CHAPTER - 5
THEORETICAL

Cyclic phosphate derivatives:

Fatty acid phosphorus derivatives are well known for many years. Naturally occurring phosphorus derivatives of fatty acids play an important role in the life process of plants and animals. In recent years, interest has arisen in the synthesis and evaluation of new phosphorus derivatives of fatty acids for their possible utilization. Cyclic phosphate derivatives containing nitrogen are useful as antineoplastics and in mice showed improved anticancer effectiveness. Cyclic phosphate derivatives are also flame retardant in polypropylene and polystyrene.

Diamond et. al. prepared phosphorus containing esters of several naturally occurring long-chain hydroxy acids. The procedure involved the reaction of acids with phosphorus trichloride (PCl₃), phosphorus oxychloride (POCl₃), dialkyl phosphorus chloridates [(RO)₂ POCI] and dialkyl phosphite [(RO)₂ POH].

Many mixed phosphates were commonly prepared by the reaction of CH₃ P(O) Cl₂ with diethanolamine followed by the reaction with (CH₃)₃ SiNC₂ H₅ gave oxazaphosphalane (I) and CH₃ P(O) Cl₂ reacted with HOCH₂ H₄ NH CH₂ CH₂ OH gave II.
Cyclic phosphate derivatives were prepared by cyclization of HOCH₂C(CH₂Br)₂CH₂OH with POCl₃. However, when the reaction was carried out with amide and Ph₂C=N=OH, the mixed cyclic phosphate was formed.

Similarly, cyclic phosphate containing nitrogen derivatives were prepared by the reaction of R-P(O)(OPh)NRSiMe₃ with RCOCl followed by HCl. A number of chiral cyclo phosphoric acids were also prepared.

Phosporus containing halogen were prepared from Cl₃P(0)Cl₂ and Me(OH)CHCH₂OH in presence of Et₃N at -20 to 50°C. Dioxa phosphorins were also prepared by cyclization of C₂H₅P(0)Cl₂ with Ac₂CH₂ in the presence of Et₃N.

Magolda and Johnson prepared phosphoryl cholines via short-chain cyclic phosphate derivatives which was a new method to prepare phospholipids. A number of short-chain
phosphorus compounds containing heteroatoms\textsuperscript{127} were obtained by reacting RRNP(O)Cl with H\textsubscript{2}NCH\textsubscript{2}CH\textsubscript{2}SH.

\[
RRNP(O)Cl + H\textsubscript{2}NCH\textsubscript{2}CH\textsubscript{2}SH \rightarrow RRN - P(O)
\]

\[R = \text{Me, H}\]

A series of 1,3,2 - oxazaphospholanes\textsuperscript{128-130} had been prepared and studied conformationally by reacting pseudoephedrine with appropriate ZP(O)Cl\textsubscript{2} reagent.

\[
\text{Ph} -- \text{CH(OH)} -- \text{CH(Me)NHMe} + \text{ClP(O)Cl-Z} \rightarrow \text{Et}_{3}\text{N}
\]

\[Z = \text{OPh, O, Ph}\]

A number of long chain cyclic phosphates\textsuperscript{131} were prepared by treating neopentylen chloro or bromophosphite with aldehyde at 120\textdegree. Similarly the synthesis of the cyclic phosphate of the enolform of an alpha hydroxy carboxylic acid chloride is described. Alcohols are phosphorylated strictly stepwise by the novel three fold activated phosphorylating agent\textsuperscript{132}.

The synthesis of some new phosphorus containing derivatives of hydroxy fatty acids is undertaken as a part of our program to prepare novel fatty compounds for their possible use as agricultural chemicals, plasticizers, surface coatings, flame retardants and hydraulic fluids.
The present work describes the successful synthesis of phosphorus derivatives from hydroxy fatty acid esters using phosphorus oxychloride (POCl₃), 2-mercaptoethanol, ethanol amine and ethylene diamine as reagents.
DISCUSSION

Reaction of palmitoyl alcohol (32) with 2-mercaptoethanol, ethanol amine and ethylene diamine.

Palmitoyl alcohol (32) was prepared by the reduction of methylhexadecanoate with lithium aluminium hydride. Compound (32) was allowed to react with phosphorus oxychloride in presence of triethyl amine in anhydrous ether at 0° to give dichlorophosphate (33). The reaction mixture was then treated separately with three different reagents like 2-mercaptoethanol, ethanol amine and ethylene diamine in presence of triethyl amine at room temperature. The stirring was continued for twelve hours. The dichlorophosphate (33) was completely converted into cyclic phosphates (34, 35, 36). Reactions are monitored on TLC plates. After work up and column chromatography separation, the pure cyclic phosphate derivatives were obtained.

\[
\text{CH}_3 - (\text{CH}_2)_{14} - \text{CH}_2\text{OH} + \text{POCl}_3 \\
\text{(32)}
\]

\[
\text{Et}_3\text{N}, \text{ dry ether, } 0°
\]

\[
[ \text{CH}_3 - (\text{CH}_2)_{14} - \text{CH}_2\text{O} - \text{P(0)Cl}_2 ]
\text{(33)}
\]

\[
\begin{align*}
\text{Et}_3\text{N,} \\
\text{H}_2\text{NCH}_2\text{CH}_2\text{NH}_2
\end{align*}
\]

\[
\begin{align*}
\text{R} - &\text{CH}_2 - \text{O} - \text{P(O)} \\
\text{(34)}
\end{align*}
\]

\[
\begin{align*}
\text{Et}_3\text{N,} \\
\text{H}_2\text{NCH}_2\text{CHOH}
\end{align*}
\]

\[
\begin{align*}
\text{R} - &\text{CH}_2 - \text{O} - \text{P(O)} \\
\text{NH} \\
\text{H}_2\text{NCH}_2\text{CH}_2\text{NH}_2
\end{align*}
\text{(35)}
\]

\[
\begin{align*}
\text{R} - &\text{CH}_2 - \text{O} - \text{P(O)} \\
\text{NH} \\
\text{H}_2\text{NCH}_2\text{CHOH}
\end{align*}
\text{(36)}
\]

R = (CH_2)_{14} - CH_3
Characterization of Product (34):

The TLC homogeneous oily product analysed for 

$C_{18}H_{37}O_{3}PS$. Its IR spectrum showed no bands for free hydroxy group (3500 cm$^{-1}$). The condensation of reagents with hydroxy function was evidenced by the appearance of bands at 1735 (R - O - P (O) -) $^{133}$, 1460 (CH$_2$S) and 1390 cm$^{-1}$ (O-CH$_2$). The NMR spectrum supported clearly to the structure of (34) by showing diagnostic signals at $\delta 4.0$ as a triplet for methylene protons attached to oxygen (R - CH$_2$ - O), $3.7$ as a triplet for O-CH$_2$ and $2.8$ as a triplet for methylene protons attached to sulphur (S - CH$_2$) in phospholane ring. These data supported the formulation of (34) as palmitoyl 1,3,2 - oxasulphaphospholanes.

The cyclic phosphate (34) was substantiated by a study of its mass spectrum. It did not show the molecular ion peak at m/z 364. The highest ion peak observed at m/z 285 (M - 79, 10) along with m/z 259 (M - 105, 10), 258 (M - 106, 20), 257 (M - 107, 85). Alpha cleavage of phosphorus containing ring was observed at m/z 123 (10) and also phospholane moiety was observed at m/z 139 (10). Other small fragments at m/z 239 (10) and 183 (50) which confirm the structure as palmitoyl 1,3,2 - oxasulphaphospholanes (Scheme - XVII).
m/z 364 (M⁺, absent)

\[ R = \text{CH}_3(\text{CH}_2)_{12} \]

Scheme-XVII
Characterization of Product (35):

The compound (35) was analysed for C_{18}H_{38}O_{3}PN. The IR spectrum showed bands at 3400 (NH), 1750 (R – O – P(O) –), 1210 (NH – CH_{2} –) and 1130 cm\(^{-1}\) (P =O). The NMR of this compound also supported its structure. It gave signals at \(\delta 3.5\) as a triplet for methylene protons attached to oxygen (OCH_{2}), 1.7 as a multiplet for methylene protons attached to nitrogen and a D_{2}O exchangeable proton of N – H at 1.5. Thus the structure of (35) was assigned as palmitoyl –1,3,2, oxazaphospholane.

