Microwave Assisted Efficient Synthesis of Imidazole-Based Privileged Structures

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A simple and efficient microwave assisted synthesis of imidazobenzoxazines, imidazobenzoxazin-5-ones, and imidazobenzoxazin-5-thiones with broad chemistry scope is described. The molecules were prepared both under conventional as well as microwave heating conditions, to provide in high yields with clean and scalable reactions a small library of imidazole-based privileged structures for drug discovery.

Introduction

In the last years, there is growing interest in designing and synthesizing new chemical libraries based on privileged structures, especially focusing on heterocyclic structures, that belong to a class of compounds with proven utility in medicinal chemistry.[1–3] The term "privileged structure" was introduced by Evans et al. as a single molecular framework able to provide ligands for diverse receptors.[4] Since then, many substructural frameworks have been described as privileged structures and, in particular, N-containing polycyclic structures have been reported to be associated with a wide range of biological activity.[1,5–9] There are almost unlimited combinations of annulated heterocyclic structures that can be designed with the aim to obtain polycyclic skeletons with diverse physical, chemical, and biological properties and with a rigid conformation, that can be further suitably decorated to obtain new molecules with biological activity. Therefore, it is very important to study and to develop new scaleable synthetic routes able to construct fused polyheterocyclic ring systems in high yields with a reduced number of synthetic and purification steps. For this purpose, microwave assisted organic synthesis (MAOS) continues to affect synthetic chemistry by allowing us to obtain rapid, reproducible, and scalable processes to synthesize new molecules in high yield. Moreover, this methodology can facilitate the discovery of new reactions, expanding the possibilities of preparing new compounds or libraries for drug discovery. The formation of heterocyclic rings by cyclization reactions is typically a process well-suited for microwave methodology. In fact, these reactions often require high temperature for many hours or even days, whereas similar or higher yields and cleaner reaction profiles can be obtained by microwave heating for a few minutes.[10–15] Our work focused on the synthesis of the benzimidazoxazine nucleus that were previously described only in 1985 by Mahesh.[16] Here, a useful protocol for the preparation of this imidazole-based privileged structures is described, starting from a previously published one-pot solution-phase synthesis methodology.[17–19] This efficient synthetic route was here exploited in the preparation of a series of substituted imidazoles (**1**−**6**, Scheme 1), a starting point to obtain new N-containing polycyclic structures (**7a**−**n**, Scheme 2). The imidazoles **4**−**6** were cyclized to prepare various imidazobenzoxazines, characterized by the presence of three different sites of structural variation, developing a protocol for parallel synthetic application using simple experimental conditions and avoiding purification steps. Moreover, we synthesized these new polycyclic heterocycles using both conventional solution-phase synthesis and microwave irradiation, with the aim to propose a comparison between these two techniques and to develop a rapid and scalable process.

Results and Discussion

The preparation of the 4,5-disubstituted 2-(2-hydroxyphenyl)-1*H*-imidazoles (**4**−**6**) was here investigated (Scheme 1): the direct preparation from salicylaldehyde led to low yields (between 30−67%) and required a chromatographic purification of the products obtained, thus making this synthetic route not suitable for scalable processes. The two-step synthesis, through the methoxy derivatives, led to pure compounds in higher yields (86−94%). Compounds **1**−**3** were thus prepared through solution-phase synthesis, starting from phenylglyoxals or diketones and *o*-methoxybenzaldehyde, ammonium acetate as an ammonia source, and a polar protic solvent, such as methanol at room temperature, to afford the best yields of 4,5-disubstituted 2-(2-methoxyphenyl)-1*H*-imidazoles. The subsequent demethylation reaction, that usually is lengthy and with poor yields, was carried out employing microwave irradiation (HBr 48%, 150 °C for 10 min), able to produce the complete conversion in the hydroxy derivative, with 86−95% isolated yields. These intermediates were directly transformed, without further purification, into the final products **7a**−**n**, as shown in Scheme 2. The nature of the imidazobenzoxazine obtained depends on the cyclizing agent employed (CH_2I_2, for compounds **7a**−**f**, CDI, 1,1′-carbonyldiimidazole for com-

