

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/lsyc20</u>

An Efficient Synthesis of Symmetrical Bisamides From Aldehydes and Amides Catalyzed by Silica-Bonded S-Sulfonic Acid Nanoparticles

Mahmood Tajbakhsh $^{\rm a}$, Rahman Hosseinzadeh $^{\rm a}$, Heshmatollah Alinezhad $^{\rm a}$ & Parizad Rezaee $^{\rm a}$

^a Department of Organic Chemistry, Faculty of Chemistry, University of Mazandaran, Babolsar, Iran Accepted author version posted online: 20 Mar 2013.

To cite this article: Mahmood Tajbakhsh , Rahman Hosseinzadeh , Heshmatollah Alinezhad & Parizad Rezaee (2013): An Efficient Synthesis of Symmetrical Bisamides From Aldehydes and Amides Catalyzed by Silica-Bonded S-Sulfonic Acid Nanoparticles, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, DOI:10.1080/00397911.2012.709573

To link to this article: <u>http://dx.doi.org/10.1080/00397911.2012.709573</u>

Disclaimer: This is a version of an unedited manuscript that has been accepted for publication. As a service to authors and researchers we are providing this version of the accepted manuscript (AM). Copyediting, typesetting, and review of the resulting proof will be undertaken on this manuscript before final publication of the Version of Record (VoR). During production and pre-press, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal relate to this version also.

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.tandfonline.com/page/terms-and-conditions

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

An efficient synthesis of symmetrical bisamides from aldehydes and amides catalyzed by silica-bonded S-sulfonic acid nanoparticles

Mahmood Tajbakhsh¹, Rahman Hosseinzadeh¹, Heshmatollah Alinezhad¹, Parizad Rezaee¹

¹Department of Organic Chemistry, Faculty of Chemistry, University of Mazandaran, Babolsar, Iran

Corresponding Author, Tel. & Fax: +98-1125342302 E-mail: tajbaksh@umz.ac.ir

Abstract

Silica-bonded S-sulfonic acid nanoparticles (SBSSANPs) was easily synthesized from silica nanoparticles and showed to be an efficient catalyst in the synthesis the symmetrical *N*,*N*'-alkylidene bisamides. Reaction of aldehydes and amides in the presence of the catalyst afforded the corresponding bisamides in good to excellent yields. The extensive range of substrates suggests general applicability of the method. Reusability of the catalyst, simple work- up procedure and short reaction times are other advantages of this protocol.

Supplemental materials are available for this article. Go to the publisher's online edition of *Synthetic Communications*® to view the free supplemental file.



KEYWORDS: Bisamides, Silica-bonded S-sulfonic acid nanoparticles, Aldehydes,

Amides, Supported catalyst

INTRODUCTION

Bisamides are an important class of organic compounds because the amide moiety is

present in many biologically significant substances.^[1] Symmetrical and unsymmetrical

N,N'-alkylidene bisamides and their derivatives are found as key structural sub-units for

the construction of peptidomimetic frameworks.^[2-4]

The preparation of symmetrical N_{N} -alkylidene bisamides is an important organic transformation and several methods reported for their synthesis. In most cases the reaction between amides and aldehydes proceed in the presence of strong acid catalysts. e.g. triflic acid^[5], sulfuric acid,^[6] hydrochloric acid^[7] or acetic acid^[8] which, among them triflic acid is a more efficient catalyst in the formation of symmetrical bisamides. These catalysts are corrosive, toxic and may destroy the acid sensitive functional groups together with other side reactions. Zhu *et al.* have reported the synthesis of fluorinecontaining N.N'-alkylidene bisamides in the presence of fluoroalkanesulfonic acids.^[9] Perumal *et al.* reported an alternative approach to synthesis symmetrical N,N'-alkylidene bisamides by reacting of aldehydes with nitriles in the presence of sulfamic acid with moderate vields.^[10] However, this reaction was limited to electron-withdrawing aromatic aldehydes and did not work for electron-rich aromatic and aliphatic aldehydes. The reaction of aldehydes with alkyl nitriles promoted by chlorosulfonic acid afforded symmetrical bisamides and applied only for electron-deficient aldehydes.^[11] Recently, Harichandran et al. have reported the synthesis of symmetrical N,N'-alkylidene bisamides by the reaction of aldehydes with amides, using phosphotungstic and boric acids as catalyst.^[12] Their method limited to the reaction of aromatic aldehydes with benzamide. the reaction time was long with moderate yield. To address the above mentioned facts, investigation to find an efficient and general method for the synthesis of symmetrical bisamides still is an important research topic.

