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Cobalt(II) Catalysed Reaction of Alkenes with Aliphatic Aldehydes and Molecular Oxygen: Scope and Mechanism

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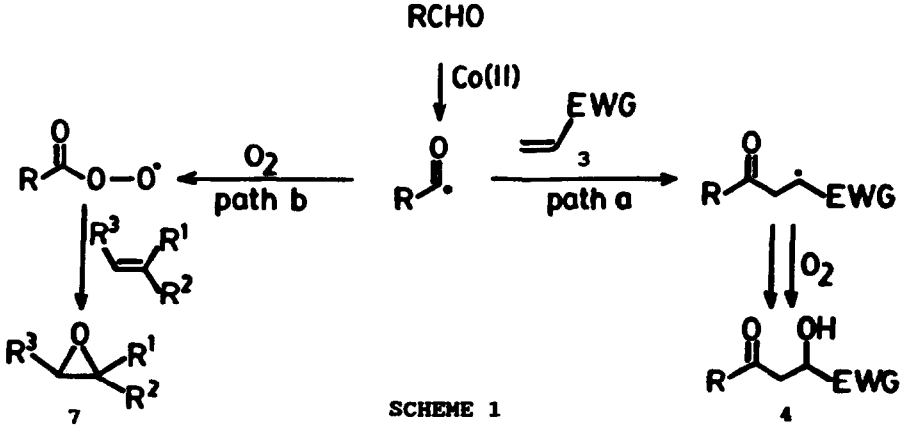
Abstract : *A variety of cobalt(II) complexes can be prepared using Schiff's bases derived from aromatic aldehydes and amines or α-aminoesters. These complexes are versatile catalyst for the reaction between aliphatic aldehydes and various alkenes. The outcome of the reaction is controlled by the electronic nature of the alkene as the electron deficient alkenes undergo oxidative addition of aldehydes followed by dioxygen incorporation to yield 2-hydroxy(acyloxy)-4-oxoesters or nitriles whereas unactivated or electron rich alkenes afford the corresponding epoxides. These reactions are proceeding via a radical pathway and a common acylcobalt intermediate is proposed for the formation of* **4** *as well as the epoxides* **7**.

INTRODUCTION

The oxidation of aldehydes by transition metal complexes is known to generate[1] the acyl radical and it is shown that cobalt(II) acetate promotes the radical chain addition of aldehyde to 1-alkene in the presence of air to afford ketones. The generation and subsequent intermolecular reaction of acyl radicals with alkenes have been

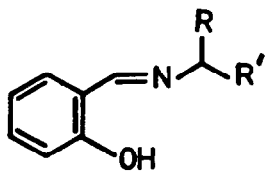


SCHEME 1

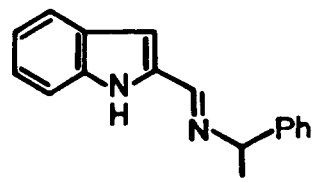
recognised as an important method of carbon-carbon bond formation as

reported[2] by Kharasch long back in 1949. The addition of acyl radicals was subsequently extended to electron deficient alkenes and this methodology has emerged as a very efficient route to the synthesis of the functionalised ketones. The synthetic potential of the acyl radical as a fundamental functionalised free radical has renewed interest in the development of direct methods for its generation and recently a series of papers have described the ability of acyl cobalt salophen[3], phenyl selenolesters[4] and S-acyl xanthates[5] serving as acyl radical precursors The acyl radical may be generated by an electron transfer process and it may involve[1b,6] either an outersphere or innersphere mode of electron transfer. If these radicals are generated by cobalt(II) complex then the resulting acyl radical may be present as an acyl cobalt intermediate. The labile nature of carbon-cobalt bond[7] will make such intermediates an attractive in situ generated precursor for the acyl radicals. The

Table 1. Schiff's Base Ligands Derived from Aldehyde, Ester and Aminoacid Ester or Amines

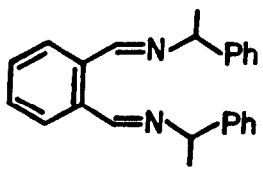


1

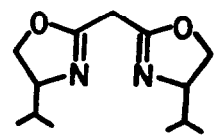


1e

a. R=Me, R'=Ph
b. R=Pr^i, R'=$-CH_2OH$
c. R=$-CH_2-Ph$, R'=CO_2Me
d. R=$-CH_2-CH_2-SMe$, R'=CO_2Me



1f

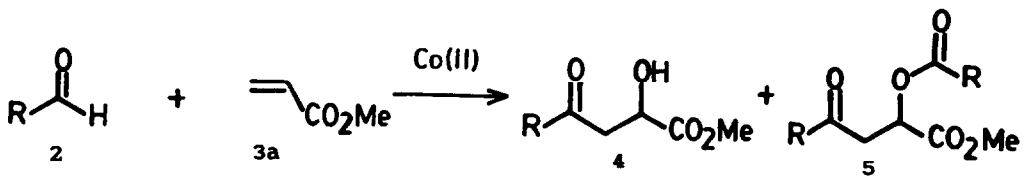


1g

formation of acyl radicals[8] using cobalt(II) complex occurs quite readily in the presence of molecular oxygen. Subsequently, these radicals may be trapped with acrylates and the resulting product radical can be terminated by the incorporation of molecular oxygen to give

2-hydroxy-4-oxoesters **4** (path a, Scheme 1). On the other hand, the reaction with unactivated alkenes leads to the formation of epoxides **7** which are derived as a result to molecular oxygen capture by the acyl radical (path b, Scheme 1). In this paper we would like to present a detailed investigation on reaction of a wide variety of alkenes with aldehyde and dioxygen in the presence of catalytic quantity of cobalt(II) complexes consisting of ligands **1a-g** derived from different Schiff's bases.

Table 2. Cobalt (II) Catalysed Reaction of Aldehydes with Methylacrylate and Dioxygen



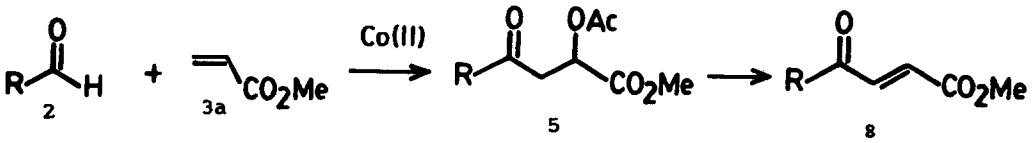
Entry	R	Ligands	Products(Yield %)	
1	C_2H_5(2a)	1a	4a(14)	5a(23)
2	C_2H_5(2a)		4a(8)[a]	5a(31)
3	$C_3^iH_7$(2b)	1a	4b(13)	5b(21)
4	$C_3^iH_7$(2b)		4b(7)[a]	5b(19)
5	$C_3^nH_7$(2c)	1a	4c(13)	5c(19)
6	$C_3^nH_7$(2c)		4c(7)[a]	5c(29)
7	$ClC_3^nH_7$(2d)		4d(17)[a]	5d(24)

