CHAPTER – 1

Fatty Acid Derivatives of Cyclic Ketones
1.1 Theoretical

Active methylene compounds are represented by the formula \( \text{CH}_2\text{XY} \), where \( X \) and \( Y \) can be carbonyl, cyanide, acid, aldehyde or any electron withdrawing group which makes the hydrogen/s bonded to \( \alpha \)-carbon acidic. Several active methylene compounds such as ethylacetoacetate, malonic ester, ketones, aldehydes have been studied for their synthetic utility. They have been used for the formation of carbon-carbon, carbon-nitrogen, carbon-sulphur, carbon-oxygen bonds due to the easy elimination of acidic hydrogen. Active methylene compounds reacts with different functional groups to yield different valuable intermediates for the synthesis of heterocycles. Active methylene compounds such as carboxylic ester when reacts with carboxylic acid yields \( \beta \)-ketoester\(^{1a}\), and with ketones yield \( \beta \)-hydroxy ester\(^{1b}\). Active methylene undergo Michael Addition\(^{2}\) reaction with double bond\(^{1c}\).

Palladium is a well known catalyst used in alkylation, allylation\(^{2}\) of active methylene compound. Kimura and coworkers\(^{3}\) has carried out the alkylation of active methylene compound (II) in the presence of Pd catalyst with triethylborane as promoter (Scheme 1.1).
The Horino et al.\textsuperscript{4} has also carried out the C-allylation of ortho-hydroxyacetophenone and its derivatives (V) with a number of allyl alcohols (IV) (Scheme 1.2).

Pd-catalysed condensation of active methylene compound with methyl-6-acetoxymethyl-hepta-2,6-dienoate (VII) resulted in six membered adduct in moderate to good yields (VIII, IX) (Scheme 1.3)\textsuperscript{5}. 

\( \text{(I)} + \text{(II)} \xrightarrow{\text{Pd(OAc)}_2 / \text{ligand}} \text{(III)} \)

\( \text{(IV)} + \text{(V)} \xrightarrow{\text{Pd(OAc)}_2 (5 \text{ mol} \%) \text{ PPh}_3 (10 \text{ mol} \%) \text{ Et}_3 \text{B (2.4 mol)}} \text{(VI)} \)
It has been found that \((\text{PPh}_3\text{Pd})/\text{tetrakis (triphenyl phosphine) Palladium}\) acts as an efficient catalyst for the alkylation of active methylene compounds by alkyl alcohols at 100°C^6.

Pd catalyses the reaction of trimethylsilylethynyl derivatives with aromatic halides in the presence of silver oxide to yield poly (aryleneethynylene)s functionalized with acetylated glucopyranosyl unit.

Rao and coworker^8 synthesized arylidene acetonitriles and arylidene heterocycles by condensation of active methylene compound (X) and carboxyl compounds (XI) in presence of anhydrous zinc chloride (Scheme 1.4).
Esters bearing a leaving group at the α position and ketones react with Bu₆CrLi₃ to produce enolates⁹.

Cyclopentanone and cyclohexanone (XIII) were alkylated with 1-octene and 1-decene (XIV) in the presence of silver (I) or silver (II) oxides under normal pressure at 80-130°C to give corresponding 2-n-alkyl cycloalkanones (XV) in 68-77% yields (Scheme 1.5)¹⁰.

\[
\begin{align*}
\text{(XIII)} & \quad \text{+} \quad \text{(XIV)} \\
& \quad \overset{\text{AgO / Ag₂O}}{\text{80 - 130°C}} \quad \text{(XV)}
\end{align*}
\]

Scheme 1.5

Ni catalyst has been found to be more efficient in alkylation of active methylene compounds than palladium, however are more sensitive than corresponding Pd ones¹¹.

