reasonable yields (55 to 77%) are obtained with the *m*- and *m*,*p*-positions (entries 8, 11, 12), the *o*-substitution (entries 6, 8), was characterized with low yields which do not exceed whatever the attempts, 29%.[12] This yield dramatically falls to 0% (entries 9, 10) when the benzene ring was *para*-substituted. This clearly demonstrates the impact of electronic influence of the benzene moiety on the kinetic of the reaction. Unexpectedly, the introduction of alkyl substituent at $N_3$ on the imidazolidine moiety proved to have a beneficial effect on the yield of the reaction, which may be attributed to an increased nucleophilic character of the sulfur atom (Table 1, entries 13, 14).

The assignment of all structures reported herein was made on the basis on their IR, NMR ($^1$H and $^{13}$C experiments including NOE difference and DEPT programs, respectively), and GC-MS spectra. In the case of solids, their elemental analyses were also performed. So, the $^1$H NMR spectra of imides **3** and **4** showed a methylene groups as a singlet with the chemical shifts values of about $\delta$ = 4.73–5.00 ppm for **3** and from $\delta$ = 4.45–4.94 ppm for **4**, respectively. The same methylene protons in N–$CH_2$–S functionalities of the 5-hydroxyimidazolidinones **5** and the cyclic *N*,*S*-acetals **6** appear as an AB system due to the diastereotopic effect with a coupling constant of $J$ = 13–15 Hz for **5** and $J$ = 12–17 Hz for benzothiazines **6** characteristic of *gem* protons. Interestingly in the latter case we found that coupling constant $J$ = 17 Hz for the majority of the tricyclic *N*,*S*-acetals **6** excepted for compounds **6e** (8-MeO benzene substituent), **6h** (naphthalene derivative) and **6i** (6,7-MeO benzene substituent) in which $J$ = 12–13 Hz. This result is in corroboration with the chemical displacement values of the angular carbon "$C_{10}$ in the ORTEP drawing, see Fig. 3 for example" ($\delta$ = 61.2–65.0 ppm) in the $^{13}$C NMR spectra compared to the same one in the *N*,*S*-acetal derivatives **6** bearing other substituents ($\delta$ = 67.5–69.3 ppm).

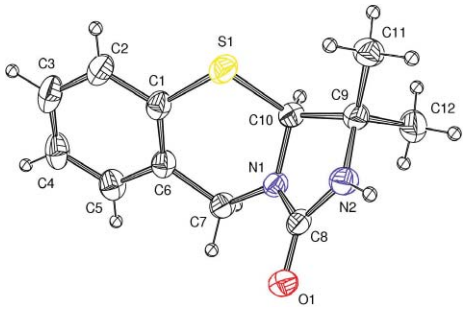



**Fig. 2** A molecular structure of imidazobenzothiazine **6a** derived from X-ray crystallographic data. Arbitrary numbering of atoms, 50% probability ellipsoids.

Likewise, the $^{13}$C NMR spectra of the cyclic *N*,*S*-acetal products **6** reveled the presence of an additional quaternary carbon in the aromatic region as the consequence of the cyclisation process. Furthermore an important shielding of the angular carbon of components **6** was observed ($\delta$ = 61.2–69.3 ppm instead of the range 83.4 to 84.8 ppm for the same

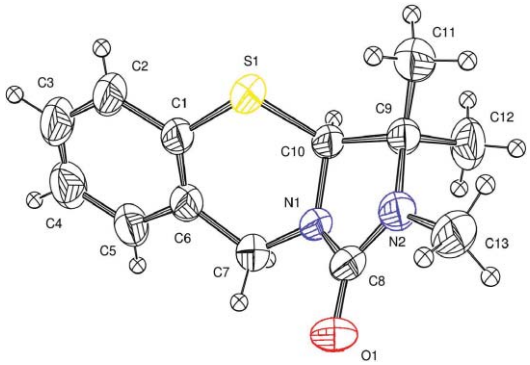



**Fig. 3** A molecular structure of imidazobenzothiazine **6j** derived from X-ray crystallographic data. Arbitrary numbering of atoms, 50% probability ellipsoids.

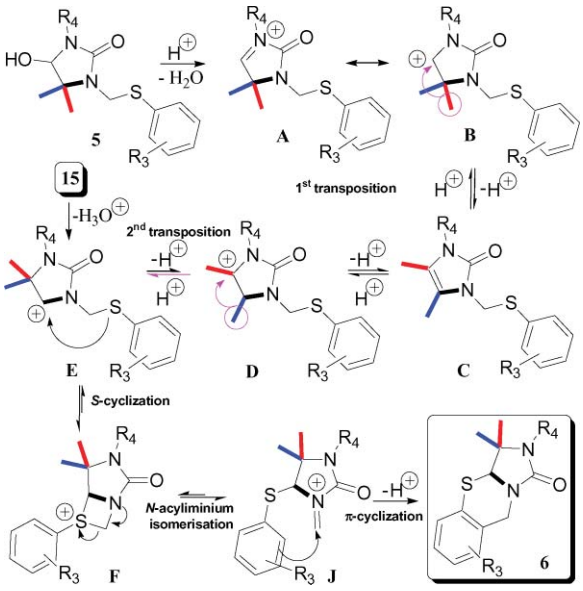
carbon in their 5-hydroxyimidazolidinones **5** congeners) which is due to the proximity of the sulfur atom instead of the oxygen one. These observations were also corroborated with similar results outlined by us in recent reports for related structures. Finally, the structures of products **6a**,**j** were unequivocally confirmed by single X-ray crystallographic analysis as shown by the ORTEP drawing in Fig. 2 for imidazo[1,3]benzothiazine **6a** and Fig. 3 for imidazo[1,3]benzothiazine **6j**.

Additionally, structure confirmation of these thiazacyclic systems was performed by two approaches as highlight in Schemes 2 and 3. So, subjection of 4-hydroxyimidazolidinone **10y** prepared as outlined above (see also Scheme 2) to our established acid-protocol, furnished the desired heterocyclic thiolactam **6a** (52% yield) by successive intramolecular thioamidoalkylation of the acyliminium ion into the intermediate thiazinium salt **I** and debenzylation (Scheme 2). In parallel experiments from 4-hydroxyimidazolidinone **10x** ($R_5$ = Et), the reaction occurred only when PTSA in catalytic amount was used (*i.e.* toluene, reflux, 48 h). The product isolated in 58% of yield was identified as imidazolone **11x** which is the consequence of the simple transposition of one methyl group.[13]

Taking into account that an enamidone function could generate an *N*-acyliminium ion under acidic conditions,[14] the cyclisation of **11x** into **6a** was achieved under drastic conditions in 67% yield (*i.e.* TFA, reflux, 48 h). This result showed that the transformation of the imidazolone **11x** into the azasulfonium salt **I** and *vice versa* was accomplished in acid medium.

In the second pathway, the good nucleophilicity of the sulfur atom was again explored. So, upon treatment with TFA (conditions (iii), Scheme 3), 4-hydroxyimidazolidinone **15j** gave the desired cyclised product **6j** (89% yield) *via* the π-cationic cyclisation of the intermediate exocyclic *N*-acyliminium ion **J**, which was obtained from the endocyclic one generated under influence of acid *via* the cyclic azasulfonium ion.[6] This sequence was generalized successfully and led to other new cyclic thioactams as **6l**–**n** (Scheme 3). Additionally as illustrated in Fig. 1, structures of **6b** ($R_4$ = Boc), **6j** ($R_4$ = Me) and **6k** ($R_4$ = Bn) were confirmed chemically by *N*-protection using classical protocols with respectively Boc, methyl and benzyl groups starting from **6a**. Finally, structures of **6a** and **6j** were proved by single X-ray crystallographic analysis, which are identical to that in the ORTEP drawing in Fig. 2 and 3.

Scheme 4 represents a plausible mechanistic rationale for the cascade process reported herein. Formation of the intermediate **C** from 5-hydroxyimidazolidinones **5**, by transposition of one methyl group under acid, accounts for the literature observations.[9] This intermediate, isolated when $R_3$ = H and $R_4$ = Bn, is in equilibrium *via* the intermediacy of **D** with the corresponding cation **E** which could also obtained directly when **15** was used as starting material. This cation **E** by successive stepwise *S*-alkylation (**F**), isomerisation (**J**) and π-cyclisation would ultimately lead to unusual cyclic *N*,*S*-acetals **6**.




**Scheme 4** Proposed mechanisms to access thiazines **6** from **5** and **15**.

## Conclusion

In summary, a one-pot synthesis of complexes heterocyclic *N*,*S*-acetals **6** was initiated by acid-catalysed rearrangement of 5-hydroxyimidazolidinones **5** and 4-hydroxyimidazolidinones **10** and **15**, respectively. During these transformations, it seems that in the case of 4-hydroxyimidazolidinones **10** it is difficult to introduce substituents in the aryl ring, while for 4-hydroxy-imidazolidinones **15** it is difficult to prepare compounds with $R_4$ = H. As a consequence, the pathway using 5-hydroxy-imidazolidinones **5** as a cation source appears to be general, easy to apply and gives moderate to good yields. In this work, a cascade process including alkyl transposition, heterocyclisation, *N*-acyliminium isomerisation, and finally a π-cyclisation was also established. Finally, the mechanistic aspect of these transformations was also addressed.

Elsewhere, we are currently investigating rational design of new hydroxyimidazolidinones as *N*-acyliminium ion precursors bearing other $C_5$-substituents and heteroatoms than sulfur and the application to multi-step synthesis, the results of which will be published in due course.

## Experimental

### General remarks

Melting points are uncorrected. IR spectra of solids (potassium bromide) were recorded on a Perkin Elmer FTIR paragon 1000 spectrophotometer. $^1$H and $^{13}$C NMR spectra were measured on a Bruker AC-200 and Bruker 300 instruments (200 and 300 MHz respectively) and chemical shifts are reported relative to $CDCl_3$ at $\delta$ 7.24 ppm (or to DMSO-$d_6$ at $\delta$ 2.49 ppm) and tetramethylsilane as an internal standard. MS spectral measurements were carried out on a AEI MS 902 S spectrometer (70 eV, electron impact). Reagents were obtained from commercial suppliers and used without further purification. Solvents were dried and purified by standard methods. A Merck silica gel 60 was used for both column chromatography (70–230 mesh) and flash chromatography (230–400 mesh). Ascending TLC was performed on precoated plates of silica gel 60 F 254 (Merck) and the spots visualized using an ultraviolet lamp or iodine vapor. Elemental analyses (C, H, N) were performed by the microanalysis laboratory of INSA at Rouen, F-76130 Mt-St-Aignan, France.

**1-Chloromethyl-5,5-dimethylhydantoin[15] (2).** To a stirred solution, at room temperature, of 1-hydroxymethyl-5,5-dimethylhydantoin (**1**, 23.7 g, 0.15 mol) in 50 mL of dry dichloromethane was added thionyl chloride (32.8 mL, 0.45 mol) at 0 °C. After stirring for 12 h at room temperature, the solution was concentrated under reduced pressure. The white solid was filtered off and washed several times with dry cyclohexane to give the suitable halide derivative **2** as a white solid in quantitative yield; mp 123–125 °C (decomposition, see ref. 15); Found: C, 40.67; H, 5.21; N, 15.66. Calc. for $C_6H_9ClN_2O_2$: C, 40.81; H, 5.14; N, 15.86%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3305 (NH), 1786 (C=O), 1727 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.45 (s, 6H, 2 × $CH_3$), 5.26 (s, 2H, $CH_2$), 6.86 (s broad, 1H, NH);$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 24.8 (2 × $CH_3$), 45.5 ($CH_2$), 59,3 (C), 154.3 ($C_2$=O), 175.6 ($C_4$=O); MS (*m*/*z*: EI) 176–178 ($M^+$).

**General procedure for *S*-alkylation of 1-chloromethyl-5,5-dimethylhydantoin (2).** To a stirred solution under an atmosphere of dry nitrogen or argon of aryl mercaptan derivative (**6a**, 0.024 mol) in 45 mL of dry DMF was added 1.3 g (0.024 mol) of sodium methoxide. After stirring for 1 h at room temperature, 1-chloromethyl-5,5-dimethylhydantoin (**2**, 3.52 g, 0.02 mol) in 15 mL of the same solvent was added slowly dropwise over a period of 20 min. The mixture was then allowed to react at ambient temperature for 12 to 24 h. After cooling, the solution was poured onto cold water and the precipitate formed was filtered off and air dried. The resultant solid was then recrystallized from the solvent indicated to give the hydantoin derivative **3** in moderate to good yields (41 to 86%). In the case of no solid was obtained, the aqueous solution was extracted three times with diethyl ether (3 × 100 mL). The combined organic layers was washed successively with water, brine and dried over $MgSO_4$. The organic phase was concentrated under reduced pressure and the crude resulting solid was purified by flash chromatography on silica gel with a mixture of cyclohexane–AcOEt (4 : 1) as eluent to give *S*-alkylated imide **3**. Recrystallization from suitable solvent afforded pure imide **3** in moderate to good yields (41 to 86%).