The mass spectrum has no molecular ion peak at m/z 347. The alpha, beta and gamma cleavage from phosphorus are at m/z 106 (80), 122 (20) and 136 (10) respectively. The presence of fragment at 289 (10) arising due to the loss of (NH–CH_{2}–CH_{2}O) from molecular ion established the position of phospholane group. Other significant mass ions were appeared at 263 (M – C_{4}H_{7} NO, 15), 262 (263 – H, 10), 261 (262 – H, 40), 260 (261-H,10), 259 [289 – (CH_{2})_{2},10], 225 (10), 58 (106-PONH,20), and 57 (58 – H, 100) (Scheme – XVIII).

Characterization of Product (36):

Elemental analysis of the product (36) corresponded to formula C_{18}H_{39}O_{2}PN_{2}. The IR spectrum of compound (36) exhibited characteristic bands at 3400 (NH), 1700 (R – O –
$R = CH_3-(CH_2)_2$

$m/z$ 347 ($M^+$, absent)

$R = CH_3-(CH_2)_{12}$

Scheme-XVIII
P(O)-, 1230 (NH - CH2-) and 1180 cm⁻¹ (P =O). In the NMR spectrum, a D₂O exchangeable proton observed at δ 5.8 as a singlet peak for NH, a triplet at 3.7 for methylene protons attached to oxygen and a triplet at 2.3 for methylene protons attached to nitrogen of phospholane ring. On the basis of spectral and combustion data the structure of the product (36) was formulated as palmitoyl 1,3,2 - diazophospholane.

The above structure was further supported by its mass spectrum having no molecular ion peak at m/z 346. The position of phospholane moiety was indicated by alpha and gamma cleavages at m/z 285 (10) and 257 (20) respectively at C-1, besides other significant peaks at m/z 256 (257 - H, 15), 225(20), 135 (M - 211, 10), 129 (40), 121(15), 105(20), 73(90), 57(80) and 43(100) (Scheme - XIX).

Reaction of methyl 12-hydroxy -cis-9-octadecenoate (37) with 2 - mercaptoethanol, ethanol amine and ethylene diamine:

The reaction of methyl 12-hydroxy - cis - 9-octadecenoate (37), with phosphorus oxychloride in presence of triethylamine gave dichlorophosphate derivative which was again treated separately with 2- mercaptoethanol, ethanol amine and ethylene diamine to yielded products (39 - 41).
Scheme-XIX

R = CH$_3$-(CH$_2$)$_{12}$
Characterization of Product (39):

The elemental analysis of the product (39) corresponded to the formula $C_{21}H_{39}O_5$ PS. The non appearance of a band at 3500 cm$^{-1}$ indicated the absence of hydroxy group in the product. A broad band centred at 1740 cm$^{-1}$ suggested the presence of ester as well as ester type phospholane group. Other bands were present at 1460 (CH$_2$-S), 1370 (O-CH$_2$) and 1170 cm$^{-1}$ (P = O). The NMR spectrum exhibited multiplets at $\delta$ 5.4 and 3.9 for olefinic and methine protons. A triplet observed at 3.8 and 2.7 for ring methylene protons attached to oxygen and sulphur respectively. These data suggested the structure (39) as methyl - 12 (1,3,2-oxasulphaphospholane) - 15 - 9 - octadecenoate.

The mass spectrum did not show molecular ion peak at m/z 434. The other significant peaks at m/z 355 (10), 295 (20) and 294 (295 - H, 35) showed the position of ring.
Alpha cleavage ion at m/z 237 (10) also confirmed phospholane ring at C - 12. Beside these ions, other ion peaks at m/z 139 (M - 295, 15) and 123 (M - 316, 100) of phospholane ring also contributed towards the assigned structure. Other fragment ions were present at m/z 197 (20), 91 (10), 85 (20) and 61 (25) (Scheme - XX).

Characterization of Product (40):

The compound (40) gave microanalysis for C_{21}H_{40}O_{5}PN. The IR displayed characteristic bands at 3400 (NH), 1740 & 1730 (R-O-P(O) and COOCH_3), 1240 (NH - CH_2 - ) and 1170 cm^{-1} (P=O). The NMR spectrum showed multiplets at 6 5.3 for olefinic protons and 2.5 for protons attached to oxygen. Two significant signals, a D_2O exchangeable singlet for NH proton at 1.9 for NH and a multiplet at 1.6 for methylene protons attached to nitrogen were also observed. On the basis of IR and NMR data, the product (40) was formulated as methyl 12-(1,3,2-oxazaphospholane) - cis-9- octadecenoate.

Mass spectrum of this compound agreed with the assigned structure by showing the peaks at m/z 295 (20), 296 (10) and 297 (30) arising from the rupture of C - O bond and other fragment at 106 (M - 311, 15) (Scheme - XXI).

72
m/z 434 (M+, absent)

\[ R = \text{CH}_3-(\text{CH}_2)_5 \]

\[ R' = \text{CH}_2-\text{CH}==\text{CH}-\text{(CH}_2)^7-\text{COOCH}_3 \]

Scheme-XX
$m/z$ 417 ($M^+$, absent)

$R = \text{CH}_3(-\text{CH}_2)_5$

$R' = \text{CH}_2-\text{CH}=\text{CH}-(\text{CH}_2)_7-\text{COOCH}_3$

Scheme-XXI
Characterization of Product (41):

Elemental analysis of the TLC homogenous product (41) corresponded to formula C_{21}H_{41}O_4PN_2. Its IR spectrum displayed bands at 3400 (NH), 1740-1705 [R-O-P(O) and COOCH], 1230 (NH – CH₂) and 1170 cm⁻¹ (P = O). The NMR spectrum gave conclusive support in favour of structure (41) by displaying characteristic signals at δ 5.4 a multiplet for olefinic protons, two D₂O exchangable proton for two NH groups observed at 5.1, a multiplet at 3.8 for methine proton (CH-0) and a triplet at 2.4 for four methylene protons of ring. The spectral data suggested the structure of compound (41) as methyl - 12 (1,3,2 - diazophospholane) - 9 - octadecenoate.

The mass spectrum of (41) further supported the structure. It did not show the molecular ion peak at m/z 416. The alpha cleavages at m/z 220 (20), 197 (10), 331(20) and 85 (15) confirm the structure (41). The C - O cleavage also showed the characteristic ion peaks at m/z 295 (20) and 121(30). Other peaks observed at m/z 293 (295-3H, 70), 262 (M-C₉H₁₄O₂, 40), 263 (260 + 3H, 45), 105 (15) and 73 (60) (Scheme - XXII).
m/z 416 (M⁺, absent)

R = CH₃-(CH₂)₅

R' = CH₂-CH=CH-(CH₂)₇-COOCH₃

Scheme-XXII
Reaction of methyl 9-hydroxy -cis-12-octadecenoate (38) with 2-mercaptoethanol and ethanol amine.

The reaction of methyl 9-hydroxy -cis-12-octadecenoate (38) was treated with phosphorus oxychloride in presence of triethylamine. The reaction gave dichlorophosphate derivative which was again treated separately with 2-mercaptoethanol and ethanol amine and triethyl amine to afford products (42, 43).

Characterization of Product (42):

Microanalysis of product (42) gave the composition as C_{21}H_{39}O_5PS. The IR spectrum had a characteristic broad band centered at 1740 (COOCH_3, R - O - P(0) ). The NMR spectrum of the compound exhibited signals at δ 5.3 a multiplet for olefinic protons and 3.9 for methine proton attached to oxygen (CH\_O). Two triplets at 3.8 and 2.7 indicated the presence of methylene protons attached to oxygen and sulphur in the ring. On the basis of above spectral and combustion data the structure of the product (42) was formulated as methyl 9- (1,3,2, -oxasulphaphospholane) -cis- 12-octadecenoate.

