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Synthesis of α-amino nitriles through Strecker reaction of aldimines and ketoimines by using nanocrystalline magnesium oxide

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Abstract

Strecker reactions of various aldimines as well as ketoimines with TMSCN proceeded smoothly under mild conditions to give the corresponding α-amino nitriles and α,α-disubstituted α-amino nitriles, respectively, in good to excellent yields in the presence of nanocrystalline magnesium oxide. The reaction proceeds through hypervalent silicate species by coordination to O^{2-}/O^{-} (Lewis basic site) of nanocrystalline magnesium oxide, proved by ^{29}Si NMR.

Keywords: Strecker reaction; α-Amino nitriles; Aldimines; Ketoimines; Trimethylsilyl cyanide; Nanocrystalline magnesium oxide

1. Introduction

α-Amino nitriles are versatile precursors for the synthesis of α-amino acids,[1] various nitrogen and sulfur containing heterocycles such as imidazoles, thiadiazoles[2] and pharmaceuticals.[3] The Strecker reaction, nucleophilic addition of cyanide ion to the imines, is of great importance to modern organic chemistry as it offers one of the most direct and viable methods for the synthesis of α-amino nitriles.[4]

The Strecker reaction has been studied extensively by using various promising Lewis acid,[5] Lewis base catalysts,[6] metal complexes and metal–salen complexes.[7] In recent years, a number of highly effective catalysts have been successfully used for asymmetric Strecker reactions, such as Lipton's cyclic dipeptide,[8a] Corey's cyclic guanidine,[8b] Jacobsen's Schiff base[8c,d] and Feng's *N*,*N*′-dioxide.[8e] Strecker methodologies for the synthesis of α-amino nitriles have been reported in ionic liquids and water instead of regular organic solvents.[9,5b]

There have been numerous reports on sulfonyl and sulfinyl imines in recent years, which are stable compounds.[10] These sulfonyl and sulfinyl groups are good activators of the C=N bond for nucleophilic addition reactions. Therefore, the addition of trimethylsilyl cyanide (TMSCN) to these imines may be a good method for obtaining α-amino nitriles. To our knowledge, there are only few reports on Strecker reaction of sulfonyl imines, using *N*-heterocyclic carbene (NHC),[11a,b] Feng's bifunctional *N*,*N*′-dioxide,[11c] Lewis acids and bases[5d,6a] as catalysts to afford α-amino nitriles in good to excellent yields. Recently, Toru et al. disclosed the Strecker reaction of sulfonyl imines in the presence of chiral additives.[12a,b] Later Ooi et al. reported Strecker reaction of *N*-arylsulfonyl imines and *N*-arylsulfonyl α-amido sulfones under phase transfer conditions.[12c,d]

Some of the Strecker methodologies rely on the use of toxic cyanide derivatives involving harsh reaction conditions, which poses problems to be addressed, particularly when large-scale applications are considered. In order to avoid partially this inconvenience, acetone cyanohydrin, diethylaluminium cyanide, TMSCN, etc. have been introduced as cyanide sources in the Strecker reaction,[12b,13] wherein TMSCN is a promising alternative, simplest, safe, easy to handle, most soluble and more effective cyanide ion source for the nucleophilic addition

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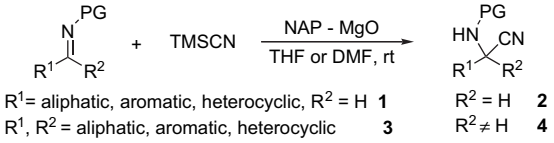
reactions. Considering the importance of the Strecker reaction for providing various chiral amino acid precursors in both laboratory and industrial scale, it is highly desirable to develop heterogeneous catalysts. However, there are only few reports that are published on Strecker reaction by using heterogeneous catalysts.[14]

Nanocrystalline metal oxides find excellent applications as active adsorbents for gases, for destruction of hazardous chemicals[15] and as catalysts for various organic transformations.[16] These high reactivities are due to high surface areas combined with unusually reactive morphologies. In continuation of our work on nanomaterials, herein we report an effective Strecker reaction of aldimines and ketoimines[10] to afford α-amino nitriles and α,α-disubstituted α-amino nitriles, respectively, in high yields by using nanocrystalline magnesium oxide (NAP-MgO) catalyst (Scheme 1).

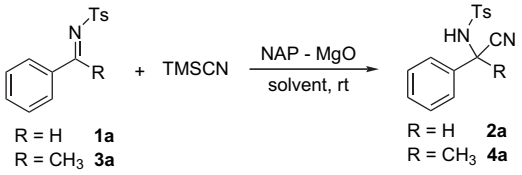


Scheme 1. NAP-MgO catalyzed Strecker reaction between aldimines or ketoimines and TMSCN.

2. Results and discussion

Various forms of magnesium oxide crystals CM-MgO (commercial MgO, SSA: 30 m^2/g), NA-MgO (NanoActive MgO, conventionally prepared MgO, SSA: 250 m^2/g), NAP-MgO (NanoActive Plus MgO, aerogel prepared MgO, SSA: 590 m^2/g) were initially evaluated in the Strecker reaction between *N*-tosyl ketoimine **3a** and TMSCN at room temperature in order to understand the relationship between structure and reactivity. All these MgO crystals catalyze the Strecker reaction in quantitative yields. However, the NAP-MgO was found to be more active than NA-MgO and CM-MgO in the Strecker reaction (Table 1).

Initially we studied the Strecker reaction with *N*-tosyl imines **1a** or **3a** as model substrates with TMSCN using NAP-MgO for optimization (Scheme 2). The reaction was performed at room temperature, between aldimine **1a** and TMSCN in the presence of NAP-MgO with different solvents like acetonitrile, toluene, DCM, DMF and THF. Among these, the rate of the reaction was fast in THF and 97% yield of α-amino nitrile **2a** obtained (Table 2, entry 5). Whereas the reaction between ketoimine **3a** and TMSCN in the presence of NAP-MgO in THF afforded the product in moderate yields and the rate of the reaction was slow (Table 2, entry 6). On switching THF to DMF, the reaction was dramatically accelerated, affording quantitative yields of the product (Table 2, entry 9). We observed, in the both cases, with aldimine **1a** and ketoimine **3a**, the reactions in the non-polar solvent, toluene took longer time. Notably, the reactions of both aldimines and ketoimines when performed in dry solvents under N_2 atmosphere require long duration with slight decrease in yields (Table 2, entries 10 and 11). This may indicate that a trace amount of moisture was important to accelerate the transformation of the substrates, which has been observed earlier by Feng et al.[11c] When this transformation was carried out on a large scale, there was a notable reduction in reaction efficiency (Table 2, entry 12). It shows that adventitious moisture may facilitate processes performed in smaller quantities.[7a]



Scheme 2. NAP-MgO catalyzed Strecker reaction between *N*-tosyl aldimine **1a** or *N*-tosyl ketoimine **3a** and TMSCN.

