

NaHSO₄-SiO₂: An Efficient Reusable Green Catalyst for Selective C-3 Propargylation of Indoles with Tertiary Propargylic Alcohols

Gohani, Mukut; H. van Tonder, Johannes; C.B. Benzuidenhoudt, Barend*⁺

Department of Chemistry, University of the Free State, P.O. Box 339, Bloemfontein 9300, SOUTH AFRICA

ABSTRACT: Although several methods for the preparation of 4° propargyl indole derivatives have been published, this synthetic transformation is complicated by the tendency of 3° propargyl alcohols to form allenium intermediates in acidic media. It is therefore a challenge to find an efficient method for the C-3 propargylation of indoles with 3° propargylic alcohols. In this paper we wish to report on the successful application of silica gel impregnated with NaHSO₄ as catalyst for the preparation of 4° propargyl indole derivatives.

KEY WORDS: Alkylation; Catalyst; Indole; Propargylic alcohols; Sodium bisulfate-silica.

INTRODUCTION

Due to the biological importance of functionalized indole derivatives, the catalytic transformation of indoles has received considerable attention [1]. The propargylation of indoles is an efficient synthetic tool to selectively obtain C-3 propargyl indoles as intermediates toward the preparation of a variety of interesting bioactive molecules [2]. C-3 propargylated indoles can be prepared either by reacting the indole with a transition metal stabilized propargylic cation [3] or activation of the propargylic alcohol function followed by direct nucleophilic substitution with indole [4]. This is attractive since it produces water as the only by-product. The most useful procedures reported lately for this transformation is based on transition-metal [5-10], Lewis acid [11-15], or Brønsted acid [16-20] catalytic methodologies. Although all of the reported methods have good merit, it is difficult to prepare 4° propargyl indole derivatives due to the tendency of 3° propargyl alcohols to form allenium

intermediates in acidic media [21-22]. It is therefore a challenge to find an efficient method for the C-3 propargylation of indoles with 3° propargylic alcohols.

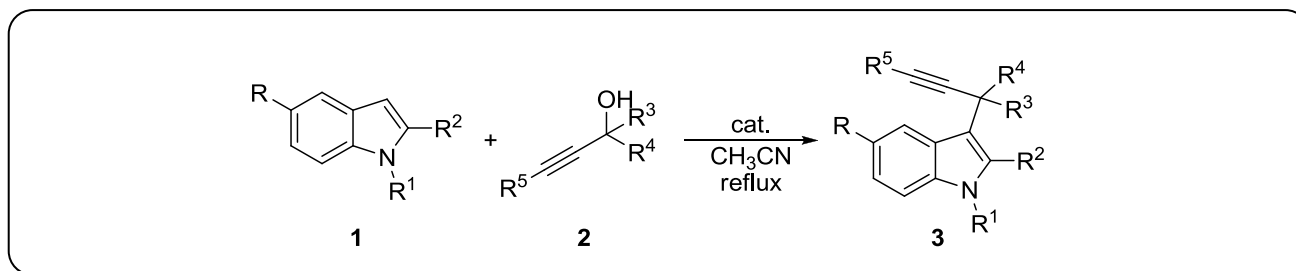
In recent years considerable attention has been paid to heterogeneous catalysts in order to replace their homogeneous counterparts due to both economic and environmental factors [23-25]. Solid acid catalysts, which are gaining popularity in organic synthesis, offer many advantages over homogeneous acids due to ease of handling, simplified separation methods, decreased plant corrosion, and environmentally safe disposal. For this reason, many solid acids have been developed to date [26]. Literature suggests that silica impregnated with NaHSO₄ (NaHSO₄-SiO₂) could be a possible heterogeneous acid catalyst for the activation of the alcohol function in propargylic alcohols as it is extensively employed for 'other' organic chemical transformations. This is due to its simple preparation, low cost and high recyclability [27-38].

* To whom correspondence should be addressed.

+ E-mail: benzuidbc@ufs.ac.za

1021-9986/15/3/11

7/§2.70



Scheme 1: $\text{NaHSO}_4\text{-SiO}_2$ catalysed propargylation of indoles.

