The Activity of Magnesium/Aluminum 'Memory Effect' Reconstructed Hydrotalcites in the Microwave-Assisted Synthesis of 2-Benzimidazolethiol and Its Alkylated Derivatives

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Received: 18.07.2013; Accepted after revision: 19.08.2013

Abstract: An efficient and practical methodology for the microwave-assisted synthesis of 2-benzimidazolethiol from 1,2-benzenediamine and carbon disulfide using reconstructed hydrotalcite is described. The corresponding mono- and dialkylated derivatives of 2-benzimidazolethiol were obtained generally in good to excellent yields after short reaction times. Reconstructed hydrotalcite proved to be an efficient and reusable heterogeneous base for the alkylation reactions.

Key words: hydrotalcite, heterogeneous bases, microwave irradiation, heterocycles, alkylations

Layered double hydroxides (LDH), or hydrotalcite-like compounds, have received considerable attention owing to their structural properties, easy recovery after a reaction, and interesting and modifiable properties as Lewis or Brønsted bases. Hydrotalcites having the general formula $[Mg_{(1-x)}Al_x(OH)_2](CO_3)_{x/2}^{2-}\cdot nH_2O$ are a class of double layered anionic clay with brucite-like $[Mg(OH)_2]$ layers, where magnesium cations are octahedrally coordinated with hydroxide ions and share edges to form the layers. When a magnesium cation is replaced by an aluminum one, a positive charge is generated in the layer, which is balanced by an anion, such as a carbonate or hydroxide ion, located between the layers.[1] Water molecules can also be present in the interlayer space.[2]

Thermal decomposition of magnesium/aluminum (Mg/Al) double layered anionic clay produces a high Mg/Al mixed oxide surface area known as calcined hydrotalcite. The hydrotalcites thus calcined can be reconstructed into the original brucite structure during subsequent aqueous treatment, owing to a peculiar memory effect.[3] The basic properties of the hydrotalcites change in both processes: calcined hydrotalcites exhibit strong Lewis base sites and the reconstructed compounds show Brønsted base ones.[4] To reconstruct hydrotalcites, microwave or ultrasonic irradiation have been employed.[5] Water,[6] aqueous solutions of sodium bicarbonate ($NaHCO_3$),[7] sodium hydroxide (NaOH),[8] and potassium hydroxide (KOH),[9] among others, have been employed as restructuring agents.

Recently, reconstructed hydrotalcites have been used as successful catalysts for esterification reactions,[10] glycerol carbonate synthesis,[3] aldol condensations,[2] the synthesis of important compounds in the cosmetic and fragrance industries,[8] and the isomerization of glucose into fructose.[11] Our research group has successfully employed calcined hydrotalcites in the macrolactonization of ω-hydroxy acids[12] and in the regioselective synthesis of silylated vicinal azidohydrins.[13] More recently, we have also applied both the parent and calcined hydrotalcites in cyanosilylation reactions over pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione (PCU).[14]

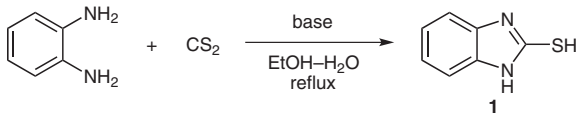
Benzimidazole and 2-benzimidazolethiol are heterocyclic rings of synthetic importance. They are present in many compounds with pharmacological activities, such as antimicrobial, antiviral, anti-inflammatory, antiulcer, antitumor, antihypertensive, antihistaminic, and anticonvulsant activity.[15] Additionally, our group has reported that 2-benzimidazolethiol is an efficient acidic corrosion inhibitor of steel grade API 5L X52.[16] We have also described the preparation of 2-(benzylthio)-1*H*-benzimidazole employing hydrotalcites and its use as an efficient acidic corrosion inhibitor of mild steel.[17]

Herein, we present a convenient and practical synthesis of 2-benzimidazolethiol and several alkylated derivatives using reconstructed hydrotalcite as a reusable heterogeneous base. These products are promising acidic corrosion inhibitors of steel.

2-Benzimidazolethiol (**1**) was prepared according to a procedure reported in the literature.[18] The refluxing of 1,2-benzenediamine and carbon disulfide in ethanol for three hours in the presence of KOH (1.05 equiv) gave product **1** in 59% yield (Table 1, entry 1). When the reaction was carried out employing the parent (HTs), calcinated (HTc), and reconstructed (HTr) hydrotalcites (100 mg) as bases under the same reaction conditions, the desired product **1** was obtained in 68, 61, and 75% yield, respectively (entries 2–4). Of these heterogeneous bases, the reaction with HTr exhibited the best results.

