Oleochemical Manufacture and Applications

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9 New chemistry of oils and fats

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9.1 Introduction

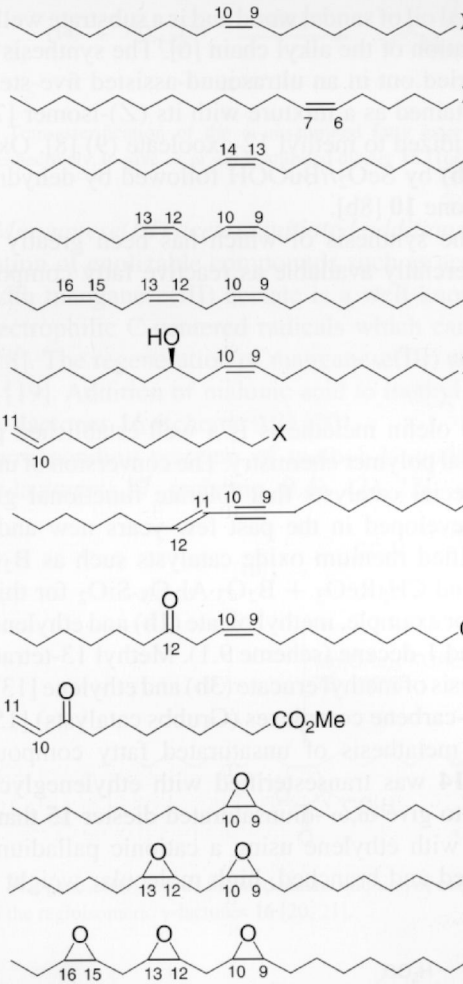
In the search for sustainable chemistry, considerable importance is being attached to renewable raw materials that exploit the synthetic capabilities of nature [1, 2]. Oils and fats of vegetable and animal origin make up the greatest proportion of renewable raw materials currently consumed in the chemical industry, since they offer possibilities for applications which can be rarely met by petrochemistry. The extent of the use of natural oils and fats in chemistry was summarized in 1988 [3] in the statement:

> 'More than 90% of oleochemical reactions have been those occurring at the fatty acid carboxy group, while less than 10% have involved transformations of the alkyl chain. However, future progress will be along the lines of these latter types of reactions with their potential for considerably extending the range of compounds obtainable from oils and fats.'

Recently, modern synthetic methods have been applied extensively to fatty compounds for the selective functionalization of the alkyl chain [4, 5]. Radical, electrophilic, nucleophilic, pericyclic and transition metal catalyzed additions to the C—C double bond of, for example, oleic acid as the prototype of a readily accessible, unsaturated fatty acid have led to a large number of novel fatty compounds from which interesting properties are expected. Functionalization of C-H bonds in the alkyl chain is also feasible with remarkable selectivity.

9.2 Reactions of unsaturated fatty compounds

Fatty materials can be processed industrially from vegetable oils in such purity that they may be used for further chemical conversions and for the synthesis of chemically pure compounds. Predominantly, oleic acid (**1a**), petroselinic acid (**2a**), erucic acid (**3a**), linoleic acid (**4a**), and linolenic acid (**5a**) have been used in the syntheses described below (figure 9.1). Ricinoleic acid (**6a**) carries an additional hydroxyl group which is useful in stereo- and regioselective syntheses. By pyrolysis of **6b** and subsequent hydrolysis, 10-undecenoic acid (**7a**), an ω-unsaturated carboxylic acid, is obtained [3], which is very useful for selective reactions. Santalbic acid (**8a**), containing a conjugated enyne system, is



(1)–(8); (11)–(13)	a	b	c
X	CO_2H	CO_2Me	CH_2OH

Figure 9.1 Starting materials for the synthesis of novel fatty acids: Oleic acid (**1a**), petroselinic acid (**2a**), erucic acid (**3a**), linoleic acid (**4a**), linolenic acid (**5a**), ricinoleic acid (**6a**), 10-undecenoic acid (**7a**), santalbic acid (**8a**), *cis*-9,10-epoxyoctadecanoic acid (**11a**), *cis*-9,10; *cis*-12,13-bisepoxyoctadecanoic acid (**12a**); *cis*-9,10; *cis*-12,13; *cis*-15,16-trisepoxyoctadecanoic acid **13a**, the respective methyl esters **1b–8b**, **11b–13b** and alcohols **1c–8c**, **11c–13c**, methyl 12-oxooctadec-10-enoate (**9**) and 9-oxo-10-undecenoic acid (**10**).

the main fatty acid in the seed oil of sandal wood and is a substrate well suited for regioselective functionalization of the alkyl chain [6]. The synthesis of methyl santalbate (**8b**) can be carried out in an ultrasound-assisted five-step reaction sequence from **6b**. It is obtained as a mixture with its (*Z*)-isomer [7]. Methyl ricinoleate (**6b**) may be oxidized to methyl 12-oxooleate (**9**) [8]. Oxidation of methyl 10-undecenoate (**7b**) by SeO_2/*t*BuOOH followed by dehydrogenation gives the ω-unsaturated enone **10** [8b].

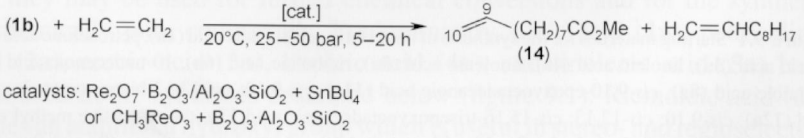
The epoxides **11–13**, the synthesis of which has been greatly improved recently [4, 5], are commercially available as reactive fatty compounds (see section 9.4).

9.2.1 *Olefin metathesis*

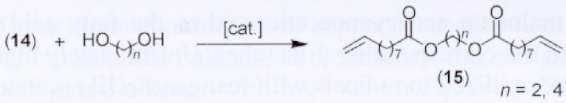
Transition metal catalyzed olefin metathesis is a well-established process in petrochemistry and industrial polymer chemistry. The conversion of unsaturated fatty acid esters needs special catalysts that tolerate functional groups [4]. Warwel and co-workers developed in the past few years new and effective heterogeneous boron modified rhenium oxide catalysts such as $B_2O_3{\cdot}Re_2O_7$ on $Al_2O_3{\cdot}SiO_2$ + $SnBu_4$ and CH_3ReO_3 + $B_2O_3{\cdot}Al_2O_3{\cdot}SiO_2$ for this purpose [9–13]. Co-metathesis of, for example, methyl oleate (**1b**) and ethylene afforded methyl 9-decenoate (**14**) and 1-decene (scheme 9.1). Methyl 13-tetradecenoate was obtained by co-metathesis of methyl erucate (**3b**) and ethylene [13]. Methyltrioxorhenium [14] and Ru-carbene complexes (Grubbs catalysts) [15] are also suitable catalysts for the metathesis of unsaturated fatty compounds. The ω-unsaturated fatty ester **14** was transesterified with ethyleneglycol and 1, 4-butanediol, respectively, to give ω,ω′-diunsaturated diester **15** that could be copolymerized effectively with ethylene using a cationic palladium catalyst to give partially cross-linked and branched, high molecular weight polymers (scheme 9.2) [16].

9.2.2 *Radical additions*

Radical additions to unsaturated fatty compounds such as oleic acid (**1a**) were reviewed in 1989 [17]. We report here on more recent results.



Scheme 9.1 Co-metathesis of methyl oleate (**1b**) and ethylene yielding methyl 9-decenoate (**14**) and 1-decene. The ester **1b** used (from high-oleic sunflower seed oil) was 87% pure, the conversions and selectivities each > 90%, and the yields of **14** were > 80% [13].

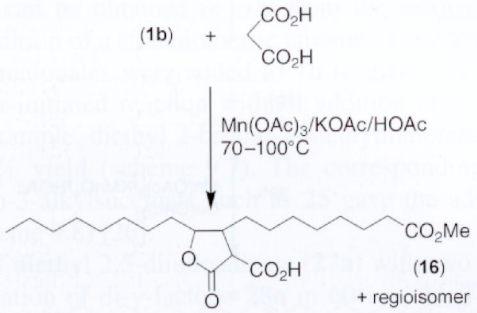


Scheme 9.2 Transesterification of the ω-unsaturated fatty ester **14** with ethyleneglycol and 1,4-butanediol, respectively, to give ω, ω′-diunsaturated diester **15** [16].

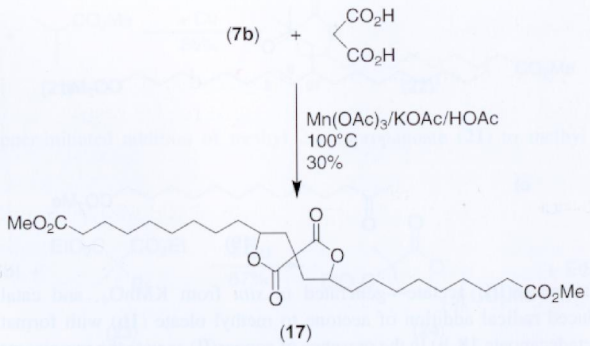
9.2.2.1 Manganese(III) acetate initiated additions

The oxidation of enolizable compounds such as acetic acid, malonic acid and acetone with manganese(III) acetate is a well-known method for the generation of electrophilic C-centered radicals which can be added to electron rich alkenes [18]. The regeneration of manganese(III) acetate is possible by anodic oxidation [19]. Addition of malonic acid to methyl oleate (**1b**) gave the regioisomeric γ-lactones **16** (scheme 9.3) [20].

The corresponding reaction of methyl 10-undecenoate (**7b**) afforded the spiro-di-γ-lactones **17** (scheme 9.4) [21, 22]. Additions of acetic acid,



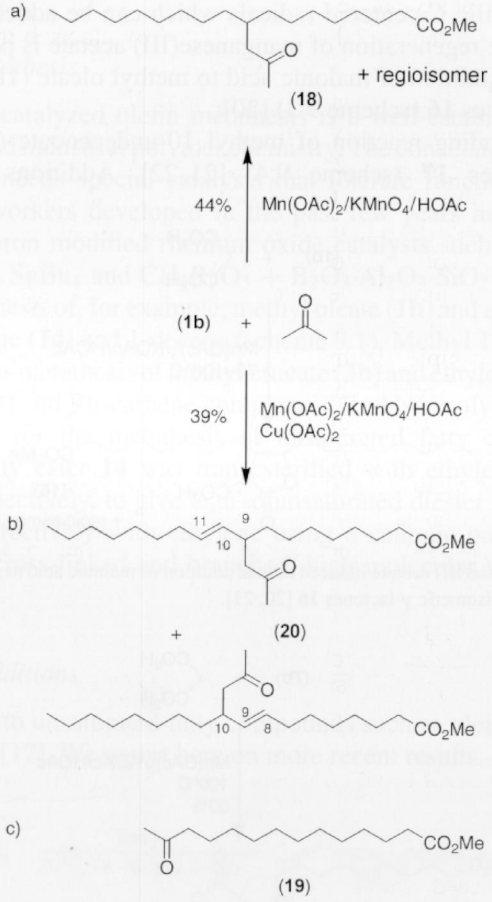
Scheme 9.3 Manganese(III) acetate induced radical addition of malonic acid to methyl oleate (**1b**) with formation of the regioisomeric γ-lactones **16** [20, 21].



Scheme 9.4 Manganese(III) acetate induced radical addition of malonic acid to methyl 10-undecenoate (**7b**) with formation of the spiro-di-γ-lactone **17** (mixture of diastereomers) [21].

monomethyl malonate and cyanoacetic acid to the fatty acid esters **1b** and **7b** also yielded the corresponding γ-lactones. Unfortunately higher carboxylic acids cannot be oxidized to radicals with manganese(III) acetate and added to alkenes [19, 20].

The addition of acetone to methyl oleate (**1b**) resulted in formation of the regioisomeric 9- and 10-acetonyloctadecanoic acid methyl esters (**18**) in a yield of 44% (scheme 9.5a). Methyl 13-oxotetradecanoate (**19**) was obtained in the corresponding reaction with methyl 10-undecenoate (**7b**) (scheme 9.5c) [20].



Scheme 9.5 Manganese(III) acetate—generated *in situ* from $KMnO_4$, and catalytic amounts of $Mn(OAc)_2$—induced radical addition of acetone to methyl oleate (**1b**) with formation of a) methyl 9(10)-acetonyloctadecanoate **18**. b) In the presence of copper(II) acetate the regioisomeric methyl 9(10)-acetonyloctadecenoates **20** were obtained. c) Addition of acetone to methyl 10-undecenoate (**7b**) gave the linear 13-oxotetradecanoic acid methyl ester (**19**) [20, 21].

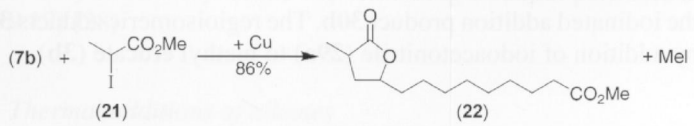
Addition of stoichiometric amounts of copper(II) acetate (a reagent used for the oxidation of nucleophilic radicals) to the reaction mixture gave two regioisomeric (*E*)-configured alkenes with high stereoselectivity. The addition of acetone, for example, to C_9 of methyl oleate (**1b**) afforded the *trans*-double bond at C_{10} while addition to C_{10} gave the *trans*-double bond at C_8 (**20**) (scheme 9.5b). This addition–elimination reaction is of importance because it allows an alkylation with retention of the double bond [20, 21].