In continuation of our work on the propargylation of indoles [40], $\text{NaHSO}_4\text{-SiO}_2$ was successfully applied as a solid reusable catalyst for the mild and efficient direct nucleophilic substitution of 3° propargyl alcohols with indole to prepare 4° C-3 propargyl indole derivatives.

EXPERIMENTAL SECTION

Preparation of $\text{NaHSO}_4\text{-SiO}_2$ catalys [42]

Silica gel [Kieselgel 60 (0.06–0.2 mm)] (15 g) was added to a magnetically stirred solution of $\text{NaHSO}_4\cdot\text{H}_2\text{O}$ (6.9 g, 50 mmol) in distilled water (100 ml) at 25 °C over a 30 minute period. Stirring was continued for 30 minutes allowing adsorption of sodium bisulfate to the surface of the silica gel. Water was removed *in vacuo* to give a powder which was dried in an oven at 120 °C (2-3 hours).

Preparation of quaternary propargyl indoles

A mixture of indole (**1**, 1.00 mmol), alkyne (**2**, 1.05 mmol) and $\text{NaHSO}_4\text{-SiO}_2$ [(w/w 40%), 10 mol%] in CH_3CN (2 mL) was heated to reflux while stirring. Upon completion of the reaction (TLC), the reaction mixture was cooled to ambient temperature and diluted with ethyl acetate (20 mL). The resulting mixture was stirred for 5 minutes and the catalyst removed by filtration after which the filtrate was washed with water (2 × 20 mL) and dried over anhydrous sodium sulfate. All solvent was removed *in vacuo* (ca. 60 °C) and the residue purified by column chromatography on silica gel (EtOAc : hexane 5 : 95, v/v). Structures for all isolated products were confirmed by spectroscopic analysis (^1H NMR, ^{13}C NMR and MS). The physical data of known compounds were identical to those reported in literature (see references in Tables 2 and 3) [40].

Recycling of the Catalyst

After diluting the reaction mixture with ethyl acetate (10 mL) and stirring it for 5 minutes, the catalyst

was filtered off, dried for 30 minutes at 80 °C and the reaction repeated.

RESULTS AND DISCUSSION

In search of an efficient heterogeneous catalyst for the preparation of 4° propargylated indole derivatives (**3**), through the condensation of indole (**1**) and an alkyne (**2**), (Scheme 1), several solid catalysts were evaluated (Table 1). $\text{NaHSO}_4\text{-SiO}_2$ (10 mol%) was found to be the superior catalyst, producing the propargylated indole (**3aa**) in 92% yield upon refluxing in CH_3CN for 120 minutes (entry 5). In the light of this result, NaHSO_4 and SiO_2 were evaluated separately as catalysts (entries 6 and 7, respectively). Only the acid salt was able to catalyse the reaction and produce the desired product, albeit in low yield. The seemingly synergistic effect between the salt and support may be the result of a stabilizing effect exerted by SiO_2 on the propargylic carbenium- or allenium ion obtained subsequent to acid assisted dehydroxylation by NaHSO_4 .

Optimal catalyst loading was established as 10 mol% (entry 5, 92%) as higher loading (entry 8) reflected similar results (89%) and a decrease in catalyst concentration (entry 9) only managed a 75% yield. Qualitative analysis by means of TLC (thin-layer chromatography) revealed solvent-free conditions to increase conversion rate significantly, but at the cost of sacrificing product selectivity (entry 10), as was established by ^1H NMR analysis of the crude product. Other solvents such as THF, CH_2Cl_2 and CH_3NO_2 were also considered but exhibited inferior results (entries 11-13). Herein $\text{NaHSO}_4\text{-SiO}_2$ is therefore reported as an effective catalyst for the preparation of 4° propargylated indole derivatives from propargyl alcohols and indoles.