SYNTHESIS 2013, 45, 3281–3287
Advanced online publication: 27.09.2013
DOI: 10.1055/s-0033-1339763; Art ID: SS-2013-M0502-OP

Table 1 Base and Heating Effect on the Synthesis of 2-Benzimidazolethiol (**1**)

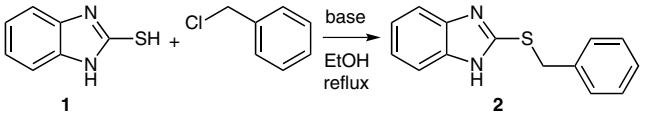


1

Entry[a]	Base	Time	Yield[c] (%)
1	KOH	3 h	59
2	HTs	3 h	68
3	HTc	3 h	61
4	HTr	3 h	75
5[b]	KOH	25 min	76
6[b]	HTr	25 min	84

[a] Reagents: 1,2-benzenediamine (1.0 g, 9.2 mmol), CS_2 (0.61 mL, 10.1 mmol), and KOH (0.54 g, 9.6 mmol) or the specified hydrotalcite (100 mg).
[b] Reaction conditions: 1,2-benzenediamine (0.5 g, 4.6 mmol), CS_2 (0.30 mL, 5.0 mmol), KOH (270 mg, 4.8 mmol) or HTr (50 mg), and microwave heating (30 W, 70 °C, using simultaneous air cooling).
[c] Isolated yield after purification.

Table 2 Alkylation of 2-Benzimidazolethiol (**1**) with Benzyl Chloride in the Presence of Different Bases



1 **2**

Entry[a]	Base	Time	Yield[d] (%)
1[b]	NaOH	2 h	87
2[b]	HTs	2 h	90
3[b]	HTc	2 h	81
4[b]	HTr	2 h	96
5[c]	NaOH	20 min	90
6[c]	HTs	20 min	91
7[c]	HTc	20 min	84
8[c]	HTr	20 min	98

[a] Reagents: 2-benzimidazolethiol (0.51 g, 3.4 mmol), benzyl chloride (0.39 mL, 3.4 mmol), and NaOH (135 mg, 3.4 mmol) or the specified hydrotalcite (135 mg).
[b] Conventional heating (reflux).
[c] Microwave heating (30 W, 70 °C, using simultaneous air cooling).
[d] Isolated yield after purification.

With the aim of improving the reaction conditions and the product yield, we decided to carry out experiments using microwave irradiation.[19] When the reaction between 1,2-benzenediamine and carbon disulfide was performed under microwave irradiation, the desired product **1** was obtained in 76% yield after only 25 minutes of reaction time using KOH (entry 5). When the heterogeneous base HTr was used under the same reaction conditions, product **1** was obtained in 84% yield (entry 6).

Following the encouraging performance of the hydrotalcites in the synthesis of thiol **1**, we decided to explore the reaction of **1** with benzyl chloride to prepare alkylated product **2**. The reaction was carried out employing conventional and microwave heating in the presence of NaOH and the three hydrotalcites. The results are summarized in Table 2 and compound **2** was obtained in good to excellent yield (81–98%). The best result was obtained with HTr and microwave heating (entry 8).

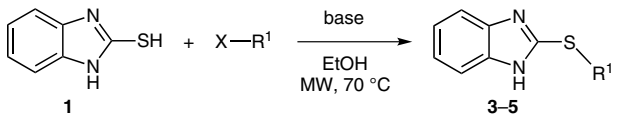
The outstanding advantages offered by hydrotalcites over common bases, such as KOH, NaOH, $NaHCO_3$, potassium carbonate, and sodium methoxide, are their recovery and reuse. In this regard, we tested the recyclability of HTr in the reaction of thiol **1** with benzyl chloride to give compound **2**. The hydrotalcite was recovered by filtration after washing with ethanol and drying at 80 °C for four hours. The recovered HTr was used without further purification for the synthesis of benzylated product **2** in a second run and displayed a very similar performance (94% yield). This result showed that HTr could be recovered without significant loss of activity.

Having successfully synthesized 2-benzimidazolethiol (**1**) and its benzylated derivative **2** using HTr, we decided to extend the application of this heterogeneous base to the synthesis of mono- and dialkylated derivatives of compound **1**.

As shown in Table 3, monoalkylated derivatives **3**–**5** were prepared in a straightforward manner. The reaction of 2-benzimidazolethiol (**1**) with the corresponding alkyl halides was performed using HTr under microwave irradiation and resulted in the corresponding alkylated products in good to excellent yields (entries 1, 3, and 5). In contrast, when the same reactions were carried out using NaOH (1 equiv) under the established reaction conditions, the desired products **3**–**5** were obtained in lower yields (entries 2, 4, and 6).

When we carried out the dialkylation of 2-benzimidazolethiol (**1**) with alkyl halides (2.3 equiv) in the presence of 260 milligrams of HTr, we obtained mixtures of the mono- and dialkylated products, which were separated by column chromatography. In all cases, the major products were the dialkylated compounds, products **6**–**10** obtained in 61–85% yield, and the corresponding monoalkylated compounds were obtained in 12–33% yield (Table 4, entries 1, 3, 5, 7, and 9). The reactions with NaOH (2 equiv) produced dialkylated compounds **6**–**10** in 50–75% yield, whereas the monoalkylated compounds were obtained in 22–44% yield (entries 2, 4, 6, 8, and 10).