Myrcene (XVI) on reaction with ethylacetoacetate (XVII) in presence of rhodium catalyst in the ionic liquid 1-ethyl-3-methyl imidazolium triflimide resulted in the formation of carbon-carbon bond in excellent yield (Scheme 1.6)¹².
Regioselective alkylation of active methylene compounds (XX) with allyl bromides and propargyl bromide on the surface of neutral alumina impregnated with sodium ethoxide or potassium tert-butoxide in solvent free environment provided 4,4-bis-functionalized-1,6-dienes (XXI) and 1,6-diynes (XXII) (Scheme 1.7).}

A good example of carbon-carbon bond formation is microwave condensation of carbonyl compounds (XXIII), N,N-dimethylformamide dimethylacetal (XXIV) and methylene active nitriles to yield 2-
pyridones (XXV) in moderate to good yields and high purities (Scheme 1.8).}

![Reaction scheme](image)

**Scheme 1.8**

3-Methylthio-1,4,2-benzodithiazin[1,1-dioxide when reacted with active methylene compounds and 4-DMAP resulted in formation of 4-dimethylaminopyridinium (1,1-dioxo-1,4,2-benzodithiazin-3-yl) methanides.

Reactions of paracyclophane with active methylene compounds in presence of polyphosphoric acid gave fused spiro pyranoindano paracyclophane derivatives.

Larsson and coworker prepared various 1-alkylthio and 1-crotylthio-1-aminoalkenes by the reaction of ketones and active methylene compounds, which were further rearranged to corresponding thioamides.
Active methylene compounds in the presence of a base easily undergo reactions with carbondisulphide giving diaxion, which on subsequent alkylation produces ketone mercaptals\(^{18}\).

Base catalyzed condensation of cyclokanones (XXVI) with n-alkylaldehydes (XXVII) in presence of H\(_2\)O yields 2-(1-hydroxyalkyl) cyclokanones (XXVIII) (Scheme 1.9)\(^{19}\).

\[
\text{O} + \text{CHO - (CH}_2\text{)}_3 - \text{CH}_3 \xrightarrow{\text{H}_2\text{O, NaOH}} \text{OH}
\]

\(25^\circ\text{C}, 3.5 \text{ hr.}
\)

\(\text{(XXVI)} \quad \text{(XXVII)} \quad \text{(XXVIII)}\)

**Scheme 1.9**

An efficient and highly enantioselective conjugate addition of alkylzinc reagents to cyclic nitroalkenes were carried out in presence of 0.5-5mol\% (CuTf)\(_2\), C\(_6\)H\(_6\) and 1-10mol\% chiral amino acid based phosphine ligands at 0\(^{0}\)C\(^{20}\).

Condensation of [hydroxy (tosyloxy) indo]-benzene with ketones in DMSO-H\(_2\)O afforded \(\alpha\)-hydroxy ketones under neutral conditions and in good yields\(^{21}\). Reaction of active methylene nitriles with pyrrole-
2-dithiocarboxylates in KOH-DMSO medium afforded 2-(1-alkylthio-2-cyanoethenyl) pyrroles in good to high yield\textsuperscript{22}.

Base catalysed reaction of active methylene compounds via radical pathway with 5-trimethylsilyl-2-cyclohexanone gave 1,4-addition product with diastereopurities\textsuperscript{23}.

Reaction of active methylene compounds with non-activated olefins under solid-liquid phase transfer conditions in the presence of iodine gave cyclopropanes of wide range\textsuperscript{24}.

Active methylene ketones when reacts with aryl or alkyl isothiocyanates leads to the formation of respective β-oxothioamides which are valuable intermediates for the synthesis of substituted thiophenes and thiazoles\textsuperscript{25}.

The active methylene moiety present in the acetonitriles and thiazolidinone and oxazolone undergoes condensation with pyridinium salts to yield 4-substituted 1,4-dihydropyridines and 1,4-dihydro (thiazolono/ oxazolono)- pyridines respectively\textsuperscript{26}.

Active methylene compounds undergoes alkylation with polymer supported alcohols in presence of TMAD and Bu\textsubscript{3}P to give desired monoalkylated product as well as bis-alkylated product\textsuperscript{27}.