9.2.2.2 Solvent-free, copper-initiated additions of 2-halocarboxylates

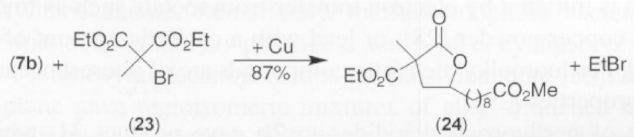
Higher carboxylic acids can be added in a very general reaction to unsaturated fatty compounds as their α-haloesters initiated by electron transfer from copper [23–26]. The addition of 2-iodocarboxylates, for example, methyl 2-iodopropanoate (**21**), to **7b** gave the γ-lactone **22** in high yields (scheme 9.6). The reaction procedure is very simple. Additions of primary, secondary and tertiary 2-haloesters such as **21** to fatty acid esters such as **1b**, **2b**, **3b** and **7b** were carried out, to give the corresponding γ-lactones (such as **22**). 2-Iodocarboxylates can be obtained *in situ* from the readily available bromo compounds by addition of a stoichiometric amount of sodium iodide.

Diethyl bromomalonates were added to **7b** to give γ-lactones **24** in good yields in a copper-initiated reaction without addition of sodium iodide. The addition of, for example, diethyl 2-bromo-2-methylmalonate (**23**) afforded γ-lactone **24** in 87% yield (scheme 9.7). The corresponding reaction with a dimethyl 2-bromo-3-alkylsuccinate such as **25** gave the addition product **26** in 50% yield (scheme 9.8) [26].

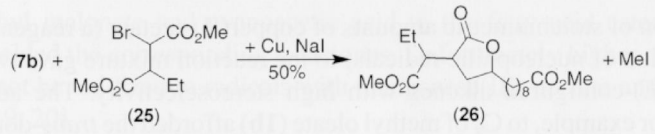
The reaction of diethyl 2,5-diiodoadipate (**27a**) with two equivalents of **7b** occurred by formation of di-γ-lactone **28a** in 60% yield. The corresponding reaction of diethyl 2,9-dibromosebacate (**27b**) was carried out by addition of



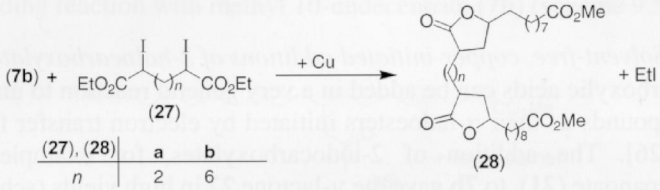
Scheme 9.6 Copper-initiated addition of methyl 2-iodopropanoate (**21**) to methyl 10-undecenoate (**7b**) [24].



Scheme 9.7 Copper-initiated addition of diethyl 2-bromo-2-methylmalonate (**23**) to methyl 10-undecenoate (**7b**) [23, 24].



Scheme 9.8 Copper-initiated addition of ethyl 2-bromo-3-ethylsuccinate (**25**) to methyl 10-undecenoate (**7b**) in the presence of sodium iodide [26].



Scheme 9.9 Reaction of diethyl α,α′-diiodoalkanedioates **27** with two equivalents of methyl 10-undecenoate (**7b**) to give bis-γ-lactones **28** [23, 24].

sodium iodide and afforded the homologous di-γ-lactone **28b** (scheme 9.9). The γ-lactones are good candidates for interesting follow-up reactions [26].

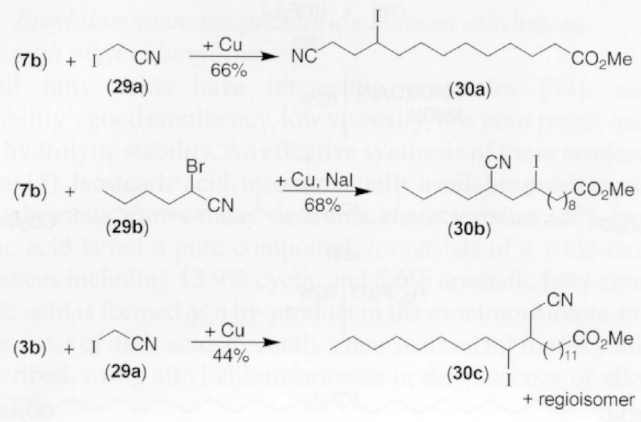
9.2.2.3 *Additions of 2-haloalkanenitriles initiated by electron transfer from copper in solvent-free systems*

2-Iodo- and 2-bromoalkanenitriles can be added to unsaturated fatty compounds in an analogous fashion to the addition of alkyl 2-haloalkanoates [24, 25]. The iodo functionality is preserved in the adduct molecule and can be used for interesting follow-up reactions. The addition of iodoacetonitrile (**29a**) to **7b** gave 12-cyano-10-iodododecanoic acid methyl ester (**30a**) in 66% yield (scheme 9.10). Reaction of **7b** and 2-bromohexanonitrile (**29b**) with added sodium iodide yielded the iodinated addition product **30b**. The regioisomeric adducts **30c** were formed by addition of iodoacetonitrile (**29a**) to methyl erucate (**3b**).

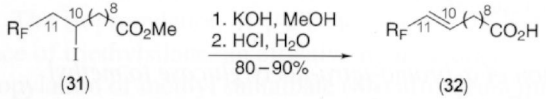
9.2.2.4 *Additions of perfluoroalkyl iodides*

Perfluoroalkyl iodides can be added to methyl 10-undecenoate (**7b**), methyl oleate (**1b**) or methyl petroselinate (**2b**) with good to very good yields when the reaction is initiated by electron transfer from metals such as finely divided silver [27], copper powder [28], or lead with a catalytic amount of copper(II) acetate [28]. Perfluoroalkylated fatty compounds are of interest because of their surfactant properties [29].

Addition of perfluoroalkyl iodides to **7b** gave product **31**, which can be reacted regioselectively with potassium hydroxide in methanol to give the corresponding linear unsaturated perfluoroalkylated carboxylic acids **32** in high



Scheme 9.10 Copper-initiated addition of iodoacetonitrile **29a** and 2-bromohexanonitrile (**29b**) to methyl 10-undecenoate (**7b**) and methyl erucate (**3b**) [24].

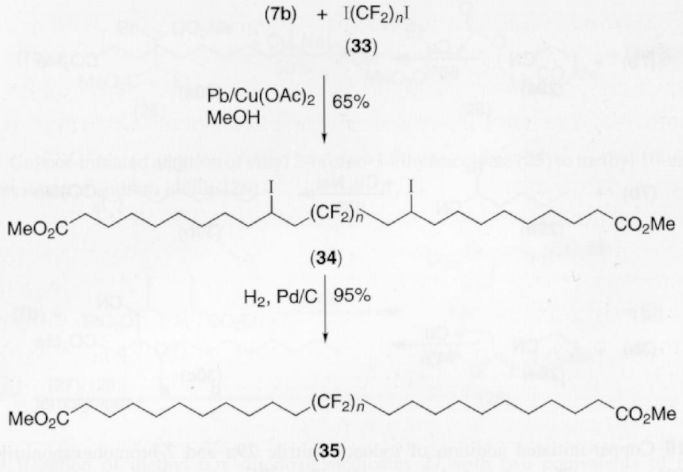


Scheme 9.11 Synthesis of 11-perfluoroalkyl-10-undecenoic acid (**32**) by regioselective elimination of HI from addition product **31** obtained by addition of perfluoroalkyl iodides to methyl 10-undecenoate (**7b**) [27].

yields (scheme 9.11) [27]. Perfluoroalkyl-1, ω-diiodides **33** were added to **7b** using the initiator system Pb/Cu(OAc)$_2$ in methanol. The diaddition product **34** was obtained in high yield. Catalytic hydrogenation afforded the long-chain dicarboxylic dimethyl esters **35**, containing a central perfluoroalkyl unit (scheme 9.12) [28].

9.2.2.5 Thermal additions of alkanes

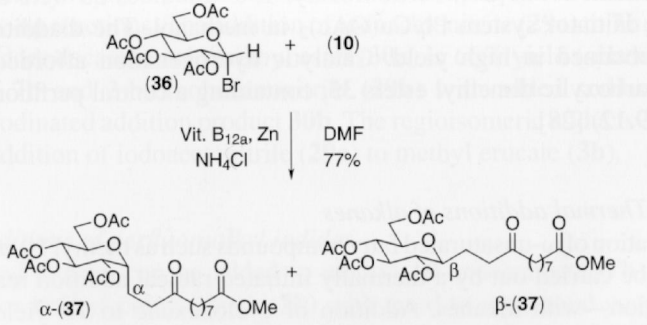
The alkylation of ω-unsaturated fatty compounds such as methyl 10-undecenoate (**7b**) can be carried out by a thermally initiated radical addition reaction—the ane reaction—with alkanes. Addition of cyclohexane to **7b** yielded methyl 11-cyclohexylundecanoate. Remarkably, thermoacidophilic bacteria such as *Alicyclobacillus acidocaldarius* produce a series of ω-cyclohexyl fatty acids of which ω-cyclohexylundecanoic acid is the most abundant [30]. In a similar reaction heptane gave regioisomeric mixtures of alkyl branched methyl C_{18} alkanoates (14% methyl stearate; 49% methyl 12-methylheptadecanoate; 25% methyl 12-ethylhexadecanoate; 12% 12-propylpentadecanoate) and toluene afforded 12-phenyldodecanoate [31].



Scheme 9.12 Radical addition of perfluoroalkyl-α,ω-diiodides (n = 4,6,8,10) to two equivalents of methyl 10-undecenoate (**7b**) with subsequent hydrogenation of the diaddition product **34** to the dicarboxylic dimethyl esters **35** [28].

9.2.2.6 *Addition of α-bromo-tetra-acetylglucose to methyl 9-oxo-10-undecenoate*

In the presence of zinc and vitamin B_{12} α-bromo-tetra-acetylglucose (**36**) was added to methyl 9-oxo-10-undecenoate (**10**), a polarity reversed unsaturated fatty compound. The product C-glucopyranoside (**37**) was formed with 77% yield and in a ratio of the α- and β-anomers of 13:1 (scheme 9.13) [8].



Scheme 9.13 Radical addition of α-bromo-tetra-acetylglucose (**36**) to methyl 9-oxo-10-undecenoate (**10**). The ratio of the anomers was [α-**37**] : [β-**37**] = 13 : 1 [8].

9.2.3 *Lewis acid induced cationic additions*

Ritter reactions with nitriles giving products equivalent to the formal addition of amides to the double bond of unsaturated fatty compounds have been reviewed quite recently [32, 33].

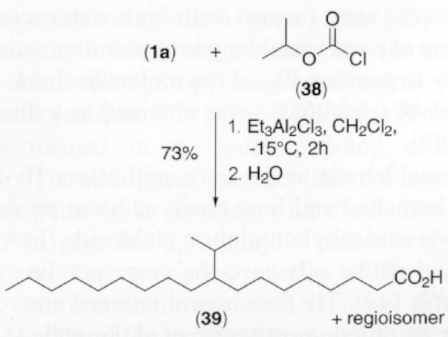
9.2.3.1 *Ethylaluminium sesquichloride induced alkylations with alkyl chloroformates*

Alkylated fatty acids have interesting properties [34], such as good 'spreadability', good emolliency, low viscosity, low pour points and good oxidative and hydrolytic stability. An effective synthesis of these products is therefore important [3]. Isostearic acid, a commercially available product used in cosmetics and lubricants shows many desirable characteristics [35], but commercial isostearic acid is not a pure compound; it consists of a wide-ranging mixture of substances including 13.9% cyclic and 5.6% aromatic fatty compounds [36]. Isostearic acid is formed as a by-product in the montmorillonite-induced dimerization process of oleic acid. Recently a new method for the alkylation of alkenes was described, using alkyl chloroformates in the presence of alkyl aluminium halides [37].

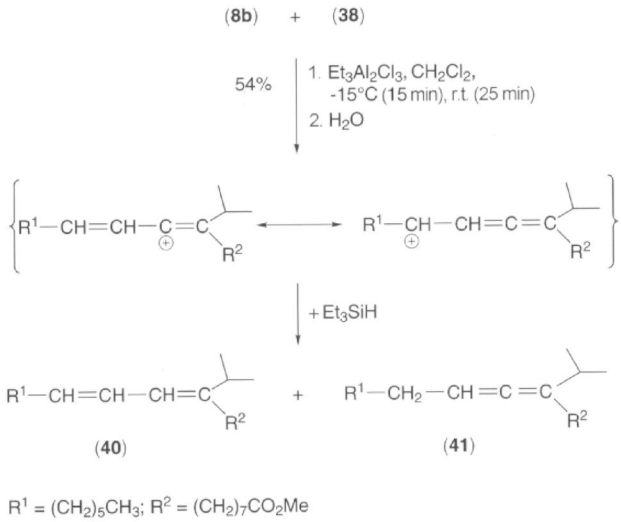
Oleic acid (**1a**) was treated with isopropyl chloroformate (**38**) mediated by ethylaluminium sesquichloride yielding 73% of a mixture of 9- and 10-isopropyloctadecanoic acid (**39**) (scheme 9.14). Methyl ricinoleate (**6b**) afforded 60% of methyl 12-hydroxyoctadecanoate isopropylated at the 9- and 10-positions. The isopropylation of 1-alkenes such as **7a** had to be carried out in the presence of triethylsilane, an effective hydride donor.

