CHAPTER III

CONVERSION OF RICINOLEIC ACID TO PGE₁
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Abstract

The strategy developed (Chapter-II) for a regiospecific two-carbon insertion and synthesis of 1,4-diketone has been extended to methyl ricinoleate, exemplifying the compatibility of the sequence with more highly functionalized starting substrates, for its conversion to methyl 9,12-dioxo-14-acetoxy-eicosanoate. The synthesis of (⁺)-11-deoxy PGE₁ methyl ester from methyl ricinoleate, utilizing in the key step a cyclooctenyl double bond protecting group ensuring regio-specific cyclisation of unsymmetrical 1,4-diketone intermediate, is reported; the former has already been converted to PGE₁ via PGA₁.
INTRODUCTION

Ricinoleic acid\(^1\), (\(\pm\)\(\left[ R-(Z)\right]\)-12-hydroxy-9-octadecenoic acid, the major (87-90\%) fatty acid in castor oil, is inexpensive and abundantly available material. In a synthetic endeavour towards prostaglandins, we were desirous of transforming ricinoleic acid into (+)-prostaglandin \(\text{E}_1\). A survey of the literature revealed that ricinoleic acid has been studied by several workers,\(^2\) in this connection, mainly for its transformation into synths for prostaglandin synthesis.

Ranganathan et al.\(^3\) synthesised \(\text{PGF}_{1\alpha}\) triacetate from methyl 10-undecenoate (2), obtained by pyrolysis of methyl ricinoleate (1). The transformation of (2) into the key synthon (6) was achieved by a sequence of reactions. (6) on Diels-Alder reaction with cyclopentadiene gave 73\% yield of a separable mixture of adducts, 2:1 in favour of the desired exo-aldehyde adduct (7). Aldehyde (7), after reduction, was treated with MEM chloride to get (8), which was converted to (10) through a sequence of reactions. The aldehyde (10) was subjected to Horner-Wittig reaction with 2-oxo heptyl phosphonate and the enone (11), thus obtained, was transformed into C-15 epimeric \(\text{PGF}_{1\alpha}\) triacetate (12) by borohydride reduction (Fig. 1).

In this Chapter we describe a new strategy for the conversion of methyl ricinoleate (1) into (+) \(\text{PGE}_1\).

FIG. 1
STRATEGY

The strategy envisaged (Fig. 2) for the transformation of castor oil - via methyl ricinoleate (1) - to (+)-11-deoxy PGE\textsubscript{1} methyl ester (26) incorporating all the 18 carbons of the castor oil backbone in the \textsubscript{C20} (26), is delineated below.

The crucial intermediate in a design of prostaglandin synthesis from acyclic precursors is the formation of an unsymmetrical 1,4-diketone, which could then be cyclised regiospecifically. Methyl ricinoleate (1) is endowed with a 12-hydroxy functionality in its structure which could be taken advantage of in its conversion to the desired 1,4-diketone (20). The conversion of (1) to (20) could be effected, after protection of the hydroxyl group, by extending the sequence developed (Chapter II) for a two-carbon insertion and synthesis of 1,4-diketone to (13), followed by elimination of the protected hydroxyl function. The stereospecific trans enone double bond in (20) was viewed to become the required \textgreek{\Delta}^{13}-trans double bond in the side chain of the target molecule (26). Further elaboration of (20) to (26) involved (i) regiospecific cyclisation (ii) reduction of cyclopentenone double bond and (iii) functionalization of \textsubscript{C15} position. The desired selective cyclisation and the subsequent reduction of the cyclopentenone
double bond could be achieved after protecting $^{13}$-double bond in (20), in a proper way. And for the functionalization of the C-15 position the $^{13}$-double bond, after regeneration, could very well serve as a handle. The series of reactions actually carried out to accomplish the synthesis of (t)-11-deoxy PGE₁ methyl ester (26) from (1) is outlined in Fig. 3.

\[ \text{Fig. 2} \]

\[ \text{Diagram showing the transformation of molecules.} \]

$\Delta$ = Protected double bond
RESULTS AND DISCUSSIONS

It was clear from the outset that C-12 hydroxyl function of methyl ricinoleate (1) would have to be protected in a manner that the sequence of reactions for a two-carbon insertion and further elaboration to 1,4-diketone (19), can be easily carried out and, after the operation, the protected hydroxyl itself can be eliminated to generate the required Δ13-double bond in (20). Of the various possibilities, the one which appeared more practical, was to protect the hydroxyl function as its acetate ester. Acetylation of the hydroxyl group was favoured for the following reasons:

(1) Acetate esters, as protective groups, are compatible with a variety of reagents and reaction conditions. Logically no difficulties can be envisaged in oxidative bis-decarboxylation (Fig. 3, step 5) and pyridinium chlorochromate oxidation (Fig. 3, Step 9). Our only concern about the stability of the acetate ester, in the sequence, was during pyrolysis of cyclobutene derivative (Fig. 3, step 6), as acetate esters are known to be labile at high temperatures.
FIG. 3: Synthesis of 15-epimeric (±)-11-deoxy PGE$_1$ (26)

10) DBU

11) Cyclopentadiene

155-160°C

12) 6% aq NaOH

13) CH$_2$N$_2$, Et$_2$O

14a) Li/liq NH$_3$, t-BuOH, Et$_2$O

14b) Na$_2$S$_2$O$_4$, NaHCO$_3$, PTC

15) 500°C/0.2 mm

16) NBS, (phCO)$_2$O

17) AgOAc, CH$_3$CO$_2$H

18) K$_2$CO$_3$, MeOH

FIG. 3: Synthesis of 15-epimeric (±)-11-deoxy PGE$_1$ (26)
(ii) Elimination of \( \beta \)-keto acetates can be effected under very mild conditions, so the protective group itself can serve the purpose of a leaving group.

Acetate esters are, however, unstable to basic conditions (pH > 8.5), so the hydrolysis of the anhydride to diacid (Fig. 3, step 4) was carried out under neutral conditions, selectively, with aqueous acetone. The protective group being labile to high temperatures, the pyrolysis of cyclobutene derivative (Fig. 3, step 6) was achieved, under well-controlled conditions, in gas phase. The sequence of reactions used to convert methyl ricinoleate (1) to (\( \pm \))-11-deoxy PGE\(_1\) methyl ester (26) is described below (Fig. 3).

Methyl ricinoleate (1), obtained by trans-esterification of castor oil with methanol in presence of catalytic amount of sodium, was purified by fractional distillation. Acetylation of (1) was effected by its treatment with acetic anhydride and pyridine (16 hr.) to furnish methyl 12-acetoxy-cis-9-octadecenoate (13) in over 98% yield. The structure of (13) was evident from its spectral data. NMR \( \delta \) (CCl\(_4\)) (Fig. 9): 5.34 (m, 2H, olefinic H), 4.76 (m, 1H, CH-O\( \text{COCH}_3\)), 3.59 (s, 3H, CO\( \text{OCH}_3\)), 1.94 (s, 3H, O\( \text{COCH}_3\)); IR (neat) (Fig. 10): 1740 cm\(^{-1}\) (C=O stretch), 1240 cm\(^{-1}\) (C-C(=O)-O stretch band for acetate).
Having protected the hydroxyl function, the conversion of (13) to the required C20 dienes (16) was brought about as follows: Acetone-sensitised irradiation (450 W medium-pressure Hg lamp) of (13) and maleic anhydride at 5-10° furnished a product which was isolated as the free dicarboxylic acid mixture (14) after aqueous acetone (1:1) hydrolysis [the yield of (14) from (13) was 98% corrected for recovery, 52% uncorrected]. The structure of (14) fits into its spectral data. NMR $\delta$(CDCl$_3$) (Fig. 11): 10.78 (b, 2H, COOH exchangeable with D$_2$O), 3.66 (s, 3H, COOCH$_3$), 4.84 (m, 1H, CH-OOCCH$_3$), 2.02 (bs, 3H, OCOCH$_3$); IR (Neat) (Fig. 12): 3010 cm$^{-1}$ (carboxylic acid O-H stretch), 1715 cm$^{-1}$ (acid C=O stretch), 1740 cm$^{-1}$ (ester C=O stretch), 1245 cm$^{-1}$ (C-C(-O)-O stretch band of acetate).

The diacid (14) was further characterised as its triester derivative (27), obtained by treatment with diazomethane. In the NMR of (27) the appearance of signals of 9 protons' intensity, at 3.59 (6H) and 3.57 (3H) was indicative of the presence of three ester groups, which was further supported by its IR (Neat): 1735 cm$^{-1}$ (ester C=O stretch).

Oxidative-bisdecarboxylation of the diacid mixture (14) with lead tetraacetate and pyridine, in a stream of dry oxygen, in refluxing benzene (30 min) furnished a product, in 47% yield, which, consequent upon cis, trans isomerisation of (13) during photoirradiation (Chapter II), must be a mixture of four diasteriomeric cyclobutenes (15). Attempts to improve
upon the yield of (15) by changing various reaction parameters - solvent, time and temperature - were not encouraging. The spectral features of (15) [NMR $\delta$ (CCl$_4$) (Fig. 13): 6.24-5.98 (two superimposed d, 2H, olefinic H), 4.82 (m, 1H, CH-OCOCH$_3$), 1.96 (s, 3H, OCOCH$_3$); IR (neat) (Fig. 14): 3120 cm$^{-1}$, 1555 cm$^{-1}$ (cyclobutene ring), 1240 cm$^{-1}$ (C-C(=O)-O band of acetate)] and microanalysis, are in accord with its structure. The mixture of cyclobutenes (15) underwent a smooth cycloreversion to furnish a neat mixture of 1,4-dienes (16), in 95% yield. This was achieved readily, under well-controlled conditions, in gas phase, i.e., on distilling (15) under reduced pressure (0.3 mm) through a heated column (450°C) filled with glass helices. The structure of the dienes (16) was evident from its spectral features. In the NMR (Fig. 15) of (16) the appearance of signals at $\delta$ 6.4-5.15 (m, 4H) and at $\delta$ 4.78 (m, 1H), $\delta$ 1.92 (s, 3H) was indicative of the presence of a conjugated diene system and of an acetate group being intact respectively. This was further supported by its IR (neat) (Fig. 16): 3025 cm$^{-1}$ (=C-H stretch band), 980 cm$^{-1}$ (C-H out-of-plane bend), 1240 cm$^{-1}$ (C-C(=O)-O stretch band of acetate); UV: $\lambda_{max}^{EtOH}$ 232 nm ($\varepsilon = 8,731$); Mass: 380 $M^+$ 1%) and microanalysis.

