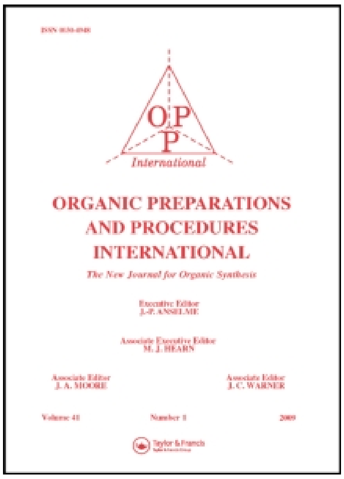

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PREPARATION AND REACTIONS OF 4-OXOCARBONYL COMPOUNDS. A REVIEW

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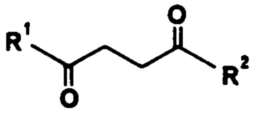
INTRODUCTION

The 4-oxocarbonyl compounds are useful intermediates in organic synthesis. They are used for the preparation of pyrroles, furans, and thiophenes, as well as in the preparation of synthetic perfumes and drugs. This review is concerned with 1,4-diketones, 4-oxoalkanals and 4-oxo esters which can be represented by the general formula 1, 2, and 3, respectively.



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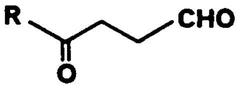

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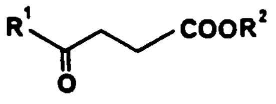

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Certain members of this class of compounds, such as cis-8-undecen-2,5-dione (1; $R^1 = CH_3$, R^2 = cis-$CH_3CH_2CH{=}CHCH_2CH_2$), 4-oxo-cis-7-decenal (2; R = cis-$CH_3CH_2CH{=}CHCH_2CH_2$), and methyl 4-oxo-cis-7-decenoate (3; R^1 = cis-$CH_3CH_2CH{=}CHCH_2CH_2$, $R^2 = CH_3$) are well known. They are useful intermediates for jasmonoids such as cis-jasmone, methyl jasmonate and γ-jasmolactone. The vast preparative potential of 4-oxocarbonyl compounds has been reviewed.[1] Recent advances, mainly after 1982, are reviewed

reviewed.[1] Recent advances, mainly after 1982, are reviewed here.

I. PREPARATION OF 1,4-DIKETONES

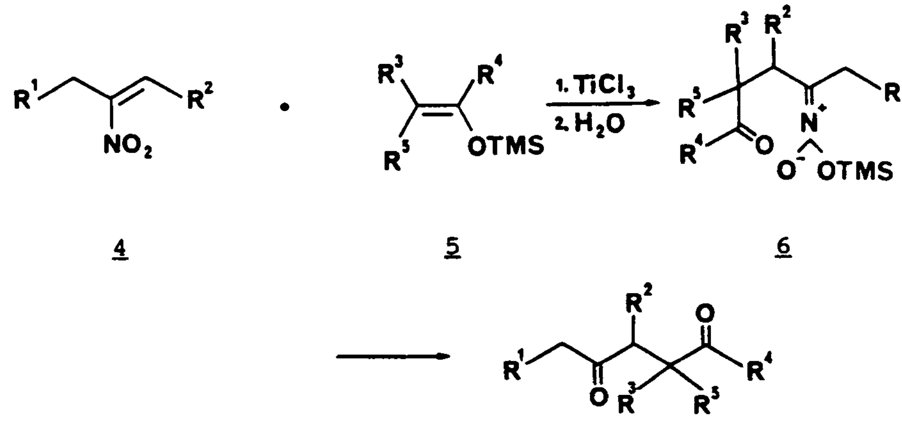
1,4-Diketones are important intermediates in the preparation of natural products such as jasmone,[1] prostaglandins,[2] steroids,[3] and terpenoids.[4] These natural products have attracted continuous attention owing to their economic values and their being convenient testing targets for many new synthetic methodologies. Many 1,4-diketones are available from mild acidic hydrolysis of furans. Simple furans are readily lithiated and then alkylated at C-2 of the furan ring, and can be converted directly into the 1,4-diketones,[5,6] or their bisethylene acetals.[6] Oxidation of 4-hydroxy ketones allows versatile synthesis; Jones reagent can be used,[7] but pyridinium chlorochromate is particulary recommended.[8] A wide range of 4,6-disubstituted pentane-2,5-diones is available from standard reactions of α-chloro ketones with sodio ethylacetoacetate.[9] A review of the formation of 1,4-diketones is given in Ref. 10.