On the other hand synthetic methodologies based on green chemistry processes are of increasing interest in organic chemistry. Although polymer-supported catalysts which

have been widely used in research and in process chemistry due to its easy recovery, but their use is also restricted because of easy damage of the organic backbone (thermal or chemical).^[13] One way to prevail over this problem of the traditional polymer-supported catalysts is to change the expensive organic polymer chain to silica having a covalently anchored organic spacer to create organic-inorganic hybrid (interphase) catalysts.^[14] In this type of solids, the reactive centers are highly mobile similar to homogeneous catalysts and at the same time it has the advantage of recyclability of the heterogeneous catalysts.

Herein we report a convenient and efficient method to prepare symmetrical bisamides by condensing different alkyl and aryl aldehydes with variety of alkyl and aryl amides using SBSSANPs as an efficient catalyst. The catalyst was prepared according to the known literature procedure,^[15] but, in the current work, the organic functional group covalently anchored onto nanosilica (with 12.6 nm average particle size), and obtained the silicabonded S-sulfonic acid nanoparticles as depicted in scheme 1.

The catalyst was characterized by thermogravimetric (TG), scanning electron microscopy (SEM), IR spectra and ion-exchange pH analysis (see the Supplementary Material, Figures 1-3, available online).

RESULTS AND DISCUSSION

Initially the reaction of 4-chloro benzaldehyde 1 (1 mmol) with benzamide 2 (2 mmol) with different amounts of catalysts were carried out in toluene at reflux temperature.

After completion of the reaction, monitored by TLC, followed by standard work-up and purification, N,N'- alkylidene bisamide **3** was obtained and the results are listed in Table 1.

As it is clear from this table, reaction in the absence of any catalyst gave very low yield of the product after 6 hrs (Table 1, entry 1). Similar results were obtained when, silica gel (SiO₂), silica nanoparticles (SiO₂ NPs) and silica sulfuric acid were applied in this reaction (Table 1, entries 2-4). Silica- bonded S-sulfonic acid (SBSSA)^[15] gave higher yield of the product under the same reaction conditions. Different amounts of the SBSSA catalyst were examined, but did not improve the yield significantly (Table 1, entries 5-9). When silica-bonded S-sulfonic acid nanoparticles (SBSSANPs) was used as catalyst, much higher yield of the product was obtained (Table 1, entries 10-13). The highest yield (97%) was achieved with 0.08 g catalyst loading (Table 1, entry 12) and higher amount of the catalyst decreased the reaction yield (Table 1, entry 13).

These observations clearly showed that the synthesized SBSSANPs is an efficient catalyst in this reaction which might be due to the higher surface area and loading in comparison with the conventional SBSSA.

This reaction was also tested in various solvents (Table 2). The results indicated that different solvents affected the efficiency of the reaction. Acetone and CH₂Cl₂ afforded moderate yields (Table 2, entries 1 and 2). No product was observed in CH₃CN and THF (Table 2, entries 3 and 4), whereas when toluene was used as solvent, excellent yield of

the product was formed (Table 2, entry 5). In addition, when the reaction was carried out under solvent-free conditions, a low yield of the product was obtained (Table 2, entry 6). The reaction did not proceed when low boiling solvents were used (Table 2, entries 1-4). This might indicate the significant effect of temperature on the reaction. However, highest yield was achieved when the reaction was carried out under reflux in toluene.

