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# (*S*)-5-Benzyl- and 5-benzylidene-imidazo-4-one derivatives synthesized and studied for an understanding of their thermal reactivity†

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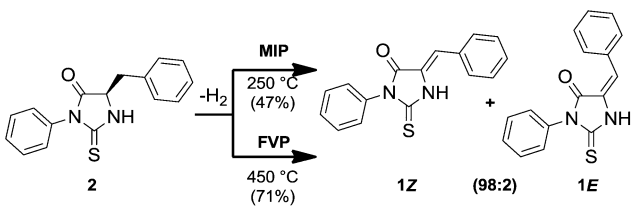
Flash vacuum as well as static pyrolysis were used to gain insight into the mechanisms of decomposition of the title compounds. They were synthesized by the use of microwave techniques that allowed better yields than the established methods. Since the benzyl compounds always open a radical channel in the thermal processes, consequently lowering the yields of other important intramolecular processes, we also started the pyrolysis with benzylidene derivatives. Detection and quantification of products accompanied by kinetic analyses were carried out for both types of compounds. The activation energies as well as the entropy contributions have been determined. Moreover, DFT calculations provided support for and corroborating of the proposed thermal pathways.

## Introduction

In a very recent paper,[1] we reported an efficient dehydrogenation reaction that allowed the synthesis of the 5-benzylidene-2-thioxoimidazolidin-4-one (**1**) core mediated by eco-friendly techniques such as Microwave Induced Pyrolysis (MIP) and Flash Vacuum Pyrolysis (FVP) (Scheme 1).

In the present contribution we synthesized other (*S*)-5-benzyl-thioxoimidazolidin-4-one and imidazolidine-2,4-dione cores in an attempt to get a comprehensive explanation on the reactivity of this useful nucleus.




Scheme 1 Synthesis of 5-benzylidene-2-thioxoimidazolidin-4-one **1** by selective dehydrogenation of (*S*)-5-benzyl-3-phenyl-2-thioxoimidazolidin-4-one **2**.

The interest in the synthesis of (*S*)-5-benzyl-imidazo-4-ones is based upon two important features. First, the widespread use of this heterocyclic nucleus in the preparation of pharmaceutically active compounds such as antimycobacterials,[2] immunomodulators,[3] anticonvulsivants,[4] and antifungals.[5] Second, it affords an interesting route towards the formation of an exocyclic double bond at $C_5$ which is difficult to obtain using conventional methods. In this regard, there have been many attempts and reactions proposed to induce the formation of the exocyclic double bond in similar heterocyclic systems, but they invariably need the use of a co-reactant or a catalyst, such as rhodium,[6] iridium,[7] or even more complex catalysts.[8]

Dehydrogenation reactions are quite common in high-temperature pyrolysis, because of the decrease in energy in the system due to aromatization and/or the formation of stable products;[9] however, selective dehydrogenations are scarce and few examples have been studied.

Our previous study, led us to put forward questions like whether the dehydrogenation reaction is a general mechanism, or whether the substitution of the benzyl imidazo core is of prime importance. Besides, it is also interesting to look into the role played by the 3p electrons and orbitals available in the sulfur atom of the thioxo compounds during the thermal transformations. We have also reported that 1,3-heterocycles in which the sulfur atom is changed by an oxygen atom, react at higher temperatures than *cis* or *trans*-thioxo analogs when subjected to FVP (Scheme 2, **3**).[10,11] As a result of the higher temperatures required for the dioxo compounds, competitive pathways open up. In the case of (*S*)-5-benzyl-imidazo-4-ones, this competitive pathway is a radical process that dramatically

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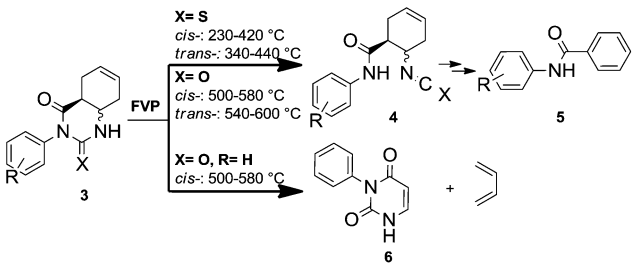
† Electronic supplementary information (ESI) available: Rate constants obtained by FVP from **7** and **8** (Tables S1 and S2), characterization of compounds **7**, **8**, **11**, **12**, **25**, **27**, **28**, **31**, and **35** and Cartesian coordinates (Å) obtained from the B3LyP(6-31+G(d,p)) computational calculations are provided. See DOI: 10.1039/c4ra11046c




Scheme 2 FVP of *cis* and *trans*-2-thio(oxo)quinazolin-4-ones.

reduces the yield of the products formed by intramolecular reactions. For his reason, we also synthesized the 5-benzylidene-imidazo-4-ones that acted as initial reagent in the thermal decomposition.

The fact that FVP is both a very useful technique to study reaction mechanisms and a powerful tool for synthetic purposes has been highlighted in several excellent reviews[12–14] and books.[15,16] The purpose of this work is to study the thermal behavior of (*S*)-5-benzyl-3-(2-chloroethyl)imidazolidine-2,4-dione **7** and 5-benzylidene-3-chloroethyl-2-oxoimidazolidin-4-one **8** (Fig. 1) in order to better understand their chemistry, in particular the structural requirements that allow dehydrogenation or dehydrochlorination reactions to occur under FVP conditions.

We pursued further to compare the results with the corresponding thio-derivatives (namely (*S*)-5-benzyl-3-(2-chloroethyl)-2-thioxoimidazolidin-4-one **9** and 5-benzylidene-3-(2-chloroethyl)-2-thioxoimidazolidin-4-one **10**), though our syntheses have resulted without exception in the cyclic compounds (*S*)-6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **11** and 6-benzylidene-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **12** which are nevertheless interesting because they allowed us to evaluate different kind (exocyclic and endocyclic) of dehydrogenations as well as to obtain essential information about the energetics required.

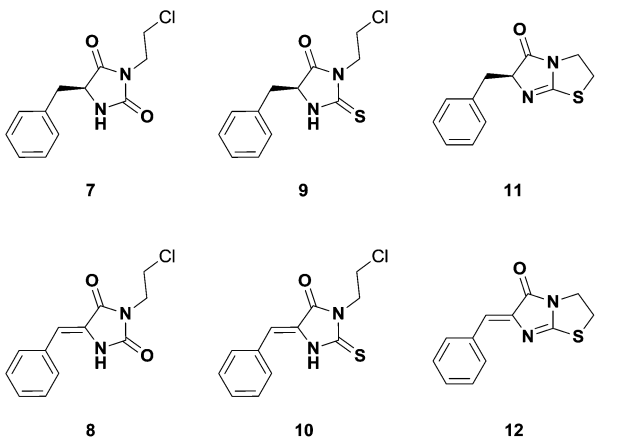



Fig. 1 Structures of (*S*)-5-benzyl-3-(2-chloroethyl)imidazolidine-2,4-dione **7** and 5-benzylidene-3-chloroethyl-2-oxoimidazolidin-4-one **8**, (2-chloroethyl)-2-thioxoimidazolidinones (**9** and **10**) and 2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-ones (**11** and **12**).

# Results and discussion

## Synthesis of (*S*)-5-benzyl-3-(2-chloroethyl)imidazolidine-2,4-dione (7) and (*S*)-6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one (11)

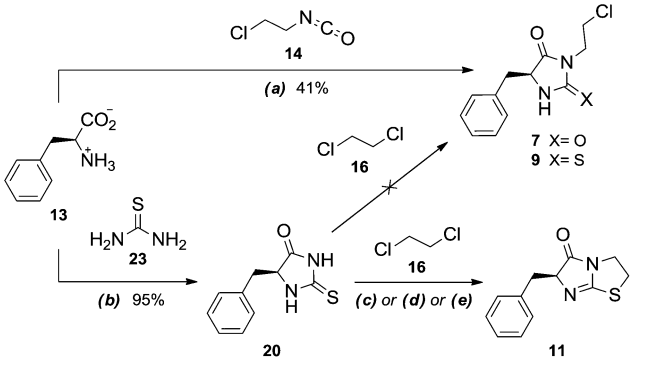
Our synthetic work was focused on the obtainment of 2-oxoimidazolidinones and 2-thioxoimidazolidinones substituted in position **3** by a chloroethyl group. It was expected that these molecules would suffer dehydrogenation or dehydrochlorination reactions allowing us to study the mechanisms and energetic requirements of both class of thermal reactions. (*S*)-5-Benzyl-3-(2-chloroethyl)imidazolidine-2,4-dione **7** was prepared by modification of known general methodologies[17,18] but employing microwave irradiation (MW) as an alternative approach.

