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COBALT MEDIATED REGIOSELECTIVE RING OPENING OF OXIRANES WITH BENZENETHIOL: A MECHANISTIC STUDY

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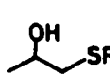
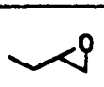
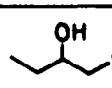
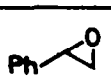
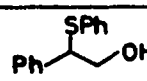
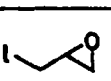
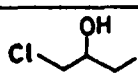
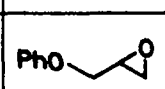
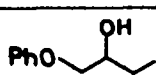
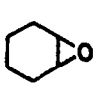
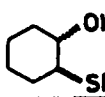
Abstract : Oxiranes are regioselectively cleaved by benzenethiol in presence of cobalt(II) chloride or $Co_2(CO)_8$ to the corresponding β-hydroxy sulfides in good yields. A mechanistic study of this reaction reveals that an electron transfer process is involved in these transformations and the reaction is proceeding via the formation of a carbon-cobalt bond.

The oxirane ring opening[1] with various nucleophiles (e.g. Me_3SiX, Me_3SiCN, Me_3SiN_3, RSH, etc.) is an important synthetic transformation for an easy access to a large number of functionalised intermediates that are required during the synthesis of natural products. These ring openings are promoted by Lewis acids such as $AlCl_3$, $ZnCl_2$, ZnI_2, $Ti(OPr^i)_4$, $VO(OPr^i)_4$ etc. and usually take place at ambient temperature over a long period of time. The opening of oxiranes with thiols is promoted by alumina[2] and very recently it is shown that such transformations could also be carried out in the presence of lanthanide complexes.[3] Based on an study from our earlier work on cobalt(II) chloride catalysed acylation of thiols[4], we envisioned that cobalt(II) complexes may also promote the opening of oxiranes with thiols. A preliminary work on cobalt(II) chloride or $Co_2(CO)_8$ catalysed opening of oxiranes with thiols showed quite promising results and a detailed account of these findings alongwith a mechanistic interpretation is presented below.

In a typical experiment dry cobalt(II) chloride (5 mol%) is dissolved in anhydrous acetonitrile (50 ml) and to this solution benzenethiol (20 mmol) and oxirane (20 mmol) are added successively at 25°C. The resulting dark green mixture is stirred under nitrogen for 12-18 hrs at this temperature and the usual work-up yielded β-hydroxy sulphides (Table 1). From the results in the table it is quite evident that these reactions proceed with a remarkable regioselectivity because in most of the cases the thiol attacks the less hindered carbon of the oxirane to give rise to secondary hydroxy sulphides. However, styrene oxide mainly gave the primary hydroxy sulfide alongwith a trace of secondary

hydroxysulphide (Tabl 1, entry 3). The crude ^{1}H-NMR of all the reaction mixture showed the presence of the other regioisomer in very small amount (≈5%). A careful monitoring of these reactions showed the presence of diphenyl disulphide as a by-product and its formation is dependent upon the quantity of cobalt(II) chloride used in the reaction. Thus when cobalt(II) chloride is used in catalytic quantity the yield of disulphide is 40% which drops to 10% if cobalt(II) chloride is used in stoichiometric amount (Table 1, entries 2, 3 and 6). It is also noteworthy that when disulphide formation is low the yield of β-hydroxy sulphide increases by approximately the same extent to which the drop in the yield of disulphide is observed. This observation coupled with the fact that disulphide formation depends upon the quantity of cobalt(II) chloride clearly indicates that it is the thiophenoxy radical and not thiophenol, that is involved in the oxirane opening. Also, the observation that the yield of β-hydroxy sulphide is dependent upon the quantity