The above structure was further supported by its mass spectrum. It did not show the molecular ion peak at m/z 434. The usual C - O fragment ions were observed at m/z 295 (30) and 139 (25) besides alpha cleavages of carbon having phosphorus group at m/z 309(10), 277 (20), 157(15) and 125...
Scheme-XXIII

$$m/z \ 434 \ (M^+, \ absent)$$

\[ R = \text{CH}_3-(\text{CH}_2)_4-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2 \]

\[ R' = (\text{CH}_2)_7-\text{COOCH}_3 \]
The other characteristic peak was observed at m/z 331 (M-C₅H₁₁O₂,40) 294 (295 - H,70), 263 (295-32,40), 262 (35) and 123(60) (Scheme - XXIII).

Characterization of Product (43):

The compound (43) was indicated to be its elemental analysis C₂₁H₄₀O₅PN. The IR spectrum exhibited bands at 3400 (NH), 1740 (R - O - P(O),1700 (ester CO), 1250 (NH - CH₂), 1170 cm⁻¹ (P = O). The NMR spectrum showed at 5.3 a multiplette for olefinic protons and at 3.8 for methine proton attached to oxygen. A D₂O exchangeable proton showed for NH proton at 1.8 and a triplet at 2.3 for methylene proton attached to nitrogen. A triplet at 3.7 for methylene protons attached to oxygen of phospholane group attached to C-9 is also observed. These spectral data confirmed the structure (43) as methyl 9-(1,3,2-oxazophospholane)-12-octadecenoate.

The mass spectrum of above further supported the structure. It did not show the molecular ion peak at m/z 417 the alpha cleavages along with three hydrogens observed at m/z 295 (70) and 263(30) confirmed the position of phosphate group at C - 9. Other prominent peaks were observed at m/z 296 (295 + H, 20) and 122 (60) showed the C - O cleavage of the phospholane group. Besides other, usual ion peaks observed at m/z 264 (263 + H,40), 157 (20), 125 (40) and 106 (30) (Scheme - XXIV).
m/z 417 ($M^+$, absent)

\[ \text{R} = \text{CH}_3-(\text{CH}_2)_4-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2 \]

\[ \text{R'} = (\text{CH}_2)_7-\text{COOCH}_3 \]

Scheme- $\times \times \times \times \imes$
EXPERIMENTAL

All melting points were observed on a Kofler apparatus and are uncorrected. All melting points are given in degree centigrade. Infrared (IR) spectra were determined using a Perking-Elmer 621 and Pye Unicam SP-3-100 spectrophotometer. IR values are given in cm$^{-1}$. Ultraviolet (UV) spectra were recorded on a Perkin Elmer 202 ultraviolet visible spectrophotometer. Nuclear magnetic resonance (NMR) spectra were run on a varian A 60 instrument. Chemical shifts are reported as (ppm) relative to tetramethyl silane (TMS). Mass spectra were measured with a JEOL JMS-D300 at 70 eV. In the absence of accurate and deuterated mass spectra the fragmentation pattern shown in discussion part may be considered as tentative. Thin layer chromatographic (TLC) plates were coated with silica gel G and sprayed with a 30% aqueous solution of perchloric acid. Petroleum ether (Pet ether) refers to a fraction of b.p 40° - 60°. The abbreviations s, d, t, m, and br denote singlet, doublet, triplet, multiplet and broad respectively. Column chromatography was carried out with silica gel G (60 - 120 mesh) using 25 - 30 g per g of material to be separated. Elution was usually effected with petroleum ether containing increasing proportions of diethyl ether. Mixture of petroleum ether (bp 40° -60°) and diethyl ether will be
referred to as PE followed by numericals to indicate the relative volumes.

With a view to limit the size of the thesis the various spectral data necessary for structure determination are only discussed. The data normally associated with fatty compounds have been deliberately omitted.

The starting materials used were either of commercial grade [10-undecenoic and octadec-(Z)-9-enoic (oleic) acid] or isolated from natural sources [12-hydroxy octadec-(Z)-9-enoic (ricinoleic) and 9-hydroxy octadec-(Z)-12-enoic (isoricinoleic) acids from Racinus communis and Wrightia tinctoria seed oils respectively, following Gunstone's partition procedure; 12,13-epoxy-(Z)-9-octadecenoate from Vernonia anthelmintica seed oil. Their methyl esters were prepared by the usual method (H+/CH₃OH). General (G.R.) grade of solvents were employed for extraction purposes and when required solvents were dried and distilled before use.

Preparation of (E)-2-enoic Acids:

The (E) - 2-hexadecenoic acid was prepared from palmitic acid following the method of Palameta and Prostenik as adopted in author's laboratory as a standard procedure.
General Procedure:

To a well stirred mixture of saturated acid (50g) and red phosphorous (2.3g), dry bromine (25ml) was added dropwise at 90° during a period of 7 hours. The mixture was vigorously stirred during the addition of bromine by using a mercury-sealed stirrer. Heating was continued for 24 hours and the cooled solution was poured into cold water and left overnight. The product taken up in ether, washed successive by 10% aqueous sodium sulphite and distilled water and dried over sodium sulphate (Na₂SO₄). The 2-bromoacid obtained after evaporation of the ether was refluxed with powdered potassium iodide (48g) in 95% ethanol (350 ml) for 6 hours. To the cooled solution potassium hydroxide (32g) was added and the mixture was refluxed for another 4 hours. Most of the alcohol was removed under reduced pressure and residue diluted with water, acidified with (dil.) hydrochloric acid and extracted with water and dried. After evaporation of the solvent, a mixture of alpha, beta unsaturated and their co-products, i.e. 2-hydroxy and 2-ethoxy acids were obtained.

The 2-hydroxy acids were separated from alpha, beta unsaturated acids as copper chelate by treatment with cupric acetate in ethanol and acetic acid. The remaining two components obtained after removal of 2-hydroxy acids were fractionated by silicagel column chromatography to afford the
individual components. Pure alpha, beta unsaturated acid was isolated by elution with pet. ether - ether (95 : 5, v/v) as a white product (yield 52%), crystallized in pet. ether-ethanol (75 : 25, v/v). The 2- enoic acids on acid catalyzed esterification yielded their corresponding esters. M.P.54° (lit. 84 m.p.53.5°).

Analysis: (Found : C, 75.47; H, 11.85; C_{16}H_{30}O_{2} requires; C, 75.53; H, 11.89%). IR (CCl₄): 1730 (COOCH₃), 1650 (-CH = CH -) and 980 (trans unsaturation). NMR (CCl₄): 7.9 (d,d,1H, -CH = CH - CO₂CH₃, J = 15 and 5 Hz), 6.0 (d,1H, CH = CH - CO₂ CH₃, J = 15 Hz), 3.71(s, 3H, -CO₂CH₃), 2.42 (M,2H), 1.3 (br, s, chain CH₂) and 0.9 (t, 3H).

Preparation of methyl -4- oxohexadec - 2(E)- enoate (18) :
Methyl 4 - oxohexadec - 2 (E) enoate (18) was prepared by chromic acid oxidation of methyl hexadec - 2 (E) enoate. The chromic acid reagent was prepared by portion wise addition of chromium trioxide (8.5 g., 0.8 mole) to a mixture of acetic anhydride (30 ml) and glacial acetic acid (60 ml) followed by dilution with benzene (25 ml) under ice cooling. To this reagent (85 ml), a solution of compound (5) (5.5 g, 0.02 mole) in benzene (50 ml) was added dropwise with stirring over a period of two hours and the temperature of reaction mixture maintained between 10° and 20°. The reaction mixture was diluted with water neutralized with ag.NaOH and
extracted with ether. The etherial extract washed with water, dried over dry sodium sulphate and solvent removed in vacuo to give the product which was subjected to column chromatography over silicagel (60 -120 mesh). Elution with PE 5 gave (18). The solid product was crystallized from hexane yielding (10g, 20%), m.p. 68° (lit. m.p. 65 - 66°)

Preparation of methyl 4-oxo - 2(E)-hexadecanoate(19):

Methyl-4-oxo-2(E)-hexadecenoate(18) (1g, 0.005 mole) in absolute ethanole (15ml), 200mg of palladium charcoal was added and hydrogen gas was passed at a pressure of 20 psi for four hours. The reaction mixture was then filtered and the solvent was evaporated on water bath. The hydrogenated product was purified by silicagel column chromatography using PE-2 as eluent yielded solid product(19), (3.9 g, 70%), m.p. 42° IR (Nujol) : 1735 (COOCH₃), 1700 (C = O), 1180 (C-CO - C stretching and bending), NMR (CDCl₃): 3.68 (s, 3H, COOCH₃), 2.64 (two overlapping, t, J = 4Hz, 4H, CO - CH₂ -CH₂ - CO₂), 2.45 (t, J = 7Hz, 2H, CH₂ - CO), 1.28 (br, b, 20 H), 0.9 (distorted, triple, 3H).