Our concern about the labile nature of acetate ester, at high temperatures, was sufficiently justified when in an
experiment the pyrolytic column got choked, resulting in increased contact time of the pyrolysate. The product from this experiment showed, on tlc, an additional spot higher in $R_f$ to that of (16). It was reasonable to assume that a part of (15) might have undergone cycloreversion followed by elimination of the 14-acetoxy group, on pyrolysis, resulting in the formation of triene/s (28) and/or (29).

The compound was isolated (5% of total pyrolysed product) by column chromatography on silica gel and its spectral features, indeed, delineated it to be a mixture of two trienes (28) and (29) (Fig. 4). That it is a mixture of two trienes was evident from its UV (Fig. 24a): $\lambda_{\text{max}}^{\text{EtOH}}$ 234 nm ($\varepsilon=12,586$) for (29) and $\lambda_{\text{max}}^{\text{EtOH}}$ 269 nm ($\varepsilon=21,333$) for (28). This was further supported by its NMR $\delta$(CCl$_4$) 6.3-5.1 (m, 6H, olefinic H), 3.6 (s, 3H, COOCH$_3$) and IR (neat): 3030 cm$^{-1}$ (= C-H stretch), 990 cm$^{-1}$ (C-H out-of-plane bend).

![FIG. 4]
With a primary aim of improving the yield of (15) the following alternative route was also investigated (Fig. 5).

Maleic anhydride, because of its ready accessibility and superior reactivity, is the most widely used C₂ unit for (2 + 2) photocycloaddition reactions. However, we desired a cyclobutene without 1,2-substituents, so the two alternatives for enhancing the yield of (15) were either the removal of adjacent carboxyl groups, from the adduct, in a more efficient way or the usage of a C₂ unit having groups more readily removed than carboxyl. The former approach still awaits an efficient method. We, therefore, thought of the latter alternative. More recently attention has been focussed on electron rich olefins such as vinylene carbonates, which add to olefins giving excellent yields of adducts.¹⁰ Therefore, for converting (13) into the required cyclobutenes (15), vinylene carbonate as a two-carbon component appeared most attractive as its adduct with an olefin yields, on hydrolysis, cis-1,2-diol and there are many efficient methods, known in literature, for deoxygenation¹¹ of vicinal diols to olefins.

Vinylene carbonate was prepared¹² from ethylene carbonate by its monochlorination followed by dehydrochlorination. Acetone-sensitized¹⁰ irradiation (450 W medium-pressure Hg lamp) of (13) and vinylene carbonate (32), at 5-10⁰ (12 hr),
FIG. 5: Synthesis of methyl 9,11-eicosadienoate (16)
furnished the required carbonate adducts mixture (33), in 70% yield. The structural features of (33) fit into its structure. In the IR (Fig. 18) of (33) the presence of the carbonate carbonyl was indicated by the absorption at 1812 cm\(^{-1}\) and this was further supported by its NMR \(\delta(CDC_13)\) (Fig. 17): 4.42-5.2 (m, 3H, CH-OCOCH\(_3\) and CH-O-C(=O)-O). Cyclic carbonates require relatively milder basic conditions for hydrolysis, when compared with acetates and esters, which was thought could be taken advantage of in the selective hydrolysis of (33). The carbonate adduct (33), when refluxed with aqueous pyridine (1:1, 16 hr), afforded the diol mixture (34), in 68% yield. The diol (34) was characterised on the basis of its spectral data NMR \(\delta(CCl_4)\) (Fig. 19): 4.28-3.38 (bm, 4H, O-H and CH-OH), 3.61 (s, 3H, COOCH\(_3\)), 4.8 (m, 1H, CH-OCOCH\(_3\)), 1.97 (s, 3H, OCOCH\(_3\)); IR (neat) (Fig. 20): 3440 cm\(^{-1}\) (O-H stretch), 1740 cm\(^{-1}\) (C=O stretch), 1240 cm\(^{-1}\) (C-C(=O)-O stretch band of acetate). The diol (34) was further characterised as its triacetate derivative (36), prepared by treatment with acetic anhydride and pyridine. In the NMR (Fig. 21) of (36) the appearance of signals at \(\delta\) 5.41-5.1 and \(\delta\) 5.0-4.58 (2m, 3H, CH-OAc), 2.04 (s, 3H, OCOCH\(_3\)) and 1.93 (s, 6H, OCOCH\(_3\)) was indicative of the presence of three acetate groups.
For reductive elimination of the diol (34) to cyclobutene derivative (15), by Eastwood deoxygenation, when (34) was treated with ethyl orthoformate in presence of catalytic amount of benzoic acid and the bath temperature maintained at 170°C (5 hr), a mixture of two compounds (tlc) was obtained. The two compounds, after separation by column chromatography on silica gel, turned out to be 1,3-dienes (16) and 2-ethoxy 1,3-dioxalan derivative (35). The formation of (16) and (35) can be rationalized as follows: It is obvious that (16) must have formed by cycloreversion of cyclobutene derivative (15), at this temperature, and (35) is a part of the reaction intermediate, that did not undergo thermal breakdown to the olefin (15). The dioxalan intermediate (35) was recognized by its NMR δ (CCl₄) (Fig. 23): 5.83 and 5.8 (two s, 1H, C-2 proton of 1,3-dioxalan ring), 4.6, 4.15 (2m, 2H, C-4 and C-5 protons of 1,3-dioxalan ring), 3.47 (q, 2H, O-CH₂-C₃H₃), 1.15 (O-CH₂-C₃H₃ protons superimposed by methylene protons). The appearance of two singlets, at 5.83 and 5.8, for C₂ proton of the 1,3-dioxalan ring is due to its being an isomeric mixture. The inference derived from this experiment was that the intermediate (35) requires a higher temperature for its complete carboxylic acid-catalysed thermal decomposition and that the resulting cyclobutene (15) would be labile to cycloreversion at that temperature. Therefore, it was
decided to convert (34) directly into the required 1,3-dienes (16) by raising the reaction temperature. Indeed, in another experiment, when the reaction temperature was raised unto 200°C (bath), complete decomposition of the intermediate (35) took place to furnish the diene mixture (16), in 69% yield. However, the overall yield of 1,3-diene (16) from (13) (42.13%), by this method, did not show any improvement over the earlier method with an overall yield of 42.83%. This lower overall yield is attributed to inferior reactivity of vinylene carbonate, as a C2 unit in (2 + 2) photocycloaddition reaction, when compared with maleic anhydride. A sample of the dienes (16) prepared in this way showed NMR, IR and UV identical to the one prepared earlier.

Photooxygenation of the dienes (16) was accomplished, when a dilute soln of (16) in MeOH: CCl4 (1:9) containing some Rose Bengal was simultaneously irradiated (125 W medium pressure Hg lamp) and treated with a steady stream of dry oxygen, to furnish the desired peroxide (17) in 80% yield. In the NMR (Fig. 25) of (17) the appearance of signals at δ 5.86, 5.82 (2s, 2H, olefinic protons) and δ 4.38 (bt, 24, H-C-O-O) was indicative of the presence of 1,4-epidioxy group.

From our previous knowledge (Chapter II) it was envisaged that treatment of the peroxide (17) with DBU followed by
exposure of the product to active alumina should bring about its rearrangement to 1,4-diketone with concomitant elimination of 14-acetoxy group, to furnish the required enedione (20), in only one step. However, when (17) was treated with DBU followed by passage of the crude product through a column of active alumina a mixture of products, including enedione (20), was obtained. Therefore, the peroxide (17) was reduced with hydrogen and Raney Ni to furnish, in over 79% yield, the saturated alcohol (18).

The spectral features of (18) [NMR $^6$ (CDCl$_3$) (Fig. 27): 4.95 (m, 1H, CH-OCOCH$_3$), 3.56 (bm, 4H, CH-OH and O-H; two protons exchangeable with D$_2$O), 2.02 and 1.98 (2s, 3H, OCOCH$_3$); IR (neat) (Fig. 28): 3420 cm$^{-1}$ (O-H stretch), 1735 cm$^{-1}$ (C=O stretch), 1245 cm$^{-1}$ (C-C(-O)-O stretch band of acetate); Mass: 416 (M$^+$ 1%) and microanalysis are consistent with its structure. The diol (18) was oxidised with pyridinium chlorochromate to afford methyl 9,12-dioxo-14-acetoxy-eicosanoate (19), as a wax, m.p. 35-36$^\circ$, in 85% yield. The structure of the dione (19) was fully borne out by its spectral data [NMR $^6$ (CCl$_4$) (Fig. 29): 5.09 (m, 1H, CH-OCOCH$_3$), 3.58 (s, 3H, COOH), 2.57 (s, 4H, OC-(CH$_2$)$_2$-CO), 1.94 (s, 3H, OCOCH$_3$); IR (CHCl$_3$) (Fig. 30): 1735 cm$^{-1}$ (b) (C=O stretch), 1245 cm$^{-1}$ (C-C(-O)-O stretch band of acetate); Mass: 412 (M$^+$ 6%) and microanalysis.
Having succeeded in extension of the sequence, for a two-carbon insertion and further elaboration, to methyl ricinoleate (1) for its conversion to 1,4-dione (19), our next aim was to achieve regiospecific cyclisation and process the resulting cyclopentanone derivative towards the target molecule (26). The diketone (19) is endowed with 14-acetoxy functionality in its structure which was thought could be taken advantage of in differentiating carbonyl functions at C-9 and C-12 for its regiospecific cyclisation, i.e., intramolecular condensation between C-8 and C-12.

