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Short communication

Zinc perchlorate hexahydrate as a new and highly efficient catalyst for synthesis of 2-hydroxysulfides by opening of epoxide rings with thiols under solvent-free conditions: Application for synthesis of the key intermediate of diltiazem

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Abstract

Commercially available zinc perchlorate hexahydrate [$Zn(ClO_4)_2{\cdot}6H_2O$] was found to be highly effective catalyst for opening of epoxide ring by thiols under solvent-free condition at room temperature for efficient synthesis of 2-hydroxysulfides. The catalytic activity of various group I/II metal perchlorates followed the order $Zn(ClO_4)_2{\cdot}6H_2O \gg Mg(ClO_4)_2{\cdot}6H_2O > Ba(ClO_4)_2{\cdot}6H_2O \ggg LiClO_4$. The $Zn(ClO_4)_2{\cdot}6H_2O$-catalysed reaction of epoxides derived from cyclic and acyclic olefines with thiols afforded β-hydroxysulfides in high yields. Reaction with cycloalkene oxides led to stereoselective formation of the *trans*-2-hydroxysulfides. Excellent regioselectivity was observed for unsymmetrical epoxides. In case of styrene oxide, the hydroxysulfide from nucleophilic attack at the benzylic carbon of the epoxide was the major product. Preferential nucleophilic attack by thiophenol took place at sterically less hindered position of the epoxide ring of unsymmetrical non-styrenoid alkene oxides. Epichlorohydrin exemplified a case of chemo- and regioselective reaction with no detectable (GC–MS) side product formation by direct displacement of the chlorine atom. The methodology was extended for an efficient synthesis of the key intermediate of diltiazem.

Keywords: Zinc perchlorate hexahydrate; Catalyst; Epoxides; Thiols; 2-Hydroxysulfides; Regioselective; Chemoselective; Solvent-free; Intermediate of diltiazem

1. Introduction

2-Hydroxysulfides are synthetic intermediates of drugs, pharmaceuticals and natural products [1]. Opening of epoxide rings by thiols constitutes common strategy for synthesis of 2-hydroxysulfides and is achieved in the presence of organic/inorganic bases [1a,2], and Lewis acids such as Al_2O_3 [3], Sn(IV) salts [4], $Ti(OPr^i)_4$ [5], $LnCl_3$ [6], Zn(II)tartrate [7], $BF_3{\cdot}OEt_2$ [8], $CoCl_2$ [9], ceric ammonium nitrate [10], montmorillonite clay [11], gallium–lithium-bis(binaphthoxide) complex [12], (salen)Cr(III) complex [13], $InCl_3$ [14], $B(C_6F_5)_3$ [15], $LiNTf_2$ [16], and $ZnCl_2$ [17]. Epoxide ring opening by thiols has also been promoted by PEG [18], HFIP [19] and Bu_3P [20]. However, one or more of disadvantages such as requirement of excess thiols, stoichiometric amount of catalyst, prolonged reaction times, elevated temperatures, halogenated solvents, special apparatus, moisture sensitive/hazardous/costly catalysts, unsatisfactory yields (due to undesirable side reactions of oxidation of the thiol or rearrangement of the epoxide) encountered with the existing protocols make the necessity to develop a better method.

We felt that a metal salt that can form a strong coordinate bond with the oxygen atom of the epoxide ring should increase the electrophilicity of the carbon atoms of the oxirane ring and assist opening of the epoxide ring by thiol to be carried out under milder conditions and in short times.