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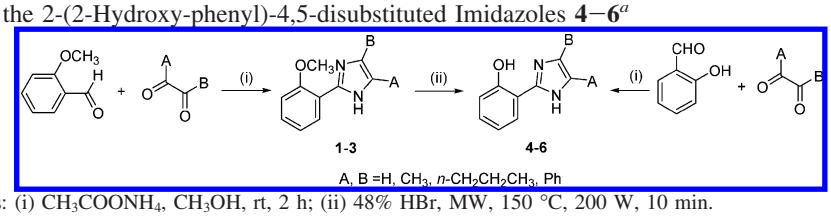
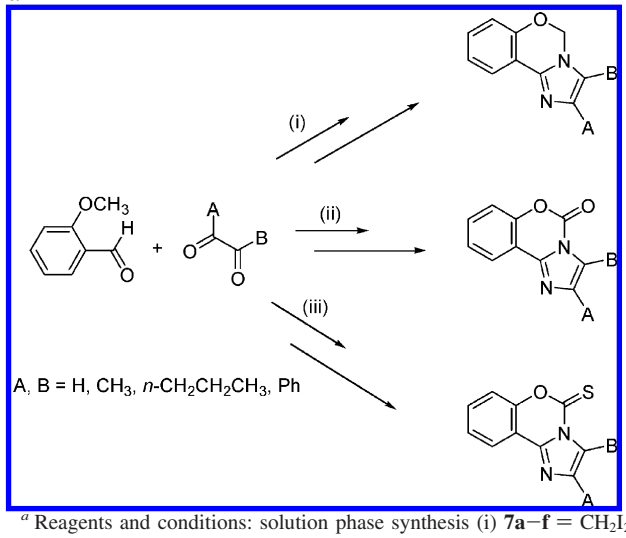
Scheme 1. Synthesis of the 2-(2-Hydroxy-phenyl)-4,5-disubstituted Imidazoles **4**−**6**[a]



[a] Reagents and conditions: (i) CH_3COONH_4, CH_3OH, rt, 2 h; (ii) 48% HBr, MW, 150 °C, 200 W, 10 min.

Scheme 2. Synthesis of the Imidazobenzoxazines, Imidazobenzoxazin-5-ones, and Imidazobenzoxazin-5-thiones **7a**−**n**[a]



[a] Reagents and conditions: solution phase synthesis (i) **7a**−**f** = CH_2I_2, Cs_2CO_3, *N*,*N*-DMF, 100 °C, 16 h, (ii) **7g**−**j** = CDI, THF, rt, 24 h; microwave heating (i) **7a**−**f** = CH_2I_2, Cs_2CO_3, CH_3CN, MW, 80 °C, 150 W, 10 min, (ii) **7g**−**j** = CDI, THF, MW, 90 °C, 240 W, 20 min, (iii) **7k**−**n** = TCDI, THF, MW, 90 °C, 240 W, 10 min + 10 min with further addition of the cyclizing agent.

pounds **7g**−**j**, and TCDI, 1,1′-thiocarbonyldiimidazole for compounds **7k**−**n**). The products were prepared first under conventional condition, and then, in order to reduce reaction times and to improve the yields, microwave heating was employed. The reaction conditions for the solution phase synthesis of the imidazobenzoxazines **7a**−**f** were investigated using different reagents: paraformaldehyde, following the procedure proposed by Burke,[20] did not afford the desired products, while CH_2Br_2 in DMF[21,16] led to low yields. The best conditions found (CH_2I_2, Cs_2CO_3, DMF, 16 h at 100 °C) determined the formation of two regioisomers, separated and isolated in yields between 50 and 70%. The imidazobenzoxazin-5-ones **7g**−**j** were prepared at first employing known procedures indicated in the literature for the synthesis of benzoxazinones,[22,23] subsequently optimized due to the different reactivity of the imidazole ring, to obtain higher and acceptable yields (between 50 and 70% using CDI in THF at rt). Interestingly, no regioselectivity was achieved when CH_2I_2 was used as a cyclizing agent (compounds **7a**−**f**), while with CDI only one isomer was recovered when a phenyl ring is connected to the imidazole (**7g** and **7h**). These findings could be correlated with the steric hindrance of the 1,1′-carbonyldiimidazole.