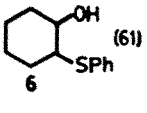
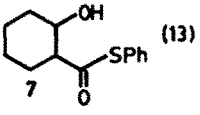
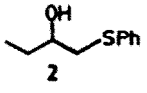
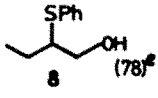
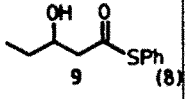
Table 1. Cobalt(II) chloride catalysed regioselective opening of oxiranes with benzenethiol

ENTRY	OXIRANE	PRODUCT[c]	ISOLATED YIELD(%)a,d (1-6)	PhS - SPh
1		 1	62	35
2		 2	58 78[b]	40 10[b]
3		 3	51 72[b]	40 10[b]
4		 4	61	35
5		 5	57	40
6		 6	50 71[b]	40 10[b]

a) All the reactions were carried out in the presence of the catalytic (0.1 mole equivalent $Co(II)Cl_2$. b) This yield is obtained when one equivalent of $Co(II)Cl_2$ is used. c) Traces of other regioisomer were obtained in all the cases. However, no attempt was made to isolate it. d) Yield based on oxirane.

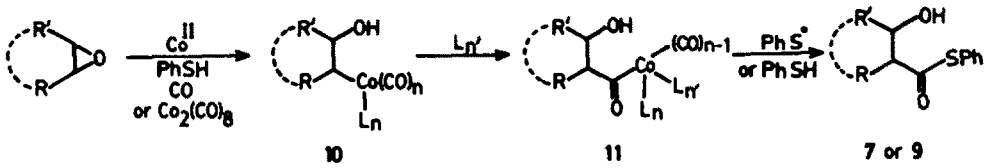
of cobalt(II) chloride clearly suggests the intermediacy of an organocobalt species during the course of this reaction. The later observation is in agreement with the work of Heck[5] who has shown earlier that the cleavage of oxiranes by cobalt complex $Co_2(CO)_8$ proceeds via a organocobalt intermediate. Inspite of many attempts the organocobalt complex could not be isolated from these reactions. However, the presence of a carbon-cobalt bond in these reactions was inferred by conducting the reaction under the atmosphere of carbon monoxide or with $Co_2(CO)_8$ complex. Interestingly, β-hydroxy thioesters were obtained alongwith β-hydroxy sulphides by the treatment of oxiranes with cobalt(II) chloride, thiophenol in an atmosphere of carbon monoxide. Similarly, $Co_2(CO)_8$ complex also gave small amounts of thioesters when reacted with oxiranes and thiophenol (Table 2).

Table 2. : Cobalt mediated cleavage of oxiranes in presence of Thiol

ENTRY	OXIRANE	REACTION CONDITIONS[c,d]	PRODUCT(S) (YIELD %)[a,b]		
1.		$Co^{II}Cl_2$, CO, 25°C, 30h	 (61) 6	 (13) 7	
2.	-do-	$Co_2(CO)_8$, 25°C, 48h	6(79)	7(15)	
3.	-do-	$Co_2(CO)_8$ (Catalytic), 25°C, 30h	6(61)	—	
4.		$Co^{II}Cl_2$, CO, 30°C, 20h	 2	 (78)[e] 8	 (8) 9
5.	-do-	$Co_2(CO)_8$, 20°C, 48h	2(62)	8(-)	9(12)

