

Solar thermochemical reactions III: A convenient one-pot synthesis of 1,2,4,5-tetrasubstituted imidazoles catalyzed by high surface area SiO₂ and induced by solar thermal energy

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Abstract

A simple, convenient and efficient method for the synthesis of 1,2,4,5-tetrasubstituted imidazole derivatives using benzoin, an aromatic aldehyde, an aromatic amine in the presence of ammonium acetate catalyzed by high surface area SiO₂ and induced by free solar thermal energy was reported.

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There is now a great demand for an alternative and freely available clean energy sources. Free solar energy does not require energy raw materials hence does not produce any associated pollutants and as a consequence is regarded as a clean reagent [1,2]. It is one key technology for solving world energy. Also, multi-component reactions (MCRs) are powerful tools in generating products in a single synthetic operation [3]. It enables straight forward access to structurally related, drug-like compounds and thereby facilitating lead generation. Such reactions have constituted an increasingly valuable approach to drug discovery efforts in recent years [4,5]. The developing of new MRCs [6] and improving known multi-component reactions are an area of considerable recent interest. We do believe that combining solar thermal energy technique with a multi-component one step reaction will be of great interest in green chemistry area. One such reaction is the synthesis of tetrasubstituted imidazoles. Tetrasubstituted imidazoles scaffold is a core constituent in many biological systems such as Olmesartan [7] as well as many natural products and pharmacologically active compounds [8]. Despite extensive synthetic approaches to such molecules, only few attempts to comprise a general method have been reported. This involves the reaction of benzil or benzoin, aromatic aldehyde and an aromatic amine in the presence of ammonium acetate and catalyzed by silica gel/NaHSO₄ [9], silica gel or zeolite Hg [10], molecular iodine [11], heteropolyacids [12], K₅COW₁₂O₄·3H₂O [13], HClO₄-SiO₂ [14]. Very recently [15] a solvent free convenient method has been reported using a silica-supported boron trifluoride [BF₃·SiO₂] as a catalyst at 140 °C. However, the use of high temperature, expensive metal precursors and catalysts that may be harmful to the environment is disadvantages to such syntheses. Green

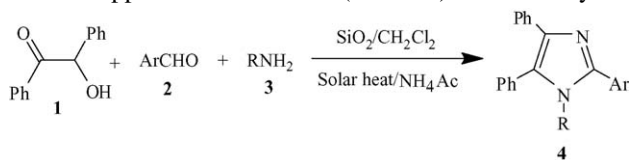
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chemistry has received considerable attention nowadays [16] and we have recently reported the first attempt to synthesize polyhydroquinoline derivatives induced by free solar thermal energy [17]. Nowadays, there is an increasing interest towards a new and economic energy sources particularly those green ones. There is no need to convince researchers by the necessity to shift towards greener techniques. Innovative chemical reactions have to make the green concepts happen. An important parameter for the economical and greenness of a reaction is that energy efficiency. High surface area fumed silica – sigma product – has a surface area equals to $390 (\pm 40) \text{ m}^2/\text{g}$ with particle size of 0.007μ and refractive index of 1.46 is a top reagent which is easy to handle, reusable with a better accessibility of the reactants to the active sites. As a part of our efforts toward the developing of useful environmentally friendly and efficient methodology for the synthesis of biologically active heterocycles [18,19] we reported herein the synthesis of tetrasubstituted imidazoles catalyzed by high surface area SiO_2 and induced by free solar thermal energy. To the best of our knowledge the combination of reusable catalyst with the free solar thermal energy to accomplish such transformation has not been reported in the literature.

Exposing a solution of benzoin, ammonium acetate, aromatic amine and aromatic aldehyde in dichloromethane to direct sunlight for 2–2.5 h (determined by TLC control), and after completion of the reaction, the mixture was cooled to room temperature. Chloroform was added to the mixture which was filtered to remove the catalyst. After evaporation of the solvent, a solid was obtained which was crystallized from the proper solvent. The generality of the method is demonstrated by using different aldehydes and amines bearing both electron donating and electron withdrawing groups as cited in Table 1. In both cases, the reaction proceeds smoothly to afford the corresponding tetrasubstituted imidazoles in high yields (80–93%) with a little bit increase when R or Ar is electron withdrawing groups. To optimize the reaction conditions, different molar ratios of reactants and catalyst were used and our study revealed that the best molar ratio of aldehyde/amine/benzoin/ammonium acetate/ SiO_2 is 1:1:1:0.1. The structure of imidazoles were confirmed by comparison with authentic specimen (^1H NMR, ^{13}C NMR and IR) spectra and mps.

