Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 1200–1210

Scope and limitations of $HClO_4$–SiO_2 as an extremely efficient, inexpensive, and reusable catalyst for chemoselective carbon–sulfur bond formation

Gopal L. Khatik, Gaurav Sharma, Raj Kumar and Asit K. Chakraborti*

Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), Sector 67, S. A. S. Nagar, Punjab 160 062, India

Received 9 September 2006; revised 7 November 2006; accepted 16 November 2006
Available online 12 December 2006

Abstract—The scope and limitations of perchloric acid adsorbed on silica gel ($HClO_4$–SiO_2) as a highly efficient, inexpensive, and reusable catalyst for chemoselective carbon–sulfur bond formation by conjugate addition of thiols to α,β-unsaturated ketones under solvent-free conditions and at rt are reported. In the case of 1,3-diphenylpropenone, the reactions were best carried out either at 80 °C under solvent-free conditions or at rt in MeOH. The reaction of aryl, arylalkyl, alkyl thiols, and alkane dithiols with cyclic and acyclic α,β-unsaturated ketones afforded excellent yields of the corresponding β-sulfidocarbonyls after 2 min to 2 h. In the case of dithiols, the bis-thia-Michael adducts were formed. The rate of the reaction was found to be dependent on the electronic and steric factors of the α,β-unsaturated ketones and the thiols. A substituent at the β-carbon of the α,β-unsaturated ketone offered steric hindrance for conjugate addition and such substrates required longer times. In case of aromatic thiols, the presence of the nitro group reduced the nucleophilicity of the sulfhydryl sulfur atom resulting in slower rate of reaction for 4-nitrothiophenol compared to that of thiophenol and 4-methylthiophenol. For alkane thiol, the reaction rate was influenced by the steric crowding of the alkyl group attached to the sulfhydryl moiety. The rate of reaction for alkane thiols was sluggish compared to that of aryl thiols. The influence of the β-substituent on the rate of thia-Michael addition was utilized for selective reaction during inter-molecular competitions of cyclohexen-2-one versus 3-methyl-2-cyclohexenone, cyclohexen-2-one versus 4-methyl-3-penten-2-one, and 4-phenyl-3-buten-2-one versus 4-methyl-3-penten-2-one with thiophenol with 100:0, 91:9, and 70:30 selectivities, respectively. The difference in the rate of reaction of thiophenol and 4-nitrothiophenol was also reflected during the inter-molecular competition for the reaction with cyclohexen-2-one with an excellent selectivity of 100:0. The influence of the steric factor of the alkyl group in alkane thiol resulted in 62:38 selectivity during the inter-molecular competition of ethane thiol and *tert*-butanethiol with cyclohexen-2-one. During inter- and intra-molecular competitions of thia- versus aza- and thia- versus oxa-Michael addition reactions, chemoselective thia-Michael addition took place. The chemoselective thia-Michael addition over aza-Michael addition during intra-molecular competion reactions with 2-aminothiophenol was utilized for an efficient one-pot synthesis of benzothiazepines.

1. Introduction

Carbon–sulfur bond formation by conjugate addition of thiols to α,β-unsaturated carbonyl compounds, has versatile applications in chemistry and biology as it plays critical roles in the (i) biosynthesis,[1] (ii) synthesis of bioactive compounds,[2] (iii) protection of the olefinic double bond of conjugated enones[3] (due to the ease of regeneration of the double bond by copper(I)-induced[4] and oxidative[3] elimination of the sulfur moiety), and (iv) generation of β-acylvinyl cation[5] and homoenolate anion[6] equivalents. These have generated interest to develop new methodologies for thia-Michael addition reaction.[7]

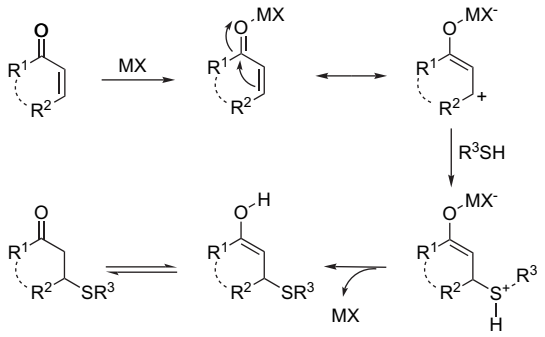
2. Results and discussion

We felt that the role of a metal catalyst is to induce electrophilic activation of the α,β-unsaturated carbonyl compound through coordination of the cationic center of the catalyst with the carbonyl oxygen of the α,β-unsaturated carbonyl compounds to increase the electrophilicity of the β-carbon (Scheme 1).

In the search for a more effective catalyst, we thought that a Lewis acid that can form a strong coordinate bond with the carbonyl oxygen atom of the α,β-unsaturated carbonyl compound should induce electrophilic activation more effectively and enable the conjugate addition to take place under mild conditions and in short times. Recently we

Keywords: C–S bond formation; Thia-Michael addition; Thiols; $HClO_4$–SiO_2; Catalyst; Selectivity; Electronic effect; Steric effect; Inter-molecular competition; Intra-molecular competition; Benzothiazepines; One-pot synthesis.
* Corresponding author. Tel.: +91 172 2214683; fax: +91 172 2214692; e-mail: akchakraborti@niper.ac.in

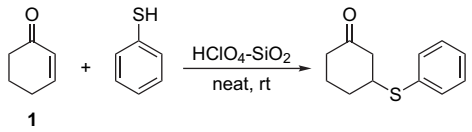
0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.11.050



Scheme 1. The role of a metal catalyst in catalyzing the thia-Michael addition reaction.

have been engaged in the development of various electrophilic activation catalysts derived from metal halides, perchlorates, tetrafluoroborates, and protic acids adsorbed on solid support for heteroatom acylation,[8] epoxide ring opening,[9] and imine[10]/dithiolane[11]/carbamate[12]/acetal[13]/acylal[14] formation, and thia-Michael addition reactions.[15] Although a comparison with the literature methods revealed that the use of $Cu(BF_4)_2 \cdot xH_2O$[15a] and $Zn(ClO_4)_2 \cdot 6H_2O$[15b] to be improved procedures, it was observed that the reactions with α,β-unsaturated ketones having an alkyl or an aryl substituent at the β-carbon took longer times (20 min–14 h). Our recent observation revealed that water plays a novel dual activation role in promoting the conjugate addition of thiols to α,β-unsaturated ketones.[16] However, this method also does not work well with these substrates. This encouraged us to develop a more effective catalyst. Recently we reported for the first time[17] that perchloric acid adsorbed on silica gel ($HClO_4$–SiO_2) is an extremely effective electrophilic activation agent for acylation reactions[8g] and subsequently found its application in dithiolane[11a] and carbamate[12a] formation. We were happy to observe that this newly introduced catalyst system has attracted the attention of other groups of researchers for various synthetic transformations.[18] Thus, we planned to explore the catalytic efficiency of $HClO_4$–SiO_2 for the thia-Michael addition reaction[19] as (i) the increasing pressure from environmentalists has led to the search for more friendly forms of catalysis and the leading contender for an environmentally acceptable alternative process is the use of supported reagents, (ii) the activity and selectivity of a reagent dispersed on the surface of a support is often improved (as the effective surface area of the reagent can be increased up to one hundred times), (iii) the good thermal and mechanical stabilities of supported reagents make them easy to handle as they are generally low toxic, non-corrosive free flowing powders, and their ease of separation from the reaction mixture through filtration and the feasibility of reuse make them suitable for meeting the requirement of triple bottom line philosophy[20] of green chemistry.

To evaluate the catalytic effect of $HClO_4$–SiO_2, 2-cyclohexen-1-one (**1**) was treated with thiophenol under various conditions (Scheme 2, Table 1). Excellent results were obtained using 0.01–1 mol % of $HClO_4$–SiO_2 affording the thia-Michael adduct in 85–99% yields after 2–20 min under solvent-free condition and at rt. However, for subsequent studies we used 1 mol % of the catalyst for ease of handling/weighing of the catalyst for small scale (2.5 mmol) reactions.



Scheme 2. The reaction of **1** with thiophenol in the presence of $HClO_4$–SiO_2.

Table 1. Reaction of **1** with thiophenol under the catalytic influence of $HClO_4$–SiO_2 and various conditions[a]

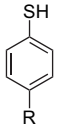
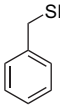
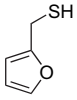
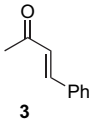
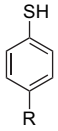
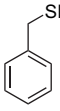
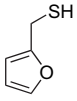
Entry	**1**[b]	Mol %[c]	Thiophenol (mmol)	Time (min)	Yield (%)[d,e]
1	2.5	1	2.75	2	99
2	5	0.1	5.5	5	90
3	10	0.01	11	20	85

[a] The α,β-unsaturated ketone was treated with the thiol in the presence of the catalyst at rt (~25–30 °C) under neat conditions.
[b] Amount of **1** (in mmol) used for the reaction.
[c] Mol % of $HClO_4$–SiO_2 used with respect to **1**.
[d] Isolated yield of the corresponding thia-Michael adduct after chromatographic purification.
[e] The product was characterized by IR, NMR, and MS.

We next planned to establish the superiority of $HClO_4$–SiO_2 over the reported catalysts, particularly $Cu(BF_4)_2 \cdot xH_2O$[15a] and $Zn(ClO_4)_2 \cdot 6H_2O$,[15b] so took 3-methyl-2-cyclohexen-1-one (**2**) and 4-phenyl-3-buten-2-one (**3**) as representatives of cyclic and acyclic α,β-unsaturated ketones, having an alkyl and aryl group at the β-carbon, respectively. Thus, in separate experiments, **2** and **3** were treated with various thiols in the presence of $HClO_4$–SiO_2 (1 mol %) and the results were compared with those obtained during the $Cu(BF_4)_2 \cdot xH_2O$ and $Zn(ClO_4)_2 \cdot 6H_2O$-catalyzed reactions (Table 2). The results clearly demonstrated that $HClO_4$–SiO_2 is a better suited catalyst in comparison to $Cu(BF_4)_2 \cdot xH_2O$ and $Zn(ClO_4)_2 \cdot 6H_2O$. An interesting observation was made during the reaction of **3**, a solid α,β-unsaturated ketone, with 4-nitrothiophenol, a solid thiol (entry 22, Table 2). After addition of $HClO_4$–SiO_2 to the heterogeneous mixture of **3** and 4-nitrothiophenol, a melt was obtained, which solidified after stirring for 15 min. The TLC and IR of the crude reaction mixture revealed that complete consumption of **3** took place. This indicated that the use of $HClO_4$–SiO_2 as a catalyst should enable the thia-Michael addition reaction to be carried out involving a solid ketone and a solid thiol under solvent-free conditions.