**5,5-Dimethyl-1-phenylthiomethylhydantoin (3a).** This product was obtained as a white solid in 79% yield; mp 106 °C (ethanol–diethyl ether); Found: C, 57.29; H, 5.38; N, 11.05. Calc. for $C_{12}H_{14}N_2O_2S$: C, 57.58; H, 5.64; N. 11,19%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3293 (NH), 1770 (C=O), 1720 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.27 (s, 6H, 2 × $CH_3$), 4.76 (s, 2H, $CH_2$), 6.48 (s broad, 1H, NH), 7.21–7.28 (m, 3H, $H_{aro}$), 7.43–7.48 (m, 2H, $H_{aro}$);$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 25.0 (2 × $CH_3$), 42.8 ($CH_2$), 58.9 (C), 128.3 ($CH_{aro}$), 129.1 (2 × $CH_{aro}$), 132.6 ($C_{aro}$–S), 133.3 (2 × $CH_{aro}$), 155.3 ($C_2$=O), 176.2 ($C_4$=O); MS (*m*/*z*: EI) 250 ($M^+$).

**1-(*o*-Bromophenyl)thiomethyl-5,5-dimethylhydantoin (3c).** This product was obtained as a white solid in 71% yield; mp 91 °C (ethanol); Found: C, 43.60; H, 3.77; N, 8.53. Calc. for $C_{12}H_{13}BrN_2O_2S$: C, 43.78; H, 3.98; N, 8.51%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3264 (NH), 1765 (C=O), 1714 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.26 (s, 6H, 2 × $CH_3$), 2.59 (s broad, 1H, NH), 4.80 (s, 2H, $CH_2$), 7.03–7.20 (m, 2H, $H_{aro}$), 7.49–7.60 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 24.7 (2 × $CH_3$), 41.8 ($CH_2$), 58.7 (C), 127.9 ($CH_{aro}$), 128.0 ($C_{aro}$–Br), 129.6 ($CH_{aro}$), 133.2 ($CH_{aro}$), 133.7 ($C_{aro}$–S), 134.4 ($CH_{aro}$), 155.0 ($C_2$=O), 176.4 ($C_4$=O); MS (*m*/*z*: EI) 328–329 ($M^+$).

**1-(*o*-Methoxyphenyl)thiomethyl-5,5-dimethylhydantoin (3d).** This product was isolated as a white solid in 41% yield; mp 126 °C (ethanol); Found: C, 55.45; H, 5.68; N, 10.05. Calc. for $C_{13}H_{16}N_2O_3S$: C, 55.70; H, 5.75; N, 9.99%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3301 (NH), 1778 (C=O), 1720 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.25 (s, 6H, 2 × $CH_3$), 3.92 (s, 3H, $OCH_3$), 4.83 (s, 2H, $CH_2$), 6.16 (s broad, 1H, NH), 6.77–6.88 (m, 2H, $H_{aro}$), 7.29–7.41 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 24.9 (2 × $CH_3$), 40.4 ($CH_2$), 55.9 ($OCH_3$), 58.7 (C), 111.0 ($CH_{aro}$), 119.3 ($C_{aro}$–S), 120.6 ($CH_{aro}$), 130.7 ($CH_{aro}$), 135.9 ($CH_{aro}$), 155.5 ($C_{aro}$–O), 159.8 ($C_2$=O), 176.4 ($C_4$=O); MS (*m*/*z*: EI) 280 ($M^+$).

**1-(*m*-Methoxyphenyl)thiomethyl-5,5-dimethylhydantoin (3e).** This product was isolated as a white solid in 47% yield; mp 93 °C (diethyl ether); Found: C, 55.39; H, 5.61; N, 9.82. Calc. for $C_{13}H_{16}N_2O_3S$: C, 55.70; H, 5.75; N, 9.99%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3270 (NH), 1772 (C=O), 1720 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.50 (s, 6H, 2 × $CH_3$), 3.94 (s, 3H, $OCH_3$), 5.00 (s, 2H, $CH_2$), 6.07 (s broad, 1H, NH), 6.95 (dd, 1H, $J$ = 2 and 8 Hz, $H_{aro}$), 7.20–7.40 (m, 3H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 24.9 (2 × $CH_3$), 42.4 ($CH_2$), 55.4 ($OCH_3$), 58.9 (C), 114.2 ($CH_{aro}$), 117.5 ($CH_{aro}$), 124.7 ($CH_{aro}$), 129.9 ($CH_{aro}$), 133.9 ($C_{aro}$–S), 155.3 ($C_{aro}$–O), 159.8 ($C_2$=O), 176.2 ($C_4$=O); MS (*m*/*z*: EI) 280 ($M^+$).

**1-(*p*-Methoxyphenyl)thiomethyl-5,5-dimethylhydantoin (3f).** This product was isolated as a white solid in 70% yield; mp 120 °C (ethanol–diethyl ether); Found: C, 55.41; H, 5.67; N, 9.86. Calc. for $C_{13}H_{16}N_2O_3S$: C, 55.70; H, 5.75; N, 9.99%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3287 (NH), 1762 (C=O), 1715 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.32 (s, 6H, 2 × $CH_3$), 3.76 (s, 3H, $OCH_3$), 4.70 (s, 2H, $CH_2$), 6.39 (s broad, 1H, NH), 6.80 (d, 2H, $J$ = 9 Hz, $H_{aro}$), 7.42 (d, 2H, $J$ = 9 Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 24.8 (2 × $CH_3$), 43.5 ($CH_2$), 55.2 ($OCH_3$), 58.7 (C), 114.5 (2 × $CH_{aro}$), 122.7 ($C_{aro}$–S), 136.1 (2 × $CH_{aro}$), 155.4 ($C_{aro}$–O), 160.1 ($C_2$=O), 176.2 ($C_4$=O); MS (*m*/*z*: EI) 280 ($M^+$).

**1-(*p*-Chlorophenyl)thiomethyl-5,5-dimethylhydantoin (3g).** This product was isolated as a white solid in 86% yield; mp 135 °C (ethanol); Found: C, 50.33; H, 4.50; N, 9.88. Calc. for $C_{12}H_{13}ClN_2O_2S$: C, 50.61; H, 4.60; N, 9.84%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3292 (NH), 1770 (C=O), 1721 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.34 (s, 6H, 2 × $CH_3$), 4.80 (s, 2H, $CH_2$), 5.87 (s broad, 1H, NH), 7.25 (d, 2H, $J$ = 9 Hz, $H_{aro}$), 7.44 (d, 2H, $J$ = 9 Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 25.0 (2 × $CH_3$), 42.8 ($CH_2$), 59.0 (C), 129.3 (2 × $CH_{aro}$), 131.2 ($C_{aro}$–Cl), 134.4 (2 × $CH_{aro}$), 134.5 ($C_{aro}$–S), 155.2 ($C_2$=O), 176.2 ($C_4$=O); MS (*m*/*z*: EI) 284 ($M^+$).

**5,5-Dimethyl-1-(*β*-naphthyl)thiomethylhydantoin (3h).** This product was isolated as a white solid in 61% yield; mp 115 °C (ethanol–diethyl ether–cyclohexane); Found: C, 63.80; H, 5.41; N, 9.21. Calc. for $C_{16}H_{16}N_2O_2S$: C, 63.98; H, 5.37; N, 9.33%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3287 (NH), 1786 (C=O), 1721 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.23 (s, 6H, 2 × $CH_3$), 4.90 (s, 2H, $CH_2$), 6.50 (s broad, 1H, NH), 7.40–7.97 (m, 7H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 24.9 (2 × $CH_3$), 42.5 ($CH_2$), 58.9 (C), 126.6 ($CH_{aro}$), 126.7 ($CH_{aro}$), 127.6 ($CH_{aro}$), 127.9 ($CH_{aro}$), 128.8 ($CH_{aro}$), 129.8 ($CH_{aro}$), 129.9 ($C_{aro}$–C), 132.0 ($CH_{aro}$), 132.7 ($C_{aro}$–S), 133.6 ($C_{aro}$–C), 155.2 ($C_2$=O), 176.2 ($C_4$=O); MS (*m*/*z*: EI) 300 ($M^+$).

**1-(*m*,*p*-Dimethoxyphenyl)thiomethyl-5,5-dimethylhydantoin (3i).** This product was obtained as a white solid in 76% yield; mp 99 °C (ethanol–cyclohexane); Found: C, 54.11; H, 5.69; N, 9.00. Calc. for $C_{14}H_{18}N_2O_4S$: C, 54.18; H, 5.85; N, 9.03%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3337 (NH), 1781 (C=O), 1720 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.29 (s, 6H, 2 × $CH_3$), 3.80 (s, 3H, $OCH_3$), 3.82 (s, 3H, $OCH_3$), 4.73 (s, 2H, $CH_2$), 6.65 (s broad, 1H, NH), 6.70–6.75 (m, 1H, $H_{aro}$), 7.01–7.04 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 24.8 (2 × $CH_3$), 43.3 ($CH_2$), 55.8 ($OCH_3$), 56.0 ($OCH_3$), 58.7 (C), 111.2 ($CH_{aro}$), 116.8 ($CH_{aro}$), 123.2 ($C_{aro}$–S), 126.9 ($CH_{aro}$), 148.9 ($C_{aro}$–O), 149.5 ($C_{aro}$–O), 155.3 ($C_2$=O), 176.2 ($C_4$=O); MS (*m*/*z*: EI) 310 ($M^+$).

**General procedure for *N*-protection of 1-arylthiomethyl-5,5-dimethylhydantoin (3).** To a stirred solution of dry acetonitrile or THF (40 mL) under an atmosphere of dry argon containing 1-arylthiomethyl-5,5-dimethylhydantoin (**3**, 0.012 mol) was added in one portion $Boc_2O$ (3.14 g, 0.014 mol) and a catalytic amount of DMAP. After being stirred at room temperature for 12 to 24 h (the reaction was monitored by TLC using precoated plate of silica gel and $CH_2Cl_2$ as eluent), the reaction mixture was concentrated *in vacuo*. The crude resulting viscous oil was purified by column chromatography on silica gel with a mixture of cyclohexane–AcOEt (1 : 4) as eluent to give *N*-protected imides **4** in quantitative yields.

**3-$^t$Butyloxycarbonyl-5,5-dimethyl-1-phenylthiomethylhydantoin (4b).** This product was obtained as a white solid in 100% yield; mp 144 °C (cyclohexane); Found: C, 58.09; H, 6.08; N, 7.77. Calc. for $C_{17}H_{22}N_2O_4S$: C, 58.27; H, 6.33; N, 7.99%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1751 (C=O), 1742 (C=O), 1735 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.49 (s, 6H, 2 × $CH_3$), 1.53 (s, 9H, 3 × $CH_3$), 4.85 (s, 2H, $CH_2$), 7.27–7.30 (m, 3H, $H_{aro}$), 7.48–7.53 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.1 (2 × $CH_3$), 28.2 (3 × $CH_3$), 43.2 ($CH_2$), 63.2 (C), 84.4 (C($^t$Bu)), 128.5 ($CH_{aro}$), 129.2 (2 × $CH_{aro}$), 132.5 ($C_{aro}$–S), 133.1 (2 × $CH_{aro}$), 148.4 ($CO_2{}^t$Bu), 155.9 ($C_2$=O), 173.9 ($C_4$=O).

**1-(*o*-Bromophenyl)thiomethyl-3-$^t$butyloxycarbonyl-5,5-dimethylhydantoin (4c).** This product was obtained as a white solid in 98% yield; mp 89 °C (cyclohexane); Found: C, 47.39; H, 4.76; N, 6.39. Calc. for $C_{17}H_{21}BrN_2O_4S$: C, 47.56; H, 4.93; N, 6.52%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1755 (C=O), 1736 (C=O), 1732 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.51 (s, 6H, 2 × $CH_3$), 1.53 (s, 9H, 3 × $CH_3$), 4.89 (s, 2H, $CH_2$), 7.09–7.28 (m, 2H, $H_{aro}$), 7.56–7.65 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.0 (2 × $CH_3$), 28.0 (3 × $CH_3$), 42.3 ($CH_2$), 63.0 (C), 84.3 (C($^t$Bu)), 128.0 ($CH_{aro}$), 128.2 ($C_{aro}$–Br), 129.9 ($CH_{aro}$), 133.4 ($CH_{aro}$), 133.5 ($C_{aro}$–S), 134.6 ($CH_{aro}$), 148.3 ($CO_2{}^t$Bu), 150.6 ($C_2$=O), 173.7 ($C_4$=O).

**3-$^t$Butyloxycarbonyl-1-(*o*-methoxyphenyl)thiomethyl-5,5-dimethylhydantoin (4d).** This product was obtained as a white solid in 96% yield; mp 79 °C (diethyl ether–cyclohexane); Found: C, 56.77; H, 6.12; N, 7.20. Calc. for $C_{18}H_{24}N_2O_5S$: C, 56.82; H, 6.36; N, 7.36%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1751 (C=O), 1736 (C=O), 1722 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.42 (s, 6H, 2 × $CH_3$), 1.52 (s, 9H, 3 × $CH_3$), 3.92 (s, 3H, $OCH_3$), 4.86 (s, 2H, $CH_2$), 6.77–6.88 (m, 2H, $H_{aro}$), 7.26–7.43 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.0 (2 × $CH_3$), 28.2 (3 × $CH_3$), 41.0 ($CH_2$), 55.9 ($OCH_3$), 63.0 (C), 84.2 (C($^t$Bu)), 111.2 ($CH_{aro}$), 119.1 ($C_{aro}$–S), 120.7 ($CH_{aro}$), 131.0 ($CH_{aro}$), 136.0 ($CH_{aro}$), 148.5 ($CO_2{}^t$Bu), 150.8 ($C^q_{aro}$–O), 159.9 ($C_2$=O), 174.0 ($C_4$=O).