Table 3 Monoalkylation of 2-Benzimidazolethiol (**1**) Using Microwave Heating



Entry[a]	Base	X	R	Time	Product	Yield[b] (%)
1	HTr	Cl	4-$ClC_6H_4CH_2$	25 min	**3**	98
2	NaOH	Cl	4-$ClC_6H_4CH_2$	25 min	**3**	51
3	HTr	Cl	2-pyridinylmethyl	30 min	**4**	94
4	NaOH	Cl	2-pyridinylmethyl	30 min	**4**	83
5	HTr	Br	$CH_2CH{=}CH_2$	35 min	**5**	77
6	NaOH	Br	$CH_2CH{=}CH_2$	35 min	**5**	67

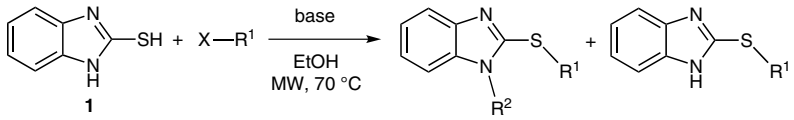
[a] Reagents: 2-benzimidazolethiol (0.51 g, 3.4 mmol), alkyl halide (3.4 mmol), and NaOH (135 mg, 3.4 mmol) or HTr (135 mg).
[b] Isolated yield after purification.

These results suggest that the deprotonation of the NH hydrogen (lower acidity than SH)[20] is more efficient with HTr, thereby favoring the formation of the dialkylated compounds.

We then observed interesting enhanced performances of related reactions using HTr. For example, the nucleophilic addition of 2-benzimidazolethiol (**1**) to phenylacetylene in the presence of NaOH (2 equiv) in ethanol under reflux for 16 hours gave *Z*-alkene **11** (92% yield),[21] whereas this product was obtained in excellent yield after 1 hour using HTr and microwave heating (Scheme 1). The S-arylation of thiol **1** with iodobenzene carried out with HTr under mild reaction conditions gave compound **12**, also in excellent yield (Scheme 1), whereas the reported method requires copper(I) iodide at high temperatures.[22]

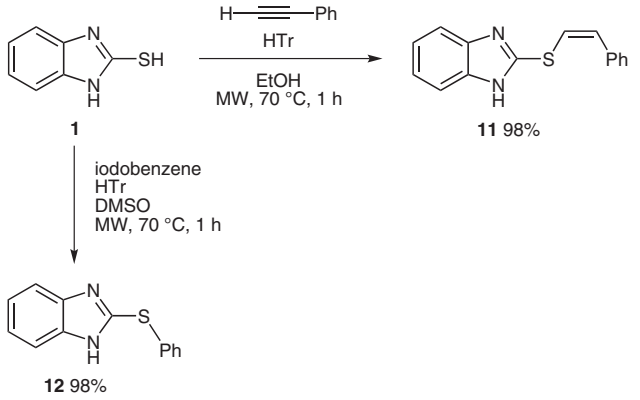
During our investigation, it was found that the reaction of 2-benzimidazolethiol (**1**) with propargyl bromide in the presence of HTr at 70 °C did not produce compound **13** after 20 minutes. Instead, tricyclic compound **14** was obtained in 95% yield (Scheme 2). The formation of product **14** proceeds through acetylene–allene isomerization followed by intramolecular cyclization.[23] The structure of

Table 4 Dialkylation of 2-Benzimidazolethiol (**1**) Using Microwave Heating

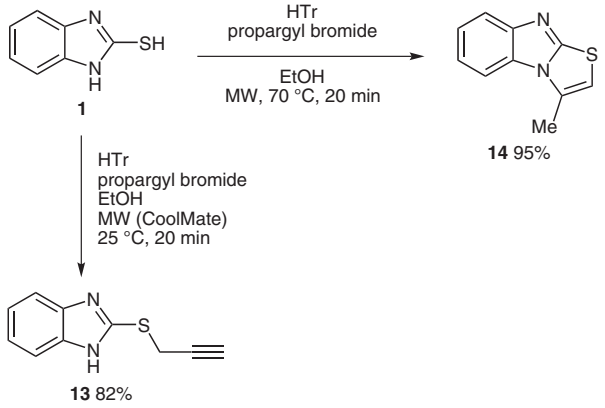


Entry[a]	Base	X	R	Time	Dialkylated product	Yield[c] (%) of dialkylated product	Yield[c] (%) of monoalkylated product
1	HTr	Cl	Bn	3.5 h	**6**	71	21
2	NaOH	Cl	Bn	3.5 h	**6**	51	38
3	HTr	Cl	4-$ClC_6H_4CH_2$	2 h	**7**	75	19
4	NaOH	Cl	4-$ClC_6H_4CH_2$	2 h	**7**	63	29
5	HTr	Cl	2-pyridinylmethyl	5 h	**8**	61	33
6	NaOH	Cl	2-pyridinylmethyl	5 h	**8**	50	44
7[b]	HTr	Br	$CH_2C{\equiv}CH$	1.3 h	**9**	85	12
8[b]	NaOH	Br	$CH_2C{\equiv}CH$	1.3 h	**9**	75	22
9	HTr	Br	$CH_2CH{=}CH_2$	3 h	**10**	80	14
10	NaOH	Br	$CH_2CH{=}CH_2$	3 h	**10**	68	24

[a] Reagents: 2-benzimidazolethiol (0.51 g, 3.4 mmol), alkyl halide (7.9 mmol), and NaOH (272 mg, 6.8 mmol) or HTr (260 mg).
[b] Microwave heating (150 W, 25 °C) employing the CoolMate system.
[c] Isolated yield after purification.