We next planned to establish the generality of the catalytic efficiency of $HClO_4$–SiO_2 for reaction of thiols with other α,β-unsaturated carbonyl compounds such as **1**, 2-cyclopenten-1-one (**4**), 3-buten-2-one (**5**), 4-methyl-3-penten-2-one (**6**), and 1,3-diphenylpropenone (**7**) (Table 3). Excellent results were obtained in each case. The reactions were completed after 2 min to 2 h (TLC, IR, and GCMS). No aqueous work-up was required for isolation of the product from the reaction mixture. After completion of the reaction, the mixture was diluted with Et_2O and passed through a plug of cotton to remove the catalyst, which separated out from the cotton on drying. Although the reaction using solid substrates such as **3** and 4-nitrothiophenol afforded excellent results under solvent-free conditions and at rt (entry 22, Table 2), in the case of **7** (a solid substrate), an initial attempt in carrying out the reaction with thiophenol at rt under

Table 2. Comparison of the catalytic efficiency of $HClO_4$–SiO_2 (**A**), $Cu(BF_4)_2 \cdot xH_2O$ (**B**), and $Zn(ClO_4)_2 \cdot 6H_2O$ (**C**) during conjugate addition of **2** and **3** with various thiols[a]

Entry	Enone	Thiol	Cat	Time (min)	Yield (%)[b,c]
	 **2**				
1		R=H	**A**	10	85
2		R=H	**B**	45	83[d]
3		R=H	**C**	60	Nil[e]
4		R=Me	**A**	10	89
5		R=Me	**B**	60	83[d]
6		R=Me	**C**	60	Nil[e]
7			**A**	10	81
8			**B**	45	81[d]
9			**C**	60	Nil[e]
10			**A**	30	80
11			**B**	60	82[d]
12			**C**	60	Nil[e]
13			**A**	30	88
14			**B**	12 h	75[d]
15			**C**	60	Nil[e]
	 **3**				
16		R=H	**A**	5	95
17		R=H	**B**	5	86[d]
18		R=H	**C**	90	89[f]
19		R=Me	**A**	30	90
20		R=Me	**B**	75	84[d]
21		R=Me	**C**	120	80[f]
22		$R=NO_2$	**A**	15	80
23		$R=NO_2$	**B**	60	60[g]
24		$R=NO_2$	**C**	60	40[g]
25			**A**	30	96
26			**B**	75	87[d]
27			**C**	120	82[f]
28			**A**	20	90
29			**B**	20	88[d]
30			**C**	120	78[f]
31			**A**	60	98
32			**B**	14 h	80[d]
33			**C**	6 h	83[f]
34			**A**	90	87
35			**B**	90	75
36			**C**	90	50

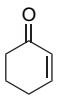
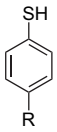
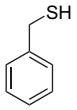
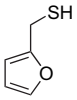
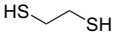
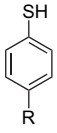
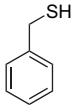
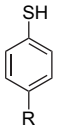
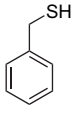
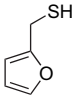
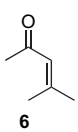
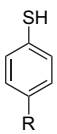
[a] The α,β-unsaturated ketone (2.5 mmol) was treated with the thiol (2.75 mmol, 1.1 equiv) in the presence of the catalyst (1 mol %) at rt (~25–30 °C) under neat conditions.
[b] Isolated yield of the corresponding thia-Michael adduct after chromatographic purification.
[c] The products were characterized by IR, NMR, and MS.
[d] Ref. 15a.
[e] The starting materials remained intact (TLC, IR, and GCMS).
[f] Ref. 15b.
[g] The thia-Michael adduct was formed in 30% yield after 15 min.

solvent-free conditions showed ~20% conversion to the thia-Michael adduct after 1 h. The conversion was increased to 60% after 30 min at 80 °C. No significant formation of the thia-Michael adduct was observed during the reaction of **7** with 4-nitrothiophenol after 2 h at rt under solvent-free conditions. However, the desired thia-Michael adduct was obtained in 75% yield after heating the reaction mixture at 80 °C for 1 h. The poor yields obtained during the reaction of **7** under solvent-free conditions were due to the fact that the reaction did not proceed toward incompletion as evidenced by the presence of unconsumed starting materials (IR and TLC). The initially formed thia-Michael adduct (a solid compound) created a heterogeneous environment and trapped the enone **7** and the thiol. This retarded the reaction rate. However, excellent results were obtained when the reactions of **7** were carried out in MeOH. Initially a clear solution was obtained after mixing **7** and the thiol in MeOH. After the addition of the catalyst, the reaction mixture became turbid and the product precipitated out after completion of the reaction and this served as visual means of monitoring the reaction. The recovered catalyst was reactivated on heating at 80 °C under reduced pressure for 24 h and reused (see Section 4).

The rate of thia-Michael addition was influenced by the steric factor of the substituent at the β-carbon atom of the enone. In general, substrates having a β-methyl/phenyl group required longer reaction time or higher reaction temperature during the reaction with a common thiol compared to that of the reaction of analogous enone devoid of a β-methyl/phenyl group. The electronic factor associated with the thiols also contributed to the overall rate of the reaction. Comparison of the results of the reaction of thiophenol and 4-methylthiophenol with a common enone (compare entries 16 and 19, Table 2; entries 19 and 20, Table 3; entries 23 and 24, Table 3) revealed that the reaction rates were faster in case of thiophenol although 4-methylthiophenol is expected to be a better nucleophile compared to thiophenol. Thus, apart from the nucleophilicity of the sulfur atom of the thiol, the acidic property of the sulfhydryl hydrogen atom was important and thiols with better acidic character reacted at a faster rate. This is in conformity with the proposed mechanism of electrophilic activation (Scheme 1). Thus, the liberation/regeneration of the catalyst takes place more efficiently for reactions with thiols in which the sulfhydryl hydrogen atom possesses better acidic property. Therefore, in general the reaction rates are faster with aromatic thiols compared to those of aliphatic thiols. The longer time required in using 4-nitrothiophenol (compare entries 1 and 2 with entry 3 and entries 23 and 24 with entry 26, Table 3) was due to the decrease in nucleophilicity of the sulfur atom of 4-nitrothiophenol compared to that of thiophenol and 4-methylthiophenol. The longer time required for conjugate addition of *tert*-butanethiol compared to that of ethane thiol (compare entry 6 with 7, and entry 31 with 32, Table 3) was due to the steric effect.

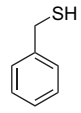
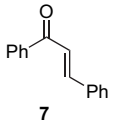
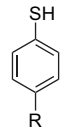
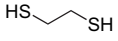
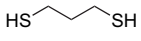
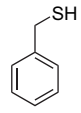
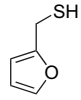
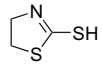
We planned to exploit the difference in the rate of reaction because of the steric and electronic factors associated with the Michael acceptors and the thiols for inter-molecular competition studies (Scheme 3). Thus, equimolar mixtures of (i) **1** and **2**, (ii) **1** and **6**, and (iii) **3** and **6** were treated with thiophenol (1.1 equiv) to demonstrate the effect of the substituent at the β-position of the enone and excellent selectivities (GCMS) of 100:0, 91:9, and 70:30, respectively, in favor of the thia-Michael addition of the substrate having

Table 3. $HClO_4$–SiO_2-catalyzed conjugate addition of α,β-unsaturated carbonyl compounds with thiols[a]

Entry	Enone	Thiol	Time (min)	Yield (%)[b,c]
	 **1**			
1		R=H	2	99
2		R=Me	2	99
3		R=NO_2	10	80
4			2	99
5			5	80
6			10	90
7			15	90
8			15	75[d]
9			20	70[d]
	 **4**			
10		R=H	2	95
11		R=Me	2	90
12			3	80
13			5	75
	 **5**			
14		R=H	2	85
15		R=Me	2	80
16			5	80
17			5	80
18			10	75
	 **6**			
19		R=H	90	85
20		R=Me	120	80

(*continued*)

Table 3. (*continued*)

Entry	Enone	Thiol	Time (min)	Yield (%)[b,c]
21			120	80
	 **7**			
22		R=H	30	60[e]
23		R=H	15	80[f]
24		R=Me	20	80[f]
25		R=NO_2	60	75[e]
26		R=NO_2	120	60[f]
27			45	85[d,f]
28			60	90[d,f]
29			60	80[f]
30			60	80[f]
31			60	79[f]
32			120	70[f,g]
33			90	78[f,h,i]

[a] The α,β-unsaturated ketone (2.5 mmol) was treated with the thiol (1.1 equiv) in the presence of $HClO_4$–SiO_2 (1 mol %) at rt (~25–30 °C) under neat conditions (except for entries 23, 24, and 26–33) at rt (except for entries 8, 9, 22, and 25).

[b] Isolated yield of the corresponding conjugate addition product obtained after chromatographic purification.

[c] The products were characterized by IR, NMR, and MS.

[d] The reaction was carried out by addition of the thiol (0.5 equiv) to the magnetically stirred mixture of the enone and the catalyst at 0 °C followed by stirring at rt (~25–30 °C).

[e] The reaction was carried out at 80 °C.

