

Reactivity of 2-Thiohydantoins Towards Various Electrophilic Reagents: Applications to the Synthesis of New 2-Ylidene-3,5-dihydro-4*H*-imidazol-4-ones.

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Abstract: A new route to 5-(imidazolidin-2-ylidene)-2-methylsulfanyl-3,5-dihydro-imidazol-4-ones **4a-c** using ketene dithioacetal intermediates **3a-c** is described. The reactivity of thiohydantoin derivatives **2a-c** towards *N,N*-dimethylformamide diethylacetal (DMF-DEA) was also explored using solvent-free technique under microwave irradiation ($\mu\omega$). The ¹H- and ¹³C-NMR spectra of some representative products are discussed.

Keywords: Thiohydantoins; ketene dithioacetal; dimethylformamide diethylacetal; microwave irradiation.

Introduction

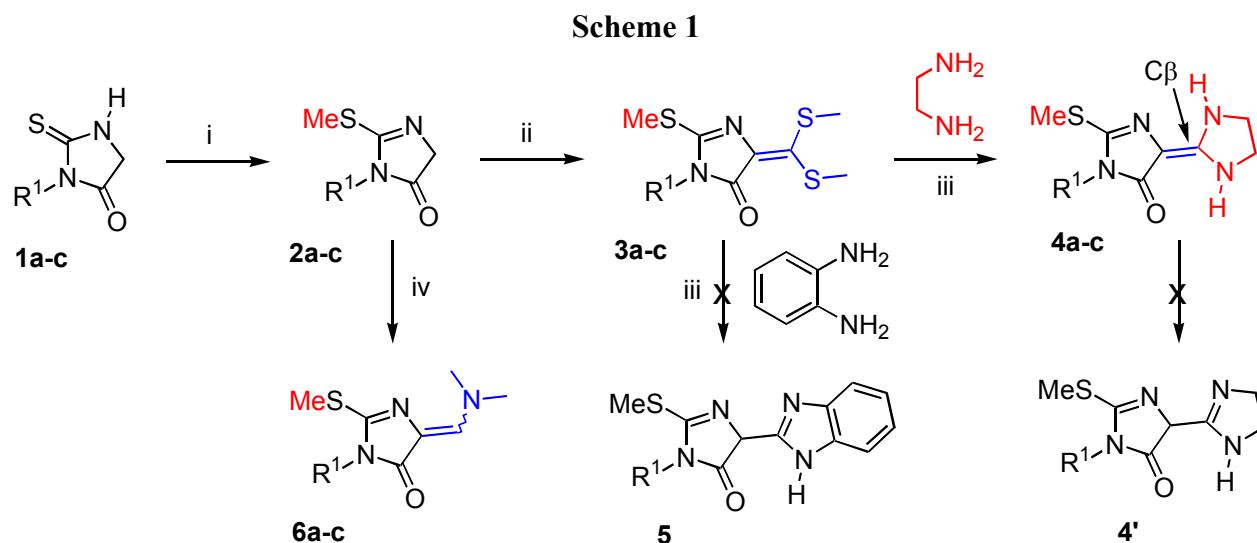
There has been much interest in the synthesis and properties of 2-thiohydantoin derivatives that are useful synthetic intermediates with a wide range of applications as therapeutics [1] as well as

fungicides and herbicides [2]. Furthermore, several 5-arylidene-3-aryl-2-thiohydantoin and their S-glucosylated derivatives [3] show potent activity against the herpes simplex virus (HSV) [4] and the human immunodeficiency virus (HIV) [5].

A series of S-alkylated 4-ylidene thiohydantoin has been developed in our laboratory as precursors for the preparation of marine alkaloid 2-aminoimidazolones [6] with protein kinase inhibition activities [7]. As part of our program directed towards new, simple and efficient procedures for the synthesis of new 2-thiohydantoin derivatives to study their biological activities, the linking of ylidene thiohydantoin to hydrophilic imidazolidines was considered. We report in this contribution our results on the preparation of 5-imidazolidin-2-yliden-3,5-dihydro-4*H*-imidazol-4-ones *via* ketene dithioacetals and the reactivity of S-alkylated thiohydantoin towards N,N-dimethylformamide diethylacetal (DMF-DEA) under microwave irradiation ($\mu\omega$).