2. Results and discussion

In search for less costly but more effective catalysts, we thought that it should be a compound of group I/II metal (so as to become cheap) with strong oxophilic central metal ion (for more effective coordination with the epoxide oxygen) and have strong electron-withdrawing counter anion (to make the central

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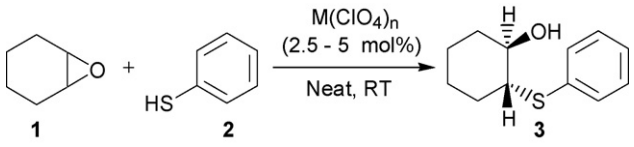


Scheme 1. Reaction of **1** with **2** catalysed by metal perchlorates.

metal ion more oxophilic). Thus, we thought of selecting group I/II metal salts of strong protic acids that should have more pronounced oxophilic property. The large negative H_0 value (−14.1) [21] makes triflic acid the strongest protic acid but its high cost does not make metal triflates attractive for large-scale applications. Moreover, TfOH is often liberated from metal triflates during the triflate-catalysed acylation reactions and may be the actual catalytic agent [22]. The *in situ* generation of TfOH might induce potential side reactions as epoxides are susceptible to protic acid-catalysed rearrangement. Further, not many metal triflates are available commercially. Perchloric acid is the second strongest protic acid and is of low cost. Various metal perchlorates are easily available. Thus, metal perchlorates are strong contenders as catalysts for industrial use [23]. Recently, we have been engaged in exploring the catalytic efficiency of metal perchlorates for electrophilic activation [24–27]. In the present study, we planned to evaluate the catalytic efficiency of various commercially available groups I and II metal perchlorates and report that zinc perchlorate hexahydrate is a new and highly efficient catalyst for synthesis of 2-hydroxysulfides by opening of epoxide rings with thiols at room temperatures and under solvent-free conditions. Our hypothesis of metal perchlorates being a strong activator of epoxide ring was reinforced by the use of $LiClO_4$ as catalyst for opening of epoxide ring by thiols [28]. However, more than stoichiometric amount of $LiClO_4$ was needed and it took prolonged time for completion of the reactions. For example, reaction of cyclohexene oxide with thiophenol was carried out in anhydrous MeCN in the presence of 1.25 equiv. of $LiClO_4$ for 48 h at 80 °C. In a recent publication although it has been reported that the epoxide ring opening of cyclohexene oxide with thiophenol was carried out at room temperature under solvent-free condition using 12.5 mol% of $LiClO_4{\cdot}3H_2O$ in 2–28 min, the use of 5 mol% of the catalyst required 24 h for completion of the reaction [29]. Our previous study on acylation [25] revealed that due to the higher charge–size ratio [30] of Mg^{2+} compared to that of Li^+, $Mg(ClO_4)_2$ was a better electrophilic activation catalyst than $LiClO_4$ and the catalytic efficiency of different metal perchlorates followed the order $Mg(ClO_4)_2 > Ba(ClO_4)_2 > LiClO_4$. Thus, we planned to evaluate the catalytic efficiency of various group I/II metal perchlorates for opening of epoxide ring by thiols.

In a model reaction, cyclohexene oxide (**1**) (2.5 mmol) was taken as a representative epoxide and treated with thiophenol (**2**) (1 equiv.) in the presence of various group I/II metal perchlorates under neat conditions at r.t. (Scheme 1).

The reactions were monitored by GC–MS and the optimum results are provided in Table 1.

The reaction was best catalysed by $Zn(ClO_4)_2{\cdot}6H_2O$ (2.5 mol%) affording 100% conversion to *trans*-2-(phenylthio)-cyclohexanol (**3**) after 30 min (entry 4, Table 1). Moderate catalytic activity was exhibited by $Mg(ClO_4)_2{\cdot}6H_2O$ with 45% conversion after 60 min (entry 3, Table 1). A 15% conversion took place with $Ba(ClO_4)_2{\cdot}xH_2O$ (5 mol%) (entry 2, Table 1) but $LiClO_4$ (entry 1, Table 1) was found to be ineffective.