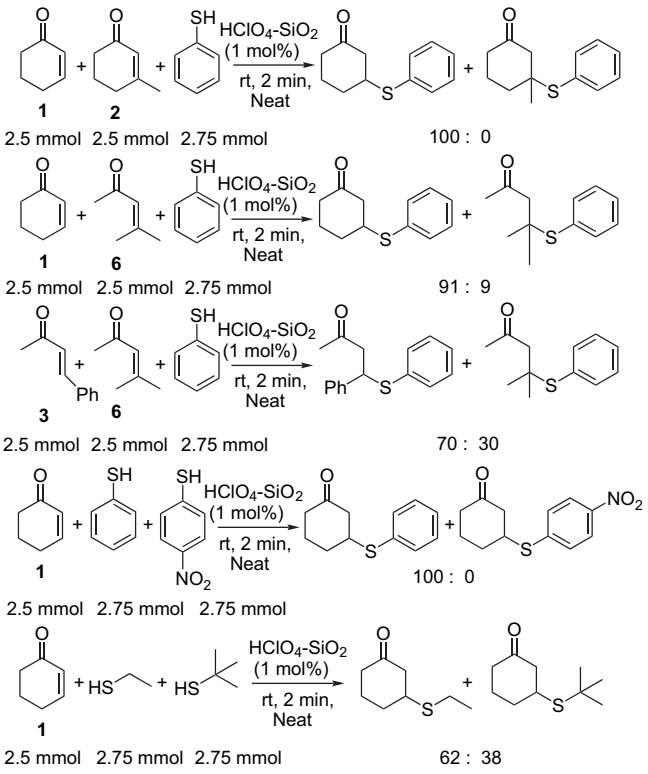
[f] The reaction was carried out in MeOH.

[g] The thia-Michael adduct was formed in 60% yield after 2 h when the reaction was carried out in MeOH at rt.

[h] The thia-Michael adduct was formed in 30% yield after 90 min when the reaction was carried out in the presence of $Cu(BF_4)_2 \cdot xH_2O$.

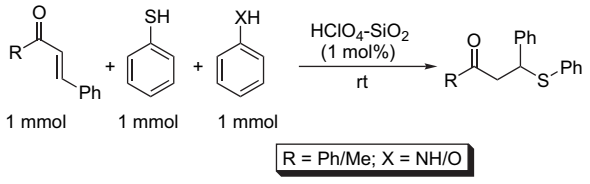
[i] No significant amount of the thia-Michael adduct was formed after 90 min when the reaction was carried out in the presence of $Zn(ClO_4)_2 \cdot 6H_2O$.

less substitution at the β-position were observed. The reaction of **1** (1 equiv) with an equimolar mixture of (i) thiophenol and 4-nitrothiophenol and (ii) ethane thiol and *tert*-butanethiol represented the selectivity of thia-Michael addition during competition between thiols of varying electronic and steric factors, respectively. Excellent selectivity (100:0) was observed in the former case. The moderate selectivity (62:38) observed during the competition of ethane thiol and *tert*-butanethiol may be due to the combined effects of the steric electronic factors. Thus, while the steric factor of *tert*-butanethiol should make its thia-Michael addition sluggish, the increased nucleophilicity due to the inductive effect of the *tert*-butyl group enhances its rate of reaction.



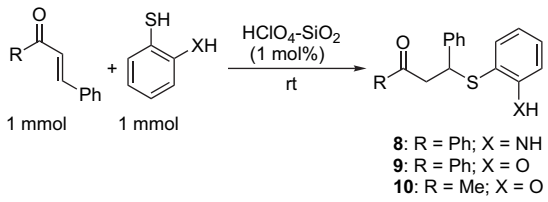
Scheme 3. Inter-molecular competition during thia-Michael addition.

We next planned to evaluate the efficiency of $HClO_4$–SiO_2 during inter- and intra-molecular competition studies of thia- versus aza- and thia- versus oxa-Michael addition reactions involving a common Michael acceptor (Schemes 4 and 5). Thus, during the inter-molecular competition reactions, the treatment of **7** separately with equimolar mixtures of (i) thiophenol and aniline, and (ii) thiophenol and phenol in MeOH at rt for 15 min afforded the thia-Michael adduct in 80 and 90% yields, respectively, as the sole product and no significant amount of the aza-Michael adduct was formed (TLC comparison with authentic sample). Exclusive formation of the thia-Michael adduct (90% yield) was observed when **3** was treated separately with equimolar mixtures of (i) thiophenol and aniline, and (ii) thiophenol and phenol at rt under solvent-free conditions for 5 min (Scheme 4).



Scheme 4. Inter-molecular competition of thia- versus aza- and thia- versus oxa-Michael addition reactions.

The excellent chemoselectivity observed during the inter-molecular competitive studies encouraged us to evaluate the chemoselective thia-Michael addition reaction during intra-molecular competition between a thiol and an amine moiety and between a thiol and a phenol moiety. Thus, when **7** was separately treated with equimolar amounts of 2-aminothiophenol and 2-hydroxythiophenol, the corresponding thia-Michael adducts **8**[7n] and **9** were formed exclusively in 85 and 81% yields after 15 and 30 min, respectively, at rt in MeOH (Scheme 5). The reaction of **3** with an equimolar amount of 2-hydroxythiophenol afforded the corresponding thia-Michael adduct **10** as the sole product in 80% yield after 10 min at rt under solvent-free conditions (Scheme 5).

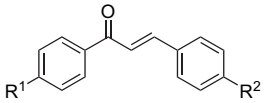
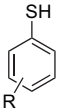


Scheme 5. Intra-molecular competition of thia- versus aza- and thia- versus oxa-Michael addition reactions.

To establish the generality of the chemoselective thia-Michael addition over aza-Michael addition during intra-molecular competition, various 1,3-diaryl propenones (**11**) were treated with 2-aminothiophenol and 4-aminothiophenol (Table 4). In each case, exclusive chemoselectivity for thia-Michael adduct formation was observed and the corresponding β-sulfidocarbonyl derivatives were formed in excellent yields.

The excellent yields of the thia-Michael adducts obtained during the reaction of 1,3-diaryl propenones (**11**) with 2-aminothiophenol encouraged us to explore the feasibility of this catalyst system for the development of a one-pot synthesis of 1,6-diaryl-1,5-benzothiazepines as the intermediately formed thia-Michael adducts are expected to undergo imine formation following a cyclodehydration process (Scheme 6). The 1,5-benzothiazepine moiety is a privileged class pharmacophore as compounds bearing this structural unit possess a broad spectrum of biological activities[21] and has stimulated interest to develop new methodologies for synthesis of 1,5-benzothiazepines. The common strategy for the construction of the 1,5-benzothiazepine moiety is

Table 4. $HClO_4$–SiO_2-catalyzed chemoselective conjugate addition of 1,3-diaryl propenones with aminothiols[a]

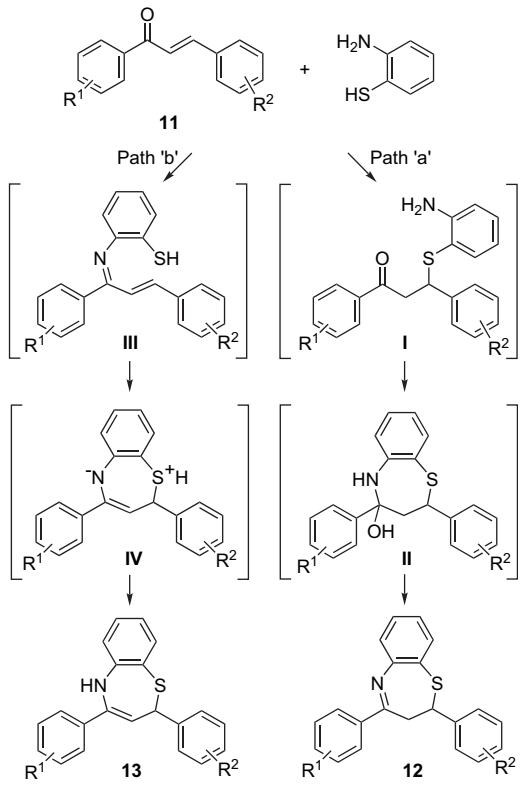
Entry	1,3-Diaryl propenones	Aminothiols	Time (min)	Yield (%)[b,c]
	 **11**			
1	R^1=R^2=H	R=2-NH_2	15	85
2	R^1=H; R^2=Cl	R=2-NH_2	20	82
3	R^1=Cl; R^2=H	R=2-NH_2	15	85
4	R^1=H; R^2=NO_2	R=2-NH_2	15	92
5	R^1=H; R^2=OMe	R=2-NH_2	25	91
6	R^1=OMe; R^2=H	R=2-NH_2	20	90
7	R^1=R^2=H	R=4-NH_2	45	85
8	R^1=H; R^2=NO_2	R=4-NH_2	25	90
9	R^1=Cl; R^2=H	R=4-NH_2	30	88
10	R^1=H; R^2=OMe	R=4-NH_2	50	85
11	R^1=OMe; R^2=H	R=4-NH_2	45	86

[a] The 1,3-diaryl propenone (1 mmol) was treated with the aminothiophenol (1 mmol) in the presence of $HClO_4$–SiO_2 (1 mol %) in methanol (1 mL) at rt (~25–30 °C).

[b] Isolated yield of the corresponding thia-Michael adduct obtained after chromatographic purification.

[c] The products were characterized by IR, NMR, and MS.

the reaction of 1,3-diaryl-2-propenones with 2-aminothiophenols.[22] The reported methodologies involve the use of inorganic supports (2 g/mmol) under heating at 80 °C for 3 h,[23] HOAc (3 mL/mmol) in DMF under microwave irradiation,[24] HOAc or TFA (1 mL/mmol) in EtOH or PhMe under reflux for 3–6 h,[25] HOAc in DMF or EtOH at 60 °C for 5 h followed by rt for overnight,[26] EtOH saturated with HCl under reflux for 3 h,[27] piperidine (1 mL/mmol) in toluene under reflux for 8 h or pyridine (15 mL/mmol) under reflux for 3 h.[28] The disadvantages such as the use of high boiling solvent (e.g., DMF) that is difficult to recover, excess amounts of acid or base, need to use special apparatus, use of corrosive (e.g., HCl gas, and TFA) and hazardous reagents (e.g., pyridine), long reaction time, etc. necessitate to develop a more effective synthetic procedure.

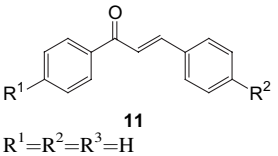


Scheme 6. Synthesis of benzothiazepines.