Preparation of 3-amino-2-methyl-4-oxoquinazoline:

In a 500 ml round bottom flask, methyl anthranilate (918.14 g, 0.12 mole) and acetic anhydride (15 g, 0.15 mole) were heated for 15 minutes at 100°. The solution was cooled,
poured on ice, stirred and solid was filtered off, then washed with water and dried. The N-acetyl ester (22.5g, 0.13 mole), m.p. 98 - 99°, thus obtained was refluxed for 19 hours with hydrazine hydrate (10 ml) in ethanol (100 ml). The solution was evaporated and crystallized from benzene: petroleu (4 : 1 v/v) to give 3-amino-2 methyl -4-oxoquinazoline (16.5 g. 76%) m.p. 148-149° (lit. 152°)\(^{17}\).

Preparation of acetylinic fatty acids:

The method of kannam et al\(^{138}\) was adopted for the preparation of 10-undecynoic acid (m.p. 42° lit.\(^{138}\) m.p. 41 - 42°) and 9-octadecynoic (m.p. 45, lit\(^{138}\) m.p. 44 - 45°) acids involving bromination - dehydrobromination of the respective olefinic acids. Ames and Bowman’s method\(^{139}\) was used for the preparation of 9-undecynoic acid (m.p. 59°, lit\(^{138}\) m.p. 58 - 59°). Methyl esters 16,18,20) of 10-undecynoic, 9-undecynoic and 9-octadecynoic acids were prepared as usual with absolute methanol containing a catalytic amount of sulphuric acid.

Preparation of 10-undecynoic acid(11):

A solution of commercial 10-undecenoic (18.4g, 0.1 mole) acid in carbon tetrachloride (75 ml) was cooled in an ice bath and bromine (16.0g, 0.1 mole) was added dropwise. The mixture after addition of all bromine was stirred for 3 hours and left overnight. Distillation of carbon
tetrachloride and workup with diethyl ether furnished 10, 11-dibromoundecanoic acid (33.7 g) as a thick viscous liquid. A mixture of dibromide (33.7 g), potassium hydroxide (68.0 g), water (15 ml) and ethanol (300 ml) was refluxed on a water bath for 12 hours. Ethanol was then removed under reduced pressure and the resultant solid was dissolved in water, acidified with cold dil. Sulphuric acid and extracted with diethyl ether, washed and dried over anhydrous sodium sulfate. Removal of the solvent yielded the crude acid which was crystallized from petroleum ether at low temperature. The crystalline 10-undecynoic acid (9.1 g), thus obtained melted at 42° (lit. 138, m.p. 41 - 42°). Analysis (Found : C, 72.56 ; H, 9.95. C_{11}H_{18}O_{2} requires : C, 72.53; H, 9.89%).

Preparation of 9-octadecynoic acid (15):

Commercial octadec-9(Z)-enoic (oleic) acid 28.2 g, 0.1 mole in carbon tetrachloride (75 ml) was cooled and bromine (16.0 g, 0.1 mole) was added drop wise as described earlier. Distillation of the solvent followed by work up with diethyl ether gave 9, 10-dibromostearic acid (44.3 g) as a thick viscous liquid. A mixture of 9, 10-dibromostearic acid (44.3 g), potassium hydroxide (88.4 g), water (15 ml) and ethanol (300 ml) was refluxed on a water bath for 12 hours. Evaporation of the solvent, acidification with cold dil. sulphuric acid and workup with diethyl ether, drying and
Evaporation of the solvent afforded the crude acid. The crude acid was crystallized from petroleum ether at low temperature. The crystalline 9-octadecynoic acid (126 g.) melted at 45° (lit.138, m.p. 44 - 45°). Analysis (Found : C, 77.12; H, 11.48 C₁₈H₃₂O₂ requires : C, 77.09; H, 11.50%).

Preparation of 9-undecynoic acid (13):

10, 11-Dibromoundecanoic acid (33.7 g) was added to a solution of potassium hydroxide (52.0 g) in water (25 ml) and the mixture was heated in an open flask so that the internal temperature rose slowly to 180° and remained there for 30 minutes. It was then dissolved in water (120 ml), acidified with cold dil. Sulphuric acid and was extracted with diethyl ether. The removal of the solvent gave a non-crystallizable oil which revealed two spots of very close Rf values on the TLC plate.

The oil was subjected to silica gel column chromatographic fractionation. Elution with petroleum ether gave 9,10-undecadienoic (allenic) acid (2.7 g) as a liquid. Analysis (Found : C: 72.47; H, 9.85. C₁₁H₁₈O₂ requires : C; 72.53; H, 9.89%).

Subsequent elution (PETO) gave 9-undecynoic acid (13,10.92 g) as a white crystalline solid and melted at 59°.
(lit138, m.p. 58 - 59°). Analysis (Found: C, 72.45; H, 9.83. \( C_{11}H_{18}O_2 \) requires; C, 72.53; H, 9.89%).

Preparation of lead tetracetate (LTA):

\( \text{Pb}_3\text{O}_4 + 8\text{C}_2\text{H}_3\text{O}_2 \rightarrow \text{Pb} (\text{C}_2\text{H}_3\text{O}_2)_4 + 2\text{Pb} (\text{C}_2\text{H}_3\text{O}_2)_2 + 4\text{H}_2\text{O} \).

A mixture of 45 g of glacial acetic acid and 10 g of acetic anhydride is placed in a 1 litre flask (3 necked) provided with a thermometer and a mercury sealed stirrer. The liquid is vigorously stirred, heated to 55 - 60° and 25 g of dry red lead powder is added in portions of 2.3 g. A fresh addition is made only after the colour due to the preceding portion has largely disappeared. The temperature was not allowed to rise above 65°. Towards the end it may be necessary to warm the flask continuously to above 80° in order to complete the reaction.

At the end of the reaction, the thick and somewhat dark solution is cooled and the precipitated LTA is filtered off (mother liquor is kept aside) and washed with glacial acetic acid. The crude product without being dried is dissolved in hot glacial acetic acid, containing a little acetic anhydride. The solution is treated with a little decolourising carbon, filtered through a hot water funnel and cooled. The white crystalline product is filtered off and dried in vacuum desiccator over KOH pellets. The yield of LTA is about 12 g.
Preparation of Palmitoyl alcohol\textsuperscript{141}(32)

Methyl palmitate (10g) was dissolved in dry ether (500 ml) and added to a stirred suspension of lithium aluminium hydride (2g) in dry ether (200 ml). After stirring for 10 minutes at room temperature, excess of hydride was carefully destroyed by the caution addition of wet ether and then water. Dil. sulfuric acid (2 lit, 2M) was added and the palmitoyl alcohol extracted with ether and dried. A white solid product was obtained which on crystallization yielded palmitoyl alcohol m.p. 50° (lit\textsuperscript{142} m.p.54°). IR (Nujol): 3350 (OH). NMR (CCl\textsubscript{4}): 4.6 (m, 2H, CH\textsubscript{2} - OH), 2.6 (br, s, 1H, OH, D\textsubscript{2}O exchangeable), 1.3 (br, s chain CH\textsubscript{2}) 0.9 (t, 3H, CH\textsubscript{3}).

Preparation of Epoxy fatty esters from olefinic fatty esters

A conventional method of Gunstone and Jacobsberg\textsuperscript{111} was used for the preparation of methyl 10, 11-epoxy undecanoate (23) and methyl 9, 10 - epoxy-octadecanoate (26).