Table 1
Reaction of **1** and **2** in the presence of various perchlorates[a]

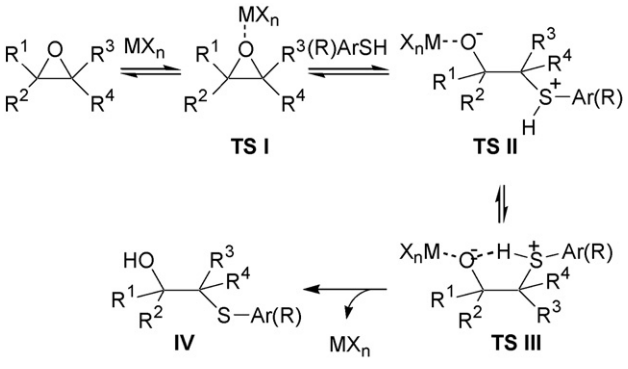
Entry	Catalyst	Time (min)	Yield (%)[b]
1	$LiClO_4$	60	Nil
2	$Ba(ClO_4)_2{\cdot}xH_2O$	60	15
3	$Mg(ClO_4)_2{\cdot}6H_2O$	60	45
4	$Zn(ClO_4)_2{\cdot}6H_2O$	30	100[c]

[a] Cyclohexene oxide (**1**) (2.5 mmol) was treated with thiophenol (**2**) (2.5 mmol, 1 equiv.) in the presence of catalyst (5 mol% except for entry 4) at r.t. (~25–30 °C) under solvent-free condition.
[b] GC–MS conversion to **3**.
[c] The reaction was carried out using 2.5 mol% of the catalyst.

The role of $Zn(ClO_4)_2{\cdot}6H_2O$ in catalysing the opening of epoxide ring by thiols may be explained by Scheme 2.

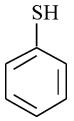
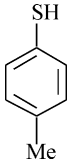
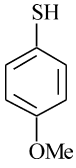
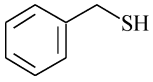
Coordination of the oxygen atom of the epoxide ring with the central metal ion of the catalyst induced 'electrophilic activation' of the oxiran ring and formed the **TS I**, which on subsequent nucleophilic attack at one of the carbon atoms constituting the epoxide ring was converted to **TS II** through opening of the epoxide ring. Intramolecular hydrogen bond formation involving the oxyanionic site and the sulfhydryl hydrogen atom in **TS II** led to **TS III**. Finally, transfer of proton from the sulfonium moiety to the oxyanionic site resulted in the formation of 2-hydroxysulfide (**IV**) and liberated the catalyst to complete the catalytic cycle.

The mechanism depicted in Scheme 2 provided rationale for poor catalytic activity of $LiClO_4$, $Ba(ClO_4)_2$ and $Mg(ClO_4)_2$. The lower charge to size (Z^2/r) value of Li^+ ($1.35\,e^2\,m^{-10}$) and Ba^{2+} ($2.94\,e^2\,m^{-10}$) ions compared to that of Zn^{2+} ion ($5.33\,e^2\,m^{-10}$) [30] make the Li^+ and Ba^{2+} ions significantly less oxophilic compared to Zn^{2+}. Thus, $Zn(ClO_4)_2{\cdot}6H_2O$ was more effective in inducing 'electrophilic activation' of the epoxide ring. Further, the strong electrophilic property of the Zn^{2+} ion delocalized the negative charge of the oxygen atom in the **TS II** and assisted the progress of the reversible reaction in the forward direction. The parallels between the catalytic



Scheme 2. Role of $Zn(ClO_4)_2{\cdot}6H_2O$ in catalysing the opening of epoxide ring by thiols.

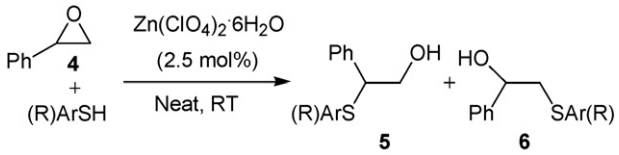
Table 2
$Zn(ClO_4)_2{\cdot}6H_2O$-catalysed epoxide ring opening of **1** by various thiols[a]