**3-$^t$Butyloxycarbonyl-1-(*m*-methoxyphenyl)thiomethyl-5,5-dimethylhydantoin (4e).** This product was obtained as a white solid in 100% yield; mp 82 °C (ethanol–diethyl ether); Found: C, 56.69; H, 6.09; N, 7.17. Calc. for $C_{18}H_{24}N_2O_5S$: C, 56.82; H, 6.36; N, 7.36%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1753 (C=O), 1737 (C=O), 1725 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.51 (s, 6H, 2 × $CH_3$), 1.53 (s, 9H, 3 × $CH_3$), 3.78 (s, 3H, $OCH_3$), 4.87 (s, 2H, $CH_2$), 6.80 (dd, 1H, $J$ = 2 and 8 Hz, $H_{aro}$), 7.04–7.08 (m, 2H, $H_{aro}$), 7.17 (dd, 1H, $J$ = 2 and 8 Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.0 (2 × $CH_3$), 28.1 (3 × $CH_3$), 42.8 ($CH_2$), 55.4 ($OCH_3$), 63.1 (C), 84.3 (C($^t$Bu)), 114.4 ($CH_{aro}$), 117.3 ($CH_{aro}$), 124.6 ($CH_{aro}$), 129.9 ($CH_{aro}$), 133.7 ($C_{aro}$–S), 148.4 ($CO_2{}^t$Bu), 150.7 ($C_{aro}$–O), 159.9 ($C_2$=O), 173.8 ($C_4$=O).

**3-$^t$Butyloxycarbonyl-1-(*p*-methoxyphenyl)thiomethyl-5,5-dimethylhydantoin (4f).** This product was obtained as a white solid in 100% yield; mp 123 °C (ethanol–diethyl ether); Found: C, 56.71; H, 6.13; N, 7.19. Calc. for $C_{18}H_{24}N_2O_5S$: C, 56.82; H, 6.36; N, 7.36%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1753 (C=O), 1736 (C=O), 1725 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.49 (s, 6H, 2 × $CH_3$), 1.53 (s, 9H, 3 × $CH_3$), 3.76 (s, 3H, $OCH_3$), 4.73 (s, 2H, $CH_2$), 6.81 (d, 2H, $J$ = 9 Hz, $H_{aro}$), 7.41 (d, 2H, $J$ = 9 Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.1 (2 × $CH_3$), 28.2 (3 × $CH_3$), 44.2 ($CH_2$), 55.4 ($OCH_3$), 63.1 (C), 84.3 (C($^t$Bu)), 114.8 (2 × $CH_{aro}$), 122.7 ($C_{aro}$–S), 136.1 (2 × $CH_{aro}$), 148.5 ($CO_2{}^t$Bu), 150.7 ($C_{aro}$–O), 160.4 ($C_2$=O), 173.8 ($C_4$=O).

**3-$^t$Butyloxycarbonyl-1-(*p*-chlorophenyl)thiomethyl-5,5-dimethylhydantoin (4g).** This product was obtained as a white solid in 100% yield; mp 114 °C (diethyl ether); Found: C, 52.86; H, 5.35; N, 7.11. Calc. for $C_{17}H_{21}ClN_2O_4S$: C, 53.05; H, 5.50; N, 7.28%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1752 (C=O), 1745 (C=O), 1737

(C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.50 (s, 6H, 2 × $CH_3$), 1.52 (s, 9H, 3 × $CH_3$), 4.82 (s, 2H, $CH_2$), 7.24 (d, 2H, $J$ = 9 Hz, $H_{aro}$), 7.42 (d, 2H, $J$ = 9 Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.1 (2 × $CH_3$), 28.1 (3 × $CH_3$), 43.2 ($CH_2$), 63.2 (C), 84.5 (C($^t$Bu)), 129.4 (2 × $CH_{aro}$), 131.0 ($C_{aro}$–Cl), 134.2 (2 × $CH_{aro}$), 134.7 ($C_{aro}$–S), 148.3 ($CO_2{}^t$Bu), 150.7 ($C_2$=O), 173.9 ($C_4$=O).

**3-$^t$Butyloxycarbonyl-5,5-dimethyl-1-(*β*-naphthyl)thiomethylhydantoin (4h).** This product was obtained as a white solid in 95% yield; mp 135 °C (diethyl ether–cyclohexane); Found: C, 62.78; H, 6.00; N, 6.84. Calc. for $C_{21}H_{24}N_2O_4S$: C, 62.98; H, 6.04; N, 6.99%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1756 (C=O), 1743 (C=O), 1736 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.44 (s, 6H, 2 × $CH_3$), 1.51 (s, 9H, 3 × $CH_3$), 4.94 (s, 2H, $CH_2$), 7.41–7.97 (m, 7H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.0 (2 × $CH_3$), 28.1 (3 × $CH_3$), 42.8 ($CH_2$), 63.1 (C), 84.3 (C($^t$Bu)), 126.6 ($CH_{aro}$), 126.7 ($CH_{aro}$), 127.6 ($CH_{aro}$), 127.8 ($CH_{aro}$), 128.9 ($CH_{aro}$), 129.7 ($CH_{aro}$), 131.9 ($CH_{aro}$), 132.7 ($C_{aro}$–S), 133.5 (2 × $C_{aro}$–C), 148.3 ($CO_2{}^t$Bu), 150.7 ($C_2$=O), 173.8 ($C_4$=O).

**3-$^t$Butyloxycarbonyl-1-(*m*,*p*-dimethoxyphenyl)thiomethyl-5,5-dimethylhydantoin (4i).** This product was obtained as a white solid in 94% yield; mp 125 °C (ethanol–diethyl ether and then cyclohexane); Found: C, 55.42; H, 6.22; N, 6.68. Calc. for $C_{19}H_{26}N_2O_6S$: C, 55.59; H, 6.38; N, 6.82%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1752 (C=O), 1745 (C=O), 1736 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.48 (s, 6H, 2 × $CH_3$), 1.52 (s, 9H, 3 × $CH_3$), 3.82 (s, 3H, $OCH_3$), 3.84 (s, 3H, $OCH_3$), 4.78 (s, 2H, $CH_2$), 6.72–6.76 (m, 1H, $H_{aro}$), 7.02–7.07 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.1 (2 × $CH_3$), 28.1 (3 × $CH_3$), 43.8 ($CH_2$), 56.0 ($OCH_3$), 56.1 ($OCH_3$), 63.1 (C), 84.4 (C($^t$Bu)), 111.4 ($CH_{aro}$), 116.7 ($CH_{aro}$), 123.0 ($C_{aro}$–S), 127.0 ($CH_{aro}$), 148.4 ($C_{aro}$–O), 149.1 ($C_{aro}$–O), 149.8 ($CO_2{}^t$Bu), 150.7 ($C_2$=O), 173.8 ($C_4$=O).

**General procedure for *N*-alkylation of 5,5-dimethyl-1-phenylthiomethylhydantoin (3a).** To a stirred mixture of 5,5-dimethyl-1-phenylthiomethylhydantoin (**3a**, 5 g, 20 mmol) and 18-C-6 (1% *w*/*w*) in 50 mL of dry toluene were added solid potassium carbonate (2.92 g, 22 mmol) and 0.1 equiv. per mmol of potassium iodide. After stirring for 25 min, 24 mmol of methyl iodide or benzyl bromide in 50 mL of dry toluene was added dropwise over a period of 20 min. The mixture was then refluxed for 24 h and cooled. After filtration over a short column of celite, the organic phase was concentrated under reduced pressure and the crude resulting solid was purified by flash chromatography on silica gel with dichloromethane as eluent to give *N*-alkylated imide **4j** or **4k**. Recrystallization from ethanol afforded pure **4j** or **4k** in 91 and 97%, respectively.

**3,5,5-Trimethyl-1-phenylthiomethylhydantoin (4j).** This product was isolated as white prisms in 91% yield; mp 73 °C (cyclohexane); Found: C, 58.87; H, 6.00; N, 10.45. Calc. for $C_{13}H_{16}N_2O_2S$: C, 59.07; H, 6.10; N, 10.60%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1772 (C=O), 1718 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.26 (s, 6H, 2 × $CH_3$), 2.83 (s, 3H, $CH_3$), 4.84 (s, 2H, $CH_2$), 7.25–7.33 (m, 3H, $H_{aro}$), 7.46–7.52 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 21.9 (2 × $CH_3$), 24.4 ($CH_3$), 42.8 ($CH_2$), 61.2 (C), 128.0 ($CH_{aro}$), 128.2 ($C_{aro}$–S), 129.0 (2 × $CH_{aro}$), 132.8 (2 × $CH_{aro}$), 153.8 ($C_2$=O), 175.5 ($C_4$=O); MS (*m*/*z*: EI) 264 ($M^+$).

**3-Benzyl-5,5-dimethyl-1-phenylthiomethylhydantoin (4k).** This product was isolated as white crystal in 97% yield; mp 97 °C (cyclohexane–diethyl ether); Found: C, 66.94; H, 5.81; N, 8.16. Calc. for $C_{19}H_{20}N_2O_2S$: C, 67.03; H, 5.92; N, 8.23%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1772 (C=O), 1716 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.14 (s, 6H, 2 × $CH_3$), 4.45 (s, 2H, $CH_2$), 4.89 (s, 2H, $CH_2$), 7.16–7.36 (m, 8H, $H_{aro}$), 7.51–7.55 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.3 (2 × $CH_3$), 43.0 ($CH_2$), 43.2 ($CH_2$), 62.2 (C), 127.8 ($CH_{aro}$), 127.9 (2 × $CH_{aro}$), 128.3 ($CH_{aro}$), 128.7 (2 × $CH_{aro}$), 129.1 (2 × $CH_{aro}$), 132.5 ($C_{aro}$–S), 133.4 (2 × $CH_{aro}$), 137.7 ($C_{aro}$–C), 154.5 ($C_2$=O), 175.5 ($C_4$=O); MS (*m*/*z*: EI) 340 ($M^+$).

**General procedure for regioselective reduction of *N*-protected-*N*-arylthiomethylhydantoin (3a = 4a and 4b–k).** To a well stirred solution of *N*-protected-*N*-arylthiomethylhydantoin (**4**, 6 mmol) in dry ethanol (60 mL) was added in portions at ambient temperature sodium borohydride (1.37 g, 36 mmol) over a period of 5 min. After complete reaction (12 to 48 h; the reaction was monitored by TLC using precoated plate of silica gel and $CH_2Cl_2$ as eluent), the excess of sodium borohydride was decomposed by careful addition of 10% HCl solution to pH = 3. After removal of the solvent under reduced pressure, the residue was diluted with $H_2O$ (40 mL) and extracted with 2 × 30 mL of $CH_2Cl_2$. The organic phase was separated, dried with $MgSO_4$, filtered and concentrated under reduced pressure, to give a solid, which was recrystallized from suitable solvent to give corresponding 5-hydroxyimidazolidinone **5** in good yields.

**4-Hydroxy-5,5-dimethyl-1-phenylthiomethylimidazolidin-2-one (5a).** This product was isolated as white crystals in 93% yield; mp 166 °C (ethanol–water); Found: C, 57.01; H, 6.14; N, 10.98. Calc. for $C_{12}H_{16}N_2O_2S$: C, 57.12; H, 6.39; N, 11.10%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3277 (NH and OH), 1698 (C=O); $^1$H NMR (300 MHz, DMSO $d_6$) $\delta$ 0.90 (s, 3H, $CH_3$), 1.05 (s, 3H, $CH_3$), 4.32 (d, 1H, $J$ = 13 Hz, $CH_2$), 4.60 (d, 1H, $J$ = 7 Hz, CH), 5.08 (d, 1H, $J$ = 13 Hz, $CH_2$), 6.07 (d, 1H, $J$ = 7 Hz, CH), 6.79 (s broad, 1H, NH), 7.17–7.30 (m, 3H, $H_{aro}$), 7.33–7.44 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, DMSO $d_6$) $\delta$ 21.9 ($CH_3$), 27.7 ($CH_3$), 43.9 ($CH_2$), 55.3 (C), 84.0 (CH), 126.4 ($CH_{aro}$), 129.0 (2 × $CH_{aro}$), 129.8 (2 × $CH_{aro}$), 134.5 ($C_{aro}$–S), 157.4 (C=O).

**3-$^t$Butyloxycarbonyl-4-hydroxy-5,5-dimethyl-1-phenylthiomethylimidazolidin-2-one (5b).** This product was isolated as white crystals in 89% yield; mp 140 °C (ethanol); Found: C, 57.59; H, 6.68; N, 7.80. Calc. for $C_{17}H_{24}N_2O_4S$: C, 57.93; H, 6.86; N, 7.95%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3399 (OH), 1770 (C=O), 1759 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.09 (s, 3H, $CH_3$), 1.46 (s, 3H, $CH_3$), 1.48 (s, 9H, 3 × $CH_3$), 3.64 (d, 1H, $J$ = 11 Hz, OH), 4.53 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.64 (d, 1H, $J$ = 11 Hz, CH), 5.22 (d, 1H, $J$ = 14 Hz, $CH_2$), 7.18–7.42 (m, 5H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 20.6 ($CH_3$), 24.9 ($CH_3$), 28.3 (3 × $CH_3$), 44.6 ($CH_2$), 61.7 (C), 82.9 (C($^t$Bu)), 83.8 (CH), 127.1 ($CH_{aro}$), 129.3 (2 × $CH_{aro}$), 130.2 (2 × $CH_{aro}$), 133.7 ($C_{aro}$–S), 150.3 ($CO_2{}^t$Bu), 153.1 (C=O).