The scope of the reaction with regard to the indole analogue was subsequently determined and it was found to be effective for the production of several

Table 1: Optimization of the propargylation reaction conditions using indole (1a) and 1-methyl-1,3-diphenylpropargyl alcohol (2a).^a

Entry	Solvent	Catalyst	Catalyst (mol%)	Yield (%)
1	CH ₃ CN	Amberlyst 15	10	85
2	CH ₃ CN	Montmorillonite clay	10	75
3	CH ₃ CN	KF-Al ₂ O ₃ ^b	10	Trace
4	CH ₃ CN	PPA-SiO ₂ ^c	10	80
5	CH ₃ CN	NaHSO ₄ -SiO ₂	10	92
6	CH ₃ CN	NaHSO ₄	10	87
7	CH ₃ CN	SiO ₂	10	Trace
8	CH ₃ CN	NaHSO ₄ -SiO ₂	15	89
9	CH ₃ CN	NaHSO ₄ -SiO ₂	5	75
10	None	NaHSO ₄ -SiO ₂	10	80 ^d
11	THF	NaHSO ₄ -SiO ₂	10	75
12	CH ₂ Cl ₂	NaHSO ₄ -SiO ₂	10	80
13	CH ₃ NO ₂	NaHSO ₄ -SiO ₂	10	85

a) Reaction conditions: Indole, alkynol (1.05 equiv), solvent, reflux, 2 h. b) Potassium fluoride on alumina.

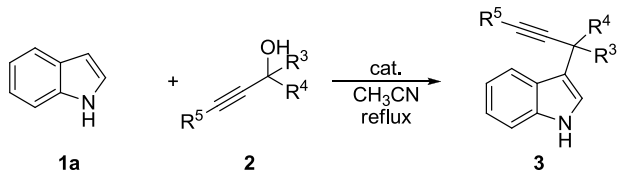
c) Polyphosphoric acid on silica. d) Reaction was performed neat at 80 °C.

Table 2: Propargylation of indole derivatives 1a-1h with 1,3-diphenyl-1-methylpropargyl alcohol (2a).^a

Entry	1	R	R ¹	R ²	3	Time (min.)	Yield (%)
1	1a	H	H	H	3aa ¹⁵	120	92 (94 ^b)
2	1b	Cl	H	H	3ba ¹⁵	120	91 (93 ^b)
3	1c	OMe	H	H	3ca ¹⁵	110	88 (88 ^b)
4	1d	H	Me	H	3da ⁴¹	120	90 (90 ^b)
5	1e	H	H	Me	3ea ⁴¹	90	82 (89 ^b)
6	1f	H	Me	Me	3fa ⁴¹	90	85 (69 ^c)
7	1g	H	H	Ph	3ga	120	88
8	1h	H	Me	Ph	3ha ⁴¹	120	89 (82 ^c)

a) Reaction conditions: Indole (1 mmol), alkynol (1.05 mmol), NaHSO₄-SiO₂ (10 mol%), CH₃CN (2 mL), reflux.

b) Yield previously obtained with Al(OTf)₃ as catalyst [15]. c) Yield obtained with PTSA as catalyst [40].

Table 3: Substitution reactions on propargyl alcohol derivatives 2b-2i with indole (1a).^a


Entry	2	R ³	R ⁴	R ⁵	3	Time (min.)	Yield (%)
1	2b	Me	4-Cl-Ph	Ph	3ab ¹⁵	120	90 (90 ^c)
2	2c	Me	Ph	4-OMe-Ph	3ac ¹⁵	120	90 (92 ^c)
3	2d	CH(CH ₂) ₂	Ph	Ph	3ad ⁴²	100	90 ^b (99 ^d)
4	2e	CH(CH ₂) ₂	Me	Ph	3ae ⁴¹	100	88 ^b (71 ^e)
5	2f	Me	Ph	ⁿ Bu	3af ⁴¹	140	67 (62 ^c)
6	2g	Me	Me	Ph	3ag ⁴¹	180	45 (54 ^c)
7	2h	Et	Ph	Ph	3ah	100	85
8	2i	Et	Ph	4-Cl-Ph	3ai	100	86

a) Reaction conditions: Indole (1 mmol), alkynol (1.05 mmol), NaHSO₄-SiO₂ (10 mol%), CH₃CN (2 mL), reflux.

b) Reaction was performed at room temperature. c) Yield previously obtained with Al(OTf)₃ [15]. d) Yield obtained with Yt(OTf)₃ [42].

e) Yield obtained with PTSA as catalyst [41].