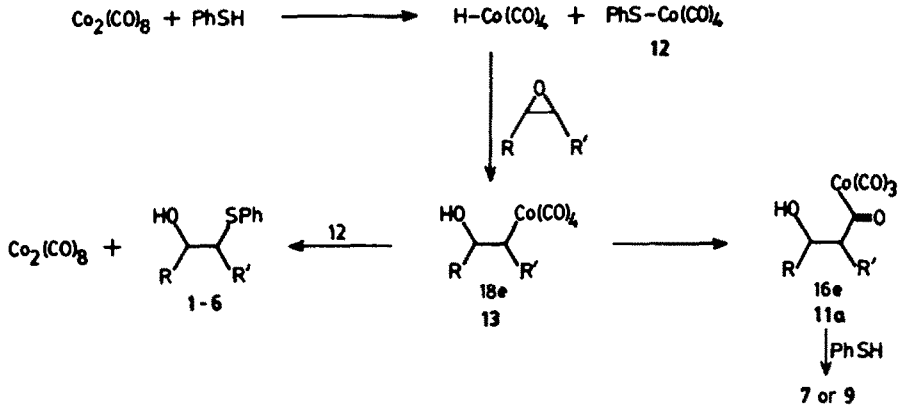
a) Yield of the isolated products. b) All the reactions gave around 5-10% of PhS-SPh. c) Carbon monoxide was bubbled slowly during the reaction. d) Anhydrous $Co(II)Cl_2$ (1 equiv.) or $Co_2(CO)_8$ (1 equiv.) were used in these reactions. e) Combined yield of both the regioisomer.

The presence of thioesters 7 and 9 can be explained if we assume the formation of a carbon-cobalt bond to give the intermediate 10, which can undergo the insertion of carbon-monoxide in carbon-cobalt bond to give an acyl cobalt complex 11 (Scheme 1). The thioester 7 or 9 can be obtained by an attack of thiophenoxy radical or thiophenol on complex 11. The insertion of carbon monoxide in carbon-cobalt bond is a very well known reaction from the work of Heck[5].



Scheme 1

Similarly, $Co_2(CO)_8$ complex is known[6] to cleave oxiranes by the reaction of $HCo(CO)_4$ which can be obtained by PhSH and $Co_2(CO)_8$ (Scheme 2). The 18e alkyl cobalt tetracarbonyl complex 13 thus obtained may lead to 16e acyl cobalt complex 11a by migration of alkyl portion from the metal to the ligand. The complex 11a may undergo the thioester formation on reaction with thiophenol. On the other hand the alkyl cobalt complex 13 may lead to the formation of β-hydroxy sulfides 1-6 by a reaction with cobalt sulphur complex 12. The catalytic nature of this reaction (Table 2, entry 3) also supports the possible role which the complex 12 may be playing in the conversion of complex 13 to compound 1-6.

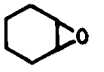
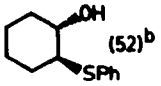
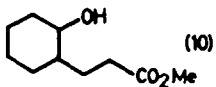
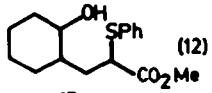
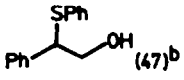
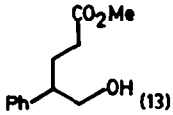
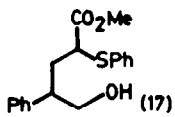


Scheme 2

In order to have an additional proof for the presence of a carbon-cobalt bond (which is potentially a carbon centred radical) these reactions when carried out, in the presence of excess of methyl acrylate, showed the formation of products 14-17 obtained due to addition of oxirane to methyl acrylate (Table 3).

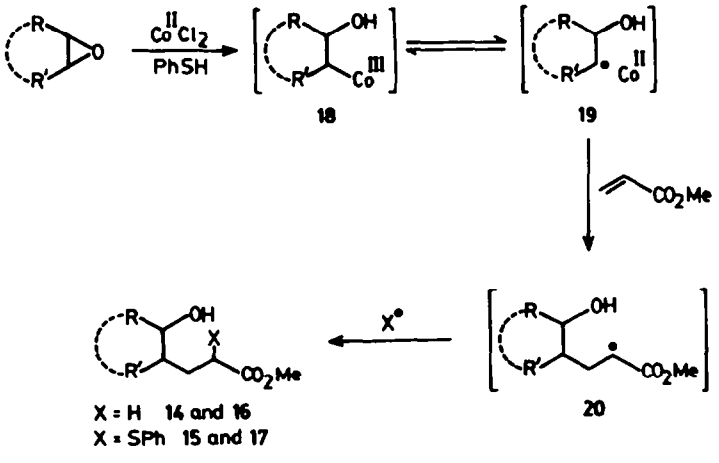
The presence of compounds 14-17 suggests the intermediacy of a carbon-centred radical 19 which may add to methyl acrylate to yield another radical 20. The radical 20 may then either pick a hydrogen atom or a thiophenoxy radical to yield compound 14 or 16 and 15 or 17, respecti-