In our first attempt, towards this end, it was envisaged that selective hydrolysis of the 14-acetoxy group, in (19), followed by protection of the resulting hydroxyl function with a bulky group (e.g., triphenylmethyl ether, TBDMS ether) might hinder the C-13 position, sterically for the generation of carbanion, effecting its selective base-catalysed cyclisation. However, when (19) was subjected to selective hydrolysis conditions (K₂CO₃ in methanol) it underwent rapid elimination of the acetoxy group followed by addition of methanol, in Michael fashion, to the resulting enedione (20) to form methyl 9,12-dioxo-14-methoxy-eicosanoate (37) (Fig. 6). In the NMR of (37) the appearance of a signal at δ3.24 was indicative of the presence of -OCH₃ group.
In another attempt, it was thought worthwhile to explore the cyclisation of the enedione (20), which could be obtained by elimination of the 14-acetoxyl group of (19). The acetoxyl group, being \( \beta \)-keto, should be labile to elimination. However, when (19) was treated with triethylamine, in refluxing CH\(_2\)Cl\(_2\), the elimination could not be achieved. The conversion of (19) to (20) was brought about by treating (19) with 1,5-diazabicyclo [5.4.0] undecene-5, in CH\(_2\)Cl\(_2\) at room temperature (30 min.), to furnish the required enedione (20) in 96\% yield. Enedione (20) was also obtained, in 88\% yield, by exposure of diketone (19) to basic alumina\( ^6 \) (grade-I). In the IR of (20) the absorptions at 1675 cm\(^{-1}\) (enone C = O stretch), 1632 cm\(^{-1}\), 980 cm\(^{-1}\) (trans-olefin) were indicative of the presence of a trans-enone system and this was further supported by its NMR \( \delta (\text{CCl}_4) \) (Fig. 31): 6.77 (dt, 1H, \( J = 16 \) Hz, \( J = 7 \) Hz, CO-CH=CH), 6.03 (d, 1H, \( J = 16 \) Hz, CO-CH = ) and UV: \( \lambda_{\text{max}}^{\text{EtOH}} \; 227 \) nm (\( \varepsilon = 6.89 \times 10^3 \)).
An attempt was made to cyclise (20), expecting C-8 C-12 mode of condensation to be the preferred one, though, theoretically, three products were possible. However, when (20) was subjected to cyclisation conditions (10% aqueous NaOH, THF) and the progress of the reaction followed, periodically, by UV, the condensation did not turn out to be selective and proceeded both ways (Fig. 7); i.e., between C-8 → C-12 and C-13 → C-9. The UV spectrum (Fig. 24b) after completion of the reaction (disappearance of the absorption at 227 nm for starting enone), showed two absorption maxima, one at 232 nm [characteristic of the chromophore in (39)] and second at 286 nm [characteristic of the chromophore in (38)]. TLC (hexane: EtOAc, 75:25) of the reaction product also indicated two

![Diagram of cyclisation of enedione (20)](image)

**Fig. 7**: Cyclisation of enedione (20)
overlapping spots, lower in $R_f$ to that of the starting enone. The formation of the compound (40), if the cyclisation proceeds by the attack of C-10 carbonion in Michael fashion at C-14, however, could not be ascertained. No attempt was made to separate these isomers.

At this stage, it became clear that the trans-double bond in (20) would have to be protected in a manner that the sequence of reactions, selective cyclisation and subsequent reduction of the cyclopentenone double bond, can be easily carried out and, after the operation, the double bond can be regenerated with the retention of its geometry. The protection of the double bond appeared imperative, in view of the situation as well, that if the desired cyclisation of (20) is achieved otherwise, to afford (38), then again $\alpha,\beta$-enone double bond of the cyclopentenone (38) would call for selectivity with respect to its reduction, in preference to the $\gamma,\delta$-enone double bond. A survey of the literature divulged that it lacks many precedents of selective reduction of $\alpha,\beta$-enone double bond, in preference to $\gamma,\delta$-enone double bond, in conjugated dienones; the converse is more frequent. The situation appeared more discouraging, in view of the fact, that in (38) the $\alpha,\beta$-enone double bond is tetrasubstituted and the $\gamma,\delta$-enone double bond disubstituted.
Of the various possibilities of protecting the enone double bond in (20) the one which appeared more practical, was to protect it as its $\pi^4s + \pi^2s$ Diels-Alder adduct.\textsuperscript{18} The cyclopentenyl protecting group was favoured as it possesses many unique advantages, which are:

i) Diels-Alder adducts are stable to both acidic and basic conditions. Logically, no difficulties can be envisaged in cyclisation (Fig. 3, step 12).

ii) The bicyclo system makes the C-13 carbon tertiary one, thus preventing undesirable condensation between C-13 and C-9 (no dehydration can take place) and ensuring only one mode of condensation\textsuperscript{19} (C-8 $\rightarrow$ C-12).

iii) The Diels-Alder and retro-Diels-Alder reactions exhibit pronounced stereochemical selectivity,\textsuperscript{20} so the geometry of the double bond is retained.

However, the thermally labile nature of Diels-Alder adducts precluded the purification of the compounds, having cyclopentenyl protecting group, by distillation. All such compounds were purified by column chromatography on silica gel.
The protective group itself possesses a highly exposed isolated double bond, so the reduction of cyclopentenone double bond (Fig. 3, step 14) called for selectivity.

The enedione (20) was converted to (21) by heating it (155-160°C), in an evacuated sealed tube, with freshly cracked cyclopentadiene and toluene, for 27 hrs. A clean reaction occurred to furnish the diketo adduct (21), in 93% yield, which from its 90 MHz $^1$H-NMR (broad multiplet for olefinic protons at $\delta$ 6.28-5.73) appeared to be a mixture of two isomers (exo and endo). TLC (25% ethyl acetate in pet ether) of the diketo adduct (21) also indicated it to be a mixture of two compounds. That (21) is a mixture of two isomers should be especially revealed by the chemical shift and multiplicity of the carbonyl methine proton, in its high field NMR, but in its 90 MHz NMR this proton is not distinctly seen. The formation of this isomeric mixture of (21) is of no consequence in the synthesis, since these centres become trigonal at a later stage, so no effort was expended to separate these isomers. The structure of (21) was evident from its spectral data. NMR (CCl$_4$, Fig. 33): 6.28-5.73 (m, 2H, olefinic H), 3.59 (s, 3H, COOCH$_3$), 3.05-2.13 (m, 11H, CH$_2$-COOCH$_3$, α to keto and allylic protons); IR (neat) (Fig. 34): 1740 cm$^{-1}$ (ester C=O stretch), 1708 cm$^{-1}$ (keto C=O stretch); Mass: 418 (M$^+$ 17%) and microanalysis.
Having protected the double bond, all was set to cyclise \(21\) regiospecifically. Indeed, when \(21\) was subjected to cyclisation conditions, \(6\%\) NaOH in methanol, the cyclopentenone \(22\) was obtained, after esterification, in 58% yield. The rest 32.59% was starting diketone (based on actual recovery by chromatography on silica gel). The progress of the reaction was followed by taking UV of the aliquots, periodically. The structure of the cyclopentenone \(22\) was fully borne out by its spectral features.

\[\text{IR (neat) (Fig. 36): 1740 cm}^{-1} \text{ (ester C=O stretch), 1698 cm}^{-1} \text{ and 1625 cm}^{-1} \text{ (five-membered ring carbonyl and enone double bond); NMR \(\delta\) (CCl}_4\) (Fig. 35): 6.3, 6.05 (2m,2H, olefinic H), 2.88-1.8 (m, 11H, CH}_2-CO_2CH}_3, seven allylic and two CH}_2-CO\}; UV: \(\lambda_{\text{max}}^{\text{EtOH}}\) 251 nm (\(\epsilon = 1.6 \times 10^4\)) and microanalysis.

Our next effort was directed towards the selective reduction of cyclopentenone double bond in \(22\). A number of methods are known in literature, for the selective reduction of an enone double bond in the presence of an isolated double bond. When \(22\) was reduced with hydrogen and 5% Rh over alumina, the isolated cyclooctetrayl double bond got reduced, selectively and completely, to form \(41\); the enone double bond remained intact, which was inferred by its UV: \(\lambda_{\text{max}}^{\text{EtOH}}\) 246 nm. In the IR (Fig. 38) of \(41\) the absorptions at 1700 cm\(^{-1}\) and 1630 cm\(^{-1}\) also indicated the presence of the enone double bond and the reduction of
the cyclopentenyl double bond was inferred by its NMR (Fig. 37) (disappearance of signal for olefinic protons).

Selective reduction of conjugated olefins in \(\alpha,\beta\)-unsaturated carbonyl compounds, using hydroxysilane-rhodium (I) complex combinations, is known. However, when (22) was treated with slight excess of triethylsilane in the presence of a catalytic amount of \((\text{Ph}_3\text{P})_3\text{RhCl}\), under nitrogen at 50°C for 2 hr., the isolated double bond again got reduced in preference to the enone double bond, to form (41). Tris-(triphenylphosphine)chlororhodium (I) catalyst is known for C=C double bond reduction of olefinic substrates. In view of the fact, that the enone double bond, in (22) is tetrasubstituted and somewhat hindered when compared with cyclopentenyl double bond which is disubstituted, strained and more exposed, the need for a more specific reagent, for the selective reduction of the former, was realized.

\[ \text{FIG. 8} \]
The metal-ammonia reduction is characterised by its ability to selectively reduce conjugated C=C double bonds to form unconjugated ketones. The reduction may be applied to compounds with any degree of substitution on the enone double bond. Isolated double bonds, unless they have very low-lying antibonding orbitals or special structural features which stabilise radical ion intermediates, are normally stable to metal-ammonia solutions. Esters are susceptible to the reduction conditions and can get converted to saturated alcohols by acyl-oxygen fission or, in hindered systems, carboxylic acids may be formed by alkyl-oxygen fission. However, metal-ammonia reductions of enones are more rapid than those of esters which has been taken advantage of in the selective reduction of the former, in presence of the latter, using a limited amount of lithium. On subjecting (22) to Birch reduction conditions (Li/lid. NH₃ in presence of 1 eq. of proton donor and quenching the reaction with solid NH₄Cl) the desired cyclopentanone (23) was obtained, in only 54% yield, along-with some aldehyde (indicated by a signal at 8 9.65 in the NMR). The formation of this small amount of aldehyde can be rationalized as follows: The liquid ammonia, used in the reaction, was undistilled commercial, so it must be containing some iron impurities. Iron catalyses the reaction of liquid NH₃ with metals to form metal amides. It is reasonable to assume that lithium amide, thus formed, must
have reacted\textsuperscript{34} with terminal ester in (22) to form amide. Amides are known\textsuperscript{35} to get converted to aldehydes by metals in liquid ammonia.