In the next phase of this study, the same molecules were prepared under microwave heating conditions, to investigate the advantages of this technique. In fact, it is well documented that MAOS can lead to rate enhancement, higher yields, less side reactions, and a better reproducibility compared to conventional heating. Compounds **7a**−**f** were synthesized varying molar ratios of Cs_2CO_3 and solvent (CH_3CN instead of DMF) with respect to the above solution phase synthesis. These new conditions led to very high yields (75−98%), also reducing the time of reaction from 16 h to 10 min. Compounds **7g**−**j** were prepared reducing the amount of cyclizing agent (CDI) utilized in the "classical" synthetic route, thus obtaining a significant increase of the yields (80−98%) and a dramatic decrease of the reaction time (20 min) (Table 1). Moreover, the various attempts made to optimize the cyclization reactions highlighted that MAOS did not have appreciable effects on the formation of the isomers. In fact, all the tests carried out did not affect the regioisomers ratio obtained with the traditional solution-phase synthesis, while having very favorable effects on yields and reaction times.

The optimized conditions found for the carbonyl compounds were then applied to the synthesis of the imidazobenzoxazin-5-thiones **7k**−**n**, also demonstrating the versatility of the technique employed. As was observed before for compounds **7g** and **7h**, only one isomer was formed in the presence of a phenyl ring on the imidazole (**7k** and **7l**).

Conclusion

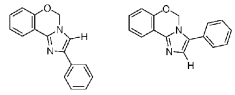
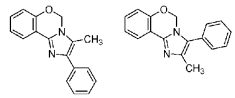
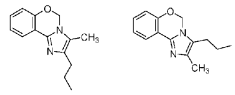
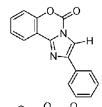
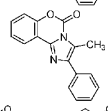
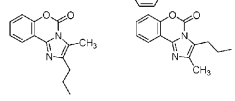
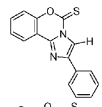
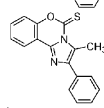
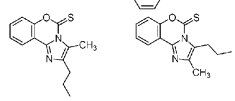
The described synthetic protocol allows for the preparation of a series of imidazobenzoxazines, imidazobenzoxazin-5-ones, and imidazobenzoxazin-5-thiones as new privileged structures potentially useful for drug discovery. A microwave-assisted synthesis was developed to provide small libraries of privileged heterocyclic structures in high yields and with clean and scalable reactions.

Experimental Section

Melting points are not corrected and were determined using a Gallenkamp melting point apparatus. Solution phase synthesis was made in parallel using a Büchi Syncore Reactor, while microwave assisted synthesis was performed using a CEM Microwave Synthesizer—Discover Model. The final products were analyzed on a ThermoQuest (Italia) FlashEA 1112 Elemental Analyzer, for C, H, N. The percentages recorded were within ±0.4% of the theoretical values. All products were also characterized by ^{1}H NMR. The ^{1}H NMR spectra were recorded on a Bruker 300 Avance spectrometer (300 MHz); chemical shifts (δ scale) are reported in parts per million (ppm) relative to the central peak of the solvent. ^{1}H NMR spectra are reported in order: multiplicity and number of protons; signals were characterized as s (singlet), dd (doublet of doublet), t (triplet), m (multiplet), br s (broad signal).