The isopropylation of methyl santalbate (**8b**) afforded a mixture of addition products **40** and **41** in 54% yield [6]. The main product was the isopropylated allenic fatty acid methyl ester **41** (scheme 9.15). The formation of **40** and **41** can be rationalized assuming regioselective addition of the isopropyl cation to C_9 of **8b**, giving the resonance-stabilized intermediate, which can be trapped by hydride transfer from triethylsilane to give **41** as the 1,4-addition product and **40** as the 1,2-addition product.

The alkylation has been applied to native oils such as sunflower oil to give the isopropylated oil with low iodine value, low acid number, and a low pour point.



Scheme 9.14 Ethylaluminium sesquichloride induced reaction of oleic acid (**1a**) with isopropyl chloroformate (**38**) [37].

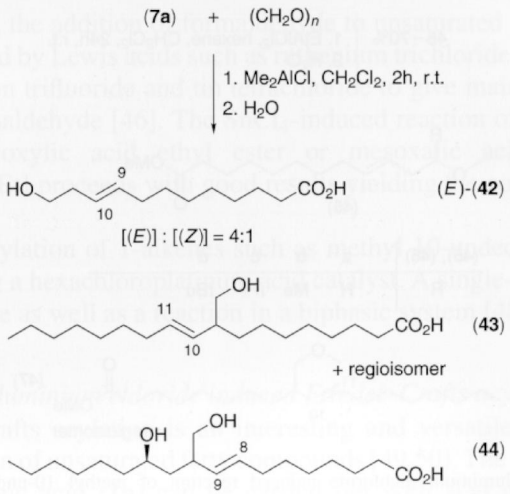


Scheme 9.15 Ethylaluminium sesquichloride induced reaction of methyl santalbate (**8b**) with isopropyl chloroformate (**38**). The allenic fatty compound **41** was obtained by 1,4-addition as main product. The formation of the minor product **40** occurred by 1,2-addition [6].

9.2.3.2 Lewis acid induced additions of aldehydes and acetals

The ene reaction of formaldehyde and alkenes is a suitable method for the synthesis of primary homoallylic alcohols, especially in the presence of alkylaluminium halides [38, 39]. The dimethylaluminium chloride (Me_2AlCl)-induced reaction of **7a** and paraformaldehyde yielded 12-hydroxy-9-dodecenoic acid (**42**) as a mixture of the (*E*)- and (*Z*)-stereoisomers in a ratio of 4:1 (scheme 9.16) [40]. It is of interest that (*Z*)-**42** induces wound healing of tissue damage in soybeans by stimulation of callus formation at the damaged site [41]. The corresponding reaction of oleic acid (**1a**) gave a regioisomeric mixture (1:1) of the branched homoallylic alcohols 9- and 10-hydroxymethyl-10(8)-octadecenoic acid (**43**). The products were formed with high stereoselectivity as pure (*E*)-adducts. The addition of paraformaldehyde to ricinoleic acid (**6a**) occurred with high regioselectivity to position C_{10} of the molecule chain. The optically active homoallylic alcohol **44** (yield 68%) was obtained as a diastereomeric mixture in a ratio of 1.2:1 [42].

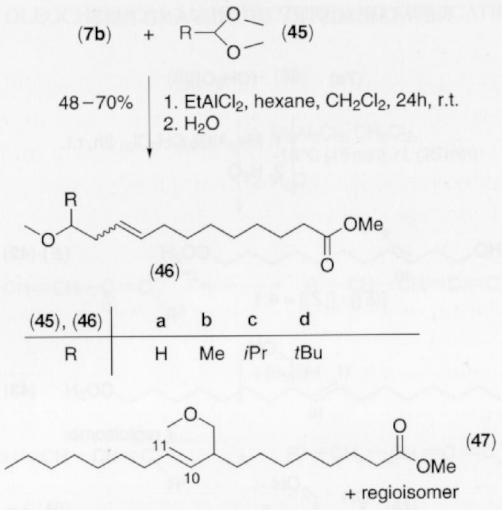
Additions of formaldehyde to the fatty acid esters **1b–3b** and **7b** afforded the corresponding branched and long-chain addition products in the presence of the stronger Lewis acid ethylaluminium dichloride ($EtAlCl_2$). Ene reactions of formaldehyde and native oils gave the corresponding di- and trifunctionalized triacylglycerols [42]. The Lewis acid induced ene reaction of jojoba oil and formaldehyde afforded a mixture of 1:1- and 1:2-adducts [43]. ω-Hydroxycarboxylic acids are of interest as polyester components.



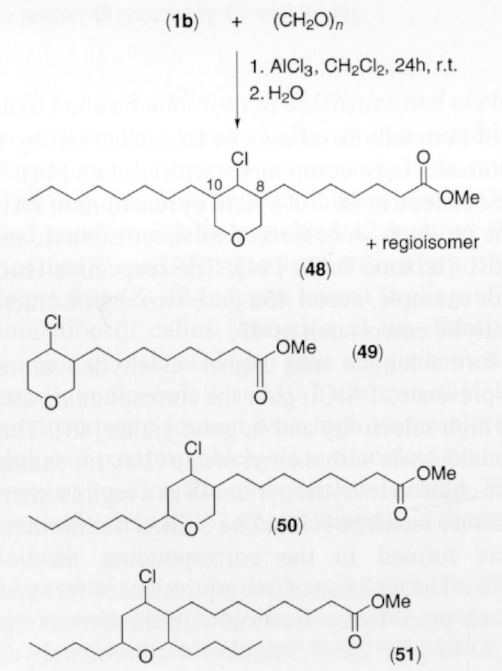
Scheme 9.16 Dimethylaluminium chloride induced addition of paraformaldehyde to 10-undecenoic acid (**7a**) to give homoallylic alcohol **42** [(*E*):(*Z*) = 4:1]. The corrresponding additions to oleic acid (**1a**) and ricinoleic acid (**6a**) gave homoallylic alcohols **43** (regioisomeric mixture) and **44** (diastereomeric mixture) [40].

The synthesis of homoallylic ethers can be carried out by $EtAlCl_2$ induced reactions of unsaturated fatty compounds with acetals [44]. The homoallylic ethers **46a–d** were obtained in 48–70% yield by reactions of **7b** with the dimethyl acetals **45a–d**. The products were formed as stereoisomeric mixtures in a ratio of [(*E*)]:[(*Z*)] ≈ 6:1 (scheme 9.17) [44]. The respective reactions of methyl oleate (**1b**) and, for example, acetal **45a** gave two regioisomeric branched (*E*)-configured homoallylic ethers such as **47**.

Additions of formaldehyde and higher aldehydes to unsaturated fatty compounds in the presence of $AlCl_3$ gave the corresponding alkyl 4-chlorotetrahydropyrans with high selectivity and in good yields [45]. The reaction of two equivalents of formaldehyde with methyl oleate (**1b**), for example, yielded 86% of the 3,5-dialkyl 4-chlorotetrahydropyrans **48** as a regioisomeric (ratio 1:1) and diastereomeric mixture (scheme 9.18). The 3-alkyl 4-chlorotetrahydropyran **49** (yield: 73%) was formed in the corresponding reaction with methyl 10-undecenoate (**7b**). The addition of one equivalent of formaldehyde to methyl ricinoleate (**6b**) took place by cyclization with the hydroxy group at C_{12} and elimination of H_2O to give the 2,5-dialkyl 4-chlorotetrahydropyran **50** as a diastereomeric mixture. The analogous reaction of **7b** and pentanal afforded the 2,3,6-trialkyl 4-chlorotetrahydropyran **51** (scheme 9.18). Variation of the alkene, on the one hand, and the carbonyl compound, on the other, leads to a broad range of alkyl chlorotetrahydropyrans.



Scheme 9.17 Ethylaluminium dichloride induced reaction of methyl 10-undecenoate (**7b**) with dimethyl acetals **45** affording homoallylic ethers **46**. Homoallylic ether **47** was obtained in the corresponding reaction of methyl oleate (**1b**) and formaldehyde dimethyl acetal **45a** as a mixture of two regioisomers [44].



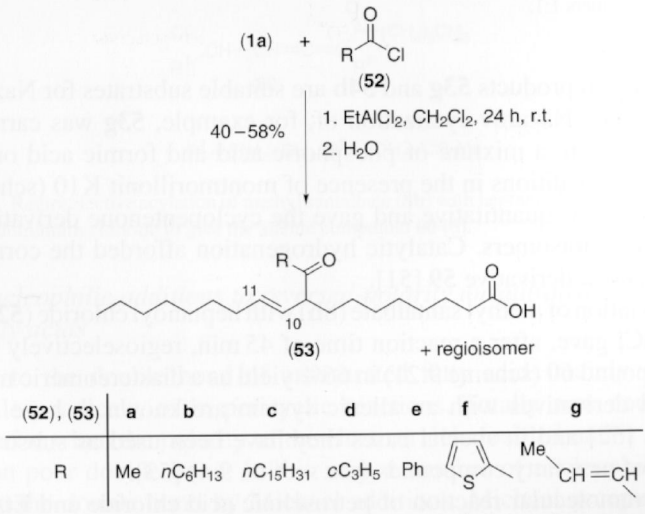
Scheme 9.18 $AlCl_3$-induced addition of two equivalents of paraformaldehyde to methyl oleate (**1b**) to give 4-chlorotetrahydropyrans **48** (mixture of two regioisomers). 4-Chlorotetrahydropyrans **49** and **50** were obtained in the corresponding reactions with methyl 10-undecenoate (**7b**) and methyl ricinoleate (**6b**). Addition of pentanal to **7b** afforded the addition product **51** [45].

Furthermore, the addition of formaldehyde to unsaturated fatty compounds could be induced by Lewis acids such as ruthenium trichloride, hexachloroplatinum acid, boron trifluoride and tin tetrachloride to give mainly 1:1- and 1:2-adducts of formaldehyde [46]. The $SnCl_4$-induced reaction of oleic acid ethyl ester with glyoxylic acid ethyl ester or mesoxalic acid diethyl ester [EtO_2CCOCO_2Et] proceeds with good results yielding the corresponding 1:1-adducts [47].

The hydrosilylation of 1-alkenes such as methyl 10-undecenoate (**7b**) was optimized using a hexachloroplatinum acid catalyst. A single-phase hydrosilylation is possible as well as a reaction in a biphasic system [48].

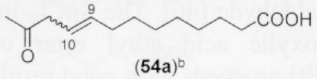
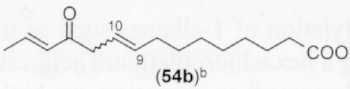
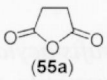
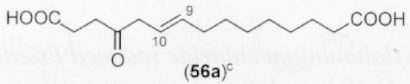
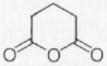
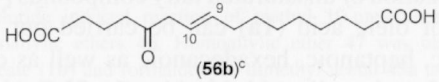
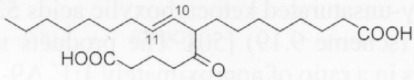
9.2.3.3 Alkylaluminium chloride induced Friedel–Crafts acylations

The Friedel–Crafts acylation is an interesting and versatile method for the functionalization of unsaturated fatty compounds [49,50]. The $EtAlCl_2$-induced acylation of oleic acid (**1a**) can be carried out with acyl chlorides derived from acetic, heptanoic, hexadecanoic as well as cyclopropanoic, benzoic and thiophene-2-carboxylic acid chlorides (**1a**:**52**:$EtAlCl_2$ =1:1:2) giving the corresponding β,γ-unsaturated ketocarboxylic acids **53** as pure (*E*) adducts in yields of 40–58% (scheme 9.19) [50]. The products were obtained as mixtures of regioisomers in a ratio of approximately 1:1. Δ9-12-ketoalkenoic acids such as **54a** and **54b** were formed by acylation reactions of **7a** with acyl chlorides. The stereoisomeric mixtures ([(*E*)]:[(*Z*)] ≈ 3:1) were isolated in yields of 50–60% (table 9.1).



Scheme 9.19 Ethylaluminium dichloride induced Friedel–Crafts acylations of oleic acid (**1a**) with acyl chlorides **52a–g** gave the unsaturated regioisomeric oxocarboxylic acids **53a–g** [49].

Table 9.1 Syntheses of β,γ-unsaturated ketones: ethylaluminium dichloride induced Friedel–Crafts acylations of 10-undecenoic acid (**7a**) and oleic acid (**1a**)[a] [49]

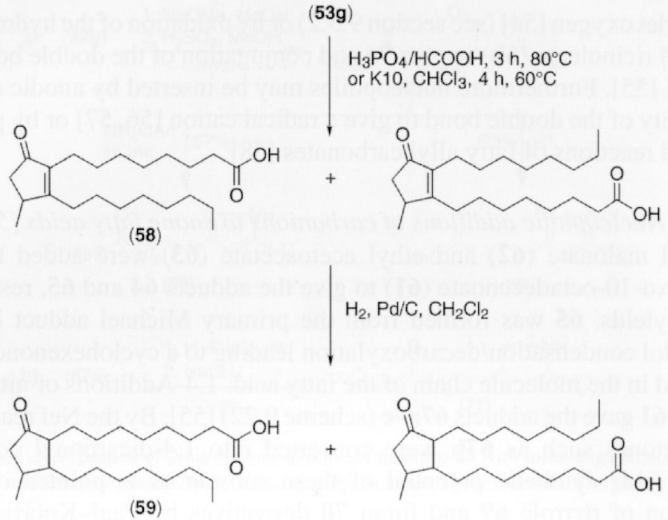
No	Alkene	Acylation agent	Product	Yield (%)
1	(**7a**)	(**52a**)	 (**54a**)[b]	50
2	(**7a**)	(**52g**)	 (**54b**)[b]	60
3	(**7a**)	 (**55a**)	 (**56a**)[c]	50
4	(**7a**)	 (**55b**)	 (**56b**)[c]	67
5	(**1a**)	(**55b**)	 (**57**)[d]	49

[a] reaction conditions: alkene:acylation agent:$EtAlCl_2$ = 1:1:2, CH_2Cl_2, r.t., 2 h.
[b] [(*E*)]:[(*Z*)] ≈ 3:1.
[c] after recrystallization the pure (*E*)-adduct was obtained.
[d] ratio of regioisomers 1:1.