**1-(*o*-Bromophenyl)thiomethyl-3-$^t$butyloxycarbonyl-4-hydroxy-5,5-dimethylimidazolidin-2-one (5c).** This product was isolated as yellow crystals in 70% yield; mp < 40 °C (diethyl ether); Found: C, 47.22; H, 5.19; N, 6.21. Calc. for $C_{17}H_{23}BrN_2O_4S$: C, 47.34; H, 5.37; N, 6.49%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3400 (OH), 1765 (C=O), 1758 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.11 (s, 3H, $CH_3$), 1.48 (s, 12H, 4 × $CH_3$), 3.81 (d, 1H, $J$ = 11 Hz, OH), 4.56 (d, 1H, $J$ = 15 Hz, $CH_2$), 4.67 (d, 1H, $J$ = 11 Hz, CH), 5.26 (d, 1H, $J$ = 15 Hz, $CH_2$), 6.98–7.07 (m, 1H, $H_{aro}$), 7.23–7.30 (m, 1H, $H_{aro}$), 7.44–7.52 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 20.6 ($CH_3$), 24.9 ($CH_3$), 28.3 (3 × $CH_3$), 43.8 ($CH_2$), 61.8 (C), 83.1 (C($^t$Bu)), 83.6 (CH), 124.3 ($C_{aro}$–Br), 127.8 ($CH_{aro}$), 128.3 ($CH_{aro}$), 129.9 ($CH_{aro}$), 133.2 ($CH_{aro}$), 135.2 ($C^q_{aro}$–S), 150.4 ($CO_2{}^t$Bu), 153.3 (C=O).

**3-$^t$Butyloxycarbonyl-4-hydroxy-1-(*o*-methoxyphenyl)thiomethyl-5,5-dimethylimidazolidin-2-one (5d).** This product was isolated as yellow crystals in 86% yield; mp 144 °C (ethanol–diethyl ether); Found: C, 56.41; H, 6.77; N, 7.18. Calc. for $C_{18}H_{26}N_2O_5S$: C, 56.52; H, 6.85; N, 7.32%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3406 (OH), 1765 (C=O), 1758 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.13 (s, 3H, $CH_3$), 1.46 (s, 12H, 4 × $CH_3$), 3.85 (d, 1H, $J$ = 11 Hz, OH), 3.88 (s, 3H, $OCH_3$), 4.52 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.65 (d, 1H, $J$ = 11 Hz, CH), 5.18 (d, 1H, $J$ = 14 Hz, $CH_2$), 6.82–6.70 (m, 2H, $H_{aro}$), 7.17–7.26 (m, 1H, $H_{aro}$), 7.36–7.40 (m, 1H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 20.5 ($CH_3$), 24.9 ($CH_3$), 28.3 (3 × $CH_3$), 43.4 ($CH_2$), 55.9 ($OCH_3$), 61.6 (C), 82.8 (C($^t$Bu)), 84.0 (CH), 111.0 ($CH_{aro}$), 120.9 ($C_{aro}$–S), 121.2 ($CH_{aro}$), 129.2

($CH_{aro}$), 132.8 ($CH_{aro}$), 150.3 ($CO_2{}^tBu$), 152.9 ($C_{aro}$–O), 158.4 (C=O).

**3-$^t$Butyloxycarbonyl-4-hydroxy-1-(*m*-methoxyphenyl)thiomethyl-5,5-dimethylimidazolidin-2-one (5e).** This product was isolated after a second chromatography purification as yellow crystals in 86% yield; mp 69 °C (ethanol–diethyl ether); Found: C, 56.38; H, 6.79; N, 7.20. Calc. for $C_{18}H_{26}N_2O_5S$: C, 56.52; H, 6.85; N, 7.32%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3403 (OH), 1759 (C=O), 1720 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.12 (s, 3H, $CH_3$), 1.46 (s, 3H, $CH_3$), 1.48 (s, 9H, 3 × $CH_3$), 3.72 (d, 1H, $J$ = 10 Hz, OH), 3.76 (s, 3H, $OCH_3$), 4.53 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.65 (d, 1H, $J$ = 10 Hz, CH), 5.21 (d, 1H, $J$ = 14 Hz, $CH_2$), 6.72 (dd, 1H, $J$ = 2 and 8 Hz, $H_{aro}$), 6.94–7.13 (m, 2H, $H_{aro}$), 7.13–7.22 (m, 1H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 20.5 ($CH_3$), 24.9 ($CH_3$), 28.3 (3 × $CH_3$), 44.4 ($CH_2$), 55.5 ($OCH_3$), 61.7 (C), 82.9 (C($^t$Bu)), 83.8 (CH), 113.4 ($CH_{aro}$), 114.7 ($CH_{aro}$), 122.0 ($CH_{aro}$), 130.2 ($CH_{aro}$), 135.0 ($C_{aro}$–S), 150.3 ($CO_2{}^tBu$), 153.0 ($C_{aro}$–O), 160.0 (C=O).

**3-$^t$Butyloxycarbonyl-4-hydroxy-1-(*p*-methoxyphenyl)thiomethyl-5,5-dimethylimidazolidin-2-one (5f).** This product was isolated as a white crystal in 93% yield; mp 66 °C (cyclohexane–diethyl ether); Found: C, 56.40; H, 6.73; N, 7.16. Calc. for $C_{18}H_{26}N_2O_5S$: C, 56.52; H, 6.85; N, 7.32%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3400 (OH), 1768 (C=O), 1758 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.15 (s, 3H, $CH_3$), 1.46 (s, 12H, 4 × $CH_3$), 3.75 (s, 3H, $OCH_3$), 4.41 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.62 (s, 1H, CH), 5.04 (d, 1H, $J$ = 14 Hz, $CH_2$), 6.50 (s broad, 1H, OH), 6.79 (d, 2H, $J$ = 9 Hz, $H_{aro}$), 7.35 (d, 2H, $J$ = 9 Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 20.6 ($CH_3$), 25.0 ($CH_3$), 28.2 (3 × $CH_3$), 46.1 ($CH_2$), 55.4 ($OCH_3$), 61.6 (C), 82.8 (C($^t$Bu)), 83.7 (CH), 114.8 (2 × $CH_{aro}$), 123.8 ($C_{aro}$–S), 133.6 (2 × $CH_{aro}$), 150.3 ($CO_2{}^tBu$), 153.1 ($C_{aro}$–O), 159.4 (C=O).

**3-$^t$Butyloxycarbonyl-1-(*p*-chlorophenyl)thiomethyl-4-hydroxy-5,5-dimethylimidazolidin-2-one (5g).** This product was isolated as white crystals in 92% yield; mp 139 °C (ethanol–diethyl ether); Found: C, 52.56; H, 5.79; N, 7.05. Calc. for $C_{17}H_{23}ClN_2O_4S$: C, 52.77; H, 5.99; N, 7.24%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3391 (OH), 1769 (C=O), 1760 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.10 (s, 3H, $CH_3$), 1.46 (s, 3H, $CH_3$), 1.47 (s, 9H, 3 × $CH_3$), 4.11 (d, 1H, $J$ = 11 Hz, OH), 4.51 (d, 1H, $J$ = 15 Hz, $CH_2$), 4.62 (d, 1H, $J$ = 11 Hz, CH), 5.19 (d, 1H, $J$ = 15 Hz, $CH_2$), 7.22 (d, 2H, $J$ = 9 Hz, $H_{aro}$), 7.33 (d, 2H, $J$ = 9 Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 20.6 ($CH_3$), 24.9 ($CH_3$), 28.3 (3 × $CH_3$), 44.4 ($CH_2$), 61.8 (C), 83.1 (C($^t$Bu)), 83.6 (CH), 129.4 (2 × $CH_{aro}$), 131.2 (2 × $CH_{aro}$), 132.3 ($C_{aro}$–Cl), 132.9 ($C_{aro}$–S), 150.3 ($CO_2{}^tBu$), 153.3 (C=O).

**3-$^t$Butyloxycarbonyl-4-hydroxy-5,5-dimethyl-1-(*β*-naphthyl)-thiomethylimidazolidin-2-one (5h).** This product was isolated as white crystals in 90% yield; mp 125 °C (cyclohexane–diethyl ether); Found: C, 62.53; H, 6.42; N, 6.79. Calc. for $C_{21}H_{26}N_2O_4S$: C, 62.66; H, 6.51; N, 6.96%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3400 (OH), 1767 (C=O), 1758 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.07 (s, 3H, $CH_3$), 1.45 (s, 12H, 4 × $CH_3$), 3.82 (d, 1H, $J$ = 11 Hz, OH), 4.61 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.67 (d, 1H, $J$ = 11 Hz, CH), 5.31 (d, 1H, $J$ = 14 Hz, $CH_2$), 7.38–7.51 (m, 3H, $H_{aro}$), 7.70–7.87 (m, 4H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 20.6 ($CH_3$), 24.9 ($CH_3$), 28.2 (3 × $CH_3$), 44.5 ($CH_2$), 61.7 (C), 82.9 (C($^t$Bu)), 83.7 (CH), 126.1 ($CH_{aro}$), 126.6 ($CH_{aro}$), 127.4 ($CH_{aro}$), 127.6 ($CH_{aro}$), 127.8 ($CH_{aro}$), 128.9 ($CH_{aro}$), 129.0 ($CH_{aro}$), 131.0 ($C_{aro}$–S), 132.1 ($C^q{}_{aro}$–C), 133.7 ($C_{aro}$–C), 150.3 ($CO_2{}^tBu$), 153.2 (C=O).

**3-$^t$Butyloxycarbonyl-4-hydroxy-1-(*m*,*p*-dimethoxyphenyl)-thiomethyl-5,5-dimethylimidazolidin-2-one (5i).** This product was isolated as white crystals in 100% yield; mp 130 °C (diethyl ether); Found: C, 55.21; H, 6.70; N, 6.55. Calc. for $C_{19}H_{28}N_2O_6S$: C, 55.32; H, 6.84; N, 6.79%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3392 (OH), 1770 (C=O), 1757 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.14 (s, 3H, $CH_3$), 1.46 (s, 12H, 4 × $CH_3$), 3.83 (d, 1H, $J$ = 10 Hz, OH), 3.84 (s, 6H, 2 × $OCH_3$), 4.45 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.62 (d, 1H, $J$ = 10 Hz, CH), 5.10 (d, 1H, $J$ = 14 Hz, $CH_2$), 6.73–6.78 (m, 1H, $H_{aro}$), 6.95–6.99 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 20.5 ($CH_3$), 25.0 ($CH_3$), 28.3 (3 × $CH_3$), 45.7 ($CH_2$), 56.0 ($OCH_3$), 56.1 ($OCH_3$), 61.6 (C), 82.9 (C($^t$Bu)), 83.8 (CH), 111.7 ($CH_{aro}$), 114.6 ($CH_{aro}$), 124.2 ($C_{aro}$–S), 124.3 ($CH_{aro}$), 148.8 ($C_{aro}$–O), 149.3 ($C_{aro}$–O), 150.3 ($CO_2{}^tBu$), 153.0 (C=O).

**4-Hydroxy-3,5,5-trimethyl-1-phenylthiomethylimidazolidin-2-one (5j).** This product was isolated as white crystals in 89% yield; mp 98 °C (diethyl ether–pentane); Found: C, 58.39; H, 6.69; N, 10.41. Calc. for $C_{13}H_{18}N_2O_2S$: C, 58.62; H, 6.81; N, 10.52%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3345 (OH), 1701 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.91 (s, 3H, $CH_3$), 1.20 (s, 3H, $CH_3$), 2.61 (s, 3H, $CH_3$), 3.20 (d, 1H, $J$ = 10 Hz, OH), 4.48 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.74 (d, 1H, $J$ = 10 Hz, CH), 5.17 (d, 1H, $J$ = 14 Hz, $CH_2$), 7.18–7.31 (m, 3H, $H_{aro}$), 7.40–7.45 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.1 ($CH_3$), 23.3 ($CH_3$), 24.6 ($CH_3$), 45.1 ($CH_2$), 59.8 (C), 83.4 (CH), 127.0 ($CH_{aro}$), 129.1 (2 × $CH_{aro}$), 130.6 (2 × $CH_{aro}$), 134.1 ($C_{aro}$–S), 157.1 (C=O).