Entry	Thiol	Time (min)	Yield (%)[b,c]
1		30	98
2		60	90
3		60	96
4		60	95

[a] Cyclohexene oxide (**1**) (2.5 mmol) was treated with thiol (2.5 mmol, 1 equiv.) in the presence of $Zn(ClO_4)_2{\cdot}6H_2O$ (2.5 mol%) at r.t. (~25–30 °C) under solvent-free condition.
[b] Isolated yield.
[c] The product was characterized by NMR and GC–MS.

activity and charge–size function of metal perchlorates was also observed during the metal perchlorate-catalysed acetylation [25], thia-Michael addition [26] and Diels-Alder [31] reactions. However, although the higher Z^2/r value of 5.56 of Mg^{2+} ion should demand it to be more oxophilic compared to Zn^{2+} ion, $Mg(ClO_4)_2{\cdot}6H_2O$ was proved to be less active than $Zn(ClO_4)_2{\cdot}6H_2O$ in catalysing the epoxide ring opening reaction (compare entries 3 and 4, Table 1). The inferior catalytic activity of $Mg(ClO_4)_2{\cdot}6H_2O$ could be explained due to the higher hydrolysis constant (pK_h value) of 11.42 of Mg^{2+} ion compared to a value of 9.6 of Zn^{2+} ion [32]. Thus, Mg^{2+} ion became susceptible to loss of oxophilic property in the presence of water of hydration and trace of moisture.

To establish the generality, **1** was treated with various aryl/alkyl thiols in the presence of $Zn(ClO_4)_2{\cdot}6H_2O$ (2.5 mol%) at r.t. under solvent-free condition (Table 3). In each occasion, the *trans*-2-aryl/alkylthiocyclohexanol was obtained in excellent yield. However, compared to the reaction of thiophenol, the reaction with electron rich aromatic thiols (entries 2 and 3, Table 2) and aryl alkyl thiol (entry 4, Table 2) took longer times. This can be explained on the basis of the mechanism depicted in Scheme 2. The overall rate of the reaction should depend on the final proton exchange step through intramolecular hydrogen bond formation via the **TS III**. As the sulfhydryl hydrogen atom in 4-methylthiophenol, 4-methoxythiophenol and α-toluenethiol is less effective in hydrogen bond formation with the oxyanionic site compared to that of thiophenol, the reaction with the former thiols took longer time. Although the sulfur atom in 4-methylthiophenol and 4-methoxythiophenol was more



Scheme 3. Regioselectivity of $Zn(ClO_4)_2{\cdot}6H_2O$-catalysed reaction of styrene oxide (**4**) with thiols.

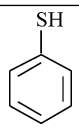
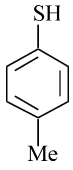
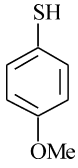
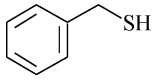
nucleophilic compared to that of thiophenol, the reaction with thiophenol was faster. This provided evidence in support of the involvement of **TS III** in the mechanism depicted in Scheme 2.

To determine regioselectivity, styrene oxide (**4**) was taken as model unsymmetrical epoxide. Nucleophilic attack at the benzylic carbon atom of the epoxide ring should lead to hydroxysulfide **5** and the reaction at the terminal carbon of the epoxide ring should form **6** (Scheme 3).

Thus, **4** was treated with various thiols in the presence of $Zn(ClO_4)_2{\cdot}6H_2O$ (2.5 mol%) at r.t. under solvent-free conditions (Table 3). In each occasion, the GC–MS showed the presence of the regioisomeric products. The major product was isolated by purification of the reaction mixture by column chromatography. On the basis of ^1H and ^{13}C NMR data, the major products were found to be the hydroxysulfides formed by reaction at the benzylic carbon atom of **4**.