4° propargylated indoles in moderate to excellent yields (Table 2). The effect of electron donating and withdrawing substituents on the benzenoid ring was assessed through the reaction of 5-chloro (**1b**) and 5-methoxy indole (**1c**) with propargylic alcohol **2a** (entries 2 and 3, respectively). Since both the desired products were obtained in excellent yields, the effect of the 5-substituent seems to be minimal. Methyl-substituted indole substrates such as 1-methyl (**1d**) (entry 4), 2-methyl (**1e**) (entry 5) and 1,2-dimethyl indole (**1f**) (entry 6) as well as 2-phenyl indole (**1g**) (entry 7) and 1-methyl-2-phenyl indole (**1h**) (entry 8) were also tested in the reaction, and all of these substrates proceeded to the desired products in high to excellent yield. Due to steric hindrance from the 2-phenyl substituent, a 9:1 mixture of the desired 3-substituted indole and 3-dienylindole **4** were obtained when 2-phenylindoles were subjected to the reaction conditions [16, 40].

Variation of the substituents on the propargylic alcohol (Table 3) indicated a significant decrease in propargyl indole yield (67%) when the terminal phenyl group (R⁵ = Ph) is replaced with a butyl entity (entry 5).

This observation suggests the phenyl unit in this position to assist in the stabilization of the intermediate propargylic carbocation (No indication of the presence of any 3-dienylindole and thus allenium carbocation formation was found by GC-MS), which contributes to the success of the transformation. Replacing the phenyl substituent on the alcoholic carbon by methyl groups (R³ and R⁴ = Me) supported the carbocation stabilization hypothesis as only a moderate yield (45%) could be obtained with this substrate under similar conditions (entry 6), even at extended reaction times. In contrast to the simple alkyl substituents, the introduction of a cyclopropyl unit to the alcoholic carbon [R³ = CH(CH₂)₂] resulted in transformation rates comparable to 2-phenyl substituted propargylic alcohols and excellent product yields (entries 3 and 4). This observation reinforces the above mentioned postulate as the cyclopropyl group has been reported to stabilize carbocationic species [39].

All reactions were analysed by GCMS and did not reveal the presence of any by-product in significant amounts. The propensity of nucleophilic substitution versus competitive water elimination was investigated

Table 4: Recyclability of NaHSO₄-SiO₂ as catalyst^{a,b}.

Entry	Product	1 st cycle	2 nd cycle	3 rd cycle	4 th cycle
1	3aa	91	90	90	89
2	3ac	90	90	89	89

a) Reaction conditions: Indole (1 mmol), alkynol (1.05 mmol), NaHSO₄-SiO₂ (10 mol%), solvent (2 mL), reflux.

b) Upon completion the reaction mixture was diluted with ethyl acetate (10 mL), stirred for 5 minutes and the catalyst recovered by means of filtration.

by subjecting ethyl-substituted propargyl alcohol and indole to the established reaction conditions (entries 7 and 8). No indication of water elimination was observed, as the products obtained could be ascribed exclusively to the direct nucleophilic substitution reaction of the OH function by the indole. It is necessary to mention that no C-2 alkylated indole products were observed or isolated for any of the reactions conducted under the optimized reaction conditions.

Recyclability of catalysts is an important aspect of a reaction from an economical and environmental point of view, and has attracted much attention in recent years. The reusability of NaHSO₄-SiO₂ was evaluated for two reactions by recovering the catalyst by means of filtration subsequent to diluting the reaction mixture with ethyl acetate (10 mL) and stirring for 5 minutes. The recovered catalyst was dried for 30 minutes at 80 °C prior to repeating the reaction. In this way the catalyst could successfully be recycled three times and results comparable to those found with fresh catalyst, could be generated for up to four cycles, indicating no observable decrease in activity or selectivity (Table 4).

CONCLUSIONS

In conclusion, a highly efficient catalyst for the synthesis of substituted quaternary C-3 propargylated indoles is reported on. Treatment of indole derivatives with 3° propargyl alcohols in the presence of NaHSO₄-SiO₂ not only afforded the products in excellent yields, but also addresses challenges associated with catalysts such as cost, ease of handling, recovery, safety and pollution. The catalyst can easily be prepared and is retrievable by simple filtration methods.

Acknowledgment

We gratefully acknowledge Sasol for financial support.

