Chapter VII

PART B

Synthesis of Undecyl Hexadecanoate and 12-Hydroxyhentriacontane

The plant *Ziziphus mauritiana* belongs to the buckthorn family (Rhamnaceae).<sup>404</sup> *Ziziphus* is a genus of about 100 species of deciduous or evergreen trees and shrubs distributed in the tropical and subtropical regions of the world. *Ziziphus mauritiana* is an example of a hardy drought species and is a dominant component of the natural vegetation of the Indian desert. *Ziziphus mauritiana* is a multipurpose tree widely popular for its fruits, fodder, fuel, medicinal and ornamental purposes. The antiinflammatory, antibacterial and antimicrobial properties of this plant<sup>405-407</sup> are found to be even higher than Penicillin and Nystatin.

The tree finds importance in dry areas, as the leaves are important famine food in Niger because they are excellent source of the essential fatty acids, Linoleic acid, alkaloids and several metals including iron, calcium, after magnesium and zinc. The leaves are helpful in asthma fever, act as an astringent, diaphoretic and are prescribed for typhoid.<sup>405</sup> In Iran, the leaves are said to be used to decrease the intake of sweets. Extract of its leaves elevates human taste threshold to sucrose solutions,<sup>406</sup> supresses sweet taste sensation in the fly *Phormia regina* and in rat and hamster.<sup>407,408</sup> It is also an important fruit tree as the fruits are rich in sugars, proteins and vitamins and are used for curing indigestion. The bitter astringent bark decoction is taken to halt diarrhea and dysentery. The tree produces firewood, charcoal, timber, and animal fodder from the leaves and provides good soil conservation.

Agarwal <i>et al</i> have isolated new aliphatic ester *undecyl hexadecanoate* (201) and a long chain alcohol *12-hydroxyhentriacontane* (208) from the hexane extract of its leaves which on repeated silica gel column chromatography yielded colourless crystals of undecyl hexadecanoate 201 with m.p. 82° and 12-hydroxyhentriacontane (208) as a white solid, m.p. 77°. The structures were elucidated by physico-chemical data.<sup>404</sup> The ester group of undecyl hexadecanoate (201) was established by its mass fragmentation pattern and its alkaline hydrolysis.<sup>409</sup>
Literature does not record any synthesis of the title compound 201 and 208.

The application of microwave heating under ‘dry reaction’ conditions is a promising alternative to polluting reactions and has been a current field of interest. Furthermore, the solid state reactions (or solvent free reactions) have many advantages, such as reduced pollution, low cost and simplicity in process and handling.

In view of the wide applicability of microwave irradiation in chemical reaction enhancement, we therefore, report novel, first synthesis of 201 and 208 by making use of ecofriendly microwave and ultrasonic energies.

A very short synthesis of undecyl hexadecanoate (201) has been achieved involving microwave assisted esterification as the key step as described below (scheme 10).

![Scheme 10](image)

**Reagents**

(a) CrO₃, conc. H₂SO₄, acetone, 71%  (b) Undecan-1-ol, p-TSA, MWI, 320 W, 4 min., 93%
Jones oxidation\textsuperscript{247} of hexadecan-1-ol (199) with chromium trioxide in conc. sulphuric acid in acetone furnished hexadecanoic acid (200) in 71\% yield. Its IR provided the prominent bands at 3400 (-COOH), 1700 (C=O) and 1590 (carboxylate anion) cm\textsuperscript{-1}. \textsuperscript{1}H NMR spectrum recorded main peaks at \(\delta\) 2.3 (t, 2H, \(J=6\)Hz, \(-CH_2COOH\)) and 11.3 (bs, 1H, -COOH, \(D_2O\) exchangeable) and absence of signal at \(\delta\) 3.6 for \(-CH_2OH\) group further confirmed the formation of product.

Microwave mediated esterification\textsuperscript{403} of hexadecanoic acid (200) with undecan-1-ol in the presence of \(p\)-toluenesulphonic acid furnished undecyl hexadecanoate (201) in 93\% yield after silica gel column chromatography using ethyl acetate:n-hexane (0.5:9.5). Its structure was confirmed on the basis of spectral studies. The IR spectrum recorded absorption bands at 2850 (C-H), 1737 (C=O), 1175 (C-O) cm\textsuperscript{-1} for aliphatic nature with the absence of band at 2920 (-COOH) cm\textsuperscript{-1}. \textsuperscript{1}H NMR spectrum exhibited peaks at \(\delta\)

\[
\begin{align*}
0.9 & \text{ (t, } J=7\text{Hz, 6H, } 2\times-CH_2CH_3) \\
1.2-1.7 & \text{ (bs, 44H, saturated methylene protons)} \\
2.3 & \text{ (t, } J=6\text{Hz, 2H, } -CH_2CH_2CO-) \\
4.1 & \text{ (t, } J=7\text{Hz, 2H, } -CH_2OCO-) \\
\end{align*}
\]

Disappearance of broad singlet at \(\delta\) 11.3 for -COOH further confirmed the formation of product.