Results and Discussion

The 3-substituted-2-thioxo-imidazolin-4-ones starting materials **1a-c** [8] used in Scheme 1 were easily prepared in good yields (96%) on a large scale (up to 20 g) by addition of commercial isothiocyanates to methyl glycinate hydrochloride in a basic medium. With the 2-thiohydantoin **1a-c** in hand, regioselective S-alkylation with 1.5 equiv. of methyl iodide and 0.5 equiv. of potassium carbonate gave the 2-methylsulfanyl-3,5-dihydro-imidazol-4-ones **2a-c** in yields ranging from 90 to 96%.



Reagents and reaction conditions: (i) MeI 1.5 equiv., K₂CO₃ 0.5 equiv., MeCN, 40°C, 14 h.; (ii) CS₂ 1.1 equiv., K₂CO₃ 2.1 equiv., MeI 2.5 equiv., MeCN, 40°C, 16 h.; (iii) (CH₂NH₂)₂ 10 equiv. or *o*-C₆H₄(NH₂)₂ 1.1 equiv., CHCl₃, 70°C, 8 days; (iv) DMF-DEA 1 equiv., $\mu\omega$ at 70°C, 1 h.

Originally synthesized by Freund in 1919 [9], ketene dithioacetals have become established intermediates in synthetic organic methodology. The sulphur atom exercises a stabilizing effect on neighboring positive as well as negative charges. This makes the double bond in ketene dithioacetals responsive towards both nucleophilic as well as electrophilic attack, an extremely useful feature for organic synthetic purposes [10].

The desired ketene dithioacetals **3a-c** are readily prepared by a one-pot reaction of **2a-c** with carbon disulfide (1.1 equiv.) in the presence of potassium carbonate in MeCN, followed by alkylation with methyl iodide (2.5 equiv.). After moderate heating at 40°C during 16 hours, the ketene dithioacetals **3a-c** are obtained in moderate to good yields (60-70%). The ketene dithioacetals **3a-c** were next reacted with a large excess of dry ethylenediamine in chloroform to afford the desired N,N-acetals **4a-c** in moderate yields (41-54%) after recrystallization from acetone. The reaction took place smoothly under mild conditions (70°C, 8 days) and was easily monitored by the evolution of methane thiol. On the other hand, when *ortho*-phenylenediamine was employed, no reaction occurred at 70°C in CHCl₃ and only the decomposition of the starting materials was observed when more forcing reaction conditions were used (neat conditions, 15 days). These results indicate that the N,N-acetal formation seems to be influenced by the electronic effects of the primary amine.

The chemical structures of the reaction products **4a-c** were determined on the basis of their spectroscopic data (¹H-, ¹³C-NMR) and HRMS analysis. In the ¹H-NMR spectra of **4a-c**, the absence of the methylene proton signal (I = 1H) and the observation of nitrogen proton signals of two protons exclude the amidine tautomer **4'**. In the ¹³C-NMR spectra of **4c**, the C-5, C β bond revealed a strong polarization (δ_{C-5} 100 and $\delta_{C\beta}$ 164.2 ppm) that is attributed to the exocyclic "push-pull" double bond structure [11].

In the course of identifying new chemical structures derived from 2-thiohydantoin for their biological activities [12], we were interested in evaluating the chemical reactivity of C-5 methylene protons. We have investigated the reactivities of 2-methylsulfanyl-3,5-dihydro-imidazol-4-ones **2a-c** with N,N-dimethylformamide diethylacetal [13] using solvent-free conditions under microwave dielectric heating ($\mu\omega$) [14]. The microwave reactor (Synthewave[®] 402 [15]) comprises a single-mode microwave cavity that operates at a frequency of 2.45 GHz with continuous microwave irradiation power from 0 to 300 W. The reaction vial is a cylindrical quartz reactor ($\varnothing = 4$ cm) which was introduced into the Synthewave[®] 402 microwave reactor. Inside the microwave cavity, the vial was exposed to microwave irradiation. The temperature was measured with an IR captor [16] (infrared thermometry). The software algorithm regulates the microwave output power so that the preselected maximum temperature is maintained for the desired reaction/irradiation time. After the irradiation period, the reaction vial is cooled rapidly to ambient temperature by compressed air (gas jet cooling). The compounds **2a-c** were converted with DMF-DEA (1.05 equiv.) into the corresponding 5-dimethylaminomethylidene-2-methylsulfanyl-3,5-dihydro-imidazol-4-ones **6a-c** [17] in yields ranging from 80 to 86% after a reaction time of 1 hour at 70°C under microwave irradiation. The products **6a-c** can exist in (*5Z*) and/or (*5E*) isomeric forms with respect to the exocyclic C=C double bond. In all cases, the compounds **6a-c** exist as single isomers, as shown by the presence of only one set of signals in