The substrate generality of the Strecker reaction was carried out initially for *N*-sulfonyl aldimines with TMSCN (Scheme 3). A variety of structurally different aldimines containing *N*-*p*-toluene sulfonyl (Ts), *N*-benzene sulfonyl (Bzs), *N*-methane sulfonyl (Ms), *N*-2,4,6-triisopropylbenzene sulfonyl (Tris) and *N*-*tert*-butyl sulfonyl (Bus) imines were employed and the results are summarized in Table 3. It was found that various

Table 1
Strecker reaction between *N*-tosyl ketoimine **3a** and TMSCN with various catalysts[a]

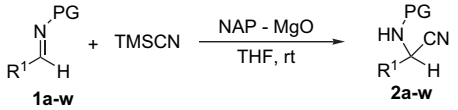
Entry	Catalyst	Time	Yield[b] (%)
1	NAP-MgO	45 min, 1 h[c]	97, 95[c]
2	NA-MgO	3 h	95
3	CM-MgO	6 h	91
4	Sil-NAP-MgO	3 h	89
5	None	8 h	18

[a] Reaction conditions: *N*-tosyl ketoimine **3a** (1 mmol), TMSCN (1.5 mmol), catalyst (0.05 g), DMF (3 mL) at room temperature.
[b] Isolated yield.
[c] Fourth cycle.

Table 2
Optimization of Strecker reaction of *N*-tosyl imines **1a** or **3a** with TMSCN catalyzed by NAP-MgO[a]

Entry	Substrate	Solvent	Time	Yield[b] (%)
1	**1a**	CH_3CN	5 min	95
2	**1a**	$PhCH_3$	12 min	90
3	**1a**	CH_2Cl_2	5 min	87
4	**1a**	DMF	4 min	92
5	**1a**	THF	2 min	97
6	**3a**	THF	3 h	72
7	**3a**	CH_3CN	3 h	80
8	**3a**	$PhCH_3$	5 h	52
9	**3a**	DMF	45 min	97
10	**1a**[c]	Dry THF	25 min	89
11	**3a**[c]	Dry DMF	6 h	82
12	**3a**[d]	DMF	8 h	78

[a] Reaction conditions: *N*-tosyl imine **1a** or **3a** (1 mmol), TMSCN (1.2 mmol for **1a**, 1.5 mmol for **3a**), catalyst (0.05 g), solvent (3 mL) at room temperature.
[b] Isolated yield.
[c] Under N_2 atmosphere.
[d] Reaction on 5 mmol scale.



Scheme 3. NAP-MgO catalyzed Strecker reaction between various aldimines and TMSCN.

aliphatic, aromatic and heterocyclic aldimines afforded good to excellent yields. Various *N*-(arylmethylidene)-4-methyl benzenesulfonamides **1a**–**1h** including α,β-unsaturated and heterocyclic aldimines have showed high reactivity with excellent yields. Moreover, other *N*-sulfonated imines such as *N*-benzene sulfonated imines **1k**–**1m**, *N*-mesylated imines **1n**–**1p** and *N*-*tert*-butyl sulfonated imine **1s** also proceeded smoothly under the optimized conditions and provided yields comparable with those of 4-methyl benzenesulfonated imines. *N*-[(4-Methoxyphenyl)methylidene]-methanesulfonamide **1p** took longer reaction time (entry 16). Aliphatic aldimines **1i**, **1j**, **1s** (entries 9, 10 and 19) furnished good yields. On the other hand, *N*-2,4,6-triisopropylbenzene sulfonated aldimines **1q**, **1r** (entries 17 and 18) gave high yields, with low reactivity, which might be due to the bulky and electron-donating groups on the aromatic ring. Where *N*-*tert*-butyl carbonyl (Boc) aldimine **1t** (entry 20) was smoothly transformed to the corresponding α-amino nitrile in good yields but unexpectedly, *N*-benzyl carbonyl (Cbz) aldimine **1u** (entry 21) was inactive and 94% of the starting material Cbz imine **1u** was recovered. In the Strecker reaction of *N*-trimethylsilyl (*N*-TMS) aldimine **1v** (entry 22), there was no product formation, but imine was decomposed. *N*-*p*-Methoxy phenyl (PMP) aldimine **1w** (entry 23) afforded the product in moderate yields on prolonged reaction time. Generally, the normal aldimines are less reactive than the activated *N*-sulfonyl aldimines.

Furthermore, many protocols are limited to aldimines only, and are not applicable to ketoimines. In practice, the catalytic Strecker reactions of ketoimines are not as easily performed as those of aldimines. However, fewer systems have been developed for cyanation of ketoimines and the generation of α,α-

Table 3
Strecker reaction of various aldimines **1a**–**1w** with TMSCN catalyzed by NAP-MgO[a]

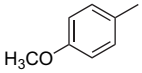
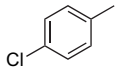
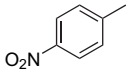
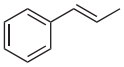
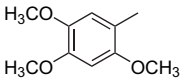
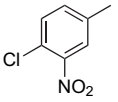
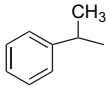
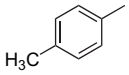
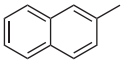
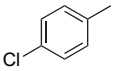
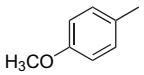
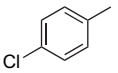
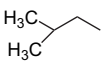
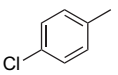
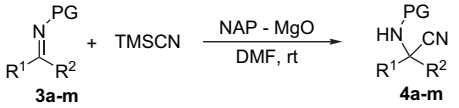
Entry	R		PG	Time (min)	Yield[b] (%)
1		(**1a**)	Ts	2	97 (**2a**)
2		(**1b**)	Ts	5	97 (**2b**)
3		(**1c**)	Ts	2	92 (**2c**)
4		(**1d**)	Ts	2	96 (**2d**)
5		(**1e**)	Ts	2	95 (**2e**)
					(*continued*)

Table 3 (*continued*)

Entry	R		PG	Time (min)	Yield[b] (%)
6		(**1f**)	Ts	2	90 (**2f**)
8		(**1g**)	Ts	4	89 (**2g**)
7		(**1h**)	Ts	2	91 (**2h**)
9		(**1i**)	Ts	2	89 (**2i**)
10		(**1j**)	Ts	2	87 (**2j**)
11		(**1k**)	Bzs	2	93 (**2k**)
12		(**1l**)	Bzs	2	94 (**2l**)
13		(**1m**)	Bzs	2	91 (**2m**)
14		(**1n**)	Ms	2	96 (**2n**)
15		(**1o**)	Ms	2	92 (**2o**)
16		(**1p**)	Ms	10	97 (**2p**)
17		(**1q**)	Tris	10	97 (**2q**)
18		(**1r**)	Tris	10	95 (**2r**)
19		(**1s**)	Bus	2	91 (**2s**)
20		(**1t**)	Boc	2	89 (**2t**)
21		(**1u**)	Cbz	30	N.R[c]
22		(**1v**)	TMS	5	N.D[d]
23		(**1w**)	PMP	120	67 (**2w**)

[a] Reaction conditions: aldimine **1a**–**w** (1 mmol), TMSCN (1.2 mmol), catalyst (0.05 g), THF (3 mL) at room temperature.
[b] Isolated yield.
[c] No reaction.
[d] Imine decomposed.