The construction of the 1,5-benzothiazepine moiety from **11** and 2-aminothiophenol may involve two pathways: (i) conjugate addition of the sulfhydryl group of 2-aminothiophenol to the α,β-unsaturated carbonyl group of **11** leading to the intermediate formation of the thia-Michael adduct **I**, which on subsequent intra-molecular nucleophilic attack by the NH_2 group on the carbonyl carbon followed by dehydration forms the 2,3-dihydro-1,5-benzothiazepine **12** (Path a)[29] and (ii) condensation of the amino group of 2-aminothiophenol with the carbonyl group of **11** leading to the intermediate formation of the aza-diene **II**, which on subsequent intra-molecular conjugate addition by the sulfhydryl group forms the isomeric 2,5-dihydro-1,5-benzothiazepine **13** (Path b)[24] (Scheme 6). Thus, the use of an effective electrophilic activation agent should make synthesis of benzothiazepines feasible under milder conditions and in shorter times, as it would accelerate both the thia-Michael addition and the imine formation steps. In this regard, a catalyst derived from a strong protic acid should be an ideal and more effective contender.

Our initial attempt to carry out the cyclodehydration of 1,3-diphenyl-1-(2-aminophenylsulfide)-2-propanone, obtained by the reaction of 1,3-diphenyl-2-propenone and 2-aminothiophenol catalyzed by $HClO_4$–SiO_2, by heating under reflux in MeOH without any catalytic assistance did not produce any significant amount of the corresponding 1,5-benzothiazepine derivative. We were delighted to observe that the 2,3-dihydro-1,5-benzothiazepine was formed in 90% yield when 1,3-diphenyl-1-(2-aminophenylsulfide)-2-propanone was heated under reflux for 40 min in MeOH in the presence of $HClO_4$–SiO_2 (1 mol %). We next planned for a one-pot synthesis of 2,3-dihydro-1,5-benzothiazepines from 1,3-diaryl propenones by reaction with 2-aminothiophenol catalyzed by $HClO_4$–SiO_2 and the desired products were formed in 80–90% yields by heating under reflux for 45–90 min in MeOH (Table 5).

Table 5. One-pot synthesis of 2,3-dihydro-1,5-benzothiazepines (**12**) by $HClO_4$–SiO_2-catalyzed tandem thia-Michael addition–cyclodehydration reaction of 1,3-diaryl-2-propenones with 2-aminothiophenol[a]

Entry	1,3-Diphenylpropenone	Time (min)	Yield (%)[b,c]
	 **11**		
1	R^1=R^2=R^3=H	90	88
2	R^1=H; R^2=Cl	60	80
3	R^1=Cl; R^2=H	45	85
4	R^1=H; R^2=NO_2	45	90
5	R^1=H; R^2=OMe	60	80
6	R^1=OMe; R^2=H	45	85

[a] The reaction of 1,3-diaryl propenone (1 mmol), and 2-aminothiophenol (1 mmol) was carried out in the presence of $HClO_4$–SiO_2 (1 mol %) in methanol (1 mL) under reflux.
[b] Isolated yield of the corresponding 2,3-dihydro-1,5-benzothiazepine (**12**) obtained after chromatographic purification.
[c] The products were characterized by IR, NMR, and MS.

3. Conclusion

In conclusion, we have described herein the scope and limitations of $HClO_4$–SiO_2 as a new and highly efficient catalyst for chemoselective carbon–sulfur bond formation by conjugate addition of thiols to α,β-unsaturated ketones. The advantages include, (i) the use of a cheap, easy to handle, and reusable catalyst, (ii) rt and non-anhydrous reaction conditions, (iii) non-aqueous work-up and ease of product isolation by filtration, (iv) short reaction times, (vi) high yields, (v) excellent chemoselectivity during inter- and intra-molecular competitions, and (vi) applicability for an easy synthesis of 2,3-dihydro-1,5-benzothiazepines.

4. Experimental

4.1. General

The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX 300 (300 MHz) spectrometer in $CDCl_3$ using

TMS as an internal standard. The IR spectra were recorded on a Nicolet Impact 400 spectrometer as KBr pellets for solid and neat for liquid samples. Mass spectra were recorded on QCP 5000 (Shimadzu) GCMS. The reactions were monitored by TLC (Merck). Evaporation of solvents was performed under reduced pressure using a Büchi rotary evaporator. Thiophenol, 4-methylthiophenol, 4-nitrothiophenol, α-toluenethiol, 2-furylmethanethiol, ethane thiol, *tert*-butanethiol, 1,2-ethanedithiol, 1,3-propanedithiol, 2-mercaptothiazole, 2-aminothiophenol, 4-aminothiophenol, 2-hydroxythiophenol, 2-cyclohexen-1-one, 3-methyl-2-cyclohexen-1-one, 2-cyclopenten-1-one, 3-buten-2-one, 4-methyl-3-penten-2-one, 4-phenyl-3-buten-2-one, $Cu(BF_4)_2 \cdot xH_2O$, and $Zn(ClO_4)_2 \cdot 6H_2O$ were purchased from Aldrich, India. Silica gel (230–400 mesh) and aqueous (48%) perchloric acid were procured from Spectrochem and Loba Chemie, India, respectively. Aniline, phenol, other reagents, and solvents were from SD Fine Chemicals, India. 1,3-Diphenyl-2-propenone,[30] 1-phenyl-3-(4-chlorophenyl)-2-propenone,[30] 1-(4-chlorophenyl)-3-phenyl-2-propenone,[30] 1-phenyl-3-(4-nitro-phenyl)-2-propenone,[30] 1-phenyl-3-(4-methoxyphenyl)-2-propenone,[30] and 1-(4-methoxyphenyl)-3-phenyl-2-propenone[30] were prepared following reported procedure.

4.1.1. Preparation of perchloric acid adsorbed on silica gel ($HClO_4$–SiO_2). The preparation of $HClO_4$–SiO_2 was carried out following the reported procedure.[8g,17] To the suspension of silica gel (23.75 g, 230–400 mesh) in Et_2O (50 mL), $HClO_4$ (1.25 g, 12.5 mmol, 1.78 mL of a 70% aqueous solution of $HClO_4$) was added and the mixture was stirred magnetically for 30 min at rt. The Et_2O was removed under reduced pressure (rotary evaporator) and the residue heated at 100 °C for 72 h under vacuum to afford $HClO_4$–SiO_2 (0.5 mmol g^{-1}) as a free flowing powder.

4.1.2. Representative experimental procedure for conjugate addition of thiol to α,β-unsaturated ketone. 3-Phenylthiocyclohexanone (entry 1, Table 1). To a magnetically stirred mixture of 2-cyclohexen-1-one (**1**) (0.24 g, 2.5 mmol) and thiophenol (0.30 g, 2.75 mmol, 1.1 equiv) was added $HClO_4$–SiO_2 (0.05 g, 0.025 mmol, 1 mol %) and the reaction mixture was stirred at rt (~25–30 °C) till completion of the reaction (2 min: TLC and IR). The reaction mixture was diluted with Et_2O (2 mL), filtered through a plug of cotton (to separate the catalyst), and the cotton plug was washed with Et_2O (2×1 mL). The combined ethereal filtrates were concentrated, adsorbed on silica gel, charged on a column of silica gel (60–120 mesh, 5 g), and eluted with hexane (to eliminate any disulfide formed) followed by 1:10 EtOAc–hexane to afford 3-phenylthiocyclohexanone (0.51 g, 99%, entry 1, Table 1) as colorless oil, identical (IR, ^1H and ^{13}C NMR, and MS) with an authentic sample.[15a] In a large-scale batch, **1** (0.96 g, 10 mmol) was treated with thiophenol (1.1 g, 11 mmol, 1.1 equiv) in the presence of $HClO_4$–SiO_2 (0.2 g, 0.1 mmol, 1 mol %) to afford 3-phenylthiocyclohexanone (2.03 g, 99%) after work-up and purification. The cotton plug retaining the recovered catalyst was put on a rb flask (25 mL) and dried in a rotary evaporator when the catalyst separated out from the cotton (0.16 g, 80%). The catalyst was activated on heating under reduced pressure (10 mmHg) at 80 °C for 24 h. The repetition of the reaction of **1** (0.24 g, 2.5 mmol) with thiophenol (0.30 g, 2.75 mmol, 1.1 equiv) in the presence of the recovered $HClO_4$–SiO_2 (0.05 g, 0.025 mmol, 1 mol %) afforded 3-phenylthiocyclohexanone (0.47 g, 93%) after work-up and purification.

4.1.3. 1,3-Diphenyl-3-thiophenyl-propanone (entry 23, Table 3). To a magnetically stirred mixture of 1,3-diphenylpropenone (**7**) (0.21 g, 1 mmol) and thiophenol (0.12 g, 1.1 mmol, 1.1 equiv) in MeOH (2 mL) was added $HClO_4$–SiO_2 (0.02 g, 0.01 mmol, 1 mol %) and the reaction mixture was stirred at rt (~25–30 °C) till completion of the reaction (15 min: TLC, IR) when the thia-Michael adduct precipitated out. The reaction mixture was diluted with EtOAc to dissolve the product (10 mL), filtered through a plug of cotton (to separate the catalyst), and the cotton plug was washed with EtOAc (2×1 mL). The combined filtrates were concentrated, and the solid residue recrystallized (EtOH) to afford 1,3-diphenyl-3-thiophenyl-propanone (0.26 g, 80%) as white solid identical (mp, IR, ^1H and ^{13}C NMR, and MS) with an authentic sample.[15a]

4.1.4. Representative experimental procedure for intermolecular competition reaction (Scheme 3). To a magnetically stirred mixture of 2-cyclohexen-1-one (**1**) (0.24 g, 2.5 mmol), 3-methyl-2-cyclohexen-1-one (0.27 g, 2.5 mmol) (**2**), and thiophenol (0.30 g, 2.75 mmol, 1.1 equiv) was added $HClO_4$–SiO_2 (0.05 g, 0.025 mmol, 1 mol %) and the reaction mixture was stirred at rt (~25–30 °C) for 2 min. The reaction mixture was diluted with Et_2O (2 mL), filtered through a plug of cotton (to separate the catalyst), and the cotton plug was washed with Et_2O (2×1 mL). The combined ethereal filtrates were concentrated and the isolated reaction mixture, without further purification, was subjected to GCMS column to afford 100% selectivity in favor of the formation of 3-phenylthiocyclohexanone.