In 1984, Louis Andre\textsuperscript{36} published a paper highlighting the usage of sodium dithionite, under phase transfer catalytic conditions, for selective reduction of enone double bond in the presence of an isolated double bond. Reduction of (22) with sodium dithionite (large excess), under the influence of phase transfer catalyst (triacryryl-methyl ammonium chloride) in refluxing benzene: water (1:1), afforded (23) in 75\% yield. The rest 19\% was starting material (based on actual recovery by column chromatography on silica gel). Sodium dithionite was added in portions as a batch of the reagent loses most of its reducing properties,\textsuperscript{37} after one hour, under the conditions used. The cyclopentanone obtained by this method was identical, in its spectral characteristics, to the product obtained earlier by Li/liq. NH\textsubscript{3} reduction. The spectral characteristics of (23) are NMR \delta (CCl\textsubscript{4}) (Fig. 39): 6.12-5.98 (m, 2H, olefinic H), 3.57 (s, 3H, COOCH\textsubscript{3}), 2.78 (m, 2H, bridgehead allylic protons), 2.6 (m, 1H, methine proton to cyclopentane carbonyl), 2.4-1.90 (m, 4H, CH\textsubscript{2}CO\textsubscript{2}CH\textsubscript{3} and CH\textsubscript{2}-C=O); IR (neat) (Fig. 40): 1740 cm\textsuperscript{-1} (ester C=O stretch and cyclopentanone C=O stretch).
At this stage it was decided to deprotect the double bond in (23), since it had served its purpose of effecting regiospecific cyclisation and selective reduction of cyclopentenone double bond. Retro-Diels-Alder of (23) was achieved readily in gas phase, i.e., distilling (23) under reduced pressure (0.2 mm) through a heated column (500°C) filled with glass helices. A remarkably clean reaction occurred to furnish, in 95% yield, the required (\(+\))-11,15-dideoxy PGE\(_1\) methyl ester (24). This compound has been prepared earlier by C.J. Sih and co-workers.\(^{39}\) The spectral characteristics of (24) are IR (neat) (Fig. 42): 1740 cm\(^{-1}\) (C=O), 970 cm\(^{-1}\) (\(\text{trans}\) CH=CH); NMR (\(\text{CCl}_4\)) (Fig. 41): 5.71-5.12 (m, 2H, olefinic protons), 3.59 (s, 3H, COOCH\(_3\)) ; Mass: 336 (M\(^+\) 39%).

In the Li/liq. NH\(_3\) reduction of (22), which is viewed to proceed via an enolate anion intermediate\(^{40a}\), it was reasonable to assume that the more thermodynamically stable\(^{40b}\) product (23), having \(\text{trans}\) relationship between the substituents on the cyclopentanone, would be formed. Nothing is known about the stereochemistry of the reduction of enones with sodium dithionite under PTC conditions. Treatment of ketone (24) with ethanolic potassium acetate (120 hr), known equilibrating conditions,\(^{41}\) led to unchanged material (tlc), thus confirming \(\text{trans}\)-relationship between the substituents on the cyclopentanone.
Our next and the ultimate interest, in the synthesis, was the conversion of (24) into the (+)-11-deoxy PGE₁ methyl ester (26). Although (24) is a compound known in the literature, however, so far there is no report of its transformation into (26). In an approach towards this target, (24) was converted into its C-15 epimeric bromo derivative by refluxing with NBS in CCl₄, in the presence of benzoyl peroxide. The crude bromide mixture on treatment with silver acetate in glacial acetic acid, furnished a mixture of C-15 epimeric acetates (25). The spectral features of (25) are IR (neat) (Fig. 44): 1240 cm⁻¹ (C-C(=O)-O) stretch band of acetate; 970 cm⁻¹ (trans-CH₂CH); NMR (CDCl₃) δ (Fig. 43): 5.5 (m, 2H, olefinic H), 5.15 (m, 1H, CH-CH-OAc), 3.6 (s, 3H, -COOCH₃), 1.97 (s, 3H, -OCOCH₃). Selective hydrolysis of this mixture (25) with K₂CO₃ in methanol, at room temperature, yielded 1:1 mixture of C-15 epimeric carbinols (26) separable on tlc (30% ethyl acetate in pet. ether; Rₚ 0.43 and 0.35). The more polar alcohol (Rₚ 0.35) is known to be the (+)-11-deoxy PGE₁ methyl ester and has been separated from its C-15 epimer (Rₚ 0.43). Both the isomers have been reported to show identical spectral data. The alcohol (26) thus synthesised was identical (NMR, IR, Mass) with 11-deoxy PGE₁ methyl ester prepared earlier by Alvarez and co-workers. The spectral features of (26) are NMR δ (CCl₄) (Fig. 45): 5.58 (m, 2H,
The hydrolysis of (26) to its corresponding acid, 11-deoxy PGE₁, is already known, which in turn has been transformed into PGE₁ via PGA₁.
EXPERIMENTAL

For general remarks see Chapter-II.

Methyl 12-Hydroxy-cis-9-octadecenoate 1

A solution of castor oil (750 g) in dry methanol (2.5 l), to which sodium (1 g) had been added, was refluxed for 2 hr. Excess of methanol was distilled off and the residue was dissolved in ether (500 ml). To it 500 ml of water was added, when a white emulsion appeared. After two hr 100 ml of 50% aq. \( \text{NH}_4\text{Cl} \) solution was added, when the aqueous and the organic layers separated distinctly. The organic layer was separated and washed with water (100 ml \times 3) and brine (100 ml \times 2). It was dried (\( \text{Na}_2\text{SO}_4 \)) and the solvent was removed to get the crude methyl ricinoleate (725 g), which on fractionation afforded pure methyl ricinoleate 1 (483 g), b.p. 167-172\(^\circ\)/0.8-1.0 mm (lit.\(^b\), b.p. 210-212\(^\circ\)/4 mm).

\(^1\text{H-NMR}\) \( ^{9}\alpha (\text{CCl}_4) : 5.42 (m, 2H, -\text{CH-CH-}), 3.61 \text{(s, 3H, COOCH}_3\text{)}, 3.55 \text{(bm, 1H, -CH-OH), 1.9-2.4 (m, 6H, allylic CH}_2\text{'s and CH}_2\text{-COOCH}_3\text{),} 1.63 \text{(s, 1H, -CH-OH exchangeable with D}_2\text{O),} 1.3 \text{(bs, 2OH, CH}_2\text{'s),} 0.88 \text{(t, 3H, -CH}_3\text{);} \quad \text{IR}^{9}\alpha \text{(Neat) } \nu_{\text{max}}: 3420, 1744 \text{ cm}\^-1.

Methyl 12-Acetoxy-cis-9-octadecenoate 13

Methyl ricinoleate 1 (10.14 g, 32.49 mmole) \( \text{Ac}_2\text{O} \) (6.62 g, 64.9 mmole) and dry pyridine (10 ml) were mixed together and
kept at r.t. (35°C) in a stoppered conical flask for 16 hr. The reaction mixture was diluted with ether (100 ml) and washed successively with 25% HCl (20 ml x 3), 10% NaHCO₃ (20 ml), water (20 ml x 3), brine (30 ml) and dried (Na₂SO₄). Solvent was removed to give colourless liquid 13 (11.37 g, 98.86% yield), b.p. 170-173°C/0.1 mm (lit.³, b.p. 203-205/4mm).

¹H-NMR δ (CDCl₃) (Fig. 9): 5.34 (m, 2H, -CH=CH-), 4.76 (m, 1H, -CH-OCOCH₃), 3.59 (s, 3H, COOCH₃), 2.45-1.9 (m, 6H, allylic protons, and CH₂-COOCH₃), 1.94 (s, 3H, OCOCH₃), 1.31 (bm, 20H, CH₂'s), 0.88 (t, 3H, -CH₃); IR (Neat)(Fig. 10): 3020, 1740, 1245, 1025 cm⁻¹.

cis-1,2-Dicarboxy-(cis/trans)-3-(2-acetoxyoctyl)-4-(7-carbomethoxyheptyl)-cyclobutane 1₄

A solution of 13 (10.14 g, 28.64 mmole) and maleic anhydride (2.81 g, 28.67 mmole) in dry acetone (300 ml) was deoxygenated with N₂ and irradiated for 12 hr (450 W medium-pressure Hg lamp) at 5-10°C, while bubbling N₂ continuously. Removal of solvent under vacuum furnished the crude photoadduct which was hydrolysed by aqueous acetone (1:1, 100 ml) for 36 hr. Acetone was distilled off and the aqueous portion, after saturating with solid NaCl, was extracted with ether (4 x 40 ml). The ether extract was
cooled and extracted with a cold solution of Na₂CO₃ (5%, 3 x 35 ml). The solvent was removed, from the ether portion, to recover 4.69 g of the starting material 13 (unreacted). The aqueous portion (Na₂CO₃ extract) was acidified with conc. HCl (pH 3), saturated with solid NaCl and then extracted with ether (2 x 35 ml) and ethyl acetate (2 x 30 ml). The ether and the ethyl acetate extracts were combined and washed with water (2 x 30 ml) and brine (30 ml) and dried. Solvent was removed to get a mixture of dicarboxylic acid 14 7.03 g, as a gum (the yield of 14 from 13 was 98% corrected for recovery, 52% uncorrected).