To study the scope of the reaction, a series of aldehydes and amides were reacted in the presence of SBSSANPs in toluene at reflux temperature (Table 3). In all cases, aromatic aldehydes substituted with either electron-donating or electron-withdrawing groups underwent the reaction smoothly and gave the products in good to excellent yields. The reaction is also compatible with aliphatic aldehydes, as propionaldehyde and formaldehyde reacted with benzamide and acetamide, the related bisamides were resulted in good yields (Table 3, entries 15, 16, 26). In some reported methods, the reaction of benzaldehyde with acetamide did not occur and only starting material was recovered in quantitative yield,¹³ but, in this method the reaction afforded the related bisamide in 83% yield (Table 3, entry 17).

In order to examine the possibility to synthesize the unsymmetrical *N*,*N*'-alkylidene bisamides, *p*- chlorobenzaldehyde (1 mmol) reacted with a mixture of benzamide (1 mmol) and acetamide (1 mmol) under same reaction conditions (Table 4). After 3 hr, 62.7% of *N*-[benzoylamino(4-chlorophenyl)methyl]-benzamide (4a), 20.7% of *N*-[acetylamino(4-chlorophenyl)methyl]-acetamide (5a) and 16.6% of *N*-(acetamido(4-chlorophenyl)methyl]-benzamide (5a) and 16.6% of *N*-(acetamido(4-chlorophenyl)methyl)benzamide (6a) was obtained (Table 4, entry 1). When, 4-

methoxybenzaldehyde and *p*-nitrobenzaldehyde were applied in this reaction, 5b and 5c was formed in 50.2% and 36.6% yield respectively and other products were obtained in lower yields (Table 4, entries 2 and 3).

All the known compounds were characterized by their melting points and comparison of their IR, ¹H-NMR and ¹³C- NMR spectra with authentic samples. The structure of unknown compounds (Table 3, entries 4, 5, 11, 12, 14, 15, 21, 22, 23, 27-31) were deduced by elemental and spectral analysis.

The reusability of SBSSANPs was also investigated in this system. Under optimized conditions after completion of the reaction, the reaction mixture was cooled and filtered off, The residue was dissolved in boiling ethanol (40 ml) and filtered off to remove the catalyst. The catalyst was washed with hot ethanol (20 ml), dried and reused directly for three subsequent runs in the reaction of 4-chloro benzaldehyde with benzamide (Table 3, entry 6). As shown in the Figure 1, the yield of product decreased slightly after four runs.

Finally, the crystallinity of the synthesized bisamides were assessed by XRD patterns (see also Supplementary Material). The XRD patterns for four samples (Table 3, entries 6, 7, 19, 26) showed that these bisamides are crystalline in nature, which could be due to the presence of the two amide groups and hard segment such as aryl rings as well as the interchain hydrogen bonds. This is in agreement with other similar studies. ^[18]

EXPERIMENTAL

General Information

All the starting materials were supplied commercially from Aldrich or Merck Chemical Co. The SBSSA catalyst was made according to the literature procedure.^[15] Nanosilica with 12.6 nm average particle size was purchased from Nissan Chemical (Tokyo, Japan). ¹H- and ¹³C-NMR spectra were recorded on a Bruker DRX-400 AVANCE (400 and 100 MHz respectively) in DMSO-d₆ as solvent. Chemical shifts are on the δ scale, relative to internal Me₄Si. Thermo gravimetric analysis (TGA) were recorded on a Stanton Redcraft STA-780 (London, UK). Scanning electron microscopic (SEM) images were observed under CAMScan-MV2300 instrument (England). X-ray powder diffraction (XRD) patterns of the PIs were recorded by an X-ray diffractometer (XRD, GBC MMA Instrument) with Be-filtered Cu K α radiation. Melting points were determined on a thermo scientific IA9200 and are uncorrected. Mass spectra were obtained on an Agilent technologies instrument and IR spectra were determined on a Shimadzu instrument.

Preparation Of 3-Mercaptopropylsilica 1 (MPS)

Silica nanoparticles was activated by refluxing in hydrochloric acid (4 M) for 24 h, washed with distillated water and dried completely.^[19] Refluxing the activated silica gel (10 g) with 3-mercaptopropyltrimethoxysilane (MPTMS, 5 mmol) in dry toluene for 18 h. The solid materials were filtered off and washed with hot toluene for 12 h in a continuous extraction apparatus (Soxhlet) and dried in oven at 110 °C overnight to give the surface-bounded thiol (MPS) group.