4.1.5. Representative experimental procedure for intermolecular competition of thia- versus aza-Michael addition reactions (Scheme 4). To a magnetically stirred mixture of 1,3-diphenylpropenone (**7**) (0.21 g, 1 mmol), aniline (0.093 g, 1 mmol) and thiophenol (0.11 g, 1 mmol) in MeOH (2 mL) was added $HClO_4$–SiO_2 (0.02 g, 0.01 mmol, 1 mol %) at rt (~25–30 °C) for 15 min. After 15 min the reaction mixture was diluted with EtOAc (10 mL), filtered through a plug of cotton (to separate the catalyst), and the cotton plug was washed with EtOAc (2×1 mL). The combined filtrates were concentrated, and the solid residue recrystallized (EtOH) to afford 1,3-diphenyl-3-thiophenyl-propanone (0.26 g, 80%) as the sole product indicating exclusive selectivity for thia-Michael addition over aza-Michael addition.

4.1.6. Representative experimental procedure for intramolecular competition of thia- versus aza-Michael addition reactions (Scheme 5). To a magnetically stirred mixture of 1,3-diphenylpropenone (**7**) (0.21 g, 1 mmol) and 2-aminothiophenol (0.13 g, 1 mmol, 1 equiv) in MeOH (2 mL) was added $HClO_4$–SiO_2 (0.02 g, 0.01 mmol, 1 mol %) at rt (~25–30 °C). After 15 min, the reaction mixture was diluted with EtOAc (10 mL), filtered through a plug of cotton (to separate the catalyst), and the cotton plug was washed with EtOAc (2×1 mL). The combined filtrates were concentrated, and the solid residue recrystallized (EtOH)

to afford 0.28 g (85%) of 3-(2-amino-phenylsulfanyl)-1,3-diphenyl-propan-1-one as the sole product indicating exclusive selectivity for thia-Michael addition over oxa-Michael addition.

4.1.7. One-pot synthesis of 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepine (entry 1, Table 5). To a magnetically stirred mixture of 1,3-diphenylpropenone (**7**) (0.21 g, 1 mmol) and 2-aminothiophenol (0.12 g, 1 mmol, 1 equiv) in MeOH (2 mL) was added $HClO_4$–SiO_2 (0.02 g, 0.01 mmol, 1 mol %) and the reaction mixture was stirred under reflux conditions till completion of the reaction (90 min: TLC and IR). The reaction mixture was diluted with EtOAc to dissolve the product (10 mL), filtered through a plug of cotton (to separate the catalyst), and the cotton plug was washed with EtOAc (2×1 mL). The combined filtrates were concentrated and purification was done using column chromatography to afford 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepine (0.27 g, 88%) as yellow solid identical (mp, IR, ^1H & ^{13}C NMR, and MS) with an authentic sample.[23]

4.1.8. Synthesis of 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepine from 1,3-diphenyl-1-(2-aminophenylsulfide)-2-propanone. To a magnetically stirred mixture of 1,3-diphenyl-1-(2-aminophenylsulfide)-2-propanone (0.33 g, 1 mmol) in MeOH (2 mL) was added $HClO_4$–SiO_2 (0.02 g, 0.01 mmol, 1 mol %) and the reaction mixture was stirred under reflux conditions till completion of the reaction (40 min: TLC and IR). The reaction mixture was diluted with EtOAc to dissolve the product (10 mL), filtered through a plug of cotton (to separate the catalyst), and the cotton plug was washed with EtOAc (2×1 mL). The combined filtrates were concentrated and purification was done using column chromatography to afford 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepine (0.28 g, 90%) as yellow solid identical (mp, IR, ^1H & ^{13}C NMR, and MS) with an authentic sample.[23]

The remaining reactions were carried out following these general procedures. In each occasion, the spectral data (IR, NMR and MS) of known compounds such as 3-phenylthio-3-methylcyclohexan-1-one[15a] (entry 1, Table 2), 3-(4-methylphenylthio)-3-methylcyclohexan-1-one[15a] (entry 4, Table 2), 3-benzylthio-3-methylcyclohexan-1-one[15a] (entry 7, Table 2), 3-(2-furfurylthio)-3-methylcyclohexan-1-one[15a] (entry 10, Table 2), 3-ethylthio-3-methylcyclohexan-1-one[15a] (entry 13, Table 2), 4-phenylthio-4-phenylbutan-2-one[15b] (entry 16, Table 2), 4-(4-methylphenylthio)-4-phenylbutan-2-one[15b] (entry 19, Table 2), 4-benzylthio-4-phenylbutan-2-one[15b] (entry 25, Table 2), 4-(2-furfurylthio)-4-phenylbutan-2-one[15b] (entry 28, Table 2), 4-ethylthio-4-phenylbutan-2-one[15b] (entry 31, Table 2), 3-(4-methylphenylthio)-cyclohexan-1-one[16] (entry 2, Table 3), 3-(4-nitro-phenylsulfanyl)-cyclohexanone[16] (entry 3, Table 3), 3-benzylthio-cyclohexan-1-one[16] (entry 4, Table 3), 3-(furan-2-ylmethylsulfanyl)-cyclohexanone[15b] (entry 5, Table 3), 3-ethylthio-cyclohexan-1-one[15b] (entry 6, Table 3), 3,3′-[1,2-dithioethyl]biscyclohexane-1-one[7q] (entry 8, Table 3), 3,3′-[1,3-dithiopropyl]biscyclohexane-1-one[7q] (entry 9, Table 3), 3-phenylsulfanyl-cyclopentanone[7q] (entry 10, Table 3), 3-*p*-tolylsulfanyl-cyclopentanone[7q] (entry 11, Table 3), 3-benzylsulfanyl-cyclopentanone[7b,c] (entry 12, Table 3), 3-ethylsulfanyl-cyclopentanone[16] (entry 13, Table 2), 4-phenylthio-butan-2-one[15a] (entry 14, Table 3), 4-(4-methylphenylthio)-butan-2-one[15a] (entry 15, Table 3), 4-benzylthio-butan-2-one[7h] (entry 16, Table 3), 1-(furan-2-ylmethylsulfanyl)-propan-2-one[15a] (entry 17, Table 3), 4-ethylthio-butan-2-one[7h] (entry 18, Table 3), 4-methyl-4-phenylsulfanyl-pentan-2-one[7l] (entry 19, Table 3), 1,3-diphenyl-3-*p*-tolylsulfanyl-propan-1-one[15a] (entry 24, Table 3), 3-benzylsulfanyl-1,3-diphenyl-propan-1-one[15b] (entry 29, Table 3), 3-(furan-2-ylmethylsulfanyl)-1,3-diphenyl-propan-1-one[15b] (entry 30, Table 3), 3-ethylsulfanyl-1,3-diphenyl-propan-1-one[15b] (entry 31, Table 3), 2,3-dihydro-2-(4-chlorophenyl)-4-phenyl-1,5-benzothiazepine[21] (entry 2, Table 5), 2,3-dihydro-2-phenyl-4-(4-chlorophenyl)-1,5-benzothiazepine[23] (entry 3, Table 5), 2,3-dihydro-2-phenyl-4-(4-nitro-phenyl)-1,5-benzothiazepine[23] (entry 4, Table 5), 2,3-dihydro-2-(4-methoxyphenyl)-4-phenyl-1,5-benzothiazepine[23] (entry 5, Table 5), 2,3-dihydro-2-phenyl-4-(4-methoxyphenyl)-1,5-benzothiazepine[23] (entry 6, Table 5), and 3-(2-amino-phenylsulfanyl)-1,3-diphenyl-propan-1-one (**8**)[7n] were found to be identical with those reported in the literature. The following compounds were unknown.

4.1.8.1. 4-(4-Nitro-phenylsulfanyl)-4-phenylbutan-2-one (entry 22, Table 2). Yellow solid, mp 68–70 °C; [Found: C, 63.80; H, 5.06; S, 10.65. $C_{16}H_{15}NO_3S$ requires C, 63.77; H, 5.02; S, 10.64%]; ν_{max} (KBr) 2925, 1712 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.11 (s, 3H), 3.08–3.11 (m, 2H), 4.95 (t, *J*=6.9 Hz, 1H), 7.20–7.39 (m, 5H), 7.61 (d, *J*=8.9 Hz, 1H), 8.02 (d, *J*=8.6 Hz, 2H), 8.17 (d, *J*=8.5 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 31.3, 46.8, 50.3, 124.4, 125.0, 126.9, 128.2, 128.5, 129.4, 140.7, 145.7, 205.2.

4.1.8.2. 4-*tert*-Butylsulfanyl-4-phenylbutan-2-one (entry 34, Table 2). Colorless oil; [Found: C, 71.16; H, 8.54; S, 13.59. $C_{14}H_{20}OS$ requires C, 71.14; H, 8.53; S, 13.57%]; ν_{max} (Neat) 1717 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.18 (s, 9H), 2.01 (s, 3H), 2.85–2.90 (m, 2H), 4.41 (t, *J*=7.3 Hz, 1H), 7.13–7.18 (m, 1H), 7.22–7.31 (m, 2H), 7.38 (d, *J*=7.3 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 30.8, 31.2, 42.5, 52.0, 44.1, 126.8, 127.6, 128.4, 144.5, 205.1.

4.1.8.3. 3-*tert*-Butylsulfanyl-cyclohexanone (entry 7, Table 3). Colorless oil; [Found: C, 64.47; H, 9.76; S, 17.23. $C_{10}H_{18}OS$ requires C, 64.46; H, 9.74; S, 17.21%]; ν_{max} (Neat) 1712 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.25 (s, 9H), 1.65 (t, *J*=8.2 Hz, 2H), 1.95–2.14 (m, 2H), 2.21–2.35 (m, 3H), 2.61–2.65 (m, 1H), 2.93 (d, *J*=3.6 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 23.6, 26.4, 30.5, 33.3, 39.7, 42.6, 49.8, 207.9.

4.1.8.4. 4-Methyl-4-*p*-tolylsulfanyl-pentan-2-one (entry 20, Table 3). Colorless oil; [Found: C, 70.24; H, 8.20; S, 14.40. $C_{13}H_{18}OS$ requires C, 70.22; H, 8.16; S, 14.42%]; ν_{max} (Neat) 1710 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.37 (s, 6H), 2.13 (s, 3H), 2.35 (s, 3H), 2.65 (s, 2H), 7.14 (d, *J*=7.6 Hz, 2H), 7.4 (d, *J*=7.6 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 21.7, 28.6, 32.7, 47.4, 54.9, 128.5, 130.0, 138.1, 139.7, 207.2.