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Reaction of active methylene compounds (XXX) with Baylis-Hillman acetates (XXIX) in N,N-dimethylformamide in the presence of a base (K₂CO₃) gives ortho-hydroxyacetophenone derivatives (XXXI) (Scheme 1.10)²⁸.

mercaptopacetic acid on condensation with ketones yielded biologically active derivatives of spiro thiazolidinone. The syntheses of spiro compounds have gained importance because of their biological significance. Certain spiro compounds showed antifungal²⁹, antibacterial³⁰,³¹, pesticidal³², and anti HIV³³,³⁴ activities. Although a large number of common spiro compounds have appeared in literature³⁵, there is sporadic reports on the synthesis of spirothiazolidin-4-ones. Karali and coworkers³⁶ have synthesized 4-aza-1-thiospiro (4.5) dec-3-one derivatives of 3-phenyl-4-(2H)-quinazolinones in good yield.
Klemmensen and coworkers\textsuperscript{37} have reported synthesis of 1,3-oxathiolan-5-one-2-spiro-1-cycloalkanes by reaction of enamines with mercaptocarboxylic acid.

Paryzek and Kielezewisky\textsuperscript{38} prepared steroidal spirothiazolidinones by reacting steroidal compounds containing carboxyl group at different positions with mercaptoacetic acid and ammonium carbonate in dry benzene to give the corresponding spirothiazolidinones.

Rajopadhye and Popp\textsuperscript{39} have prepared 5, 3-phenylmethylspiro[3H-indole-3,2'-thiazolidine]-2,4'(1H) diones by the cyclocondensation of thiolactic acid with substituted isatin-3-amines in dry toluene.

Joshi and coworkers\textsuperscript{40} have reported the synthesis of spiro [3H-indole-3,2'-thiazolidine]-2(1H), 4'-diones by the reaction of mercaptoacetic acid with 3-arylimino-2H-indol-2-ones, which were prepared in situ by condensation of isatin with aromatic amines in dry toluene.

Al-Thebeiti and coworker\textsuperscript{41} have obtained spirothiazolidinones by treating cycloalkylidene-3-aminoquinazolinone derivatives with mercaptoacetic acid. The quinazoline derivatives were prepared by reacting 3-amino-2-methyl-3H-quinazolin-4-one with cyclic ketones.
It has been reported that cyclic ketones when incorporated in some structures, generally, found to enhance the antimicrobial activities. Keeping this in view, we have prepared the fatty derivatives of cyclic-ketones by taking methyl undec-10-enaote as the substrate and silver oxide as catalyst. Literature survey has revealed that this work has not been done earlier on fatty acid esters.
1.2 Results and Discussion

The synthesis of compound 3a, 3b, 4a and 4b have been performed by the reaction of methyl undec-10-enoate (1) and cyclic ketones (2a, b) in presence of silver oxide as catalyst. The cyclic ketone derivatives of methyl undec-10-enoate was prepared following the method of Yamamoto et al.\textsuperscript{43} by refluxing methyl undec-10-enoate with cyclic ketones (molar ratio, 1: 5) at 130–140\degree C (Scheme i).

\begin{align*}
&\text{CO}_2\text{Me} \quad + \quad \text{O} \\
&(\text{1}) \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad
Reaction of methyl undec-10-enoate (1) with cyclopentanone (2a)

Methyl undec-10-enoate (1) and cyclopentanone (2a) (molar ratio 1:5) were refluxed for 5 hrs at 130-132°C in presence of silver oxide catalyst. The progress of the reaction was monitored by TLC. The product on usual work up and column chromatographic purification yielded compound 3a as minor and compound 4a as major product.

Structure elucidation of compound 3a

The structure of 3a was established by IR, $^1$HNMR, MS data and elemental analysis. IR spectra gave characteristic peaks at 1734 and 1710 cm$^{-1}$ for ester carbonyl and keto group respectively. It suggests that the reaction has taken place at the α carbon and carbonyl groups are intact. In product 3a, a band at 1641 cm$^{-1}$ showed the presence of double bond that reaction has taken place at the α carbon of compound (1).