[a]These reactions are carried out using $CoCl_2$ as catalyst

RESULTS AND DISCUSSION

Preparation of Cobalt(II) Complexes. A variety of cobalt(II) complexes can be prepared by mixing $CoCl_2$ and the ligands **1a-g** which can be obtained by reaction of aromatic aldehydes with amines and α-amino esters (Table 1). The cobalt(II) complexes derived from these ligands have tetrahedral geometry as revealed by their UV-visible spectra .However, an unambiguous proof for the structure of these complexes is lacking and future studies involving single crystal X-ray will be utilized to

Table 3. Cobalt(II) Catalysed Reaction of Aldehydes with Methyl acrylate in the Presence of Acetic anhydride and Dioxygen: Synthesis of Enoates

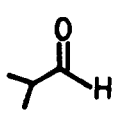
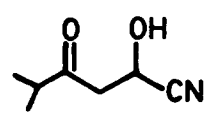
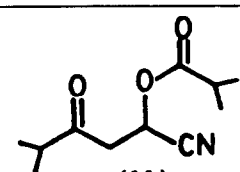
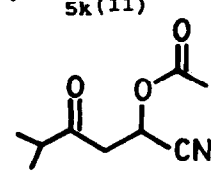


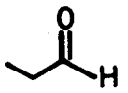
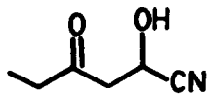
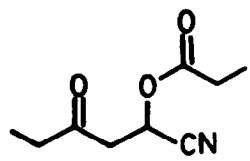
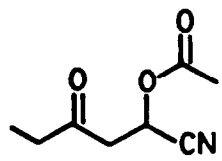
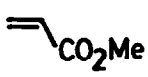
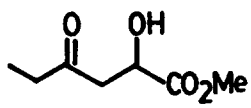
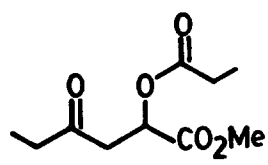
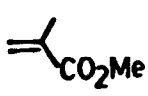
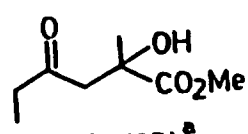
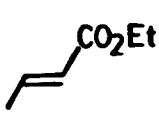
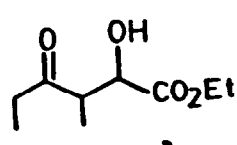
Entry	R	Products (Yield%)[a]	
1	C_2H_5(2a)	5e(75)	8a(69)
2	$C^n_3H_7$(2c)	5f(72)	8b(68)
3	$C^i_3H_7$(2b)	5g(77)	8c(87)
4	$C^n_5H_{11}$(2e)	5h(71)	8d(67)
5	$C^n_6H_{13}$(2f)	5i(72)	8e(85)
6	$ClC^n_3H_6$(2d)	5j(56)	-

[a]These reactions are carried out using $CoCl_2$ as catalyst

unambiguously prove the structure for the complexes. Most of these complexes are stable in air and are soluble in acetonitrile and exhibit green or blue colour in this solvent. *However, these reactions were performed by in situ generated catalysts.*

Table 4. Cobalt(II) Catalysed Reaction of Aldehydes with Electron Deficient Alkenes in the Presence of Dioxygen

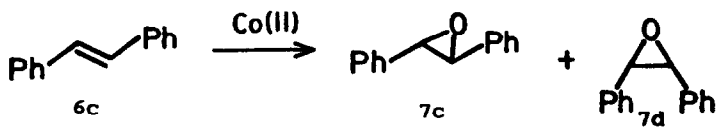
Entry	Aldehyde	Alkene	Ligand	Products(Yield%)
1	 2b	 3b		 4e (26)[a]
				 5k(11)
2				 5l(56)[a]

3	 2a		 4f (25)[a]	 5m (10)
4				 5n (58)[a]
5		1g	4f (12)	5m (22)
6	 3a	1d	 4a (13)	 5a (19)
7		1g		5a (31)
8	 3c			 4g (37)[a]
9	 3d			 4h (63)[a]

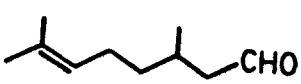
[a]These reactions are carried out using $CoCl_2$ as catalyst

Reaction with Electron Deficient Alkenes. The cobalt(II) catalysed reaction of electron deficient alkenes with aldehydes and dioxygen afforded a mixture of 2-hydroxy and 2-acyloxy-4-oxoesters in good yields. The reaction between various aldehydes and methyl acrylate are controlled by the nature of the ligands as indicated from the results compiled in table 2. The catalyst derived from ligand **1a** is quite efficient in affecting this transformation and the ratio of 2-hydroxy and 2-acyloxy esters remained unaffected when the reactions were conducted with different catalysts. The reaction using catalyst from ligand **1d** provided mainly the oligomeric products. Similarly, the polymerisation was found to be the major pathway if the reactions were carried out under nitrogen

Table 5: Cobalt(II) Catalysed Reaction of Aldehyeds with (E)-Stilbene in the Presence of Dioxygen

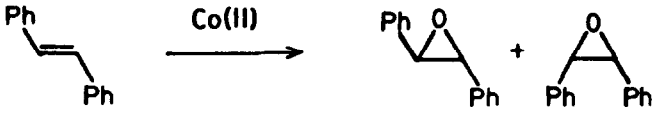


6c 7c 7d

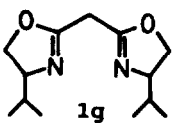
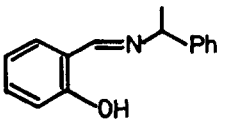
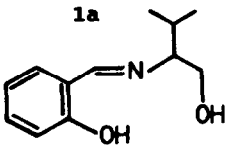
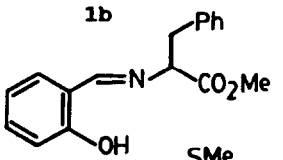
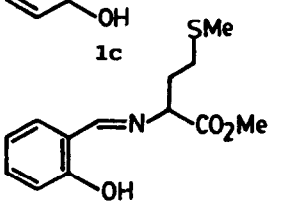
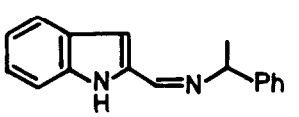
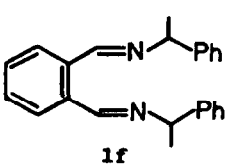
Entry	Aldhyde	Ligand	Epoxide(%Yield) (7c:7d)
1	**2a**	**1a**	62 (90:10)
2	**2b**		90 (100:0)
3		**1b**	87 (100:0)
4		**1c**	89 (0:100)
5		**1d**	53 (58:41)
6		**1e**	91 (100:0)
7		**1f**	90 (100:0)
8	 **2g**	**1g**	66 (100:0)

atmosphere. Interestingly, these reactions can be performed in the presence of excess of acetic anhydride to afford the corresponding 2-acetoxy compounds in high yields. It is noteworthy that no 2-acyloxy compounds were obtained under these conditions (Table 3). Once again, the catalyst derived from ligand **1a** was found to be quite suitable for this reaction, however, the other complexes were also able to affect this

Table 6. Cobalt(II) Catalysed Reaction of 2-Methylpropnal with (E)-Stilbene and Dioxygen: The Role of the Ligands on the Stereochemistry