4.1.8.5. 4-Benzylsulfanyl-4-methyl-pentan-2-one (entry 21, Table 3). Colorless oil; [Found: C, 70.20; H, 8.17; S, 14.43. $C_{13}H_{18}OS$ requires C, 70.22; H, 8.16; S, 14.42%];

ν_{max} (Neat) 1709 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.44 (s, 6H), 2.10 (s, 3H), 2.66 (s, 2H), 3.76 (s, 2H), 7.17–7.34 (m, 5H); δ_C (75 MHz, $CDCl_3$) 29.0, 32.7, 33.8, 44.8, 55.1, 127.5, 129.1, 129.5, 138.5, 207.2.

4.1.8.6. 3-(4-Nitro-phenylsulfanyl)-1,3-diphenyl-propan-1-one (entry 25, Table 3). White solid, mp 87–89 °C; [Found: C, 69.60; H, 4.76; S, 8.79. $C_{21}H_{17}NO_3S$ requires C, 69.40; H, 4.71; S, 8.82%]; ν_{max} (KBr) 1679 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.61–3.66 (m, 2H), 5.20 (t, *J*=6.8 Hz, 1H), 7.34–7.37 (m, 4H), 7.42–7.47 (m, 4H), 7.49–7.63 (m, 1H), 7.89–7.91 (m, 2H), 8.03–8.06 (m, 2H), 8.17–8.20 (m, 1H); δ_C (75 MHz, $CDCl_3$) 45.6, 47.1, 124.4, 124.9, 126.9, 128.2, 128.4, 128.6, 129.2, 129.4, 129.5, 134.1, 140.8, 145.8, 196.7.

4.1.8.7. 3-[2-(3-Oxo-1,3-diphenyl-propylsulfanyl)-ethylsulfanyl]-1,3-diphenyl-propan-1-one (entry 27, Table 3). White solid, mp 158–160 °C; [Found: C, 75.24; H, 5.90; S, 12.59. $C_{32}H_{30}O_2S_2$ requires C, 75.26; H, 5.92; S, 12.56%]; ν_{max} (KBr) 1675 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.43 (d, *J*=3.1 Hz, 4H), 3.46–3.49 (m, 4H), 4.48 (s, 2H), 7.21–7.33 (m, 10H), 7.44 (d, *J*=7.6 Hz, 4H), 7.53 (d, *J*=7.4 Hz, 2H), 7.88 (d, *J*=7.1 Hz, 4H); δ_C (75 MHz, $CDCl_3$) 31.2, 44.4, 45.3, 127.3, 127.8, 128.0, 128.6, 133.2, 136.7, 141.8, 196.6; *m/z* (MALDI TOF/TOF) 533.69 ($M+Na^+$), 549.688 ($M+K^+$).

4.1.8.8. 3-[3-(3-Oxo-1,3-diphenyl-propylsulfanyl)-propylsulfanyl]-1,3-diphenyl-propan-1-one (entry 28, Table 3). White solid, mp 88–90 °C; [Found: C, 75.51; H, 6.16; S, 12.24. $C_{33}H_{32}O_2S_2$ requires C, 75.53; H, 6.15; S, 12.22%]; ν_{max} (KBr) 1682 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.64–1.71 (m, 2H), 2.17–2.45 (m, 4H), 3.49–3.57 (m, 4H), 4.47–4.54 (m, 2H), 7.16–7.88 (m, 16H), 7.89 (d, *J*=7.3 Hz, 4H); δ_C (75 MHz, $CDCl_3$) 29.0, 29.1, 30.7, 127.8, 128.4, 128.6, 129.0, 129.1, 133.7, 137.3, 142.6, 197.3; *m/z* (MALDI TOF/TOF) 547 ($M+Na^+$), 563.698 ($M+K^+$).

4.1.8.9. 3-*tert*-Butylsulfanyl-1,3-diphenyl-propan-1-one (entry 32, Table 3). White solid, mp 73–75 °C; [Found: C, 76.44; H, 7.45; S, 10.72. $C_{19}H_{22}OS$ requires C, 76.46; H, 7.43; S, 10.74%]; ν_{max} (KBr) 1682 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.22 (s, 9H), 3.46–3.50 (m, 2H), 4.65 (t, *J*=7.0 Hz, 1H), 7.15–7.20 (m, 2H), 7.40–7.53 (m, 6H), 7.89 (d, *J*=7.9 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 31.6, 42.6, 44.4, 47.6, 126.8, 127.8, 128.1, 128.4, 128.5, 133.1, 136.9, 144.8, 197.0.

4.1.8.10. 3-(4,5-Dihydro-thiazol-2-ylsulfanyl)-1,3-diphenyl-propan-1-one (entry 33, Table 3). White solid, mp 130–132 °C; [Found: C, 66.04; H, 5.26; N, 4.25; S, 19.53. $C_{18}H_{17}NOS_2$ requires C, 66.02; H, 5.23; N, 4.28; S, 19.58%]; ν_{max} (KBr) 1678 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.04–3.22 (m, 2H), 3.52–3.67 (m, 2H), 3.84–3.92 (m, 1H), 3.98–4.07 (m, 1H), 6.81 (t, *J*=7.5 Hz, 1H), 7.31–7.35 (m, 5H), 7.43–7.48 (m, 2H), 7.54–7.59 (m, 1H), 7.98 (d, *J*=7.2 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 27.5, 38.7, 52.4, 56.6, 127.3, 128.2, 128.4, 128.7, 128.9, 133.5, 136.1, 136.7, 196.3, 196.6; *m/z* (EI): 327 (M^+).

4.1.8.11. 3-(2-Amino-phenylsulfanyl)-3-(4-chloro-phenyl)-1-phenyl-propan-1-one (entry 2, Table 4). White crystalline solid, mp 128–129 °C; [Found: C, 68.57; H, 4.94; N, 3.83; S, 8.75. $C_{21}H_{18}ClNOS$ requires C, 68.56; H, 4.93; N, 3.81; S, 8.72%]; ν_{max} (KBr) 1676, 3364 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.48–3.69 (m, 2H), 4.47 (s, 2H), 4.72 (t, *J*=7.1 Hz, 1H), 6.53 (t, *J*=7.2 Hz, 1H), 6.68 (d, *J*=7.7 Hz, 1H), 7.02–7.21 (m, 6H), 7.41–7.57 (m, 3H), 7.89 (d, *J*=7.3 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 44.4, 46.7, 115.4, 115.7, 118.6, 128.6, 129.0, 129.2, 129.5, 131.4, 133.9, 137.1, 138.2, 140.8, 149.9, 197.4; *m/z* (APCI) 368 (MH^+).

4.1.8.12. 3-(2-Amino-phenylsulfanyl)-1-(4-chloro-phenyl)-3-phenyl-propan-1-one (entry 3, Table 4). White crystalline solid, mp 100–102 °C; [Found: C, 68.58; H, 4.93; N, 3.85; S, 8.74. $C_{21}H_{18}ClNOS$ requires C, 68.56; H, 4.93; N, 3.81; S, 8.72%]; ν_{max} (KBr) 1685, 3364 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.46–3.65 (m, 2H), 4.44 (s, 2H), 4.72 (t, *J*=7.1 Hz, 1H), 6.52 (t, *J*=7.2 Hz, 1H), 6.65 (d, *J*=8.1 Hz, 1H), 7.05–7.37 (m, 9H), 7.78 (d, *J*=8.4 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 44.6, 47.6, 115.5, 116.2, 118.6, 127.9, 128.2, 129.0, 129.5, 130.0, 131.3, 135.6, 138.3, 140.2, 141.9, 150.1, 196.5; *m/z* (APCI) 368 (MH^+).

4.1.8.13. 3-(2-Amino-phenylsulfanyl)-3-(4-nitro-phenyl)-1-phenyl-propan-1-one (entry 4, Table 4). White crystalline solid, mp 127–129 °C; [Found: C, 66.67; H, 4.83; N, 7.45; S, 8.50. $C_{21}H_{18}N_2O_3S$ requires C, 66.65; H, 4.79; N, 7.40; S, 8.47%]; ν_{max} (KBr) 1675, 3467 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.56–3.77 (m, 2H), 4.50 (s, 2H), 4.82 (t, *J*=8.0 Hz, 1H), 6.50 (t, *J*=7.1 Hz, 1H), 6.69 (d, *J*=7.7 Hz, 1H), 6.94–7.19 (m, 2H), 7.32–7.57 (m, 5H), 7.91 (d, *J*=7.1 Hz, 2H), 8.05 (d, *J*=8.0 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 43.8, 46.4, 114.82, 115.5, 118.7, 124.1, 128.6, 129.0, 129.3, 131.7, 134.2, 136.8, 138.0, 147.4, 149.9, 196.9.

4.1.8.14. 3-(2-Amino-phenylsulfanyl)-3-(4-methoxyphenyl)-1-phenyl-propan-1-one (entry 5, Table 4). White crystalline solid, mp 106–109 °C; [Found: C, 72.72; H, 5.84; N, 3.87; S, 8.85. $C_{22}H_{21}NO_2S$ requires C, 72.70; H, 5.82; N, 3.85; S, 8.82%]; ν_{max} (KBr) 1679, 3362 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.49–3.75 (m, 2H), 3.76 (s, 3H), 4.45 (s, 2H), 4.72 (t, *J*=7.1 Hz, 1H), 6.54 (t, *J*=7.2 Hz, 1H), 6.68–6.79 (m, 3H), 7.08–7.25 (m, 4H), 7.41–7.57 (m, 3H), 7.88 (d, *J*=7.7 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 44.8, 47.7, 114.3, 115.4, 116.5, 118.6, 128.6, 129.1, 129.2, 131.1, 133.8, 138.2, 149.9, 159.2, 197.8; *m/z* (APCI) 364 (MH^+).