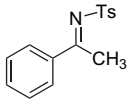
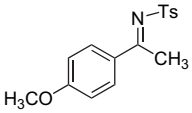
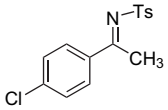
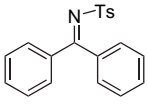
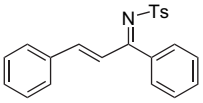
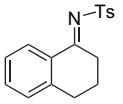
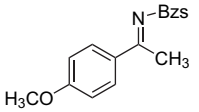
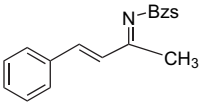
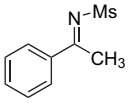
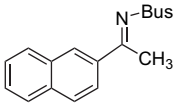
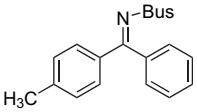
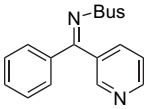
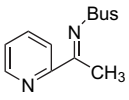
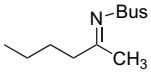


Scheme 4. NAP-MgO catalyzed Strecker reaction between various ketoimines and TMSCN.

disubstituted α-amino nitriles. Jacobsen's Schiff base catalysts,[17a,b] Shibasaki's Gd-complex catalysts,[17c,d] Vallee's metal complex catalysts[17e,f] and more recently Feng's *N*,*N*′-dioxide catalysts[17g,11c] have been developed for Strecker reaction of ketoimines. These potential precursors to quaternary α-amino acids display a wide assortment of interesting biological properties and are important chiral building blocks for pharmaceuticals.[18] Herein, we report an effective Strecker reaction of ketoimines by using nanocrystalline magnesium oxide catalyst (NAP-MgO) (Scheme 4).

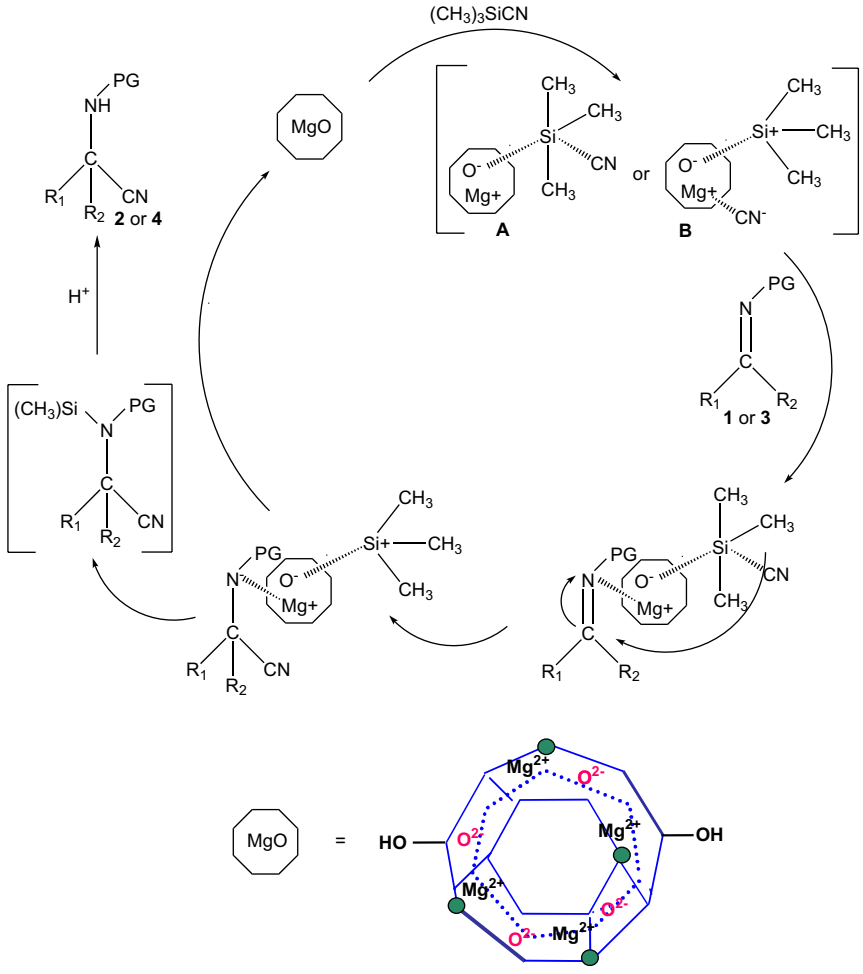
Substrate generality has been surveyed as shown in Table 4. A variety of structurally different ketoimines containing *N*-*p*-toluene sulfonyl (Ts), *N*-benzene sulfonyl (Bzs), *N*-methane sulfonyl (Ms), *N*-*tert*-butyl sulfonyl (Bus) imines were employed and the results are summarized in Table 4. The Strecker reaction of aromatic ketoimines **3a**–**3k** as well as heterocyclic ketoimines **3l**, **3m** has been achieved with excellent yields. Aliphatic ketoimine **3n** (entry 14) showed high reactivity in cyanation reaction under these optimized conditions and high yields are obtained. Generally, aliphatic imines are more reactive than aromatic imines because of resonance stabilization in the latter. And α,β-unsaturated ketoimines such as chalcone **3e** and benzylidene acetone **3h** furnished high yields (entries 5 and 8), but the rate of the reaction is slow, as compared to other aromatic ketoimines. Sterically hindered ketoimines **3d**, **3e**, **3k**, **3l** (entries 4, 5, 11 and 12) also furnished α,α-disubstituted α-amino nitriles with high yields. Most of the products **2** and **4** in Tables 3 and 4 can be directly subjected to acid hydrolysis to produce the corresponding amino acids.