**3-Benzyl-4-hydroxy-5,5-dimethyl-1-phenylthiomethylimidazolidin-2-one (5k).** This product was isolated as white crystals in 84% yield; mp 161 °C (diethyl ether–pentane); Found: C, 66.49; H, 6.31; N, 8.02. Calc. for $C_{19}H_{22}N_2O_2S$: C, 66.64; H, 6.48; N, 8.18%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3280 (OH), 1679 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.72 (s, 3H, $CH_3$), 1.07 (s, 3H, $CH_3$), 2.71 (d, 1H, $J$ = 9 Hz, OH), 4.12 (d, 1H, $J$ = 16 Hz, $CH_2$), 4.31 (d, 1H, $J$ = 16 Hz, $CH_2$), 4.44 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.72 (d, 1H, $J$ = 9 Hz, CH), 5.26 (d, 1H, $J$ = 14 Hz, $CH_2$), 7.07–7.31 (m, 8H, $H_{aro}$), 7.40–7.44 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.9 ($CH_3$), 25.4 ($CH_3$), 43.2 ($CH_2$), 45.4 ($CH_2$), 60.5 (C), 84.8 (CH), 127.1 (2 × $CH_{aro}$), 127.7 ($CH_{aro}$), 128.5 ($CH_{aro}$), 128.7 (2 × $CH_{aro}$), 129.2 (2 × $CH_{aro}$), 130.6 ($C_{aro}$–S), 131.1 (2 × $CH_{aro}$), 139.4 ($C_{aro}$–C), 157.1 ($C_2$=O).

**General procedure for cyclisation of 5-hydroxyimidazolidinones 5.** To a stirred and cold solution of 5-hydroxyimidazolidinone **5** (2.5 mmol) was added neat TFA (4 mL). After 24 h of reaction at room temperature under stirring, the reaction mixture was diluted with water (5 mL) and $CH_2Cl_2$ (10 mL) and neutralized with 10% NaOH aqueous solution. The solution was extracted twice with $CH_2Cl_2$ (10 mL). The organic layer was washed with water, separated, dried over $MgSO_4$ and evaporated. The resulting residue was purified by flash chromatography ($SiO_2$, $CH_2Cl_2$–hexane (9 : 1)) to give the tricyclic product **6** as white crystals in 21 to 91% yields.

**2,3,3*a*,9-Tetrahydro-3,3-dimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6a).** This product was isolated as white crystals in 56–92% yield; mp 162 °C (diethyl ether–pentane); Found: C, 61.35; H, 5.85; N, 11.79. Calc. for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02; N, 11.96%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3249 (NH), 1703 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.40 (s, 3H, $CH_3$), 1.43 (s, 3H, $CH_3$), 4.30 (d, 1H, $J$ = 17 Hz, $CH_2$), 4.81 (s, 1H, CH), 4.87 (d, 1H. $J$ = 17 Hz, $CH_2$), 5.13 (s broad, 1H, NH), 7.08–7.22 (m, 4H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.9 ($CH_3$), 28.7 ($CH_3$), 43.9 ($CH_2$), 55.8 (C), 69.2 (CH), 125.8 ($CH_{aro}$), 127.1 ($CH_{aro}$), 127.9 ($CH_{aro}$), 129.3 ($CH_{aro}$), 130.6 ($C_{aro}$–S), 131.8 ($C_{aro}$–C), 159.7 (C=O); MS (*m*/*z*: EI) 234 ($M^+$).

**X-Ray crystallographic analysis of benzothiazinone (6a)‡.** $C_{12}H_{14}N_2OS$, Mr = 234.31, monoclinic, $P2_1/c$, $a$ = 7.569(2), $b$ = 18.652(2), $c$ = 8.388(2) Å, $\beta$ = 103.69(3)°, $V$ = 1150.6(7) Å$^{-3}$, $Z$ = 4, $D_x$ = 1.353 mg m$^{-3}$, $\lambda$ (Mo K$\alpha$) = 0.71073 Å, $\mu$ = 2.61 cm$^{-1}$, $F(000)$ = 496, $T$ = 293 K. The sample (0.45*0.32*0.32 mm) is studied on an automatic diffractometer CAD4 NONIUS

‡ CCDC reference numbers 266273–266274. For crystallographic data in CIF format see DOI: 10.1039/b508214e

with graphite monochromatized Mo Kα radiation.[16] The cell parameters are obtained by fitting a set of 25 high-theta reflections. The data collection ($2\theta_{max} = 54°$, scan $\omega/2\theta = 1$, $t_{max} = 60$ s, range HKL: H 0,9 K 0,23 L-10,10) gives 2687 unique reflections from which 1868 with $I > 2.0\sigma(I)$. After Lorenz and polarization corrections[17] the structure was solved with SIR-97[18] which reveals the non hydrogen atoms of the compound. After anisotropic refinement a Fourier difference reveals many hydrogen atoms. The whole structure was refined with SHELXL97 by the full-matrix least-square techniques (use of $F$ square magnitude; $x, y, z, \beta_{ij}$ for S, C, O and N atoms, $x, y, z$ in riding mode for H atoms; 149 variables and 2505 observations; calc. $w = 1/[\sigma^2(Fo^2)+(0.057P)^2]$ where $P = (Fo^2 + 2Fc^2)/3$ with the resulting $R = 0.035$, $Rw = 0.094$ and $Sw = 1.043$ (residual $\Delta\rho \leq 0.27$ eÅ$^{-3}$).

Atomic scattering factors from International Tables for X-ray Crystallography (1992). Ortep views realized with PLATON98[20] and Ortep-3 for Windows.[21] All the calculations were performed on a Pentium NT Server computer. See the electronic supplementary information for further data for compound **6a**.

**5-Bromo-2,3,3*a*,9-tetrahydro-3,3-dimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6c).** This product was isolated as white crystals in 21% yield; mp 184 °C (ethanol); Found: C, 45.87; H, 4.07; N, 8.84. Calc. for $C_{12}H_{13}BrN_2OS$: C, 46.02; H, 4.18; N, 8.94%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3249 (NH), 1703 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.41 (s, 3H, $CH_3$), 1.49 (s, 3H, $CH_3$), 4.24 (d, 1H, $J = 17$ Hz, $CH_2$), 4.82 (s, 1H, CH), 4.88 (d, 1H, $J = 17$ Hz, $CH_2$), 5.03 (s broad, 1H, NH), 6.94–7.12 (m, 2H, $H_{aro}$), 7.41–7.45 (m, 1H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.7 ($CH_3$), 28.6 ($CH_3$), 43.9 ($CH_2$), 55.9 (C), 69.3 (CH), 123.6 ($C_{aro}$–Br), 126.1 ($CH_{aro}$), 126.5 ($CH_{aro}$), 131.1 ($CH_{aro}$), 132.5 ($C_{aro}$–S), 133.1 ($C_{aro}$–C), 159.1 (C=O); MS ($m/z$: EI) 311 ($M^+$).

**2,3,3*a*,9-Tetrahydro-5-methoxy-3,3-dimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6d).** This product was isolated as yellow crystals in 29% yield; mp 182 °C (ethanol–diethyl ether); Found: C, 58.91; H, 5.87; N, 10.36. Calc. for $C_{13}H_{16}N_2O_2S$: C, 59.07; H, 6.10; N, 10.60%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3260 (NH), 1698 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.38 (s, 3H, $CH_3$), 1.47 (s, 3H, $CH_3$), 3.86 (s, 3H, $OCH_3$), 4.30 (d, 1H, $J = 17$ Hz, $CH_2$), 4.73 (s, 1H, CH), 4.87 (d, 1H, $J = 17$ Hz, $CH_2$), 5.35 (s broad, 1H, NH), 6.66 (d, 1H, $J = 7$ Hz, $H_{aro}$), 6.76 (d, 1H, $J = 7$ Hz, $H_{aro}$), 7.07 (t, 1H, $J = 7$ Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 23.7 ($CH_3$), 28.7 ($CH_3$), 43.4 ($CH_2$), 55.8 (C), 56.1 ($OCH_3$), 67.8 (CH), 108.3 ($CH_{aro}$), 120.1 ($CH_{aro}$), 120.5 ($C_{aro}$–S), 125.5 ($CH_{aro}$), 130.9 ($C_{aro}$–C), 155.9 ($C_{aro}$–O), 159.5 (C=O); MS ($m/z$: EI) 264 ($M^+$).

**2,3,3*a*,9-Tetrahydro-8-methoxy-3,3-dimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6e).** This product was isolated as white prisms in 77% yield; mp 176 °C (ethanol–diethyl ether); Found: C, 58.88; H, 5.95; N, 10.50. Calc. for $C_{13}H_{16}N_2O_2S$: C, 59.07; H, 6.10; N, 10.60%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3425 (NH), 1709 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.76 (s, 3H, $CH_3$), 1.48 (s, 3H, $CH_3$), 3.77 (s, 3H, $OCH_3$), 4.15 (d, 1H, $J = 12$ Hz, $CH_2$), 4.67 (s broad, 1H, NH), 4.80 (s, 1H, CH), 5.01 (d, 1H, $J = 12$ Hz, $CH_2$), 6.69–6.77 (m, 2H, $H_{aro}$), 6.98 (d, 1H, $J = 8$ Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 24.9 ($CH_3$), 28.4 ($CH_3$), 42.2 ($CH_2$), 55.4 ($OCH_3$), 60.2 (C), 64.8 (CH), 112.8 ($CH_{aro}$), 114.2 ($CH_{aro}$), 121.6 ($C_{aro}$–S), 128.9 ($CH_{aro}$), 135.1 ($C_{aro}$–C), 158.3 ($C_{aro}$–O), 159.6 (C=O); MS ($m/z$: EI) 264 ($M^+$).

**2,3,3*a*,9-Tetrahydro-3,3-dimethylimidazo[5,1-*b*][1,3]naphthen-1-one (6h).** This product was isolated as white crystals in 61% yield; mp 260 °C (ethanol–DMF); Found: C, 67.33; H, 5.54; N, 9.77. Calc. for $C_{16}H_{16}N_2OS$: C, 67.58; H, 5.67; N, 9.85%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3199 (NH), 1727 (C=O); $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 0.42 (s, 3H, $CH_3$), 1.52 (s, 3H, $CH_3$), 4.19 (d, 1H, $J = 12$ Hz, $CH_2$), 4.94 (d, 1H, $J = 12$ Hz, $CH_2$), 5.83 (s, 1H, CH), 7.24 (s broad, 1H, NH), 7.32 (d, 1H, $J = 9$ Hz, $H_{aro}$), 7.45–7.60 (m, 2H, $H_{aro}$), 7.76 (d, 1H, $J = 9$ Hz, $H_{aro}$), 7.91 (d, 1H, $J = 8$ Hz, $H_{aro}$), 8.04 (d, 1H, $J = 8$ Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 25.1 ($CH_3$), 29.8 ($CH_3$), 43.5 ($CH_2$), 59.2 (C), 61.2 (CH), 122.8 ($CH_{aro}$), 125.3 ($C_{aro}$–C), 125.4 ($CH_{aro}$), 126.6 ($CH_{aro}$), 127.2 ($CH_{aro}$), 128.2 ($CH_{aro}$), 128.9 ($CH_{aro}$), 131.9 ($C_{aro}$–C), 132.2 ($C_{aro}$–C), 133.7 ($C_{aro}$–S), 158.9 (C=O); MS ($m/z$: EI) 284 ($M^+$).

**2,3,3*a*,9-Tetrahydro-6,7-dimethoxy-3,3-dimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6i).** This product was isolated as white crystals in 55% yield; mp 207 °C (ethanol); Found: C, 57.01; H, 6.03; N, 9.36. Calc. for $C_{14}H_{18}N_2O_3S$: C, 57.12; H, 6.16; N, 9.52%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3234 (NH), 1704 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.77 (s, 3H, $CH_3$), 1.50 (s, 3H, $CH_3$), 3.82 (s, 6H, 2 × $OCH_3$), 4.09 (d, 1H, $J = 13$ Hz, $CH_2$), 4.74 (s, 1H, CH), 4.98 (d, 1H, $J = 13$ Hz, $CH_2$), 5.47 (s broad, 1H, NH), 6.51 (s, 1H, $H_{aro}$), 6.68 (s, 1H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 24.8 ($CH_3$), 28.5 ($CH_3$), 42.5 ($CH_2$), 56.0 ($OCH_3$), 56.2 ($OCH_3$), 60.2 (C), 65.0 (CH), 110.8 ($CH_{aro}$), 112.5 ($CH_{aro}$), 121.3 ($C_{aro}$–S), 125.3 ($C_{aro}$–C), 147.4 ($C_{aro}$–O), 148.3 ($C_{aro}$–O), 159.6 (C=O); MS ($m/z$: EI) 294 ($M^+$).

**Procedure for *N*-protection of *N*,*S*-acetal cyclic compound 6a by Boc group; access to 2-$^t$butyloxycarbonyl-2,3,3*a*,9-tetrahydro-2,3,3-trimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6b).** According to the typical procedure reported above for *N*-protected imide **4**, this product was obtained in quantitative yield as a white–yellow solid by reaction of 2,3,3*a*,9-tetrahydro-3,3-dimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one **6a** with $Boc_2O$ and melted at 140 °C (diethyl ether–cyclohexane); Found: C, 61.00; H, 6.44; N, 8.25. Calc. for $C_{17}H_{22}N_2O_3S$: C, 61.05; H, 6.63; N, 8.38%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1706 (C=O), 1698 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 01.53 (s, 9H, 3 × $CH_3$), 1.55 (s, 3H, $CH_3$), 1.67 (s, 3H, $CH_3$), 4.32 (d, 1H, $J = 17$ Hz, $CH_2$), 4.78 (s, 1H, CH), 4.98 (d, 1H, $J = 17$ Hz, $CH_2$), 7.11–7.16 (m, 4H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 22.5 ($CH_3$), 25.8 ($CH_3$), 28.2 (3 × $CH_3$), 43.9 ($CH_2$), 60.3 (C), 67.5 (CH), 82.9 (C($^t$Bu)), 126.0 ($CH_{aro}$), 127.3 ($CH_{aro}$), 127.8 ($CH_{aro}$), 129.2 ($CH_{aro}$), 129.6 ($C_{aro}$), 131.2 ($C_{aro}$), 149.7 ($CO_2{}^t$Bu), 150.4 (C=O), 153.5 (C=O).