Solution Phase Synthesis. General Procedure for the Synthesis of the 2-Methoxyphenyl-imidazoles 1−**3.** The

Table 1. Synthesis of Imidazobenzoxazines, Imidazobenzoxazin-5-ones, and Imidazobenzoxazin-5-thiones **7a−n**

entry	structures	Time[a]	Yields (%)[a,b]	Time[c]	Yields (%)[c,b]
7a and 7b		16 h	85	10 min	90
7c and 7d		16 h	70	10 min	88
7e and 7f		16 h	50	10 min	75
7g		24 h	70	20 min	80
7h		24 h	60	20 min	98
7i and 7j		24 h	60	20 min	86
7k		-[d]	-[d]	10+10[e] min	85
7l		-[d]	-[d]	10+10[e] min	90
7m and 7n		-[d]	-[d]	10+10[e] min	87

[a] Conventional heating. [b] Isolated yield. [c] MAOS. [d] Not synthesized using conventional heating. [e] After 10 min another amount of TCDI was added.

opportune glyoxal or diketone (1.00 mmol) in 5.00 mL methanol was added dropwise to a solution of 2-methoxybenzaldehyde (1.20 mmol) and ammonium acetate (4.87 mmol) in 5.00 mL methanol, and the mixture was stirred at room temperature for 2 h. The solvent was evaporated and the residue was partitioned between aqueous $NaHCO_3$ solution and ethyl acetate. The organic phase was dried over Na_2SO_4, and the solvent was removed in vacuo. The crude products were then crystallized from methylene chloride/*n*-hexane.

2-(2-Methoxyphenyl)-5-phenyl-1*H*-imidazole (1). Yield 86%. mp 116−118 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.90 (br s, 1H), 8.20 (dd, 1H), 7.89 (dd, 2H), 7.64 (d, 1H), 7.38 (m, 3H), 7.18 (m, 2H), 7.05 (m, 1H), 3.94 (s, 3H).

2-(2-Methoxyphenyl)-4-methyl-5-phenyl-1*H*-imidazole (2). Yield 92%. mp 126−128 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.10 (dd, 1H), 7.72 (d, 2H), 7.35 (m, 3H), 7.21 (t, 1H), 7.13 (d, 1H), 7.03 (t, 1H), 3.95 (s, 3H), 2.50 (s, 3H).

2-(2-Methoxyphenyl)-4-methyl-5-propyl-1*H*-imidazole (3). Yield 94%. mp 106−108 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.99 (dd, 1H), 7.25 (m, 1H), 7.08 (d, 1H), 6.97 (t, 1H), 3.92 (s, 3H), 2.50 (s, 3H), 2.12 (br s, 2H), 1.55 (m, 2H), 0.89 (s, 3H).

General Procedure for the Direct Synthesis of the 2-Hydroxyphenyl-imidazoles 4−6. The opportune glyoxal or diketone (1.00 mmol) in 5.00 mL methanol was added dropwise to a solution of 2-hydroxybenzaldehyde (1.20 mmol) and ammonium acetate (4.87 mmol) in 5.00 mL methanol, and the mixture was stirred at room temperature for 2 h. The solvent was evaporated and the residue was partitioned between aqueous HCl solution and methylene chloride. Then, the aqueous phase was neutralized with K_2CO_3, and the products were extracted with methylene chloride. The organic phase was dried over Na_2SO_4, and the solvent was removed in vacuo. The crude products were purified by flash chromatography on silica gel using methylene chloride.

2-(5-Phenyl-1*H*-imidazol-2-yl)phenol (4). Yield 30%. mp 176−178 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 13.00 (s, 1H), 12.94 (s, 1H), 7.84 (m, 4H), 7.42 (t, 2H), 7.26 (t, 2H), 6.95 (m, 2H).

2-(4-Methyl-5-phenyl-1*H*-imidazol-2-yl)phenol (5). Yield 60%. mp 217−219 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 13.01 (s, 1H), 12.77 (s, 1H), 7.83 (d, 1H), 7.64 (m, 2H), 7.47 (t, 2H), 7.26 (m, 2H), 6.93 (m, 2H), 2.50 (s, 3H).