(*S*)-5-Benzyl-3-(2-chloroethyl)imidazolidine-2,4-dione **7** was prepared by carefully reacting L-phenylalanine **13** with 2-chloroethylisocyanate **14** in $CH_3NO_2$ (Scheme 3). The synthesis is tricky because of the intrinsic high reactivity of **14** which decomposes easily, as we demonstrated recently.[19]

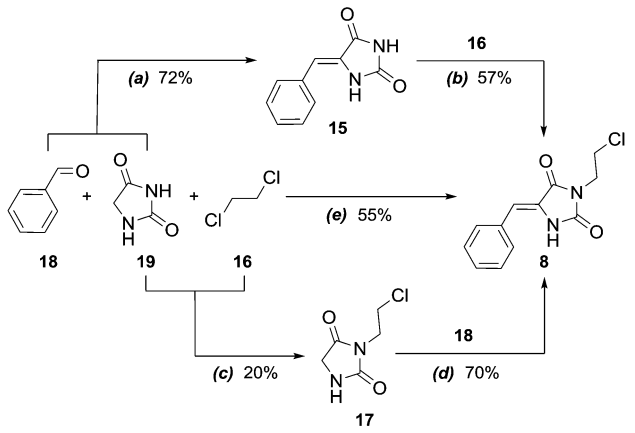
Since the thio-analog of **14** was unavailable to us, we developed a 2-step strategy to obtain (*S*)-5-benzyl-3-(2-chloroethyl)-2-thioxoimidazolidin-4-one **9**. In spite of our efforts, the attempts were unsuccessful because the end product was always the bicyclic compound **11**. We formed (*S*)-5-benzyl-2-thioxoimidazolidin-4-one **20** from L-phenylalanine **13** and thiourea **23** and reacted it with 1,2-dichloroethane. Although several conditions and temperatures were used, the method afforded only the cyclization to the (*S*)-6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **11** (Scheme 3).

## Synthesis of 5-benzylidene-3-(2-chloroethyl) imidazolidine-2,4-dione (8) and 5-benzylidene-2,3-dihydroimidazo[2,1-*b*] thiazol-6(5*H*)-one (12)

5-Benzylidene-3-(2-chloroethyl)imidazolidine-2,4-dione **8** was prepared by modifying existing procedures[20,21] in order to increase the yield of the reaction and by trying a one pot synthesis (Scheme 4). First, we attempted to obtain **8** in a two-step reaction, preparing the 5-benzylidene-imidazolidine-2,4-dione **15** by MW irradiation (72%) which later reacted with




Scheme 3 Synthesis of (*S*)-5-benzyl-3-(2-chloroethyl)-2-oxoimidazolidin-4-one **7** and (*S*)-6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **11**.



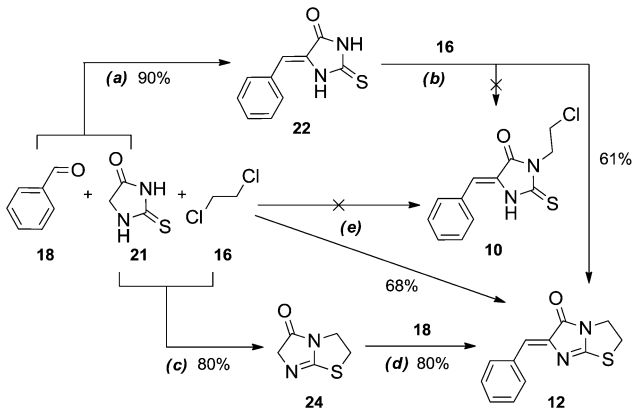

(a) $NaHCO_{3(aq)}$, MW, 140 °C, 10 min ; (b) $Et_3N$, MW, 175 °C, 10 min; (c) $K_2CO_{3(aq)}$, MW, 175 °C, 10 min; (d) $NaHCO_{3(aq)}$, MW, 140 °C, 10 min; (e) $Et_3N$, MW, 175 °C, 20 min.

Scheme 4 Synthesis of 5-benzylidene-3-chloroethyl-2-oxoimidazolidin-4-one **8** by different methodologies.

1,2-dichloroethane **16** in the presence of $Et_3N$ yielding **8** in an overall 41% yield (paths (a) and (b)).

A second methodology involved the preparation of the 3-(2-chloroethyl)imidazolidine-2,4-dione **17** (20%) and later its reaction with benzaldehyde **18**,which yielded the desired product (paths (c) and (d), 14%). Nevertheless, the simplest one pot reaction of the three reagents proved to be the best procedure to obtain **8** in 55% yield (path E) with a ratio between isomers $Z : E > 98\%$ as reported elsewhere for other benzylidene analogs.[1]

The use of equivalent procedures to afford 5-benzylidene-3-(2-chloroethyl)-2-thioxoimidazolidin-4-one **10**, resulted in the bicyclic product 6-benzylidene-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **12**.[22,23] The synthesis of **12** was performed in three different ways in order to find the best methodology (Scheme 5).




(a) $NaHCO_{3(aq)}$, MW, 140 °C, 10 min; (b) $Et_3N$, MW, 175 °C,10 min; (c) $K_2CO_{3(aq)}$, MW, 175 °C,10 min; (d) $NaHCO_{3(aq)}$, MW, 140 °C 10 min; (e) $Et_3N$ MW, 175 °C,15 min.

Scheme 5 Synthesis of 5-benzylidene-2,3-dihydroimidazo[2,1-*b*]thiazol-6(5*H*)-one **12**.

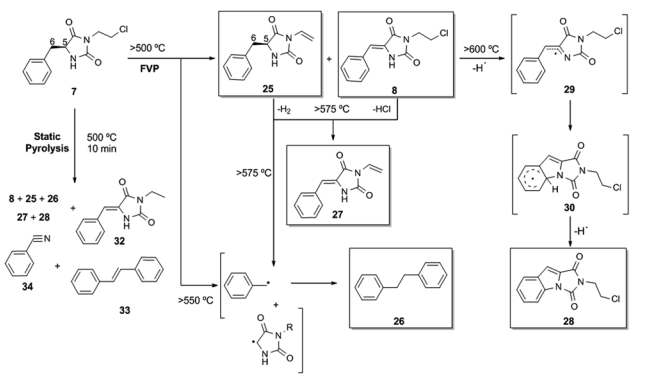
Thus, the thioxoimidazolidinone precursor **22** was prepared from **18** and **21** using MW irradiation at 140 °C (90%), and then reacted with **16** under MW irradiation at 175 °C yielding **12** in 55% overall yield (paths (a) and (b)). On the other hand, **12** could be also obtained from the imidazothiazolone **24** and benzaldehyde in 64% overall yield (paths (c and d)). Here again, the simplest one-pot reaction was the best procedure to obtain **12** in the highest yield (68%, path (e)).

The difficulties found in the preparation of both 2-thioxoimidazolidinones **9** and **10** can be attributed to multiple reasons. One of them is the high reactivity of the thiol tautomer of the thioxoimidazolidinone precursors (**20**–**22**), towards the alkylation that led to the bicyclic imidazothiazolones (**11**, **12** and **24**) without detection of 2-chloroethyl-2-thioxoimidazolidin-4-ones (Schemes 3 and 5). These findings agree with literature data,[24,25] especially when the alkylation reaction is performed with dibromoalkanes where the corresponding bicyclic compounds are obtained.[26] Although we have performed the reactions with 1,2-dichloroethane, which is less reactive than 1,2-dibromoethane, the cyclization could not be avoided. Many attempts to perform a sequence of protection and deprotection reactions of the thiol group in **20** and **22** led to unsuccessful results.

## Reactivity by flash vacuum pyrolysis

(S)-5-Benzyl-3-(2-chloroethyl)imidazolidine-2,4-dione **7** was subjected to flash vacuum pyrolysis (FVP) (Scheme 6). Sakaizumi *et al.*,[27] reported that the main product of the vacuum pyrolysis of 2-chloroethylisocyanate **14** is vinyl isocyanate produced by dehydrochlorination of the precursor between 100–900 °C, with a maximum at 800 °C. In our case, FVP reactions of **7** below 500 °C were unsuccessful, recovering only the starting material. Above 500 °C the two expected reactions took place, namely the dehydrochlorination leading to **25** and the dehydrogenation leading to **8**, though their yields were low (Scheme 6 and Table 1).