**General procedure for *N*-alkylation of 2,3,3*a*,9-tetrahydro-3,3-dimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6a); access to tricyclic systems 6j and 6k.** To a stirred solution under an atmosphere of dry argon of 2,3,3*a*,9-tetrahydro-3,3-dimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (**6a**, 702 mg, 3 mmol) in 30 mL of dry THF was added in three portions (86.4 mg, 3.6 mmol) of sodium hydride (60% in mineral oil). After stirring for 35 min at room temperature, methyl iodide (3.6 mmol) or benzyl chloride (3.6 mmol) in 15 mL of the same solvent was added slowly dropwise over a period of 15 min. The mixture was then allowed to react at ambient temperature for 60 h. After cooling, the solution was poured onto water and the precipitate formed was filtered and dried. The resultant solid was recrystallized from ethanol to give the *N*-alkylated cyclic derivative **6j** (62% yield) and **6k** (58% yield).

**2,3,3*a*,9-Tetrahydro-2,3,3-trimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6j).** This product was isolated as white crystals in 62% yield; mp 98 °C (diethyl ether); Found: C, 62.66; H, 6.25; N, 11.09. Calc. for $C_{13}H_{16}N_2OS$: C, 62.87; H, 6.49; N, 11.28%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1694 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.28 (s, 3H, $CH_3$), 1.41 (s, 3H, $CH_3$), 2.74 (s, 3H, $CH_3$), 4.28 (d, 1H, $J = 17$ Hz, $CH_2$), 4.82 (s, 1H, CH), 4.88 (d, 1H, $J = 17$ Hz. $CH_2$), 7.07–7.18 (m, 4H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 21.5 ($CH_3$), 23.6 ($CH_3$), 24.8 ($CH_3$), 44.4 ($CH_2$), 58.8 (C), 68.5 (CH), 125.8 ($CH_{aro}$), 127.1 ($CH_{aro}$), 127.9 ($CH_{aro}$), 129.3 ($CH_{aro}$), 130.9 ($C_{aro}$–S), 131.9 ($C_{aro}$–C), 158.5 (C=O); MS ($m/z$: EI) 248 ($M^+$).

**2-Benzyl-2,3,3*a*,9-tetrahydro-3,3-dimethylimidazo[5,1-*b*][1,3]-benzothiazin-1-one (6k).** This product was isolated as white crystals in 58% yield; mp 112 °C (cyclohexane); Found: C, 70.20; H, 6.08; N, 8.51. Calc. for $C_{19}H_{20}N_2OS$: C, 70.34; H,

6.21; N, 8.63%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1694 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.24 (s, 3H, $CH_3$), 1.27 (s, 3H, $CH_3$), 4.23 (d, 1H, $J$ = 16 Hz, $CH_2$), 4.36 (d, 1H, $J$ = 16 Hz, $CH_2$), 4.61 (d, 1H, $J$ = 16 Hz, $CH_2$), 4.81 (s, 1H, CH), 5.01 (d, 1H, $J$ = 16 Hz, $CH_2$), 7.11–7.30 (m, 9H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 22.2 ($CH_3$), 25.1 ($CH_3$), 43.1 ($CH_2$), 44.4 ($CH_2$), 59.6 (C), 68.7 (CH), 125.8 ($CH_{aro}$), 127.0 ($CH_{aro}$), 127.1 ($CH_{aro}$), 127.2 (2 × $CH_{aro}$), 127.8 ($CH_{aro}$), 128.5 (2 × $CH_{aro}$), 129.3 ($CH_{aro}$), 130.6 ($C_{aro}$–S), 131.7 ($C_{aro}$–C), 139.2 ($C_{aro}$–C), 158.8 (C=O); MS (*m*/*z*: EI) 324 ($M^+$).

**General procedure for *N*-alkylation of 5,5-dimethylhydantoin (8).** To a stirred mixture of 5,5-dimethylhydantoin (**8**, 2.56 g, 20 mmol) and 18-C-6 (1% *w*/*w*) in 50 mL of dry toluene were added solid potassium carbonate (2.92 g, 24 mmol) and 0.1 equiv. per mmol of 5,5-dimethylhydantoin (**8**) of potassium iodide. After stirring for 25 min, *o*-ethylthiobenzyl bromide (**7x**, 5.52 g, 24 mmol) or *o*-benzylthiobenzyl bromide (**7y**, 7.04 g, 24 mmol)[5a,6] in 50 mL of dry toluene was added dropwise over a period of 20 min. The mixture was then refluxed for 48 h under stirring and cooled. After filtration over a short column of celite, the organic phase was concentrated under reduced pressure and the crude resulting solid was purified by flash chromatography on silica gel with dichloromethane as eluent to give 3-alkylated-5,5-dimethylhydantoin derivative **9x** or **9y**. All data for these products are as follows.

**3-(*o*-Ethylthiobenzyl)-5,5-dimethylhydantoin (9x).** This product was isolated as an uncolored oil in 63% yield; Found: C, 60.18; H, 6.35; N, 9.87. Calc. for $C_{14}H_{18}N_2O_2S$: C, 60.40; H, 6.52; N, 10.06%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3294 (NH), 1761 (C=O), 1712 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.29 (t, 3H, $J$ = 7 Hz, $CH_3$), 1.44 (s, 6H, 2 × $CH_3$), 2.95 (q, 2H, J = 7 Hz, $CH_2$), 4.83 (s, 2H, $CH_2$), 6.20 (s broad, 1H, NH), 7.00–7.21 (m, 3H, $H_{aro}$), 7.33–7.38 (m, 1H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 14.5 ($CH_3$), 25.2 (2 × $CH_3$), 28.4 ($CH_2$), 40.1 ($CH_2$), 59.0 (C), 126.5 ($CH_{aro}$), 126.6 ($CH_{aro}$), 128.0 ($CH_{aro}$), 130.4 ($CH_{aro}$), 134.9 ($C_{aro}$–S), 135.8 ($C_{aro}$–C), 156.6 ($C_2$=O), 177.3 ($C_4$=O); MS (*m*/*z*: EI) 278 ($M^+$).

**3-(*o*-Benzylthiobenzyl)-5,5-dimethylhydantoin (9y).** This product was isolated as a white–yellow solid in 73% yield; mp 88 °C (ethanol–cyclohexane); Found: C, 66.86; H, 5.78; N, 8.02. Calc. for $C_{19}H_{20}N_2O_2S$: C, 67.03; H, 5.92; N, 8.23%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3300 (NH), 1774 (C=O), 1714 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.44 (s, 6H, 2 × $CH_3$), 4.09 (s, 2H, $CH_2$), 4.78 (s, 2H, $CH_2$), 6.00 (s broad, 1H, NH), 7.02–7.07 (m, 1H, $H_{aro}$), 7.13–7.33 (m, 8H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 25.3 (2 × $CH_3$), 39.9 ($CH_2$), 40.0 ($CH_2$), 59.0 (C), 126.7 ($CH_{aro}$), 127.3 ($CH_{aro}$), 127.6 ($CH_{aro}$), 128.1 ($CH_{aro}$), 128.6 (2 × $CH_{aro}$), 129.1 (2 × $CH_{aro}$), 132.6 ($CH_{aro}$), 134.3 ($C_{aro}$–S), 137.0 ($C_{aro}$–C), 137.4 ($C_{aro}$–C), 156.4 ($C_2$=O), 177.2 ($C_4$=O); MS (*m*/*z*: EI) 340 ($M^+$).

**3-(*o*-Ethylthiobenzyl)-4-hydroxy-5,5-dimethylimidazolidin-2-one (10x).** According to the typical procedure reported above for sodium borohydride reduction of *N*-protected imide **4**, this product was obtained in 94% yield as a white solid by reduction of 3-(*o*-ethylthiobenzyl)-5,5-dimethylhydantoin (**9x**) with 6 mole equiv. of $NaBH_4$ at 20 °C for 24 h in ethanol and melted at 129 °C (ethanol); Found: C, 59.77; H, 7.05; N, 9.81. Calc. for $C_{14}H_{20}N_2O_2S$: C, 59.97; H, 7.19; N, 9.99%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3299 (NH and OH), 1693 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.19 (s, 3H, $CH_3$), 1.26 (s, 3H, $CH_3$), 1.29 (t, 3H, $J$ = 7 Hz, $CH_3$), 2.92 (q, 2H, $J$ = 7 Hz, $CH_2$), 4.06 (d, 1H, $J$ = 10 Hz, OH), 4.39 (d, 1H, $J$ = 10 Hz, CH), 4.41 (d, 1H, $J$ = 15 Hz, $CH_2$), 4.75 (d, 1H, $J$ = 15 Hz, $CH_2$), 4.80 (s broad, 1H, NH), 7.12–7.35 (m, 4H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 14.3 ($CH_3$), 22.2 ($CH_3$), 27.8 ($CH_2$). 28.2 ($CH_3$), 41.7 ($CH_2$), 56.5 (C), 86.7 (CH), 126.2 ($CH_{aro}$), 128.1 ($CH_{aro}$), 128.9 ($CH_{aro}$), 129.5 ($CH_{aro}$), 135.7 ($C_{aro}$–S), 136.7 ($C_{aro}$–C), 159.7 (C=O).

**3-(*o*-Benzylthiobenzyl)-4-hydroxy-5,5-dimethylimidazolidin-2-one (10y).** According to the typical procedure reported above for reduction of *N*-protected imide **4**, this product was obtained in 84% yield as a white–yellow solid by reduction of 3-(*o*-ethylthiobenzyl)-5,5-dimethylhydantoin (**9y**) with 6 mole equiv. of $NaBH_4$ at 20 °C for 24 h in ethanol and melted at 150 °C (ethanol); Found: C, 66.54; H, 6.21; N, 8.03. Calc. for $C_{19}H_{22}N_2O_2S$: C, 66.64; H, 6.48; N, 8.18%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3363 (NH and OH), 1680 (C=O); $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.10 (s, 3H, $CH_3$), 1.12 (s, 3H, $CH_3$), 4.15 (d, 1H, $J$ = 15 Hz, $CH_2$), 4.23 (s, 2H, $CH_2$), 4.33 (d, 1H, $J$ = 7 Hz, CH), 4.41 (d, 1H, $J$ = 15 Hz, $CH_2$), 5.91 (d, 1H, $J$ = 7 Hz, OH), 6.73 (s broad, 1H, NH), 7.19–7.39 (m, 9H, $H_{aro}$); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 22.1 ($CH_3$), 27.9 ($CH_3$), 36.5 ($CH_2$), 40.6 ($CH_2$), 55.6 (C), 85.7 (CH), 125.7 ($CH_{aro}$), 127.2 ($CH_{aro}$), 127.4 ($CH_{aro}$), 127.5 ($CH_{aro}$), 128.1 ($CH_{aro}$), 128.5 (2 × $CH_{aro}$), 129.0 (2 × $CH_{aro}$), 134.9 ($C_{aro}$–S), 136.9 ($C_{aro}$–C), 137.2 ($C_{aro}$–C), 158.9 (C=O).

**1-(*o*-Ethylthiobenzyl)-4,5-dimethylimidazol-2(3*H*)-one (11x) by simple transposition of 4-hydroxyimidazolidinone 10x in acid medium.** To a stirred solution of 4-hydroxyimidazolidinone (**10x**, 560 mg, 2 mmol) in dry toluene was added a catalytic amount of PTSA. After 48 h of reaction at reflux under stirring, the reaction mixture was cooled, concentrated under reduced pressure, diluted with water (10 mL) and $CH_2Cl_2$ (15 mL) and neutralized slowly on cooling with 5% NaOH aqueous solution. The solution was extracted twice with $CH_2Cl_2$ (15 mL). The organic layer was washed with water, brine, dried over $MgSO_4$ and evaporated. The resulting oily residue was purified by flash chromatography using a mixture of cyclohexane–AcOEt (1 : 1) as eluent to give the imidazolone derivative **11x** as yellow oil in 58% yield; Found: C, 64.00; H, 6.76; N, 10.45. Calc. for $C_{14}H_{18}N_2OS$: C, 64.09; H, 6.91; N, 10.68%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3332 (NH), 1692 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.30 (t, 3H, $J$ = 7 Hz, $CH_3$), 1.74 (s, 3H, $CH_3$), 1.96 (s, 3H, $CH_3$), 2.92 (q, 2H, $J$ = 7 Hz, $CH_2$), 4.91 (s, 2H, $CH_2$), 7.11–7.21 (m, 3H, $H_{aro}$), 7.31–7.34 (m, 1H, $H_{aro}$), 9.79 (s broad, 1H, NH); MS (*m*/*z*: EI) 262 ($M^+$).