¹H-NMR δ (CDCl₃) (Fig.11): 10.78 (b, 2H, -COOH exchangeable with D₂O), 4.84 (m, 1H, -CH-0Ac), 3.66 (s, 3H, COOCH₃), 2.8 (m, 2H, carboxyl methine protons), 2.29 (t, 2H, J = 7Hz, CH₂-COOCH₃), 2.02 (bs, 3H, -OCOCH₃), 1.85-1.02 (bm, 27H, CH₂'s), 0.87 (s, 3H, -CH₃); IR (Neat) (Fig. 12): 3020, 1720, 1735, 1250 cm⁻¹.

A part of 14 was converted to its tri-ester 27 by treatment with diazomethane and further purified by column chromatography on silica gel to get a thick liquid, which was characterised as such.

¹H-NMR δ (CCl₄): 4.69 (φ, 1H, -CH-0Ac), 3.59 (s, 6H, COOCH₃), 3.57 (s, 3H, COOCH₃), 2.6 (m, 2H, carbomethoxy methine protons), 2.22 (t, 2H, J = 7Hz, CH₂-COOCH₃), 1.96, 1.94 (2s, 3H, -OCOCH₃), 1.75-1.03 (bm, 27H, CH₂'s), 0.87 (t, 3H, -CH₃); IR (Neat) ʋₐₘₙₐₓ: 1735, 1435, 1370, 1240, 1025 cm⁻¹
The diacid 14 (6.37 g, 13.55 mmole) was taken in dry benzene (225 ml) and dry pyridine (2.18 g, 27.59 mmole) was added to it. The reaction mixture was refluxed, in a stream of oxygen, and lead tetraacetate (12.25 g, 27.65 mmole) was added at once. Refluxing was continued for another 30 minutes and it was then brought to room temperature. Ethylene glycol (1.5 ml) was then added and reaction mixture was stirred for another 15 minutes, to destroy excess lead tetraacetate. The material was then filtered through celite and washed with benzene (4 x 30 ml). The combined filtrates were washed successively with dil. HNO₃ (15%, 3 x 35 ml), water (1 x 30 ml), aqueous NaHCO₃ (1 x 30 ml) and again with water (3 x 30 ml) and brine (1 x 35 ml) and dried over anhydrous sodium sulphate. The solvent was removed, under reduced pressure, to give a crude product, which was purified by column chromatography on silica gel (120 g) to furnish an isomeric mixture of cyclobutenes 15 (2.44 g, 47.37% yield) as a liquid.

**H-NMR** δ(CCl₄) (Fig. 13): 6.24-5.98 (two superimposed d, 2H, olefinic H), 4.82 (m, 1H, -CH-OAc), 3.59 (s, 3H, COOCH₃), 2.22 (m, 4H, allylic protons at ring junction and -CH₂-COOCH₃), 1.96 (s, 3H, COOCH₃), 1.31 (bm, 26H, CH₂'s), 0.89 (t, 3H, -CH₃);
IR (Neat) (Fig. 14): 3120, 3040, 2930, 2860, 1740, 1240, 1030, 725 cm⁻¹. (Found C, 72.30; H, 10.38; C₂₃H₄₀O₄ requires C, 72.63; H, 10.52%).

Methyl 14-Acetoxy-9,11-eicosadienoate 1₆ from 1₅

The cyclobutene 1₅ (2.45 g, 6.44 mmole) was taken in a 5 ml round bottomed flask fitted to an electrically heated column (12.5 x 1.5 cm), filled with glass helices, which in turn was connected to a cold trap. The flask was heated to 235° (bath temp.), under vacuum (0.2-0.3 mm), while the temperature of the column was maintained at 450°C, whereby an isomeric mixture of dienes 1₆ (2.37 g, 94.5% yield) distilled over as a colourless liquid.

¹H NMR δ(CCl₄) (Fig. 15): 6.4-5.1 (m, 4H, olefinic H), 4.78 (m, 1H, CH-OAc), 3.58 (s, 3H, COOCH₃), 2.48-1.9 (m, 6H, allylic protons and CH₂COOCH₃), 1.92 (s, 3H, OCOCH₃), 1.88-1.08 (m, 22H, CH₂'s), 0.88 (t, 3H, -CH₃); IR (Neat) (Fig. 16): 3025, 2920, 2845, 1740, 1370, 1240, 980, 725 cm⁻¹; UV: λₘₐₓ 232 nm (ε = 8,731); Mass: m/e 380 (M⁺, 1%), 349 (1%), 320 (90%), 289 (10%), 177 (7%), 150 (10%), 106 (12%), 67 (29%), 57 (100%), 43 (73%). (Found C, 72.01; H, 10.58; C₂₃H₄₀O₄ requires C, 72.63; H, 10.52%).

Preparation of vinylene carbonate 3₂

Vinylene carbonate, based on earlier procedure, was prepared as follows:
Freshly distilled ethylene carbonate \(30\) (100 g, 1.16 mole) was taken in a quartz immersion well and was simultaneously irradiated (125 W medium-pressure mercury lamp) and treated with a steady stream of chlorine at 63-70°C (temperature maintained by circulating hot water in the outer jacket). After 6 hr the gain in wt. was 41 g (1.15 mol for monochloro substn.). Vacuum rectification afforded pure monochloro vinylene carbonate \(31\) (94 g, 67%), b.p. 115-116°C/10 mm (lit.\(^{12}\) b.p. 106-107/10-11 mm). PMR (\(\text{CDCl}_3\)):

6.43 (dd, 1H, J = 5Hz, chloromethine proton), 4.85 (dd, 1H, J = 10Hz, J = 5Hz, methylene proton), 4.55 (dd, 1H, J = 10Hz, J = 2 Hz, methylene proton); IR \(^{12}\) (Neat) \(\nu_{\text{max}}\): 1825 cm\(^{-1}\).

To a stirred refluxing mixture of \(31\) 94g (0.77 mole) in 150 ml of dry ether was added 101 g (1 mole) of redistilled pure triethylamine over 4 hr. After a total of 32 hr. of refluxing the dark solid was collected and washed with benzene-ether (300 ml). After distillation of the solvent and excess of triethylamine, further distillation at 25 mm afforded 38.7 g (59% yield) of pure vinylene carbonate \(32\), b.p. 70°C/25 mm (lit.\(^{12}\) b.p. 73-74°C/32 mm).

PMR \(\text{CDCl}_3\): 7.18(s); IR \(^{12}\) (Neat) \(\nu_{\text{max}}\): 3170, 1830 cm\(^{-1}\).

\[\text{cis-1,2-Carbonyldioxy-(cis/trans)-3-(2-acetoxy-octyl)-4-(7-carbomethoxyheptyl)-cyclobutane 33}\]

A solution of \(13\) (12.39 g, 35 mmole) and vinylene
carbonate 32 (3.76 g, 44.76 mmole) in dry acetone (350 ml) was deoxygenated with N₂ and irradiated (450 W medium-pressure-mercury lamp) for 12 hr. at 5-10⁰C, while bubbling nitrogen continuously. The solvent was removed and the residue was dissolved in ether, when the dimer of vinylene carbonate remained insoluble (0.421 g, white fluffy solid) and was filtered off. Ether was flashed off and the residue was chromatographed on SiO₂-IIb column (210 g, 4 cm x 105 cm) (TLC: 40% ethyl acetate in pet. ether). The following pooled fractions were collected:

Frac. 1  Pet. ether  3 x 100 ml
Frac. 2  5% EtOAc in pet. ether  6 x 100 ml  1.40 g, starting material 13
Frac. 3  5% EtOAc in pet. ether  7 x 100 ml  1.36 g, streak on TLC, discarded
Frac. 4  15% EtOAc in pet. ether  8 x 100 ml  9.13 g, thick liquid, Rf : 0.57
Frac. 5  20% EtOAc in pet. ether  2 x 100 ml

Pooled fraction (4 + 5) was identified as the carbonate adduct 33 (9.13 g, yield 59.32% uncorrected for recovery of 13). ¹H NMR (CDCl₃) (Fig. 17): 5.2-4.42 (bm, 3H, -CH-O-C(=O)-O-CH- and -CH-OAc), 3.66 (s, 3H, COOCH₃), 2.28 (t, 3H, J = 7Hz, CH₂-COOCH₃), 2.02 (s, 3H, OCOC₃H₃), 1.85-1.05 (bm, 26H, CH₂'s), 0.87 (t, 3H, -CH₃); IR (Neat) (Fig. 18): 2940, 2860, 1812, 1738,1370, 1240, 1130 cm⁻¹.
cis-1,2-Dihydroxy-(cis/trans)-3-(2-acetoxy-octyl)-4-(7-carbomethoxyheptyl)-cyclobutane 34

The carbonate adduct 33 (1.0 g, 28.28 mmole) was taken in 80 ml of aqueous pyridine (1:1) and refluxed gently over a period of 16 hr. It was diluted with ether and the aqueous portion was separated, saturated with solid NaCl and extracted with ether (3 x 15 ml). The ether portion and ether extracts were combined and washed with 25% HCl (3 x 15 ml), water (1 x 20 ml), 10% aqueous NaHCO₃ (2 x 15 ml) and again with water (1 x 20 ml) and brine (1 x 20 ml) and dried. Ether was flashed off and the residue was purified by column chromatography on SiO₂-gel (25 g) to afford 1,2-cyclobutane diol 34 (0.643 g, 68.40% yield) as a viscous liquid. PMR δ(CDCl₃) (Fig. 19): 4.99-4.57 (m, 1H, -CH₂-OAc), 4.28-3.38 (bm, 4H, -O-H, -CH₂-OH), 3.61 (s, 3H, COOCH₃), 1.97 (s, 3H, COOCH₃), 2.22 (t, 3H, CH₂-COOCH₃), 1.8-1.07 (bm, 26H, CH₂'s), 0.87 (t, 3H, -CH₃); IR (Neat) (Fig. 20): OH 3440 cm⁻¹; COOCH₃ and COOCH₃ 1740 cm⁻¹; OCOC₂H₅ 1240; 1370, 1030 cm⁻¹.