A. Routes Based on Michael Addition

The use of aliphatic nitro compounds in organic synthesis has been well documented.[11] The synthetic application of aliphatic nitro compounds includes interconversions of functional groups as well as C-C bond forming processes. Nitro olefins are synthetic equivalents to ketone functionalites.[12]

Aliphatic conjugated nitro olefins 4 undergo a Lewis acid-catalyzed reaction with trimethyl silyl enol ethers 5 to give Michael-type addition products.[13] These intermediates 6 are transformed in good yield *in situ* into 1,4-diketones 1 *via* the

Nef reaction.



4 5 6

1

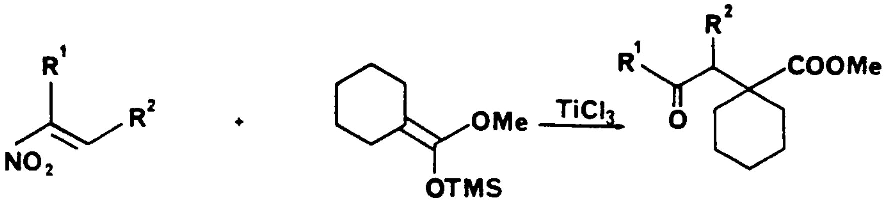
$\underline{4}$ $R^1 = H, CH_3$ $\underline{5}$ $R^3 = (CH_2)_n$ $n = 3$ to 4

$R^2 = H, CH_3$ $R^4 = n\text{-}C_6H_{13}$

$R^5 = H, CH_3$

This method thus allows the regioselective introduction of 2-oxoalkyl substituents to a ketone functionality by a one-pot reaction. Some results are shown in Table 1. The nitro olefins have been prepared from appropriate nitroalkanes and an aldehyde followed by dehydration. Nitro olefins are very sensitive to highly alkaline conditions, but they tolerate an acidic environment very well. Other additions of conjugated nitro olefins have been reviewed.[14a] Similarly, the niro olefins 4 react under somewhat modified conditions with ketene silyl acetals 7 to afford the methyl 4-oxoalkanoates 3. Other additions of this type of conjugated nitro olefins 4 have been reviewed.[14] The reactions utilizing ketene silyl acetals have been recently reviewed in detail.[14b]

The nitro group is a function of great synthetic potential in organic chemistry because of the versatility with which it



4 7 3

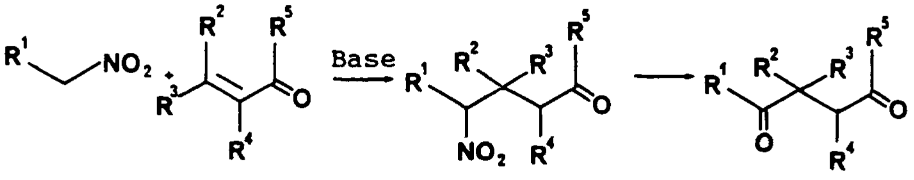
may react. In particular, it is well known that nitro alkanes 8 undergo base catalyzed 1,4-addition to various α,β-unsaturated carbonyl compounds 9. These reactions are typically run as homogeneous solutions of the reactants in an organic solvent using soluble organic bases (e.g., tetramethylguanidine,[15-18] potassium fluoride/18-crown-6, sodium hydride/18-crown-6,[17] diisopropylamine,[16,19] potassium t-butoxide,[16,20] alkoxides,[21] tri-n-butylphosphine,[22,23] triphenylphosphine,[20,24] 1,5-diazabicyclo[5.4.0]undecene-5[25] and tetrabutylammonium fluoride[20]). A wide variety of Michael reactions by

TABLE 1. Synthesis of 1,4-Diketones 1 from Nitro Olefines 4 and Silyl Enol Ethers 5

Nitro Olefin 4		Silyl Enol Ether 5			Lewis Acid	1,4-Diketone 1
R^1	R^2	R^3	R^4	R^5		Yield (%)
H	H			H	$SnCl_4$	85
Me	H	$-(CH_2)_4-$		H	$TiCl_4$	76
H	Me			H	$AlCl_3$	63
H	H			Me	$TiCl_4$	70
Me	H	$-(CH_2)_4-$		Me	$TiCl_4$	82
H	Me			Me	$SnCl_4$	71
H	H	$-(CH_2)_3CHMe-$		H	$SnCl_4$	63
H	H	H	$Me(CH_2)_5$	H	$SnCl_4$	65
H	H	$-(CH_2)_3-$		H	$SnCl_4$	70
H	H			Me	$SnCl_4$	41
Me	H	$-(CH_2)_3-$		Me	$SnCl_4$	41

heterogeneous catalysts (e.g., KF-alumina[26,27] and alumina[28]) have already been reported in the literature.