**General procedure for *S*-alkylation of 3-bromomethyl-5,5-dimethylhydantoin (13).** By using same protocol described above for *S*-alkylation of 3-bromomethyl-5,5-dimethylhydantoin (**2**), reaction of 3-bromomethyl-5,5-dimethylhydantoin (**13**)[14] with 1.2 mole equiv. of substituted thiophenol **12j,l–n** in the presence of MeONa (1.2 mole equiv.) in dry DMF at ambient temperature for 12 to 24 h give suitable *S*-alkylated products **14j,l–n** in good yields.

**1,5,5-Trimethyl-3-phenylthiomethylhydantoin (14j).** This product was isolated as a white solid in 85% yield; mp 77 °C (ethanol); Found: C, 59.07; H, 6.10; N, 10.60. Calc. for $C_{13}H_{16}N_2O_2S$: C, 58.81; H, 6.02; N, 10.45%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1776 (C=O), 1713 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.26 (s, 6H, 2 × $CH_3$), 2.83 (s, 3H, $CH_3$), 4.84 (s, 2H, $CH_2$), 7.25–7.31 (m, 3H, $H_{aro}$), 7.48–7.52 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 21.8 (2 × $CH_3$), 24.3 ($CH_3$), 42.6 ($CH_2$), 61.1 (C), 127.9 ($CH_{aro}$), 128.9 (2 × $CH_{aro}$), 132.6 (2 × $CH_{aro}$), 132.7 ($C_{aro}$–S), 153.6 ($C_2$=O), 175.3 ($C_4$=O); MS (*m*/*z*: EI) 264 ($M^+$).

**3-(*o*-Bromophenyl)thiomethyl-1,5,5-trimethylhydantoin (14l).** This product was isolated after a second chromatography purification as a white–yellow solid in 85% yield; mp 110 °C (ethanol–cyclohexane); Found: C, 45.31; H, 4.29; N, 8.00. Calc. for $C_{13}H_{15}BrN_2O_2S$: C, 45.49; H, 4.40; N, 8.16%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1775 (C=O), 1715 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.28 (s, 6H, 2 × $CH_3$), 2.83 (s, 3H, $CH_3$), 4.88 (s, 2H, $CH_2$), 7.08–7.28 (m, 2H, $H_{aro}$), 7.56–7.67 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 21.9 (2 × $CH_3$), 24.4 ($CH_3$), 42.1 ($CH_2$), 61.2 (C), 127.9 ($C_{aro}$–Br), 127.9 ($CH_{aro}$), 129.5 ($CH_{aro}$), 133.3 ($CH_{aro}$),

134.1 ($C_{aro}$–S), 134.2 ($CH_{aro}$), 153.7 ($C_2$=O), 175.5 ($C_4$=O); MS (*m*/*z*: EI) 342 ($M^+$).

**3-(*o*-Methoxyphenyl)thiomethyl-1,5,5-trimethylhydantoin (14m).** This product was isolated as an uncolored oil in 75% yield; Found: C, 57.00; H, 6.02; N, 9.37. Calc. for $C_{14}H_{18}N_2O_3S$: C, 57.12; H, 6.16; N, 9.52%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1781 (C=O), 1714 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.19 (s, 6H, 2 × $CH_3$), 2.79 (s, 3H, $CH_3$), 3.92 (s, 3H, $OCH_3$), 4.85 (s, 2H, $CH_2$), 6.76–6.88 (m, 2H, $H_{aro}$), 7.29–7.42 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 21.9 (2 × $CH_3$), 24.4 ($CH_3$), 40.6 ($CH_2$), 55.9 ($OCH_3$), 62.1 (C), 111.0 ($CH_{aro}$), 119.5 ($C_{aro}$–S), 120.5 ($CH_{aro}$), 130.6 ($CH_{aro}$), 135.7 ($CH_{aro}$), 154.0 ($C_{aro}$–O), 159.8 ($C_2$=O), 175.7 ($C_4$=O); MS (*m*/*z*: EI) 294 ($M^+$).

**3-(*m*,*p*-Dimethoxyphenyl)thiomethyl-1,5,5-trimethylhydantoin (14n).** This product was isolated as an uncolored oil in 66% yield; Found: C, 55.39; H, 6.02; N, 8.51. Calc. for $C_{15}H_{20}N_2O_4S$: C, 55.54; H, 6.21; N, 8.64%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1770 (C=O), 1714 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.25 (s, 6H, 2 × $CH_3$), 2.82 (s, 3H, $CH_3$), 3.82 (s, 3H, $OCH_3$), 3.84 (s, 3H, $OCH_3$), 4.77 (s, 2H, $CH_2$), 6.74 (d, 1H, $J$ = 8 Hz, $H_{aro}$), 7.01–7.06 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 22.0 (2 × $CH_3$), 24.5 ($CH_3$), 43.5 ($CH_2$), 56.0 ($OCH_3$), 56.1 ($OCH_3$), 61.3 (C), 111.3 ($CH_{aro}$), 116.6 ($CH_{aro}$), 123.6 ($C_{aro}$–S), 126.7 ($CH_{aro}$), 149.1 ($C_{aro}$–O), 149.5 ($C_{aro}$–O), 154.0 ($C_2$=O), 175.6 ($C_4$=O); MS (*m*/*z*: EI) 324 ($M^+$).

**General procedure for regioselective reduction of 1,5,5-trimethylhydantoin derivatives 14j,l–n.** By using same protocol described above for reduction of the positional isomers *N*-protected imides **4**, treatment of imides **14j**,**l**–**n** with $NaBH_4$ (6 mole equiv.) in dry ethanol at 20 °C for 12 to 46 h (monitored by TLC using $CH_2Cl_2$ as eluent) gives suitable 4-hydroxyimidazolidinones **15j**,**l**–**n** in good yields.

**4-Hydroxy-1,5,5-trimethyl-3-phenylthiomethylimidazolidin-2-one (15j).** This product was isolated as a white solid in 82% yield; mp 105 °C (ethanol); Found: C, 58.33; H, 6.65; N, 10.22. Calc. for $C_{13}H_{18}N_2O_2S$: C, 58.62; H, 6.81; N, 10.52%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3311 (OH), 1682 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.90 (s, 3H, $CH_3$), 1.21 (s, 3H, $CH_3$), 2.60 (s, 3H, $CH_3$), 3.58 (s broad, 1H, OH), 4.46 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.72 (d, 1H, $J$ = 10 Hz, CH), 5.15 (d, 1H, $J$ = 14 Hz, $CH_2$), 7.13–7.30 (m, 3H, $H_{aro}$), 7.40–7.44 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.1 ($CH_3$), 23.2 ($CH_3$), 24.6 ($CH_3$), 45.0 ($CH_2$), 59.8 (C), 84.3 (CH), 127.0 ($CH_{aro}$), 129.1 (2 × $CH_{aro}$), 130.6 (2 × $CH_{aro}$), 134.0 ($C_{aro}$–S), 157.2 (C=O).

**3-(*o*-Bromophenyl)thiomethyl-4-hydroxy-1,5,5-trimethylimidazolidin-2-one (15l).** This product was isolated as a white solid in 90% yield; mp 110 °C (ethanol–diethyl ether); Found: C, 45.04; H, 4.69; N, 8.02. Calc. for $C_{13}H_{17}BrN_2O_2S$: C, 45.22; H, 4.96; N, 8.11%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3309 (OH), 1685 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.90 (s, 3H, $CH_3$), 1.21 (s, 3H, $CH_3$), 2.60 (s, 3H, $CH_3$), 3.58 (s broad, 1H, OH), 4.46 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.72 (d, 1H, $J$ = 10 Hz, CH), 5.15 (d, 1H, $J$ = 14 Hz, $CH_2$), 7.13–7.30 (m, 3H, $H_{aro}$), 7.40–7.44 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.0 ($CH_3$), 23.2 ($CH_3$), 24.6 ($CH_3$), 44.2 ($CH_2$), 59.8 (C), 84.1 (CH), 124.7 ($C_{aro}$–Br), 127.7 ($CH_{aro}$), 128.0 ($CH_{aro}$), 130.4 ($CH_{aro}$), 133.1 ($CH_{aro}$), 135.4 ($C_{aro}$–S), 157.1 (C=O).

**4-Hydroxy-3-(*o*-methoxyphenyl)thiomethyl-1,5,5-trimethylimidazolidin-2-one (15m).** This product was isolated as a white solid in 69% yield; mp 117 °C (ethanol–ethyl acetate); Found: C, 56.57; H, 6.65; N, 9.23. Calc. for $C_{14}H_{20}N_2O_3S$: C, 56.73; H, 6.80; N, 9.45%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3305 (OH), 1687 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.92 (s, 3H, $CH_3$), 1.20 (s, 3H, $CH_3$), 2.57 (s, 3H, $CH_3$), 3.90 (s, 4H, OH and $OCH_3$), 4.47 (d, 1H, $J$ = 13 Hz, $CH_2$), 4.73 (d, 1H, $J$ = 10 Hz, CH), 5.11 (d, 1H, $J$ = 13 Hz, $CH_2$), 6.81–6.88 (m, 2H, $H_{aro}$), 7.18–7.21 (m, 1H, $H_{aro}$), 7.38–7.42 (m, 1H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.1 ($CH_3$), 23.3 ($CH_3$), 24.6 ($CH_3$), 43.8 ($CH_2$), 55.9 ($OCH_3$), 59.7 (C), 84.6 (CH), 110.9 ($CH_{aro}$), 121.0 ($CH_{aro}$), 121.3 ($C_{aro}$–S), 129.1 ($CH_{aro}$), 133.2 ($CH_{aro}$), 157.1 ($C_{aro}$–O), 158.5 (C=O).

**4-Hydroxy-3-(*m*,*p*-dimethoxyphenyl)thiomethyl-1,5,5-trimethylimidazolidin-2-one (15n).** This product was isolated as a white–yellow solid in 95% yield; mp 92 °C (ethanol); Found: C, 55.03; H, 6.56; N, 8.40. Calc. for $C_{15}H_{22}N_2O_4S$: C, 55.19; H, 6.79; N, 8.58%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3308 (OH), 1687 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.90 (s, 3H, $CH_3$), 1.20 (s, 3H, $CH_3$), 2.57 (s, 3H, $CH_3$), 3.81 (s, 3H, $OCH_3$), 3.82 (s, 3H, $OCH_3$), 4.09 (d, 1H, $J$ = 10 Hz, OH), 4.38 (d, 1H, $J$ = 14 Hz, $CH_2$), 4.70 (d, 1H, $J$ = 10 Hz, CH), 5.06 (d, 1H, $J$ = 14 Hz, $CH_2$), 6.73 (d, 1H, $J$ = 8 Hz, $H_{aro}$), 6.94–6.99 (m, 2H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.0 ($CH_3$), 23.4 ($CH_3$), 24.6 ($CH_3$), 45.9 ($CH_2$), 56.0 ($OCH_3$), 56.1 ($OCH_3$), 59.8 (C), 84.4 (CH), 111.6 ($CH_{aro}$), 114.7 ($CH_{aro}$), 124.4 ($CH_{aro}$), 124.6 ($C_{aro}$–S), 148.7 ($C_{aro}$–O), 149.2 ($C_{aro}$–O), 157.1 (C=O).

**General procedure for cyclisation of 4-hydroxyimidazolidinones 10x,y and 15j,l–n; access to tricyclic *N*,*S*-acetals 6a and 6j,l–n.** By using the well-established acid protocol described above for cyclisation of 4-hydroxyimidazolidinones **5**, *N*-acyliminium ions precursors **10x**,**y** and **15j**,**l**–**n** after treatment with TFA at ambient temperature for 24 h led to suitable cyclised products **6a** and **6j**,**l**–**n**, respectively, in appreciable to good yields.

**2,3,3*a*,9-Tetrahydro-3,3-dimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6a).**

*Method A.* This product, which was identical to that described above, was obtained from hydroxylactam **10y** and TFA at reflux for 48 h in 52% yields.

*Method B.* Product **6a** was also obtained in 67% yield from imidazolone **11x** by refluxing in TFA for 48 h.

**2,3,3*a*,9-Tetrahydro-2,3,3-trimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6j).** This product, which was identical to that described above, was obtained from 4-hydroxyimidazolidinone **15j** and neat TFA at room temperature for 48 h in 89% yield.

**X-Ray crystallographic analysis of benzothiazinone (6j)‡.** $C_{13}H_{16}N_2OS$, $M_r$ = 248.34, orthorhombic, $Pna2_1$, $a$ = 19.225(8), $b$ = 10.950(4), $c$ = 6.047(9) Å, $V$ = 1273(2) Å$^{-3}$, $Z$ = 4, $D_x$ = 1.296 Mg.m$^{-3}$, $\lambda$(Mo K$\alpha$) = 0.71073 Å, $\mu$ = 2.40 cm$^{-1}$, $F(000)$ = 528, $T$ = 293 K. The sample (0.36*0.32*0.30 mm) is studied on an automatic diffractometer CAD4 NONIUS with graphite monochromatized Mo K$\alpha$ radiation.[16] The cell parameters are obtained by fitting a set of 25 high-theta reflections. The data collection ($2\theta_{max}$ = 54°, scan $\omega/2\theta$ = 1, $t_{max}$ = 60 s, range HKL: H 0,24 K 0,13 L 0,7) gives 1511 unique reflections from which 1209 with $I > 2.0\sigma(I)$. After Lorenz and polarization corrections[17] the structure was solved with SIR-97[18] which reveals the non hydrogen atoms of the compound. After anisotropic refinement a Fourier difference reveals many hydrogen atoms. The whole structure was refined with SHELXL97[19] by the full-matrix least-square techniques (use of $F$ square magnitude; $x$, $y$, $z$, $\beta_{ij}$ for S, C, O and N atoms, $x$, $y$, $z$ in riding mode for H atoms; 155 variables and 1209 observations; calc. $w = 1/[\sigma^2(Fo^2) + (0.109P)^2]$ where $P = (Fo^2 + 2Fc^2)/3$ with the resulting $R$ = 0.048, $Rw$ = 0.145 and $Sw$ = 1.057 (residual $\Delta\rho \leq 0.40$ eÅ$^{-3}$).