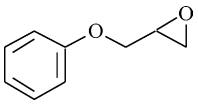
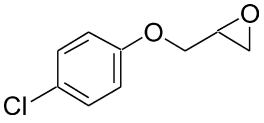
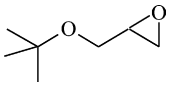
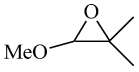
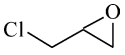
The formation of the hydroxysulfide (**5**) as the major product could be explained on the basis of the proposed mechanism (Scheme 2). In the **TS I**, the coordination of the epoxide oxygen

Table 3
Regioselectivity of epoxide ring opening of **4** by various thiols catalysed by $Zn(ClO_4)_2{\cdot}6H_2O$[a]

Entry	Catalyst	Yield (%)[b]	Ratio (**5**:**6**)[c]
1		99	98:2
2		98	97:3
3		96	95:5
4		95	92:8

[a] **4** (2.5 mmol) was treated with the thiol (2.5 mmol, 1 equiv.) in the presence of $Zn(ClO_4)_2{\cdot}6H_2O$ (2.5 mol%) under solvent-free condition at r.t. (~25–30 °C) for 1 h.
[b] Isolated yield.
[c] Determined by GC–MS of the isolated reaction mixture and NMR of the column purified major product.

Table 4
$Zn(ClO_4)_2·6H_2O$-catalysed epoxide ring opening of different epoxides with **2**[a]

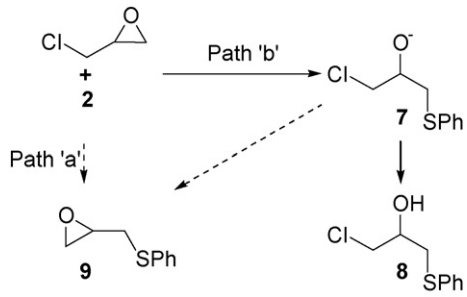
Entry	Epoxide	Yield (%)[b,c]
1		83[d,e]
2		98[f]
3		95[f]
4		95[f]
5		80[f]
6		97[f]

[a] The epoxide (2.5 mmol) was treated with **2** (2.5 mmol, 1 equiv.) in the presence of $Zn(ClO_4)_2·6H_2O$ (2.5 mol%) under solvent-free condition at r.t. (~25–30 °C) for 1 h (except for entry 1).
[b] Isolated yield.
[c] The structure of the product was established by NMR and MS.
[d] The reaction was carried out for 20 min.
[e] The *trans*-2-thiophenylcyclopentanol was the only product formed.
[f] The hydroxysulfide from nucleophilic attack at the less substituted carbon of the epoxide ring was the only product formed [36].

atom with the Zn^{2+} ion induced positive charge on oxygen. The positive charge on oxygen was delocalized through the carbon atoms of the epoxide ring. Since the phenyl group helped stabilization of the positive charge on the benzylic carbon of the epoxide ring through resonance effect, the positive charge of oxygen atom was delocalized largely on the benzylic carbon and made it more electrophilic compared to the terminal carbon atom. Therefore, selective nucleophilic attack took place at this centre. Similar regioselectivity was observed during the Lewis acid catalysed reaction of **4** with amines [33].

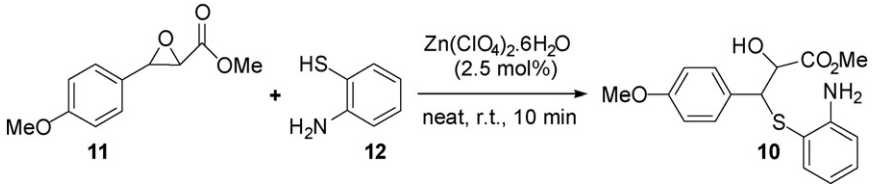
We next planned to establish the generality of the $Zn(ClO_4)_2·6H_2O$-catalysed epoxide opening reaction with other epoxides. Thus, different symmetrical and non-styrenoidal unsymmetrical epoxides were treated with **2** in the presence of $Zn(ClO_4)_2·6H_2O$ (2.5 mol%) under solvent-free conditions at r.t. (Table 4).