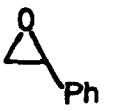
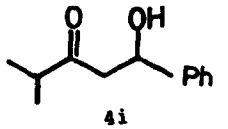
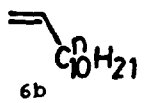
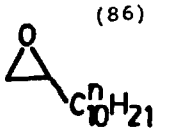
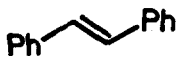
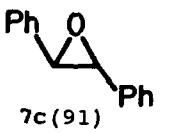
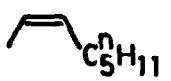
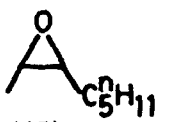
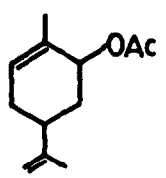
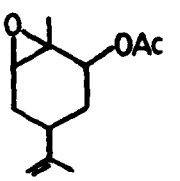
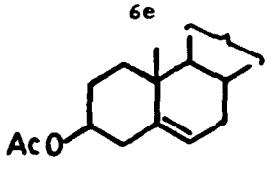
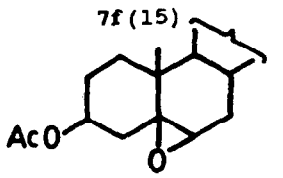
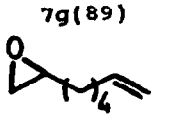


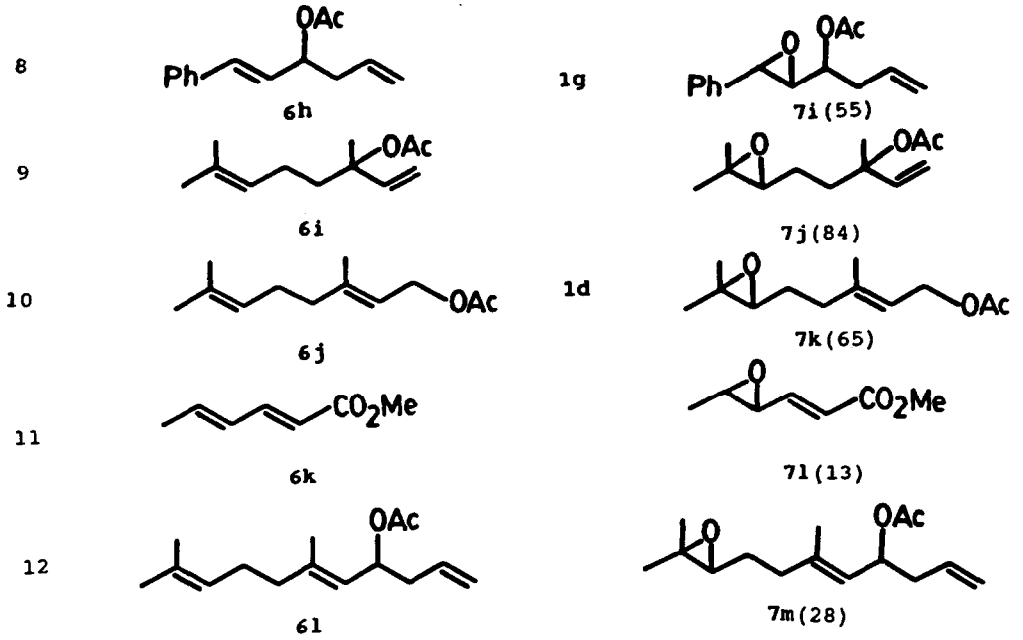
6c 7c 7d

Entry	Ligand	Yield (%)	
1	 1g	86	-
2	 1a	90	-
3	 1b	90	-
4	 1c	87	-
5	 1d	-	89
6	 1e	31	22
7	 1f	91	-

transformation only in modest yields. The formation of 2-hydroxy compound was suppressed considerably in the presence of acetic anhydride. The 2-acetoxy esters 5 were converted to the corresponding (E)-enoates 8 on treatment with triethyl amine in acetonitrile (Table 3).

Table 7. Cobalt(II) Catalysed Epoxidation of Various Alkenes with 2-MethylPropanal and Dioxygen

Entry	Alkene	Ligand	Products (Yield %)
1	 6a	1a	 7a  4i (86)
2	 6b		 7b(62)
3	 6c		 7c(91)
4	 6d		 7e(45)
5	 6e		 7f(15)
6	 6f		 7g(89)
7	 6g		 7h(65)

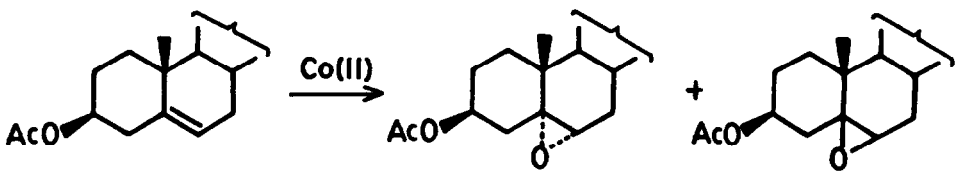


The addition of aldehydes to methyl acrylate was successful only if an excess of the latter is used. However, no adduct was formed if the aldehydes and methyl acrylate were used in stoichiometric amounts. Aldehydes mainly gave the corresponding carboxylic acid and 1,2-diketone under these conditions and no attempt was made to optimize the formation of these products. These reactions were also extended to other electron deficient alkenes using different cobalt(II) complexes. Thus, the treatment of aldehydes with acrylonitrile gave the corresponding 2-hydroxy and 2-acyloxy-4-oxonitriles respectively in moderate yields (Table 4, entries 1-5). These reactions can also be performed in the presence of acetic anhydride to give the corresponding 2-acetoxy-4-oxonitriles in good yields. Similarly, methyl methacrylate underwent a smooth reaction with propanal to furnish 2-hydroxy-2-methyl-4-oxoester as the only isolable product (Table 4, entry 8). The reaction with ethyl crotonate and propanal leads to a 1:1 mixture of syn and anti-diastereomers (Table 4, entry 9).