Preparation of methyl 10 ,11 - epoxy-undecanoate (23):

An equimolar amount of methyl 10- undecanoate (10 g 0.05 mole) reacted with m-chloroperbenzoic acid (m CPBA) (8.5g, 0.05 mole) in chloroform (200 ml) at room temperature for 3 -4 hours. Usual extraction and purification by silicagel column chromatography at PE 3% gave(23) (6 g). IR
Preparation of Epoxide

The first report on the preparation, characterization and application of *m*-chloroperbenzoic acid (*m* CPBA) dates back of 1955, when the epoxidation of trans-stilbene was described by Lynch and Pansacker\(^{112}\). Subsequently this versatile reagent of unique property was found to oxidise diverse class of compound under generally mild conditions\(^{113}\). Gunstone and Jacobsberg\(^{114}\) have successfully exploited *m*-CPBA with long-chain unsaturations. Now the reagent is widely used for a number of preparations especially epoxidation, both of short as well as long-chain substrates but in fact, on laboratory scale. The epoxide was also prepared by a different route, using a procedure in which iodohydrin was converted to the corresponding epoxide\(^{115}\).

Preparation of methyl 9,10-epoxy octadecanoate (26):

Reaction of methyl octadec-9(\(Z\))-enoate (3) (15 g, 0.05 mole) was carried out in chloroform (300 ml) using *m*-CPBA (8.5 g, 0.05 mole) under similar conditions as stated earlier, yielded product (26) (13.5 g). IR (nujol): 1740 (COOCH\(_3\), 1285, 1240 (C - C and C - O ring), 1185, 1170 (C - O)
and 870 cm\(^{-1}\) (epoxy group). NMR (CDCl\(_3\)): 3.6 (s, 3H, COOCH\(_3\)), 2.7 (t, 2H, -CH - CH - ), 1.3 (br, s, Chain CH\(_2\)), 0.9 (t, 3H, CH\(_3\)).

**Extraction of Epoxy Acid from *Vernonia anthelmintica* Seed Oil**

The seed samples were purchased by commercial seed suppliers. The oils were extracted repeatedly with petroleum ether (bp. 40 - 60\(^\circ\)) in a soxhlet apparatus. The analytical values of seed and oil were determined according to AOCS methods\(^{109}\).

Seed oil was refluxed with ethanolic potassium hydroxide. The unsaponifiable material was removed by diethyl ether extraction and the free fatty acids were obtained by acidification with dil. H\(_2\)SO\(_4\) of aqueous layer followed by extraction with diethyl ether.

The methyl ester of *V. anthelmintica*\(^{110}\) seed oil was transesterified with 0.5% NaOMe solution under reflux for 20 minutes; cooled and then acidified with acetic acid. After usual work up, methyl vernoleate (29) was separated into non-oxygenated and oxygenated fractions by preparative TLC, using silicagel G.

**General procedure for the preparation of Aziridines/Azirines:**

Equimolar amount of methyl ester of olefinic/acetylenic fatty acids and 3-amino-2-methyl-4-oxoquinazoline in dry
Dichloromethane was stirred for 15-20 minutes followed by the addition of lead tetracetate (LTA) in several portions over 3-hours duration. The reaction mixture was further stirred for additional 30 minutes, filtered and washed with dry dichloromethane. The combined filtrate and washing on evaporation to dryness gave reaction products.

Reaction of methyl undec-10-enoate (1) with 3-amino-2-methyl-4-oxoquinazoline in presence of LTA:

Methyl undec-10-enoate (1) (1.9 g, 0.01 mole) on reaction with 3-amino-2-methyl-4-oxoquinazoline (0.8g, 0.01 mole) as detailed above in the presence of LTA (4g, 0.01 mole) gave an oily product. This on separation by column chromatography afforded the product (2) (1.1 g, 33%) with PE 60 as solid, m.p. 55° along with unreacted ester.

Analysis—(Found: C, 67.87; H, 7.85; N, 11.29%; Calcd. for C_{21}H_{29}O_{3}N_{3}: C, 67.90; H, 7.86; N, 11.31%). IR (nujol): 1725 (COOCH_{3}) 1695 (\text{C=O}), 1605, 775 (unsaturation of quinazoline ring), 1210 (N-N), 110 (C-N), 1020 (\text{-C-O-}), 835 (aziridine ring moiety). NMR (CDCl_{3}): 8.2 (m, 2H, quinazoline ring), 7.6 (m, 2H, quinazoline ring), 3.65 (s, 3H, COOCH_{3}), 2.7 (s, 3H, quinazoline ring CH_{3}), 2.67 - 2.38 (m, 3H, methylene and methine protons of aziridine ring), 2.3 (m, 2H, CH_{2} - COOCH_{3}), 2.15 (m, CH_{2} alpha to aziridine ring) 1.28 br, s, Chain CH_{2}. Ms: m/z, 371(M).
Reaction of methyl octadec-9(Z)-enoate (3) with 3-amino-2-methyl-4-oxoquinazoline in presence of LTA:

Reaction of methyl octadec-9(Z)-enoate (3) (3 g, 0.01 mole) with 3-amino-2-methyl-4-oxoquinazoline (0.9 g, 0.01 mole) in presence of LTA (4 g, 0.01 mole) as described earlier afforded the oily product which was chromatographed on silica gel. The product (4) was eluted with PE 55 as an oil yielded (2.2 g, 50%) along with unreacted ester. Analysis-(Found : C, 71.60; H, 9.20; N, 8.92%; Calcd. for C\textsubscript{28}H\textsubscript{43}N\textsubscript{3}O\textsubscript{3} : C, 71.61; H, 9.22; N, 8.94%). IR (Neat): 1740 (COOCH\textsubscript{3}), 1680 (C=O), 1600, 775 (unsaturation of quinazoline ring), 1235 (N - N), 1665 (C - N), 1020 (C-O), 830 (\textdelta\textsubscript{1} aziridine ring). NMR (CCl\textsubscript{4}): 8.0 (m, 2H, quinazoline ring), 7.43 (m, 2H, quinazoline ring) 3.6 (s, 3H, COOCH\textsubscript{3}), 2.75 (m, 2H aziridine ring in part merged with methyl singlet at 2.6), 2.6 (s, 3H, quinazoline ring CH\textsubscript{3}), 2.2 (m, 2H, CH\textsubscript{2} alpha to carbonyl), 1.9 (m, 4H, 2x CH\textsubscript{2} alpha to aziridine ring), 1.28 (br, s, CH\textsubscript{2}), 0.9 (t 3H, CH\textsubscript{3}). MS : m/z 470(M+1), 469(M).

Reaction of methyl hexadec-2(E) enoate (5) with 3-amino-2-methyl-4-oxoquinazoline:

Reaction of methyl hexadec-2(E) enoate (5) (1.04 g, 0.005 mole) with 3-amino-2-methyl-4-oxoquinazoline (0.4 g, 0.005 mole) under similar conditions as stated earlier in
presence of LTA (2g, 0.005 mole) gave an oily product which was chromatographed on silica gel and elution with PE 60 gave solid product (6) (1.2 g, 70%) m.p. 35. Analysis—(Found: C, 70.69; H, 8.91; N, 9.50%; Calcd. for C_{26}H_{39}N_{3}O_{3}: C, 70.71; H, 8.90; N, 9.51%). IR (nujol): 1735 (COOCH$_3$), 1695 (-CO-), 1600, 775 (unsaturation of quinazoline ring), 1225 (N=N), 1185 (C=N), 1020 (C-O), 875 (trans aziridine ring), NMR (CDCl$_3$): 7.7 (m, quinazoline ring), 7.3 (m, 2H, quinazoline ring), 3.7 (s, 3H, COOCH$_3$), 3.2 (m, 1H, C-2 proton of aziridine ring), 2.9 (m, 1H, C-3 proton of aziridine ring), 2.7 (s, 3H, quinazoline ring CH$_3$), 1.4 (br, s, chain CH$_2$), 0.9 (t, 3H, CH$_3$). MS: m/z 441(M).