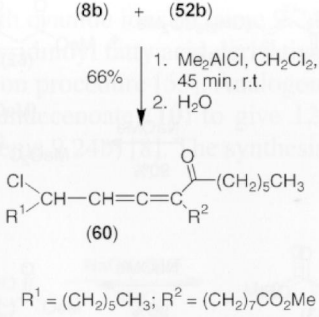
The addition products **53g** and **54b** are suitable substrates for Nazarov reactions [51]. The Nazarov cyclization of, for example, **53g** was carried out by heating for 2 h in a mixture of phosphoric acid and formic acid or by modified reaction conditions in the presence of montmorillonit K10 (scheme 9.20). The reaction was quantitative and gave the cyclopentenone derivative **58** as a mixture of regioisomers. Catalytic hydrogenation afforded the corresponding cyclopentanone derivative **59** [51].

The acylation of methyl santalbate (**8b**) with heptanoyl chloride (**52b**) induced by Me_2AlCl gave, after a reaction time of 45 min, regioselectively the allenic fatty compound **60** (scheme 9.21) in 66% yield as a diastereomeric mixture [6]. Fatty acid derivatives with an allenic system are known to have interesting properties [52] and in special cases they have been used as substrates in the synthesis of new fatty compounds (see section 9.4) [53].

The intramolecular reaction of petroselinic acid chloride and $EtAlCl_2$ took place by cyclization with high regio- and stereoselectivity to give a cyclohexanone derivative with an exocyclic (*E*)-configured double bond [49b, 50].



Scheme 9.20 Nazarov cyclization of allyl vinyl ketone **53g** followed by hydrogenation of the cyclopentenones **58** to give the regioisomeric cyclopentanones **59. 53g** was obtained by Friedel–Crafts acylation of methyl oleate (**1b**) with crotonic acid chloride (**52g**) [51].



Scheme 9.21 Regioselective acylation of methyl santalbate (**8b**) with heptanoyl chloride (**52b**), induced by dimethylaluminium chloride to give the allenic compound **60** [6].

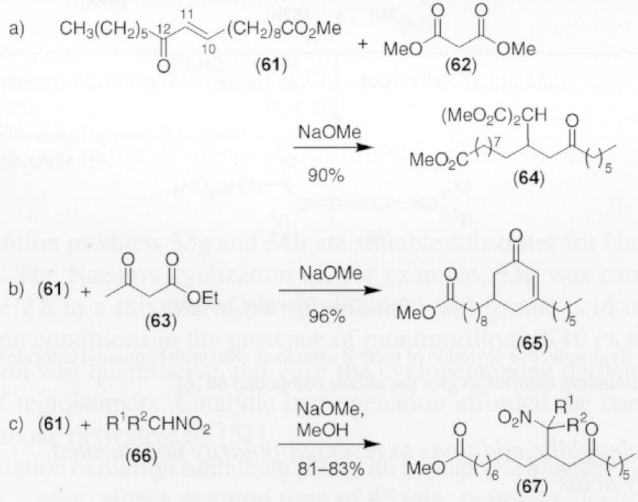
9.2.4 *Nucleophilic additions to reversed-polarity unsaturated fatty acids*

Additions to the double bond of unsaturated fatty acids mainly occur with electrophiles, radicals, or in pericyclic reactions. Totally new coupling possibilities arise when the polarity of the electron rich double bond is reversed to an electron poor double bond. In this way, a number of nucleophiles may be coupled to the double bond by Michael additions. Michael acceptors derived from fats such as the enone fatty ester **10** can be prepared in different ways: by SeO_2 oxidation of unsaturated fatty compounds [54], by photo-oxygenation

with singlet oxygen [54] (see section 9.3.2) or by oxidation of the hydroxy group of methyl ricinoleate (**6b**) to give **9a** and conjugation of the double bond yields enone **61** [55]. Furthermore nucleophiles may be inserted by anodic change of the polarity of the double bond to give a radical cation [56, 57] or by palladium catalyzed reactions of fatty allyl carbonates [58].

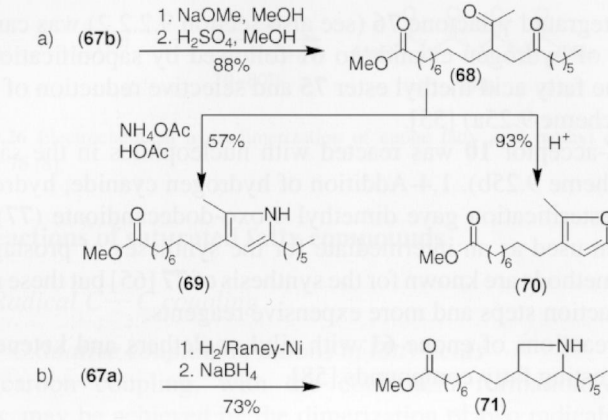
9.2.4.1 Nucleophilic additions of carbanions to enone fatty acids [55]

Dimethyl malonate (**62**) and ethyl acetoacetate (**63**) were added to methyl (*E*)-12-oxo-10-octadecenoate (**61**) to give the adducts **64** and **65**, respectively, in good yields. **65** was formed from the primary Michael adduct by subsequent aldol condensation/decarboxylation leading to a cyclohexenone which is integrated in the molecule chain of the fatty acid. 1,4-Additions of nitroalkanes **66a–c** to **61** gave the adducts **67a–c** (scheme 9.22) [55]. By the Nef reaction [59] γ-nitroketones such as **67b** were converted into 1,4-dicarbonyl compounds **68**. The wide synthetic potential of these substances is pointed out in the production of pyrrole **69** and furan **70** derivatives by Paal–Knorr syntheses (scheme 9.23a) [55, 60]. Pyrrolidine fatty acids such as **71** were obtained by reductive cyclization of the nitroalkane adducts **67a** (scheme 9.23b). Compound



66, 67	a	b	c
R^1	H	Me	Me
R^2	H	H	Me

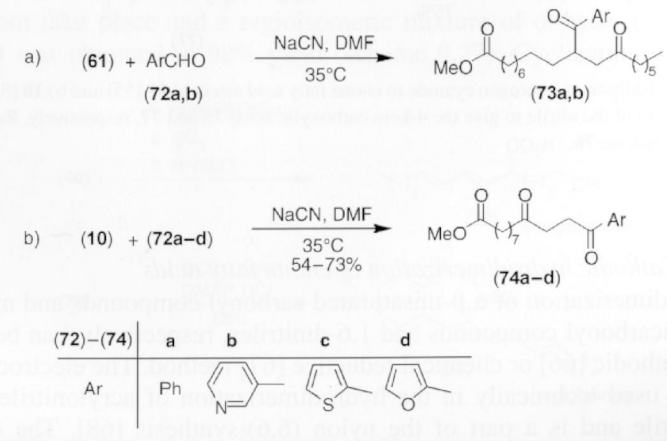
Scheme 9.22 Michael addition of a) malonate **62**, b) ethyl acetoacetate **63** and c) nitroalkanes **66a–c** to the enone fatty acid ester **61** [55].



Scheme 9.23 a) Nef reaction of γ-nitroketone **67b** to 1,4-diketone **68** with following reaction to pyrrole derivative **69** and furan derivative **70**. b) Reductive cyclization of γ-nitroketone **67a** giving pyrrolidine derivative **71** [55].

71 was also synthezised from methyl ricinoleate (**6b**) by reaction with sodium azide [61].

Aromatic aldehydes **72** can be added by Stetter reaction [62] to the enone **61** by reversal of polarity with cyanide ions (scheme 9.24a). In this way, benzoyl-**73a** (yield: 44%) and 3-pyridinoyl fatty acid derivatives **73b** (yield: 84%) were obtained by simple reaction procedure [55]. Analogous additions were carried out to methyl 9-oxo-10-undecenoate (**10**) to give 12-aryl-substituted methyl dodecanoates **74a–d** (scheme 9.24b) [8]. The synthesis of the fatty acid methyl

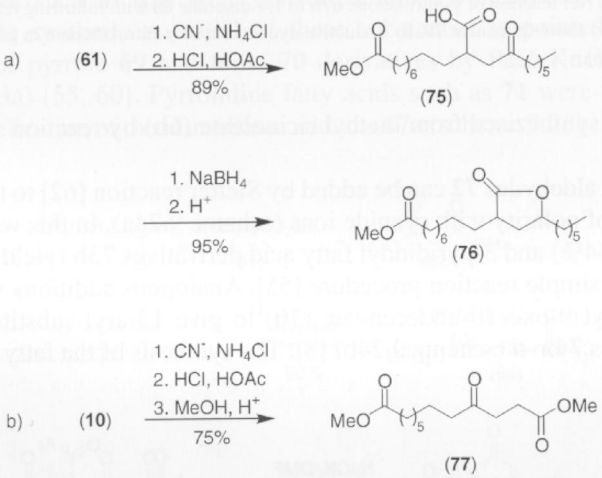


Scheme 9.24 Additions of aromatic and heteroaromatic aldehydes **72** to a) enone **61** [55] and to b) enone **10** [8] to give the aryl-substituted 1,4-diketo fatty acid ester **73** and **74**, respectively.

ester with an integrated γ-lactone **76** (see also section 9.2.2.2) was carried out by 1,4-addition of hydrogen cyanide to **61** followed by saponification of the nitrile to give the fatty acid methyl ester **75** and selective reduction of the keto functionality (scheme 9.25a) [55].

The Michael-acceptor **10** was reacted with nucleophiles in the same way as enone **61** (scheme 9.25b). 1,4-Addition of hydrogen cyanide, hydrolysis of the nitrile and esterification gave dimethyl 4-oxo-dodecandioate (**77**) [8]. **77** has already been used as an intermediate for the syntheses of prostaglandins [63, 64]. Other methods are known for the synthesis of **77** [65] but these methods require more reaction steps and more expensive reagents.

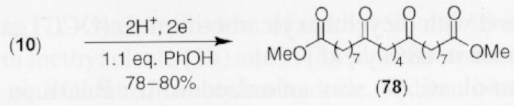
Mukayama reactions of enone **61** with silyl enolethers and ketene acetals gave many interesting fatty compounds [58].



Scheme 9.25 Addition of hydrogen cyanide to enone fatty acid esters a) **61** [55] and b) **10** [8], followed by saponification of the nitrile to give the 4-keto carboxylic acids **75** and **77**, respectively. Reduction of **75** gave the γ-lactone **76**.

9.2.4.2 Cathodic hydrodimerization of enone fatty acids

The hydrodimerization of α,β-unsaturated carbonyl compounds and nitriles to give 1,6-dicarbonyl compounds and 1,6-dinitriles, respectively, can be carried out by a cathodic [66] or chemical reductive [67] method. The electrochemical method is used technically in the hydrodimerization of acrylonitrile to give adipodinitrile and is a part of the nylon (6,6)-synthesis [68]. The cathodic hydrodimerization of enone fatty ester **10** yielded the C_{22} diketodiester **78** (scheme 9.26) [8].



Scheme 9.26 Electrochemical hydrodimerization of enone fatty acid methyl ester **10** to give the diketoester **78** [8].

9.3 Reactions of saturated fatty compounds

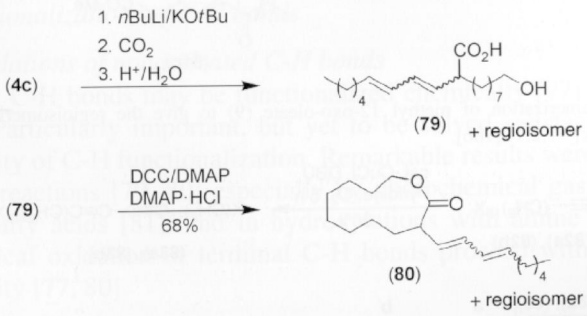
9.3.1 Radical C—C coupling

9.3.1.1 Oxidative coupling of anions of fatty acids

Carbon-carbon coupling, with the concurrent formation of symmetrical products, may be achieved by the dimerization of two radicals. Radicals may be formed selectively under mild conditions in high concentrations by the oxidation of anionic precursors. Unsaturated fatty acids possess several sites with comparably high C-H acidities which are suitable for anionization: a) the 11-CH-bond of methyl 12-oxo-oleate (**9**) has a pK_s-value of about 13; b) the CH-bond in α-position to the ester functionality has a pK_s-value of 24; and c) that of the 11-CH-bond of methyl linoleate (**4b**) of approximately 37.

For radical α,α′-dimerization fatty acid methyl esters such as **7b** were anionized with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) LDA in THF and oxidatively coupled with copper(I) bromide to 2,3-dialkylsuccinic diesters. The dimeric products were obtained in yields of 56–73% [4, 55a].