In each case, the corresponding 2-hydroxysulfide was formed in high yields. Excellent regioselectivity was observed



Scheme 4. Chemo- and regioselectivity of $Zn(ClO_4)_2·6H_2O$-catalysed reaction of epichlorohydrin with **2**.

for non-styrenoidal unsymmetric epoxides. The regioselectivity was controlled by the steric and electronic factors surrounding the epoxide ring carbon atoms. Selective nucleophilic attack by the thiol took place at the less substituted carbon atom of the epoxide ring due to the steric effect. However, in case of entry 5 (Table 4), the resonance/electronic effect of the OMe group also contributed to the overall regioselectivity of epoxide ring opening. The formation of the regioisomeric alcohol by nucleophilic attack of thiophenol at the methoxy substituted (less substituted) carbon atom of the epoxide ring as the sole product indicated that the resonance effect of the methoxy group and the steric effect of the geminal dimethyl groups were in consonance in controlling the regioselectivity of the epoxide ring opening for this substrate. The regioselectivity was established by the GC–MS analyses of the product. The GC–MS of the crude reaction mixture exhibited a single peak at *m*/*z* 212 indicating the formation of only one of the two possible regioisomers. The ion peaks at 153 (M^+–Me_2COH), 59 (M^+-153) and 43 ($MeCO^+$, 100%) in the mass spectrum of the product were diagnostic of the formation of the regioisomer by nucleophilic attack at the less substituted carbon atom of the epoxide. The formation of this regioisomer was further confirmed by comparison of the ^1H NMR data of an authentic compound prepared by an alternate route [36]. However, the product obtained after chromatographic (60–120 mesh silica-gel) purification of the crude reaction mixture tends to generate small amount of impurity on storing probably as the result of hydrolytic decomposition of the mixed acetal moiety as indicated by IR (appearance of a peak at 1720 cm^{-1}) and NMR. The reaction of epichlorohydrin (entry 6, Table 4) provided excellent example of chemo- and regioselectivity and afforded 97% yield of the hydroxysulfide corresponding to nucleophilic attack at the terminal carbon of the epoxide moiety. No significant amount of the product from nucleophilic substitution of the chlorine atom was observed (GC–MS). Nucleophilic attack on epichlorohydrin generally results in the formation of



Scheme 5. Improved synthesis of **10**.

a new methyloxirane **9**. The reaction, in principle, may proceed via two distinct pathways: (i) direct displacement of chlorine (path a) or (ii) initial attack on the epoxide (path b) followed by protonation of the alkoxide anion to form the hydroxysulfide (**8**) or extrusion of the chlorine atom to give **9** (Scheme 4) [34]. It is anticipated that the strong electron-withdrawing nature of the ClO_4^- counter anions in $Zn(ClO_4)_2$ make the Zn^{2+} sufficiently electrophilic so as to hold the negative charge of the alkoxide anion generated after the nucleophilic attack on the metal complexed epoxide. Thus, the free alkoxide anion is not available for subsequent elimination of the chloride anion.

We next planned to extend this new methodology of regioselective epoxide ring opening by thiol for an improved synthesis of the key intermediate **10** of the antihypertensive drug diltiazem (Scheme 5). The treatment of 3-(4-methoxyphenyl)glycidate (**11**) with 2-aminothiophenol (**12**) afforded **10** in 75% yield after 10 min at r.t. The reported methodology for the synthesis of **10** involves a two-step procedure: the reaction of **11** with 2-nitrothiophenol in the presence of $SnCl_2$ followed by the reduction of the isolated 2-hydroxy-(2-nitrophenyl)sulfide derivative by $FeSO_4$ under reflux [35].

3. Conclusion

We have described herein a highly efficient catalyst for epoxide ring opening by thiols to afford efficient synthesis of 2-hydroxysulfides under solvent-free conditions at room temperature. The advantages include: (i) the use of small amount (2.5 mol%) of cheap, easy to handle and commercially available catalyst; (ii) room temperature reaction conditions; (iii) short reaction times; (iv) high yields. With increasing environmental concerns [37] the solvent-free reaction conditions should make this methodology environmentally friendly and applicable for large-scale operations. The industrial utility of this methodology has been demonstrated by an improved synthesis of the key intermediate of antihypertensive drug diltiazem.