Atomic scattering factors from International Tables for X-ray Crystallography (1992). Ortep views realized with PLATON98[20] and Ortep-3 for windows.[21] All the calculations were performed on a Pentium NT Server computer. See the electronic supplementary information for further data on compound **6j**.

**5-Bromo-2,3,3*a*,9-tetrahydro-2,3,3-trimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6l).** This product was isolated as an uncolored oil in 100% yield; Found: C, 47.58; H, 4.41; N, 8.34. Calc. for $C_{13}H_{15}BrN_2OS$: C, 47.71; H, 4.62; N, 8.56%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1703 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.29 (s, 3H, $CH_3$), 1.47 (s, 3H, $CH_3$), 2.74 (s, 3H, $CH_3$), 4.23 (d, 1H, $J$ = 16 Hz, $CH_2$), 4.84 (s, 1H, CH), 4.89 (d, 1H, $J$ = 16 Hz,

$CH_2$), 6.96 (dd, 1H, $J = 2$ and 7 Hz, $H_{aro}$), 7.09 (d, 1H, $J = 7$ Hz, $H_{aro}$), 7.41 (dd, 1H, $J = 2$ and 7 Hz, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 21.1 ($CH_3$), 23.3 ($CH_3$), 24.6 ($CH_3$), 44.1 ($CH_2$), 58.8 (C), 68.4 (CH), 123.2 ($C_{aro}$–Br), 125.8 ($CH_{aro}$), 126.3 ($CH_{aro}$), 130.9 ($CH_{aro}$), 132.5 ($C_{aro}$–S), 133.0 ($C_{aro}$–C), 157.9 (C=O); MS (*m*/*z*: EI) 326–328 ($M^+$).

**2,3,3*a*,9-Tetrahydro-5-methoxy-2,3,3-trimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6m).** This product was isolated as a white solid in 100% yield; mp 124 °C (ethanol–hexane); Found: C, 60.18; H, 6.34; N, 9.87. Calc. for $C_{14}H_{18}N_2O_2S$: C, 60.40; H, 6.52; N, 10.06%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1694 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.28 (s, 3H, $CH_3$), 1.46 (s, 3H, $CH_3$), 2.75 (s, 3H, $CH_3$), 3.86 (s, 3H, $OCH_3$), 4.31 (d, 1H, $J = 17$ Hz, $CH_2$), 4.75 (s, 1H, CH), 4.91 (d, 1H, $J = 17$ Hz, $CH_2$), 6.68–6.79 (m, 2H, $H_{aro}$), 7.02–7.11 (m, 1H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 21.2 ($CH_3$), 23.5 ($CH_3$), 24.7 ($CH_3$), 43.8 ($CH_2$), 56.0 ($OCH_3$), 58.9 (C), 67.1 (CH), 108.3 ($CH_{aro}$), 120.2 ($CH_{aro}$), 120.5 ($C_{aro}$–S), 125.4 ($CH_{aro}$), 131.1 ($C_{aro}$–C), 155.9 ($C_{aro}$–O), 158.3 (C=O); MS (*m*/*z*: EI) 278 ($M^+$).

**2,3,3*a*,9-Tetrahydro-6,7-dimethoxy-2,3,3-trimethylimidazo[5,1-*b*][1,3]benzothiazin-1-one (6n).** This product was isolated as a white solid in 44% yield; mp 183 °C (ethanol); Found: C, 58.23; H, 6.31; N, 8.82. Calc. for $C_{15}H_{20}N_2O_3S$: C, 58.42; H, 6.54; N, 9.08%; IR $\nu_{max}$ (KBr)/cm$^{-1}$ 1690 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.68 (s, 3H, $CH_3$), 1.46 (s, 3H, $CH_3$), 2.72 (s, 3H, $CH_3$), 3.83 (s, 3H, $OCH_3$), 3.84 (s, 3H, $OCH_3$), 4.13 (d, 1H, $J =$ 12 Hz, $CH_2$), 4.66 (s, 1H, CH), 5.05 (d, 1H, $J = 12$ Hz, $CH_2$), 6.55 (s, 1H, $H_{aro}$), 6.70 (s, 1H, $H_{aro}$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.5 ($CH_3$), 25.2 ($CH_3$), 26.1 ($CH_3$), 43.4 ($CH_2$), 56.0 ($OCH_3$), 56.2 ($OCH_3$), 63.3 (C), 64.0 (CH), 111.3 ($CH_{aro}$), 112.7 ($CH_{aro}$), 121.5 ($C_{aro}$–S), 125.8 ($C_{aro}$–C), 147.4 ($C_{aro}$–O), 148.2 ($C_{aro}$–O), 158.4 (C=O); MS (*m*/*z*: EI) 308 ($M^+$).

## Acknowledgements

We are grateful to Johnson & Johnson, Pharmaceutical R. & D., Division of Janssen-Cilag, for support of this research. We thank also the Region of "Haute Normandie" for a Regional-Industrial Graduate Fellowship, (BRI/2000–2003), attributed to A. P. We are grateful also to Dr Loïc Toupet (University of Rennes) and Dr Samuel Petit (University of Rouen) for X-ray crystallographic analysis.

## References

1 (*a*) For interesting reviews, see: L. F. Tietze and U. Beifuss, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 131; (*b*) L. F. Tietze, *Chem. Rev.*, 1996, **96**, 115.
2 (*a*) K. C. Nicolaou and N. A. Petasis, in *Strategies and Tactics in Organic Synthesis*, ed. L. Lindberg, Academic Press, New York, 1984, vol. 1, pp. 155–173; (*b*) D. P. Curran, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 4, ch. 4.2; (*c*) T. L. Ho, *Tandem Organic Reactions*, Wiley, New York, 1992; (*d*) H. Waldmann, in *Domino Reaction in Organic Synthesis Highlight II*, ed. H. Waldmann, VCH, Weinheim, 1995, pp. 193–202.
3 (*a*) For representatives reviews in this area, see: H. Hiemstra and W. N. Speckamp, in *The Alkaloids*, ed. A. Brossi, Academic Press, New York, 1988, vol. 32, ch. 4, pp. 271–339; (*b*) W. N. Speckamp and H. Hiemstra, *Tetrahedron*, 1985, **41**, 4367; (*c*) H. Hiemstra and W. N. Speckamp, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 2, pp. 1047–1082; (*d*) H. Koning and W. N. Speckamp, in *Stereoselective Synthesis [Houben–Weyl]*, ed. G. Helmchen, R. W. Hoffmann, J. Muzler and E. Schaumann, Thieme, Stuttgart, 1996, vol. 3, pp. 1952–2010; (*e*) W. N. Speckamp and M. J. Moolenaar, *Tetrahedron*, 2000, **56**, 3817.
4 (*a*) For C–N bonds forming *via* the *N*-acyliminium chemistry, see: P. Aeberli and W. J. Houlihan, *J. Org. Chem.*, 1968, **33**, 2402; (*b*) J. B. P. A. Wijnberg and W. N. Speckamp, *Tetrahedron*, 1978, **34**, 2399; (*c*) H. H. Wasserman, S. L. Henke, P. Luce and E. Nakanishi, *J. Org. Chem.*, 1990, **55**, 5821; (*d*) H. H. Wasserman, S. L. Henke and E. Nakanishi, *J. Org. Chem.*, 1992, **57**, 2641; (*e*) O. Surygina, M. Ehwald and J. Liebscher, *Tetrahedron Lett.*, 2000, **41**, 5479; (*f*) H. Sun and K. D. Moeller, *Org. Lett.*, 2002, **4**, 1547; (*g*) A. R. Katritzky, Y.-J. Xu, H.-Y. He and P. J. Steel, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1767; (*h*) A. R. Katritzky, H.-Y. He and A. K. Verma, *Tetrahedron: Asymmetry*, 2002, **13**, 933; (*i*) A. Fogain-Ninkam, A. Daïch, B. Decroix and P. Netchitaïlo, *Eur. J. Org. Chem.*, 2003, 4273; (*j*) A. Cul, A. Daïch, B. Decroix, G. Sanz and L. Van Hijfte, *Tetrahedron*, 2004, **60**, 11029. For C–O linkages forming *via* the *N*-acyliminium species see: (*k*) H. W. Moore, L. Hernandez, Jr., D. M. Kunert, F. Mercer and A. Sing, *J. Am. Chem. Soc.*, 1981, **103**, 1769; (*l*) A. Mamouni, A. Daïch, Š. Marchalín and B. Decroix, *Heterocycles*, 2001, **54**, 275; (*m*) P. Pigeon, J. Sikoraiová, Š. Marchalín and B. Decroix, *Heterocycles*, 2002, **56**, 129; (*n*) J. Sikoraiová, A. Chihab-Eddine, Š. Marchalín and A. Daïch, *J. Heterocycl. Chem.*, 2002, **39**, 383; (*o*) J. Sikoraiová, Š. Marchalín, A. Daïch and B. Decroix, *Tetrahedron Lett.*, 2002, **43**, 4747; (*p*) A. Cul, A. Chihab-Eddine, A. Pesquet, Š. Marchalín and A. Daïch, *J. Heterocycl. Chem.*, 2003, **40**, 499; (*q*) A. S. Kende, J. I. M. Hernando and J. B. J. Milbank, *Tetrahedron*, 2002, **58**, 61; (*r*) C. Agami, A. Beauseigneur, S. Comesse and L. Dechoux, *Tetrahedron Lett.*, 2002, **43**, 4747. For C–O/C–N and/or C–S linkages forming, *via* the *N*-acyliminium species see: (*s*) N. Mizutani, W.-H. Chiou and I. Ojima, *Org. Lett.*, 2002, **4**, 4575; (*t*) H. H. Wasserman, Y. O. Long, R. Zhang, A. J. Carr and J. Parr, *Tetrahedron Lett.*, 2002, **43**, 3347.
5 (*a*) N. Hucher, A. Daïch, P. Netchitaïlo and B. Decroix, *Tetrahedron Lett.*, 1999, **40**, 3363; (*b*) Another example of this process was reported recently during their synthesis of azabicyclo[4.4.0]alkane amino acids by Rh-catalyzed cyclocarbonylation of amide-olefins. For this end, see ref. 4*s*, above.
6 (*a*) N. Hucher, B. Decroix and A. Daïch, *J. Org. Chem.*, 2001, **66**, 4695; (*b*) N. Hucher, A. Pesquet, P. Netchitaïlo and A. Daïch, *Eur. J. Org. Chem.*, 2005, 2758.
7 Only one report concerning similar phenomenon using a tandem aza-Cope isomerisation/*O*-cyclisation was pointed in the literature. See H. Ent, H. De Koning and W. N. Speckamp, *Heterocycles*, 1990, **30**, 501.
8 N. Hucher, A. Daïch and B. Decroix, *Org. Lett.*, 2000, **2**, 1201.
9 T. L. Hough, *J. Heterocycl. Chem.*, 1989, **26**, 1523.
10 A. Guzmán and M. Romero, *Can. J. Chem.*, 1990, **68**, 791.
11 H. Hilpert, *Tetrahedron*, 2001, **57**, 7675.
12 Under these conditions the substituted thiophenol, which resulted from the N–$CH_2$–S functionality cleavage, was recovered in appreciable quantity.
13 (*a*) H. Kohn and Z.-K. Liao, *J. Org. Chem.*, 1982, **47**, 2787; (*b*) Z.-K. Liao and H. Kohn, *J. Org. Chem.*, 1985, **50**, 1884.
14 (*a*) M. A. Brodney and A. Padwa, *J. Org. Chem.*, 1999, **64**, 556; (*b*) A. Padwa and A. G. Waterson, *Tetrahedron*, 2000, **56**, 10159; (*c*) N. Hucher, A. Daïch and B. Decroix, *J. Heterocycl. Chem.*, 1998, **35**, 1477.
15 J. Casanova and A. G. Ciba-Geigy, *Chem. Abs.*, 1973, **80**, 48541.
16 C. K. Fair, *MolEN, An Interactive Intelligent System for Crystal Structure Analysis*, User Manual, Enraf-Nonius, Delft, The Netherlands, 1990.
17 A. L. Spek, *HELENA, Program for the handling of CAD4-Diffractometer output SHELX(S/L)*, Utrecht University, Utrecht, The Netherlands, 1997.
18 A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori and R. Spagna, *J. Appl. Crystallogr.*, 1999, **32**, 115.
19 G. M. Sheldrick, *SHELXS-97, Program for Solution of Crystal Structures*, University of Göttingen, Germany, 1997.
20 A. L. Spek, *PLATON, A Multipurpose Crystallographic Tool*, Utrecht University, Utrecht, The Netherlands, 1998.
21 L. J. Farrugia, *J. Appl. Crystallogr.*, 1997, **30**, 565.