Scheme 1 Microwave-assisted syntheses of products **11** and **12** in the presence of reconstructed hydrotalcites



Scheme 2 Microwave-assisted synthesis of products **13** and **14** in the presence of reconstructed hydrotalcites

tricyclic compound **14** was confirmed by ^{1}H and ^{13}C NMR spectroscopy. Signals for the CH_3 and =CH moieties of compound **14** appeared at δ = 2.56 and 6.20 ppm, respectively, in the ^{1}H NMR spectrum.

To prevent the formation of **14**, we carried out a microwave irradiation experiment with intense simultaneous cooling using the CEM CoolMate system. After performing the reaction for 20 minutes at 25 °C, the desired product **13** was obtained in 82% yield (Scheme 2). The ^{1}H NMR spectrum of alkyne **13** exhibited a singlet at δ = 3.17 ppm (≡CH) and a doublet at δ = 4.11 ppm (CH_2) for the propargyl fragment, whereas signals at δ = 20.3 (CH_2), 74.6 (≡CH), and 80.6 (≡C) ppm appeared in the ^{13}C NMR spectrum.

In conclusion, we have successfully developed a convenient and practical synthesis of 2-benzimidazolethiol and several alkylated derivatives using HTr. This protocol offers several advantages, such as using a reusable and efficient heterogeneous base and notable process simplicity. The compounds reported herein are presently being evaluated as acidic corrosion inhibitors of steel.

Commercially available reagents and solvents were used as received. Flash column chromatography was performed on Kieselgel silica gel 60 (230–400 mesh). Melting points were determined using a Fisher-Johns apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Bruker Alpha FT-IR/ATR (attenuated total reflection) spectrometer. The NMR spectra were obtained using JEOL ECA-500 (500 MHz) and JEOL Eclipse-400 (400 MHz) spectrometers. Chemical shifts (δ) are given in ppm downfield from TMS as an internal reference. The ^{13}C NMR spectra of compounds **2**, **3**, **5**, **6**, and **8** were recorded overnight. High-resolution mass spectra (HRMS) were recorded on JEOL JMS-SX 102a and Agilent-MSD-TOF-1069A spectrometers. Microwave irradiation experiments were performed using a Discover System (CEM Corporation) single-mode microwave with standard sealed microwave glass vials. Simultaneous air jet cooling (3–4 bar) during microwave irradiation was performed using a compressor. Microwave irradiation experiments using liquid cooling were performed on a CEM CoolMate employing a microwave-transparent cooling fluid (Galden HT-55). Reaction temperatures were monitored using an IR sensor on the outside wall of the reaction vials or a fiber-optic probe protected by a sapphire immersion well inserted directly into the reaction mixture. The nitrogen adsorption–desorption isotherm of HTr was obtained at –196 °C on Micromeritics ASAP 2020 equipment. Powder X-ray diffraction (XRD) was performed using a Philips X'Pert Instrument with Cu-Kα radiation (45 kV, 40 mA). Compounds **2**–**6** and **10**–**14** are known heterocyclic compounds; dialkylated products **7**–**9** are new.

Synthesis and Characterization of Reconstructed Hydrotalcite

A solution of NaOH (14 g, 0.35 mol) and Na_2CO_3 (12.8 g, 0.093 mol) in deionized H_2O (100 mL) was added slowly dropwise using an addition funnel to a 250-mL Erlenmeyer flask containing $Mg(NO_3)_2{\cdot}6H_2O$ (25.6 g, 0.1 mol) and $Al(NO_3)_3{\cdot}9H_2O$ (18.7 g, 0.05 mol) in deionized H_2O (70 mL). The white gel obtained was then stirred and heated at 60 °C for 24 h. The resulting gel was allowed to cool and was then washed with deionized H_2O until a pH of 9 was achieved. After vacuum filtration, the wet solid was dried at 120 °C for 18 h in an oven to obtain dry HTs. Then, HTc was formed by heating HTs (2 g) at 450 °C (10 °C·min^{-1}) in a tubular furnace under air flow for 8 h. To obtain HTr, HTc (1.0 g) was treated with an MeOH–H_2O mixture (1:1, 100 mL) for 4 h at 60 °C. Then, the solid was recovered by filtration and dried at 110 °C (10 °C·min^{-1}) for 1 h.

The XRD pattern of HTr showed peak intensities and the sharpness of (0 0 3), (0 0 6), and (0 0 9) planes, which were directly proportional to the crystallinity of the material. The degree of reconstruction could be estimated by comparing the peak intensities of (0 0 3), (0 0 6), and (0 0 9) planes of each sample with those of the HTs sample after 4 h reconstruction time. The nitrogen adsorption–desorption isotherm of HTr showed a type II isotherm as defined by IUPAC and a hysteresis loop type H3 under the same classification, typical of slit-shaped pores. The HTr surface area, pore volume, and pore size were 48.95 m$^2{\cdot}$g^{-1}, 0.24 cm$^3{\cdot}$g^{-1}, and 193.38 Å, respectively.