Table 4
Strecker reaction of various ketoimines **3a**–**3n** with TMSCN catalyzed by NAP-MgO[a]

Entry	Ketoimine		Time (min)	Yield[b] (%)
1		(**3a**)	45	97 (**4a**)
2		(**3b**)	60	97 (**4b**)
3		(**3c**)	55	93 (**4c**)
4		(**3d**)	45	92 (**4d**)
5		(**3e**)	90	97 (**4e**)
6		(**3f**)	60	94 (**4f**)
7		(**3g**)	30	96 (**4g**)
8		(**3h**)	60	96 (**4h**)
9		(**3i**)	40	95 (**4i**)
10		(**3j**)	30	96 (**4j**)
11		(**3k**)	45	91 (**4k**)
12		(**3l**)	30	94 (**4l**)
13		(**3m**)	30	96 (**4m**)
14		(**3n**)	15	91 (**4n**)

[a] Reaction conditions: ketoimine **3a**–**n** (1 mmol), TMSCN (1.5 mmol), catalyst (0.05 g), DMF (3 mL) at room temperature.
[b] Isolated yield.

As to the mechanism, we assumed that the cyanation of imines with TMSCN proceeds through the formation of two active intermediates either hypervalent silicate **A** or nucleophilic cyanide ion **B** coordinated with the NAP-MgO as illustrated in Scheme 5. There are extensive literature precedents that TMSCN reacts rapidly with alcohols and phenols to produce HCN and this has been demonstrated to be the actual cyanating agent in the Strecker reactions involving TMSCN.[7a–c,13d,e] In our present system, however, the substrates have proved to be inert to HCN. The substrate **3a** was treated with ethyl cyanoformate followed by addition of acetic acid[11c] (see Section 4.5). This method is an alternative way instead of using TMSCN and phenol that could produce HCN, which could serve as a cyanating agent. The product **4a** was not obtained



Scheme 5. Plausible mechanism for the Strecker reaction using NAP-MgO.

in the present system and also the evolved gas fragment m/z=26, due to CN^- ion was not observed in TGA–DTA–MS of TMSCN treated NAP-MgO. So we assumed that intermediate **B** may not be the active intermediate in the present system. Therefore, we assumed that the reaction proceeds through the possible active intermediate hypervalent silicate **A** in the present system as showed in Scheme 5.[11a,c,19]

Trimethylsilyl cyanide was activated by O^{2-}/O^- (Lewis base) of NAP-MgO catalyst, which forms a hypervalent silicate **A**, coordinates with O^{2-}/O^- of the NAP-MgO, resulting in the cyanide group being polarized to acquire more reactivity; meanwhile, imine **1** or **3** was activated by Mg^{2+}/Mg^+ (Lewis acid) of NAP-MgO. The highly reactive cyanide ion attacks the imine, resulting in the formation of a nitrogen anion intermediate, which coordinates with Mg^{2+}/Mg^+ (Lewis acid) of NAP-MgO. Thereafter the *N*-TMS intermediate was formed and hydrolyzed to Strecker product **2** or **4** due to the cleavage of the rather labile N–Si bond by a trace amount of moisture present in the solvent, which is important to accelerate the transformation of the substrates, as observed earlier by Feng et al.[11c]

In order to confirm the hypothesis of hypervalent silicate intermediate **A**, ^{29}Si NMR (400 MHz) analyses were carried out at 25 °C in $CDCl_3$.[19] All the experiments were performed in $CDCl_3$, as detailed in Section 4. The ^{29}Si NMR spectra were recorded using tetramethyl silane as an internal standard. As illustrated in Table 5, entry 1, TMSCN affords a signal at δ=−11.45 ppm {lit.:[19] δ=−11.5 ppm}. When TMSCN is added to the solution of NAP-MgO, another signal was found at δ=7.07 ppm {lit.:[19] δ=7.1 ppm} (Table 5, entry 2). When imine was added to the solution of NAP-MgO and TMSCN, an identical spectrum was observed as to NAP-MgO (Table 5, entry 3). The spectral changes strongly indicate that the environments around the silicon atoms of some TMSCN species are changed when NAP-MgO is present. It is possible that these silicon atoms of TMSCN could form five- or six-coordinated hypervalent silicate species by coordination with

Table 5
^{29}Si NMR chemical shifts of several systems[a]

Entry	Components	δ (ppm)
1	TMSCN	−11.45
2	TMSCN+NAP-MgO	7.07, −11.45
3	TMSCN+NAP-MgO+imine	7.06, −11.45
4	TMSCN+Sil-NAP-MgO	7.05, −11.43

[a] Reaction conditions: ketoimine **3a** (0.1 mmol), TMSCN (0.15 mmol), catalyst (0.005 g), $CDCl_3$ (0.5 mL) at 25 °C.

O^{2-}/O^{-} (Lewis basic site) of NAP-MgO, but not the Bronsted basic site (Scheme 5).[20] This is proved, when TMSCN is added to the solution of Sil-NAP-MgO, an almost identical spectrum was observed as to NAP-MgO (Table 5, entry 4).

To understand the relationship between structure and reactivity of the catalyst in the Strecker reaction, it is important to know the structure and nature of the reactive sites of NAP-MgO. NAP-MgO has single-crystallite, three-dimensional polyhedral structure, which possesses high surface concentrations of edge/corner and various exposed crystal planes (such as 002, 001, 111), leading to inherently high surface reactivity per unit area. Thus, NAP-MgO indeed displayed the highest activity compared to that of NA-MgO and CM-MgO. Besides this, the NAP-MgO has Lewis acid sites Mg^{2+}, Lewis basic sites O^{2-} and O^{-}, lattice-bound and isolated Bronsted hydroxyls and anionic and cationic vacancies.[20] Strecker reactions are known to be driven by base catalysts,[6] and accordingly, the surface −OH, O^{2-} sites of these oxide crystals are expected to trigger these reactions. To examine the role of −OH, the Sil-NAP-MgO[20e] devoid of free −OH, were tested in Strecker reactions. It is found that the rate of the reaction was slow, and longer reaction time was required in Strecker reaction (Table 1, entry 4). Although both NAP-MgO and NA-MgO possess defined shapes and the same average concentrations of surface −OH groups, a possible rationale for the display of higher reactivity to α-amino nitriles by the NAP-MgO is that the presence of more surface Lewis acid sites Mg^{2+} ions (20%) and −OH groups present on the edge and corner sites on the NAP-MgO, which are stretched in three-dimensional space, are more isolated and accessible for the reactants. Thus, NAP-MgO indeed displayed the highest activity compared to NA-MgO and CM-MgO. In the Strecker reaction, O^{2-}/O^{-} (Lewis base) of NAP-MgO activates the trimethylsilyl cyanide, which forms a hypervalent silicate, coordinates with O^{2-}/O^{-} of the NAP-MgO. The Strecker reaction proceeds via dual activation of both substrates (electrophiles and nucleophiles) by NAP-MgO. Thus, the Lewis base moiety (O^{2-}/O^{-}) of the catalyst activates the TMSCN and the Lewis acid moiety (Mg^{2+}/Mg^{+}) activates the nitrogen of aldimines or ketoimines (Scheme 5).[13e,21]

The NAP-MgO was reused for four cycles with consistent activity (Table 1, entry 1). After completion of the reaction, catalyst was centrifuged and washed properly for several times. The recovered catalyst was activated at 250 °C for 1 h under nitrogen atmosphere, before reuse.