each of ^1H - and ^{13}C -NMR, but differentiation between (*Z*)- and (*E*)- form is not possible on the basis of chemical shifts. However, the two isomeric forms are easily be differentiated on the basis of the magnitude of the long range heteronuclear ^{13}C - ^1H coupling constants, $^3J_{\text{CH}}$ which have been used for determination of configuration in various systems [18]. Generally, the magnitude of coupling constant for *cis*-configuration around the C=C double bond is smaller (2-6 Hz) than that observed for *trans*-oriented nuclei (8-12 Hz). In the case of compound **6a** ($\text{R}^1 = \text{Me}$), the magnitude of coupling constant $^3J_{\text{CH}} = 3.4$ Hz showed that **6a** exists in the (*Z*) form. Similar coupling constants have also been observed in some oxazolones derivatives with an analogous structural element [19].

Conclusions

In summary, the major significance of these results is the development of a versatile and practical route of N,N-acetal derivatives of 2-methylsulfanyl-3,4-dihydro-imidazol-4-ones *via* ketene dithioacetals. The extension of this strategy to other aliphatic primary diamines with these ketene dithioacetals is presently in progress and may complement those existing in the literature. Work is also in progress to study the protein kinase C inhibition activities of these new imidazolones [20]. The results of these pharmacological studies will be reported elsewhere in due course.

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Experimental

General

Thin-layer chromatography (TLC) was accomplished on 0.2-mm precoated plates of silica gel 60 F-254 (Merck). Visualization was made with ultraviolet light (254 and 365 nm) or with a fluorescence indicator. For preparative column chromatography, silica gel 60F 254 Merck (230-240 Mesh ASTM) was used. Melting points were determined on a Kofler melting point apparatus and are uncorrected. ^1H - NMR spectra were recorded on a Bruker AC 300 P (300 MHz) spectrometer, ^{13}C -NMR spectra on a Bruker AC 300 P (75 MHz) spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Unless otherwise stated, δ values refer to singlet absorptions. Data are given in the following order: δ value, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), number of protons, coupling constants J are given in Hertz. The mass spectra (HRMS) were taken on a Varian MAT 311 at a ionizing potential of 70 eV in the Centre Régional de Mesures Physiques de l'Ouest (CRMPO, Rennes). Solvents were evaporated with

a Buchi rotary evaporator. All reagents were purchased from Acros and Aldrich and were used without purification.

General procedure for the preparation of 2-methylsulfanyl-3,5-dihydro-imidazol-4-ones 2a-c.

To a suspension of thiohydantoin (**1**, 20 mmol.) and potassium carbonate (1.38 g., 10 mmol.) in anhydrous acetonitrile (50 mL) was added dropwise over 30 minutes methyl iodide (4.26 g., 30 mmol.). The reaction mixture was heated in a thermostated oil bath at 40°C during 14 hours with vigorous magnetic stirring. The reaction mixture was allowed to cool down to room temperature. After elimination of solvent *in vacuo*, the crude reaction mixture was triturated with diethyl ether (40 mL). After standing for 1 hour, the insoluble salt (KI) was filtered off and washed with diethyl ether (10 mL). The combined filtrates were dried over MgSO₄, filtered and elimination of the solvent by rotary evaporation afforded the desired 2-methylsulfanyl-3,5-dihydro-imidazol-4-one **2**. The crude products **2a** and **2c** were purified by recrystallization from pentane and **2b** by flash chromatography on silica gel 60F 254 (Merck) with the appropriate eluent.