At 550 °C, $C_5$–$C_6$ cleavage of **7** becomes dominant and the main product observed was 1,2-diphenylethane **26**, resulting from the dimerization of benzyl radicals. At 575 °C a new product (**27**) involving both extrusions appears. We propose that




Scheme 6 Pyrolysis of (S)-5-benzyl-3-(2-chloroethyl)imidazolidine-2,4-dione **7** between 500–600 °C.

Table 1 FVP reactions of 7

| | Yield of products[a], % | | | |
|---|---|---|---|---|
| $T$ (°C) | 7 | 26 | 8+25 | Minor compounds |
| 500 | 96.7 | — | 3.3 (40 : 60)[c] | — |
| 550 | 73.8 | 12.2 | 2.9 (45 : 55)[c] | — |
| 575 | 67.1 | 14.8 | 3.2 (38 : 62)[c] | 27 |
| 600[b] | 54.5 | 20.0 | 4.8 (79 : 21)[c] | 27, 28 |
| 625[b] | 11.0 | 39.4 | 7.2 (76 : 24)[c] | 27, 28 |
| 650[b] | 4.1 | 43.1 | 6.2 (74 : 26)[c] | 27, 28 |

[a] Determined by GC-MS analysis. [b] The presence of coke was observed. [c] Ratio 8 : 25.

Table 2 FVP reactions of 8

| | Yield of products[a], % | | | |
|---|---|---|---|---|
| $T$ (°C) | 8 | 27 | 28 | 31 |
| 525 | 94.1 | 3.7 | 2.2 | 0 |
| 550 | 74.4 | 4.8 | 18.9 | 1.9 |
| 575 | 53.5 | 11.7 | 27.3 | 7.5 |
| 600 | 45.7 | 11.9 | 36.1 | 6.3 |
| 650 | 33.7 | 21.7 | 34.2 | 10.4 |
| 675 | 26.5 | 23.8 | 36.9 | 12.8 |
| 700[b] | 19.8 | 24.2 | 34.3 | 14.1 |
| 750[b] | 16.8 | 27.9 | 34.0 | 14.7 |

[a] Determined by GC-MS analysis. [b] The presence of coke was detected.

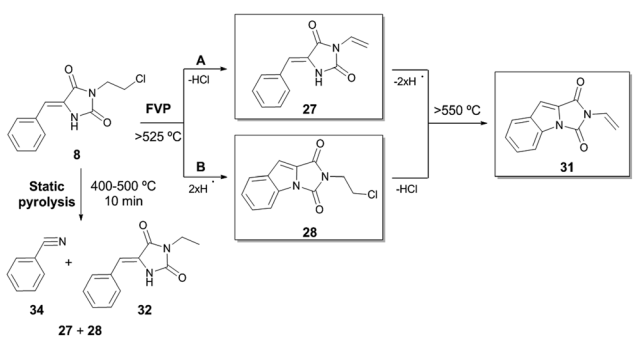
27 principally originates from 8, because the dominance of the benzylic $C_5$–$C_6$ cleavage in 25 would increase the amount of 26 which is the main product of the reaction. However, a further increase in temperature (over 600 °C) yields another heterocyclic compound (28) which is formed through an intra-molecular aromatic insertion (intermediates 29 and 30). This appears to be an exclusive product from benzylidene hydantoines since to the best of our knowledge, we have found no literature evidence of this process occurring in other cores. We have already observed this kind of reaction in the FVP of 5-benzyl-3-phenyl-2-thioxoimidazolidin-4-one.[1] Compounds similar to 28 are interesting in pharmaceutical chemistry because of their antifungal activities[28] and for this reason many other synthetic methods have been described.[29]

Compounds 8 and 27 were obtained as a mixture of the $Z$ and $E$ isomers under all conditions. $^1$H-NMR analysis of those mixtures indicated that in thermal equilibrium, the ratio between isomers $Z$ : $E$ is approximately 98 : 2 as was previously observed by us in the case of 5-benzylidene-3-phenyl-2-thioxoimidazolidin-4-one 1.[1]

In order to obtain relevant information on the mechanism without the interference of the radical reactions, *i.e.*, to suppress the formation of 1,2-diphenylethane 26, FVP of 5-benzylidene-3-(2-chloroethyl)imidazolidine-2,4-dione 8 was performed (Scheme 7 and Table 2).

As can be seen in Scheme 7, two main products were obtained under FVP at all temperatures, both described and obtained also in the FVP of 7. One of them (27) corresponds to the dehydrochlorination process (path A), and the other (28) arises from an intra-molecular aromatic insertion (path B). These results corroborate our previous assumption about the origin of 27 in the FVP of 7.

Over 550 °C, a new product, 31 is obtained. It could arise from dehydrochlorination when the precursor is 28 and/or from aromatic insertion when the precursor is 27. At present we cannot distinguish between paths A or B to produce 31 and perhaps both routes take place. It is important to note that this compound was not detected when the FVP started from 7 probably due to the characteristics of the FVP technique that allows the isolation of kinetically controlled products due to the short contact times.




Scheme 7 Pyrolysis of 5-benzylidene-3-(2-chloroethyl) imidazolidine-2,4-dione 8 at 400–750 °C.

## Reactivity by static pyrolysis

Earlier work,[1] reported the decomposition of 2 by MIP and confirmed the selectivity of the dehydrogenation process observed by FVP. As compounds 7 and 8 do not react at the highest temperatures reached by the microwave assisted reactions (300 °C), we studied their decomposition by static pyrolysis using a sealed tube with the main goal of increasing the yield of products 27, 28 and 31. Due to the long contact times of the static pyrolysis, complex mixtures were obtained in the whole range of temperatures studied (Schemes 6 and 7, static pyrolysis). The reaction mixtures were therefore analyzed by GC/MS.

The static pyrolysis of 7 and 8 were performed at 500 °C in glass cells. After 10 minutes 77% conversion of 7 into products 8, 25, 26, 27, 28, a new compound 32 and different products of fragmentation and recombination such as stilbene 33 and benzonitrile 34 was reached (Scheme 6, static pyrolysis). Similarly, compound 8 yielded compounds 27, 28, 32, benzonitrile 34 and other trace components (Scheme 7, static pyrolysis). The new compound 32 could arise from the hydrogenation of 27 or by elimination of chlorine followed by hydrogenation. In order to evaluate its source, the same procedure was performed in deactivated quartz cells. In these cases, the amount of 32 was much lower than in glass cells, suggesting that 32 is formed by hydrogen abstraction from the surface of the glass reactor.

Although it was not possible to increase the yield of the desired products by static experiments, relevant information about the stability of compounds **8**, **25–28**, **31** was retrieved. Compounds **27** and **28** appear to be the most stable ones, while **8**, **25** and **31** decompose under these conditions.