3. Conclusion

In conclusion, nanocrystalline MgO has been demonstrated to be an effective catalyst for the cyanation of aldimines as well as ketoimines to afford α-amino nitriles and α,α-disubstituted α-amino nitriles, respectively, in high yields. To conclude, the simplicity of our procedure, the mildness of the reaction conditions, high yields, together with the ability to easy separation of reaction mixture, especially the reusability of the catalyst demonstrates our method to be practical for the synthesis of α-amino nitriles.

4. Experimental section

4.1. General remarks

Nanocrystalline MgO samples were obtained from Nano-Scale Materials Inc., Manhattan, Kansas, USA. All catalysts are calcined at 400 °C for 4 h before use. All chemicals were purchased from Aldrich Chemicals and S.D Fine Chemicals, Pvt. Ltd., India and used as received. All solvents were used LR grade and used as received from S.D Fine Chemicals Pvt. Ltd., India. ACME silica gel (100–200 mesh) was used for column chromatography and thin layer chromatography was performed on Merck precoated silica gel 60-F_{254} plates. Melting points were measured in open capillary tubes and are uncorrected. The IR spectra of all compounds were recorded on a Perkin–Elmer, SpectrumGX FTIR spectrometer using KBr pellet method. The IR values are reported in reciprocal centimetres (cm^{-1}). The ^{1}H and ^{13}C NMR spectra were recorded on a Varian-Gemini 200 MHz and Bruker-Avance 300 MHz Spectrometer. The ^{29}Si NMR spectra were recorded on a Varian-Unity 400 MHz Spectrometer. Chemical shifts (δ) are reported in parts per million, using TMS (δ=0) as an internal standard in $CDCl_3$. All the mass spectra were recorded on QSTAR XL high resolution mass spectrometer (Applied Biosystems, Foster city, USA). Substrate imines **1a–s**,[10] **1t–v**,[22] **3a–n**[10] were prepared according to reported literature methods.

4.2. Preparation of the different types of nanocrystalline MgO catalysts[20c–e]

Preparation of NA-MgO:[20c,d] Several grams of commercially available MgO was boiled in 500 mL of distilled water overnight (with magnetic stirring in a 1 L flask equipped with a reflux condenser). After cooling, the slurry was filtered and the filter cake was dried in an oven at 120 °C. The dried powder was broken into pieces and heat treated to 500 °C under vacuum in a Pyrex reaction tube that fit into a cylindrical furnace. Heating took about 12 h, and the sample was maintained at 500 °C for several hours, usually overnight. The vacuum reached about 1×10^{-3} Torr.

Preparation of NAP-MgO:[20c,d] In a three-necked 2 L round bottom flask equipped with a mechanical stirrer, water cooled condenser, and argon inlet with a three-way stopcock was placed 300 mL of toluene. In another flask, 2.4 g (0.1 mol) of Mg turnings was allowed to react with 100 mL of CH_3OH under argon. The resultant 1 M solution of $Mg(OCH_3)_2$ was added dropwise to the toluene with vigorous stirring under argon. Then 4 mL (0.22 mol) of distilled water was added dropwise from a syringe over a 30 min period. This solution was stirred at room temperature under argon overnight. The resultant slightly milky solution (gel-like) was placed in an autoclave, slowly heated to 265 °C, vented, and thus converted to a $Mg(OH)_2$ aerogel.[20c] After cooling, the slurry was filtered, and the filter cake was dried in an oven at 120 °C. The dried powder was broken into pieces and heat treated to 500 °C under vacuum in a Pyrex reaction tube that fit into a cylindrical furnace. Heating took about

12 h, and the sample was maintained at 500 °C for several hours, usually overnight. The vacuum reached about 1×10^{-3} Torr.

Preparation of Sil-NAP-MgO:[20e] A mixture of 0.5 g of NAP-MgO and 0.3 g of methoxytrimethyl silane in 20 mL of toluene was refluxed for 7 h and the reaction mixture was allowed to cool and centrifuged to obtain silylated NAP-MgO, which was washed several times with *n*-pentane.

4.3. Typical procedure for the Strecker reaction of aldimines

To a stirred solution of NAP-MgO (0.05 g) in THF (4 mL), TMSCN (1.2 mmol) was added in one portion at ambient temperature. After 5 min, aldimine **1** (1 mmol) was added to the reaction mixture and stirred at room temperature. After completion of the reaction (as monitored by TLC), the catalyst was centrifuged, and washed with ethyl acetate (3×5 mL). The combined organic solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel (100–200 mesh) using ethyl acetate/hexane in varying proportions as an eluent to afford the pure product **2**. The physical data of the known products **2c**, **2e**, **2g**, **2h**, **2q**, **2t** and **2w** were comparable to the literature data.[5a,11a] The physical data of the new products are given below.

4.3.1. N-(Cyanophenylmethyl)-4-methylbenzenesulfonamide (**2a**)

R_f 0.52 (hexane/EtOAc 6:4), colourless solid; mp 152–154 °C. IR (KBr): 3255, 2228, 1334, 1156 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=2.48 (s, 3H), 5.02 (d, J=9.4 Hz, 1H), 5.47 (d, J=9.4 Hz, 1H), 7.37 (d, J=8.3 Hz, 2H), 7.39–7.5 (m, 5H), 7.81 (d, J=8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz): 21.7, 48.2, 116.2, 127.0, 127.2, 129.3, 129.8, 129.9, 131.9, 135.8, 144.6. Mass (ESI): *m/z* 309 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{15}H_{14}N_2O_2NaS$: 309.0673. Found: 309.0682.

4.3.2. N-[Cyano-(4-methoxyphenyl)methyl]-4-methylbenzenesulfonamide (**2b**)

R_f 0.62 (hexane/EtOAc 5:5), colourless solid; mp 128–129 °C. IR (KBr): 3268, 2244, 1348, 1158, 1093 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=2.48 (s, 3H), 3.81 (s, 3H), 5.02 (d, J=8.7 Hz, 1H), 5.39 (d, J=8.7 Hz, 1H), 6.88 (d, J=8.3 Hz, 2H), 7.35 (d, J=8.7 Hz, 2H), 7.37 (d, J=8.7 Hz, 2H), 7.79 (d, J=8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): 21.4, 47.6, 55.4, 114.4, 116.5, 124.1, 127.1, 128.5, 129.8, 136.1, 144.4, 160.5. Mass (ESI): *m/z* 339 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{16}H_{16}N_2O_3NaS$: 339.0779. Found: 339.0785.

