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Solvent-free synthesis of *N*-sulfonylimines using microwave irradiation

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Abstract

N-Sulfonylimines are prepared expeditiously in a one-pot solventless operation by microwave thermolysis of aldehydes and sulfonamides in the presence of benign reagents, calcium carbonate and montmorillonite K 10 clay.

N-Sulfonylimines continue to attract the attention of chemists as versatile synthetic intermediates. As electron deficient imines, they find elegant application in inverse electron demand Diels–Alder chemistry,[1–4] stable and reactive alkenes in ene reactions,[5] aza-aldehyde equivalents in addition reactions[6] and valuable precursors for the preparation of optically active 2-imidazolines.[7] There are several methods available for the preparation of *N*-sulfonylimines namely via the rearrangement of oxime *O*-sulfinates,[8] Lewis acid catalyzed reactions of sulfonamides with aldehyde precursors,[9,10] the addition of *N*-sulfinyl sulfonamides to aldehydes in the presence of boron-trifluoride etherate,[11] the utilization of in situ generated *N,N'*-ditosyltellurodiimide from tellurium metal and chloramine T,[12] using tetraethyl orthosilicate,[13] or halogen-mediated conversion of *N*-(trimethylsilyl) imines in the presence of corresponding sulfonyl chloride.[14]

Herein, we report a novel solvent-free synthesis of *N*-sulfonylimines which utilizes the relatively benign reagents such as calcium carbonate and montmorillonite K 10 clay and a clean energy source, microwave irradiation. Since the appearance of first article on the use of microwave (MW) energy in a chemical reaction,[15] the approach has now developed into a useful technique for a variety of applications in organic synthesis,[16–19] especially noteworthy are the solventless reactions conducted on mineral oxides.[18–20] Recently, a new dimension has been added to these solid state reactions wherein the non-microwave absorbing benign reagents[20] are being exploited in selective synthetic manipulation. Since only the polar reactants adsorbed on such surfaces absorb microwave energy, a variety of such supports

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can be utilized for the enhancement of organic reactions using a microwave oven. These solvent-free MW-assisted reactions[18–20] provide an opportunity to work with open vessels, thus avoiding the risk of high pressure development and increasing the potential of such reactions to upscale.

A straightforward extension of our clay-catalyzed protocols[19i,j] to reaction of aryl aldehydes with sulfonamides failed on various mineral surfaces presumably due to rapid decomposition of the aldehydes at elevated reaction temperatures. However, success was achieved by the condensation of the preformed acetals with sulfonamides but the yields were modest (See entries 1 and 3, Table 1). Because of the added attraction of a concise approach amenable to one-pot protocol, we explored a variety of reaction conditions and several reagents, such as $CH(OCH_3)_3$, calcium carbonate and K 10 clay materials to generate the corresponding aldehyde acetals in situ (Table 1). Finally, we have succeeded in finding an optimum combination of calcium carbonate and K 10 clay (9:2, w/w) that works most efficiently.

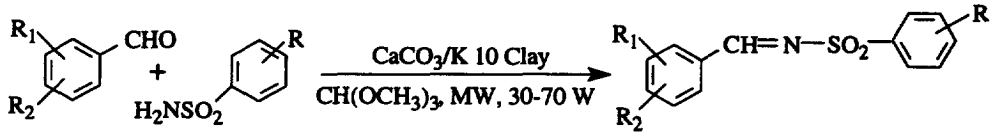

Table 1

Microwave-assisted synthesis of *N*-sulfonyl imines from aryl aldehyde acetals[a] or arylaldehydes in one-pot reaction with trimethyl orthoformate[b] and sulfonamides using calcium carbonate and K 10 clay

Entry	R_1	R_2	R	Microwave irradiation			m. p.	Yield
				Time (min)	Power (W)	Temperature[c] (°C)	(°C)	(%)[d]
1[a]	H	H	H	9	30	195-199	77-80	60
2[b]	H	H	H	9	30	180-185	78-81	89
3[a]	H	H	4-CH_3	6	45	186-192	109-110	69
4[b]	H	H	4-CH_3	6	45	186-195	109-110	91
5[b]	H	H	4-Cl	12	30	165-169	108-110	83
6[b]	H	H	2-$COOCH_3$	8	30	180-183	118-122	82
7[b]	4-Br	H	4-CH_3	6	75	200-210	182-185	90
8[b]	4-OAc	H	4-CH_3	9	30	165-171	121-123	76
9[b]	3-OCH_3	4-OCH_3	4-CH_3	9	30	191-198	114-117	88
10[b]	3-OCH_3	4-$OCH(CH_3)_2$	4-CH_3	6	45	167-173	132-134	80
11[b]	3-OAc	4-OAc	H	8	30	178-182	189-192	52

[a]Procedure: A mixture of sulfonamides (10 mmol), $CaCO_3$ (9 g), K 10 clay (2 g) and aldehyde acetal (11 mmol) were homogenized using A-10 (AKA) mixer and was placed in a glass tube for microwave irradiation.