Reaction of methyl 12-hydroxyoctadec-9(Z) -enoate (7) with 3-amino-2-methyl-4-oxoquinazoline:

Methyl 12-hydroxy octadec-9 (Z) enoate (7) (3.1 g, 0.01 mole) reacted with 3-amino-2-methyl-4-oxoquinazoline (0.09 g, 0.01 mole) in a similar manner as indicated, before in presence of LTA (4 g, 0.01 mole) gave an oily product which on purification by silica gel column chromatography (PE 20) yielded product (8) (2.4 g, 50%). Analysis—(Found: C, 69.24; H, 8.90; N, 8.66%; Calcd. for C$_{28}$H$_{43}$N$_{3}$O$_{4}$: C, 69.25; H, 8.92; N, 8.65%). IR (nujol): 3350 (OH), 1740 (COOCH$_3$), 1680 (-CO-), 1605, 785 (unsaturation of quinazoline ring), 1205 (N=N), 1175 (C=N), 1020 (C-O), 835 (trans aziridine ring) NMR (CDCl$_3$):
8.12 (m, 2H, quinazoline ring), 7.4 (m, 2H, quinazoline ring), 4.4 (m, 1H, CH-OH), 3.6 9 (s, 3H, COOCH₃), 2.64 (s, 3H, quinazoline ring methyl), 2.61 (CH-OH, D₂O exchangeable), 2.4 (m, 2H, methine aziridine ring), 2.2 (m, 2H, CH₂ alpha to ester carboxyl), 1.9 (m, 4H, 2 x CH₂, alpha to aziridine ring), 1.3 (br, s, chain CH₂), 0.9 (t, 3H, CH₃). MS: m/z 455 (M - 30).

Reaction of methyl 9-hydroxy octadec-12 (Z) enoate (9) with 3-amino-2-methyl-4-oxoquinazoline:

Methyl 9-hydroxy octadec-12 (Z) enoate (9) (3.1 g, 0.01 mole) with 3-amino-2-methyl-4-oxoquinazoline (0.8 g, 0.01 mole) was stirred in presence of LTA (4 g, 0.01 mole) in the same manner as that of methyl 12-hydroxy octadec-9(Z) enoate (7). The reaction mixture was chromatographed on silica gel and eluted with PE 50 yielded product 10 (2.2 g, 46%).

Analysis—(Found: C, 69.24; H, 8.90; N, 8.66%; Calcd. for C₂₈H₄₃N₃O₄: C, 69.25; H, 8.92; N, 8.65%). IR (nujol): 3350 (OH), 1740 (COOCH₃), 1680 (-CO-), 1600, 775 (unsaturation of quinazoline ring), 1240 (N - N), 1190 (C - N), 1010 (C - O), 825 (cis aziridine ring), NMR (CDCl₃): 8.15 (m, 2H, quinazoline ring), 7.8 (m, 2H, quinazoline ring), 5.04 (m, 1H, CH-OH), 3.7 (s, 3H, COOCH₃), 2.7 (s, 3H, quinazoline ring methyl), 2.54 (br, s, 1H, CH - OH, D₂O exchangeable), 2.4 (m, 2H, aziridine ring) 2.2 (m, 2H, CH₂, alpha to carbonyl), 1.9 (m, 4H, 2 x CH₂ alpha to aziridine ring), 1.3 (br, s, chain CH₂), 0.9 (t, 3H, CH₃). MS: m/z, 414 (M - CH₃ - (CH₂)₄).
Reaction of methyl 10-undecynoate (11) with 3-amino-2-methyl-4-oxoquinazoline:

Reaction of 3-amino-2-methyl-4-oxoquinazoline (0.8 g, 0.01 mole) with methyl 10-undecynoate (11) (1.9 g, 0.01 mole) in presence of LTA (4 g, 0.01 mole) as detailed above. On final work up and column chromatographic separation afforded the product (12) (PE 20%) yielded 26% with unreacted ester (11). Analysis—(Found: C, 68.26; H, 7.35; N, 11.36%; Calcd. for C_{21}H_{27}N_{3}O_{3}: C, 68.27; H, 7.36; N, 11.37%). IR (nujol): 1775 (azirine ring), 1740 - 1680, 1600, 1470, 1430, 1380, 1295, 1150, 870 and 700 cm^{-1};

NMR (CCl₄): 8.9 (m, HC - C -); 7.7-7.3 (m, 4H, quinazoline unsaturation), 4.3 (m, H - C - C -); 3.6 (s, 3H, COOCH₃), 2.5 (s, 3H, quinazoline methyl), 2.23 (m, 2H, CH₂ alpha to carbonyl group), 2.0 (m, 2H, CH₂ alpha to azirine ring), 1.2 (br, s, chain CH₂), MS : m/z 369 (M).

Reaction of methyl 9-undecynoate (13) with 3-amino-2-methyl-4-oxoquinazoline:

Methyl 9-undecynoate (13) (1.9 g, 0.01 mole), with 3-amino-2-methyl-4-oxoquinazoline (0.8 g, 0.01 mole), in presence of LTA (4 g, 0.01 mole) as described earlier.
afforded the product (14) (PE 10%) yielded 32%. Analysis—
(Found: C, 68.26; H, 7.35; N, 11.36%; Calcd. for C_{21}H_{27}N_{3}O_{3}: C,
68.27; H, 7.36; N, 11.37%). IR (neat): 1770 (azirine ring),
1745, 1680, 1625, 1440, 1370, 1170, 1020, 790, 760 cm\(^{-1}\). NMR
(CCl\(_{4}\)): 7.6 – 7.3 (m, 4H, quinazoline unsaturation) 3.6 (s,
3H, COOCH\(_{3}\)), 2.4 (t, 2H, CH\(_{2}\) alpha to azirine ring), 2.26
(t, 2H, CH\(_{2}\) alpha to carbonyl group), 2.2 (s, 3H, CH\(_{3}\)– C – C–)
1.4 (s, 3H, CH\(_{3}\) C – C –), 1.2 (br, s, chain CH\(_{2}\)).

MS: m/z M\(^+\) (369) absent.

Reaction of methyl 9-octadecynoate (15) with 3-amino-2-
methyl-4-oxoquinazoline:

A similar treatment of reaction of methyl 9-
octadecynoate (15) (1.47 g, 0.005 mole) with 3-amino-2-
methyl-4-oxoquinazoline (0.4 g, 0.005 mole) in presence of LTA
(2g, 0.005 mole) finally gave product (16) (PE 30%) yielded
25%. Analysis—(Found: C, 71.90; H, 8.82; N, 8.98%; Calcd. for
C\(_{28}\)H\(_{41}\)N\(_{3}\)O\(_{3}\): C, 71.91; H, 8.83; N, 8.98%). IR (neat): 1775
(azirine ring), 1740, 1680, 1595, 1455, 1430, 1370, 1160, 870,
770, 720 cm\(^{-1}\), NMR (CDCl\(_{3}\)): 7.7 – 7.3 (m, 4H, quinazoline
unsaturation), 3.6 (s, 3H, COOCH\(_{3}\)) 2.9 (t, 2H, – C – C – CH\(_{2}\),
2.4 (s, 3H, quinazoline ring CH\(_{3}\)), 2.1 (t, 2H, CH\(_{2}\) alpha to

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Preparation of $\gamma$-dodecyl-$\gamma$-butyrolactone (20):

To an equimolar solution of methyl $\gamma$-oxohexadecanoate (19) (2.8 g, 0.01 mole) and sodium borohydride in 20 ml ethanolic NaOH (4%) was stirred for one hour at 15 – 20°. Solvent was evaporated and the product was extracted with ether washed with water and dried on sodium sulphate. The compound (20) was purified by silica gel column chromatography using petroleum ether as an eluent. A solid product was obtained yielded (2.3 g, 85%) m.p. 43°. Analysis—(Found: C, 75.53; H, 11.87%; Calcd. for C$_{16}$H$_{30}$O$_2$: C, 75.54; H, 11.88%). IR (nujol): 1765 ($\gamma$-lactone – CO) 1460, (CH$_2$ CH$_2$ CO), 1380 (OCH$_2$ wagging), 1185 (strong C – C – O asym) NMR (CDCl$_3$); 4.49 (m, 1H, – CH), 2.74 – 2.1 (m, 4H, ring methylene protons), 1.28 (br, s, chain CH$_2$), MS: m/z 254 ($\gamma$).