Linoleic acid (**4a**) was deprotonated with the Schlosser base BuLi/*t*-BuOK [69] and the anion was trapped with CO_2. Because of deprotonation as well at C_2 as at C_{11} a 1:1-mixture of di- and tricarboxylic acids was obtained (yield: 78%). In the corresponding reaction of linoleic alcohol (**4c**) deprotonation at C_2 did not take place and a regioisomeric mixture of ω-hydroxy carboxylic acids **79** was obtained in 90% yield (scheme 9.27). Cyclization of **79** using



Scheme 9.27 Synthesis of ω-hydroxy carboxylic acid **79** (regioisomeric mixture) by deprotonation of linoleic alcohol (**4c**) and addition of CO_2 followed by cyclization to macrolides **80** (isomeric mixture) [70b].

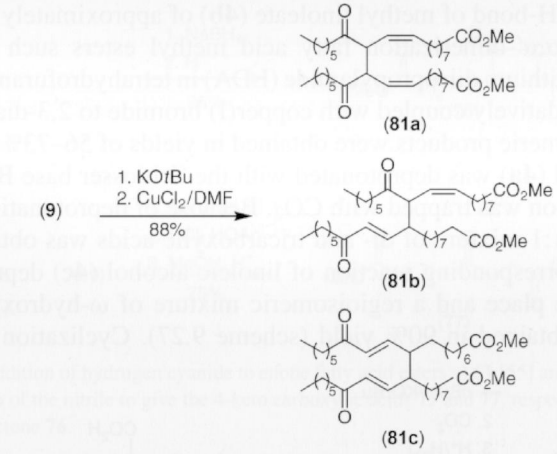
the dilution method with dicyclohexylcarbo-diimide (DCC) gave **80** and regioisomeric macrolides in 68% yield [70b].

Methyl 12-oxo-oleate (**9**) was anionized with *t*-BuOK in THF at −78°C and coupled with $CuCl_2$ in dimethyl formamide (DMF) to give the dimers **81a–c**. The three regioisomers were statistically formed in a ratio of 1:2:1 (scheme 9.28) [70b].

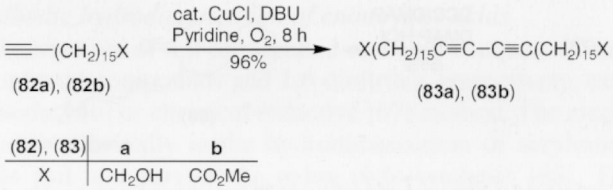
The dimerization of 17-octadecyn-1-ol (**82a**) could be carried out with oxygen in the presence of one equivalent of copper(I) ions and one equivalent of diamine with formation of hexatriaconta-17,19-diene-1,36-diol **83a** in a yield of 94% [71]. Using 1,8-diazabicyclo [5.4.0] undec-7-ene (DBU) as base the reaction time could be shortened compared to the analogous reaction with tetramethylethyl-enediamine (TMEDA). Ester **82b** was dimerized in the same way with DBU to product **83b** (yield: 96%) (scheme 9.29).

9.3.1.2 *Radical C—C coupling of halide fatty acids with activated olefins*

Reductive alkylations of C—C double bonds activated by electron withdrawing substituents can be carried out in radical reactions with alkyl halides and



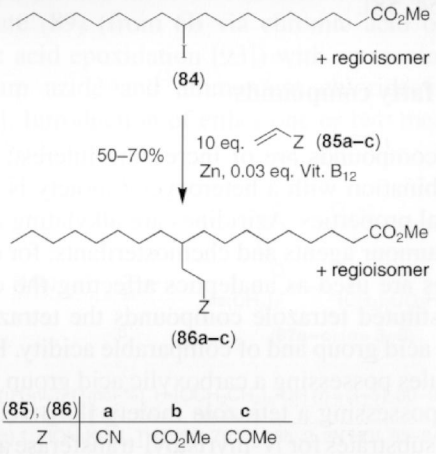
Scheme 9.28 Dimerization of methyl 12-oxo-oleate (**9**) to give the regioisomeric dimers **81a–c** ([**81a**]:[**81b**]:[**81c**]=1:2:1) [70b].



Scheme 9.29 Oxidative dimerization of 17-octadecyn-1-ol (**82a**) and methyl 17-octadecynoate (**82b**) to give the diynes **83a** and **83b**, respectively [71].

tributyltin hydride [72–74a]. A mixture of methyl 9- and 10-iodostearate (**84**) was obtained from methyl oleate (**1b**) and HI by phase transfer catalysis. **84** was reacted with 0.2 equivalent of tributyltin hydride, sodium borohydride and 10 equivalents of activated olefin such as acrylonitrile (**85a**) and methyl acrylate (**85b**) to give the adducts **86a** and **86b** in good yields. In an alternative way the reductive addition can be carried out with zinc and vitamin B_{12} as catalyst to avoid the toxic tin compound [72, 74a]. Several activated olefins were used and the adducts **86a–c** were obtained in good yields (scheme 9.30) [74b].

The anodic homo- and heterocoupling of fatty acids (Kolbe electrolysis) has been used by Schäfer to synthesize many interesting compounds and was reviewed quite recently [75,76].



Scheme 9.30 Reductive alkylation of activated olefins **85a–c** with methyl 9(10)-iodostearate (**84**) to the adducts **86a–c** [74b].

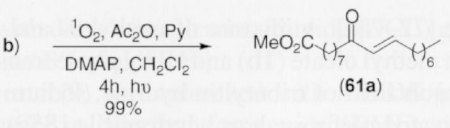
9.3.2 Functionalizations of C-H bonds

9.3.2.1 Oxidations of nonactivated C-H bonds

Nonactivated C-H bonds may be functionalized chemically [77] or enzymatically [78]. Particularly important, but yet to be solved satisfactorily, is the regioselectivity of C-H functionalization. Remarkable results were obtained in chlorination reactions [79, 80] especially by photochemical gas phase chlorination of fatty acids [81], and in hydroxylations with amine oxides [8a]. Electrochemical oxidation of terminal C-H bonds proceed with satisfactory regioselectivity [77, 80].

9.3.2.2 Oxidations of allylic C-H bonds

Allylic C-H bonds can be oxidized by a great variety of oxidizing reagents. The allylic oxidation of **1b** and **7b** with SeO_2/tBuOOH [8, 54] is possible but



Scheme 9.31 Photo-oxygenation of methyl oleate (**1b**) with singlet oxygen and tetraphenylporphyrin as sensitizer to give the α,β-unsaturated ketone **61** (mixture of regioisomers) [58].

more favourable is the corresponding reaction of, for example, **1b** with singlet oxygen to give a hydroperoxide which is reduced to the corresponding allylic alcohol [54]. In the presence of acetic anhydride and pyridine methyl oleate (**1b**) can be directly oxidized with singlet oxygen to the regioisomeric mixture of the corresponding α,β-unsaturated ketones **61a**, regioisomers of the ketone **61** (scheme 9.31) [54, 58].

9.4 Heterocyclic fatty compounds

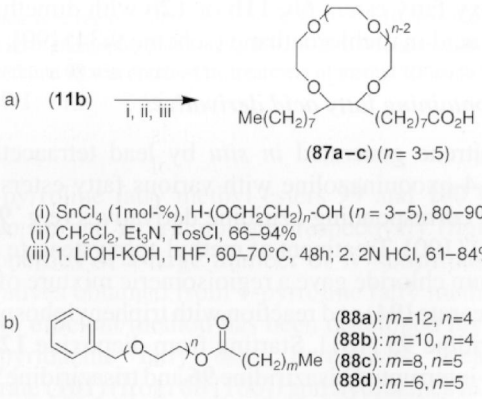
Heterocyclic fatty compounds are of increasing interest, since the lipophilic alkyl chain in combination with a heterocyclic moiety is expected to possess promising biological properties. Aziridines are alkylating agents and therefore well known as antitumour agents and chemosterilants, for example [82]. Some 1,5-dialkyltetrazoles are used as analeptics affecting the central nervous system [83]. In 5-substituted tetrazole compounds the tetrazole ring is isosteric with the carboxylic acid group and of comparable acidity. Hence for all biologically active molecules possessing a carboxylic acid group there is a theoretical nitrogen analogue possessing a tetrazole moiety [83]. Tetrazole analogues of fatty acid ethers are substrates for *N*-myristoyl-transferase and its coenzyme and show antiviral (including HIV) and antifungal activity [84]. Studies on 1,3,4-oxadiazole fatty acid derivatives are not well known although 1,3,4-oxadiazoles in general have a wide variety of uses, particularly as biologically active compounds in medicine and in agriculture [85]. Latest developments including heterocycles on novel long-chain fatty compounds [86] and the synthesis of special fatty acids [87] have been reviewed recently. The synthesis of various fatty compounds containing heterocyclic functionalities have been already mentioned.

9.4.1 O- and S-Heterocyclic fatty acids

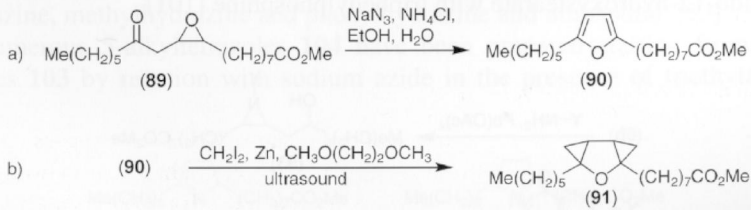
Epoxy fatty compounds are the most important fatty heterocycles, having industrial applications as PVC stabilizers and in photochemical cationic curing [88], [89] and synthetic applications as reactants for transformation into further interesting fatty heterocycles. The epoxidation of unsaturated fatty acids has been reviewed recently [90]. Crown ethers derived from unsaturated fatty acids, such as **1a, 2a** and **7a** were obtained by reacting the corresponding epoxy

derivatives (e.g. **11b**) under Lewis acid catalysis with tri-, tetra- or pentaethylene glycol followed by tosylation of the hydroxy function, cyclization with alkali hydroxides and saponification of the methyl esters **87a–c** (scheme 9.32a) [91]. In this context, it is most interesting that fatty acid-oligo(ethylene glycol) esters have been shown to form ion channels in lipid membranes. The ion channel formers were prepared in a two-step sequence. Monobenzyl ethers, obtained by Williamson reaction of tetra- or pentaethylene glycol with benzyl bromide, were esterified with different fatty acids to the corresponding oligo(ethylene glycol) fatty ester **88a–d** (scheme 9.32b) [92].

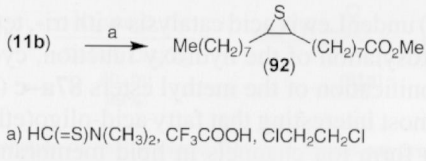
With regard to the pharmacological significance of 2,5-disubstituted furanoid compounds an efficient synthetic method for the preparation of furan **90** has been developed. This method involves conversion of methyl (*Z*)-9,10-epoxy-12-oxo-octadecanoate (**89**) (from **6b** via chromic acid oxidation to **9b** and *m*-chloroperbenzoic acid epoxidation [93]) with ammonium azide, generated *in situ* from sodium azide and ammonium chloride in aqueous ethanol (scheme 9.33a) [94]. Introduction of either one or two methyl groups into the



Scheme 9.32 a) Conversion of methyl epoxystearate **11b** to crown ethers **87a–c** [91]. b) Oligo(ethylene glycol) fatty esters **88a–d**, active as ion channel formers in lipid membranes [92].



Scheme 9.33 a) 2,5-Disubstituted furan **90** by reaction of methyl (*Z*)-9,10-epoxy-12-oxo-octadecanoate (**89**) with ammonium azide [94]. b) Ultrasound-assisted Simmons–Smith reaction of furan **90** to form tricyclo derivative **91** [98].



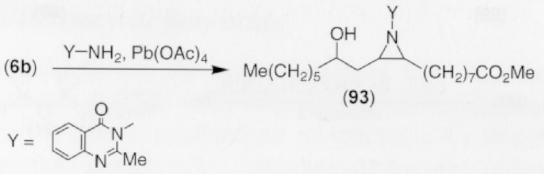
Scheme 9.34 Methyl 9,10-epithiostearate (**92**) by reaction of epoxide **11b** with dimethylthioformamide and trifluoroacetic acid in dichloroethane [99].

furan ring of a 2,5-disubstituted C_{18} furan fatty acid is possible [95, 96]. A phenyl substituent at the 3- or 4-position of the furan ring was introduced via **89** as a key intermediate [97]. Ultrasound-assisted Simmons–Smith reaction involving zinc and diiodomethane in 1,2-dimethoxyethane provides a unique method for the cyclopropanation of olefinic bonds in fatty acids and also in triacylglycerols as substrates which also can contain hydroxy groups. Furan **90** was reacted in this manner to form a novel tricyclo derivative **91** (scheme 9.33b) [98].

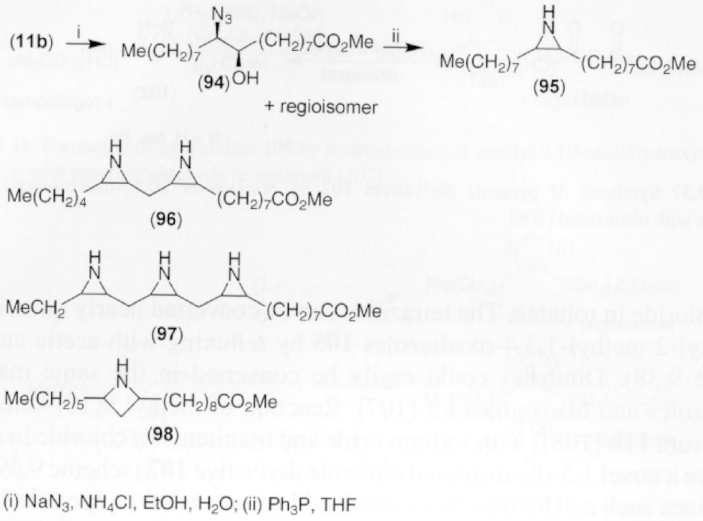
A number of epithio C_{18} fatty esters (e.g. **92**) resulted in the conversion of the corresponding epoxy fatty esters **6b, 11b** or **12b** with dimethylthioformamide and trifluoroacetic acid in dichloroethane (scheme 9.34) [99].