### Kinetic measurements from flash vacuum pyrolysis

More information on the reaction mechanism was derived from kinetic measurements carried out on **7** and **8** through the use of FVP. The rate constants for the reactions of **7** and **8** are given in Tables S1 and S2 in ESI data,† while the activation parameters in Table 3. Rate constants were measured at particular temperatures from the change of the relative concentrations of the starting materials as determined by $^1$H NMR and GC and averaged over at least three determinations. Reaction times were calculated as $V_0/m$ (contact time), $V_0$ being the volume of the reaction tube inside the hot zone and $m$, the carrier gas flow. Arrhenius parameters were derived *via* the classical equation ($\ln k$ *vs.* $1/T$). In order to validate the system, the kinetic parameters from the pyrolysis of ethyl acetate were measured and compared with those reported for a static system; these results, together with a detailed description of the methodology, have been described elsewhere.[1]

Even though the calculated parameters describe the sum of various processes, they highlight the differences between the reactions of two imidazolidine-2,4-dione derivatives. For compound **7** the positive value of activation entropy ($\Delta S^{\#} = 0.8$ e.u.) indicates that the mechanism is driven by a radical process like the one proposed for the formation of the main product observed (**26**) while for **8** this value is negative (−36.0 e.u.) in agreement with a concerted mechanism. In fact, the parameters obtained for **8**, are similar to those reported in the gas phase reaction for 5-benzyl-3-phenyl-2-thioxoimidazolidin-4-one **2**, where a concerted $H_2$ elimination was proposed.[1]

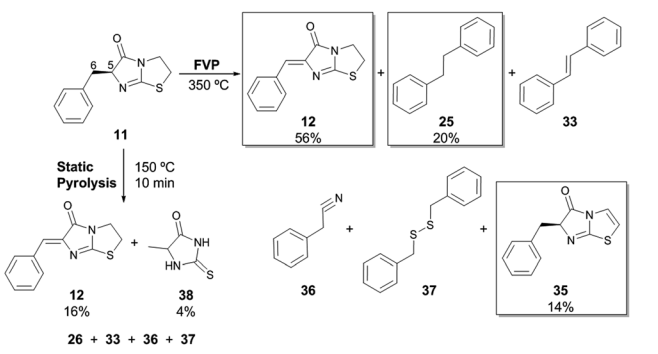
From the calculation of $\Delta G^{\#}$, it is possible to conclude that radical mechanisms affording benzyl radicals have a slightly smaller free energy demand than the concerted ones yielding dehydrogenation or dehydrochlorination products. This can be rationalized by the increasingly important contribution of the entropy term, because at higher temperatures it cannot be neglected in the calculation of $\Delta G^{\#}$.

On the other hand, (*S*)-6-benzyl-2,3-dihydroimidazo[2,1-*b*]-thiazol-5(6*H*)-one **11** and 5-benzylidene-2,3-dihydroimidazo-[2,1-*b*]thiazol-6(5*H*)-one **12** were subjected to pyrolysis in gas phase. Unfortunately, the low vapour pressures and the lability of these compounds difficult the study and promoted decomposition of substrates in the sample probe. In the case of **12** all efforts to achieve volatilization of the sample failed. Nevertheless, for **11** it was possible and the FVP reactions were carried out at 350 °C affording as main products 1,2-diphenylethane **26**, 5-benzylidene-2,3-dihydroimidazo[2,1-*b*]thiazol-6(5*H*)-one **12** and (*S*)-6-benzylimidazo[2,1-*b*]thiazol-5(6*H*)-one **35** among others (which included even coke, Scheme 8).

Exocyclic (**12**) and endocyclic (**35**) dehydrogenation reactions are competing with the radical fragmentation of the weak $C_5$–$C_6$ in **11**. Exocyclic dehydrogenation appears to be more easily achieved than the other processes. According to the yields obtained, the relatively low amount of **35** could also be due to its inherent instability, which would, upon reaction, generate more fragmentation products. We propose this hypothesis due to the fact that in the static pyrolysis performed at low temperatures (150 °C, 10 min) **35** was not detected. Calculations to estimate the energies required for each process are therefore needed to support or discard the mechanisms.

The reaction temperatures required for any pyrolysis of **11** are lower than those required for **7**. This fact allows us to obtain a smaller number of kinetically controlled products thus improving the selectivity of the process. This is one of the most relevant pieces of information obtained from static experiments, where oxo derivatives are much more stable (requiring temperatures higher than 400 °C to react) in comparison with their thio analogues. As it was stated above, this behavior was also observed for *cis* and *trans*-2-thio(oxo)quinazolin-4-ones **3**.[10]

It is well known that charge density can be distributed over the molecule by the appropriate interaction with the electron lone pairs or with 3p orbitals available on heteroatoms. The more electronegative the atom containing the lone pair is, the less able it is to donate electron density. For this reason, sulfur is a more effective stabilizer of charge density than oxygen. We




Scheme 8 Pyrolysis of (*S*)-6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **11**.

Table 3 Activation parameters for FVP reactions of **7** and **8**

| Comp. | $E_a$ (kcal mol$^{-1}$) | $\log(A)/\Delta S^{\#}$ (u.e.) | $\Delta H^{\#a}$ (kcal mol$^{-1}$) | $\Delta G^{\#a}$ (kcal mol$^{-1}$) |
|---|---|---|---|---|
| **7** | 45.6 | 13.41/0.80 | 43.9 | 43.2 |
| **8** | 14.5 | 5.37/−36.0 | 12.8 | 44.2 |

[a] Determined at 600 °C.

believe that this is the reason why the imidazothiazolone **11** reacts at lower temperatures than the oxygenated ones, affording the same kind of products.

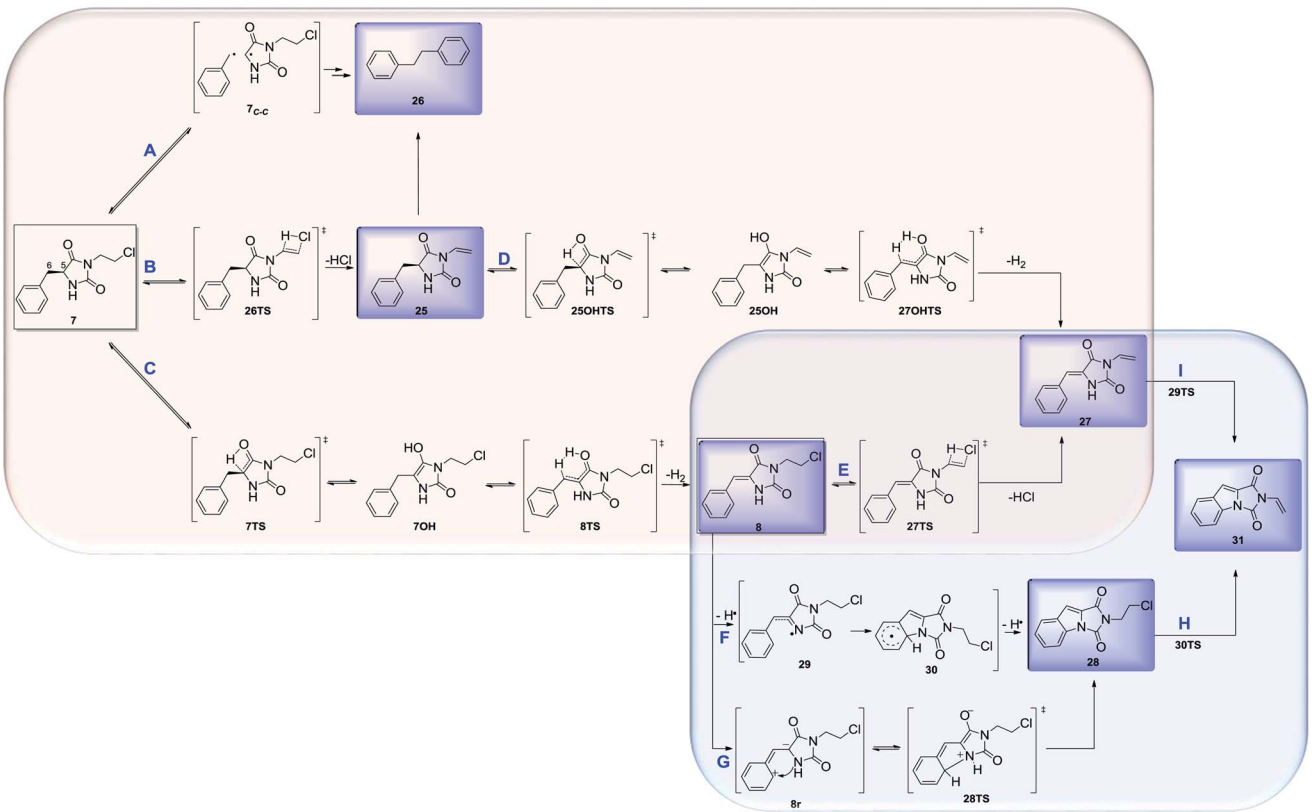
## Theoretical study

Quantum chemical calculations, using the DFT level of theory (B3LYP/6-31+G(d,p) functional), have been carried out in order to investigate the reaction mechanisms in the gas phase pyrolysis of imidazolidine-2,4-dione derivatives (**7**, **8**) as well as the imidazothiazolone **11**. In all cases, full geometry optimizations were performed, followed by harmonic frequency calculations at the same level of theory, which also allowed characterization of the nature of the stationary points.