2-Benzimidazolethiol (1)

To a suspension of HTr (50 mg) in EtOH–H_2O (9:1, 5 mL) were added 1,2-benzenediamine (500 mg, 4.6 mmol) and CS_2 (0.30 mL, 380 mg, 5.0 mmol), and the mixture was placed in a microwave reactor (30 W, 70 °C, simultaneous air cooling) for 25 min. Then, HTr was filtered off and washed with EtOH (10 mL). The EtOH used to wash the HTr was combined with the filtered reaction mixture and the whole was vacuum evaporated, and the resulting desired product was purified by column chromatography (EtOAc–hexane, 10:90) and recrystallization (EtOH–H_2O, 1:1).

Yield: 580 mg (84%); white solid; mp 302–305 °C (Lit.[18] 303–304 °C).

Monoalkylated 2-Benzimidazolethiols 2–5; General Procedure
A mixture of HTr (135 mg) in EtOH (7 mL) was placed in a microwave tube having a magnetic stirrer. Subsequently, 2-benzimidazolethiol (**1**) (510 mg, 3.4 mmol) and an alkyl halide (3.4 mmol) were added to the mixture, which was heated under microwave irradiation (30 W, 70 °C, simultaneous air cooling) for the time given in Table 2, entry 8, or Table 3. Then, HTr was filtered off and washed with EtOH (10–15 mL). The EtOH used to wash the HTr was combined with the filtered reaction mixture and the whole was vacuum evaporated, and the residue was purified by column chromatography (EtOAc–hexanes, 20:80, 10:90, or 5:95) and/or recrystallization (EtOH–H_2O, 1:1).

2-(Benzylthio)-1*H*-benzimidazole (2)
The title compound was prepared from **1** (510 mg, 3.4 mmol) and benzyl chloride (0.39 mL, 3.4 mmol) according to the above general procedure.

Yield: 790 mg (98%); white solid; mp 183–184 °C (Lit.[24] 184–185 °C).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.57 (s, 2 H, SCH_2), 7.09–7.14 (m, 2 H, ArH), 7.21–7.32 (m, 3 H, ArH), 7.43–7.45 (m, 4 H, ArH), 12.58 (br s, 1 H, NH).

^{13}C NMR (100.5 MHz, DMSO-d_6): δ = 35.7 (SCH_2), 111.0 (ArCH), 118.0 (ArCH), 122.0 (2 ArCH), 127.9 (ArCH), 129.0 (2 ArCH), 129.4 (2 ArCH), 136.0 (C_{ipso}), 138.3 (C_{ipso}), 144.2 (C_{ipso}), 150.3 (N=C–S).

2-(4-Chlorobenzylthio)-1*H*-benzimidazole (3)
The title compound was prepared from **1** (510 mg, 3.4 mmol) and 4-chlorobenzyl chloride (540 mg, 3.4 mmol) according to the above general procedure.

Yield: 800 mg (98%); white solid; mp 179–180 °C (Lit.[25] 180–181 °C).

^{1}H NMR (500 MHz, DMSO-d_6): δ = 4.52 (s, 2 H, SCH_2), 7.06–7.12 (m, 2 H, ArH), 7.31–7.34 (m, 2 H, ArH), 7.36–7.48 (m, 4 H, ArH), 12.56 (br s, 1 H, NH).

^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 34.8 (SCH_2), 110.9 (ArCH), 117.9 (ArCH), 122.0 (2 ArCH), 128.9 (2 ArCH), 131.2 (2 ArCH), 132.4 (C_{ipso}), 136.2 (C_{ipso}), 137.6 (C_{ipso}), 144.2 (C_{ipso}), 149.9 (N=C–S).

2-(2-Pyridinylmethylthio)-1*H*-benzimidazole (4)
The title compound was prepared from **1** (510 mg, 3.4 mmol) and 2-pyridinylmethyl chloride hydrochloride (550 mg, 3.4 mmol) according to the above general procedure.

Yield: 770 mg (94%); white solid; mp 100–101 °C (Lit.[26] 100–102 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.41 (s, 2 H, SCH_2), 7.16–7.20 (m, 2 H ArH), 7.22–7.26 (m, 1 H, ArH), 7.35 (d, *J* = 7.8 Hz, 1 H, ArH), 7.54 (br s, 2 H, ArH), 7.67 (td, *J* = 7.7, 1.7 Hz, 1 H, ArH), 8.60 (d, *J* = 4.3 Hz, 1 H, ArH), 13.04 (br s, 1 H, NH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 38.1 (SCH_2), 110.7 (ArCH), 118.3 (ArCH), 122.1 (2 ArCH), 123.0 (ArCH), 123.8 (ArCH), 135.3 (C_{ipso}), 138.0 (ArCH), 144.1 (C_{ipso}), 149.1 (ArCH), 151.1 (N=C–S), 158.0 (C_{ipso}).