Table 3. : Cobalt(II) chloride mediated reaction of oxiranes with thiophenol in the presence of methyl acrylate

ENTRY	OXIRANE	PRODUCT(S) (YIELD %)[a,d]		
1.		 (52)[b] **6**	 (10) **14**	 (12) **15**
2.	-do-	6 (67)[c]	14 (-)	15 (5)
3.		 (47)[b] **3**	 (13) **16**	 (17) **17**
4.	-do-	3 (61)[c]	16 (8)	17 (7)

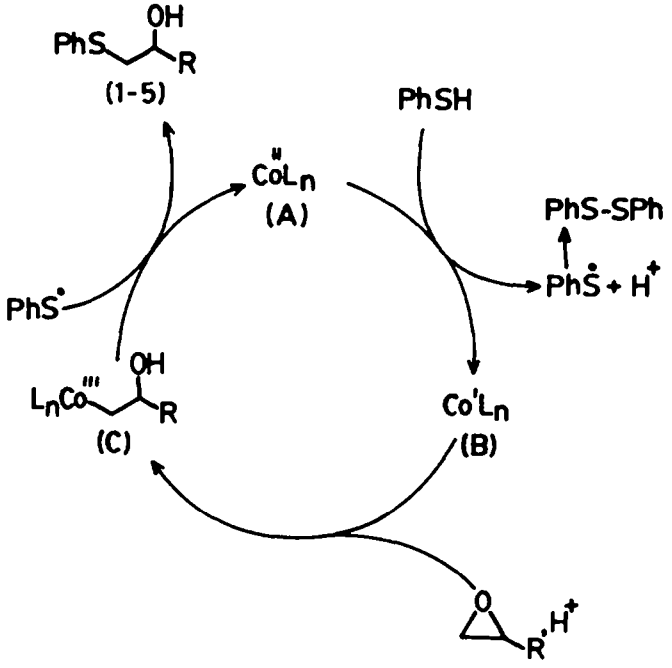
a) PhS-SPh is obtained in minor amounts (≃ 8-10%) in all the reactions. b) These reactions are carried out in the presence of 1 equiv. of anhyd. $Co(II)Cl_2$). c) These reactions are carried out in the presence of catalytic (30 mg) amount of anhyd. $Co(II)Cl_2$). d) All the reactions are carried out in acetonitrile in the presence of 10 fold excess of methyl acrylate at 60°C.

vely (Scheme 3). The homolytic cleavage of a carbon-cobalt bond under thermal condition is quite well known[7] from the earlier work in the literature.



Scheme 3

In the light of the above observations a preliminary mechanistic explanation can be offered as shown in Scheme 4. According to this scheme the catalytic role of cobalt(II) chloride can be explained by assuming that the reaction is initiated by a electron transfer from benzenethiol to cobalt(II) complex (A) to give rise to a cobalt(I) species (B) and thiophenoxy radical. Cobalt(I) species (B) then reacts with the oxirane in an S_N2 manner to give a hydroxy organocobalt(III) intermediate (C), which is then attacked by thiophenoxy radical in an S_H2 fashion to yield β-hydroxysulphides **1-5**. Oxidation of thiol[8] by cobalt(II) complexes is very well precedented in the literature. The high regioselectivity in the oxirane opening suggests an S_N2 type of attack by "super nucleophile Co(I)" species as shown earlier by Heck[5] and Jensen[9]. Similarly, there



Scheme 4

is precedent from the work of Johnson et al.[10] that a carbon-cobalt bond can be cleaved by a thiophenoxy radical to give rise to a carbon-sulphur bond.