4.3.3. N-[Cyano-(4-nitrophenyl)methyl]-4-methylbenzenesulfonamide (**2d**)

R_f 0.52 (hexane/EtOAc 6:4), orange solid; mp 120–122 °C. IR (KBr): 3279, 2238, 1338, 1159, 1523 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=2.5 (s, 3H), 5.36 (d, J=9.8 Hz, 1H), 5.56 (d, J=9.8 Hz, 1H), 7.38 (d, J=8.3 Hz, 2H), 7.71 (d, J=8.3 Hz, 2H), 7.79 (d, J=9.1 Hz, 2H), 8.28 (d, J=9.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=21.6, 47.5, 115.4, 124.3, 127.2, 128.2, 130.2, 135.5, 138.7, 145.2, 148.5. Mass (ESI): *m/z* 354 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{15}H_{13}N_3O_4NaS$: 354.0524. Found: 354.0529.

4.3.4. N-[Cyano-(2-furyl)methyl]-4-methylbenzenesulfonamide (**2e**)

R_f 0.6 (hexane/EtOAc 5:5), colourless solid; mp 98–100 °C. IR (KBr): 3260, 2243, 1341, 1162, 1090 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=2.47 (s, 3H), 5.3 (d, J=9.2 Hz, 1H), 5.5 (d, J=9.2 Hz, 1H), 6.35 (dd, J=3.4, 1.6 Hz, 1H), 6.48 (d, J=3.4 Hz, 1H), 7.34 (d, J=8.3 Hz, 2H), 7.4 (d, J=1.6 Hz, 1H), 7.77 (d, J=8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=21.5, 42.2, 110.3, 110.9, 114.6, 127.2, 129.9, 135.9, 144.0, 144.3, 144.6. Mass (ESI): *m/z* 299 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{13}H_{12}N_2O_3NaS$: 299.0466. Found: 299.0474.

4.3.5. N-[(E)-1-Cyano-3-phenyl-2-propenyl]-4-methylbenzenesulfonamide (**2f**)

R_f 0.46 (hexane/EtOAc 6:4), colourless solid; mp 99–101 °C. IR (KBr): 3236, 2228, 1353, 1162, 1638 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=2.47 (s, 3H), 3.65 (dd, J=7.9, 6.1 Hz, 1H), 5.06 (d, J=7.9 Hz, 1H), 6.06 (dd, J=6.1, 16 Hz, 1H), 6.86 (d, J=16 Hz, 1H), 7.06–7.11 (d, J=8.3 Hz, 2H), 7.28–7.33 (m, 5H), 7.35 (d, J=8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=21.5, 35.8, 113.6, 126.2, 126.9, 127.5, 128.2, 128.3, 128.7, 129.9, 130.0, 143.3, 146.1. Mass (ESI): *m/z* 335 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{17}H_{16}N_2O_2NaS$: 335.0830. Found: 335.0842.

4.3.6. N-[Cyano-(2,4,5-trimethoxyphenyl)methyl]-4-methylbenzenesulfonamide (**2g**)

R_f 0.52 (hexane/EtOAc 6:4), colourless solid; mp 174–175 °C. IR (KBr): 3264, 2244, 1341, 1165, 1075, 1096 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ=2.45 (s, 3H), 3.81 (s, 3H), 3.86 (s, 6H), 5.29 (d, J=9.2 Hz, 1H), 5.43 (d, J=9.2 Hz, 1H), 6.45 (s, 1H), 6.7 (s, 1H), 7.3 (d, J=8.1 Hz, 2H), 7.73 (d, J=8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=21.5, 44.8, 56.1, 56.3, 56.5, 97.2, 111.6, 112.3, 116.8, 127.1, 129.7, 136.4, 143.0, 144.1, 151.2. Mass (ESI): *m/z* 399 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{18}H_{20}N_2O_5NaS$: 399.0990. Found: 399.0996.

4.3.7. N-[Cyano-(4-chloro-3-nitrophenyl)methyl]-4-methylbenzenesulfonamide (**2h**)

R_f 0.34 (hexane/EtOAc 6:4), yellow solid; mp 125–127 °C. IR (KBr): 3315, 2323, 1334, 1157, 1540 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=2.5 (s, 3H), 5.44 (d, J=9.4 Hz, 1H), 5.5 (d, J=9.4 Hz, 1H), 7.37 (d, J=8.3 Hz, 2H), 7.62–7.69 (m, 2H), 7.76 (d, J=8.3 Hz, 2H), 7.86 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=21.6, 46.9, 115.1, 124.3, 127.1, 128.6, 130.2, 131.6, 132.5, 132.9, 135.4, 145.3, 147.9. Mass (ESI): *m/z* 388 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{15}H_{12}N_3O_4NaSCl$: 388.0134. Found: 388.0121.

4.3.8. N-(Cyanophenylmethyl)benzenesulfonamide (**2k**)

R_f 0.49 (hexane/EtOAc 6:4), light yellow solid; mp 100–102 °C. IR (KBr): 3284, 2244, 1330, 1164 cm^{-1}. ^1H

NMR ($CDCl_3$, 300 MHz): δ=5.13 (d, J=9.1 Hz, 1H), 5.48 (d, J=9.1 Hz, 1H), 7.39–7.49 (m, 5H), 7.54–7.68 (m, 3H), 7.92 (d, J=7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=48.2, 116.2, 127.0, 127.2, 129.3, 129.4, 129.9, 132.0, 133.6, 138.9. Mass (ESI): *m/z* 295 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{14}H_{12}N_2O_2NaS$: 295.0517. Found: 295.0516.

*4.3.9. N-[Cyano-(4-methylphenyl)methyl]benzenesulfonamide (**2l**)*

R_f 0.36 (hexane/EtOAc 6:4), colourless solid; mp 112–113 °C. IR (KBr): 3280, 2234, 1335, 1164 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.36 (s, 3H), 5.2 (d, J=9.1 Hz, 1H), 5.42 (d, J=9.1 Hz, 1H), 7.17 (d, J=8.1 Hz, 2H), 7.32 (d, J=8.1 Hz, 2H), 7.53–7.67 (m, 3H), 7.89–7.93 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=21.1, 47.9, 116.4, 126.9, 127.2, 129.0, 129.3, 129.9, 133.5, 138.9, 139.9. Mass (ESI): *m/z* 309 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{15}H_{14}N_2O_2NaS$: 309.0673. Found: 309.0679.