2-(4-Methyl-5-propyl-1*H*-imidazol-2-yl)phenol (6). Yield 67%. mp 132−134 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 13.21 (s, 1H), 12.35 (s, 1H), 7.74 (d, 1H), 7.16 (m, 1H), 6.86 (m, 2H), 2.50 (s, 3H), 2.18 (br s, 2H), 1.58 (m, 2H), 0.90 (t, 3H).

General Procedure for the Synthesis of the Imidazobenzoxazines 7a−f. A solution of the opportune hydroxyphenyl-imidazole (1.00 mmol), CH_2I_2 (4.00 mmol), and Cs_2CO_3 (7.20 mmol) in 2 mL dry *N*,*N*-DMF was heated at 100 °C for 16 h. The reaction mixture was then treated with methylene chloride and washed many times with water. The organic phase was dried over Na_2SO_4 and the solvent was removed in vacuo. The regioisomers so obtained were separated on silica gel using methylene chloride/*n*-exane = 1/1.

2-Phenyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazine (7a). mp 134−138 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.75 (m, 3H), 7.64 (s, 1H), 7.27 (m, 3H), 7.10 (m, 3H), 5.89 (s, 2H). Anal. ($C_{16}H_{12}N_2O$) C, H, N: C_{calc} 77.40%, C_{found} 77.00%, H_{calc} 4.87%, H_{found} 4.84%, N_{calc} 11.28%, N_{found} 10.97%.

3-Phenyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazine (7b). mp 144−148 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.72 (dd, 1H), 7.37 (m, 4H), 7.28 (m, 2H), 7.21 (s, 1H), 7.08 (m, 2H), 5.96 (s, 2H). Anal. ($C_{16}H_{12}N_2O$) C, H, N: C_{calc} 77.40%, C_{found} 77.04%, H_{calc} 4.87%, H_{found} 4.86%, N_{calc} 11.28%, N_{found} 11.07%.

3-Methyl-2-phenyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazine (7c). mp 129−132 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.70 (dd, 1H), 7.58 (br s, 2H), 7.31 (t, 2H), 7.23 (m, 1H), 7.14 (m, 1H), 7.05 (m, 2H), 5.86 (s, 2H), 2.33 (s, 3H). Anal. ($C_{17}H_{14}N_2O \cdot 0.2H_2O$) C, H, N: C_{calc} 76.78%, C_{found} 76.79%, H_{calc} 5.45%, H_{found} 5.31%, N_{calc} 10.53%, N_{found} 10.36%.

2-Methyl-3-phenyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazine (7d). mp 116−120 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.69 (dd, 1H), 7.40 (br s, 2H), 7.26 (m, 4H), 7.05 (m, 2H), 5.76 (s, 2H), 2.13 (s, 3H). Anal. ($C_{17}H_{14}N_2O$) C, H, N: C_{calc} 77.84%, C_{found} 77.95%, H_{calc} 5.38%, H_{found} 5.41%, N_{calc} 10.68%, N_{found} 10.65%.

3-Methyl-2-propyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazine (7e). mp 90−93 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.57 (dd, 1H), 7.15 (m, 1H), 6.99 (m, 2H), 5.73 (s, 2H), 2.31 (t, 2H), 2.06 (s, 3H), 1.46 (m, 2H), 0.77 (t, 3H). Anal. ($C_{14}H_{16}N_2O$) C, H, N: C_{calc} 73.66%, C_{found} 73.33%, H_{calc} 7.06%, H_{found} 7.12%, N_{calc} 12.27%, N_{found} 11.88%.