Catalyst Preparation (2)

To a magnetically stirred mixture of 3-mercaptopropylsilica (1, 5 g) in CHCl₃ (20 mL), chlorosulfonic acid (1.00 g, 9 mmol) was added dropwise at 0 °C during 2 h. The mixture was stirred for 2 h until all HCl was removed from reaction vessel. The mixture was then filtered, washed with methanol (30 mL) and dried at room temperature to give the silica bonded functionalized sulfonic acid nanoparticles **2** (SBSSANPs) as a cream powder.

Analysis Of The Sbssanps

Scanning electron microscopy was used to study the structure of the catalyst. Comparing the primary particle size and the size of finally nanoparticles, the SEM morphologies show that the particles are approximately 30-40 nm in size, and they show some degree of aggregation. The catalyst shows characteristic IR peaks at around 3100-3700, 2928, 2852, 1020-1250 and 650 cm⁻¹ due to O-H of silanols, C–H stretching vibrations, Si–O–Si stretching vibrations and –SO₃H groups, respectively.^[20] Quantitative determination of the organic functional group covalently anchored onto the surface in compound **2** was performed with thermogravimetric analysis (TGA). Typically a loading at ca. 1.20 mmol/g for surface bound –SO₃H group was obtained. When sulfonated product **2** was placed in an aqueous NaCl solution, the solution pH dropped instantaneously to pH≈1.62, as ion exchange occurred between protons and sodium ions (proton exchange capacity: 1.19 mmol/g of sulfonic acid **2**) which is in good agreement with the result obtained from TGA and titration analysis.

A General Procedure For The Synthesis Of Symmetrical Bisamides 3

A mixture of aldehyde (1 mmol), amide (2 mmol) and SBSSANPs (0.08 g) in toluene (7 mL) was heated under reflux. The completion of the reaction was followed by TLC analysis. After vigorously stirring for the appropriate time a white viscous solid was obtained. The mixture was cooled and filtered, the residue was boiled in ethanol (40 ml). The catalyst was removed by simple filtration on a sintered glass funnel (Porosity Grades 5) and washed with hot ethanol. The combined ethanolic solution concentrated under vacuum to afford the products, which were purified by recrystallisation in the suitable solvent (ethanol or acetone). The reaction times, the yields and the melting points are listed in Table 3. The analytical data for the new products are shown in the Supplementary Material.

CONCLUSION

In conclusion, we have developed a highly efficient synthesis of symmetrical bisamides from aldehydes and amides under simple reaction conditions. Mild heterogeneous reaction conditions, using inexpensive range of substrate compatibility and simple work up procedure are the main advantages of this protocol, for the synthesis of *N*,*N*'- alkylidene bisamides from aldehydes and amides.

SUPPLEMENTARY DATA AVAILABLE

¹H-NMR and ¹³C- NMR spectra; SEM morphologies; XRD patterns; FTIR spectra; thermal gravimetrical and ion-exchange pH analyses of the materials are available online in the Supplementary Material.

ACKNOWLEDGMENTS

We are thankful to the Research Council of Mazandaran University for the partial support of this work.

REFERENCES

1. Yamazaki, T.; Numani, K. Y.; Goodman, M. Cyclic retro-inverso dipeptides with two aromatic side chains. II. Conformational analysis. *Biopolymers* **1991**, *31*, 1513-1528.

2. Pallai, P. V.; Struthers, R. S.; Goodman, M.; Moroder, L.; Wunsch E.; Vale, W. Partial retro-inverso analogs of somatostatin: pairwise modifications at residues 7 and 8 and at residues 8 and 9. *Biochemistry* **1985**, *24*, 1933-1941.

3. Nunami, K. I.; Yamazaki, T.; Goodman, M. Cyclic retro-inverso dipeptides with two aromatic side chains. I. Synthesis. *Biopolymers* **1991**, *31*, 1503-1512.