4.1.8.15. 3-(2-Amino-phenylsulfanyl)-1-(4-methoxyphenyl)-3-phenyl-propan-1-one (entry 6, Table 4). White crystalline solid, mp 104–105 °C; [Found: C, 72.71; H, 5.83; N, 3.86; S, 8.84. $C_{22}H_{21}NO_2S$ requires C, 72.70; H, 5.82; N, 3.85; S, 8.82%]; ν_{max} (KBr) 1666, 3462 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.45–3.65 (m, 2H), 3.83 (s, 3H), 4.46 (s, 2H), 4.73 (t, *J*=7.1 Hz, 1H), 6.52 (t, *J*=7.3 Hz, 1H), 6.67 (d, *J*=7.6 Hz, 1H), 6.89 (d, *J*=7.2 Hz, 2H), 7.04–7.22 (m, 7H), 7.88 (d, *J*=8.1 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 43.6, 47.2, 55.5, 113.7, 114.8, 115.7, 117.9, 127.2, 127.6, 128.3, 129.8, 130.4, 130.5, 137.6, 141.8, 149.5, 163.6, 195.6; *m/z* (APCI) 364 (MH^+).

4.1.8.16. 3-(4-Amino-phenylsulfanyl)-1,3-diphenyl-propan-1-one (entry 7, Table 4). White crystalline solid, mp 98–99 °C; [Found: C, 75.62; H, 5.70; N, 4.23; S, 9.60. $C_{21}H_{19}NOS$ requires C, 75.64; H, 5.74; N, 4.20; S,

9.62%]; ν_{max} (KBr) 1677, 3379, 3470 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.58 (br s, 2H), 3.50–3.65 (dd, *J*=6.5 Hz, 17.0 Hz, 2H), 4.70 (t, *J*=7.1 Hz, 1H), 6.53 (d, *J*=6.7 Hz, 2H), 7.10 (d, *J*=6.8 Hz, 2H), 7.23–7.26 (m, 5H), 7.40–7.45 (m, 2H), 7.52–7.54 (m, 1H), 7.87 (d, *J*=8.5 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 44.2, 49.6, 115.3, 121.1, 127.1, 127.9, 128.1, 128.3, 128.6, 133.3, 136.6, 136.9, 141.5, 146.9, 197.3.

4.1.8.17. 3-(4-Amino-phenylsulfanyl)-3-(4-nitro-phenyl)-1-phenyl-propan-1-one (entry 8, Table 4). Yellow solid, mp 134–136 °C; [Found: C, 66.63; H, 4.75; N, 7.42; S, 8.43. $C_{21}H_{18}N_2O_3S$ requires C, 66.65; H, 4.79; N, 7.40; S, 8.47%]; ν_{max} (KBr) 1678, 3380, 3493 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.59 (br s, 2H), 3.55–3.71 (m, 2H), 4.74 (t, *J*=6.2 Hz, 1H), 6.51 (d, *J*=8.5 Hz, 2H), 7.04(d, *J*=8.5 Hz, 2H), 7.34 (d, *J*=8.7 Hz, 2H), 7.42–7.47 (m, 2H), 7.55–7.60 (m, 1H), 7.89 (d, *J*=8.7 Hz, 2H), 8.07 (d, *J*=8.7 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 44.1, 49.5, 115.9, 119.9, 124.1, 128.9, 129.3, 134.1, 134.5, 137.0, 137.4, 147.3, 148.0, 150.1, 197.0; *m/z* (EI) 378 $(M)^+$.

4.1.8.18. 3-(4-Amino-phenylsulfanyl)-1-(4-chloro-phenyl)-3-phenyl-propan-1-one (entry 9, Table 4). White solid, mp 124–126 °C; [Found: C, 68.52; H, 4.97; N, 3.80; S, 8.69. $C_{21}H_{18}ClNOS$ requires C, 68.56; H, 4.93; N, 3.81; S, 8.72%]; ν_{max} (KBr) 1671, 3326, 3416 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.56 (br s, 2H), 3.49–3.60 (m, 2H), 4.67 (t, *J*=7.2 Hz, 1H), 6.52 (d, *J*=8.5 Hz, 2H), 7.09 (d, *J*=8.5 Hz, 2H), 7.19–7.24 (m, 5H), 7.40 (d, *J*=8.6 Hz, 2H), 7.80 (d, *J*=8.6 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 44.7, 50.1, 115.8, 121.4, 127.8, 128.4, 128.9, 129.4, 130.0, 135.7, 137.2, 140.2, 142.0, 147.5, 196.7; *m/z* (EI) 367 (M^+).

4.1.8.19. 3-(4-Amino-phenylsulfanyl)-3-(4-methoxyphenyl)-1-phenyl-propan-1-one (entry 10, Table 4). White solid; [Found: C, 72.68; H, 5.84; N, 3.84; S, 8.80. $C_{22}H_{21}NO_2S$ requires C, 72.70; H, 5.82; N, 3.85; S, 8.82%]; ν_{max} (KBr) 1681, 3375 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.56 (br s, 2H), 3.49–3.60 (m, 2H), 3.76 (s, 3H), 4.68 (t, *J*=7.2 Hz, 1H), 6.53 (d, *J*=8.4 Hz, 2H), 6.76 (d, *J*=8.6 Hz, 2H), 7.10–7.17 (m, 4H), 7.39–7.44 (m, 2H), 7.47–7.53 (m, 1H), 7.85 (d, *J*=7.3 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 44.9, 50.0, 56.0, 114.2, 115.8, 128.6, 129.1, 129.4, 133.6, 134.0, 134.5, 137.1, 137.4, 147.4, 159.1, 198.0; *m/z* (EI) 363 (M^+).

4.1.8.20. 3-(4-Amino-phenylsulfanyl)-1-(4-methoxyphenyl)-3-phenyl-propan-1-one (entry 11, Table 4). White solid, mp 138–140 °C; [Found: C, 72.66; H, 5.83; N, 3.84; S, 8.81. $C_{22}H_{21}NO_2S$ requires C, 72.70; H, 5.82; N, 3.85; S, 8.82%]; ν_{max} (KBr) 1670, 3368, 3465 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.48–3.54 (m, 2H), 3.70 (br s, 2H), 3.85 (s, 3H), 4.70 (t, *J*=7.2 Hz, 1H), 6.52 (d, *J*=8.5 Hz, 2H), 6.89 (d, *J*=8.9 Hz, 2H), 7.10 (d, *J*=8.5 Hz, 2H), 7.14–7.19 (m, 1H), 7.20–7.24 (m, 4H), 7.86 (d, *J*=8.9 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 44.3, 50.3, 56.0, 114.4, 115.8, 121.6, 122.5, 128.4, 128.8, 130.9, 131.4, 137.1, 142.2, 147.5, 164.1, 196.4; *m/z* (EI) 363 (M^+).

4.1.8.21. 3-(2-Hydroxy-phenylsulfanyl)-1,3-diphenyl-propan-1-one (9) (Scheme 5). White solid, mp 103–106 °C; [Found: C, 75.44; H, 5.45; S, 9.57. $C_{21}H_{18}O_2S$ requires C, 75.42; H, 5.42; S, 9.59%]; ν_{max} (KBr) 1682, 3347 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.48–3.71 (m, 2H), 4.50–4.55 (m, 1H), 6.68 (t, *J*=7.5 Hz, 1H), 6.97 (d, *J*=7.9 Hz, 1H), 7.04 (d, *J*=7.9 Hz, 1H), 7.14–7.24 (m, 5H), 7.40–7.45 (m, 2H), 7.50–7.57 (m, 2H), 7.93 (d, *J*=7.2 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 44.1, 49.3, 115.9, 117.8, 120.8, 128.1, 128.2, 128.8, 129.2, 129.3, 132.4, 134.2, 136.9, 137.6, 141.9, 158.7, 197.8.

4.1.8.22. 4-(2-Hydroxy-phenylsulfanyl)-4-phenylbutan-2-one (10) (Scheme 5). White solid, mp 74–76 °C; [Found: C, 70.60; H, 5.96; S, 11.79. $C_{16}H_{16}O_2S$ requires C, 70.56; H, 5.92; S, 11.77%]; ν_{max} (KBr) 1706, 3307 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.14 (s, 3H), 2.97–3.16 (m, 2H), 4.31–4.36 (m, 1H), 6.71 (t, *J*=7.5 Hz, 1H), 6.95 (d, *J*=7.92 Hz, 1H), 7.03–7.09 (m, 3H), 7.17–7.26 (m, 4H); δ_C (75 MHz, $CDCl_3$) 31.0, 48.8, 48.8, 115.8, 117.5, 120.8, 127.9, 128.2, 129.1, 132.4, 137.6, 141.5, 158.5, 206.4; *m/z* (EI) 272 (M^+).