The possibility of recycling the catalyst was detected. For this purpose, the reaction of benzoin, benzaldehyde, aniline and ammonium acetate as a model reaction was restudied. Our study revealed that the catalyst was reusable without appreciable reduction (82–93%) in the catalytic activity.



1. Experimental

High surface SiO_2 is commercially available from sigma products.

Typical procedure for the synthesis of tetrasubstituted imidazoles: To a solution of benzoin (1 mmol), aldehyde (1 mmol), amine (1 mmol) and amm. acetate (1 mmol) in dichloromethane (10 mL) was added high surface SiO_2 (0.1 mol%). The reaction mixture was exposed to direct sunlight for 2–2.5 h by (TLC control). The mixture was filtered to separate the catalyst which was washed with dichloromethane (5 mL) and dried to be reused. The catalyst could be directly used with the same efficiency for four times after that a graduable decline in activity was observed. The combined solvent was removed under reduced pressure to afford the crude product which was purified by crystallization from $\text{EtOH}-\text{H}_2\text{O}$ (10:1). The products were characterized by IR, NMR and through comparison of their physical properties with those reported in literature.

1.1. 1-Benzyl-2,4,5-triphenyl-1H-imidazole (4b)

IR (KBr): $\nu_{\text{max}} = 1600, 1580, 1480 \text{ cm}^{-1}$; ^1H NMR (DMSO- d_6 , 300 MHz, δ ppm): 5.25 (s, 2H, CH_2), 6.71–6.88 (m, 20H, Ar-H).

1.2. 1,2-Di(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (4h)

IR (KBr): $\nu_{\text{max}} = 1598, 1496 \text{ cm}^{-1}$; ^1H NMR (DMSO- d_6 , 300 MHz, δ ppm): 6.92–7.66 (m, 18H, Ar-H); ^{13}C NMR (DMSO- d_6 , 75 MHz, δ ppm): 127.1, 127.5, 127.9, 128.3, 128.4, 130.0, 130.2, 130.4, 131.1, 131.3, 133.3, 133.8, 134.7, 137.6, 138.7, 145.6.

Table 1
Solar thermal energy/SiO₂ synthesis of 1,2,4,5-tetrasubstituted imidazoles **4a–h**.

Compd. ^a	Ar	R	Time (h)	Yield (%)	m.p. (°C)	Lit. m.p. (°C)	Ref.
4a	C ₆ H ₅	C ₆ H ₅	2	88	218–220	216–218	[13]
4b	C ₆ H ₅	C ₆ H ₅ CH ₂	2	80	163–165	163–165	[14]
4c	4-Cl-C ₆ H ₄	C ₆ H ₅	2	93	160–161	160–162	[14]
4d	4-OH-C ₆ H ₄	C ₆ H ₅	2	85	281–282	280–281	[14]
4e	4-CH ₃ -C ₆ H ₄	C ₆ H ₅	2	90	185–178	185–188	[14]
4f	3-NO ₂ -C ₆ H ₄	4-CH ₃ -C ₆ H ₄	2.5	89	149–151	149–150	[8]
4g	4-OH-C ₆ H ₄	4-CH ₃ -C ₆ H ₄	2	84	>280	>270	[10]
4h	4-Cl-C ₆ H ₄	4-Cl-C ₆ H ₄	2	90	188–189	187–189	[8]

^a All compounds were characterized by IR, NMR and m.p.

1.3. 2-(3-Nitrophenyl)-4,5-diphenyl-1-(4-tolyl)-1H-imidazole (**4f**)

IR (KBr): ν_{\max} = 1588, 1506, 1334 cm⁻¹; ¹H NMR (DMSO-*d*₆, 300 MHz, δ ppm): 2.13 (s, CH₃), 6.95–8.22 (m, 18H, Ar-H); ¹³C NMR (DMSO-*d*₆, 75 MHz, δ ppm): 21.22 (CH₃), 122.7, 123.2, 126.8, 127.1, 128.7, 128.8, 129.1, 130.4, 130.4, 131.5, 132.2, 132.7, 134.1, 134.3, 134.4, 137.7, 139.2, 144.1, 148.1.

2. Conclusions

We have developed an efficient, simple and environmentally friendly process for the synthesis of the interesting 1,2,4,5-tetrasubstituted imidazoles, with expected biological activity, with a good yield and economic gain. The catalyst is recoverable and several runs without the loss of activity were achieved.

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