2-Methyl-3-propyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazine (7f). oil. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.57 (dd, 1H), 7.16 (m, 1H), 7.00 (m, 2H), 5.73 (s, 2H), 2.43 (t, 2H), 2.00 (s, 3H), 1.34 (m, 2H), 0.76 (t, 3H). Anal. ($C_{14}H_{16}N_2O$) C, H, N: C_{calc} 73.66%, C_{found} 73.73%, H_{calc} 7.06%, H_{found} 7.32%, N_{calc} 12.27%, N_{found} 11.96%.

General Procedure for the Synthesis of the Imidazobenzoxazin-5-ones 7g−j. A solution of the opportune hydroxyphenyl-imidazole (1.00 mmol) and 1,1′-carbonyldiimidazole (CDI; 3.00 mmol) in 2 mL THF was stirred at room temperature for 24 h. The solvent was then concentrated under reduced pressure and the imidazobenzoxazinones were purified on silica gel using methylene chloride/*n*-hexane = 1/1.

2-Phenyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazin-5-one (7g). mp 200−204 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.36 (s, 1H), 8.07 (dd, 1H), 7.94 (dd, 2H), 7.55 (m, 1H), 7.40 (m, 4H), 7.25 (m, 1H). Anal. ($C_{16}H_{10}N_2O_2 \cdot 0.2H_2O$) C, H, N: C_{calc} 72.28%, C_{found} 72.35%, H_{calc} 3.94%, H_{found} 3.93%, N_{calc} 10.53%, N_{found} 10.36%.

3-Methyl-2-phenyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazin-5-one (7h). mp 140−143 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.00 (br s, 1H), 7.62 (br s, 2H), 7.49 (m, 1H), 7.33 (m, 5H), 2.64 (s, 3H). Anal. ($C_{17}H_{12}N_2O_2$) C, H, N: C_{calc} 73.90%, C_{found} 73.64%, H_{calc} 4.38%, H_{found} 4.48%, N_{calc} 10.14%, N_{found} 9.93%.

3-Methyl-2-propyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazin-5-one (7i). mp 81−83 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.90 (dd, 1H), 7.44 (m, 1H), 7.30 (m, 2H), 3.21 (s, 3H), 2.41 (t, 2H), 1.52 (m, 2H), 0.80 (t, 3H). Anal. ($C_{14}H_{16}N_2O_2$) C, H, N: C_{calc} 69.41%, C_{found} 69.68%, H_{calc} 5.82%, H_{found} 5.95%, N_{calc} 11.56%, N_{found} 11.26%.

2-Methyl-3-propyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazin-5-one (7j). mp 78−80 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.90 (dd, 1H), 7.46 (m, 1H), 7.32 (m, 2H), 2.79 (t, 2H), 2.11 (s, 3H), 1.48 (m, 2H), 0.78 (t, 3H). Anal. ($C_{14}H_{16}N_2O_2$) C, H, N: C_{calc} 69.41%, C_{found} 69.78%, H_{calc} 5.82%, H_{found} 5.97%, N_{calc} 11.56%, N_{found} 11.35%.

Microwave Assisted Synthesis. General Procedure for the Synthesis of the 2-Hydroxyphenyl-imidazoles 4−6 from the Methoxy Derivatives 1−3. A solution of the opportune methoxyphenyl-imidazole (0.4 mmol) in 2 mL 48% HBr was prepared in a sealed 10 mL vial. The mixture was irradiated for 10 min, setting the temperature at 150 °C and the maximal power output at 200 W. During this period, the reaction vessel was stirred and cooled (2 atm air). The reaction mixture was neutralized with an aqueous saturated $NaHCO_3$ solution. The products were then extracted with ethyl acetate, and the solvent was concentrated under reduced pressure. The products so obtained were used in the successive reaction without further purification. Yields: 95% (compound **4**), 95% (compound **5**) and 86% (compound **6**).