References and notes

1. Fujita, E.; Nagao, Y. *Bioorg. Chem.* **1977**, *6*, 287.
2. (a) Fluharty, A. L. *The Chemistry of the Thiol Group*; Patai, S., Ed.; Wiley Interscience: New York, NY, 1974; p 589; Part 2; (b) Kumar, A.; Salunkhe, R. V.; Rane, R. A.; Dike, S. Y. *J. Chem. Soc., Chem. Commun* **1991**, 485.
3. Trost, B. M.; Keeley, D. E. *J. Org. Chem.* **1975**, *40*, 2013.
4. Cohen, T.; Mura, A. J., Jr.; Shull, D. W.; Fogel, E. R.; Ruffner, R. J.; Falck, J. R. *J. Org. Chem.* **1976**, *41*, 3218.
5. Bakuzia, P.; Bakuzis, M. L. F. *J. Org. Chem.* **1981**, *46*, 235.
6. Cherkauskas, J. P.; Cohen, T. *J. Org. Chem.* **1992**, *57*, 6.
7. (a) Zeolites: Sreekumar, R.; Rugmini, P.; Padmakumar, R. *Tetrahedron Lett.* **1997**, *38*, 6557; (b) CdI_2: Saito, M.; Nakajima, M.; Hashimoto, S. *Tetrahedron* **2000**, *56*, 9589; (c) $InBr_3$: Bandini, M.; Cozzi, P. G.; Giacomini, M.; Melchiorre, P.; Selva, S.; Umani-Ronchi, A. *J. Org. Chem.* **2002**, *67*, 3700; (d) $Hf(OTf)_3$: Kobyashi, S.; Ogawa, C.; Kawamura, M.; Sugiura, M. *Synlett* **2001**, 983; (e) $Na_2CaP_2O_7$: Zahouily, M.; Abrouki, Y.; Rayadh, A. *Tetrahedron Lett.* **2002**, *43*, 7729; (f) KF/NP: Abrouki, Y.; Zahouily, M.; Rayadh, A.; Bahlaouan, B.; Sebti, S. *Tetrahedron Lett.* **2002**, *43*, 8951; (g) $Bi(NO_3)_3$: Srivastava, N.; Banik, B. K. *J. Org. Chem.* **2003**, *68*, 2109; (h) $Bi(OTf)_3$: Alam, M. M.; Varala, R.; Adapa, S. R. *Tetrahedron Lett.* **2003**, *44*, 5115; (i) Al_2O_3: Cheng, S.; Comer, D. D. *Tetrahedron Lett.* **2002**, *43*, 1179; (j) Nafion® SAC-13: Wabnitz, T. C.; Yu, J.-Q.; Spencer, J. B. *Synlett* **2003**, 1070; (k) Ionic liquids: Yadav, J. S.; Reddy, B. V. S.; Baishya, G. *J. Org. Chem.* **2003**, *68*, 7098; (l) Ionic liquids: Ranu, B. C.; Dey, S. S.; Hajra, A. *Tetrahedron* **2003**, *59*, 2417; (m) Ionic liquids: Ranu, B. C.; Dey, S. S. *Tetrahedron* **2004**, *60*, 4183; (n) $InCl_3$: Ranu, B. C.; Dey, S. S.; Samanta, S. *ARKIVOC* **2005**, *iii*, 44; (o) I_2: Chu, C.-M.; Gao, S.; Sastry, M. N. V.; Yao, C.-F. *Tetrahedron Lett.* **2005**, *46*, 4971; (p) KF/Al_2O_3: Yang, L.; Xu, L.-W.; Xia, C.-G. *Tetrahedron Lett.* **2005**, *46*, 3279; (q) $H_3PW_{12}O_{40}$: Firouzabadi, H.; Iranpoor, N.; Jafari, A. A. *Synlett* **2005**, 299; (r) SDS: Firouzabadi, H.; Iranpoor, N.; Jafari, A. A. *Adv. Synth. Catal.* **2005**, *347*, 655; (s) β-Cyclodextrin: Krishnaveni, N. S.; Surendra, K.; Rao, K. R. *Chem. Commun.* **2005**, 669.
8. (a) Chakraborti, A. K.; Shivani. *J. Org. Chem.* **2006**, *71*, 5785; (b) Chakraborti, A. K.; Gulhane, R. *Synlett* **2004**, 627; (c) Chakraborti, A. K.; Gulhane, R.; Shivani. *Synthesis* **2004**, 111; (d) Chakraborti, A. K.; Gulhane, R.; Shivani. *Synlett*

2003, 1805; (e) Chakraborti, A. K.; Sharma, L.; Gulhane, R.; Shivani. *Tetrahedron* **2003**, *59*, 7661; (f) Chakraborti, A. K.; Gulhane, R. *Tetrahedron Lett.* **2003**, *44*, 6749; (g) Chakraborti, A. K.; Gulhane, R. *Chem. Commun.* **2003**, 1896; (h) Chakraborti, A. K.; Gulhane, R. *Tetrahedron Lett.* **2003**, *44*, 3521.

9. (a) Shivani; Chakraborti, A. K. *J. Mol. Catal. A: Chem.* **2006**. doi:10.1016/j.molcata.2006.08.047; (b) Chakraborti, A. K.; Kondaskar, A.; Rudrawar, S. *Tetrahedron* **2004**, *60*, 9085; (c) Chakraborti, A. K.; Rudrawar, S.; Kondaskar, A. *Eur. J. Org. Chem.* **2004**, 3597; (d) Chakraborti, A. K.; Rudrawar, S.; Kondaskar, A. *Org. Biomol. Chem.* **2004**, *2*, 1277; (e) Chakraborti, A. K.; Kondasker, A. *Tetrahedron Lett.* **2003**, *44*, 8315.
10. Chakraborti, A. K.; Bhagat, S.; Rudrawar, S. *Tetrahedron Lett.* **2004**, *45*, 7641.
11. (a) Rudrawar, S.; Besra, R. C.; Chakraborti, A. K. *Synthesis* **2006**, 2767; (b) Besra, R. C.; Rudrawar, S.; Chakraborti, A. K. *Tetrahedron Lett.* **2005**, *46*, 6213.
12. (a) Chakraborti, A. K.; Chankeshwara, S. V. *Org. Biomol. Chem.* **2006**, *4*, 2769; (b) Chankeshwara, S. V.; Chakraborti, A. K. *Synthesis* **2006**, 2784; (c) Chankeshwara, S. V.; Chakraborti, A. K. *Tetrahedron Lett.* **2006**, *47*, 1087; (d) Chankeshwara, S. V.; Chakraborti, A. K. *J. Mol. Catal. A: Chem.* **2006**, *253*, 198.
13. Kumar, R.; Chakraborti, A. K. *Tetrahedron Lett.* **2005**, *46*, 8319.
14. Kumar, R.; Thilagavathi, R.; Gulhane, R.; Chakraborti, A. K. *J. Mol. Catal. A: Chem.* **2006**, *250*, 227.
15. (a) $Cu(BF_4)_2 \cdot xH_2O$: Garg, S. K.; Kumar, R.; Chakraborti, A. K. *Tetrahedron Lett.* **2005**, *46*, 1721; (b) $Zn(ClO_4)_2 \cdot 6H_2O$: Garg, S. K.; Kumar, R.; Chakraborti, A. K. *Synlett* **2005**, 1370; (c) Montmorillonite K-10: Sharma, G.; Kumar, R.; Chakraborti, A. K. *J. Mol. Catal. A: Chem.* **2006**. doi:10.1016/j.molcata.2006.08.021.
16. Khatik, G. L.; Kumar, R.; Chakraborti, A. K. *Org. Lett.* **2006**; *8*, 2433.
17. $HClO_4$–SiO_2 is not commercially available and was prepared for the first time by Chakraborti et al. (vide Ref. 8g) and was patented [Chakraborti, A. K.; Gulhane, R. Indian Patent, 266/DEL/2003 (10-3-2003)].
18. (a) Agarwal, A.; Rani, S.; Vankar, Y. D. *J. Org. Chem.* **2004**, *69*, 6137; (b) Misra, A. K.; Tiwari, P.; Madhusudan, S. K. *Carbohydr. Res.* **2005**, *340*, 325; (c) Mukhopadhyay, B.; Russell, D. A.; Field, R. A. *Carbohydr. Res.* **2005**, *340*, 1075; (d) Khan, A. T.; Parvin, T.; Choudhury, L. K. *Synthesis* **2006**, 2497; (e) Das, B.; Venkateswarlu, K.; Majhi, A.; Reddy, M. R.; Reddy, K. N.; Rao, Y. K.; Ravikumar, K.; Sridhar, B. *J. Mol. Catal. A: Chem.* **2006**, *246*, 276.
19. After the completion of this work a related report appeared in the literature [Khan, A. T.; Ghosh, S.; Choudhury, L. H. *Eur. J. Org. Chem.* **2006**, 2226] and prompted us to report our results on the scope and limitation of the use of this self-developed catalyst for carbon–sulfur bond formation.
20. Tundo, P.; Anastas, P.; Black, D. S.; Breen, J.; Collins, T.; Memoli, S.; Miyamoto, J.; Polyakoff, M.; Tumas, W. *Pure Appl. Chem.* **2000**, *72*, 1207.
21. (a) Anticonvulsant: Sarro, G. D.; Chimirri, A.; Sarro, A. D.; Gitto, R.; Grasso, S.; Zappalá, M. *Eur. J. Med. Chem.* **1995**, *30*, 925; (b) Ca^{+2} Channel antagonist: Kurokawa, J.; Adachi-Akahane, S.; Nagao, T. *Eur. J. Pharmacol.* **1997**, *325*, 229; (c) Anti-HIV: Grandolini, G.; Perioli, L.; Ambrogi, V. *Eur. J. Med. Chem.* **1999**, *34*, 701; (d) Squalene synthetase inhibitor: Yang, X.; Buzon, L.; Hamanaka, E.; Liu, K. K.-C. *Tetrahedron: Asymmetry* **2000**, *11*, 4447 and the references therein; (e) V_2 Arginine vasopressin receptor antagonist: Urbanski, M. J.; Chen, R. H.; Demarest, K. T.; Gunnet, J.; Look, R.; Ericson, E.; Murray, W. V.; Rybczynski, P. J.; Zhang, X. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 4031; (f) HIV-1 Reverse transcriptase inhibitor: Santo, R. D.; Costi, R. *IL Farmaco* **2005**, *60*, 385.
22. Lévai, A. *J. Heterocycl. Chem.* **2000**, *37*, 199 and the references therein.
23. Kodomari, M.; Noguchi, T.; Aoyama, T. *Synth. Commun.* **2004**, *34*, 1783.
24. Patel, V. M.; Desai, K. R. *Indian J. Chem.* **2004**, *43B*, 199.
25. (a) Lévai, A. *J. Heterocycl. Chem.* **2004**, *41*, 399; (b) Lévai, A. *J. Heterocycl. Commun.* **2002**, *8*, 227; (c) Lévai, A. *J. Heterocycl. Commun.* **2002**, *8*, 375.
26. Micheli, F.; Degiorgis, F.; Feriani, A.; Paio, A.; Pozzan, A.; Zarantonello, P.; Seneci, P. *J. Combi. Chem.* **2001**, *3*, 224.
27. Pant, S.; Singhal, B.; Upreti, M.; Pant, U. *Molecules* **1998**, *3*, 159.
28. (a) Upreti, M.; Pant, S.; Dandia, A.; Pant, U. C. *Indian J. Chem.* **1997**, *36B*, 1181; (b) Pant, S.; Sharma, A.; Sharma, S. K.; Pant, U. C.; Goel, A. K. *Indian J. Chem.* **1996**, *35B*, 794.
29. Dandia, A.; Sati, M.; Loupy, A. *Green Chem.* **2002**, *4*, 599.
30. Bhagat, S.; Sharma, R.; Sawant, D. M.; Sharma, L.; Chakraborti, A. K. *J. Mol. Catal. A: Chem.* **2005**, *244*, 20.