9.4.2 *Nitrogen-containing fatty acid derivatives*

Reaction of the nitrene generated *in situ* by lead tetraacetate oxidation of 3-amino-2-methyl-4-oxoquinazoline with various fatty esters (i.e. **1b, 6b** and **10b**) furnished the corresponding aziridine derivatives (e.g. **93**) in about 50% yield (scheme 9.35) [100]. Treatment of methyl epoxystearate **11b** with sodium azide and ammonium chloride gave a regioisomeric mixture of methyl 9,10(10, 9)-azidohydroxystearate (**94**) and reaction with triphenylphosphine afforded the corresponding aziridine **95** [101]. Starting from diepoxide **12b** and triepoxide **13b** the methylene-interrupted bisaziridine **96** and trisaziridine **97** were obtained respectively (scheme 9.36) [102]. Both compounds showed considerable cytotoxic, antimicrobial and neuroprotective activity as well as a significant antitumour promoting effect. Azetidine **98** was obtained by treatment of methyl 10-azido-12-hydroxystearate with triphenylphosphine [101].



Scheme 9.35 Formation of aziridine derivative **93** by reaction of the nitrene generated *in situ* by lead tetraacetate oxidation of 3-amino-2-methyl-4-oxoquinazoline with methyl ricinoleate (**6b**) [100].



Scheme 9.36 Synthesis of aziridine **95** by treatment of methyl epoxystearate (**11b**) with sodium azide and ammonium chloride to a regioisomeric mixture of methyl 9.10(10.9)-azidohydroxystearate (**94**) followed by reaction with triphenylphosphine [101]. Bisaziridine **96** and trisaziridine **97** were synthesised analogously [102]. Azetidine **98** was obtained by treatment of methyl 10-azido-12-hydroxystearate with triphenylphosphine [101].

Isomers of 1-pyrroline fatty methyl esters **99** and **100** were derived from methyl ricinoleate **6b** and *iso*-ricinoleate, respectively (figure 9.2) [61, 103]. The physical properties of a large number of *N*-substituted pyrrolinium and pyrrolidine derivatives obtained from 1-pyrroline fatty methyl ester were studied [104, 105]. An efficient method has been developed for the preparation of pyrazole and pyridazine fatty ester derivatives. Reaction of methyl 10, 12-dioxostearate (**101**) (from **6b** [106]) and hydrazines in water at 60°C with ultrasound gave pyrazole derivatives **102** in high yields (scheme 9.37) [106]. The latter compound **102** could also be obtained from a novel C_{18} keto-allenic ester methyl 12-oxo-9,10-octadienoate (prepared from **6b**) by reaction with hydrazine, methylhydrazine and phenylhydrazine and ultrasound [53].

Numerous 5-alkyltetrazoles **104** have been prepared starting from fatty nitriles **103** by reaction with sodium azide in the presence of triethylamine

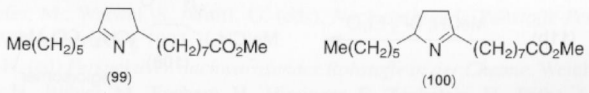
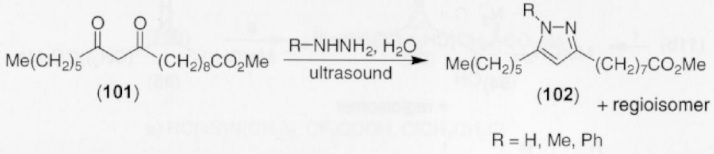
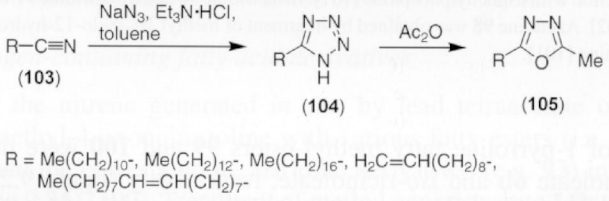


Figure 9.2 1-Pyrroline fatty methyl esters **99** and **100** derived from methyl ricinoleate **6b** and *iso*-ricinoleate [61, 103].

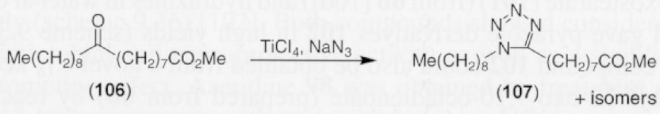


Scheme 9.37 Synthesis of pyrazole derivatives **102** by reaction of 10,12-dioxostearate **101** and hydrazines with ultrasound [106].

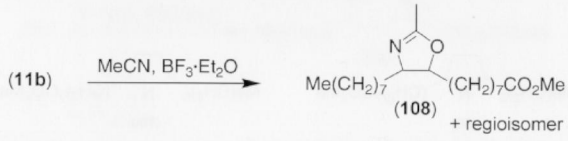
hydrochloride in toluene. The tetrazoles can be converted nearly quantitatively to 5-alkyl-2-methyl-1,3,4-oxadiazoles **105** by refluxing with acetic anhydride (scheme 9.38). Dinitriles could easily be converted in the same manner to bistetrazoles and bisoxadiazoles [107]. Reaction of methyl 9(10)-ketostearate (**106**) (from **11b** [108]) with sodium azide and titanium(IV) chloride in acetonitrile gave a novel 1,5-disubstituted tetrazole derivative **107** (scheme 9.39) [107]. Oxazolines such as **108** have been obtained by conversion of epoxide **11b** with nitriles in the presence of boron trifluoride etherate (scheme 9.40) [107].



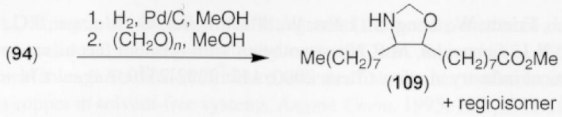
Scheme 9.38 Preparation of 5-alkyltetrazoles **104** from fatty nitriles **103** by reaction with sodium azide in the presence of triethylamine hydrochloride in toluene and subsequent reaction with acetic anhydride to form 5-alkyl 2-methyl-1,3,4-oxadiazoles **105** [107].



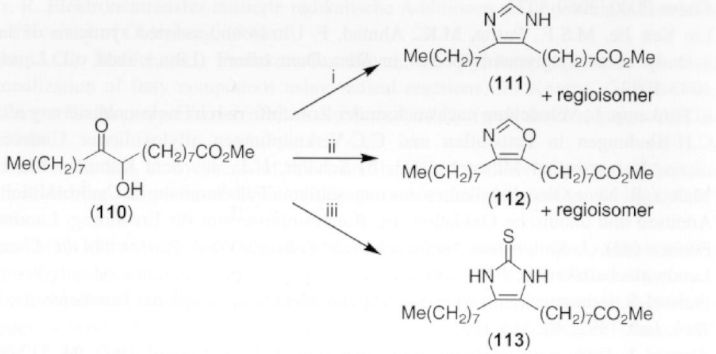
Scheme 9.39 Reaction of methyl 9(10)-ketostearate **106** with sodium azide and titanium(IV) chloride in acetonitrile to 1,5-disubstituted tetrazole derivative **107** [107].



Scheme 9.40 Oxazoline **108** was obtained by conversion of epoxide **11b** with acetonitrile in the presence of boron trifluoride etherate [107].



Scheme 9.41 Formation of oxazolidine **109** by hydrogenation of methyl 9,10-azidohydroxystearate **94** and reaction with paraformaldehyde in methanol [107].



(i) $HCONH_2$; (ii) $HCONH_2$, conc. H_2SO_4; (iii) NH_4SCN, dioxan

Scheme 9.42 Methyl 9(10)-hydroxy-10(9)-oxostearate **110** was converted with (i) formamide to imidazole **111** and (ii) formamide in the presence of sulfuric acid to oxazole derivative **112**. Reaction with ammonium thiocyanate in dioxan (iii) yielded an imidazolinethione **113** [107].

Hydrogenation of methyl 9,10-azidohydroxystearate (**94**) furnished the corresponding amino alcohol. The latter was reacted with aldehydes such as paraformaldehyde in methanol to give oxazolidines such as **109** (scheme 9.41) [107]. Another useful precursor, methyl 9(10)-hydroxy-10(9)-oxostearate (**110**) (obtained by dimethyl sulfoxide (DMSO) oxidation of epoxide **11b** in the presence of boron trifluoride etherate [109]) was converted to imidazole **111** with formamide, to oxazole derivative **112** with formamide in the presence of sulfuric acid, and to imidazolinethione **113** with ammonium thiocyanate in dioxan (scheme 9.42) [107]. Variation of the amide allows access to a great variety of substituted oxazole and imidazole derivatives.

References

1. Eggersdorfer, M., Warwel, S., Wulff, G. (eds). *Nachwachsende Rohstoffe-Perspektiven für die Chemie*. Weinheim: VCH; 1993.
2. Eierdanz, H. (ed) *Perspektiven nachwachsender Rohstoffe in der Chemie*. Weinheim: VCH; 1996.
3. Baumann, H., Bühler, M., Fochem, H., Hirsinger, F., Zoebelein, H., Falbe, J. Natural fats and oils-renewable raw materials for the chemical industry. *Angew. Chem.* 1988; **100**: 42-62; *Angew. Chem. Int. Ed. Engl.* 1988; **27**: 41-62.

4. Biermann, U., Friedt, W., Lang, S., Lühs, W., Machmüller, G., Metzger, J.O., Rüsch gen. Klaas, M., Schäfer, H.J., Schneider, M.P. New syntheses with oils and fats as renewable raw materials for the chemical industry. *Angew. Chem.* 2000; **112**: 2292-2310; *Angew. Chem. Int. Ed.* 2000; **39**: 2206-2224.
5. Knothe, G., Derksen, J.T.P. (eds). *Recent Developments in the Synthesis of Fatty Acid Derivatives*. Champaign: AOCS Press; 1999.
6. Biermann, U., Lützen, A., Lie Ken Jie, M.S.F., Metzger, J.O. Regioselective cationic 1,2-and 1,4-additions forming carbon-carbon bonds to methyl santalbate, a conjugated enyne. *Eur. J. Org. Chem.* 2000: 3069-3073.
7. Lie Ken Jie, M.S.F., Pasha, M.K., Ahmad, F. Ultrasound-assisted synthesis of santalbic acid: a study of triacylglycerol species in *Santalbum album* (Linn.) seed oil. *Lipids*. 1996; **31**: 1083-1089.
8. a) Hinkamp, L. Veredelung nachwachsender Rohstoffe durch Funktionalisierung nicht aktivierter C,H-Bindungen in Fettstoffen und C,C-Verknüpfungen allyloxidierter Undecensäure, PhD thesis, University of Münster, 1993; b) Schäfer, H.J., aus dem Kahmen, M., Hinkamp, L., Maletz, R. Neue Oleochemikalien aus ungesättigten Fettsäuren durch Cycloaddition, nukleophile Addition und anodische Oxidation. In: Bundesministerium für Ernährung, Landwirtschaft und Forsten (ed). *3. Symposium Nachwachsende Rohstoffe, Perspektiven für die Chemie*. Münster: Landwirtschaftsverlag; 1994: 217-234.
9. Warwel, S. Industriechemikalien durch Olefin-Metathese natürlicher Fettsäureester. *Nachr. Chem. Tech. Lab.* 1992; **40**: 314-320.
10. Warwel, S. Fatty-acids as chemical raw materials, *Fat Sci. Technol.* 1992; **94**: 512-523.
11. Warwel, S., Bavaj, P., Ecklentz, B., Harperscheid, M., Rüsch gen. Klaas, M., Thomas, S. Industriechemikalien durch Metathese und Oxidation ungesättiger Fettstoffe. In: Eggersdorfer, M., Warwel, S., Wulff, G. (eds). *Nachwachsende Rohstoffe – Perspektiven für die Chemie*, Weinheim: VCH; 1993: 69-95.
12. Warwel, S., Jägers, H.-G., Thomas, S. Metathesis of unsaturated fatty acid esters - a simple approach to long-chained dicarboxylic acids. *Fat Sci. Technol.* 1992; **94**: 323-328.
13. a) Wolff, B. Palladium katalysierte Ketonisierung von höhermolekularen α-Olefinen und endständig ungesättigter Fettsäureester mit Sauerstoff und Wasserstoffperoxid, PhD thesis, RWTH Aachen, 1994; b) Warwel, S., Bavaj, P., Rüsch gen. Klaas, M., Wolff, B. Polymerbausteine aus Pflanzenölen durch katalystische Reaktionen. In: Eierdanz, H. (ed) *Perspektiven nachwachsender Rohstoffe in der Chemie*. Weinheim: VCH; 1996: 119-135.
14. Herrmann, W.A., Wagner, W., Flessner, U.N., Volkhardt, N., Komter, H. Methyltrioxorhenium as catalyst for the olefine metathesis. *Angew. Chem.* 1991; **103**: 1704-1706; *Angew. Chem. Int. Ed.* 1991; **30**: 1636-1638.
15. Grubbs, R.H., Tumas, W. Polymer synthesis and organotransition metal chemistry. *Science*. 1989; **243**: 907-915.
16. Warwel, S., Brüse, F., Demes, C., Kunz, M., Rüsch gen. Klaas, M. Polymers and surfactants on the basis of renewable resources. *Chemosphere*. 2001; **43**: 39-48.
17. Metzger, J.O., Riedner, U. Free-radical additions to unsaturated fatty acids. *Fat Sci. Technol.* 1989; **91**: 18-23.
18. Melikyan, G.G. Manganese(III) mediated reactions of unsaturated systems. *Synthesis*. 1993: 833-850.
19. Shundo, R., Nishigushi, I., Matsubara, Y., Toyoshima, M., Hirashima, T. Novel carboxymethylation of styrene derivatives by M_n^{3+}-mediated electrooxidation. *Chem. Letters*. 1991: 185-188.
20. Metzger, J.O., Linker, U. Free-radical additions to unsaturated fatty acids. *Fat Sci. Technol.* 1991; **93**: 244-249.
21. Linker, U. Funktionalisierung ungesättigter Fettsäuren durch radikalische C,C-Verknüpfungsreaktionen, PhD thesis, University of Oldenburg, 1991.