Reaction with Unactivated Alkenes. Cobalt(II) catalysed reaction of unactivated alkenes with aldehydes and dioxygen results in the formation of the corresponding epoxides. Thus, (E)-stilbene can be converted to anti epoxide with various aldehydes (Table 5). Best results are obtained by employing 2-methylpropanal, however, other aldehydes are also

efficient but afford moderate yields of the epoxides. A small amount of the corresponding syn epoxide is also observed in these reactions. Propanal and catalyst derived from ligand **1a** provide a mixture of anti and syn epoxides with the former as the major product whereas 2-methylpropanal affords the anti epoxide exclusively (Table 5, entries 1 and 2). The epoxidation of (E)-stilbene using citronellal results into the formation of the lactone besides trans-stilbene oxide (Table 5, entry 8). The lactone may be derived from citronellal via an epoxidation of

Table 8. Cobalt(II) Catalysed Epoxidation Of Cholesterylacetate with 2-Methylpropanal and dioxygen



6f 7g (α) 7g (β)

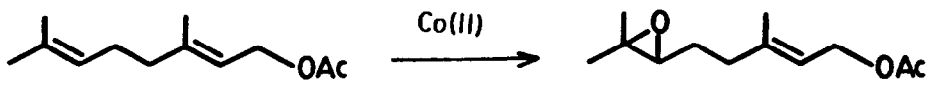
Entry	Ligand	Yield (%) α-Epoxide : β-Epoxide
1	**1a**	89(75:25)
2	**1g**	87(80:20)
3	**1d**	89(58:42)

the double bond followed by intramolecular cyclisation. The epoxidation of (E)-stilbene with 2-methylpropanal and dioxygen in the presence of various catalysts is presented in table 6. It is quite clearly evident from these results that the ratio of syn and anti epoxides is controlled by the nature of the ligand on the metal. Thus, catalyst from ligands **1a-b, 1d-f** and **1g** mainly provided the trans epoxides whereas catalyst **1c** favour the formation of the syn-epoxide (Table 6, entries 1-7). In view of these observations it can be concluded that the ligands derived from salicylaldehyde and amines or α-amino esters encourage the formation of the syn epoxide which may be formed via a radical process. A variety of alkenes were epoxidised using 2-methylpropanal and cobalt(II) catalysts derived from different ligands. All the catalysts from ligands **1a-g** mentioned in table 1 are capable of effecting the epoxidation and the results using these catalysts are presented in table 7. Styrene **6a** is a borderline case as both the addition of aldehyde and the epoxide are

obtained under these conditions, whereas 1-dodecene 6b was epoxidised in high yield without any observable addition product. The geometrically pure alkenes i.e. (E)-stilbene and (Z)-2-octene were smoothly transformed to the corresponding epoxides along with small amounts of the regioisomeric epoxides (Table 7, entries 3-4). 1,7-Octadiene was monoepoxidised in moderate yields whereas dienes with electronically dissimilar double bonds were chemoselectively epoxidised to the corresponding monoepoxides (Table 7, entries 5,7-11). It is noteworthy that in these cases no regioisomeric epoxides were observed which is in contrast to the similar epoxidation[9] using nickel(II) complexes. The monoepoxidation of the triene clearly indicates that these epoxidations are quite facile in the case of highly substituted double bonds (Table 7, entry 12).

The epoxidation of cholesteryl acetate was examined in the presence of different ligands under these conditions. It is noteworthy that the major product in each case was found to be the α-epoxide (Table 8) which

Table 9. Cobalt(II) Catalysed Selective Epoxidation of Geranylacetate with 2-Methylpropanal and Dioxygen



6j 7k

Entry	Ligand	Yield(%)
1	1g	60
2	1a	67
3	1c	65
4	1d	66

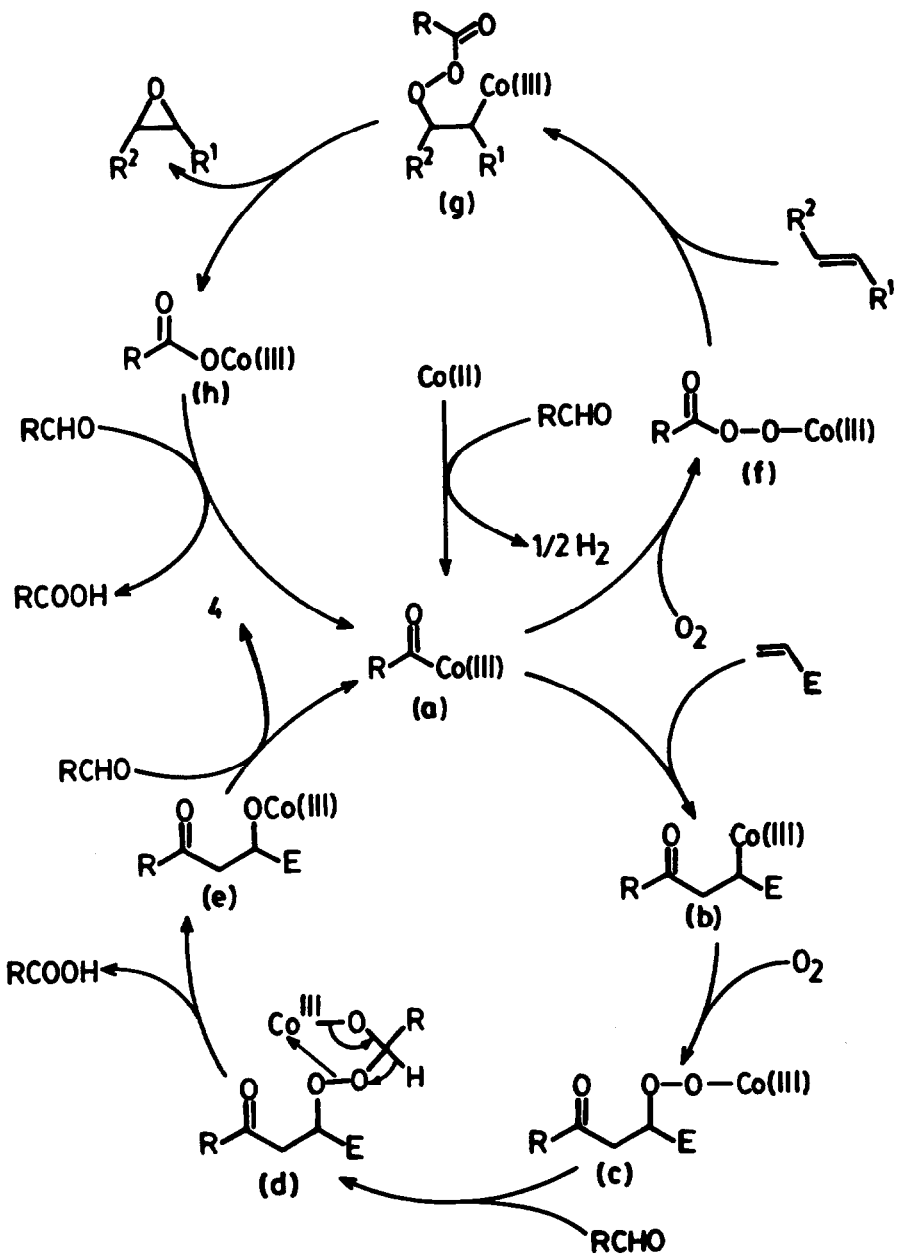
is similar to the reaction[10] using mCPBA. This observation clearly suggests that cobalt(II) catalysed epoxidations are mechanistically quite different from the corresponding nickel(II) promoted[9] epoxidations. The chemoselectivity during the epoxidation of dienes was further probed by using geranyl acetate and subjecting it to the epoxidation in the presence of different ligands (Table 9). It is clearly evident from

these studies that changing the ligand has no effect on the chemoselectivity of the epoxidation. However, there is slight effect on the chemical yield of epoxides by changing the ligand as indicated by some improvement in the yield of epoxidation in going from **1g** to **1a** .