*4.3.10. N-[Cyano-(2-napthyl)methyl]benzenesulfonamide (**2m**)*

R_f 0.5 (hexane/EtOAc 6:4), colourless solid; mp 164–166 °C. IR (KBr): 3275, 2250, 1331, 1156 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ=5.08 (d, J=8.8 Hz, 1H), 5.66 (d, J=8.8 Hz, 1H), 7.49–7.68 (m, 5H), 7.82–7.98 (m, 7H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ=48.5, 116.2, 123.9, 126.6, 127.2, 127.3, 127.5, 127.8, 128.2, 129.5, 129.7, 132.8, 133.7, 139.1. Mass (ESI): *m/z* 345 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{18}H_{14}N_2O_2NaS$: 345.0673. Found: 345.0683.

*4.3.11. N-(Cyanophenylmethyl)methanesulfonamide (**2n**)*

R_f 0.55 (hexane/EtOAc 5:5), white solid; mp 104–106 °C. IR (KBr): 3252, 2244, 1324, 1161 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.13 (s, 3H), 5.02 (d, J=8.3 Hz, 1H), 5.56 (d, J=8.3 Hz, 1H), 7.43–7.48 (m, 3H), 7.52–7.56 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=41.8, 48.3, 117.0, 127.2, 129.5, 130.1, 131.8. Mass (ESI): *m/z* 233 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_9H_{10}N_2O_2NaS$: 233.0360. Found: 233.0368.

*4.3.12. N-[(4-Chlorophenyl)cyanomethyl]methanesulfonamide (**2o**)*

R_f 0.52 (hexane/EtOAc 6:4), colourless solid; mp 154–155 °C. IR (KBr): 3217, 2250, 1324, 1157 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.16 (s, 3H), 4.89 (br s, 1H), 5.56 (br s, 1H), 7.45 (d, J=8.7 Hz, 2H), 7.52 (d, J=8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=41.9, 47.7, 116.8, 128.4, 128.6, 129.8, 134.9. Mass (ESI): *m/z* 261 ($M+NH_4^+$). HRMS (ESI): Anal. Calcd for $C_9H_9N_2O_2NaSCl$: 266.9970. Found: 266.9972.

*4.3.13. N-[Cyano-(4-methoxyphenyl)methyl]methanesulfonamide (**2p**)*

R_f 0.45 (hexane/EtOAc 5:5), white solid; mp 143–144 °C. IR (KBr): 3206, 2244, 1315, 1157, 1073 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.13 (s, 3H), 3.83 (s, 3H), 4.75 (d, J=8.7 Hz, 1H), 5.5 (d, J=8.7 Hz, 1H), 6.93 (d, J=8.3 Hz, 2H), 7.45 (d, J=8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=41.9, 48.0, 55.4, 114.9, 116.5, 126.8, 128.7, 161.3. Mass (ESI): *m/z* 263 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{10}H_{12}N_2O_3NaS$: 263.0466. Found: 263.0473.

*4.3.14. N-[(4-Chlorophenyl)cyanomethyl]-2,4,6-triisopropylbenzenesulfonamide (**2r**)*

R_f 0.49 (hexane/EtOAc 8:2), colourless solid; mp 117–118 °C. IR (KBr): 3371, 2238, 1322, 1148 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.28 (d, J=5.3 Hz, 6H), 1.31 (d, J=5.3 Hz, 12H), 2.92 (septet, J=6.8 Hz, 1H), 4.03 (septet, J=6.8 Hz, 2H), 4.98 (d, J=8.6 Hz, 1H), 5.47 (d, J=8.6 Hz, 1H), 7.18 (s, 2H), 7.37 (d, J=8.7 Hz, 2H), 7.43 (d, J=8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=23.5, 24.7, 24.8, 29.9, 34.2, 47.9, 116.4, 124.1, 128.6, 129.5, 131.7, 150.4, 153.8. Mass (ESI): *m/z* 455 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{23}H_{29}N_2O_2NaSCl$: 455.1535. Found: 455.1539.

*4.3.15. N-[1-Cyano-(3-methyl)butyl]-2-methyl-2-propanesulfonamide (**2s**)*

R_f 0.52 (hexane/EtOAc 6:4), white solid; mp 102–103 °C. IR (KBr): 3275, 2238, 1331, 1145 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.01 (d, J=3.1 Hz, 3H), 1.03 (d, J=3.1 Hz, 3H), 1.44 (s, 9H), 1.72–1.78 (m, 2H), 1.83–1.97 (m, 1H), 4.35 (q, 1H), 4.65 (d, J=9.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=21.7, 21.9, 24.0, 24.5, 43.7, 44.2, 60.4, 119.0. Mass (ESI): *m/z* 255 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{10}H_{20}N_2O_2NaS$: 255.1143. Found: 255.1149.

4.4. Typical procedure for the Strecker reaction of ketoimines

To a stirred solution of NAP-MgO (0.05 g) in DMF (4 mL), TMSCN (1.5 mmol) was added in one portion at ambient temperature. After 5 min, ketoimine **3** (1 mmol) was added to the reaction mixture and stirred at room temperature. After completion of the reaction (as monitored by TLC), the catalyst was centrifuged, and washed with ethyl acetate (3×5 mL), water (2×5 mL) was added to the filtrate, and then the reaction mixture was extracted with ethyl acetate (2×5 mL). The combined organic layers were washed with brine (2×5 mL), and dried over anhydrous Na_2SO_4. The protocol involving addition of water followed by extraction with ethyl acetate is required to remove DMF from reaction mixture. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel (100–200 mesh) using ethyl acetate/hexane in varying proportions as an eluent to afford the pure product **4**. The physical data of the known products **4a–4f** were comparable to the literature data.[11b,c] The physical data of the new products are given below.

*4.4.1. N-[1-Cyano-(4-methoxyphenyl)ethyl]benzenesulfonamide (**4g**)*

R_f 0.46 (hexane/EtOAc 5:5), colourless solid; mp 151–153 °C. IR (KBr): 3269, 2249, 1342, 1156, 1091 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.94 (s, 3H), 3.8 (s, 3H), 5.28 (s, 1H), 6.77 (d, J=8.9 Hz, 2H), 7.36 (d, J=8.9 Hz, 2H), 7.42–7.58 (m, 3H), 7.73 (d, J=8.1 Hz, 2H). ^{13}C NMR

($CDCl_3$, 75 MHz): δ=30.1, 55.4, 56.1, 114.0, 119.2, 127.1, 127.3, 128.6, 128.9, 132.9, 140.1, 160.1. Mass (ESI): *m/z* 339 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{16}H_{16}N_2O_3NaS$: 339.0779. Found: 339.0766.