2-(Allylthio)-1*H*-benzimidazole (5)
The title compound was prepared from **1** (510 g, 3.4 mmol) and allyl bromide (0.29 mL, 3.4 mmol) according to the above general procedure.

Yield: 830 mg (77%); white solid; mp 134–135 °C (Lit.[25] 133.5–135 °C).

^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.91–3.93 (m, 2 H, SCH_2), 5.05–5.08 (m, 1 H, $=CH_2$), 5.25–5.30 (m, 1 H, $=CH_2$), 5.92–6.01 (m, 1 H, =CH), 7.06–7.10 (m, 2 H, ArH), 7.41 (br s, 2 H, ArH), 12.52 (br s, 1 H, NH).

^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 34.4 (SCH_2), 110.8 (ArCH), 117.9 (ArCH), 118.9 ($=CH_2$), 121.9 (2 ArCH), 134.3 (=CH), 136.0 (C_{ipso}), 144.2 (C_{ipso}), 149.9 (N=C–S).

Dialkylated 2-Benzimidazolethiols 6–10; General Procedure
A mixture of HTr (260 mg) in EtOH (7 mL) was placed in a microwave tube having a magnetic stirrer. Subsequently, 2-benzimidazolethiol (**1**) (0.51 g, 3.4 mmol) and an alkyl halide (7.9 mmol) were added to the mixture, which was heated under microwave irradiation [30 W, 70 °C, simultaneous air cooling, except in the case of the formation of **9** (see below)] for the time given in Table 4. Then, HTr was filtered off and washed with EtOH (10–15 mL). The EtOH used to wash the HTr was combined with the filtered reaction mixture and the whole was vacuum evaporated, and the residue was purified by column chromatography (EtOAc–hexanes, 20:80, 10:90, or 5:95) and recrystallization (EtOH–H_2O, 1:1).

1-Benzyl-2-(benzylthio)-1*H*-benzimidazole (6)
The title compound was prepared from **1** (0.51 g, 3.4 mmol) and benzyl chloride (0.91 mL, 7.9 mmol) according to the above general procedure.

Yield: 790 mg (71%); white solid; mp 85–86 °C (Lit.[27] 93–93.5 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.64 (s, 2 H, SCH_2), 5.23 (2 H, NCH_2), 7.09–7.12 (m, 2 H, ArH), 7.17–7.19 (m, 2 H, ArH), 7.22–7.33 (m, 7 H, ArH), 7.39–7.43 (m, 2 H, ArH), 7.76 (d, *J* = 8.05 Hz, 1 H, ArH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 37.6 (SCH_2), 47.7 (NCH_2), 109.4 (ArCH), 118.6 (ArCH), 122.2 (ArCH), 122.3 (ArCH), 127.0 (2 ArCH), 127.8 (ArCH), 128.0 (ArCH), 128.8 (2 ArCH), 128.9 (2 ArCH), 129.2 (2 ArCH), 135.7 (C_{ipso}), 136.3 (C_{ipso}), 136.7 (C_{ipso}), 143.7 (C_{ipso}), 151.8 (N=C–S).

1-(4-Chlorobenzyl)-2-(4-chlorobenzylthio)-1*H*-benzimidazole (7)
The title compound was prepared from **1** (0.51 g, 3.4 mmol) and 4-chlorobenzyl chloride (1.27 g, 7.9 mmol) according to the above general procedure.

Yield: 790 mg (75%); white solid; mp 74–75 °C.

IR (neat): 3053, 3024, 2919, 1713, 1490, 1322, 1092, 795, 734 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 4.58 (s, 2 H, SCH_2), 5.32 (s, 2 H, NCH_2), 7.06 (d, *J* = 8.5 Hz, 2 H, ArH), 7.11–7.17 (m, 2 H, ArH), 7.28–7.33 (m, 4 H, ArH), 7.40–7.45 (m, 3 H, ArH), 7.57–7.60 (m, 1 H, ArH).

^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 35.5 (SCH_2), 46.5 (NCH_2), 110.4 (ArCH), 118.4 (ArCH), 122.4 (ArCH), 122.6 (ArCH), 128.9 (2 ArCH), 129.2 (2 ArCH), 129.3 (2 ArCH), 131.3 (2 ArCH), 132.6 (C_{ipso}), 132.8 (C_{ipso}), 135.8 (C_{ipso}), 136.6 (C_{ipso}), 137.3 (C_{ipso}), 143.5 (C_{ipso}), 151.3 (N=C–S).

HRMS-ESI-TOF: *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{16}Cl_2N_2S$: 399.0484; found: 399.0487.

1-(2-Pyridinylmethyl)-2-(2-pyridinylmethylthio)-1*H*-benzimidazole (8)
The title compound was prepared from **1** (0.51 g, 3.4 mmol) and 2-pyridinylmethyl chloride hydrochloride (1.29 g, 7.9 mmol) according to the above general procedure.

Yield: 688 mg (61%); white solid; mp 81–82 °C.