The $^1$HNMR spectrum of 3a gives a triplet of doublet doublet at $\delta$ 5.8 for C10-methine proton. The two double doublets at $\delta$ 5.01 and $\delta$ 4.95 coupled with each other and with the adjacent methine proton were assigned to the two terminal olefinic proton, $H_z$-11 and $H_E$-11 respectively. It shows a singlet at $\delta$ 3.67 indicating three hydrogen’s of ester methyl. Detailed $^1$HNMR spectra of 3a is given in experimental section.
In EIMS spectrum of 3a, the molecular ion peak was absent, characteristic fragment ions observed at m/z 210, 138, 124. Base peak appears at m/z 74 and a peak characteristic of cyclopentanone appears at m/z 55. The fragmentation pattern is shown in Chart 1.

On the basis of the above facts, 3a was characterized as methyl 2 -(2'-cyclopentanonyl) undec-10-enoate.

Structure elucidation of compound 4a

Two characteristic bands at 1732 cm\(^{-1}\) and 1708 cm\(^{-1}\) appears for ester group and ring carbonyl in IR of compound 4a. Absence of band for double bond indicates the product formation due to the reaction of double bond with \(\alpha\)-carbon of cyclopentanone. A sharp singlet at \(\delta\) 3.66 was assigned to three protons of ester group. A multiplet at \(\delta\) 2.32 – 2.13 showed the presence of five hydrogen’s attached to the C’s alpha to \(>\text{C}=\text{O}\) of cyclopentanone and ester carbonyl. A broad singlet at \(\delta\) 1.25 shows the presence of chain methylene protons. Detailed \(^1\text{H}\) NMR data are given in experimental section.
Chart 1: Mass fragmentation of compound 3a
The EIMS spectrum of \( \text{4a} \) is also in accordance with the proposed structure (Chart 2). The molecular ion peak for \( \text{4a} \) was observed at \( m/z \) 282 which is in agreement with the molecular formula \( \text{C}_{17}\text{H}_{30}\text{O}_3 \). The base peak was displayed at \( m/z \) 84. The other characteristic fragment ions appear at \( m/z \) 251 and 141. On the basis of the above spectral data \( \text{4a} \) was characterized as methyl 11- (2'-cyclopentanonyl) undecanoate.

![Structure of 4a](image)

\( \text{(4a)} \)

**Reaction of methyl undec-10-enoate (1) with cyclohexanone (2b)**

Methyl undec-10-enoate (1) was allowed to react with cyclohexanone (2b) under the similar conditions as described earlier. Final work up yielded a semisolid mass which on chromatographic separation and purification over silica gel gave a minor product \( \text{3b} \) and a major product \( \text{4b} \).

**Structure elucidation of compound 3b**

The structure of \( \text{3b} \) was determined by its IR, \(^1\text{HNMR} \) and \(^{13}\text{CNMR} \). In IR, it gave the ketone absorption band at 1710 cm\(^{-1} \). Band for double bond appears at 1640 cm\(^{-1} \). Other significant bands were
Chart 2: Mass fragmentation of compound 4a
present at 1742 (ester carbonyl), 1438 (for cyclohexanone, CH-stretching), 2926 (chain carbon). Its $^1$HNMR had very much resemblance to that of compound 3a except an increase of 2 protons in cyclohexanone (2 cyclic ketone protons). Its $^{13}$CNMR give signals at $\delta_c$ 213.5 and 174.2 for carbonyl of cyclohexanone and ester. Peaks at $\delta_c$ 142 and 112.14 indicates the presence of double bond. The nature chemical shift of other carbon atoms are presented in experimental section.