With the exception of our recent work, there are, to the best of our knowledge, no previous mechanistic studies on the gas phase dehydrogenation of benzyl imidazolidinones.[1] Therefore, we propose the set of reactions depicted in Scheme 9 to account for the whole reaction mechanism of imidazolidinones. We suggest three main paths for reaction of **7**, namely, a stepwise one, *via* a radical intermediate (path A) that has to do with the dissociation of the $C_5$–$C_6$ bond, and two concerted routes (paths B or C) that lead to the dehydrochlorination and dehydrogenation compounds, respectively. For all possible reaction mechanisms, radical routes are expected to give positive entropies of activation and concerted mechanisms negative values, as was stated above.

Calculations through concerted routes (Table 4) show that the dehydrochlorination (path B, **25TS** = 53.5 kcal mol$^{-1}$) requires less energy than the dehydrogenation which is achieved from the enol ***7OH*** (path C, **7TS** = 76.9 kcal mol$^{-1}$). This trend corresponds to the experimental results obtained at low temperatures (500–575 °C) where the ratio **8**/**25** is lower than one (Table 1). On the other hand, the most energetic process calculated was the cleavage of the $C_5$–$C_6$ bond to afford benzyl radicals through path A, which is in disagreement with the experimental results, where 1,2-diphenylethane **26** is the main product; however, it is important to remember that at high temperatures the positive term $T\Delta S^{\#}$ is not negligible and it could compensate the energy requirement to the cleavage.

Starting from **8**, we postulate different concerted ways for the synthesis of **27** and **28**. The energy required for the dehydrochlorination is almost the same than for **7** (path E, **27TS** = 54.0 kcal mol$^{-1}$); nevertheless, the energy required to reach the concerted transition state **28TS** (path G, 112.0 kcal mol$^{-1}$) is too high to be achieved and its formation seemed rather unlikely; for this reason, a lower energy possibility (path F) postulates first the loss of radical hydrogen (91.7 kcal mol$^{-1}$) and then a radical insertion to the aromatic ring, with formation of a new five-membered heterocycle. Thus, a comparison of the energy barriers for dehydrochlorination and aromatic insertion allows us to propose that compound **31** would be principally obtained from **28** rather than being formed from **27**.

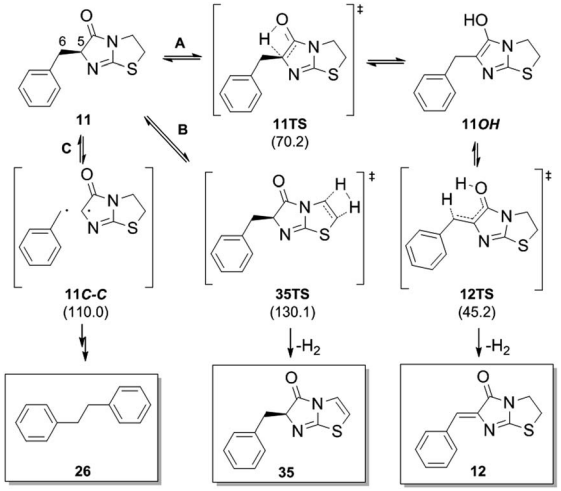



Scheme 9 Reaction mechanism for pyrolysis of **7** and **8**.

Table 4 B3LYP energies of transient species involved in the proposed mechanisms for FVP of **7** and **8**

| Path | A | B | C | | D | | E | F | G | H | I |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Species | **7C–C** | **25TS** | **7TS** | **8TS** | **25OHTS** | **27OHTS** | **27TS** | **29** | **28TS** | **30TS** | **29TS** |
| $\Delta E^a$ | 110.0 | 53.5 | 76.9 | 45.2 | 73.2 | 44.1 | 54.0 | 91.7 | 112.0 | ~50 | ~90 |

[a] Values in kcal mol$^{-1}$.




Scheme 10 Proposed mechanisms for the FVP reaction of **11** at B3LyP/6-31+G(d,p) theoretical level.

The reaction paths of compound **11** were calculated and led us to conclude that the concerted endocyclic dehydrogenation to afford **35** is the most energetic process (Scheme 10, path B, **35TS** = 130.1 kcal mol$^{-1}$) (*cf.* the $C_5$–$C_6$ cleavage, path C, **11*C–C*** = 110.0 kcal mol$^{-1}$ and the exocyclic dehydrogenation, path A, **11TS** = 70.2 kcal mol$^{-1}$ and **12TS** = 45.2 kcal mol$^{-1}$). These calculations are in agreement with the fact that compound **12** is obtained in 56% yield while 26 and 35 are obtained in low yields, 20% and 14% respectively. Despite the fact that the experimental energy barrier obtained was much lower than the calculated numbers, we believe that the overall trend of the calculations is quite significant, because we can explain not only the percentage of products obtained but also corroborate our assumptions about the dehydrogenation, cyclization[1] and tautomerization[11] performed in our previous studies.

# Conclusions

New synthetic methodologies to obtain 3-(2-chloroethyl) imidazolidine-2,4-dione (**7** and **8**) and 2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one (**11** and **12**) derivatives are described together with studies of their reactivity. Under thermal conditions, these compounds undergo fragmentation, dehydrogenation, dehydrochlorination and cyclization or a combination of these reactions to give the corresponding dehydrogenated products. This work shows once again the scope of the FVP methodology to form C–C double bonds through simple dehydrogenation and dehydrohalogenation process.

We found that thio compounds react at lower temperatures than the oxygenated counterparts. This fact was explained by the capacity of sulfur atoms to conjugate electrons as well as charge density.

Through experimental observations and quantum chemical calculations, we were able to rationalize the sequence and the energy requirements of the different processes for each compound. For (*S*)-5-benzyl-3-(2-chloroethyl)imidazolidine-2,4-dione (**7**) the sequence established was cleavage of benzylic bond, dehydrochlorination and exo-dehydrogenation to afford the benzyliden derivative; while for (*S*)-6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one (**11**) it was exocyclic dehydrogenation, cleavage of benzylic bond and a new endocyclic dehydrogenation.

# Experimental

### General methods

FVP reactions were carried out in a Vycor glass reactor using a tube furnace with a temperature-control device. Oxygen-free dry nitrogen was used as the carrier gas. Contact times were around $10^{-2}$ s and a pressure of 0.02 Torr was used. Products were trapped at liquid air temperature, extracted with a solvent, and subjected to different analyses or separation techniques. In all FVP experiments, the recovery of material was >90%. Static pyrolysis were performed by introducing each of the substrates into the reaction tube (1.5 × 12 cm Pyrex) that was then cooled in liquid nitrogen and sealed under vacuum. The sealed ampoule was finally placed in the Vycor glass reactor. The products of pyrolysis were then extracted with solvent (acetone-$d_6$) and subjected to different analyses or separation techniques. Reactions under microwave irradiation were performed in cylindrical borosilicate tubes ($\Phi$ = 1.5 cm) located in a Anton Paar Monowave 300 reactor (2.455 GHz), with adjustable power within the range 0–300 W and a wave guide (monomode) fitted with a stirring device and IR and Ruby temperature detectors. (*S*)-5-Benzyl-3-(2-chloroethyl)imidazolidine-2,4-dione **7**, 5-benzylidene-3-(2-chloroethyl)imidazolidine-2,4-dione **8**, (*S*)-6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **11** and 5-benzylidene-2,3-dihydroimidazo[2,1-*b*]thiazol-6(5*H*)-one **12** were prepared by modifying a procedure described in the literature.[17,18] All compounds were characterized by standard spectroscopic techniques ($^1$H NMR, $^{13}$C NMR, HMBC, HSQC, UV, IR) and mass spectrometry, and all data are in agreement with the proposed structures. $^1$H, $^{13}$C, HSQC and HMBC spectra were recorded in

acetone-$d_6$ with a Bruker Advance II 400 MHz spectrometer (BBI probe, *z* gradient) ($^1$H at 400.16 MHz and $^{13}$C at 100.56 MHz). Chemical shifts are reported in parts per million (ppm) downfield from TMS. The spectra were measured at 22 °C. Absorption spectra of the solutions were recorded with a UV-1601 Shimadzu spectrophotometer using a quartz cell with an optical path length of 1 cm and acetonitrile as solvent. Infrared solid spectra were recorded with an FTIR Bruker IFS 28v spectrometer, with a resolution of 2 $cm^{-1}$ in the range from 4000 to 400 $cm^{-1}$ by using KBr disks. All calculations were performed with the Gaussian 09 program system[30] by using a DFT-B3LYP/6-31+G(d,p) approach. Transition-state theory was used to evaluate the energy of the different channels. The transition states were characterized by the presence of one negative frequency and the internal reaction's coordinate (IRC) method was applied to verify that the correct states were connected. Though we knew that more precise methods were available, we had to make a compromise between the size of the molecules under study and the computational cost. Gas chromatography/mass spectrometry (GC/MS) analyses were performed with a Shimadzu GC/MS-QP 5050 spectrometer equipped with a VF column (30 m × 0.25 × mm × 5 μ) by using helium as eluent at a flow rate of 1.1 mL $min^{-1}$. The injector and ion source temperature was 280 °C, the oven heating ramp was 15 °C $min^{-1}$ from 150 up to 280 °C, and the interface temperature was 280 °C. The pressure in the MS instrument was $10^{-5}$ Torr, precluding ion-molecule reactions from taking place, and MS recordings were made in the electron impact mode (EI) at ionization energy of 70 eV.