The formation of a reduced cobalt species was observed as shown in the cyclic voltammogram (Figure 1). It is clear from the C.V. scan that cobalt(II) chloride and benzenethiol react to give a reduced species (Figure 1, bold line) of cobalt as shown by the appearance of peaks

in the region of negative potential. The peak A may be due to the formation of PhS-SPh and the peak B may result due to cobalt(I) species. Peak C is due to the oxidised species of benzenethiol or cobalt complex. The reduced species then disappears after the addition of oxirane (Fig.1b dotted line) and at the same time one observes the appearance of the oxidised species (peak D) as indicated in the positive potential region of the scan.

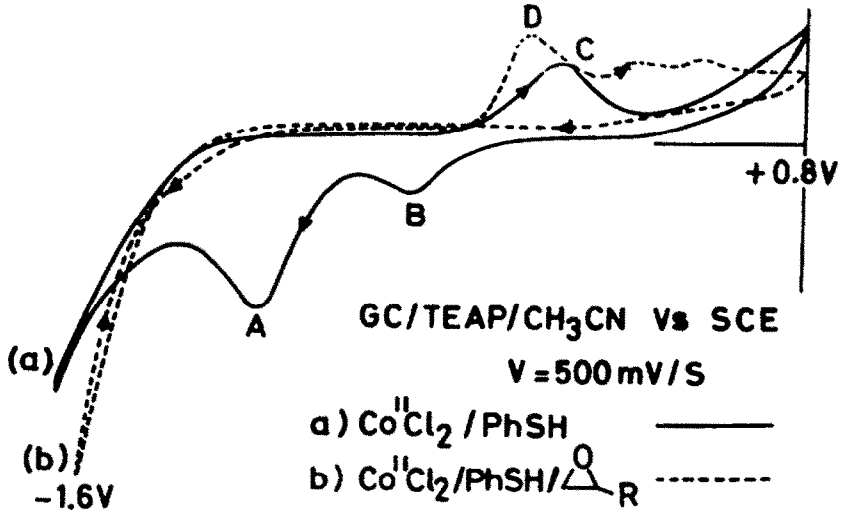


Fig. 1. : Cyclic Voltammogram at a glassy carbon electrode in tetraethylammonium perchlorate and CH_3CN of a) $Co(II)Cl_2$ and benzenethiol (bold line); b) $Co(II)Cl_2$ and benzenethiol after addition of styrene oxide (dotted line). Scan initiated at +0.8V versus SCE in negative direction at 500 mV/s.

The rigorous delineation of mechanism is not possible at this stage as the reactive species are too labile to allow the direct examination of the intermediates. However, a mechanistic study based on product analysis and cyclic voltammogram, indicates that these reactions may be proceeding via a carbon-cobalt bond formation.

We thank Dr. R.N. Mukherjee for the help during the cyclic voltammogram experiments.

EXPERIMENTAL

General Methods. IR spectra were obtained in CH_2Cl_2. ^1H-NMR spectra were measured in CCl_4 on EM-390, WP-80 and G-300 using TMS as the internal standard. $Co(II)Cl_2$ was purchased from Loba, Bombay and dried at 110°C for 3 hrs. $Co_2(CO)_8$ was purchased from Alfa Products and used

without purification. The voltammogram experiment was carried out using Princeton applied research M-370 electrochemistry system.

General procedure for cobalt(II) chloride catalysed cleavage of oxiranes with benzenethiol. Anhydrous cobalt(II) chloride (25 mg) is dissolved in dry acetonitrile (50 ml) and benzene thiol (20 mmol) and oxirane (20 mmol) are added successively to this solution at 25°C. The resulting dark green mixture is stirred under nitrogen for 12-18 hrs at this temperature. Acetonitrile is removed under vacuum and the residue taken into ether and washed successively with saturated solution of sodium bicarbonate and water. Drying ($MgSO_4$) and evaporation of ether gave a residue which on column chromatography (SiO_2, ether-pet. ether) yielded β-hydroxy sulphides.