The diol 34 (100 mg) was mixed with pyridine (2 ml) and Ac₂O (2 ml) and kept at r.t. in a stoppered 10 ml flask, for 16 hr. The mixture was diluted with ether (30 ml) and washed successively with water (2 x 10 ml), 25% HCl (3 x 10 ml), 10% NaHCO₃ (2 x 10 ml), water (2 x 10 ml) and brine (15 ml).
and dried. Ether was flashed off and the residue was chromatographed on silica gel (4.0 g) to furnish pure tri-acetate derivative 36 (120 mg, 83.33% yield) as a liquid. PMR δ(CCl₄) (Fig. 21): 5.41-5.1 and 5.0-4.58 (2H, 3H, CH-0Ac and cyclobutane CH-0Ac) 3.61 (s, 3H, COOCH₃), 2.22 (t, 3H, J = 7Hz, -CH₂-COOCH₃), 2.04 (s, 3H, OCOCH₃), 1.93 (s, 6H, -OCOCH₃), 1.82-1.05 (bm, 26H, CH₂'s), 0.88 (t, 3H, -CH₃); IR (Neat) (Fig. 22): COOCH₃ and OCOCH₃ 1740 cm⁻¹; OCOCH₃ 1240 cm⁻¹.

Methyl 14-Acetoxy-9,11-eicosadienoate 16 from 34

Diol 34 (0.8 g, 1.94 mmole), triethyl orthoformate (2 ml) and benzoic acid (0.05 g) were heated in a 5 ml r.b. flask, arranged for distillation. Bath temperature was gradually raised so that EtOH started slowly distilling and then the bath temperature was raised from 140-150°C. It was maintained at this temperature, for 8 hr, when no more EtOH distilled. The reaction mixture was diluted with ether (30 ml) and washed successively with aq. 10% NaHCO₃ (3 x 15 ml), water (2 x 15 ml) and brine (1 x 20 ml) and dried. The solvent was removed to get a coloured residue (0.7125 g). It was taken in a 5 ml r.b. flask, arranged for distillation, and 0.05 g of benzoic acid was added to it. The flask was heated, in an oil bath, slowly and the temp. was maintained
between 180-200°C, for 4 hr. The reaction mixture was
diluted with ether (30 ml) and washed with 10% aqueous
NaHCO₃ (3 x 15 ml), water (2 x 15 ml) and brine (20 ml).
Ether was flashed off to get 0.6532 g of the crude
product, which was purified by column chromatography on
silica gel (8.0 g) to afford pure 1,3-diene 16 (0.5134 g,
69.94% yield) as a neat liquid. The diene 16 prepared
by this method was identical (NMR, IR, UV) with 16
prepared earlier by oxidative bis-decarboxylation followed
by pyrolysis of 14.

Methyl 14-Acetoxy-9,12-peroxy-eicos-10-enoate 17

A solution of diene 16 (5g, 13.15 mmole) and Rose Bengal
(0.5 g, 0.49 mmole) in 1200 ml of dry methanol: CCl₄ (1:9)
was simultaneously irradiated with 125 W medium pressure
mercury lamp (RCA) and treated with a continuous stream of
dry oxygen for 72 hr., while circulating an ice-cold solution
of 1% aqueous potassium chromate both as a filter and as a
coolant. After the reaction was complete (tlc), solvent
was removed under reduced pressure, at room temperature
(30°C), and the residue was chromatographed on silica gel
(100 g) to give the adduct 17 (4.3 g, 79.3% yield) as a
liquid. PMR δ(CCl₄) (Fig. 25): 5.86, 5.82 (two s, 2H, olefinic
protons), 4.95 (m, 1H, -CH-OAc), 4.38 (bt, 2H, H-C-O-O),
3.58 (s, 3H, COOCH₃), 2.22 (t, 2H, J = 7Hz, -CH₂-COOCH₃),
1.96 (s, 3H, OCOCH₃), 1.82-1.1 (bm, 26H, CH₂'s), 0.88 (t,
3H, -CH₃); IR (Neat) (Fig. 26): COOCH₃ and OCOCH₃ 1740 cm⁻¹;
OCOCH₃ 1240, 2940, 2860, 1440, 1380, 1030, 725 cm⁻¹.

Methyl 14-Acetoxy-9,12-dihydroxysicosanoate ¹⁸

Endoperoxide ¹⁷ (3.49 g, 11.18 mmole) was taken in
methanol (100 ml) and stirred over Raney Ni (1.05 g, 30%) under hydrogen atmosphere for 6 hr. Methanol was decanted off and the catalyst was washed with methanol (3 x 15 ml). The combined solvent was removed under reduced pressure to give the crude diol (3.5 g), which on purification by chromatography on silica gel (20 g) afforded pure 1,4-diol ¹⁸ (2.79 g, 79.26% yield) as a liquid. PMR $ (CCl₄) (Fig. 27):
4.95 (m, 1H, -CH-OAc), 3.6 (s, 3H, COOCH₃), 3.56 (bm, 4H,
-CH-OH and -CH-OH; two H exchangeable with D₂O), 2.22 (t, 2H, J = 7Hz, CH₂-COOCH₃), 2.02 and 1.98 (2s, 3H, -OCOCH₃),
1.9-1.1 (bm, 30H, CH₂'s), 0.88 (t, 3H, -CH₃); IR (Neat) (Fig.28):
OH 3420 cm⁻¹; COOCH₃ and OCOCH₃ 1735 cm⁻¹; OCOCH₃ 1245; 2940,
2860, 1440, 1375, 1030 cm⁻¹; Mass: m/e 416 (M⁺ 1%), 338(20%),
320 (3%), 253 (30%), 241(81%), 227 (100%), 155 (35%), 81 (53%),
55 (71%), 43(72%). (Found C,67.09; H, 10.38; C₂₃H₄₄O₆ requires C, 66.34; H, 10.57%).

Methyl 14-Acetoxy-9,12-dioxeicosanoate ¹⁹

To a suspension of pyridinium chlorochromate (4.35 g,
20.18 mmole) in dry CH₂Cl₂ (50 ml) was added the diol ¹⁸
(2.8 g, 6.73 mmol), at room temperature (37°C). After stirring for 3 hr, the reaction mixture was diluted with ether (50 ml). The solvent was decanted and the residue was washed with ether (3 x 20 ml). The combined solvent was passed through a short silica gel column. Removal of solvent gave the crude dione (2.62 g), which was further purified by silica gel (50 g) chromatography to afford pure 19 (2.37 g, 85.55% yield) as a wax (m.p. 35-36°C).

PMR $\delta$ (CCl$_4$) (Fig. 29): 5.09 (m, 1H, -CH-OAc), 3.58 (s, 3H, COOCH$_3$), 2.57 (s, 4H, CO-(CH$_2$)$_2$-CO), 2.5-2.1 (m, 6H, CH$_2$-COOCH$_3$ and CH$_2$-CO-(CH$_2$)$_2$-CO-CH$_2$), 1.94 (s, 3H, COCH$_3$), 1.75-1.1 (bm, 20H, CH$_2$'s), 0.88 (t, 3H, -CH$_3$); IR (CHCl$_3$) (Fig. 30: 3015, 2940, 2860, 1730, 1440, 1370, 1245, 1030 cm$^{-1}$; Mass: m/e 412 (M$^+$ 6%), 352 (38%), 321 (24%), 241 (17%), 210 (100%), 195 (48%), 139 (59%), 111 (43%), 83 (28%), 43 (67%).

(Found C, 66.16; H, 9.93; C$_{23}$H$_{40}$O$_6$ requires C, 66.99; H, 9.7).
was chromatographed on silica gel (35 g) to furnish enedione 20 (1.78 g, 95% yield) as a liquid, b.p. 235-240°C/0.1 mm (bath temp.) PMR δ(CCl₄) (Fig. 31): 6.77 (dt, 1H, J = 16Hz, J = 7Hz, -CO-CH=CH-), 6.03 (d, 1H, J = 16H, -CO-CH=CH-), 3.6 (s, 3H, COOCH₃), 2.9-2.03 [bm, 10H, -CO-(CH₂)₂-CO-,CH₂-C=O, CH₂-COOCH₃ and allylic protons], 1.9-1.05 (bm, 18H, CH₂'s), 0.88 (t, 3H, -CH₃); IR (Neat)(Fig. 32): COOCH₃ 1740 cm⁻¹; trans-enone 1695, 1675, 1632, 980 cm⁻¹; ketone C=O 1715 cm⁻¹; UV: λₑₒₑ 227 nm (ε = 6.89 x 10³); Mass: m/e 352 (M⁺ 53%), 321 (32%), 241 (10%), 195 (58%), 167 (58%), 139 (100%), 111 (64%), 83 (30%), 55 (68%), 41 (22%). (Found C, 71.70; H, 10.89; C₂₁H₃₆O₄ requires C, 71.59; H, 10.22%).

(b) Basic alumina (Grade-I, 3.0 g) was filled in a column (1 cm x 30 cm) and diketone 19 (0.1 g, 0.24 mmol) was loaded on it, by dissolving in 1 ml of methylene chloride (dry). It was then eluted with another 2 ml of dry CH₂Cl₂ so as to bring the compound in the middle of the column. After 12 hr., the column was eluted with ethyl acetate (75 ml). The solvent was removed to get 0.092 g of the crude product, which was purified by chromatography on silica gel to afford enedione 20 (0.0732 g, 85.9% yield). The enedione prepared by this method showed NMR, IR, UV identical to 20 prepared earlier by treatment of 19 with DBU.
Generation of cyclopentadiene from the dimer: A 100 ml r.b.
flask containing 20 ml of dicyclopentadiene was set up
for fractional distillation, at atmospheric pressure. The
flask was gently heated and the contents were allowed to
come to a brisk reflux, whereupon the monomer began to
distil at 40-42°C. Distillation was continued at a rate
so as to keep the distillate temperature below 45°C.