### Synthesis of (*S*)-5-benzyl-3-(2-chloroethyl)imidazolidine-2,4-dione (7)

L-Phenylalanine **13** (496 mg, 3.0 mmol) and 2-chloroethylisocyanate **14** (446 mg, 3.3 mmol) were placed in a cylindrical borosilicate tube in that order. Nitromethane (0.3 mL) was added solely to homogenize the mixture. The tube was then introduced into the Anton Paar microwave reactor. The mixture was stirred at room temperature and then irradiated at 100 °C for 10 min. The reaction products were extracted with ethyl acetate (3 × 15 mL), the organic layer was dried over anhydrous $Mg_2SO_4$, and after removal of the solvent under reduced pressure, the solid was recrystallized from toluene to give the pure title compound **7** (310 mg, 41%) as white powder. $\nu_{max}$ (KBr)/$cm^{-1}$ = 3292 (NH st), 2924 (C–H $sp^3$ st), 1773 (C=O st), 1721 (C=O st). $\lambda_{max/nm}$ [$\varepsilon$/$M^{-1}$ $cm^{-1}$]($CH_3CN$) = 191 [(1 × $10^2$ ± 0.006)$10^6$]. $^1$H NMR $\delta_H$ (ppm) (400.16 MHz, acetone-$d_6$, 22 °C) = 7.24 (m, 5H, Ar-H), 4.42 (m, 1H, C5–H), 3.55 (m, 4H, $CH_2$–$CH_2$–Cl), 3.15 (dd, $J_1$ = 14.1 Hz, $J_2$ = 4.5 Hz, 1H, C6–$H_a$), 2.99 (dd, $J_1$ = 14.1 Hz, $J_2$ = 6.1 Hz, 1H, C6–$H_b$). $^{13}$C NMR $\delta_c$ (ppm) (100.56 MHz, acetone-$d_6$) = 173.9, 156.9, 136.5, 130.6 (×2), 129.1(×2), 127.7, 58.7, 40.8, 40.3, 38.0. GC-MS *t* (min) = 7.82, *m*/*z* (EI, %): 65(10), 91(100), 92(11), 252(5, $M^{+\bullet}$), 254(2, $M^{+\bullet}$ + 2).

### Synthesis of 5-benzylidene-3-(2-chloroethyl) imidazolidine-2,4-dione (8)

**8** was prepared by three different ways modifying existing procedures.[18,19]

**Method (a) and (b).** In a cylindrical borosilicate tube were placed benzaldehyde **18** (0.5 mL, 4.9 mmol), imidazolidine-2,4-dione **19** (410 mg, 4.1 mmol) and saturated $NaHCO_3$ solution (1.0 mL). After introduction into the Anton Paar microwave reactor, the mixture was irradiated at 140 °C for 10 min. The crude was partitioned with ethyl acetate (3 × 15 mL) and the organic layer dried over anhydrous $Mg_2SO_4$ to obtain the pure 5-benzylidene-imidazolidine-2,4-dione **15** (60.1 mg, 72%). Then, compound **15** (0.3 mmol), 1,2-dichloroethane **16** (1.0 mL, 12.6 mmol) and $Et_3N$ (1 mL) were placed in the borosilicate tube and irradiated at 175 °C for 10 min. The reaction products were extracted performing the same procedure as before to obtain the pure 5-benzylidene-3-(2-chloroethyl)imidazolidine-2,4-dione **8** (42.8 mg, 57%, global yield: 41%).

**Method (c) and (d).** In a cylindrical borosilicate tube thioxoimidazolidin-4-one **19** (713 mg, 7.1 mmol), 1,2-dichloroethane **16** (1.2 mL, 15.1 mmol) and $K_2CO_3$ (2.9 g, 21.1 mmol) were placed. The mixture was irradiated at 175 °C for 10 min. The reaction products were extracted as in method A and B to obtain the pure 3-(2-chloroethyl)imidazolidine-2,4-dione **17** (760 mg, 20%). Then, compound **17** (4.7 mmol), benzaldehyde **18** (0.5 mL, 4.5 mmol) and $NaHCO_3$ saturated solution (1.0 mL) were introduced in the borosilicate tube and irradiated at 140 °C for 10 min. The reaction crude was extracted to obtain the pure 5-benzylidene-3-(2-chloroethyl)imidazolidine-2,4-dione **8** (70%, global yield: 14%).

**Method (e).** In a cylindrical borosilicate tube, benzaldehyde **18** (1.0 mL, 9.8 mmol), imidazolidine-2,4-dione **19** (634 mg, 3.4 mmol), 1,2-dichloroethane **16** (1.0 mL, 12.6 mmol) and $Et_3N$ (1.0 mL) were placed. Subsequently the mixture was irradiated at 175 °C during 20 min. The reaction mixture was extracted to obtain the pure 5-benzylidene-3-(2-chloroethyl)imidazolidine-2,4-dione **8** (55%) as white powder. $\nu_{max}$ (KBr)/$cm^{-1}$ = 1720 (C=O st), 2925 (C–H $sp^3$ st). $\lambda_{max/nm}$ [$\varepsilon$/$M^{-1}$ $cm^{-1}$]($CH_3CN$) = 315 [(1.81 ± 0.01)$10^4$]. $^1$H NMR $\delta_H$ (ppm) (400.16 MHz, acetone-$d_6$, 22 °C) = 9.65 (broad s. 1H, N–H), 7.63 (d, $J$ = 7.2, 2H, Ar-$H_o$), 7.43 (t, $J$ = 7.4 Hz, 2H, Ar-$H_m$), 7.36 (t, $J$ = 7.4 Hz, 1H, Ar-$H_p$), 6.63 (s, 1H, =C6–H); 3.90 (m, 4H, $CH_2$–$CH_2$–Cl). $^{13}$C NMR $\delta_c$ (ppm) (100.56 MHz, DMSO-$d_6$) = 163.8, 154.3, 129.3 (×2), 128.9 (×2), 128.6, 109.9, 40.6, 39.9. GC-MS *t* (min) = 9.10, *m*/*z* (EI, %): 63(13), 64(5), 89(37), 90(44), 91(7), 116(28), 117(100), 118(16), 144(5), 172(13), 187 (18), 188 (33), 250 (68, $M^{+\bullet}$), 251(14), 252(23).

### Synthesis of 5-benzyl-2-thioxoimidazolidin-4-one (20)

In a cylindrical borosilicate tube, L-phenylalanine **7** (4.0 g, 24.0 mmol), thiourea **23** (5.6 g, 73.7 mmol) and *tert*-butylammonium perchlorate (341 mg, 1.0 mmol) were placed. After introduction into the Anton Paar microwave reactor, it was irradiated at 190 °C for 15 min. The reaction products were extracted with ethyl acetate (3 × 15 mL) and the organic layer dried over anhydrous $Mg_2SO_4$ to obtain the pure 5-benzyl-2-thioxoimidazolidin-4-one, **20** (95%).