General procedure for $Co_2(CO)_8$ catalysed cleavage of oxiranes with benzenethiol. Benzenethiol (25 mmol) and oxirane (25 mmol) are added successively to a solution of $Co_2(CO)_8$ (50 mg) in dry diethyl ether (80 ml). The resulting mixture is purged with carbon monoxide and stirred at 20°C for 48 hrs. Ether layer is washed successively with saturated solution of ammonium chloride, sodium bicarbonate and water. Drying ($MgSO_4$) and evaporation of ether gave a residue which on column chromatography (SiO_2, hexane-ether) gave β-hydroxy thioester.

General procedure for cobalt(II) chloride mediated cleavage of oxiranes with benzenethiol in the presence of carbon monoxide. Benzenethiol (30 mmol) and oxirane (30 mmol) are added successively to a solution of anhydrous cobalt(II) chloride (30 mmol) in dry acetonitrile (150 ml) at 30°C. Carbon monoxide is bubbled slowly into this mixture for 30 hrs at 30°C. Acetonitrile is removed under reduced pressure and the residue is dissolved in ether. The ether layer is washed with saturated solution of ammonium chloride and water. Drying ($MgSO_4$) and evaporation of ether gave a gum which was purified by column chromatography (SiO_2, ether-pet. ether) to yield β-hydroxy sulphide and β-hydroxy thioester.

General procedure for cobalt(II) chloride mediated cleavage of oxiranes with benzenethiol in the presence of methyl acrylate. Benzenethiol (10 mmol), oxirane (10 mmol) and methyl acrylate (100 mmol) are added to a solution of anhydrous cobalt(II) chloride (10 mmol) in dry acetonitrile (200 ml) and the mixture is stirred under nitrogen for 48 hrs at 60°C. Acetonitrile and excess methyl acrylate is removed under reduced pressure to yield a residue which is dissolved in ether and the ether layer is washed successively with saturated solution of ammonium chloride and water. Drying ($MgSO_4$) and evaporation of ether gave a semi-solid which on column chromatography (SiO_2, hexane-ether) yielded β-hydroxy

sulphide and hydroxy esters.

2-Phenylthiopropan-2-ol (1) : Prepared as described above in 62% yield. IR 3715 cm^{-1} ; ^{1}H-NMRδ1.18 (d, 3H, J = 6.8 Hz), 2.86 (d, 2H, J = 6.9 Hz), 3.76 (m, 1H), 7.12-7.57 (m, 5H).

2-Phenylthiobutan-2-ol (2) : Prepared as described above in 58% yield. This is also prepared by using 1 equiv. of $Co(II)Cl_2$ in 78% yield. IR 3772 cm^{-1} ; ^{1}H-NMRδ0.95 (t, 3H, J = 7 Hz), 1.51 (m, 2H), 2.81 (dd, 1H, J = 17.5 Hz and 8.7 Hz), 3.1 (dd, 1H, J = 15.6 Hz and 5.2 Hz), 3.56 (m, 1H), 7.17-7.56 (m, 5H) (Found : C, 65.87; H, 7.74, Calc for $C_{10}H_{14}OS$: C, 65.93; H, 7.69%).

2-Phenylthio-2-phenylethan-1-ol (3) : Prepared according to the procedure described above in 52% yield. It is also prepared by using 1 equiv. of $Co(II)Cl_2$ in 72% yield : IR 3340 cm^{-1} ; ^{1}H-NMRδ3.65 (d, 2H, J = 7 Hz), 4.70 (t, 1H, J = 6.9 Hz), 7.12-7.55 (m, 10H).