MECHANISM

The dichotomous nature of these reactions suggests that a common intermediate may be involved whose reactivity is dependent upon the nature of the alkene. The catalytic nature of this reaction may be explained by an initial redox reaction of aldehyde with cobalt(II) to give an acylcobalt complex (**a**) (Scheme 2). The later will react with the electron deficient alkene to give an organocobalt adduct (**b**) which may undergo the insertion of dioxygen to yield a peroxycobalt intermediate (**c**). The reaction of (**c**) with aldehyde may provide a labile intermediate (**d**) which will fragment readily to afford the alkoxycobalt complex (**e**) and the corresponding carboxylic acid. A redox reaction between another molecule of aldehyde and the complex (**e**) may provide the 2-hydroxy-4-oxoesters or nitriles **4** and the acylcobalt complex (**a**) will be regenerated to complete the cycle. Alternatively, in the presence of unactivated alkenes the acylcobalt complex (**a**) will undergo the insertion of dioxygen, instead of addition to the alkene, to yield a peroxyacylcobalt species (**f**) which may react with the alkene to give a peroxyacyl organocobalt intermediate (**g**). A homolytic fragmentation of the later will afford the corresponding epoxide and the cobalt carboxylate (**h**) which may interact with aldehyde via redox process to regenerate the acylcobalt complex (**a**). The acylcobalt complex is known to undergo 1,4-addition to electron deficient alkene[3] under thermal or photochemical conditions. The cobalt(II) catalysed epoxidation of the alkenes with dioxygen is also known to occur via a β-peroxy radical which resembles[11] the proposed intermediate (**g**). The mechanism proposed in scheme 3 is in agreement with the observation that (E)-stilbene affords a mixture of anti and syn epoxides under these conditions. The formation of syn-stilbene oxide clearly suggests that these epoxidations are proceeding via a radical pathway. Thus, the peroxycobalt complex (**j**) obtained by the insertion of dioxygen on acylcobalt complex (**i**) will add to the alkene to give an β-peroxy organocobalt (**k**) where the carbon-cobalt bond may behave as a carbon-centered radical. Rotation around the bond and subsequent intramolecular fragmentation will afford the syn-epoxide (**7d**) (Scheme 3). Finally, the presence of a common intermediate (**a**) is demonstrated by performing the reaction in the

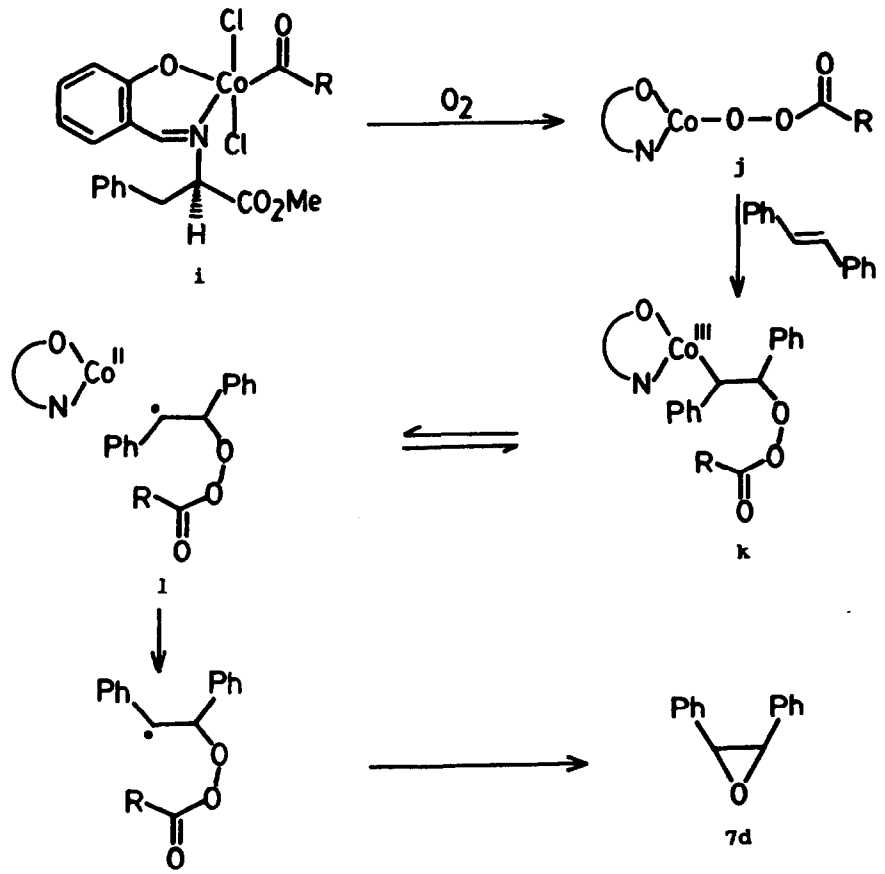
presence of a mixture of the electronically dissimilar alkenes. Thus, 2-methylpropanal reacted with both stilbene and excess of methyl acrylate



E=EWG

SCHEME 2

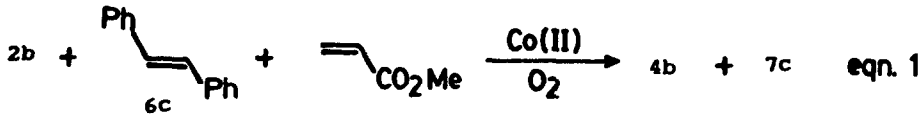
to afford a mixture of the corresponding epoxide 7c and 2-Hydroxy-4-oxoester 4b in good yields (eq. 1). In order to further