### Synthesis of (*S*)-6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one (11)

First, compound **20** (118 mg, 0.6 mmol), 1,2-dichloroethane **16** (0.3 mL, 3.8 mmol) and $Et_3N$ (0.1 mL) were placed in the

microwave vial and subjected to 15 min irradiation at 100 °C. The reaction products were extracted to obtain the pure 6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **11** (61%, global yield: 58%). In other vial, compound **20** (436.7 mg, 2.1 mmol), 1,2-dichloroethane **16** (0.3 mL, 3.8 mmol), $K_2CO_3$ (815 mg, 8.2 mmol) and acetone (1.0 mL) were placed. The mixture was stirred at room temperature for 48 h. The reaction products were extracted to obtain the pure 6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **11** (229 mg, 47%, global yield: 45%). The last procedure consisted in placing compound **20** (450 mg, 2.2 mmol), 1,2-dichloroethane **16** (0.3 mL, 3.8 mmol) and $K_2CO_3$ (810 mg, 8.2 mmol) in the borosilicate tube. The mixture was irradiated with MW at 110 °C for 30 minutes. The reaction products were extracted as usual to obtain the pure 6-benzyl-2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **11** (52%, global yield: 49%). $\nu_{max}$ (KBr)/$cm^{-1}$ = 1708 (C=O st), 1769 (C=O st), 2925 (C–H $sp^3$ st), 3276 (N–H st). $\lambda_{max/nm}$ [$\varepsilon$/$M^{-1}$ $cm^{-1}$]($CH_3CN$) = 267 [(4.61 ± 0.01)$10^4$]. $^1$H NMR $\delta_H$ (ppm) (400.16 MHz, acetone-$d_6$, 22 °C) = 7.52 (m, 5H, Ar-H), 4.43 (m, 1H, C5–H), 3.58 (m, 4H, $CH_2$–$CH_2$–Cl), 3.16 (dd, $J_1$ = 15.1 Hz, $J_2$ = 5.4 Hz, 1H, C6–$H_a$), 3.01 (dd, $J_1$ = 15.2 Hz, $J_2$ = 6.3 Hz, 1H, C6–$H_b$). $^{13}$C NMR $\delta_c$ (ppm) (100.56 MHz, acetone-$d_6$) = 173.9, 156.9, 136.5, 130.6 (×2), 129.1 (×2), 127.7, 58.7, 40.8, 40.3, 38.0. GC-MS *t* (min) = 7.52. *m*/*z* (EI, %) = 51(3), 65(8), 77(3), 91(100), 92(9), 206(17, $M^{+\bullet}$ – CH≡CH), 232 (2, $M^{+\bullet}$).

### Synthesis of 5-benzylidene-2,3-dihydroimidazo[2,1-*b*]thiazol-6(5*H*)-one (12)

**Method (a) and (b).** In a microwave vial, benzaldehyde **18** (0.5 mL, 4.9 mmol), 2-thioxoimidazolidin-4-one **21** (649 g, 5.6 mmol) and saturated $NaHCO_3$ solution (1.0 mL) were placed. After introduction into the Anton Paar microwave reactor, it was irradiated at 140 °C for 10 min. The reaction products were extracted with ethyl acetate (3 × 15 mL) and the organic layer dried over anhydrous $Mg_2SO_4$ to obtain the pure 5-benzylidene-2-thioxoimidazolidin-4-one **22** (61.2 mg, 90%). Then, compound **22** (0.3 mmol), 1,2-dichloroethane **16** (1.0 mL, 12.6 mmol) and $Et_3N$ (1.0 mL) were placed in a vial and irradiated with MW at 175 °C for 10 min. The reaction products were extracted to obtain the pure 5-benzylidene-2,3-dihydroimidazo[2,1-*b*]thiazol-6(5*H*)-one **12** (61%, global yield: 55%).

**Method (c) and (d).** In a microwave vial, thioxoimidazolidin-4-one **23** (705 mg, 6.8 mmol), 1,2-dichloroethane (1.3 mL, 16.4 mmol) and $K_2CO_3$ (2.5 g, 18.0 mmol) were placed. The mixture was irradiated at 175 °C for 10 min. The reaction products were extracted to obtain the pure 2,3-dihydroimidazo[2,1-*b*]thiazol-5(6*H*)-one **24** (680 mg, 80%). Then, compound **24** (4.8 mmol) and benzaldehyde **18** (0.5 mL, 4.9 mmol), in presence of $NaHCO_3$ (1.0 mL), were placed in the borosilicate tube and irradiated at 140 °C for 10 min. The reaction products were extracted with ethyl acetate (3 × 15 mL) and the organic layer dried over anhydrous $Mg_2SO_4$ to obtain the pure 5-benzylidene-2,3-dihydroimidazo[2,1-*b*]thiazol-6(5*H*)-one **12** (80%, global yield: 64%).

**Method (e).** In a cylindrical vial were placed benzaldehyde **18** (1.0 mL, 9.8 mmol), 2-thioxoimidazolidin-4-one **21** (0.5 g, 3.5 mmol), 1,2-dichloroethane **16** (1.0 mL, 12.6 mmol) and $Et_3N$ (1.0 mL). The mixture was irradiated with MW at 175 °C for 15 min. The reaction products were extracted as usual to obtain the pure 5-benzylidene-2,3-dihydroimidazo[2,1-*b*]thiazol-6(5*H*)-one **12** (547 mg, 68%) as yellow powder. $\nu_{max}$ (KBr)/$cm^{-1}$ = 1713 (C=O st), 2906 (C–H $sp^3$ st). $\lambda_{max/nm}$ [$\varepsilon$/$M^{-1}$ $cm^{-1}$]($CH_3CN$) = 366 [(4.67 ± 0.01)$10^4$]. $^1$H NMR $\delta_H$ (ppm) (400.16 MHz, acetone-$d_6$, 22 °C) = 8.16 (m, 2H, Ar-$H_o$), 7.42 (m, 3H, Ar-$H_p$, Ar-$H_m$), 6.73 (s, 1H, =C6–H), 3.98 (m, 4H, $CH_2$–$CH_2$–Cl). $^{13}$C NMR $\delta_c$ (ppm) (100.56 MHz, acetone-$d_6$) = 132.4 (×2), 130.3, 129.4(×2), 122.9, 41.6, 35.1. *m*/*z* (EI, %) = 51(5), 59(6), 60(10), 63(10), 76(5), 86(18), 89(40), 90(11), 102(7), 115(7), 116(60), 117(8), 122(7), 142(14), 147(6), 174(12), 201(16), 202(57, $M^{+\bullet}$ – $CH_2$=$CH_2$), 203(7), 229(11), 230(100, $M^{+\bullet}$).

### Thermal reactions of 7, 8 and 11

**Flash vacuum pyrolysis reaction.** In a typical experiment, samples of **7**, **8** or **11** (30 mg) were pyrolyzed. After the reaction, the crudes were extracted with acetone-$d_6$ and subjected to GC/MS and NMR analysis. The mixtures were also purified by preparative thin-layer chromatography (dichloromethane/hexane, 6 : 4) to afford products **25**, **27**, **28**, **31**, **33** and **35**.

**Static pyrolysis.** Each of the substrates (**7**; 5.0 mg, 20.0 μmolar **8**; 5.0 mg, 21.6 μmol) were introduced into the reaction tube (1.5 × 12 cm Pyrex), cooled in liquid nitrogen, sealed under vacuum (0.06 mbar) and then placed in the Vycor glass reactor for 10 min at 400 °C for **7** and 400 °C and 500 °C for **8**. The pyrolysis products were then extracted with solvent (acetone-$d_6$) and subjected to different analyses or separation techniques to afford products **8**, **25**, **26**, **27**, **28** and **32**. Compounds **26**, **33**, **34**, **36**, **37** and **38** were characterized by comparison with authentic samples.

*Data for 5-benzyl-3-vinylimidazolidine-2,4-dione,* ***25****.* GC/MS *t* (min) = 6.20, *m*/*z* (EI, %) = 42(6), 43(30), 44(6), 58(8), 65(11), 83(9), 91(100), 92(14), 100(24), 117(13), 149(7), 216(8, $M^{+\bullet}$).