4. Rodriguez, M.; Dubreuil, P.; Bali, J. P.; Martinez, J. Synthesis and biological activity of partially modified retro-inverso pseudopeptide derivatives of the c-terminal tetrapeptide of gastrin. *J. Med. Chem.* **1987**, *30*, 758-763.

5. Fernandez, A. H.; Alvarez, R. M.; Abajo, T. M. Improved synthesis of symmetrical *N*,*N*'-alkylidene bisamides. *Synthesis* **1996**, 1299-1301.

6. Magat, E. E.; Faris, B. F.; Reith, J. E.; Salisbury, L. F. Acid-catalyzed reactions of nitriles. II. polyamides from formaldehyde and dinitriles. *J. Am. Chem. Soc.* **1951**, *73*, 1028-1031.

 Brace, N. O.; Mantell, G. J. Hydrophobic compounds and polymers from long chain alkanamide-formaldehyde condensation reactions. *J. Org. Chem.* 1961, *26*, 5176-5180.

8. Noyes, W. A.; Forman, D. B. Aldehyde—Amide condensation. I. reactions between aldehydes and acetamide. *J. Am. Chem. Soc.* **1933**, *55*, 3493-3494.

9. Zhu, S.; Xu, G.; Chu, Q.; Xu, Y.; Qui, C. Synthesis of fluorine-containing symmetrical *N*,*N*'-alkylidene bisamides. *J. Fluorine Chem.* **1999**, *93*, 69-71.

10. Selvam, N. P.; Saranya, S.; Perumal, P. T. A convenient and efficient protocol for the synthesis of symmetrical *N*,*N*'-alkylidine bisamides by sulfamic acid under solvent-free conditions. *Can. J. Chem.* **2008**, *85*, 32-38.

11. Anary-Abbasinejad, M.; Mosslemin, M. H.; Hassanabadi, A. Synthesis of symmetrical bisamides by reaction between aromatic aldehydes and alkyl nitriles in the presence of chlorosulfonic acid. *J. Chem. Res.* **2009**, *4*, 218-219.

(a) Harichandran, G.; Amalraj, S. D.; Shanmugam, P. An efficient synthesis of symmetrical *N*,*N* -alkyl- idene bisamides catalyzed by phosphortungstic acid. *Indian J. Chem. Sect B.* 2011, *50B*, 77-82; (b) Harichandran, G.; Amalraj, S. D.; Shanmugam, P. Boric acid catalyzed efficient synthesis of symmetrical *N*,*N* -alkylidene bisamides. *J. Iran. Chem. Soc.* 2011, *8*, 298-305.

Sherrington, D. C. Polymer-supported in synthesis, in: J. H. Clark (Ed.),
 Chemistry of Waste Minimization, Blackie Academic, London, 1995.

(a) Lu, Z. L.; Lindner, E.; Mayer, H. A. Applications of sol-gel-processed interphase catalysts. *Chem. Rev.* 2002, *102*, 3543-3578; (b) Wight, A. P.; Davis, M. E.
Design and preparation of organic-inorganic hybrid catalysts. *Chem. Rev.* 2002, *102*, 3589-3614.

15. Niknam, K.; Saberi, D.; Sadegheyan, M.; Deris A. Silica-bonded S-sulfonic acid: an efficient and recyclable solid acid catalyst for the synthesis of 4,4'- (arylmethylene) bis(1H-pyrazol-5-ols). *Tetrahedron Lett.* **2010**, *51*, 692–694.

16. Anary-Abbasinejad, M.; Mosslemin, M. H.; Hassanabadi, A.; Tajik, S. *p*-Toluene Sulfonic Acid-Catalyzed, Solvent-Free Synthesis of symmetrical bisamides by reaction between aldehydes and amides. *Synth. Commun.* **2010**, *40*, 2209-2214.

17. Mohammad Shafiee, M. R. One-pot preparation of *N*,*N*'-alkylidene bisamide derivatives catalyzed by silica supported polyphosphoric acid (SiO₂-PPA). *J Saudi Chem Soc In Press*. Available online 20 June **2011**, doi:10.1016/j.jscs.2011.06.005.