4. Experimental

The ^1H and ^{13}C NMR spectra were recorded on Bruker Avance DPX 300 (300 MHz) spectrometer in $CDCl_3$ using TMS as internal standard. The IR spectra were recorded on Nicolet Impact 400 spectrometer as KBr pellets for solid and neat for liquid samples. The reactions were monitored by TLC (silica gel-G) and Shimadzu QP 5000 GC–MS. Evaporation of solvents was performed at reduced pressure, using a Büchi rotary evaporator.

*4.1. Typical procedure for opening of epoxide ring by thiol: trans-2-(Phenylthio)cyclohexanol (**3**)*

To a magnetically stirred mixture of cyclohexene oxide (**1**) (0.245 g, 0.25 mL, 2.5 mmol) and thiophenol (**2**) (0.275 g, 0.25 mL, 2.5 mmol) in a flame dried round bottom flask under nitrogen was added $Zn(ClO_4)_2{\cdot}6H_2O$ (23 mg, 2.5 mol%) under neat condition at room temperature and the mixture was stirred magnetically till complete consumption of **1** (30 min, GC–MS). The mixture was diluted with water (25 mL) and extracted with Et_2O (3× 10 mL). The combined Et_2O extracts were washed with brine (2× 10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to afford *trans*-2-(phenylthio)cyclohexanol (**3**) (0.51 g, 98%) which was in full agreement with the spectral data of the authentic sample [3].

4.2. Spectral data of representative compounds

*4.2.1. Trans-2-(Phenylthio)cyclohexanol (**3**) (entry 1, Table 2)*

IR (neat): 3429, 3056, 2932, 1582, 1477, 1066 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ = 7.3 (m, 5H), 3.3 (m, 1H), 3.0 (bs, 1H, D_2O exchangeable), 2.7 (m, 1H), 2.1 (m, 2H), 1.7 (m, 2H), 1.3 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 23.89, 25.67, 32.23, 33.57, 55.67, 71.62, 127.23, 128.52, 132.55, 133.23; MS (EI): *m/z* 208 (M^+).

4.2.2. 2-Methyl-2-hydroxypropanal O-methyl-S-phenyl acetal (entry 5, Table 4)

IR (neat): 3457, 3058, 2974, 2931, 1580, 1438, 1376, 1089 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ = 1.33 (s, 6H), 2.62 (bs, 1H), 3.42 (s, 3H), 5.51 (s, 1H), 7.19–7.37 (m, 2H), 7.46–7.59 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 25.11, 25.27, 57.68, 73.39, 103.51, 127.44, 129.14, 135.78; MS (EI): *m/z* 212 (M^+), 167 (M^+-45), 153 (M^+–Me_2COH), 103 (M^+–SPh), 71 (M^+–SPh–OMe), 59 (M^+-153), 43 (100%).

*4.3. Improved synthesis of 3-[(2-aminophenyl)thio]-3-[4-(methoxyphenyl)]-2-hydroxypropionate (**10**)*

To the magnetically stirred mixture of 3-(4-methoxyphenyl)glycidate (**11**) (0.21 g, 1 mmol) and 2-aminothiophenol (**12**) (0.15 g, 0.13 mL, 1.2 equiv.) was added $Zn(ClO_4)_2{\cdot}6H_2O$ (2.3 mg, 2.5 mol%) and the mixture was stirred at r.t. under nitrogen. After completion of the reaction (10 min, TLC) the reaction mixture was diluted with CH_2Cl_2 (15 mL), washed with water (5 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuum to afford methyl-3-[(2-aminophenyl)thio]-3-[4-(methoxyphenyl)]-2-hydroxypropionate (**10**) (0.25 g, 75%) of. The spectral data IR (KBr): 2954, 1729, 1610, 1512, 1480, 1248, 1179, 1925 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.29–7.38 (m, 2H), 7.07–7.13 (m, 2H), 6.81–6.84 (m, 2H), 6.57–6.73 (m, 2H), 4.48–4.50 (m, 2H), 3.79 (s, 3H), 3.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.53, 55.56, 55.73, 74.08, 113.76, 115.24, 118.71, 125.84, 129.50, 130.55, 131.82, 137.57, 148.90, 159.0, 172.08; MS (APCI) = 333.6 (M + 1) were identical with those of authentic compound [35].