*Data for (Z)-5-benzylidene-3-vinylimidazolidine-2,4-dione,* ***27****.* $\lambda_{max/nm}$ [$\varepsilon$/$M^{-1}$ $cm^{-1}$]($CH_3CN$) = 316 [(1.87 ± 0.01)$10^4$] $M^{-1}$ $cm^{-1}$. $^1$H NMR $\delta_H$ (ppm) (400.16 MHz, acetone-$d_6$, 22 °C) = 5.50 (dd, $J_1$ = 410.1 Hz, $J_2$ = 16.3 Hz, 2H); 6.67 (s, 1H); 6.76 (c, $J_1$ = 16.3 Hz, $J_2$ = 9.8 Hz, 1H); 7.38 (t, $J$ = 7.3 Hz, 1H); 7.45 (t, $J$ = 7.2, 2H); 7.66 (d, $J$ = 7.3, 2H) ppm. $^{13}$C NMR $\delta_c$ (ppm) (100.56 MHz, DMSO-$d_6$) = 102.9, 110.4, 124.3, 128.8, 128.9 (×2), 129.3. GC-MS *t* (min) = 7.10, *m*/*z* (EI, %) = 63(10), 64(5), 89(31), 90(37), 116(24), 117(100), 118(9), 172(9), 213(8), 214(84, $M^{+\bullet}$).

*Data for 2-(2-chloroethyl)-1H-imidazo[1,5-a]indole-1,3(2H)-dione,* ***28****.* $\lambda_{max/nm}$ [$\varepsilon$/$M^{-1}$ $cm^{-1}$]($CH_3CN$) = 202 [(2.54 ± 0.01) $10^5$], 235 [(4.26 ± 0.01)$10^4$], 319 [(7.12 ± 0.01)$10^4$]. $^1$H NMR $\delta_H$ (ppm) (400.16 MHz, acetone-$d_6$, 22 °C) = 4.00 (m, 4H); 7.33 (s, 1H); 7.37 (t, $J$ = 7.8 Hz, 1H); 7.58 (t, $J$ = 7.7 Hz, 1H); 7.85 (t, $J$ = 7.6 Hz, 2H) ppm. $^{13}$C NMR $\delta_c$ (ppm) (100.56 MHz, DMSO-$d_6$) = 41.2, 41.6, 109.1, 124.9, 129.2, 113.7, 125.3, 133.5, 133.7, 149.5, 159.54 ppm. GC-MS *t* (min) = 6.06, *m*/*z* (EI, %) = 62(5), 63(5), 88(10), 89(6), 114(13), 115(45), 116(6), 143(100), 144(12), 199(6), 248(23, $M^{+\bullet}$), 250(8).

*Data for 2-vinyl-1H-imidazo[1,5-a]indole-1,3(2H)-dione,* ***31****.* This compound was characterized by GC-MS *t* (min) = 5.91, *m*/*z*

(EI, %) = 43(10), 44(6), 62(9), 88(20), 89(6), 114(18), 115(68), 116(8), 143(100), 144(11), 212(40, $M^{+\bullet}$), 213(15).

*Data for (Z)-5-benzylidene-3-ethylimidazolidine-2,4-dione,* ***32.*** This compound was characterized by GC-MS *t* (min) = 6.89, *m*/*z* (EI, %) = 43(24), 44(15), 63(9), 89(25), 90(34), 116(19), 117(100), 118(11), 187(6), 188(6), 215(1), 216(81, $M^{+\bullet}$), 217(13).

*Data for 6-benzylimidazo[2,1-b]thiazol-5(6H)-one,* ***35.*** GC/MS *t* (min) = 6.89, *m*/*z* (EI, %) = 44(9), 91(36), 105(15), 116(14), 119(39), 128(9), 142(9), 143(29), 157(8), 191(9), 201(7), 202(16), 107(30), 208(8), 220(8), 221(100), 222(17), 229(7), 230(25, $M^{+\bullet}$).

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## Notes and references

1 A. J. Pepino, W. J. Peláez, E. L. Moyano and G. A. Argüello, *Eur. J. Org. Chem.*, 2012, **18**, 3424–3430.
2 K. Kieć-Kononowicz and E. Szymańska, *Il Farmaco*, 2002, **57**, 909–916.
3 V. Chazeau, M. Cussac and A. Boucherle, *Eur. J. Med. Chem.*, 1992, **27**, 625.
4 J. Thenmozhiyal, P. Wong and W. Chui, *J. Med. Chem.*, 2004, **47**, 1527–1535.
5 J. Marton, J. Enisz, S. Hosztafi and T. Tímar, *J. Agric. Food Chem.*, 1993, **41**, 148–152.
6 U. Hintermai, T. Gutel, A. Slawin, D. Cole-Hamilton, C. Santini and Y. Chauvin, *J. Organomet. Chem.*, 2008, **693**, 2407–2414.
7 J. Choi, A. MacArthur, M. Brookhart and A. Goldmanm, *Chem. Rev.*, 2011, **111**, 1761–1779.
8 M. Lezanska, G. Szymanski, P. Pietrzyk, Z. Sojka and J. Lercher, *J. Phys. Chem. C*, 2007, **111**, 1830–1839.
9 R. F. C. Brown, in *Pyrolytic Methods in Organic Chemistry: Application of Flow and Flash Vacuum Pyrolytic Techniques*, ed. H. Wasserman, Academic Press, New York, 1980.
10 W. J. Peláez, Z. Szakonyi, F. Fülöp and G. I. Yranzo, *Tetrahedron*, 2008, **64**, 1049–1057.
11 W. J. Peláez, A. G. Iriarte, Z. Szakonyi, F. Fülöp and G. A. Argüello, *J. Anal. Appl. Pyrolysis*, 2012, **96**, 181–187.
12 H. McNab, *Contemp. Org. Synth.*, 1996, **3**, 373–396.
13 M. Karpf, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 414–430.
14 U. E. Wiersum, *J. R. Neth. Chem. Soc.*, 1982, **101**, 317–332.
15 (*a*) Y. Vallée, in *Gas Phase Reactions in Organic Synthesis*, Gordon & Breach, London, 1997; (*b*) *Applied Pyrolysis Handbook*, ed. P. Thomas Wampler, CRC Press-Taylor & Francis Group, Boca Ratón, 2007.
16 P. Edman, *Acta Chem. Scand.*, 1950, **4**, 277–282.
17 K. Faghihi, K. Zamani and A. Mobinikhaledi, *Turk. J. Chem.*, 2004, **28**, 345–350.
18 K. Schologl, F. Wessel, O. Kraupp and H. Storma, *J. Med. Pharm. Chem.*, 1961, **4**, 231–258.
19 G. A. Martinez Córdoba, L. A. Ramos, S. E. Ulic, J. L. Jios, C. O. DellaVédova, A. J. Pepino, M. A. Burgos Paci, G. A. Argüello, M. Ge, H. Beckers and H. Willner, *J. Phys. Chem. A*, 2011, **115**, 8608–8615.
20 J. Marton, J. Enisz, S. Hosztafi and T. Tímar, *J. Agric. Food Chem.*, 1993, **41**, 148–152.
21 J. C. Thenmozhiyal, P. T.-H. Wong and W.-K. Chui, *J. Med. Chem.*, 2004, **47**, 1527–1535.
22 J. C. Kim, L. K. Yun, Y. S. Koh, U. C. Yoon, M. Y. Pack and K. H. Moon, *Yakhak Hoechi*, 1983, **27**, 309–314.
23 K. Kieć-Kononowicz, J. K. Wojciechowska, C. E. Müllerc, U. Geis, W. Ksiazek and E. Szymańska, *J. Heterocycl. Chem.*, 1999, **36**, 257–264.
24 E. Szymańska, K. Kieć-Kononowicz, A. Białecka and A. Kasprowicz, *Il Farmaco*, 2002, **57**, 39–44.
25 E. Szymańska and K. Kieć-Kononowicz, *Il Farmaco*, 2002, **57**, 355–362.
26 K. Kieć-Kononowicz, J. K. Wojciechowska, C. E. Müller, B. Schumacher, E. Pekala and E. Szymańska, *Eur. J. Med. Chem.*, 2001, **36**, 407–419.
27 T. Sakaisumi, M. Nishikawa, T. Nagashima, N. Kuze and O. Ohashi, *J. Anal. Appl. Pyrolysis*, 2000, **55**, 1–11.
28 P. Kutschy, M. Suchý, M. Dzurilla, M. Takasugi and V. Kováčik, *Collect. Czech. Chem. Commun.*, 2000, **65**, 1163–1172.
29 A. R. Katritzky, S. K. Singh and S. Bobrov, *J. Org. Chem.*, 2004, **69**, 9313–9315.
30 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven Jr, J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Ioslowski and D. J. Fox, *Gaussian 09, Revision B.01*, Gaussian, Inc., Wallingford CT, 2010.