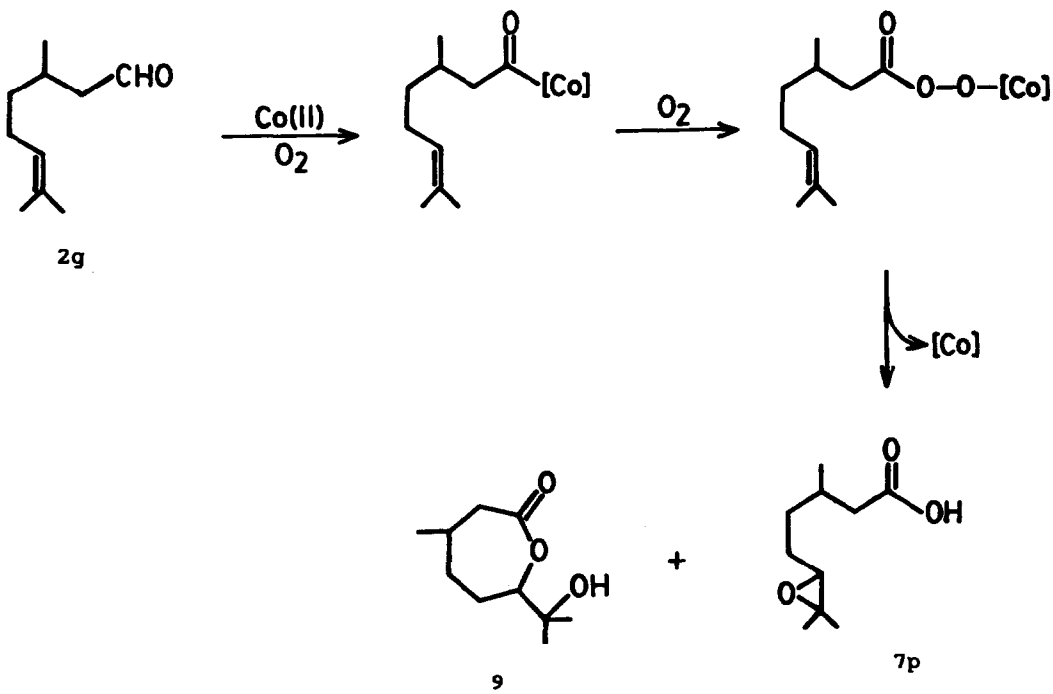
SCHEME 3

demonstrate the intermedicacy of a acylcobalt intermediate, we undertook a study on reaction with citranellal 2g which afforded a mixture of compounds from which two compounds were isolated in moderate yields (Scheme 4). The formation of the epoxy acid 7p and the lactone 9 clearly indicate that the products are obtained by intramolecular epoxidations which occur as a consequence to the incorporation of dioxygen in the initially formed acylcobalt complex from citronellal. The initially formed epoxy acid 7p undergoes intramolecular lactonisation to yield 9.

The above reaction clearly support that these transformations are proceeding via a common intermediate whose reactivity is dependent upon



the nature of the alkene. Further evidence in support of this mechanism is also reflected in the observation[12] that for each equivalent of 2 or 7,that is being formed, one equivalent of the corresponding carboxylic acid is also obtained. Finally, in order to prove the changes in the oxidation state of cobalt complex, as described in the catalytic cycle (Scheme 2), the reaction was followed by UV-visible spectroscopy. Thus,



SCHEME 4

the reaction between propanal 2a and methyl acrylate 3a was monitored periodically with UV-visible spectrometer and the spectrum at different time is presented in fig. 1. It is clearly evident that the cobalt(II) complex from ligand 1a (spectrum a, fig. 1) disappears after 15h (spec trum b, Fig. 1) and as soon as reaction goes to completion it reappears (spectrum c, Fig. 1). The UV-visible monitoring of the reaction strongly supports the catalytic cycle proposed in scheme 2.

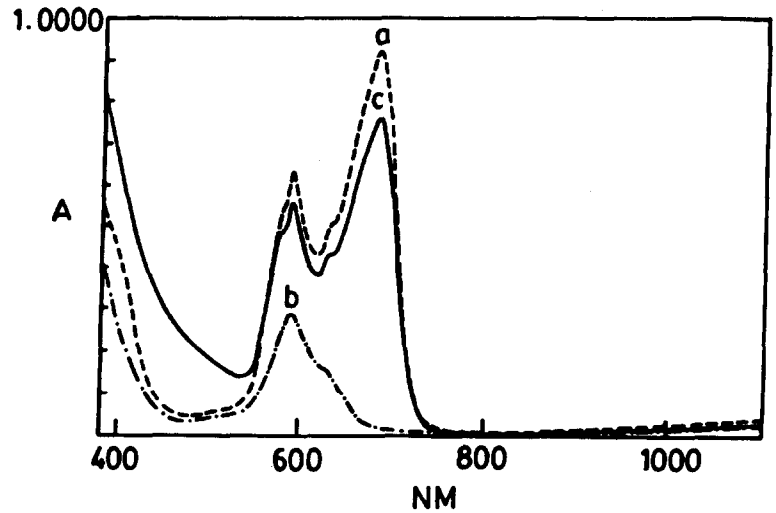


Fig1. UV-Visible spectra of the reaction between 2a and 3a with catalyst derived from ligand 1a. [a]Spectrum at the beginning of the reaction. [b]Spectrum of the reaction mixture after 15h. [c]Spectrum of the isolated catalyst after the completion of the reaction.

In conclusion, the cobalt(II) complexes derived from Schiff's bases are versatile catalysts for the reaction of aliphatic aldehydes with a wide range of alkenes in the presence of dioxygen. The electronic nature of alkene control the outcome of the reaction as the electron deficient olefins undergo addition of aldehyde followed by oxygen incorporation to yield 2-hydroxy(acyloxy)-4-oxo-esters or nitriles whereas unactivated and electron rich alkenes are converted to the corresponding epoxides. These reactions are shown to occur via a radical pathway and a common acylcobalt intermediate is proposed for the formation of 4 as well as the epoxides 7.

EXPERIMENTAL

Methods and Materials. Infra red spectra were recorded on a Perkin Elmer 1320 spectrometer. The ^1H NMR spectra were recorded on Bruker WP-80 and Jeol PMX-60 spectrometers. Elemental analysis was conducted using Coleman automatic C, H and N analyser. Analytical thin layer chromatography was performed on silica gel (Acme) coated glass plates. Column chromatography was performed using 100-200 mesh (Acme) silica gel or neutral alumina. Aldehydes and alkenes were purchased commercially and purified prior to use. The $CoCl_2$ was purchased from Loba (India) and it was heated to 110°C for 3h and crushed to powder before use.

General Procedure for the Synthesis of Epoxides. Aldehyde (10 mmol) and unactivated alkene (5 mmol) were added to a stirred solution of ligand and $CoCl_2$ (1:1) (~5 mol %) in anhydrous acetonitrile (30 mL). The mixture was stirred at room temperature under dioxygen baloon for 20-30 h. The solvent was evaporated in vacuo, and the residue was dissolved in ether. The ether layer was washed with saturated sodium bicarbonate solution (3x15 mL), brine solution (2x20 mL) and water (2x20 mL). Drying (Na_2SO_4) and evaporation yielded a residue which was purified by flash column chromatography.

General Procedure for the Synthesis of 2-Hydroxy and 2-acyloxy-4-oxoesters. Aldehyde (10 mmol) and electron deficient alkene (30 mmol) were added to a stirred solution of ligand and $CoCl_2$ (1:1) or $CoCl_2$ (5 mol %) in anhydrous acetonitrile (60 mL). The mixture was stirred at ambient temperature (25°C) for 20-24h. The workup and purification were followed as described in the above procedure.

General Procedure for the Synthesis of 2-Acetoxy-4-oxoesters. Aldehyde (10 mmol), electron deficient alkene (30 mmol) and acetic anhydride (30 mmol) were added to a stirred solution of ligand and $CoCl_2$(1:1) or $CoCl_2$ (~ 5 mol %) in anhydrous acetonitrile (60 mL). The mixture was stirred at ambient temperature (25°C) for 20-24h. The usual workup followed by column chromatography afforded the compound.

General Procedure for the Synthesis of Methyl-4-oxoenoates. Methyl 2-acetoxy-4-oxonoate (4 mmol) and triethylamine (5 mmol) were stirred at 50°C in acetonitrile for 4h. Removal of solvent followed by column chromatography yielded the compound.

Preparation of Schiff's Base Ligands. The Schiff's base ligands were prepared by the reaction of salicylaldehyde with methyl ester of

aminoacids and methyl benzyl amine. Bisoxazoline **1g** was prepared[13] accoroding to Masamune's procedure, however, tributyltinchloride was used as a catalyst for dehydration.