The spectral data of the synthesized product was found to be compatible with those cited in the literature.\textsuperscript{404}

As a part of our continuing efforts\textsuperscript{39,168} towards the use of both microwave energy under solvent free conditions and the use of ultrasonic waves, a very simple synthesis of 12-hydroxyhentriacontane (208) has been developed. The key steps include microwave assisted monobromination of diols and Zn(Cu) couple catalyzed conjugate addition of alkyl halide to \(\alpha,\beta\)-unsaturated carbonyl compound using aqueous sonochemical conditions, as outlined in scheme 11.
Reagents

(a) PBr₃, pyridine, dry ether, 0°, 81%  
(b) 48% HBr, Bu₄N⁺I⁻, MWI, 355 W, 5 min., 80%  
(c) DHP/I₂, MWI, 600 W, 3 min, 94%  
(d) 66, Mg, CuI, dry ether, 0°, 78%  
(e) CBr₄, PPh₃, 77%  
(f) Mg, THF, dry ether, 0°, 75%  
(g) PDC, dry DCM, 0°, 70%  
(h) 66, Zn(Cu), 62%  
(i) NaBH₄/Al₂O₃, MWI, 640 W, 1 min., 92%

Nonan-1-ol (124) was converted to its bromo derivative (66) in 81% yield using phosphorous tribromide and pyridine in anhyd. ether at 0°. Its characterization was done by IR spectrum, which reported a band at 580 (−Br) cm⁻¹ and absence of band at 3400 (−OH) cm⁻¹. Its ¹H NMR spectrum showed a signal at δ 3.5 (t, J=6 Hz, 2H, −CH₂C=OBr).

Microwave irradiation of a mixture of 1,10-decanediol (105), 48% aq. hydrobromic acid and tetrabutylammonium iodide as phase transfer catalyst furnished 10-bromodecan-1-ol (118) in 80% yield. Its IR spectrum recorded the absorption bands at 3400 (−OH) and 560 (−Br) cm⁻¹. Its ¹H NMR spectrum showed a signal at δ 3.3 (t, J=6 Hz, 2H, −CH₂CH₂Br).

Tetrahydroxylation⁷⁴ of 10-bromodecan-1-ol (118) DHP and iodine via microwave irradiation yielded 10-bromo-1-tetrahydroxyloxydecane (202) in 94% yield. The structure was confirmed by the spectroscopic data. IR spectrum showed main bands at...
1120 (C-O) and 540 (-Br) cm$^{-1}$ and its $^1$H NMR spectrum recorded prominent signals at $\delta$ 3.3-3.9 (m, 6H, -CH$_2$C=Br, -CH$_2$C=O$, -OCH$_2$CH$_2$-) and 4.9 (t, $J$=4Hz, 1H, -OCHO$-)$. Absence of broad D$_2$O exchangeable signal at $\delta$ 4.0 for hydroxyl group further confirmed the formation of product.

Cuprous iodide$^{208}$ catalyzed coupling of nonylmagnesium bromide with 10-bromo-1-tetrahydropyranoloxodecane (202) in anhyd. diethyl ether at 0° gave 1-tetrahydropyranoloxo nonadecane (203) in 78% yield after silica gel column chromatography using 2% ethyl acetate in $n$-hexane as the eluant. The prominent absorption bands in IR spectrum were observed at 1210, 1120 (C-O) cm$^{-1}$ with the absence of band at 540 cm$^{-1}$ for -Br group and in the $^1$H NMR spectrum the main signals recorded were at $\delta$ 1.1-1.6 (bs, 40H, saturated methylene protons), 3.3-3.8 (m, 4H, -CH$_2$C=O$, -OCH$_2$CH$_2$-) and 4.9 (t, $J$=4Hz, 1H, -OCHO$-)$. On treatment of 1-tetrahydropyranoloxynonadecane (203) with triphenylphosphine and carbon tetrabromide in dry DCM, 1-bromononadecane (204) was obtained in 77% yield.