3-Methyl-2-methylsulfanyl-3,5-dihydroimidazol-4-one (2a). Yield = 95 %; mp = 80-82°C (from pentane); ¹H-NMR (CDCl₃) δ: 2.56 (s, 3H), 3.06 (s, 3H), 4.14 (s, 2H); ¹³C-NMR (CDCl₃) δ: 12.3 (q, *J* = 143 Hz), 26.2 (q, *J* = 141 Hz), 59.0 (t, *J* = 144 Hz, C-5), 164.2 (m, C-2, C=N), 180.0 (m, C-4, C=O); HRMS (*m/z*): found 144.0360 (calc. for C₅H₈N₂OS, M⁺ requires: 144.0357).

3-Butyl-2-methylsulfanyl-3,5-dihydroimidazol-4-one (2b). Yield = 96 %; viscous oil; *R_f* = 0.6 (CH₂Cl₂); ¹H-NMR (CDCl₃) δ: 0.94 (t, 3H, *J* = 7.3 Hz), 1.23-1.40 (m, 2H), 1.55-1.65 (m, 2H), 2.55 (s, 3H), 3.47 (t, 2H, *J* = 7.4 Hz), 4.12 (s, 2H); ¹³C-NMR (CDCl₃) δ: 12.4 (q, *J* = 143 Hz), 13.5 (qt, *J* = 125, 3.8 Hz), 19.9 (tm, *J* = 121 Hz), 30.7 (tm, *J* = 125 Hz), 40.3 (tm, *J* = 139, 4.5 Hz), 59.0 (t, *J* = 144 Hz, C-5), 164.0 (m, C-2, C=N), 179.9 (m, C-4, C=O); HRMS (*m/z*): found 186.0833 (calc. for C₈H₁₄N₂OS, M⁺ requires: 186.0827).

2-Methylsulfanyl-3-phenyl-3,5-dihydroimidazol-4-one (2c). Yield = 90 %; mp = 84-86°C (from pentane); ¹H-NMR (CDCl₃) δ: 2.49 (s, 3H), 4.34 (s, 2H), 7.26-7.29 (m, 2H, Ar), 7.39-7.50 (m, 3H, Ar); ¹³C-NMR (CDCl₃) δ: 12.8 (q, *J* = 143 Hz), 59.4 (t, *J* = 144 Hz), 127.4 (dt, *J* = 162, 6.2 Hz), 129.3 (dt, *J* = 162, 7.5 Hz), 129.5 (dm, *J* = 163 Hz), 132.1 (t, *J* = 7.8 Hz), 163.9 (m, C-2, C=N), 179.0 (t, *J* = 3.5 Hz, C-4, C=O); HRMS (*m/z*): found 206.0498 (calc. for C₁₀H₁₀N₂OS, M⁺ requires: 206.0514).

General procedure for the preparation of ketene dithioacetals 3a-c.

A mixture of 2-methylsulfanyl-3,5-dihydro-imidazol-4-one **2** (20 mmol.) and carbon disulfide (1.68 g., 22 mmol.) in acetonitrile (50 mL) was treated with anhydrous potassium carbonate (5.53 g., 40 mmol.) under vigorous magnetic stirring at room temperature. Methyl iodide (8.52 g., 60 mmol.)

was added dropwise during 45 minutes to the dianionic ambident compound formed. The reaction mixture was stirred for 16 hours at 40°C. The solvent was removed *in vacuo* and diethyl ether (100 mL) was poured into the crude reaction mixture. Insoluble salts were filtered off and the filtrate was dried over MgSO₄. The solvent was eliminated in a rotary evaporator and the crude reaction mixture gave oil that crystallized on standing. Compounds **3(a-c)** were used without further purification.