Ligand(1a). Prepared from salicylaldehyde and (S)-(-)-α-Methyl benzyl amine in 89% yield as yellow solid. ^{1}H NMR (CCl_4) δ 1.55(d, 3H, J=7.0Hz), 4.2(q,1H,J=6.0Hz), 6.5-7.0(m, 5H), 7.1(s,5H), 8.2(s,1H). IR(KBr): 2980,1620,1575 cm^{-1}. Anal. Calcd. for $C_{15}H_{15}ON$: C, 79.97; H, 6.70. Found:C, 80.00; H, 6.91. M.P.: 66-67°C.

Ligand(1b). Prepared from salicylaldehyde and valinol in 91% yield as yellow solid. ^{1}H NMR (CCl_4) δ0.9(d, 6H), 1.25-2.0(m, 1H), 2.85(q, 1H), 3.5(d, 2H) 6.4-7.1(m, 5H), 8.05(s, 1H). Anal Calcd. for $C_{12}H_{17}O_2N$: C, 69.54; H, 8.2. Found: C,69.56; H, 8.29.

Ligand(1d). Prepared from salicylaldehyde and Methyl ester of L-Methionine in 79% yield as brown colour oil. ^{1}H NMR (CCl_4) 2.0(s, 3H), 2.05-2.5(m, 4H), 3.7(s,3H), 4.05(t, 1H), 6.9(d, 3H), 7.05(d, 2H), 8.2(s,1H). Anal. Calcd. for $C_{13}H_{17}O_3NS$: C,58.42; H,6.40. Found: C,58.46; H,6.52.

Methyl 2-hydroxy-4-oxohexanoate (4a). Isolated as a clear liquid in 14% yield by column chromatography on silica gel. ^{1}H NMR (CCl_4) δ 1.1 (t, 3H, J=6.0Hz), 2.4 (q, 2H, J=6.0Hz), 2.8 (d, 2H, J=6.0Hz), 3.8 (s, 3H), 4.3 (t, 1H, J=6.0Hz). IR (thin film) : 3450, 2980, 1750, 1720 cm^{-1}. Anal. Calcd. for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found : C, 52.52; H, 7.45.

Methyl 2-hydroxy-5-methyl-4-oxo-hexanoate (4b). Isolated as a clear, colourless liquid in 13% yield by column chromatography on silica gel. ^{1}H-NMR (CCl_4) δ 1.0 (d, 6H, J=7Hz), 2.1-2.7 (m, 1H), 2.8 (d, 2H, J=7.0Hz), 3.8 (s, 3H), 4.2 (t, 1H, J=6.0Hz). IR (neat) : 3450, 2980, 1755, 1730 cm^{-1}. Anal. Calcd. for $C_8H_{14}O_4$: C, 55.15; H, 8.10. Found : C, 55.49; H, 8.34.

Methyl 2-hydroxy-4-oxoheptanoate (4c). Isolated as a clear, colourless oil in 13% yield by column chromatography. ^{1}H NMR (CCl_4) δ 1.0 (t, 3H, J=6.0Hz), 1.1-1.9 (m, 2H), 2.25 (t, 2H, J=6.0 Hz), 2.75 (d, 2H, J=6.0 Hz), 3.7 (s, 3H), 4.1 (t, 1H). IR (neat) : 3460, 2990, 1745, 1725 cm^{-1}. Anal. Calcd. for $C_8H_{14}O_4$: C, 55.15; H, 8.10. Found : C, 55.29; H, 8.23.

2-Hydroxy-5-methyl-4-oxohexanitrile (4e). Isolated as a clear liquid in 26% yield by column chromatography. ^{1}H NMR (CCl_4) δ 1.1 (d, 6H, J=7Hz), 2.2-2.75 (m, 1H), 2.95 (d, 2H, J=7Hz), 4.6-4.9 (t, 1H, J=6Hz). IR (neat)

3450, 2260, 1710 cm^{-1}.

Methyl 2-hydroxy-2-methyl-4-oxohexanoate (4g). Isolated as a clear, colourless oil in 37% yield by Kugelrohr distillation. ^1H NMR (CCl_4) δ 0.6-1.1 (t, 3H, J=6.0 Hz), 1.2 (s, 3H), 2.0-2.6 (q, 2H, J=6.0Hz), 2.45 (s, 2H), 3.6 (s, 3H). IR (neat) 3470, 1730 cm^{-1}.

Methyl 2-propionoxy-4-oxohexanoate (5a). Isolated as an oil in 23% yield by column chromatography on silica gel. ^1H NMR (CCl_4) δ 0.95(t,3H, J=6.0Hz), 1.10 (t, 3H, J=6.0Hz), 2.10 (q, 2H, J=6.0Hz),2.30 (q,2H, J=6.0Hz), 2.75 (d, 2H, J=6.0Hz), 3.6 (s, 3H), 5.15 (t, 1H, J=6.0Hz). IR (thin film) : 2980, 1750 cm^{-1}. Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.52; H, 7.40. Found : C, 55.61; H, 7.80.

Methyl 2-isobutyryloxy-4-oxoheptanoate (5b). Isolated as a clear, colourless oil in 21% yield by column chromatography on silica gel. ^1H-NMR (CCl_4) δ 1.0(d, 6H, J=7.0Hz), 1.2 (d, 6H, J=7.0Hz), 2.1-2.8 (m, 2H), 2.9 (d, 2H, J=6.0Hz), 3.8 (s, 3H), 5.6 (t, 1H, J=6.0Hz). IR (thin film) : 2985, 1765, 1750, 1720 cm^{-1}. Anal. Calcd. for $C_{12}H_{20}O_5$: C, 58.99; H, 8.20. Found : C, 59.09; H, 8.46.

Methyl 2-butyryloxy-4-oxoheptanoate (5c). Isolated as a clear oil in 31% yield by column chromatography on silica gel. ^1H NMR (CCl_4) δ 0.7(t,3H, J=6.0Hz), 0.9 (t, 3H, J=6.0Hz), 1.2-1.8 (m, 4H), 2.1(t, 2H, J=6.0Hz),2.35 (t, 2H, J=6.0Hz), 2.8 (d, 2H, J=6.0Hz), 3.6 (s, 3H), 5.2 (t, 1H, J=6.0 Hz). IR (thin film) : 2990, 1770, 1755, 1725 cm^{-1}. Anal. Calcd. for $C_{12}H_{20}O_5$: C, 58.99; H, 8.20. Found : C, 59.00; H, 8.67.

Methyl 2-acetoxy-4-oxohexanoate (5e). Isolated as an oil in 75% yield by column chromatography on silica gel. ^1H-NMR (CCl_4) δ 1.1 (t, 3H, J=6.0Hz), 2 (s, 3H), 2.35 (q, 2H,J= 6.0Hz), 2.8 (d, 2H, J=6.5Hz), 3.6 (s, 3H), 5.2 (t, 1H, J=6.0 Hz). IR (thin film) : 2980, 1770, 1720 cm^{-1}. Anal. Calcd. for $C_9H_{14}O_5$: C, 53.45; H, 6.90. Found : C, 53.65; H, 7.01.