Received : June 9, 2014 ; Accepted : Apr. 27, 2015

REFERENCES

- [1] Bandini M., Eichhozer, A., Catalytic Functionalization of Indoles in a New Dimension, *Angew. Chem. Int. Ed.*, **48**(51): 9608-9644 (2009).
- [2] Sanz R., Miguel D., Gohain M., Garcia-Garcia. P., Fernández-Rodríguez M.A., González-Pérez A., Nieto-Faza O., de Lera A.R., Rodríguez F., Synthesis of Diverse Indole-Containing Scaffolds by Gold(I)-Catalyzed Tandem Reactions of 3-Propargylindoles Initiated by 1,2-Indole Migrations: Scope and Computational Studies, *Chem. Eur. J.*, **16**(32): 9818-9828 (2010).
- [3] Müller T.J.J., Stereoselective Propargylations with Transition-Metal-Stabilized Propargyl Cations, *Eur. J. Org. Chem.*, **2001**(11): 2021-2033 (2001).
- [4] Emer E., Sinisi R., Capdevila M.G., Petruzzello D., De Vincentiis F., Cozzi P.G., Direct Nucleophilic S_N1-Type Reactions of Alcohols, *Eur. J. Org. Chem.*, **2011**(4): 647-666 (2011).
- [5] Georgy M., Boucard V., Debleds O., Dal Zotto C., Campagne J. -M., Gold(III)-Catalyzed Direct Nucleophilic Substitution of Propargylic Alcohol, *Tetrahedron*, **65**(9): 1758-1766 (2009).
- [6] Kanao K., Matsuzawa H., Miyake Y., Nishibayashi Y., Ruthenium-Catalyzed Enantioselective Propargylation of Indoles with Propargylic Alcohol, *Synthesis*, **2008**(23): 3869-3873 (2008).
- [7] Whitney S., Grigg R., Derrick A., Keep A., *Org. Lett.*, [Cp*IrCl₂]₂-Catalyzed Indirect Functionalization of Alcohols: Novel Strategies for the Synthesis of Substituted Indoles, *Org. Lett.*, **9**(17): 3299-3302 (2007).
- [8] Matsuzawa H., Kanao K., Miyake Y., Nishibayashi Y., Remarkable Effect of N-Substituent on Enantioselective Ruthenium-Catalyzed Propargylation of Indoles with Propargylic Alcohols, *Org. Lett.*, **9**(26): 5561-5564 (2007).