5-(Bis-methylsulfanyl-methylene)-3-methyl-2-methylsulfanyl-3,5-dihydro-imidazol-4-one (3a). Yield = 60 %; mp = 60-62°C (from ether); ¹H-NMR (CDCl₃) δ: 2.58 (s, 3H), 2.63 (s, 3H), 2.73 (s, 3H), 3.14 (s, 3H); ¹³C-NMR (CDCl₃) δ: 12.7 (q, *J* = 143 Hz), 18.4 (q, *J* = 141 Hz), 19.2 (q, *J* = 142 Hz), 26.5 (q, *J* = 140 Hz), 135.4 (m, C-6), 149.0 (m, C-5), 157.4 (m, C-2, C=N), 163.9 (m, C-4, C=O); HRMS (*m/z*): found 248.0115 (calc. for C₈H₁₂N₂OS₃, M⁺ requires: 248.0112).

5-(Bis-methylsulfanyl-methylene)-3-butyl-2-methylsulfanyl-3,5-dihydro-imidazol-4-one (3b). Yield = 68 %; mp = 45-48°C; ¹H-NMR (CDCl₃) δ: 0.95 (t, 3H, *J* = 7.2 Hz), 1.34 (sext, 2H, *J* = 7.6 Hz), 1.64 (quint, 2H, *J* = 7.4 Hz), 2.58 (s, 3H), 2.64 (s, 3H); 2.75 (s, 3H), 3.58 (t, 2H, *J* = 7.3 Hz); ¹³C-NMR (CDCl₃) δ: 12.3 (q, *J* = 143 Hz), 13.7 (qt, *J* = 125, 3.8 Hz), 18.4 (q, *J* = 141 Hz), 19.2 (q, *J* = 142 Hz), 19.9 (tm, *J* = 121 Hz), 30.7 (tm, *J* = 125 Hz), 40.3 (tm, *J* = 139, 4.5 Hz), 135.4 (m, C=), 149.0 (m, C-5), 160.1 (m, C-2, C=N), 165.9 (m, C-4, C=O); HRMS (*m/z*): found 290.0589 (cal. for C₁₁H₁₉N₂OS₃, M⁺ requires: 290.0581).

5-(Bis-methylsulfanyl-methylene)-2-methylsulfanyl-3-phenyl-3,5-dihydro-imidazol-4-one (3c). Yield = 70 %; mp = 90-92°C (from ether); ¹H-NMR (CDCl₃) δ: 2.58 (s, 3H), 2.59 (s, 3H), 2.79 (s, 3H), 7.27-7.33 (m, 5H, Ar), 7.38-7.50 (m, 3H, Ar); ¹³C-NMR (CDCl₃) δ: 13.2 (q, *J* = 143 Hz), 18.5 (q, *J* = 142 Hz), 19.4 (q, *J* = 142 Hz), 127.2 (ddd, *J* = 164, 7.3, 5.5 Hz, C-3'), 128.9 (dt, *J* = 162, 7.5 Hz, C-4'), 129.4 (dd, *J* = 162, 7.3 Hz, C-2'), 132.8 (t, 9 Hz, C-1'), 134.8 (s); 150.2 (hp, *J* = 4.8 Hz, C-5); 156.7 (q, *J* = 5 Hz, C-2, C=N), 163.1 (s, C-4, C=O); HRMS (*m/z*): found 310.0257 (calc. for C₁₃H₁₄N₂OS₃, M⁺ requires: 310.0268).

General procedure for the preparation of 5-(imidazolidin-2-ylidene)-2-methylsulfanyl-3,5-dihydro-imidazol-4-ones 4a-c.

A mixture of ketene dithioacetal (**3**, 2.4 mmol.), chloroform (10 mL) and freshly distilled ethylene diamine (0.14 g., 1.2 mmol.) was heated with vigorous magnetic stirring in a thermostated oil bath at 70°C for 8 days (the reaction was monitored by TLC with methylene chloride as eluent). Volatile components were evaporated *in vacuo*, acetone (10 mL) was added to the residue, and the resulting precipitate was collected by filtration and washed with acetone (1 mL). The product was dried over CaCl₂ to give the expected compound as yellowish needles. It is recommended to handle it in the dark under an inert atmosphere at 4°C.