Methyl 2-acetoxy-4-heptanoate (5f). Isolated as a clear, colourless oil in 72% yield by column chromatography on silica gel. ^1H NMR (CCl_4) δ 0.85 (t, 3H), 1.1-1.8 (m, 2H), 2.0 (s, 3H), 2.25 (t, 2H, J=6.0Hz), 3.7 (s, 3H), 5.15 (t, 1H, J=6.0Hz). IR (thin film) : 1770, 1720 cm^{-1}.Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found : C, 55.61; H, 7.71.

Methyl 2-acetoxy-5-methyl-4-oxohexanoate (5g). Isolated as a clear, yellow oil in 77% yield by column chromatography on silica gel. ^1H NMR (CCl_4) δ 1 (d, 6H, J=7.0Hz), 1.9 (s, 3H), 2.1-2.6 (m, 1H), 2.75 (d, 2H,

J=6.0Hz), 3.55 (s, 3H), 5.1 (t, 1H, J=6.0Hz). IR(neat) : 1740, 1710 cm^{-1}. Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found C, 55.34; H, 7.68.

Methyl 2-acetoxy-4-oxononanoate (5h). Isolated as a clear liquid in 71% yield by column chromatography. ^1H NMR (CCl_4) δ 0.9 (t, 3H), 1.1-1.8 (m, 6H), 2.0 (s, 3H), 2.35 (t, 2H), 2.8 (d, 2H, J=6.0Hz), 3.65 (s, 3H), 5.25 (t, 1H, J=6.0Hz). IR (neat) : 1760, 1725 cm^{-1}.

Methyl 2-acetoxy-4-oxodecanoate (5i). Isolated as a liquid in 72% yield by column chromatography on silica gel. ^1H NMR (CCl_4) δ 0.5-1 (t, 3H, J=6Hz), 1-1.7 (m, 8H), 2.0 (s, 3H), 2.1-2.5 (t, 3H, J=6.0Hz), 2.6-2.85 (d, 2H, J=6.0Hz), 3.6 (s, 3H), 5.1-5.35 (t, 1H, J=6.0Hz). IR (neat) : 1740, 1710 cm^{-1}. Anal. Calcd. for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found C, 60.33, H, 8.30.

2-acyloxy-5-methyl-4-oxohexanitrile (5k). Isolated as a clear, yellow oil in 11% yield by column chromatography on silica gel. ^1H NMR (CCl_4) δ 1.1 (d, 12H, J = 7.0 Hz), 2.2-2.8 (m, 2H), 2.85 (d, 2H, J = 6.0 Hz), 5.5 (t, 1H, J = 6 Hz). IR (neat) 2260, 1740, 1710 cm^{-1}.

2-acetoxy-5-methyl-4-oxohexanitrile (5l). Isolated as an oil in 56% yield by column chromatography. ^1H NMR (CCl_4) δ 1.1 (d, 6H, J=7.0Hz), 2 (s, 3H), 2.25-2.75 (m, 1H), 2.95 (d, 2H, J=6.0Hz), 5.4 (t, 1H, J=6.0Hz). IR (neat): 2260, 1740, 1710 cm^{-1}.

2-Acetoxy-4-oxohexanitrile (5n). Isolated as a clear liquid in 58% yield by column chromatography. ^1H NMR ($CDCl_3$) δ 1.2 (t, 3H, J=6.0Hz), 2 (s, 3H), 2.1-2.6 (q, 2H, J=6.0Hz), 2.8-3 (d, 2H, J=6.0Hz), 5.4-5.6 (t, 1H, J=6.0Hz). IR (CCl_4) 2230, 1740, 1705 cm^{-1}.

5,6-Epoxy cholesteryl acetate (7g). Isolated as a mixture of α:β (76:24) isomer (89%) by column chromatography on silica gel. ^1H NMR ($CDCl_3$) δ 2.9 (s, 1H), 2.0 (s, 3H), 1.8-0.8 (m, 44H). IR(KBr) : 2950, 1720, 1370, 1250 cm^{-1}. M.P. : α, 102°C; β, 112°C.

4-Acetoxy-5,6-epoxy-6-Phenyl-1-hexene (7i). Isolated as a colourless oil in 55% yield by column chromatography on silica gel. ^1H NMR ($CDCl_3$) δ 2 (s, 3H), 2.4 (t, 2H, J=6.0Hz), 2.9 (dd, 1H, J=2.0Hz and J=6.0Hz), 3.55 (d, 1H, J=2.0Hz), 4.5-6 (m, 4H), 7.1 (s, 5H). IR (neat) : 2900, 1725, 1630, 1360, 1230 cm^{-1}.

3-Acetoxy-3,7-dimethyl-6,7-epoxy-1-octene (7j). Isolated as a clear, colourless liquid in 84% yield by column chromatography on silica gel. ^1H

NMR ($CDCl_3$) δ 1.1(s,3H),1.2 (s, 3H), 1.45(s,3H), 1.85(s, 3H), 1.6-2.0(m,4H),2.4(t, 1H, J=6.5Hz), 4.8-5.2 (m, 2H), 5.45-6.0(m, 1H). IR (neat) 2900, 1725, 1630, 1360, 1240 cm^{-1}.

Methyl 4,5-epoxyhex-2-enoate (7l). Isolated as an oil in 13% yield by column chromatography on silica gel ^1H NMR($CDCl_3$) δ 1.1 (d, 3H, J=6.5Hz), 3.6 (s, 3H), 4.6 (s, 3H), 5.7-7 (m, 2H). IR(neat) : 2950, 1720, 1650, 1260.

4-Acetoxy-6,10-dimethyl, 9,10-epoxyundec-1,5-diene (7m). Isolated as an oil in 23% yield by column chromatography on silica gel. ^1H NMR($CDCl_3$) δ 1.1 (s, 3H), 1.25(s,3H), 1.4-1.7(m,4H), 1.6 (s, 3H), 1.85(s, 3H), 2.0-2.4(m, 3H), 4.6-5.0(m,2H),. IR (neat) : 3080, 1730, 1635, 1370, 1240 cm^{-1}.

Methyl 5-methyl-4-oxohex-2-enoate (8c). Isolated as a gum in 74% yield by column chromatography on silica gel. ^1H NMR (CCl_4) δ 1-1.4 (d, 6H, J=6.0Hz), 2.5-3 (m, 1H), 3.6 (s, 3H), 6.4 (d, 1H, J=14 Hz), 6.9 (d, 1H, J=14Hz) IR (neat) 1710, 1600 cm^{-1}. Anal. Calcd. for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found : C, 61.82; H, 7.51. λ_{max} Calcd. : 237 nm. Found : 234 nm.

Methyl-4-oxodec-2-enoate (8e). Isolated as an oil in 76% yield by column chromatography on silica gel. ^1H NMR (CCl_4) δ 0.6-1 (t, 3H,J =6.0Hz), 1-1.7 (m, 8H), 2.4-2.7 (t, 2H, J=6Hz), 3.65 (s, 3H), 6.2 (d, J=14 Hz), 7.0 (d, 1H, J=14Hz). IR (neat) 1710, 1600 cm^{-1}. Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found : C, 66.49; H, 8.90.

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