General Procedure for the Synthesis of the Imidazobenzoxazines 7a−f. A solution of the opportune hydroxyphenyl-imidazole (1.00 mmol), CH_2I_2 (4.00 mmol), and Cs_2CO_3 (10.00 mmol) in 2 mL CH_3CN was prepared in a sealed 10 mL vial. The mixture was irradiated for 10 min, setting the temperature at 80 °C and the maximal power output at 150 W. During this period, the reaction vessel was stirred and cooled (2 atm air). Then, Cs_2CO_3 was filtered off and the solvent was concentrated under reduced pressure. The regioisomers so obtained were separated on silica gel using methylene chloride/*n*-exane = 1:1.

General Procedure for the Synthesis of the Imidazobenzoxazin-5-ones 7g−j. A solution of the opportune hydroxyphenyl-imidazole (0.80 mmol) and 1,1′-carbonyldiimidazole (CDI; 2.00 mmol) in 2 mL THF was prepared in a sealed 10 mL vial. The mixture was irradiated for 20 min, setting the temperature at 90 °C and the maximal power output at 240 W. During this period, the reaction vessel was stirred and cooled (2 atm air). The solvent was then concentrated under reduced pressure and the imidazobenzoxazinones were purified on silica gel using methylene chloride/*n*-hexane = 1/1.

General Procedure for the Synthesis of the Imidazobenzoxazin-5-thiones 7k−n. A solution of the opportune hydroxyphenyl-imidazole (0.80 mmol) and 1,1′-thiocarbonyldiimidazole (TCDI; 2.00 mmol) in 2 mL THF was prepared in a sealed 10 mL vial and was irradiated for 10

min, setting the temperature at 90 °C and the maximal power output at 240 W. The mixture so obtained was further added of TCDI (1.00 mmol) and heated at 90 °C for other 10 min, with the maximal power output at 240 W. During this period, the reaction vessel was stirred and cooled (2 atm air). The solvent was then concentrated under reduced pressure and the imidazobenzoxazinthiones were purified on silica gel using methylene chloride/*n*-hexane = 1/1.

2-Phenyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazin-5-thione (7k). mp 206−208 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.60 (s, 1H), 8.23 (d, 1H), 8.10 (d, 2H), 7.73 (m, 2H), 7.58 (m, 1H), 7.48 (t, 2H), 7.39 (t, 1H). Anal. ($C_{16}H_{10}N_2OS$) C, H, N: C_{calc} 69.04%, C_{found} 68.77%, H_{calc} 3.62%, H_{found} 3.55%, N_{calc} 10.06%, N_{found} 9.94%.

3-Methyl-2-phenyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazin-5-thione (7l). mp 158−160 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.14 (d, 1H), 7.70 (m, 2H), 7.51 (m, 6H), 2.91 (s, 3H). Anal. ($C_{17}H_{12}N_2OS$) C, H, N: C_{calc} 69.84%, C_{found} 69.45%, H_{calc} 4.14%, H_{found} 4.14%, N_{calc} 9.58%, N_{found} 9.37%.

3-Methyl-2-propyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazin-5-thione (7m). mp 117−119 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.06 (d, 1H), 7.58 (m, 2H), 7.46 (t, 1H), 2.71 (s, 3H), 2.56 (t, 2H), 1.64 (m, 2H), 0.92 (t, 3H). Anal. ($C_{14}H_{16}N_2OS$) C, H, N: C_{calc} 65.09%, C_{found} 65.49%, H_{calc} 5.46%, H_{found} 5.79%, N_{calc} 10.84%, N_{found} 10.46%.

2-Methyl-3-propyl-5*H*-imidazo[1,2-*c*][1,3]benzoxazin-5-thione (7n). mp 98−100 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.09 (dd, 1H), 7.61 (m, 2H), 7.48 (t, 1H), 3.21 (t, 2H), 2.27 (s, 3H), 1.62 (m, 2H), 0.91 (t, 3H). Anal. ($C_{14}H_{16}N_2OS$) C, H, N: C_{calc} 65.09%, C_{found} 65.29%, H_{calc} 5.46%, H_{found} 5.45%, N_{calc} 10.84%, N_{found} 10.58%.

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References and Notes

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