On the basis of above spectral discussion, the structure of compound 3b was assigned as methyl 2-(2'-cyclohexanonyl) undec-10-enoate.

\[
\begin{align*}
\text{Structure elucidation of compound 4b} \quad (3b)
\end{align*}
\]

The compound had an elemental composition corresponding to formula C$_{18}$H$_{32}$O$_3$. The structure of 4b was established on the basis of IR, $^1$HNMR and $^{13}$CNMR. Its IR spectrum exhibits band at 1740 and
1712 cm\(^{-1}\) for ketone and ester group. Band for double bond was absent thus showing the participation of double bond in the formation of compound. Its \(^1\)HNMR gives signals at \(\delta\) 3.64 for 3 protons of methyl ester. A peak at \(\delta\) 2.36 - 2.20 integrates for 5 protons attached to the \(\alpha\) carbons of cyclohexanone and fatty ester. It exhibits peaks at \(\delta\) 1.64 - 1.56 for 6 protons of cyclohexanone along with other fatty ester signals. In \(^{13}\)CNMR, signals appear at \(\delta_c\) 213.7 and 174.4 for carbonyl of cyclohexanone and ester. Carbon \(\alpha\) to carbonyl ester appears at \(\delta\) 51.29. The chemical shifts for other carbon atoms are given in experimental section.

On the basis of above facts, the product 4b was characterized as methyl 11-(2'-cyclohexanonyl) undecanoate.
Reaction of cyclicketone derivatives (4a), (4b) with mercaptoacetic acid.

A further reaction was carried out on the ketone group of 4a, 4b with mercaptoacetic acid and ammonium carbonate leading to the formation of spiro derivatives 5a and 5b, respectively (Scheme ii).

**Reaction of methyl 11-(2'-cyclopentanonyl) undecanoate (4a) with mercaptoacetic acid**

The mixture of 4a, mercaptoacetic acid and ammonium carbonate in dry benzene was refluxed for 25 hrs with azeotropic removal of water (Scheme ii).

\[
\text{Reaction: } \text{(4a, b)} \xrightarrow{\text{1. HSCH}_2\text{COOH}} \xrightarrow{\text{2. (NH}_4)_2\text{CO}_3\text{ dry benzene}} \text{(5a, b)}
\]

- \(n = 1\) (4a, 5a)
- \(n = 2\) (4b, 5b)

**Scheme ii** : Preparation of methyl-1-aza-2-oxo-4-thiaspiro [4.4] - nonane \& [4.5]- decane -6- undecanoate
After completion of reaction the solvent was removed under pressure. The semisolid mass so obtained was extracted with diethyl ether, washed with water and dried over anhyd. sodium sulphate. The solvent was evaporated and the crude solid product was recrystallized from petroleum ether: benzene (4:1, v/v). The reaction is expected to occur via ketimine intermediate which is formed by the reaction of 4a with ammonia from ammonium carbonate followed by cyclocondensation with mercaptoacetic acid giving spiro compound.

**Structure elucidation of compound 5a**

It was a white crystalline solid, m.p. 58°C. Its microanalysis corresponds to C_{19}H_{33}O_{3}NS. The structure of 5a is fully established by IR and ¹H NMR spectra. IR spectrum of 5a shows the absence of absorption band in the region of 1712 – 1708 cm⁻¹. It showed characteristic bands at 3182.41, 1676.53 cm⁻¹ showing the presence of NH stretching and amide group. A peak at 649.73 cm⁻¹ indicated the C-S stretching. The ¹H NMR Spectrum of 5a showed signals as assigned in experimental section. The chemical shift at δ 7.26 was assigned for the NH Proton. A singlet at δ 3.58 was assigned for the ring methylene proton. On the basis of the above fact the product 5a was characterized as methyl 1-aza-2-oxo-4-thiaspiro[4.4]-nonane-6-undecanoate.
Reaction of methyl 11-(2'-cyclohexanonyl) undecanoate (4b) with mercaptoacetic acid

Methyl 11- (2'-cyclohexanonyl) undecanoate (4b) reacted with mercaptoacetic acid and ammonium carbonate in dry benzene under the similar conditions as discussed earlier. The completion of reaction was checked by TLC. The reaction mixture obtained after the removal of solvent under reduced pressure, was extracted with diethyl ether. Evaporation of diethyl ether gave crude solid which was recrystalized with petroleum ether: benzene (4:1, v/v).