IR (neat): 3053, 3010, 2954, 2932, 1588, 1565, 1478, 1419, 985, 737 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.79 (s, 2 H, SCH_2), 5.38 (s, 2 H, NCH_2), 6.77 (d, *J* = 7.85 Hz, 1 H, ArCH), 7.12–7.23 (m, 5 H, ArCH), 7.45–7.50 (m, 2 H, ArCH), 7.56–7.60 (m, 1 H, ArCH), 7.70–7.73 (m, 1 H, ArCH), 8.52–8.56 (m, 2 H, ArCH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 39.0 (SCH_2), 49.5 (NCH_2), 109.5 (ArCH), 118.5 (ArCH), 121.0 (ArCH), 122.3 (ArCH), 122.4 (ArCH), 122.5 (ArCH), 122.8 (ArCH), 123.5 (ArCH), 136.4 (C_{ipso}),

136.8 (ArCH), 137.1 (ArCH), 143.7 (C_{ipso}), 149.66 (ArCH), 149.67 (ArCH), 151.7 (N=C–S), 155.5 (C_{ipso}), 156.7 (C_{ipso}).

HRMS-ESI-TOF: *m/z* $[M + H]^+$ calcd for $C_{19}H_{16}N_4S$: 333.1168; found: 333.1169.

1-(2-Propyn-1-yl)-2-(2-propyn-1-ylthio)-1*H*-benzimidazole (9)
The title compound was prepared from **1** (0.51 g, 3.4 mmol) and propargyl bromide (0.70 mL, 7.9 mmol) according to the above general procedure. The reaction was carried out under microwave irradiation employing the CoolMate system (150 W, 25 °C).

Yield: 650 mg (85%); white solid; mp 70–71 °C.

IR (neat): 3268 (≡C–H), 2966, 2925, 2123 (C≡C), 1612, 1462, 1433, 737, 660 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 3.19 (s, 1 H, C≡CH), 3.42 (s, 1 H, C≡CH), 4.17 (s, 2 H, SCH_2), 5.06 (s, 2 H, NCH_2), 7.17–7.24 (m, 2 H, ArH), 7.55–7.59 (m, 2 H, ArH).

^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 21.1 (SCH_2), 33.6 (NCH_2), 74.8 (≡CH), 76.5 (≡CH), 78.2 (C, alkyne), 80.3 (C, alkyne), 110.5 (ArCH), 118.6 (ArCH), 122.6 (ArCH), 122.8 (ArCH), 136.1 (C_{ipso}), 143.3 (C_{ipso}), 149.9 (N=C–S).

HRMS-ESI-TOF: m/z $[M + H]^+$ calcd for $C_{13}H_{10}N_2S$: 227.0637; found: 227.0633.

1-Allyl-2-(allylthio)-1*H*-benzimidazole (10)
The title compound was prepared from **1** (0.51 g, 3.4 mmol) and allyl bromide (0.68 mL, 7.9 mmol) according to the above general procedure.

Yield: 540 mg (80%); colorless liquid.[27]

^1H NMR (500 MHz, DMSO-d_6): δ = 3.96–3.99 (m, 2 H, SCH_2), 4.74–4.77 (m, 2 H, NCH_2), 4.88–4.93 (m, 1 H, $=CH_2$), 5.07–5.10 (m, 1 H, $=CH_2$), 5.12–5.16 (m, 1 H, $=CH_2$), 5.26–5.31 (m, 1 H, $=CH_2$), 5.86–6.02 (m, 2 H, =CH), 7.11–7.16 (m, 2 H, ArH), 7.39–7.43 (m, 1 H, ArH), 7.52–7.56 (m, 1 H, ArH).

^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 34.9 (SCH_2), 46.1 (NCH_2), 110.2 (ArCH), 117.7 ($=CH_2$), 118.3 (ArCH), 118.9 ($=CH_2$), 122.1 (ArCH), 122.2 (ArCH), 132.9 (=CH), 134.0 (=CH), 136.5 (C_{ipso}), 143.5 (C_{ipso}), 151.2 (N=C–S).

(*Z*)-2-(2-Phenylethenylthio)-1*H*-benzimidazole (11)
A mixture of HTr (80 mg) in EtOH (7 mL) was placed in a microwave tube having a magnetic stirrer. Subsequently, 2-benzimidazolethiol (**1**) (150 mg, 1 mmol) and phenylacetylene (0.14 mL, 1.25 mmol) were added to the mixture, which was heated under microwave irradiation (30 W, 70 °C, simultaneous air cooling) for 1 h. Then, HTr was filtered off and washed with EtOH (15 mL). The EtOH used to wash the HTr was combined with the filtered reaction mixture and the whole was vacuum evaporated, and the residue was purified by column chromatography (EtOAc–hexanes, 20:80).

Yield: 840 mg (98%); white solid; mp 134–135 °C (Lit.[21] 130–132 °C).

^1H NMR (400 MHz, DMSO-d_6): δ = 6.88 (d, J_{cis} = 10.8 Hz, 1 H, =CH), 7.16–7.18 (m, 2 H, ArH), 7.32 (d, J_{cis} = 10.7 Hz, 1 H, =CH), 7.33 (br s, 1 H, ArH), 7.43–7.60 (m, 6 H, ArH), 12.86 (br s, 1 H, NH).