Enedione 20 (0.5 g, 1.42 mmole), cyclopentadiene (3.5 ml)
and dry toluene (3.5 ml) were taken in a long oyxex tube,
having a standard joint. To it a pinch of hydroquinone
(antipolymeric, 0.01 g) was added. The tube was evacuated,
at -50°C, and then sealed under vacuum. It was heated, in an
oil bath, at 135-140° for 10 hr. and then at 155-160° for
another 17 hr. The solvent and other volatile material was
removed under high vacuum and the residue was purified by
chromatography on silica gel (5.0 g) to furnish the adduct 21
(0.540 g, 91% yield) as a liquid. PMR (CCl₄) (Fig. 33):
6.28-5.73 (m, 2H, olefinic H), 3.59 (s, 3H, COOCH₃), 3.05-2.13
(bm, 11H, CH₂-COOCH₃, -CH₂-CO-(CH₂)₂-CO-CH₃ and allylic protons),
1.82-1.04 (bm, 23H, CH₂'s and ring junction methine protons),
0.87 (t, 3H, -CH₃); IR (Neat) (Fig. 34): COOCH₃ 1740 cm⁻¹;
C=O 1708; 3060, 2940, 2860, 1360,1175, 725 cm⁻¹; Mass: m/e
418 (M⁺ 17%), 352 (11%), 353 (100%), 321 (99%), 209(22%), 139(18%),
111 (35%), 66 (74%), 55 (43%).

(Found C, 74.64; H, 9.98; C_{26}H_{42}O_4) requires C, 74.64; 
H, 10.04%).

(exo/endo)-2-[3-Oxo-2-(6-carbomethoxy-hexyl)-cyclopent-1-enyl] - 
(endo/exo)-3-hexylbicyclo[2,2.1] hept-5-ene (22)

1,4-Diketo adduct 21 (1.81 g, 4.33 mmole) was taken in 
90 ml of ethanol and to it 6% aqueous sodium hydroxide (28.86 ml, 
43.25 mmole) was added. The mixture was refluxed, with 
stirring under N₂, for 24 h. The progress of the reaction 
was followed by recording UV of the aliquots, after every 
3 hr. Ethanol was distilled off, under reduced pressure, and 
the aqueous portion was acidified with conc. HCl (pH ~ 3). It 
was saturated with solid NaCl and then extracted with ether 
(4 x 20 ml). The ether extracts were combined and washed 
with water (2 x 20 ml), brine (25 ml) and dried. Ether was 
flashed off and the crude was esterified with CH₂N₂ to give 
crude material (1.73 g). It was chromatographed on SiO₂-IIb column (45 g, 2 cm x 55 cm) (TLC: 25% ethyl acetate in pet. 
ether). The following pooled fractions were collected:

<table>
<thead>
<tr>
<th>Frac.</th>
<th>pet. ether</th>
<th>volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>11 x 40 ml</td>
</tr>
<tr>
<td>2</td>
<td>5% EtOAc in</td>
<td>8 x 20 ml</td>
</tr>
<tr>
<td></td>
<td>pet. ether</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5% EtOAc in</td>
<td>11 x 20 ml</td>
</tr>
</tbody>
</table>
|       | pet. ether | 0.59 g, liquid, 
|       | 0.35, starting material |

Rᵢ: 0.35, starting material 21
Solvent was removed from fraction 4 to yield the cyclopentenone adduct 22 (1.0 g, 57.80% yield, without taking into account the recovered diketone 21) as a liquid.

PMR 6(CCl₄) (Fig. 35): 6.3, 6.05 (2m, 2H, -CH = CH -), 3.6 (s, 3H, COOCH₃), 2.88 (bm, 2H, bridgehead allylic protons), 2.7-1.8 (m, 9H, CH₂-COOCH₃, CH₂-CO and five allylic protons), 1.78-1.03 (bm, 21H, CH₂'s and ring junction methine proton), 0.88 (t, 3H, -CH₃); IR (Neat) (Fig.36): COOCH₃ 1740 cm⁻¹; five-membered ring C=O and enone double bond 1698, 1625 cm⁻¹; 3060, 2940, 2860, 1440, 1360, 730 cm⁻¹; UV: λmax 251 nm (ε = 1.6 x 10⁴).

(Found C, 78.68; H, 10.23; C₂₆H₄₀D₃ requires C, 78.0; H, 10.0%).

(endo/exo)-2-[3-Oxo-2-(6-carbomethoxyhexyl)-cyclopentyl]-
(endo/exo)-3-hexylbicyclo[2.2.1]hept-5-ene (23)

(a) To a stirred solution of Li metal (0.1 g, 0.014 g-atom) in 40 ml of liquid ammonia (commercial, undistilled) was added dropwise a soln. of cyclopentenone adduct 22 (0.1 g, 0.25 mmole) and dry t-butanol (0.0185 g, 0.25 mmole) in 6 ml of dry ether, under nitrogen atmosphere, at -50°C. The reaction mixture was stirred for 30 minutes and then NH₄Cl
(5 g) was added. The ammonia was allowed to evaporate and then 20 ml of water and 20 ml of ether were added. The ether layer was separated and the aqueous layer was saturated with NaCl and extracted with ether (3 x 15 ml). The ether extracts were combined and washed with 5% HCl (1 x 15 ml), water (1 x 15 ml) and brine (1 x 15 ml) and dried. Solvent was stripped off to give the crude product which was purified by column chromatography on silica gel (6.0 g) to afford cyclopentanone 23 (0.0537 g, 53.43%) as a liquid.

(b) To a solution of cyclopentenone adduct 22 (0.220 g, 0.55 mmole) in 25 ml of benzene: water (1:1) were added NaHCO₃ (2.50 g, 29.76 mmole), Na₂S₂O₄ (0.86 g, 4.94 mmole) and tricaprylylmethyl ammonium chloride (0.2415 g, 0.49 mmole). The mixture was refluxed, with stirring under nitrogen atmosphere, for two hr. After this, more of Na₂S₂O₄ (3.64 g, 20.09 mmole) was added (4 hr), in portions of 0.43 g each every 30 minutes. The progress of the reaction was followed by tlc (20% EtOAc in pet. ether). The benzene layer was separated and the aqueous portion was extracted with benzene (3 x 15 ml). The combined benzene extracts were washed with water (2 x 15 ml), brine (15 ml) and dried. The solvent was removed and the crude material was chromatographed on SiO₂-gel column (1 cm x 30 cm, 10g) (TLC: 25% EtOAc in pet. ether). The following pooled fractions were collected:
Frac. 1 pet ether 3 x 20 ml -

Frac. 2 4\% EtOAc in pet. ether 3 x 20 ml -

Frac. 3 4\% EtOAc in pet. ether 6 x 20 ml 0.167 g, liquid, R_f: 0.49

Frac. 4 4\% EtOAc in pet. ether 3 x 20 ml 0.042g, liquid, R_f: 0.40. starting material 22

Solvent was removed from fraction 3 to yield the cyclopentanone 23 (0.167 g, 75.53\% yield, without taking into account the recovered cyclopentanone 22) as a liquid. A sample of 23 showed NMR and IR identical with cyclopentanone prepared earlier by Li/liq. NH_3 reduction of 22. PMR δ(CDCl_3) (Fig. 39): 6.12-5.98 (m, 2H, -CH=CH-), 3.57 (s, 3H, COOCH_3), 2.78 (m, 2H, allylic bridgehead protons), 2.6 (m, 1H, -CH-C=O), 2.4-1.90 (m, 4H, -CH_2-COOCH_3 and -CH_2-C=O), 1.88-1.05 (bm, 27H, CH's and CH_2's), 0.89 (t, 3H, -CH_3); IR (Neat) (Fig. 40): COOCH_3 and cyclopentanone C = O 1740 cm^{-1}; 3080, 2940, 2860, 1470, 1265, 730 cm^{-1}.

(Found C, 78.21; H, 10.12; C_{26}H_{42}O_3 requires C, 77.61; H, 10.44\%).

(\pm)-11,15-dideoxy PGE_1 Methyl Ester (24)

The cyclopentanone adduct 23 (0.320 g, 0.79 mmole) was taken in a 5 ml r.b. flask fitted to an electrically heated column (1.5 cm x 12 cm), filled with glass helices, which in turn was connected to a cold trap. The flask was heated to
240-260°C (bath temperature), under vacuum (0.2-0.3 mm), while the temperature of the column was maintained at 500°C, whereby (+)-11,15-dideoxy PGE$_1$ methyl ester 24 (0.2549, 95.13% yield) distilled over as a pale yellow liquid. It was purified by column chromatography on silica gel (5.0 g) to get pure 24.

PMR $^6$(CCl$_4$) (Fig. 41): 5.71-5.12 (m, 2H, -CH=CH), 3.59 (s, 3H, -C00CH$_3$), 2.65-1.85 (m, 8H, -CH$_2$-C0OCH$_3$, -CH$_2$-C0-CH-, -CH$_2$-CH=CH-CH-), 1.8-1.1 (bm, 20H, CH$_2$'s), 0.88 (t, 3H, -CH$_3$); IR (Neat) (Fig. 42): C0OCH$_3$ and cyclopentanone C=O 1740 cm$^{-1}$; trans-CH=CH 970 cm$^{-1}$; 2980, 2940, 2860, 1460, 1120 cm$^{-1}$; Mass: m/e 336 (M$^+$ 39%), 305(24%), 304(28%), 194(57%), 109(100%), 96(48%), 83(45%), 67(43%), 55(67%).

Equilibration of side chains in 11,15-dideoxy PGE$_1$ Methyl Ester (24) (Presuming that the cis-isomer is also present).

To a solution of the ketone 24 (0.250 g) in absolute ethanol (125 ml) was added anhydrous potassium acetate (5.5 g) and the mixture was stirred at room temperature (35°C) for 123 hr. Ethanol was removed in a stream of N$_2$ and then under high vacuum. The residue was partitioned between ether (60 ml) and water (50 ml). It was acidified (pH ~3) with 10% aq. HCl and the ether portion was separated. The aqueous portion was saturated with NaCl and extracted with ether (2 x 25 ml).
The combined ether portion was washed with water (2 x 20 ml), brine (1 x 20 ml) and dried. The solvent was removed to get a pale yellow liquid having its tlc ($R_f$ and colour) identical to the starting ketone 24.