- [9] Inada Y., Yoshikawa M., Milton M.D., Nishibayashi Y., Uemura S., Ruthenium-Catalyzed Propargylation of Aromatic Compounds with Propargylic Alcohols, *Eur. J. Org. Chem.*, **2006**(4): 881-890(2006).
- [10] Kennedy-Smith J.J., Young L.A., Toste F.D., Ruthenium-Catalyzed Aromatic Propargylation, *Org. Lett.*, **6**(8):1325-1327(2004).
- [11] Yadav J.S., Subba Reddy B.V., Raghavendra Rao K.V., Narayana Kumar G.G.K.S., Sc(OTf)₃-Catalyzed Alkylation of Indoles with Propargyl Alcohols: an Expedient Synthesis of 3-Substituted Indoles, *Tetrahedron Lett.*, **48**(31):5573-5576 (2007).
- [12] Jana U., Maiti S., Biswas S., An FeCl₃-Catalyzed Highly C3-Selective Friedel-Crafts Alkylation of Indoles with Alcohols, *Tetrahedron Lett.*, **48**(40): 7160-7163 (2007).
- [13] Yadav J.S., Subba Reddy B.V., Raghavendra Rao K.V., Narayana Kumar G.G.K.S., Indium(III) Bromide Catalyzed Rapid Propargylation of Heteroaromatic Systems by α -Aryl-Substituted Propargyl Alcohols, *Synthesis*, **2007**(20): 3205-3210(2007).
- [14] Srihari P., Bhunia D.C., Sreedhar P., Mandal S.S., Shyam Sunder Reddy J., Yadav J.S., Iodine-Catalyzed C- and O-Nucleophilic Substitution Reactions of Aryl-Propargyl Methanols, *Tetrahedron Lett.*, **48**(46):8120-8124(2007).
- [15] Gohain M., Marais C., Bezuidenhout B.C.B., An Al(OTf)₃-Catalyzed Environmentally Benign Process for the Propargylation of Indoles, *Tetrahedron Lett.*, **53**(35): 4704-4707 (2012).
- [16] Sanz R., Gohain M., Miguel D., Martínez A., Rodríguez F., Synthesis of 3-Allenylindoles and 3-Dienylindoles by Brønsted Acid Catalyzed Allenylation of 2-Arylindoles with Tertiary Propargylic Alcohols, *Synlett*, **2009**(12): 1985-1989(2009).
- [17] Sanz R., Miguel D., Álvarez-Gutiérrez J.M., Rodríguez F., Brønsted Acid Catalyzed C3-Selective Propargylation and Benzoylation of Indoles with Tertiary Alcohols, *Synlett*, **2008**(7):975-978 (2008).
- [18] Shirakawa S., Kobayashi S., Surfactant-Type Brønsted Acid Catalyzed Dehydrative Nucleophilic Substitutions of Alcohols in Water, *Org. Lett.*, **9**(2): 311-314 (2007).
- [19] Motokura K., Nakagiri N., Mizugaki T., Ebitani K., Kaneda K., Nucleophilic Substitution Reactions of Alcohols with Use of Montmorillonite Catalysts as Solid Brønsted Acids, *J. Org. Chem.*, **72**(16):6006-6015(2007).
- [20] Le Bras J., Muzart J., Brønsted-Acid-Catalyzed Coupling of Electron-Rich Arenes with Substituted Allylic and Secondary Benzylic Alcohols, *Tetrahedron*, **63**(33):7942-7948(2007).
- [21] Olah G.A., Laali K.K., Wang Q., Prakash G.K.S., "Onium Ions"; John Wiley & Sons, Inc., New York, (1998).
- [22] Ohta A., Dahl K., Raab R., Geitner J., Huisgen R., Diazodiphenylmethane and Monosubstituted Butadienes: Kinetics and a New Chapter of Vinylcyclopropane Chemistry, *Helv. Chim. Acta*, **91**(5):783-804 (2008).
- [23] Sartori G., Maggi R., *Chem. Rev.*, **111**: PR181-PR214 (2011).
- [24] Fricke R., Kosslick H., Lischke G., Richter M., Incorporation of Gallium into Zeolites: Syntheses, Properties and Catalytic Application, *Chem. Rev.*, **100**(6): 2303-2406 (2003).
- [25] Chakroborti A.K., Gulhane R., Perchloric Acid Adsorbed on Silica Gel as A New, Highly Efficient, and Versatile Catalyst for Acetylation of Phenols, Thiols, Alcohols, and Amines, *Chem. Commun.*, **2003**(15): 1896-1897 (2003).
- [26] Wilson K., Clark J.H., Solid Acids and Their Use as Environmentally Friendly Catalysts in Organic Synthesis, *Pure Appl. Chem.*, **72**(7): 1313-1319 (2000).
- [27] Wu L., Yang C., Zhang C., Yang L., HClO₄-SiO₂ and NaHSO₄-SiO₂: Two Efficient Heterogeneous Catalysts for Synthesis of N-Acylsulfonamides under Solvent-Free Conditions, *Lett. Org. Chem.*, **6**(3): 234-236 (2009).
- [28] Rostamizadeh S., Shadjou N., Amani A.M., Balalaie S., Silica Supported Sodium Hydrogen Sulfate (NaHSO₄/SiO₂): A Mild and Efficient Reusable Catalyst for the Synthesis of Aryl-14-H-dibenzo [a,j]xanthenes under Solvent-free Conditions, *Chinese Chem. Lett.*, **19**(10): 1151-1155 (2008).
- [29] Kolvari E., Sodium Hydrogen Sulfate: Safe and Efficient, *Synlett*, **2006**(12): 1971-1972 (2006).
- [30] Breton G.W., Selective Monoacetylation of Unsymmetrical Diols Catalyzed by Silica Gel-Supported Sodium Hydrogen Sulfate, *J. Org. Chem.*, **62**(25):8952-8954(1997).
- [31] Ramesh C., Banerjee J., Pal R., Das B., Silica Supported Sodium Hydrogen Sulfate and Amberlyst-15: Two Efficient Heterogeneous Catalysts for Facile Synthesis of Bis- and Tris(1H-indol-3-yl)methanes from Indoles and Carbonyl Compounds, *Adv. Synth. Catal.*, **354**(5):557-559 (2003).