Structure elucidation of compound 5b

It was a white crystalline solid, m.p. 63°C. Its elemental composition corresponds to formula C_{20}H_{35}O_{3}NS. Its structure was deduced by IR and $^1$HNMR. Its IR spectrum gives bands at 3111.2 (NH), 1730.78 (ester), 1601.15 (CONH) and 649.50 (C-S stretching) cm$^{-1}$. Absence of band for carbonyl group shows the formation of spiro
compound by participation of carbonyl carbon. In $^1$HNMR, a peak at $\delta$ 7.24 indicates one proton of NH. A peak at $\delta$ 3.57 as a singlet shows two protons of ring methylene along with other fatty acid signals.

On the basis of above facts, the compound 5b was characterised as methyl 1-aza-2-oxo-4-thiaspiro [4.5] decane-6-undecanoate.

(5b)
1.3 Experimental

The IR spectra were recorded on Shimadzu 8201 PC spectrophotometer (Kyoto, Japan) in KBr pellets. $^1$HNMR spectra were recorded on Bruker DRX-300 (Fallenden, Switzerland) at 300 MHz using TMS as an internal standard. $^{13}$CNMR spectra were recorded at 75 MHz. Chemical shift were measured in δ ppm, CDCl$_3$ was used as the solvent. The abbreviations, 's, dd, t, tdd, m, and brs' denote 'singlet, double doublet, triplet, triplet of doublet doublet, multiplet, broad singlet' respectively. Mass spectra were carried out on Jeol-D300 (EI) (Tokyo, Japan) spectrometer operating at 70 eV.

Thin layer chromatography was performed with silica gel G (about 0.25 mm layer, Merck, Mumbai, India) to access the progress of the reaction and purity of the compounds synthesized. Petroleum ether-diethyl ether and glacial acetic acid (4:1:2 drops, v/v) was used as developer. Column chromatography was carried out using silica gel [60-120 mesh, (Merck, Mumbai, India)] using 25-30 gm per gm. of compound to be separated. Elution was usually affected with petroleum ether containing increasing proportions of diethyl ether. Dry benzene was prepared according to standard procedure. Anhydrous Na$_2$SO$_4$ was used as drying organic extracts after reaction work up. All solvents were
distilled before used.

Cyclopentanone was obtained from Wilson laboratories (Mumbai, India). Cyclohexanone, mercaptoacetic acid and ammonium carbonate were obtained from Merck (Mumbai, India). Silver oxide was purchased from BDH (Mumbai, India). Undec-10-enoic acid (Fluka, Bucks, Switzerland) was used to prepare methyl ester by the usual method (H⁺, CH₃OH).

**Reaction of methyl undec-10-enoate (1) with cyclopentanone (2a)**

The fatty acid derivatives of cyclic ketone were prepared by adopting the procedure of Yamamoto et al.⁴³. Methyl undec-10-enoate (1.98 gm, 1.0x10⁻² mol) was refluxed with cyclopentanone (5 mL, 5.6 x10⁻² mol) at 130-132°C in the presence of silver oxide (2.32 gm, 1.0 x10⁻² mol) for 5 hrs. After completion, the excess of cyclopentanone was distilled at reduced pressure. The product obtained was extracted with diethyl ether. Ethereal layer was washed with water and dried over anhyd. sodium sulphate. On evaporation of diethyl ether a brown liquid product was obtained. The crude product was adsorbed on a column of silica gel and elution with petroleum ether-diethyl ether (96:4, v/v) yielded compound 3a.
Further, elution with petroleum ether –diethyl ether (92:8, v/v) gave 4a.

Methyl 2-(2′-cyclopentanonyl) undec-10-enoate (3a)

Colourless liquid.

Yield : 27.6%

IR (KBr) : 2900 (CH Stretching), 1734 (>C=O, ester), 1710 (>C=O, cyclopentanone), 1641 (C=C) cm⁻¹.