22. Ahmed, M.A., Mustafa, J., Osman, S.M. Manganese(III) acetate-mediated one-pot synthesis of some novel macrolides from long-chain fatty acids. *J. Chem. Research* (S). 1991: 48-49.
23. Metzger, J.O., Mahler, R. Radical additions of activated haloalkanes to alkenes initiated by electron-transfer from copper in solvent-free systems. *Angew. Chem.* 1995; **107**: 1012-1016; *Angew. Chem. Int. Ed.* 1995; **34**: 902-906.
24. Metzger, J.O., Mahler, R., Francke, G. Radical additions of alkyl 2-haloalkanoates and 2-haloalkanenitriles to alkenes initiated by electron transfer from copper in solvent-free systems. *Liebigs Ann./Recueil.* 1997: 2303-2313.
25. Mahler, R. Elektronentransfer initiierte radikalische Additionen an ungesättigte Fettstoffe, PhD thesis, University of Oldenburg, 1994.
26. Metzger, J.O., Mahler, R., Francke, G., Hayen, A. Synthesis of new oleochemicals: Functionalization of fatty compounds using radical reactions. In: Knothe, G., Derksen, J.T.P. (eds). *Recent Developments in the Synthesis of Fatty Acid Derivatives*. Champaign: AOCS Press; 1999: 90-99.
27. Metzger, J.O., Linker, U. Synthesis of linear and branched perfluoroalkylated carboxylic acids by radical-addition of perfluoroalkyl iodides to unsaturated fatty-acids. *Liebigs Ann.* 1992: 209-216.
28. Metzger, J.O., Mahler, R., Schmidt, A. Electron transfer initiated free radical additions of perfluoroalkyl iodides and diiodides to alkenes. *Liebigs Ann.* 1996: 693-696.
29. Greiner, J., Manfredi, A., Riess, G.J. Synthesis and preliminary evaluation of 2-(f-alkyl)-ethyl glycosides, a series of new f-alkylated surfactants for in vivo uses, *New J. Chem.* 1989; **13**: 247-254.
30. a) Floss, H.G. Natural products derived from unusual variants of the shikimate pathway. *Nat. Prod. Rep.* 1997; **14**: 433-452; b) Handa, S., Floss, H.G. Biosynthesis of omega-cyclohexyl fatty acids in *Alicyclobacillus acidocaldarius*: The stereochemistry of the initial 1,4-conjugate elimination. *Chem. Commun.* 1997: 153-154.
31. Metzger, J.O., Bangert, F. Ane additions to unsaturated fatty compounds - thermally initiated additions of alkanes to methyl 10-undecenoate. *Fat Sci. Technol.* 1995; **97**: 7-9.
32. Biermann, U., Metzger, J.O. Lewis acid-catalyzed additions to unsaturated fatty acids I: $SnCl_4$-catalyzed additions of nitriles to methyl oleate and ethyl 10-undecenoate. *Fat Sci. Technol.* 1990; **92**: 133-134.
33. Biermann, U., Fürmeier, S., Metzger, J.O. Some carbon, nitrogen- and carbon, oxygen-bond forming additions to unsaturated fatty compounds. *Fett/Lipid* 1998; **100**: 236-246.
34. Kinsman, D.V. Branched-chain fatty acids. In: Johnson, R.W., Fritz, E. (eds). *Fatty Acids in Industry*. New York: Marcel Dekker; 1989: 233-276.
35. Johnson, Jr., R.W., Cantrell, R.R. Branched-chain acids. In: *Kirk-Othmer Encyclopedia of Chemical Technology*. 4th edn. New York: Wiley; 1993; Vol 5: 189-192.
36. Technical Data Sheet, Emersol 874 Isostearic Acid, Henkel Corporation, USA, 1999.
37. Biermann, U., Metzger, J.O. Friedel–Crafts alkylation of alkenes: Ethylaluminium sesquichloride induced alkylations with alkyl chloroformates. *Angew. Chem.* 1999; **111**: 3874-3876; *Angew. Chem. Int. Ed.* 1999; **38**: 3675-3677.
38. Snider, B.B., Rodini, D.J., Kirk, T.C., Cordova, R. Dimethylaluminium chloride catalyzed ene reactions of aldehydes. *J. Am. Chem. Soc.* 1982; **104**: 555-563.
39. Snider, B.B., Phillips, G.B. Ethylaluminum dichloride catalyzed ene reactions of aldehydes with non-nucleophilic alkenes. *J. Org. Chem.* 1983; **48**: 464-469.
40. a) Biermann, U., Metzger, J.O. Lewis acid-catalyzed additions to unsaturated fatty compounds II: Alkylaluminium halide catalyzed ene reactions of unsaturated fatty compounds and formaldehyde. *Fat Sci. Technol.* 1991; **93**: 282-284; b) Metzger, J.O., Biermann, U. Alkylaluminium chloride catalyzed ene reactions of formaldehyde with unsaturated carboxylic acids, esters and alcohols. *Synthesis.* 1992: 463-465.
41. Blée, E. Oxygenated fatty acids and plant defenses, *INFORM.* 1995; **6**: 852-861.

42. Metzger, J.O., Biermann, U., Francke, G., Mahler, R. Bereitstellung neuartiger Fettstoffe. In: Fachagentur Nachwachsende Rohstoffe (ed). *Chemische Nutzung heimischer Pflanzenöle.* Münster: Landwirtschaftsverlag; 1998: 144-176.
43. Mc Lellan, J.F., Mortier, R.M., Orszulik, S.T., Paton, R.M. Hydroxymethylation of jojoba oil by Lewis acid-catalyzed ene reaction with formaldehyde. *J. Am. Oil Chem. Soc.* 1994; **71**: 231-232.
44. Metzger, J.O., Biermann, U. Ethylaluminium dichloride induced reactions of acetals with unsaturated carboxylic esters: Synthesis of homoallyl ethers. *Liebigs Ann.* 1996: 1851-1854.
45. Metzger, J.O., Biermann, U. Aluminium chloride induced additions of formaldehyde to alkenes. *Bull. Soc. Chim. Belg.* 1994; **103**: 393-397.
46. Behr, A., Handwerk, H.-P. Katalytische Verknüpfung ungesättigter Fettstoffe mit Formaldehyd. *Fat Sci. Technol.* 1992; **94**: 443-447.
47. Behr, A., Fiene, M. Lewis-acid catalysed ene reaction of electron-deficient aldehydes and ketones at unsaturated fatty acid derivatives. *Eur. J. Lipid Sci. Technol.* 2000; **102**: 212-217.
48. Behr, A., Toslu, N. Hydrosilylation reactions in single and two phases. *Chem. Eng. Technol.* 2000; **23**: 122-125.
49. a) Biermann, U., Metzger, J.O. Lewis acid-induced additions to unsaturated fatty compounds III: Alkylaluminium halide induced Friedel–Crafts acylations of unsaturated fatty compounds. *Fat Sci. Technol.* 1992; **94**: 329-332; b) Metzger, J.O., Biermann, U. Alkylaluminium dichloride induced Friedel–Crafts acylation of unsaturated carboxylic acids and alcohols. *Liebigs Ann.* 1993: 645-650.
50. Biermann, U., Metzger, J.O. Synthesis of new oleochemicals: Products of Friedel–Crafts reactions of unsaturated fatty compounds. In: Knothe, G., Derksen, J.T.P. (eds). *Recent Developments in the Synthesis of Fatty Acid Derivatives.* Champaign: AOCS Press; 1999: 80-89.
51. Metzger, J.O., Biermann, U. Lewis acid induced additions to unsaturated fatty compounds IV: Synthesis of cyclopentenones from Friedel–Crafts acylation products of unsaturated fatty compounds with α,β-unsaturated acyl chlorides. *Fett/Lipid.* 1998; **100**: 2-6.
52. Lie Ken Jie, M.S.F. The synthesis of rare and unusual fatty acids. *Prog. Lipid Res.* 1993; **32**: 151-194.
53. Lie Ken Jie, M.S.F., Lau, M.M.L. Ultrasound-assisted synthesis of pyrazole fatty ester derivatives from a key C_{18} keto-allenic ester. *Chem. Phys. Lipids.* 1999; **101**: 237-242.
54. Schäfer, H.J., Zobel, M. Palladium(O)-catalyzed reactions of nucleophiles with allyl carbonates of unsaturated fatty acids. In Knothe, G., Derksen, J.T.P. (eds). *Recent Developments in the Synthesis of Fatty Acid Derivatives.* Champaign: AOCS Press; 1999: 59-79.
55. a) Maletz, R., Schäfer, H.J., Quermann, R. Conversion of unsaturated fatty acids-nucleophilic additions to methyl (E)-12-oxo-10-octadecenoate. *Fett/Lipid.* 1996; **98**: 370-379; b) Maletz, R. Neue Oleochemikalien durch nukleophile Additionen an Oxoricinolsäure und Umwandlungen 2,2′-verknüpfter Dimerfettsäuren, PhD thesis, University of Münster, 1994.
56. a) Baltes, H., Steckhan, E., Schäfer, H.J. Anodic-oxidation of organic-compounds. 21. Anodic-oxidation of conjugated dienes. *Chem. Ber.* 1978; **111**: 1294-1314; b) Baltes, H., Storck, L., Schäfer, H.J. Anodic-oxidation of organic-compounds. 22. Anodic hydroxylation and acetamidation of conjugated dienes, *Chem. Ber.* 1979; **112**: 807-817; c) Shono, T., Ikeda, A. The anodic oxidation of 1,3-dienes, *Chem. Lett.* 1976; **4**: 311-314.
57. a) Plate, M. Untersuchung zur mittenständigen Funktionalisierung ungesättigter Fettsäuren, PhD thesis, University of Münster, 1997; b) Plate, M., Schäfer, H.J. Anodische Addition von Alkoholen an Konjuenfettsäuremethylester. In: Fachagentur Nachwachsende Rohstoffe (ed). *5th Symposium Nachwachsende Rohstoffe.* Münster: Landwirtschaftsverlag; 1997: 195-198.
58. a) Zobel, M. Untersuchungen zur chemischen Umwandlung von ungesättigten Fettsäuren aus Pflanzenölen an der Doppelbindung, PhD thesis, University of Münster, 1997; b) Zobel, M., Schäfer, H.J. Nukleophile Additionen an Ölsäure, 10-Undecensäure und Ricinolsäure. In: Fachagentur Nachwachsende Rohstoffe (ed). *5th Symposium Nachwachsende Rohstoffe* Münster: Landwirtschaftsverlag; 1997: 186-190.