3-Chloro-1-phenylthiopropan-2-ol (4) : Prepared according to the procedure described above in 61% yield : IR 3365 cm^{-1} ; ^{1}H-NMRδ3.08 (d, 2H, J = 6.8 Hz), 3.60 (d, 2H, J = 7 Hz), 3.79 (m, 1H), 7.10- 7.76 (m, 5H) (Found : C, 53.4; H, 5.48, Calc for $C_9H_{11}OSCl$: C, 53.33; H, 5.43).

3-Phenoxy-1-phenylthiopropan-2-ol (5) : Prepared according to the procedure described above in 57% yield : IR 3410 cm^{-1}; ^{1}H-NMRδ3.12 (d, 2H, J = 6.7 Hz), 3.79 (d, 2H, J = 6.9 Hz), 4.12 (m, 1H), 6.80-7.76 (m, 10H) (Found : C, 69.17; H, 6.11, Calc for $C_{15}H_{16}O_2S$: C, 69.23; H, 6.15).

2-Phenylthiocyclohexan-1-ol (6) : Prepared according to the procedure described above in 59% yield. It is also prepared by using 1 equiv. of $Co(II)Cl_2$ in 71% yield : IR 3338 cm^{-1} ; ^{1}H-NMRδ1.34-2.43 (m, 8H), 2.89 (m, 1H), 3.46 (m, 1H).

2-Hydroxycyclohexanecarboxylic acid phenylthioester (7) : Prepared according to the procedure described above in 13% yield : IR 3415, 1705 cm^{-1} ; ^{1}H-NMRδ1.37-2.35 (m, 9H), 3.82 (m, 1H), 6.87-7.41 (m, 5H), (Found : C, 66.18, H, 6.81, Calc for $C_{13}H_{16}O_2O$: C, 66.1, H, 6.77).

3-Hydroxypentanoic acid phenylthioester (9) : Prepared according to the procedures described above in 12% yield : IR 3322, 1700 cm^{-1} ; ^{1}H-NMR δ 0.91(t, 3H, J = 7 Hz), 1.78 (m, 2H), 2.33 (d, 2H, J = 6.8 Hz), 3.81 (m, 1H), 7.18-7.61 (m, 5H).

Methyl-3-(2'-hydroxycyclohexyl)propionate (14) : Prepared according to the procedure described above in 10% yield : IR 3325, 1720 cm^{-1} ; ^{1}H-NMRδ1.35-2.41 (m, 13 H), 3.69 (s, 3H), 3.73 (m, 1H).

Methyl-3-(2'-hydroxycyclohexyl)-2-phenylthiopropionate (15) : Prepared

according to the procedure described above in 12% yield : IR 3385, 1725 cm^{-1} ; ^{1}H-NMRδ 1.29-2.37 (m, 11H), 3.61 (t, 1H, J = 6.9 Hz), 3.74 (s, 3H), 3.77 (m, 1H), 7.11-7.56 (m, 5H), (Found : C, 65.37 ; H, 7.54, Calc for $C_{16}H_{22}O_3S$: C, 65.3; H, 7.48).

Methyl-5-hydroxy-4-phenylpentanoate (16) : Prepared according to the procedure described above in 13% yield : IR 3351, 1720 cm^{-1} ; ^{1}H-NMR δ 1.69(m, 2H), 2.15-2.67 (m, 3H), 3.57 (d, 2H, J = 6.8 Hz), 3.72 (s, 3H), 7.18-7.45 (m, 5H), (Found : C, 69.19 ; H, 7.61, Calc for $C_{12\ 16}O_3$: C, 69.23; H, 7.69).

Methyl-5-hydroxy-4-phenyl-2-phenylthiopentanoate (17) : Semi- solid : IR 3359, 1720 cm^{-1}, ^{1}H-NMR δ1.67 (m, 2H), 2.38 (m, 1H), 3.17- 3.45 (m, 3H), 3.71 (s, 3H), 6.91-7.78 (m, 10H), (Found : C, 68.39; H, 6.38, Calc for $C_{18}H_{20}O_3S$: C, 68.35; H, 6.32).

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