¹HNMR (CDCl₃) δ : 5.8 (1H, tdd $J_{H-\text{CH}_2} = 6.6$ Hz, $J_{H-H_2}=10.2$ Hz, $J_{H-H} = 17.2$ Hz, H₂C=CH-); 5.01 (1H, dd, $J_{H-H_2} = 10.2$ Hz, $J_{H_2-H_2} = 2.1$ Hz, H₂C=CH-), 4.95 (1H, dd, $J_{H-H} = 17.2$ Hz, $J_{H_2-H_2} = 2.1$ Hz, H₂C=CH-), 3.67 (3H, s, OMe), 2.23-2.28 (4H, m, at carbon α to >C=O), 2.05(2H, m CH₂-CH=CH₂), 1.29 (10H, brs, CH₂).

MS m/z (%) : 221 (M-CO₂ Me, 1.0), 210 (3.6), 138 (8.6), 124(43), 96 (68), 74 (100), 55 (98), 42 (78).

Anal : Calculated for C₁₇H₂₈O₃: C, 72.8; H, 10.4.

found: C, 71.9; H, 10.4%.

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Methyl 11-(2'-cyclopentanonyl) undecanoate (4a)

colourless liquid

Yield : 53.6%

IR (KBr) : 2927.2 (CH Stretching), 1732 (>C=O, ester),
          1708 (>C=O, cyclopentanone), 1460 (CH,
          cyclopentanone) cm⁻¹.

¹HNMR (CDCl₃) δ : 3.66 (3H, s, CO₂Me), 2.13-2.32 (5H, m, p α to
          >C=0), 1.25 (18 H, brs, CH₂).

MS m/z (%) : 283 (M⁺, 5.9), 282, (M⁺, 1.5), 252 (11.5),
          251 (10.2), 223 (6.3), 199 (7.5), 141 (4.8), 112
          (10.5), 84 (100), 55 (28.78).

Anal : Calculated for C₁₇H₃₀O₃: C, 70.23; H, 11.45
         found: C, 70.27; H, 11.42%.

Reaction of methyl undec-10-enoate (1) with cyclohexanone (2b):

Methyl undec-10-enoate (1.98 gm, 1.0 x10⁻² mol) reacted with
cyclohexanone (5mL, 4.8x10⁻² mol) in presence of silver oxide (2.32
gm, 1.0 x10⁻² mol) at 140°C for 8 hrs in the same manner as in preceding
reaction. After final workup TLC showed 2 spots. The crude on
mass column chromatography with silica gel gave 3b on elution with

30
petroleum ether: diethyl ether (96:4 \text{ v/v}). On further elution, by petroleum ether: diethyl ether (92:8 \text{ v/v}) it gave 4b.

**Methyl 2 – (2'-cyclohexanonyl) undec-10-enoate (3b)**

Colourless liquid

**Yield** : 27.2%

**IR (KBr)** : 2926 (CH stretching), 1742 (CO\textsubscript{2}Me), 1710 (>C=O, cyclohexanone), 1640 (C=C), 1438 (CH stretching, cyclohexanone) \text{ cm}\textsuperscript{-1}.

**\textsuperscript{1}HNMR (CCl\textsubscript{4}) \textdelta** : 5.73 (1H, tdd, J\textsubscript{H-H\textsubscript{2}CH\textsubscript{2}} = 6.1 Hz, J\textsubscript{H-H\textsubscript{2}} = 10.2 Hz, J\textsubscript{H-H\textsubscript{2}CH\textsubscript{2}} = 17.1 Hz, CH\textsubscript{2}=CH-), 4.90 (1H, dd, J\textsubscript{H-H\textsubscript{2}} = 10.2 Hz, J\textsubscript{H-H\textsubscript{2}CH} = 2.1 Hz, HE=C=CH-), 4.87 (1H, dd, J\textsubscript{H-H\textsubscript{2}} = 17.2 Hz, J\textsubscript{H-H\textsubscript{2}CH} = 2.1 Hz, H\textsubscript{2}C=CH-), 3.67 (3H, s, OMe), 2.22-2.25 (4H, m, at C’s α to >C=O), 2.02 (2H, m, CH\textsubscript{2}-CH=CH\textsubscript{2}), 1.55 (6H, m, hexyl protons), 1.18-1.30 (10H, brs, CH\textsubscript{2})