(+)-11-Deoxy-15-acetoxyprostaglandin $E_1$ Methyl Ester (25)

To a solution of (+)-11,15-dideoxy PG$E_1$ methyl ester 24 (0.110 g, 0.32 mmole) in dry CCl$_4$ (12 ml) was added N-bromo succinimide (0.0611 g, 0.34 mmole) and benzoyl peroxide (0.010 g). The mixture was refluxed under anhydrous conditions, for 1 hr, when the whole of the solid (succinimide) had come to the surface. It was filtered off and the solvent was removed, under reduced pressure, to give a light yellow liquid (allylic bromide, 0.128 g). The crude bromide (0.128 g, 0.30 mmole) was taken in glacial acetic acid (8 ml) and silver acetate (0.0740 g, 0.44 mmole) was added to it. The flask was covered with a thin Al foil and the mixture was refluxed, with stirring and maintaining anhydrous conditions, for 1 hr. It was brought to room temperature and filtered. The filtrate was diluted with ether (60 ml) and washed with water (3 x 15 ml), 10% aqueous NaHCO$_3$ (3 x 15 ml) again with water (2 x 15 ml) and brine (15 ml) and dried. The solvent was removed to get the crude product (0.0942 g), which was purified by column chromatography on silica gel (8 g) to afford pure acetate 25 (0.067 g, 52% yield) as a liquid.
PMR $\delta$(CCl$_4$) (Fig. 43): 5.5 (m, 2H, -CH=CH-), 5.15 (m, 1H, -CH-CH-OAc), 3.6 (s, 3H, -COOCH$_3$), 2.6-1.9 (m, 6H, -CH$_2$-COOCH$_3$, -CH-CH= and -CH$_2$-CO-CH-), 1.97 (s, 3H, -OCOCH$_3$), 1.8-1.06 (bm, 20H, CH$_2$'s), 0.9 (t, 3H, -CH$_3$);

IR (Neat) (Fig. 44): COOCH$_3$, OCOCH$_3$ and cyclopentanone C=O 1740 cm$^{-1}$; OCOCH$_3$ 1240 cm$^{-1}$; trans-CH=CH 970 cm$^{-1}$; 2940, 2860, 1440, 1370, 1025 cm$^{-1}$.

(+)-11-Deoxy PGE$_1$ Methyl Ester and (+)-15-epi-11-deoxy PGE$_1$ Methyl Ester (epimeric mixture 26)

To a stirred solution of the acetate 25 (0.060 g, 0.152 mmole) in dry methanol (5 ml) was added K$_2$CO$_3$ (0.0231 g, 0.167 mmole), when the suspension turned yellow instantly. It was stirred, at room temperature (35°C), for 20 minutes. Methanol was removed under vacuum and the residue was diluted with water (5 ml) and extracted with ether (3 x 15 ml). The aqueous layer, which remained coloured even after extraction with ether, was acidified with conc. HCl (pH~3) and extracted with ethyl acetate (4 x 10 ml). The combined ether and EtOAc extracts were washed with water (2 x 10 ml) and brine (10 ml) and dried. The solvent was removed to get the crude product (0.045 g), which was loaded on a silica gel (6 g) column and eluted with 20% ethyl acetate in pet. ether to get a mixture of C-15 epimeric alcohols 26 (0.036 g, 68% yield) as a liquid. This appeared to be a 1:1 mixture of two isomers,
separable on tlc (30% ethyl acetate in pet. ether; Rp 0.43 and Rp 0.35).

PMR$^{43}$ $^6$(CCl$_4$) (Fig. 45): 5.58 (m, 2H, CH=CH), 4.05 (bm, 1H, =CH-CH-OH), 3.61 (s, 3H, COOCH$_3$), 2.65-1.92 (m, 6H, -CH$_2$-COOCH$_3$, CH$_2$-CO-CH and =CH-CH), 1.85-1.05 (bm, 21H, CH$_2$'s), 0.9 (t, 3H, -CH$_3$), 2.95 (b, 1H, CH-OH exchangeable with D$_2$O);

IR$^{43}$ (neat) (Fig. 46): OH 3470 cm$^{-1}$; COOCH$_3$ and cyclopentanone C=O 1740 cm$^{-1}$; trans-CH=CH 970 cm$^{-1}$, 2960, 2940, 2860cm$^{-1}$;

Mass$^{43}$ (Fig. 47): m/e 352 (M$^+$ 3%), 334 (3%), 281 (55%), 249 (49%), 193 (26%), 109(45%), 83 (100%), 69(40%), 55(70%).
Fig. 9: PMR spectrum of methyl 12-acetoxy-cis-9-octadecenoate (13)
Fig. 10: IR spectrum of methyl 12-acetoxy-st-5,9-octadecenoate (13)
Fig. 11: PMR spectrum of cis-1,2-dicarboxy-(cis/trans)-3-(?-acetoxyoctyl)-4-(7-carbomethoxyheptyl)-cyclobutane (14)
Fig. 12: IR spectrum of cis-1,2-dicarboxy-(cis/trans)-3-(2-acetoxyoctyl)-4-(7-carboxyhexyl)-cyclobutane (14)
Fig. 13: PMR spectrum of (cis/trans)-3-(2-acetoxyoctyl)-
-4-(7-carbomethoxyheptyl)-cyclobut-1-ene (15)
Fig. 14: IR spectrum of (cis/trans)-3-(2-acetoxyoctyl)-4-\((7\text{-carboxymethoxyheptyl})\)-cyclobut-1-ene (15)
Fig. 15: PMR spectrum of methyl 14-acetoxy-9,11-eicosadienoate (16)
Fig. 16: IR spectrum of methyl 14-acetoxy-9,11-eicosadienoate (16)
Fig. 17: PNR spectrum of cis-1,2-carbonyldioxy-(Cis-trans)-
3-(2-acetoxyoctyl)-4-(7-carbomethoxyheptyl)-
cyclobutane (33).
Fig. 18: IR spectrum of \( \text{cis-1,2-carbonyldi oxy-} \) 
\( \text{thoxyhapty 1) -cyclobutane} \) (33)

![IR Spectrum Diagram](image-url)
Fig. 19: PMR spectrum of cis-1,2-dihydroxy-3-acetoxy-1-cyclobutane (24)
Fig. 20: IR spectrum of cis-1,2-dihydroxy-(cis/trans)-3-(2-acetoxyoctyl)-cyclobutane (34)
Fig. 21: PMR spectrum of cis-1,2-diacetoxoy-(cis/trans)-
3-(2-acetoxoctyl)-4-(7-carbethoxyheptyl)-
cyclobutane (36)
Fig. 22: IR spectrum of cis-1,2-diacetoxy-(cis/trans) -3-(2-acetoxyoctyl)-4-(7-carboxethoxyheptyl)-cyclobutane (36)
Fig. 23: PMR spectrum of (endo/exo)-2-(2-acetoxy-octyl)-(endo/exo)-3-(7-carbomethoxyheptyl)-endo and exo-6-ethoxy-5,7-dioxa-cis-bicyclo[3.2.0]heptane (35)
Fig. 24a: UV spectrum of the trienes from the pyrolysis of (15)

Fig. 24b: UV spectrum of the enone (20) and its cyclisation products
Fig. 25: PMR spectrum of methyl 14-acetoxy-9,12-peroxy-eicos-10-enoate (17)
Fig. 27: PMR spectrum of methyl 14-acetoxy-9,12-dihydroxyicosanoate (18)
Fig. 28: IR spectrum of methyl 14-acetoxy-9,12-dihydroxyeicosanoate (18).
Fig. 29: PMR spectrum of methyl 14-acetoxy-9,12-dioxoicosanoate (19)
Fig. 30: IR spectrum of methyl 14-acetoxy-9,12-dioxo-eicosanoate (19)
Fig. 31: $^1$H NMR spectrum of methyl 9,12-dioxo-eicos-13-enoate (25)
Fig. 32: IR spectrum of methyl 9,12-dioxo-docos-trans-13-enoate (20)
Fig. 33: PMR spectrum of (endo/exo)-2-(11-carbamethoxy-1,4-dioxo-undecyl)-(endo/exo)-3-hexylbicyclo[2.2.1]hept-5-ene (21)
Fig. 34: IR spectrum of (endo/exo) 2-(11-carboxymethoxy-1,4-
dioxy-undecyl)-endo/3-hexylbicyclo[2.2.1]
Fig. 35: PRR spectrum of (endo/exo)-2-[(6-carboxyhexyl)oxy]hept-5-ene (22).
Fig. 37: PMR spectrum of (endo/exo)-2-[3-oxo-2-(6-carboxyhexyl)-cyclopent-1-enyl]-(endo/exo)-3-hexylbicyclo[7.2.1]heptane (41)
Fig. 38: IR spectrum of (endo/exo)-2-[5-oxo-2-(6-carboxymethoxy-hexyl)-cyclopent-7-enyl]-(endo/exo)-3-hexylbicyclo-[2.2.1]heptane (41)
Fig. 39: PMR spectrum of (endo/expo)-2-[3-oxo-2-(6-carboxethoxyhexyl)-cyclopentyl]- (exo/endo)-3-hexylbicyclo[2.2.1]hept-5-ene (23)
Fig. 40: IR spectrum of (endo/exo)-2-[3-oxo-2-(6-carbomethoxyhexyl)-cyclopentyl]-(exo/endo)-3-hexylbicyclo[2.2.1]hept-5-ene (23)
Fig. 41: PMR spectrum of 11,15-dideoxy DGE, Methyl Ester (24).
Fig. 42: IR spectrum of 11,15-dideoxy PGE₁ Methyl Ester (24)
Fig. 43: PMR spectrum of (+)-11-deoxy-15-acetoxyprostaglandin E₁, Methyl Ester (25)
Fig. 44: IR spectrum of (±)-11-deoxy-15-acetoxyrostaglandin E1 Methyl Ester (25)
Fig. 45: PMR spectrum of (+)-11-deoxy PGE1 Methyl Ester and (+)-15-en1-11-deoxy PGE1 Methyl Ester (26)
Fig. 46: IR spectrum of (r)-11-deoxy PGE$_1$ Methyl Ester and (t)-15-epi-11-deoxy PGE$_1$ Methyl Ester (26)
Fig. 47: Mass spectrum of (+)-11-deoxy PG E\(_2\) Methyl Ester and (+)-15-epi-11-deoxy PG E\(_2\) Methyl Ester (26)
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