^{13}C NMR (100.5 MHz, DMSO-d_6): δ = 111.5 (ArCH), 118.3 (ArCH), 120.0 (=CH), 122.4 (2 ArCH), 128.2 (=CH), 128.5 (ArCH), 129.0 (2 ArCH), 129.2 (2 ArCH), 136.3 (2 C_{ipso}), 143.8 (C_{ipso}), 147.8 (N=C–S).

2-(Phenylthio)-1*H*-benzimidazole (12)
A mixture of HTr (100 mg) in dry DMSO (3 mL) was placed in a microwave tube having a magnetic stirrer. Subsequently, 2-benzimidazolethiol (**1**) (0.3 g, 2 mmol) and iodobenzene (0.23 mL, 2 mmol) were added to the mixture, which was heated under microwave irradiation (30 W, 70 °C, simultaneous air cooling) for 1 h. Then, HTr was filtered off and washed with EtOH (15 mL). The EtOH used to wash the HTr was combined with the filtered reaction mixture and the whole was vacuum evaporated, and the residue was purified by column chromatography (EtOAc–hexanes, 20:80).

Yield: 772 mg (98%); white solid; mp 200–201 °C.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.17 (s, 2 H, ArH), 7.27–7.80 (m, 7 H, ArH), 12.79 (br s, 1 H, NH).

^{13}C NMR (100.5 MHz, DMSO-d_6): δ = 116.0 (2 ArCH), 122.7 (2 ArCH), 128.7 (ArCH), 130.2 (2 ArCH), 131.8 (2 ArCH, C_{ipso}), 140.2 (2 C_{ipso}), 147.2 (N=C–S).

2-(2-Propyn-1-ylthio)-1*H*-benzimidazole (13)
A mixture of HTr (135 mg) in EtOH (7 mL) was placed in a microwave tube having a magnetic stirrer. Subsequently, 2-benzimidazolethiol (**1**) (0.51 g, 3.4 mmol) and propargyl bromide (0.30 mL, 3.4 mmol) were added to the mixture, which was heated under microwave irradiation employing the CoolMate system (150 W, 25 °C) for 20 min. Then, HTr was filtered off and washed with EtOH (15 mL). The EtOH used to wash the HTr was combined with the filtered reaction mixture and the whole was vacuum evaporated, and the residue was purified by column chromatography (EtOAc–hexanes, 5:95) and recrystallization (EtOH–H_2O, 1:1).

Yield: 520 mg (82%); white solid; mp 163–164 °C (Lit.[23] 164–165 °C).

^1H NMR (500 MHz, DMSO-d_6): δ = 3.17 (s, 1 H, ≡CH), 4.11 (d, *J* = 1.9 Hz, 2 H, CH_2), 7.07–7.17 (m, 2 H, ArH), 7.37 (br s, 1 H, ArH), 7.51 (br s, 1 H, ArH), 12.64 (br s, 1 H, NH).

^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 20.3 (CH_2), 74.6 (≡CH), 80.6 (C, alkyne), 111.1 (ArCH), 118.1 (ArCH), 121.8 (ArCH), 122.4 (ArCH), 136.0 (C_{ipso}), 144.1 (C_{ipso}), 148.9 (N=C–S).

3-Methylbenzo[*d*]thiazolo[3,2-*a*]imidazole (14)
A mixture of HTr (135 mg) in EtOH (7 mL) was placed in a microwave tube having a magnetic stirrer. Subsequently, 2-benzimidazolethiol (**1**) (0.51 g, 3.4 mmol) and propargyl bromide (0.30 mL, 3.4 mmol) were added to the mixture, which was heated under microwave irradiation (30 W, 70 °C, simultaneous air cooling) for 20 min. Then, HTr was filtered off and washed with EtOH (15 mL). The EtOH used to wash the HTr was combined with the filtered reaction mixture and the whole was vacuum evaporated, and the residue was purified by column chromatography (EtOAc–hexanes, 10:90).

Yield: 610 mg (95%); white solid; mp 159–160 °C (Lit.[23] 159–161 °C).

^1H NMR (500 MHz, $CDCl_3$): δ = 2.56 (s, 3 H, CH_3), 6.20 (s, 1 H, =CH), 7.12 (t, *J* = 7.7 Hz, 1 H, ArCH), 7.27 (t, *J* = 7.7 Hz, 1 H, ArCH), 7.61 (d, *J* = 8.1 Hz, 1 H, ArCH), 7.71 (d, *J* = 8.2 Hz, 1 H, ArCH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.5 (CH_3), 104.6 (=CH), 110.5 (ArCH), 119.1 (ArCH), 120.6 (ArCH), 123.2 (ArCH), 129.9 (C_{ipso}), 130.3 (C_{ipso}), 148.5 (N=C–S), 157.3 (=CMe).

Acknowledgment

The authors would like to thank Consejo Nacional de Ciencia y Tecnología (CONACyT) (project 181448) for financial support. GENS and RS wish to acknowledge the SNI (Sistema Nacional de Investigadores) for the distinction of their membership and the stipend received. We also wish to thank Rebeca Yépez for her technical assistance, Teresa Cortez for her help with NMR experiments, and Dr. Delia Soto-Castro for her help with HRMS.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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