59. a) Pinnick, H.W. The Nef reaction. *Org. React.* 1990; **38**: 655-792; b) Noland, W.E. The Nef reaction. *Chem. Rev.* 1955; **55**: 137-155.
60. Jones, R.A. *The Chemistry of Heterocyclic Compounds-Pyrroles.* New York: Wiley; 1990: 206.
61. Lie Ken Jie, M.S.F., Syed-Rahmatullah, M.S.K. Synthesis and properties of a novel 1-pyrroline fatty ester derivative from methyl isoricinoleate. *J. Chem. Soc. Perkin Trans 1.* 1991: 421-424.
62. Stetter, H. Catalyzed addition of aldehydes to activated double-bonds - new synthetic approach. *Angew. Chem.* 1976; **88**: 695-704; *Angew. Chem. Int. Ed. Engl.* 1976; **15**: 639-647.
63. a) Hardegger, E., Schenk, H.P., Broger, E. Synthese der DL-Form eines natürlichen Prostaglandins. *Helv. Chim. Acta.* 1967; **50**: 2501-2504; b) Samuelsson, B., Ställberg, G. Structure and synthesis of a derivative of prostaglandin E_1. *Acta Chem. Scand.* 1963; **17**: 810-816.
64. Novák, L., Baán, G., Marosfalvi, J., Szántay, C. Application of carbonyl umpolung to prostaglandin synthesis. 3. Synthesis of 11-deoxy prostaglandin synthons. *Chem. Ber.* 1980; **113**: 2939-2949.
65. a) Yura, Y., Ide, J. A total synthesis of a *di*-prostaglandine B_1. *Chem. Pharm. Bull.* 1969; **17**: 408-410; b) Naora, H., Ohnuki, T., Nakamura, A. An improved synthesis of methyl 7-(2-hydroxy-5-oxo-1-cyclopentenyl)heptanoate. *Bull. Chem. Soc. Jpn.* 1988; **61**: 993-994.
66. a) Baizer, M.M. Electrolytic reductive coupling. *J. Electrochem. Soc.* 1964; **111**: 215-222; b) Baizer, M.M., Danley, D.E. Discovery, development and commercialization of the electrochemical adiponitrile process - Armstrong Lecture 1. *Chem. Ind.* 1979: 435-447.
67. a) Bowers, K.W., Giese, R.W., Grimshaw, J., House, H.O., Kolodny, N.H., Kronberger, K., Roe, D.K. Reactions involving electron transfer. I. Reduction of 2,2,6,6-tetramethyl-4-hepten-3-one. *J. Am. Chem. Soc.* 1970; **92**: 2783-2799; b) House, H.O., Giese, R.W., Kronberger, K., Kaplan, J.P., Simeone, J.F. Reactions involving electron transfer. II. Reductions of enones with alkali metal solutions. *J. Am. Chem. Soc.* 1970; **92**: 2800-2810.
68. Danley, D.E. Development and commercialization of the Monsanto electrochemical adiponitrile process. In: Genders, J.D., Pletcher, D. (eds). *Electrosynthesis* New York: Electrosynthesis Company Inc.; 1990: 147-167.
69. Hartmann, J., Schlosser, M. Trimethylsilylmethylpotassium and other outstanding metallating agents. *Helv. Chim. Acta.* 1976; **59**: 453-466.
70. a) Quermann, R., Maletz, R., Schäfer, H.J. Conversion of fatty acids and derivatives IV: conversion of fatty acid methyl esters into dialkylated succinic esters by oxidative coupling of their enolates. *Liebigs Ann. Chem.*; 1993: 1219-1223; b) Quermann, R. C,C-Verknüpfungen über Anionenchemie auf Basis nachwachsender Rohstoffe, PhD thesis, University of Münster, 1991.
71. Augustin, K.E., Schäfer, H.J. Conversion of oleic acid to 17-substituted and 18-substituted stearic acid derivatives by way of the acetylene zipper. *Liebigs Ann. Chem.* 1991: 1037-1040.
72. a) Scheffold, R. Vitamin-B_{12}, catalyst for C,C-bonding formation in organic-chemical syntheses. *Chimia.* 1985; **39**: 203-212; b) Albrecht, S., Scheffold, R. Vitamin-B_{12}-catalyzed synthesis of c-glycosides. *Chimia.* 1985; **39**: 211-212.
73. Giese, B., Dupuis, J. Diastereoselective syntheses of c-glycopyranosides. *Angew. Chem.* 1983; **95**: 633-634; *Angew. Chem. Int. Ed. Engl.* 1983; **22**: 622-623.
74. a) Scheffold, R. *et al.* Vitamin-B_{12}-mediated electrochemical reactions in the synthesis of natural-products. *Pure Appl. Chem.* 1987; **59**: 363-372; b) Hollah, P. Radikalische C,C-Verknüpfungen an Fettsäurederivaten, Diploma thesis, University of Münster, 1992.
75. a) Schäfer, H.J. Recent contributions of Kolbe electrolysis to organic synthesis. *Top. Curr. Chem.* 1990; **152**: 91-151; b) Degner, D. Organic electrosyntheses in industry. *Top. Curr. Chem.* 1988; **148**: 1-95.
76. Weiper-Idelmann, A., aus dem Kahmen, M., Schäfer, H.J., Gockeln, M. Electroorganic synthesis 65. Anodic homocoupling of carboxylic acids derived from fatty acids. *Acta Chem. Scand.* 1998; **52**: 672-682.
77. a) Davies, J.A., Watson, P.L., Liebman, J.F., Greenberg, A. *Selective Hydrocarbon Activation, Principles and Progress.* Weinheim: VCH; 1990; b) Mansuy, D. Biomimetic catalysts for selective

oxidation in organic-chemistry. *Pure Appl. Chem.* 1990; **62**: 741-766; c) Reiser, O. Oxidation of weakly activated C-H bonds. *Angew. Chem.* 1994; **106**: 73-76; *Angew. Chem. Int. Ed. Engl.* 1994; **33**: 69-72; d) Schäfer, H.J. Electrochemical conversion of alkanes. In: Patai, S., Rapoport, Z. (eds). *Chemistry of Alkanes and Cycloalkanes.* New York: Wiley; 1992: 781-808.

78. a) Bühler, M., Schindler, J. Aliphatic hydrocarbons In: Rehm, J., Reed, G. (eds). *Biotechnology.* Weinheim: VCH; 1984; Vol 6a: pp 329-385; b) Kieslich, K. *Microbial Transformations of Non-Steroid Cyclic Compounds.* Stuttgart: Thieme; 1976.
79. a) Cramer, E., Schäfer, H.J. Regioselective C-H-functionalization of fatty acids and their methyl esters. *Fat Sci. Technol.* 1988; **90**: 351-357; b) Smith, J.R.L., Norman, R.O.C., Rowley, A.G. Amine oxidation. Part VIII. Evidence for intramolecular hydrogenation transfer in amine radical cations. *J. Chem. Soc., Perkin Trans 1.* 1973: 566-571; c) Deno, N.C., Pohl, D.G. Oxidations of cyclohexane, 1-octyl trifluoroacetate, heptane, and decane which stop at the alcohol stage. *J. Am. Chem. Soc.* 1974; **96**: 6680-6682.
80. Hembrock, A., Schäfer, H.J. Anodic oxidation. 33. Selectivity of the anodic oxidation of CH-group and CH_2-group—selective oxidation of steroids at C-6, *Angew. Chem.* 1985; **97**: 1048-1049; *Angew. Chem. Int. Ed. Engl.* 1985; **24**: 1055-1056.
81. Hinkamp, L., Schäfer, H.J., Wippich, B., Luftmann, H. Regioselective conversion of nonactivated CH-bonds. 6. Selective omega-chlorination to (omega-2)-chlorination of fatty acids by way of adsorption on alumina. *Liebigs Ann. Chem.* 1992: 559-563.
82. a) Deyrup, J.A. Aziridines. In: Hassner, A. (ed). *Heterocyclic Compounds – Small Ring Heterocycles.* New York: Interscience Publishers, Inc., 1983; vol 42, part 1: 1-214; b) Dermer, O.C., Ham, G.E. (eds). *Ethylenimine and Other Aziridines – Chemistry and Application.* New York: Academic Press; 1969.
83. Butler, R.N. Tetrazoles. In: Potts, K.T. (ed). *Comprehensive Heterocyclic Chemistry – Five-membered Rings with Two or More Nitrogen Atoms.* Oxford: Pergamon Press; 1984; vol 5, part 4A: 791-838.
84. Müller, R.A., Nugent, S.T. Fatty Acid Analogs and Prodrugs, U.S. Patent 5719290-A, 1993.
85. a) Hill, J. 1,3,4-Oxadiazoles. In: Potts, K.T. (ed). *Comprehensive Heterocyclic Chemistry – Five-membered Rings with Two or More Oxygen, Sulfur or Nitrogen Atoms.* Oxford: Pergamon Press; 1984; vol 6, part 4B: 427-446.
86. Gunstone, F.D. Novel long-chain compounds produced through neighboring group participation. In: Knothe, G., Derksen, J.T.P. *Recent Developments in the Synthesis of Fatty Acid Derivatives.* Champaign: AOCS Press; 1999: 1-19.
87. Lie Ken Jie, M.S.F., Cheung, S.W.H. Synthesis of special fatty acids: a review. In: Knothe, G., Derksen, J.T.P. (eds). *Recent Developments in the Synthesis of Fatty Acid Derivatives.* Champaign: AOCS Press; 1999: 20-43.
88. Crivello, J.V., Narayan, R. Epoxidized triglycerides as renewable monomers in photoinitiated cationic polymerization. *Chem. Mater.* 1992; **4**: 692-699.
89. Metzger, J.O. Organic reactions without organic solvents and oils and fats as renewable raw materials for the chemical industry. *Chemosphere.* 2000; **43**: 83-87.
90. a) Rüsch gen. Klaas, M., Warwel, S. New oxidation methods for unsaturated fatty acids, esters, and triglycerides. In: Knothe, G., Derksen, J.T.P. (eds). *Recent Developments in the Synthesis of Fatty Acid Derivatives.* Champaign: AOCS Press; 1999: 157-181 and references cited therein; b) Piazza, G.J. Some recent advances in epoxide synthesis. In: Knothe, G., Derksen, J.T.P. (eds). *Recent Developments in the Synthesis of Fatty Acid Derivatives.* Champaign: AOCS Press; 1999: pp. 183-195 and references cited therein.
91. aus dem Kahmen, M. Synthese und Anwendung von Fettsäurekronenethern und mittenständige Verknüpfungsreaktionen von Konjuenfettsäuremethylestern: Ein Beitrag zur Veredelung nachwachsender Rohstoffe, PhD thesis, University of Münster, 1993.
92. Renkes, T., Schäfer, H.J., Siemens, P.M., Neumann, E. Fatty acid-oligo(ethylene glycol) ester forms ion channels in lipid membranes. *Angew. Chem. Int. Ed.* 2000; **39**: 2512-2516.

93. Lie Ken Jie, M.S.F., Lam, C.H. Fatty Acids, Part 14. Synthesis of furanoid esters from naturally occurring unsaturated fatty ester. *Chem. Phys. Lipids.* 1977; **20**: 1-12.
94. Lie Ken Lie, M.S.F., Syed-Rahmatullah, M.S.K., Wong, K.P. Efficient synthesis of long-chain furanoid fatty ester derivative from methyl ricinoleate. *Nat. Prod. Lett.* 1992: 93-98.
95. Lie Ken Jie, M.S.F., Wong, K.P. A novel method for the introduction of a methyl-group into the furan ring of a 2,5-disubstituted C-18 furanoid fatty ester via a malonic acid function. *Lipids.* 1991; **26**: 837-841.
96. Lie Ken Jie, M.S.F., Wong, K.P. Synthesis of dimethyl-substituted C-18 furanoid fatty ester. *J. Am. Oil Chem. Soc.* 1992; **69**: 485-487.
97. Lie Ken Jie, M.S.F., Wong, K.P. Synthesis of phenyl substituted C-18 furanoid fatty esters. *Lipids.* 1993; **28**: 43-46.
98. Lie Ken Jie, M.S.F., Lam, W.L.K. Ultrasound in lipid chemistry, cyclopropanation of unsaturated fatty esters and triglycerides. *J. Am. Oil Chem. Soc.* 1988; **65**: 118-121.
99. Lie Ken Jie, M.S.F., Zheng, Y.F. Synthesis and physical properties of some 2,3-epithio-C-18 and 2,2′-epithio-C-18 faffy acid derivatives. *Chem. Phys. Lipids.* 1988; **49**: 167-178.
100. Ahmad, M.B., Rauf, A., Osman, S.M. Aziridination of olefinic and hydroxyolefinic fatty esters. *Ind. J. Chem.* 1988; **27B**: 1140-1141.
101. Lie Ken Jie, M.S.F., Syed-Rahmatullah, M.S.K. Synthesis and spectroscopic properties of long-chain aza, aziridine and azetidine fatty esters. *J. Am. Oil Chem. Soc.* 1992; **69**: 359-362.
102. Metzger, J.O., Fürmeier, S. New type of skipped oligoaziridines: synthesis of new fatty acid derivatives containing aziridine functions. *Eur. J. Org. Chem.* 1999: 661-664.
103. Lie Ken Jie, M.S.F., Syed-Rahmatullah, M.S.K., Lam, C.K., Kalluri, P. Ultrasound in fatty acid chemistry – synthesis of a 1-pyrroline fatty acid ester isomer from methyl ricinoleate. *Lipids.* 1994; **29**: 889-892.
104. Lie Ken Jie, M.S.F., Syed-Rahmatullah, M.S.K. Preparation and some spectroscopic properties of N-heterocyclic derivatives of a novel 1-pyrroline C-18 fatty ester. *Lipids.* 1991; **26**: 842-846.
105. Lie Ken Jie, M.S.F., Syed-Rahmatullah, M.S.K. Further chemical reactions of 1-pyrroline fatty ester – N-substituted pyrrolinium and pyrrolidine derivatives. *Chem. Phys. Lipids.* 1995; **77**: 179-186.
106. Lie Ken Jie, M.S.F., Kalluri, P. Synthesis of pyrazole fatty ester derivatives in water – a sonochemical approach. *J. Chem. Soc., Perkin Trans. 1.* 1995: 1205-1206.
107. a) Fürmeier, S., Metzger, J.O. Synthesis of new heterocyclic fatty compounds. In: *23rd World Congress of the International Society of Fat Research (ISF)*, Brighton, U.K., Champaign: AOCS Press; 1999: 80; b) Metzger, J.O., Fürmeier, S., Biermann, U. Synthesis of new heterocyclic fatty compounds. In: *91th AOCS Annual Meeting & Expo*, San Diego, USA, Champaign: AOCS Press; 2000: S81.
108. a) Stoll, G., Worschech, K. Verfahren zur Herstellung von Ketonverbindungen, DE 40 18 262 A1 (Offenlegungsschrift, Henkel KGaA); b) Stoll, G., Worschech, K. Ketofettsäure-Derivate – Ein einfaches Verfahren zu ihrer Herstellung. *Fat Sci. Technol.* 1992; **94**: 332-337.
109. Brousse, E., Lefort, M.D. Oxydation d'époxystéarate de méthyle en acyloine par le diméthylsulfoxyde. *C. R. Acad. Sc. Paris.* 1965; **261**: 1990-1991.