5-(Imidazolidin-2-ylidene)-3-methyl-2-methylsulfanyl-3,5-dihydro-imidazol-4-one (4a): Yield = 41 %, mp = 124-126°C (from acetone); ¹H-NMR (DMSO-d₆) 2.48 (s, 3H), 3.54 (m, 2H), 3.58 (m, 2H), 7.60 (br s, 1H, NH), 7.90 (br s, 1H, NH); ¹³C-NMR (DMSO-d₆, TMS) δ: 13.4 (q, *J* = 141 Hz), 42.6 (t, *J* = 145 Hz), 43.7 (t, *J* = 144 Hz), 100.7 (s, C-5, C=), 134.5 (q, *J* = 4.8 Hz, C-2, C=N), 163.8 (s, Cβ, C=), 179.8 (s, C-4, C=O); HRMS, (*m/z*): found 212.0739 (calc. for C₉H₁₂N₄OS requires 212.0732).

3-Butyl-5-(imidazolidin-2-ylidene)-2-methylsulfanyl-3,5-dihydro-imidazol-4-one (4b): Yield = 43 %, mp = 98-100°C (from acetone); ¹H-NMR (DMSO-d₆) δ: 0.91 (t, *J* = 7.2 Hz), 1.34 (sext, 2H, *J* = 7.6 Hz), 1.64 (quint, 2H, *J* = 7.4 Hz), 2.58 (s, 3H), 3.50 (m, 2H), 3.56 (m, 2H), 3.60 (t, 2H, *J* = 7.3 Hz), 7.64 (br s, 1H, NH), 7.93 (br s, 1H, NH); ¹³C-NMR (DMSO-d₆, TMS) δ: 12.4 (q, *J* = 143 Hz), 13.5 (qt, *J* = 125, 3.8 Hz), 19.9 (tm, *J* = 121 Hz), 30.7 (tm, *J* = 127 Hz), 40.3 (tm, *J* = 139, 4.5 Hz), 42.1 (t, *J* = 145 Hz), 43.9 (t, *J* = 144 Hz), 101.4 (s, C-5, C=), 140.8 (q, *J* = 5.2 Hz, C-2, C=N), 164.6 (s, Cβ, C=), 178.9 (s, C-4, C=O); HRMS, (*m/z*): found 254.1209 (calc. for C₁₁H₁₉N₄OS requires 254.1201).

5-(Imidazolidin-2-ylidene)-2-methylsulfanyl-3-phenyl-3,5-dihydro-imidazol-4-one (4c): Yield = 54 %, mp = 228-230°C (from acetone); ¹H-NMR (DMSO-d₆) δ: 2.40 (s, 3H), 3.55-3.58 (m, 4H), 7.28-7.50 (m, 5H, Ar), 7.62 (br s, 1H, NH), 7.95 (br s, 1H, NH); ¹³C-NMR (DMSO-d₆, TMS) δ: 13.6 (q, *J* = 142 Hz), 42.6 (t, *J* = 144 Hz), 43.8 (t, *J* = 144 Hz), 100.4 (s, C-5, C=), 127.0 (dm, *J* = 162 Hz, C-3', Ar), 127.3 (dt, *J* = 162, 7.5 Hz, C-4', Ar), 128.8 (dd, *J* = 162, 8 Hz, C-2', Ar), 134.80 (td, *J* = 9, 1.2 Hz, C-1', Ar), 135.5 (q, *J* = 5 Hz, C-2, C=N), 164.2 (s, Cβ, C=), 180.0 (s, C-4, C=O); HRMS, (*m/z*): found 274.0864 (calc. for C₁₃H₁₄N₄OS requires 274.0888).

General procedure for the preparation of 5-dimethylaminomethylene-2-methylsulfanyl-3,5-dihydro-imidazol-4-one 6a-c under microwave irradiation.

A mixture of 2-methylsulfanyl-3,5-dihydro-imidazol-4-one (**2**, 6.9 mmol.) and commercial dimethylformamide diethylacetal (1.01 g., 6.9 mmol.) was placed in a cylindrical quartz reactor (Ø = 4 cm). The reactor was then introduced into a Synthewave[®] 402 Prolabo microwave reactor [2.45 GHz, adjusted power within the range 0-300 W and a wave guide (single mode T₀₁) fitted with a stirring device and an IR temperature detector]. The reaction mixture was irradiated at 20% power level (60 W) for 1 hour at 70°C. Then the mixture was allowed to cool down and a solid formed rapidly (~ 5 min.) at 25°C. The crude solid was extracted with methylene chloride (20 mL) and the reactor was washed (CH₂Cl₂ : 10 mL). Volatile components of the combined layers were eliminated in a rotary evaporator under reduced pressure and the crude reaction mixture was purified by flash chromatography on silica gel 60 F 254 (Merck) with the appropriate eluent. Concentration of the desired fraction gave the expected product **6** as yellowish needles.