**\textsuperscript{13}CNMR (CDCl\textsubscript{3}) \textdelta\textsubscript{C}** : 213.5 (>C=0, cyclohexanone), 174.2 (>C=0, ester), 50.6 (C-2'), 51.3 (-OMe), 41.8
Methyl 11-(2'-cyclohexanonyl) undecanoate (4b)

Colourless liquid

Yield : 51.8%

IR (KBr) : 2928 (CH stretching), 1740 (CO<sub>2</sub>Me), 1712 (>CO, cyclohexanone), 1446 (CH stretching, cyclohexanone) cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ : 3.64 (3H, s, OCH<sub>3</sub>), 2.36-2.20 (5H, m, protons α to >C=O), 1.64-1.56 (6H, m, hexyl protons), 1.25 (18 H, brs, CH<sub>2</sub>).

<sup>13</sup>C NMR (CDCl<sub>3</sub>) δ:<sub>c</sub> : 213.7 (>C=O, cyclohexanone), 174.4 (>C=O, ester), 51.4 (C-2'), 51.29 (-OMe), 42.0 (C-6'), 34.1 (C-2), 33.7, 29.8, 29.5, 29.4, 29.2, 29.1, 27.8, 27.93, 25.0, 24.8.

Anal : Calculated for C<sub>18</sub>H<sub>32</sub>O<sub>3</sub>: C, 72.97; H, 10.81 found : C, 72.94; H, 10.79%.
General procedure for the preparation of spiro compounds (5a, b)

Mercaptoacetic acid (0.184 gm, 2.0x10^-2 mol) and ammonium carbonate (2.97 gm, 3.0x10^-2 mol) was added to the methyl 11-(2'-cyclopentanonyl) undecanoate, (4a), (0.584 gm, 2.0x10^-3 mol) in dry benzene (25 mL). The reaction mixture was refluxed for 25 hrs on hot plate and collecting the generated water in an azeotropic collector. The progress of the reaction was monitored by TLC. After the completion of reaction, the solvent was distilled off under reduced pressure. The residue so obtained was extracted with diethyl ether and washed with water and dried over anhyd. sodium sulphate. The solvent was evaporated and crude solid product was recrystallized from petroleum ether: benzene (4:1, v/v) to give 5a. Similar reaction was carried out on cyclohexanone derivative 4b, with mercaptoacetic acid to afford 5b.

*Methyl 1-aza-2-oxo-4-thiaspiro [4.4]-nonane-6-undecanoate (5a)*

White crystalline solid

**Yield** : 56.2%, m.p. 58°C.

**IR (KBr)** : 3182.41 (NH), 1727.56 (>C=O, ester), 1676.53 (-CONH), 649.73 (C-S) cm⁻¹.
$^1$HNMR (CDCl$_3$) $\delta$ : 7.26 (1H, s, NH), 3.66 (3H, s, CO$_2$Me), 3.58 (2H, s, 3-C), 2.32-2.28 (2H, t, 2-C), 1.51 (4H, m, pentyl protons).

Anal : Calculated for C$_{19}$H$_{33}$O$_3$NS : C, 64.22; H, 9.29; N, 3.94. found : C, 64.25; H, 9.26; N, 3.91%.

*Methyl 1-aza-2-oxo-4-thiaspiro [4.5]-decane-6-undecanoate (5b)*

White crystalline solid

Yield : 54.3%, m.p., 63°C

IR (KBr) : 3111.2 (NH), 1730.78 (>C=O, ester), 1601.15 (-CONH), 649.50 (C-S) cm$^{-1}$.

$^1$HNMR (CDCl$_3$) $\delta$ : 7.24 (1H, s, NH), 3.64 (3H, s, OMe), 3.57 (2H, s, 3-C), 2.32-2.29 (2H, t, 2-C), 1.29-1.27 (18 H, brs, CH$_2$).

Anal : Calculated for C$_{20}$H$_{35}$O$_3$NS : C, 65.46; H, 9.48; N, 3.79. found : C, 65.49; H, 9.46; N, 3.80%.
1.4 References