(a) Harings, J. A. W.; Asselen, O.; Graf, R.; Broos, R.; Rastogi, S. The Role of superheated water on the crystallization of *N*,*N*'-1,2-ethanediyl-bis(6-hydroxy-hexanamide): implications on crystallography and phase transitions. *Crystal Growth Design.* 2008, *8*, 2469-2477; (b) Zweep, N.; Hopkinson, A.; Meetsma, A.; Browne, W. R.; Feringa, B. L.; Esch, J. H.; Balancing hydrogen bonding and van der waals interactions in cyclohexane-based bisamide and bisurea organogelators. *Langmuir* 2009, *25*, 8802–8809.

 Javanbakht, M.; Ganjali, M. R.; Norouzi, P.; Badiei, A.; Hasheminasab, A.;
 Abdouss, M. Carbon paste electrode modified with functionalized nanoporous silica gel as a new sensor for determination of silver ion. *Electroanalysis* 2007, *19*, 1307-1314.

20. (a) Yuan, X.; Lee, H. I; Kim, J. W.; Yie, J. E.; Kim, J. M. Periodic mesoporous organosilicas functionalized with sulfonic acid group. synthesis and alkylation of phenol, *Chem. Lett. 32*, **2003**, 650-651; (b) Lee, B.; Kim, Y.; Lee, H.; Yi, J. Synthesis of functhionalized porous silicas via templating method as heavy metal ion adsorbent: the

introduction of surface hydrophilicity onto the surface of adsorbents. Microporous

Mesoporous Mater. 50, 2001, 77-90.

Table 1. One-pot condensation reaction between 4-chlorobenzaldehyde and benzamide in



the presence of different catalysts

Entry	catalyst	Catalyst loading (g)	Time (h)	Yield $(\%)^a$
1		No Catalyst	6	10
2	SiO ₂ NP ^b	0.05	12	38
3	SiO ₂	0.05	12	15
4	Silica Sulforic acid	0.1 (0.28 mmol)	6	31
5	SBSSA ^c	0.05 (0.017 mmol)	3	45
6		0.08 (0.030 mmol)	3	60
7		0.1 (0.034 mmol)	3	73
8		0.15 (0.051 mmol)	3	73
9		0.20 (0.068 mmol)	3	74
10	SBSSANPs	0.03 (0.036 mmol)	3	78
11		0.05 (0.060 mmol)	3	80
12		0.08 (0.096 mmol)	3	97
13		0.1 (0.120 mmol)	3	88

^{*a*} Isolated yield.

^b SiO₂ with 12.6 nm average particle size.

^c Non-nanoparticles silica-bonded S- sulfonic acid.

Table 2. Solvent effect on the reaction between 4-chlorobenzaldehyde (1 mmol) and

benzamide (2 mmol) catalyzed by SBSSANPs (0.08 g)

Entry	Solvent ^{<i>a</i>}	Time (h)	Yield $(\%)^b$
1	Acetone	18	36
2	CH ₂ Cl ₂	16	42
3	CH ₃ CN	24	0
4	THF	24	0
5	Toluene	3	97
6	Neat ^c	4	8

^{*a*} The reaction was carried out in 7 mL of solvent at reflux.

^b Isolated yield.

 c The reaction was carried out at 100 $^\circ$ C.