Preparation of 2 - Undecyl 1,3 - cyclo pentane dione (21)

Methyl $\gamma$ - oxohexadecanoate (19) (2 g, 0.01 mole) reacted promptly with sodium ethoxide (3 ml, 0.02 mole) in presence of boiling toluene (50 ml). Cyclization of the reactant was observed within 45 minutes on refluxing on water bath. After complete work up with dichloromethane, the solvent was evaporated under reduced pressure, the product was crystallised in acetone yielded a solid product (21) (97%) melting at 96°. Chromatographic behaviour of the
product (21) i.e. higher Rf value than the substrate and a shorter time indicated that the cyclization followed an intramolecular route. Analysis-(Found: C, 76.12; H, 11.17%; Calcd. for C₁₆H₂₈O₂: C, 76.14; H, 11.18%). IR (nujol): 3000 broad (bonded OH), 1725, 1695, (CO), NMR (CDCl₃): 2.6 (s, 4H, ring methylene protons), 2.2 - 2.45 (m, 1H, ring methine proton), 1.27 (br, s, chain CH₂), 0.87 (t, 3H, CH₃), MS: m/z, 252 (M+).

Preparation of 3-methoxy-2-undecylcyclopent-2-en-1-one (22):

Cyclopentadione (21) (100 mg, 0.005 mole) was refluxed with 10% borontrichloride in methanol (5 ml) for 20 minutes on water bath. The solvent was evaporated and worked up by ether, washed with water and dried. On evaporation of solvent the product was purified by column chromatography. Elution with petroleum ether (PE 10) gave solid product (22), yield (0.11 g, 80%), m.p. 44. Analysis-(Found: C, 86.43; H, 12.78%; Calcd. for C₁₇H₃₀O₂: C, 86.45; H, 12.80%). IR (KBr): 1700 (CO), 1660 (> C = C <), 1200 (ether), NMR (CCl₄): 3.62 (s, 3H, methoxy protons), 2.53 (overlapped t, 2H, ring methylene alpha to carbonyl group), 2.38 (t, J = 6.5 Hz, 4H, alpha to olefinic group), 1.2 (br, s, chain CH₂), 0.9 (t, 3H, CH₃.)
Reaction of epoxy fatty esters with 2-mercaptoacetic acid

General Procedure:

A solution of equimolar amounts of epoxy esters and 2-mercaptoacetic acid in chloroform (25 ml) were refluxed for 80 hours. After completion of reaction the mixtures were worked up and washed with water and dried over sodium sulphate. The solvent was evaporated and the products were fractionated over silica gel column chromatography.

Reaction of methyl 10, 11-epoxy undecanoate (23) with 2-mercaptoacetic acid:

Methyl 10, 11-epoxy undecanoate (23), (1.07 g, 0.005 mole) and 2-mercaptoacetic acid (0.46 g, 0.005 mole) were refluxed under similar reaction conditions as that of above. The two products (24, 25) were isolated by silica gel column chromatography product (24) obtained 65% yield at PE 20% and product (25) obtained (35%) yield at PE 35%. Analysis-(Found: C, 58.30; H, 8.39%; Calcd. for C_{14}H_{24}O_4S: C, 58.31; H, 8.38%).

Product (24), IR (nujol): 1745, 1735 (lactone CO and ester CO), 1470, 1300, 1300, 1170 cm^{-1}. NMR (CCl_4: 4.04 (m, 1H, -CH-), 3.6 (s, 3H, COOCH_3), 3.1 (s, 2H, CH_2-S), 2.6 (d, 2H, -CH_2-), 2.2 (2H, CH_2 alpha to carbonyl group), 1.3 (br, s, chain CH_2). MS: m/z 288 (M+). Analysis-(Found: C, 54.87; H, 8.54%; Calcd. for C_{14}H_{26}O_5S: C, 54.88; H, 8.55%).
Product (25): IR (nujol): 3500 (OH), 1745, 1720 (ester and chain CO), 1450, 1370, 1300, 1180 cm⁻¹, NMR (CCl₄): 4.9 (m, 1H, CH·O), 4.6 (d, 2H, CH₂), 4.0 (s, 2H, CH₂SH), 3.9 and 3.7 (broad, SH, OH, D₂O exchangeable), 3.6 (s, 3H, COOCH₃), 2.2 (t, 2H, CH₂ alpha to carbonyl group). MS: m/z 306 (M⁺) absent.

Reaction of methyl 9, 10- epoxyoctadecanoate (26) with 2-mercaptoacetic acid:

Methyl 9, 10- epoxy octadecanoate (26) was treated with 2-mercaptoacetic acid in chloroform as described earlier and reaction mixture was subjected to silica gel chromatography. Product (27) (60.9% PE 10); Analysis - (Found: C, 65.23; H, 9.89%; Calcd. for C₂₁H₃₈O₄S: C, 65.25; H, 9.90%). IR (neat): 1745 and 1725 (lacton CO and ester CO), 1470, 1370, 1300, 1170 cm⁻¹, NMR (CCl₄), 4.0 (m, 2H, -CH-), 3.6 (s, 3H, COOCH₃), 3.4 (s, 2H, CH₂-S), 2.2 (t, 2H, CH₂ alpha to carbonyl), 1.3 (br, s, chain CH₂), 0.9 (t, 3H, CH₃). MS: m/z M⁺ (386) absent.

Product (28) (40.5% PE 20%). Analysis - (Found: C, 62.33; H, 9.95%; Calcd. for C₂₁H₄₀O₅S: C, 62.34; H, 9.96%). IR (nujol): 3350 (OH), 1735 and 1720 (CO), 1450, 1370, 1290, 1180 cm⁻¹, NMR (CDCl₃): 4.1 - 3.3 (broad, 6H, CHO, CH₂-S, SH, OH), 3.6 (s, 3H, COOCH₃), 2.3 (t, 2H, CH₂ alpha to carbonyl group), 1.24 (br, s, chain CH₂) 0.9 (t, 3H, CH₃). MS: m/z, M⁺ (404) absent.

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Reaction of methyl 12, 13-epoxy-octadec-9(\(\underline{Z}\))-enoate (29) with 2-mercaptoacetic acid:

Methyl 12, 13-epoxy-octadec-9(\(\underline{Z}\))-enoate (29) was allowed to react with 2-mercaptoacetic acid under similar conditions as stated earlier. The products (30, 31) were purified by silica gel column chromatography.

Product (30) 61.1% PE 7). Analysis - (Found: C, 65.58; H, 9.42%; Calcd. for C\(_{21}\)H\(_{36}\)O\(_4\)S: C, 65.59; H, 9.43%). IR (neat), 2900 (CH\(_2\) stretching), 1760 and 1730 (lactone CO and ester CO), 1610 (C = C), 1470, 1380, 1260, 1180, cm\(^{-1}\), NMR (CDCl\(_3\)): 5.5 (m, 2H, CH=CH), 4.0 (m, 2H, CH-O, CH-S), 3.5 (s, 3H, COOCH\(_3\)), 3.6 (s, 2H, CH\(_2\)-S), 2.3 (t, 2H, CH\(_2\) alpha to carbonyl), 1.23 (br, s, chain CH\(_2\)), 0.9 (t, 3H, CH\(_3\)). MS: m/z, M\(^+\) (384) absent.

Product (31) (39.4%, PE-10). Analysis - (Found: C, 62.66; H, 9.50%; Calcd. for C\(_{21}\)H\(_{38}\)O\(_5\)S: C, 62.65; H, 9.51%). IR (neat): 3400 (OH), 1740 and 1720 (ester CO and chain CO), 1620 (C = C), 1450, 1370, 1290, 1180 cm\(^{-1}\), NMR (CCl\(_4\)): 5.4 (m, 2H, CH = CH), 4.7 (m, 2H, CHO), 4.2 (s, 2H, CH\(_2\)), 3.6 (s, 3H, COOCH\(_3\)), 3.3 (s, 1H, SH, D\(_2\)O exchangeable), 3.1 (s, 1H, OH, D\(_2\)O exchangeable), 2.2 (t, 2H, CH\(_2\) alpha to carbonyl), 1.3 (br, s, chain CH\(_2\)), 0.8 (t, 3H, CH\(_3\)). MS: m/z M\(^+\) (402) absent.
General method of preparation of cyclic phosphate derivatives:

Treating the requisite alcohol and hydroxy acid esters with stoichiometric amounts of phosphorus oxychloride and triethyl amine in anhydrous ether at 0° generates in one hour the dichlorophosphate in quantitative yield. Again triethyl amine (2 equivalent) and 2-mercaptoethanol/ethanolamine/ethylene diamine (1 equivalent) was added in situ. After 12 hours at room temperature, the dichlorophosphate was completely converted into cyclic phosphate as indicated by TLC. Purification by silica gel chromatography provided pure cyclic phosphate derivatives using petroleum ether solvent.