4.4. Spectral data of unknown compounds

4.4.1. 2-(4-Methylphenyl)thio-2-phenyl-ethanol (Table 3, entry 2)

Colourless oil; IR (neat): 3403, 3060, 3026, 2922, 2871, 1599, 1491, 1451, 1055 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.02–7.31 (m, 9H), 4.19–4.24 (t, 1H, J = 6.8 Hz,), 3.85–3.88 (m, 2H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.94,

137.35, 132.80, 129.70, 129.40, 128.26, 127.85, 127.30, 64.70, 55.67, 20.82; MS (EI): (m/z) = 244 (M^+); Anal. Calcd for $C_{15}H_{16}OS$ (244.35) C, 73.73; H, 6.60; S, 13.12. Found C, 73.78; H, 6.63; S, 13.09.

4.4.2. 2-(4-Methoxyphenyl)thio-2-phenyl-ethanol (Table 3, entry 3)

Colourless oil; IR (neat): 3412, 3061, 3027, 2938, 2836, 1462, 1591, 1246, 1030, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.04–7.13 (m, 7H), 6.59 (d, 2H, J = 8.7 Hz), 3.97 (t, 1H, J = 6.9 Hz), 3.70 (m, 2H), 3.53 (s, 3H); ^{13}C NMR (375 MHz, $CDCl_3$): δ = 159.46, 139.01, 135.64, 128.23, 127.88, 127.27, 123.33, 114.18, 64.42, 56.44, 54.95; MS (EI): (m/z) = 260 (M^+); Anal. Calcd for $C_{15}H_{16}O_2S$ (260.35) C, 69.20; H, 6.19; S, 12.32. Found C, 69.16; H, 6.23; S, 12.28.

4.4.3. 1-(4-Chlorophenoxy)-3-phenylthiopropan-2-ol (Table 4, entry 3)

Colourless oil; IR (neat): 3423, 3062, 2927, 2875, 1588, 1489, 1242, 1171, 1091 cm^{-1}; ^1H NMR (300 MHz; $CDCl_3$) δ: 7.20–7.41 (m, 7H), 6.78–6.81 (d, 2H, J = 8.9 Hz), 4.05–4.12 (m, 1H), 3.95–4.01 (m, 2H), 3.10–3.27 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 37.34, 68.37, 70.28, 115.68, 125.91, 126.56, 129.02, 129.23, 129.67, 134.87, 156.81. MS (EI): (m/z) 294 (M^+), 296 ($M^+ + 2$), 123. Anal. Calcd for $C_{15}H_{15}ClO_2S$: C, 61.11; H, 5.13; S, 10.88. Found C, 61.01; H, 5.31; S, 10.79.

4.4.4. 1-tert-Butoxy-3-phenylthiopropan-2-ol (Table 4, entry 4)

Colourless oil; IR (neat): 3427, 3057, 2973, 2927, 1582, 1477, 1366, 1194, 1085, 1022 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.12–7.41 (m, 5H), 3.78–3.88 (m, 1H), 3.37–3.49 (m, 2H), 3.07 (t, 2H, J = 5.5 Hz), 1.17 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.43, 37.15, 63.90, 69.30, 73.29, 126.14, 128.90, 129.33, 135.82. MS (EI): (m/z) = 240 (M^+), 110. Anal. Calcd for $C_{13}H_{20}O_2S$ (240.1): C, 64.96, H, 8.39; S, 13.34. Found C, 64.90; H, 8.56; S, 13.26.

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