(5Z) 5-Dimethylaminomethylene-3-methyl-2-methylsulfanyl-3,5-dihydroimidazol-4-one (**6a**): Yield = 86 %; mp = 134-136°C; R_f = 0.7 (AcOEt); $^1\text{H-NMR}$ (CDCl_3) δ : 2.57 (s, 3H), 3.12 (s, 3H), 3.22 (br s, 3H), 3.55 (br s, 3H), 6.95 (s, 1H, =CH); $^{13}\text{C-NMR}$ (CDCl_3) δ : 13.1 (q, J = 142 Hz), 26.8 (q, J = 140 Hz), 47.0 (m), 116.0 (s, C-5), 139.1 (d, J = 165 Hz, =CH), 148.5 (m, C-2, C=N), 170.4 (dm, J = 3.4 Hz, C-4, C=O); HRMS, (m/z): found 199.0782 (calc. for $\text{C}_8\text{H}_{13}\text{N}_3\text{OS}$ requires 199.0779).

(5Z) 3-Butyl-5-dimethylaminomethylene-2-methylsulfanyl-3,5-dihydroimidazol-4-one (**6b**): Yield = 80 %; mp = 80-82°C; R_f = 0.6 (Et_2O); $^1\text{H-NMR}$ (CDCl_3) δ : 0.86 (t, 3H, J = 7.2 Hz), 1.24 (sext, 2H, J = 7.3 Hz), 1.55 (quint, 2H, J = 7.3 Hz), 2.51 (s, 3H), 3.09 (br s, 3H), 3.50 (br s, 3H), 3.52 (t, 2H, J = 7.1 Hz), 6.87 (s, 1H, =CH). $^{13}\text{C-NMR}$ (CDCl_3) δ : 13.4 (q, J = 142 Hz), 14.2 (qt, J = 125, 3.8 Hz), 20.1 (tm, J = 125 Hz), 30.4 (tm, J = 125 Hz), 40.5 (tm, J = 139, 4.5 Hz), 47.6 (m), 116.4 (s, C-5), 139.1 (d, J = 165 Hz, =CH), 149.6 (m, C-2, C=N), 170.1 (dm, J = 3.7 Hz, C-4, C=O); HRMS, (m/z): found 241.1241 (calc. for $\text{C}_{11}\text{H}_{19}\text{N}_3\text{OS}$ requires 241.1249).

(5Z) 5-Dimethylaminomethylene-2-methylsulfanyl-3-phenyl-3,5-dihydroimidazol-4-one (**6c**): Yield = 82 %; mp = 138-140°C; R_f = 0.5 (AcOEt); $^1\text{H-NMR}$ (CDCl_3) δ : 2.56 (s, 3H), 3.21 (br s, 3H), 3.63 (br s, 3H), 7.07 (s, 1H, =CH), 7.34-7.53 (m, 5H, Ar). $^{13}\text{C-NMR}$ (CDCl_3) δ : 13.3 (q, J = 142 Hz), 39.4 (qm, J = 138 Hz), 46.2 (tq, J = 138 Hz), 115.2 (d, J = 5 Hz, C-5), 127.2 (ddd, J = 163, 7.3, 5.4 Hz, Ar), 128.2 (dt, J = 161, 7.5 Hz, Ar), 129.1 (dd, J = 162, 7.9 Hz, Ar), 133.9 (t, J = 9.2 Hz, Ar), 139.1 (dt, J = 166, 3.4 Hz, =CH), 146.7 (t, J = 4.8 Hz, C-2, C=N), 169.1 (d, J = 3.1 Hz, C-4, C=O); HRMS, (m/z): found 261.0924 (calc. for $\text{C}_{13}\text{H}_{15}\text{N}_3\text{OS}$ requires 261.0936).

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Samples Availability: Available from the authors.