[b]Procedure: To a mixture of sulfonamides (10 mmol), $CaCO_3$ (9 g) and K 10 clay (2 g), aldehyde (10 mmol) and trimethyl orthoformate (20 mmol) was added and the mixture were homogenized using A-10 (AKA) mixer. The contents were placed in a glass tube and subjected to microwave irradiation in a Prolabo MW oven (Maxidigest 350 with sample mixing device).

[c]final temperature measured by both, digital (Testo 901) and infrared (Amir 7812) thermometer.

[d]Isolated yield (Unoptimized) of products identified by ^1H and ^{13}C NMR spectra recorded on Varian (300 MHz) spectrometer.

That the effect may not be purely thermal[21] is supported by the fact that, in the case of the microwave-assisted reactions, the product yields (91%) were not attainable at 165°C when the same reaction was subjected to conventional heating in an oil bath at the same temperature; only poor yield of the product (46%) was obtained with incomplete consumption of the starting material (entry 1, Table 2). Additionally, we find that the microwave-assisted reactions are more efficient, convenient and cleaner.

Table 2
A comparison of the results obtained using microwave and conventional heating protocols

Entry	Time (min)	Procedure				Yield (%)
		Conventional heating[a]		Microwave heating[b]		
		Temp. (°C)	Yield (%)	Power (W)	Temp (°C)	
1	2	160	46	120	160-165	91
2	3	160	54	75	185-190	90
3	6	160	58	45	187-192	91
4	9	160	56	30	185-192	92

[a]Procedure: Benzaldehyde (10 mmol), *p*-toluenesulfonamide (10 mmol), trimethyl orthoformate (20 mmol) without solvent (neat) in the presence of *p*-TsOH as a catalyst.
[b]Procedure: see Table 1.

The present one-pot and high yielding protocol for preparation of *N*-sulfonylimines[22] provides a better alternative to the existing methods due to its shorter reaction time, simple reaction procedure and the formation of cleaner products that can be used for synthetic applications without further purification (Table 1).[23]

In conclusion, a simple, rapid and high yielding microwave-accelerated method for the synthesis of *N*-sulfonylimines is developed that occurs under solvent-free conditions using calcium carbonate and K 10 clay.

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22. General procedure: aromatic aldehydes (10 mmol) and trimethylorthoformate (20 mmol) was added to a mixture of sulfonamide (10 mmol), finely powdered calcium carbonate (9 g) and K 10 clay (2 g). The solid homogenized mixture was placed in a modified reaction tube which was connected to a removable cold finger and sample collector to trap the ensuing methanol and methylformate. The reaction tube is inserted into Maxidigest MX 350 (Prolabo) microwave reactor equipped with a rotational mixing system. After irradiation for a specified period (see Table 1), the contents were cooled to room temperature and mixed thoroughly with ethylacetate (2×20 mL). The solid inorganic material was filtered off and solvent was evaporated to afford the residue which was crystallized from the mixture of hexane and ethylacetate.
23. ^{1}H (300 MHz) and ^{13}C NMR spectra (75.4 MHz) for entries in Table 1 (in $CDCl_3$, referenced to TMS): Entry 5: ^{1}H NMR: δ 9.02 (1H, s), 7.44–7.96 (9H, m); ^{13}C NMR: δ 170.9, 140.2, 136.7, 135.2, 132.1, 131.4, 129.5, 129.2; Entry 6: ^{1}H NMR: δ 9.0 (1H, s), 7.42–8.24 (9H, m), 3.86 (3H, s); ^{13}C NMR: δ 172.1, 167.2, 136.2, 135.1, 133.4, 132.8, 132.2, 131.4, 131.1, 130.6, 129.5, 129.2, 53.0; Entry 7: ^{1}H NMR: δ 8.98 (1H, s), 7.34–7.84 (8H, m), 2.4 (3H, s); ^{13}C NMR: δ 168.7, 144.8, 134.8, 132.6, 132.4, 131.2, 130.2, 129.8, 126.4, 21.3; Entry 9: ^{1}H NMR: δ 8.92 (1H, s), 7.84 (2H, d), 7.4–7.48 (2H, m), 7.3 (2H, d), 6.9 (1H, d), 3.96 (3H, s), 3.88 (3H, s), 2.40 (3H, s); ^{13}C NMR: δ 165.5, 155.2, 149.6, 144.3, 135.6, 129.7, 129.1, 127.9, 125.4, 110.5, 110.1, 56.2, 56.1, 21.3.