Downloaded by [University of Chicago Library] at 01:39 21 April 2013

Table 3. Synthesis of symmetrical bisamides using SBSSANPs under optimized

	$R_1 H + 2$	0 R ₂ NH ₂ —	SBSSANPs Toluene, Reflux	$\rightarrow R_2 \xrightarrow{\mathbf{N}}_{\mathbf{H}} \mathbf{R}_2$	$ \begin{array}{c} 1 \\ $		
conditions_1 2 3							
Entry ^a	R ₁	R ₂	Time	Yield	Found	mp(°C)	Reported
			(h)	(%) ^b			[Lit]
1	C ₆ H ₅	C ₆ H ₅	4	93	236-		237-238 ^[5]
					238		
2	4-CH ₃ C ₆ H ₄	C ₆ H ₅	6	91	230-		242-243 [5]
					234		
3	4-CN C ₆ H ₄	C ₆ H ₅	3	98	240-		230-234
					243		[12b]
4	$3-Br C_6H_4$	C ₆ H ₅	3	93	215-		-
					217		
5	$4-Br C_6H_4$	C ₆ H ₅	3	89	259-		-
					260		
6	4-Cl C ₆ H ₄	C ₆ H ₅	3	97	257-		230-232
					261		[12b]
7	3-O ₂ N C ₆ H ₄	C ₆ H ₅	3	97	227-		190-192
					230		[16]
8	$4-O_2NC_6H_4$	C ₆ H ₅	3	97	265-		265-267 [5]
					267		
9	4-MeO C ₆ H ₄	C ₆ H ₅	8	77	224-		221-222 [5]

					226	
10	Furfuryl	C ₆ H ₅	5	94	201-	206-208
					205	[12a]
11	PhCO	C ₆ H ₅	8	87	294	-
					dec.	
12	4-Acetamido	C ₆ H ₅	8	83	159-	-
	C ₆ H ₄				161	
13	4-FC ₆ H ₄	C ₆ H ₅	3	97	252-	226-228
					255	[12b]
14	2-Cl-5- O ₂ N	C ₆ H ₅	3	93	255-	-
	C ₆ H ₃				258	
15	Et	C ₆ H ₅	8	87	165-	-
					168	
16	Н	C ₆ H ₅	4	96	225-	216-218 [6]
					227	
17	Ph	CH ₃	6	83	228-	239-240 [5]
					231	
18	4-CH ₃ C ₆ H ₄	CH ₃	6	90	258-	269-270 ^[5]
					262	
19	4-Cl C ₆ H ₄	CH ₃	3	93	256-	258-259 [5]
					258	
20	$4-O_2N C_6H_4$	CH ₃	3	98	267-	270-272 [5]
					269	

21	$4-FC_6H_4$	CH ₃	3	96	268-	259-261
					271	[17]
22	4-Pyridyl	CH ₃	8	89	261-	-
					264	
23	2-Naphthyl	CH ₃	6	87	220-	-
					223	
24	4-MeO C ₆ H ₄	CH ₃	8	79	216-	221-222 [5]
					218	
25	Ph CH=CH-	CH ₃	6	92	193-	195-197
					195	[16]
26	Н	CH ₃	3	93	191-	196-198 [5]
					193	
27	Ph	4-CH ₃	5	82	210-	-
		C ₆ H ₄			214	
28	4-Cl C ₆ H ₄	4-CH ₃	4	91	170-	-
		C ₆ H ₄			172	
29	4-O ₂ N C ₆ H ₄	4-CH ₃	4	93	220-	-
		C ₆ H ₄			223	
30	4-O ₂ N C ₆ H ₄	3-C1	4	92	242-	-
		C ₆ H ₄			244	
31	4-CN C ₆ H ₄	3-C1	4	91	228-	-
		C ₆ H ₄			230	

^aOptimized conditions: aldehyde (1 mmol), amide (2 mmol), SBSSANPs (0.08 g),

Toluene at reflux temperature.

^b Isolated yield.

Table 4. Synthesise of unsymmetrical N,N'-alkylidene

bisamides

Entry ^a	R1	Product	Time (h)	Yield (%) ^b
1	4-Cl C ₆ H ₄	4a	3	62.7
		5a		20.7
		6a		16.6
2	4-MeO C ₆ H ₄	4b	3	30.7
		5b		50.2
		6b		19.1
3	$4-O_2N C_6H_4$	4c	3	18.6
		5c		63.6
		6c		17.8

^aReaction conditions: aldehyde (1 mmol), acetamide (1 mmol), benzmide (1 mmol),

SBSSANPs (0.08 g), Toluene, reflux.

^bRatio determined by ¹H-NMR analysis.

Scheme 1. Preparation of silica-bonded S-sulfonic acid nanoparticles (SBSSANPs).