*4.4.2. N-[(E)-1-Cyano-1-methyl-3-phenyl-2-propenyl]-benzenesulfonamide (**4h**)*

R_f 0.43 (hexane/EtOAc 6:4), colourless solid; mp 126–127 °C. IR (KBr): 3252, 2238, 1338, 1163, 1122 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.8 (s, 3H), 5.41 (s, 1H), 5.89 (d, *J*=16.2 Hz, 1H), 6.83 (d, *J*=16.2 Hz, 1H), 7.29–7.32 (m, 5H), 7.47 (t, *J*=7.6 Hz, 2H), 7.58 (t, *J*=7.6 Hz, 1H), 7.85 (d, *J*=7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=28.5, 54.5, 118.2, 125.3, 127.0, 127.7, 128.6, 128.9, 129.1, 133.2, 133.3, 134.4, 140.1. Mass (ESI): *m/z* 335 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{17}H_{16}N_2O_2NaS$: 335.0830. Found: 335.0834.

*4.4.3. N-(Cyanophenylethyl)methanesulfonamide (**4i**)*

R_f 0.42 (hexane/EtOAc 5:5), colourless solid; mp 81–82 °C. IR (KBr): 3258, 2242, 1329, 1165 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.96 (s, 3H), 2.81 (s, 3H), 6.3 (s, 1H), 7.37–7.46 (m, 3H), 7.62–7.64 (d, *J*=7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=30.4, 42.5, 56.5, 119.6, 125.5, 129.1, 129.5, 137.5. Mass (ESI): *m/z* 247 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{10}H_{12}N_2O_2NaS$: 247.0517. Found: 247.0514.

*4.4.4. N-[1-Cyano-(2-naphthyl)ethyl]-2-methyl-2-propane-sulfonamide (**4j**)*

R_f 0.4 (hexane/EtOAc 6:4), white solid; mp 142–144 °C. IR (KBr): 3283, 2232, 1304, 1157 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.45 (s, 9H), 2.16 (s, 3H), 4.54 (s, 1H), 7.5–7.56 (m, 2H), 7.64 (d, *J*=9.1 Hz, 1H), 7.81–7.92 (m, 3H), 8.12 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=24.2, 30.0, 57.4, 61.0, 119.8, 122.1, 124.9, 127.0, 127.2, 127.6, 128.5, 129.4, 132.8, 133.2, 136.1. Mass (ESI): *m/z* 334 ($M+NH_4^+$). HRMS (ESI): Anal. Calcd for $C_{17}H_{20}N_2O_2NaS$: 339.1143. Found: 339.1131.

*4.4.5. N-[1-Cyano-(4-methylphenyl)phenylmethyl]-2-methyl-2-propanesulfonamide (**4k**)*

R_f 0.36 (hexane/EtOAc 6:4), colourless solid; mp 153–155 °C. IR (KBr): 3214, 2238, 1314, 1126 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.48 (s, 9H), 2.37 (s, 3H), 4.74 (s, 1H), 7.19 (d, *J*=8.3 Hz, 2H), 7.34 (d, *J*=9.1 Hz, 2H), 7.38–7.43 (m, 3H), 7.48 (d, *J*=8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=21.1, 24.3, 61.3, 64.6, 96.1, 119.1, 126.8, 128.9, 129.2, 129.7, 136.1, 139.2. Mass (ESI): *m/z* 360 ($M+NH_4^+$). HRMS (ESI): Anal. Calcd for $C_{19}H_{22}N_2O_2NaS$: 365.1299. Found: 365.1290.

*4.4.6. N-[1-Cyano-(phenyl)-3-pyridylmethyl]-2-methyl-2-propanesulfonamide (**4l**)*

R_f 0.52 (hexane/EtOAc 6:4), yellow solid; mp 170–172 °C. IR (KBr): 3284, 2264, 1311, 1126 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.56 (s, 9H), 7.31–7.45 (m, 6H), 7.52 (dd, *J*=6.4, 8.7 Hz, 1H), 8.01 (s, 1H), 8.12 (d, *J*=8.7 Hz, 1H), 8.18 (d, *J*=6.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=24.2, 29.6, 61.3, 62.0, 116.3, 125.0, 126.4, 126.7, 127.1, 129.3, 129.5, 132.8, 135.7, 141.1, 145.6. Mass (ESI): *m/z* 352 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{17}H_{19}N_3O_2NaS$: 352.1044. Found: 352.1031.

*4.4.7. N-[1-Cyano-1-(3-pyridyl)ethyl]-2-methyl-2-propane-sulfonamide (**4m**)*

R_f 0.52 (hexane/EtOAc 6:4), brown solid; mp 98–100 °C. IR (KBr): 3228, 2244, 1306, 1126 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.38 (s, 9H), 1.99 (s, 3H), 6.11 (s, 1H), 7.28 (t, *J*=6.1 Hz, 1H), 7.69–7.8 (m, 2H), 8.51 (d, *J*=6.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=24.1, 30.6, 40.8, 57.1, 60.7, 120.1, 124.0, 138.1, 148.8, 156.1. Mass (ESI): *m/z* 290 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{12}H_{17}N_3O_2NaS$: 290.0939. Found: 290.0943.

*4.4.8. N-[1-Cyano-1-methylpentyl]-2-methyl-2-propane-sulfonamide (**4n**)*

R_f 0.44 (hexane/EtOAc 6:4), colourless solid; mp 110–112 °C. IR (KBr): 3268, 2227, 1301, 1124 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=0.97 (t, *J*=6.8 Hz, 3H), 1.35–1.41 (m, 2H), 1.44 (s, 9H), 1.47–1.59 (m, 2H), 1.75 (s, 3H), 1.8–1.87 (m, 1H), 1.92–2.03 (m, 1H), 4.71 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=13.7, 22.2, 24.2, 26.4, 27.2, 41.5, 54.2, 60.6, 120.3. Mass (ESI): *m/z* 269 ($M+Na^+$). HRMS (ESI): Anal. Calcd for $C_{11}H_{22}N_2O_2NaS$: 269.1299. Found: 269.1289.

*4.5. Typical procedure for the Strecker reaction of ketoimine **3a** with ethyl cyanoformate*

Ethyl cyanoformate (2 mmol) was added to a stirred solution of NAP-MgO (0.05 g) and ketoimine **3a** (1 mmol) in 3 mL of DMF at room temperature, followed by addition of acetic acid (2 mmol). Reaction was monitored by thin layer chromatography (TLC), after 3 h of stirring no product was present by TLC.

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