The main absorption band in IR spectrum was observed at 580 (-Br) cm$^{-1}$ with the absence of 1120 (C-O) cm$^{-1}$ stretching frequency. $^1$H NMR spectrum depicted the presence of the main peak at $\delta$ 1.2-1.6 (bs, 32H, saturated methylene protons) and 3.3 (t, $J$=6Hz, 2H, -CH$_2$Br). Disappearance of signal at $\delta$ 3.3-3.8 (m, 4H, -CH$_2$C=O$, -OCH$_2$CH$_2$-) and 4.9 (t, $J$=4Hz, 1H, -OCHO$-) further confirmed the formation of bromide.

Grignard reaction of nonadecylmagnesium bromide, (prepared from 1-bromononadecane (204) and magnesium turnings in anhyd. ether under N$_2$ atmosphere) with acrolein gave the crude (205 which was purified via silica gel column chromatography using 10% ethyl acetate in $n$-hexane as the eluant to furnish pure compound (205) in 75% yield. Its IR spectrum recorded absorption bands at 3350 (-OH), 1640 (C=C) and 1160 (C-O) cm$^{-1}$. The $^1$H NMR spectrum recorded signals at $\delta$ 3.2 (bs, 1H, -OH, D$_2$O exchangeable), 3.9-4.4 (m, 1H, -CH$_2$CH(OH)$-), 5.0-5.4 (m, 2H, -CH=CH$_2$) and 5.7-6.3 (m, 1H, -CHCH=CH$_2$). Absence of band at 580 (-Br) and 1700 (C=O) cm$^{-1}$ and signal at $\delta$ 3.3 for -CH$_2$Br and 10.0 for -CHO in IR and $^1$H NMR spectrum respectively further confirmed the structure.

Oxidation of compound (205) with pyridinium dichromate$^{250}$ in anhyd. dichloromethane furnished the corresponding ketone (206) in 70% yield. Its IR spectrum provided the prominent bands at 1700 (C=O), 1660 (C=C) and 1210 (C-O) cm$^{-1}$ with the disappearance of band for 3350 cm$^{-1}$ for hydroxyl group. The $^1$H NMR spectrum showed
distinguishing signals at $\delta$ 2.3 ($t, J=6\text{Hz}, 2\text{H}, -\text{CH}_{2}\text{CH}_{2}\text{CO}-$), 5.7-6.1 (m, 1H, -CHCH=CH$_2$) and 6.3-6.7 (m, 2H, -CH=CH$_2$). Absence of signal at $\delta$ 3.2 for hydroxyl group and 3.9-4.4 corresponding to -CH$_2$CH(OH)- confirmed the formation of compound 206.

Ultrasonic irradiation$^{166(a)}$ of an aq. ethanol mixture of 1-bromononane (66) and docos-1-en-3-one (206) in the presence of zinc-copper couple furnished compound (207) was obtained in 62% yield after subsequent purification via silica gel column chromatography using 10% ethyl acetate in $n$-hexane as the eluant. Its IR spectrum provided the prominent absorption bands at 1710 (C=O), cm$^{-1}$. The $^1$H NMR spectrum recorded signals at $\delta$ 0.9 ($t, J=6\text{Hz}, 6\text{H}, 2\times-\text{CH}_{2}\text{CH}_3$), 1.2-1.7 (bs, 52H, saturated methylene protons), 2.1-2.5 (m, 4H, -CH$_2$COCH$_2$). Absence of signals at 1660 (C=C) cm$^{-1}$ and 5.7-6.1 (m, 1H, -CHCH=CH$_2$) and 6.3-6.7 (m, 2H, -CH=CH$_2$) further provided the confirmation of the structure.

Microwave assisted reduction of aliphatic ketone (207) using NaBH$_4$ doped on alumina afforded the title compound 12-hydroxyhentriaccntane (208) in 92% yield. Its structure confirmation was done on the basis of spectral data. The prominent absorption band in the IR spectrum was observed at 3430 (-OH) cm$^{-1}$ with absence of band at 1710 (C=O) cm$^{-1}$. The $^1$H NMR spectrum recorded the main peaks at $\delta$: 0.9 ($t, J=6\text{Hz}, 6\text{H}, 2\times-\text{CH}_{2}\text{CH}_3$) 1.1-1.6 (bs, 52H, saturated methylene protons) 1.8-2.0 (m, 4H, -CH$_2$CH(OH)CH$_2$) 3.7 ($t, J=8\text{Hz}, 1\text{H}, -\text{CH}_{2}\text{CH(OH)-}$) 4.2 (bs, 1H, -OH, D$_2$O exchangeable) Disappearance of signal at $\delta$ 2.1-2.5 (m, 4H, -CH$_2$COCH$_2$) further confirmed the formation of product. The spectroscopic data was found to be compatible with the values reported in literature.$^{404}$