Reaction of palmitoyl alcohol (32) with 2-mercaptoethanol, ethanol amine, ethylene diamine:

The reaction of palmitoyl alcohol (32) (1.2g, 0.005 mole) phosphorus oxychloride (0.4 ml, 0.005 mole) and triethylamine (0.7 ml, 0.005 mole) in anhydrous ether afforded dichlorophosphate which on further treatment with triethylamine (1.4 ml, 0.01 mole) and 2-mercapto ethanol, (0.34 ml, 0.005 mole)/ethanol amine, (0.3 ml, 0.005 mole)/ethylene diamine (0.3 ml, 0.005 mole) under similar condition as that of above. On purification over silica gel column chromatography yielded products ((34 - 36).
Product 34: (50% PE 20). Analysis — (Found: C, 59.30; H, 10.22%; Calc'd. for C₁₈H₃₇O₇PS: C, 59.32; H, 10.23%). IR (neat): 1735 [R-O-P(O)], 1460 (CH₂S), 1390 (OCH₂), 1240, 1220, 1170 cm⁻¹; NMR (CDCl₃): 4.0 (t, J = 7Hz, 2H, CH₂-O), 3.7 (t, 2H, ring OCH₂), 2.8 (t, 2H, S-CH₂), 1.3 (br, s, chain CH₂), 0.9 (t, 3H, CH₃), MS: m/z M⁺ (364) absent.

Product 35: (58% PE 25). Analysis — (Found: C, 62.20; H, 11.00; N, 4.01%; Calc'd. for C₁₈H₃₈O₃PN: C, 62.22; H, 11.02; N, 4.02%). IR (neat): 3400 (NH), 1750 [R-O-P(O)], 1465 (CH₂-N), 1390 (CH₂-O), 1300, 1210, 1130 cm⁻¹; NMR (CCl₄): 3.5 (t, 4H, CH₂-O), 1.71 (t, 2H, CH₂ - N), 1.53 (s, 1H, NH, D₂O exchangeable), 1.3 (br, s, chain CH₂), 0.9 (t, 3H, CH₃), MS: m/z M⁺ (347) absent.

Product 36: (60% PE 27). Analysis — (Found: C, 62.41; H, 11.33; N, 8.06%; Calc'd. for C₁₈H₃₉O₂PN₂: C, 62.40; H, 11.34; N, 8.08%). IR (nujol): 3400 (NH), 1700 [R-O-P(O)], 1470, 1400, 1380, 1300, 1170 cm⁻¹; NMR (CCl₄): 5.8 (s, NH, D₂O exchangeable 3.7 (t, 2H, CH₂O), 2.3 (t, 4H, CH₂-N), 1.3 (br, s, chain CH₂), 0.9 (t, 3H, CH₃), MS: m/z M⁺ (346) absent.
Reaction of methyl 12-hydroxy-cis-9-octadecenoate (37) methyl 
9-hydroxy-12-octadecenate (38) with 2-mercaptoethanol/amine/
ethylene diamine:

A similar reaction of compound 37 and 28 (1.5 g, 0.005 mole), phosphorus oxychloride (0.4 ml, 0.005 mole) and triethylamine (0.7 ml, 0.005 mole) in anhydrous ether as that of earlier gave dichlorophosphate which again on treatment, at room temperature, with triethylamine (1.4 ml, 0.01 mole) and 2-mercaptoethanol (0.4 ml, 0.005 mole)/ethanol amine (0.3 ml, 0.005 mole)/ethylene diamine (0.3 ml, 0.005 mole) gave product 39 - 43. These were purified on silica gel column chromatography.

Product 39 : (62% PE 10). Analysis - (Found : C, 58.02; 
H, 9.03%; Calcd. for C_{21}H_{39}O_{5}PS:C, 58.04; H, 9.04%). IR 
(neat) : 1740 (COOCH_{3}), 1700 [R-O-P(O)], 1460, 1440, 1370, 
1200, 1170 cm^{-1}, NMR (CCl_{4}) : 5.4 (m, 2H, CH = CH), 3.9 (m, 
1H, CH - O), 3.8 (t, 2H, CH_{2}O), 2.7 (t, 2H, CH_{2}S), 1.64 (t, 
4H, CH_{2} alpha to olefinic bound), 1.3 (br, s, chain CH_{2}), MS: 
m/z, M^{+} (434) absent.

Product 40 : (59% PE 15). Analysis - (Found : C, 60.41; 
H, 9.66; N, 3.34%; Calcd. for C_{21}H_{40}O_{5}PN:C, 60.42; H, 9.65; 
N, 3.35%). IR (neat) : 3400 (NH), 1740 [R-O-P(O)], 1730 
(COOCH_{3}), 1470, 1430, 1240, 1170 cm^{-1} NMR 
(CDCl_{3}) : 5.3(t,2H,CH=CH),3.6(s,3H,COOCH_{3}),2.5(m,1H,CHO), 2.2
(t, 2H, CH$_2$ alpha to carbonyl), 1.9 (s, 1H, NH, D$_2$O exchangeable), 1.6 (t, 4H, CH$_2$ alpha to olefinic bond), 1.3 (br, s, chain CH$_2$), 0.8 (t, 3H, CH$_3$), MS: m/z M$^+$ (417) absent.

Product 41: (60% PE 15). Analysis - (Found: C, 60.55; H, 9.90; N, 6.70%; Calcd. for C$_{21}$H$_{41}$O$_4$PN$_2$: C, 60.56; H, 9.91; N, 6.72%). IR (neat): 3400 (NH), 1740 (COOCH$_3$), 1705 [R-O-P(0)], 1460, 1430, 1370, 1230, 1170 cm$^{-1}$ NMR (CCl$_4$): 5.4 (m, 2H, CH = CH), 3.8 (m, 1H, CH - O), 3.6 (s, 3H COOCH$_3$), 2.4 (t, 4H, CH$_2$ - N), 2.2 (t, 2H, CH$_2$, alpha to carbonyl), 2.0 (s, 2H, 2 x NH, D$_2$O exchangeable), 1.7 (t, 4H, CH$_2$ alpha to olefinic bond) 1.3 (br, s, chain CH$_2$), 0.9 (t, 3H, CH$_3$), MS: m/z M$^+$ (416) absent.

Product 42: (55% PE 10). Analysis - (Found: C, 58.03; H, 9.02%; Calcd. for C$_{21}$H$_{39}$O$_5$PS: C, 58.04; H, 9.04%). IR (neat): 1740-1700 (COOCH$_3$, R-O-P(0)). NMR (CCl$_4$): 5.3 (m, 3H, CH = CH), 3.9 (t, 1H, CH - O), 3.8 (t, 4H, 2 x CH$_2$-N), 3.6 (s, 3H, COOCH$_3$), 2.7 (t, 2H, CH$_2$ - S), 2.2 (t, 2H, CH$_2$ alpha to carbonyl), 1.7 (t, 4H, CH$_2$ alpha to olefinic bond, 1.3 (br, s, chain CH$_2$), 0.9 (t, 3H, CH$_3$) MS: M$^+$ (434) absent.

Product 43: (61% PE 20). Analysis - (Found: C, 60.40; H, 9.66; N, 3.33%; Calcd. for C$_{21}$H$_{40}$O$_5$PN: C, 60.41; H, 9.65;
N, 3.33%). IR (neat): 3400 (NH), 1740 (COOCH₃), 1700 [R-O-P(O)], 1430, 1460, 1370, 1250, 1170 cm⁻¹. NMR (CDCl₃): 5.3 (t, 2H, CH = CH), 3.8 (m, 1H, CHO), 3.6 (s, 3H, COOCH₃), 3.7 (t, 2H, CH₂O), 2.3 (t, 2H, CH₂N) 2.1 (t, 2H, CH₂ alpha to carbonyl), 1.8 (s, 1H, NH, D₂O exchangeable) 1.6 (t, 4H, CH₃ alpha to olefinic bond) 1.3 (br, s, chain CH₂), 0.9 (t, 3H, CH₃). MS: m/z M⁺ (417) absent.