- [32] Ramesh C., Mahender G., Ravindranath N., Das B., A Simple, Mild and Efficient Procedure for Selective Cleavage of Prenyl Esters Using Silica-Supported Sodium Hydrogen Sulphate as A Heterogenous Catalyst, *Tetrahedron Lett.*, **44**(7):1465-1467(2003).
- [33] Karimi A.R., Alimohammadi Z., Azizian A., Mohammadi A.A., Mohammadizadeh M.R., Solvent-Free Synthesis of Tetrasubstituted Imidazoles on Silica Gel/NaHSO₄ Support, *Catal. Commun.*, **7**(9): 728-732 (2006).
- [34] Bazgir A., Microwave-Assisted Efficient Synthesis of Diimines in Dry Media Using Silica Gel Supported Sodium Hydrogen Sulfate as Reusable Solid Support, *J. Chem. Res.*, **2006**(1): 1-2 (2006).
- [35] Das B., Laxminarayana K., Krishnaish M., Srinivas Y., An Efficient and Convenient Protocol for the Synthesis of Novel 12-Aryl-or 12-Alkyl-8,9,10,12-tetrahydrobenzo-[a]xanthen -11-one Derivatives, *Synlett*, **2007**(20): 3107-3112 (2007).
- [36] Gopalkrishnan M., Sureshkumar P., Thanusu J., Kanagarajan V., Three Components Coupling Catalysed by NaHSO₄.SiO₂-A Convenient Synthesis, Antibacterial and Antifungal Activities of Novel 6-Aryl-1,2,4,5-tetrazinan-3-ones, *J. Enzym. Inhib. Med. Chem.*, **23**(1): 87-93 (2008).
- [37] Das B., Veeranjanyulu B., Krishnaiah M., Balasubramanyam P., Synthesis of Gem-Dihydroperoxides from Ketones Using Silica-Supported Sodium Hydrogen Sulfate as a Heterogeneous Catalyst, *J. Mol. Catal. A-Chem.*, **284**(1-2): 116-119 (2008).
- [38] Sapkal S.B., Shelke K.F., Shingate B.B., Shingare M.S., NaHSO₄/SiO₂: An Efficient Catalyst for the Synthesis of β -Enaminones and 2-Methylquinolin-4(1H)-ones under Solvent-Free Conditions, *J. Korean Chem. Soc.*, **54**(6): 723-726 (2010).
- [39] Gohain M., Marais C., Bezuidenhout B.C.B., Al(OTf)₃: An Efficient Recyclable Catalyst for Direct Nucleophilic Substitution of the Hydroxy Group of Propargylic Alcohols with Carbon-and Heteroatom-Centered Nucleophiles to Construct C-C, C-O, C-N and C-S Bonds, *Tetrahedron Lett.*, **53**(9): 1048-1050 (2012).
- [40] Sanz R., Miguel D., Martinez A., Gohain M., García-García P., Fernández-Rodríguez M.A., Álvarez E., Rodríguez F., Brønsted Acid Catalyzed Alkylation of Indoles with Tertiary Propargylic Alcohols: Scope and Limitations, *Eur. J. Org. Chem.*, **2010**(36): 7027-7039 (2010).
- [41] Rao W., Zhang X., Sze E.M.L., Chan P.W.H., Ytterbium(III) Triflate-Catalyzed Amination of 1-Cyclopropylprop-2-yn-1-ols as an Expedient Route to Conjugated Enynes, *J. Org. Chem.*, **74**(4): 1740-1743 (2009).
- [42] Azarifar D., Forghaniha A., A Novel Chemoselective Reaction of Aldehydes with 2-Mercaptoethanol Catalyzed by SiO₂-NaHSO₄ under Solvent-free Condition, *J. Chin. Chem. Soc.*, **53**(5), 1189-1192 (2006).