The Nef reaction is one of the most important transformations of a nitro group into a carbonyl group.[11] Therefore, 1,4-diketones were obtained by the Nef reaction from 4-nitro carbonyl compounds 10. A number of methods have been devised for accomplishing this transformation including the classical Nef reaction[29] by solvolysis of alkali nitronates with acid (e.g., amine/HCl,[30] NaOH/HCl,[31] or basic SiO_2[32]).



8 9 10 1

Such variations include reductive (e.g., $TiCl_3$[33]) and oxidative conditions (e.g., permanganate,[32] persulfate,[34] hydrogen peroxide,[35] molybdenum complex,[36] ceric ammonium nitrate,[37] or electrochemical oxidation[23,38-40]). Results of the electrochemical Nef reaction of 4-nitro carbonyl compounds are shown in Table 2.

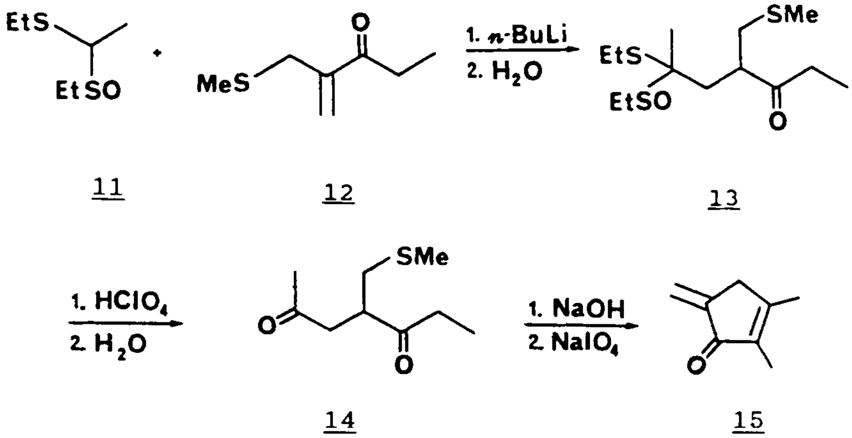
Michael addition of the anions of acyclic dithio acetal S-oxides 11 with α,β-unsaturated ketones 12 and the deprotection of dithioacetal S-monoxide group 13 afforded the 1,4-diketone 14. The base catalyzed cyclization of 14 gave methylenemycin B 15.[41]

B. Using Organosulfur and Organophosphorus Agents

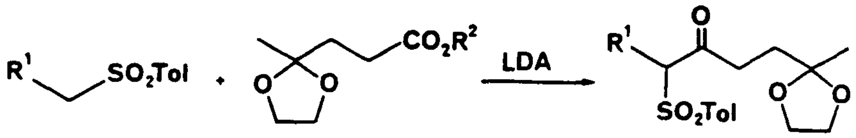
1,4-diketones were prepared by the condensation of α-sulfonyl carbanions of alkyl or alkenyl sulfones 16 with esters

TABLE 2. Conversion of 4-Nitrocarbonyl Compounds 10 into 4-Oxocarbonyl Compounds by Electrolysis

4-Nitrocarbonyl Compounds 10						4-Oxocarbonyl	
R^1	R^2	R^3	R^4	R^5	Reaction Conditions	Compound Yield (%)	Ref.
$n\text{-}C_7H_{15}$	H	H	H	CH_3	$MeOH\text{-}HCO_2Na$	90	38
C_2H_5	CH_3	CH_3	H	CH_3	$AqMeOH\text{-}HCO_2Na$	60	38
$n\text{-}C_7H_{15}$	H	H	H	OEt	$EtOH\text{-}HCO_2Na$	72	38
$(CH_2)_2CO_2Et$	H	H	H	CH_3	$EtOH\text{-}HCO_2Na$	88	38
$CH_3(OAc)CH_2CH_2$	H	H	H	OEt	$EtOH\text{-}CH_3CO_2Na$	62	38
$n\text{-}C_5H_{11}$	H	H	H	CN	$MeOH\text{-}HCO_2Na$	88	38
CH_3	H	H	H	CH_3	$DMF\text{-}Bu_4NBr$	82-86	39
CH_3	H	H	CH_3	OMe	$CH_3CN\text{-}Bu_4NBr$	98	39
CH_3	Ph	H	H	OMe	$CH_3CN\text{-}Bu_4NBr$	68	39
$n\text{-}C_4H_9$	CH_3	H	H	OMe	$CH_3OH\text{-}CH_3CO_2K$	88	40
$n\text{-}C_5H_{11}$	CH_3	H	H	OMe	$CH_3OH\text{-}CH_3CO_2K$	85	40

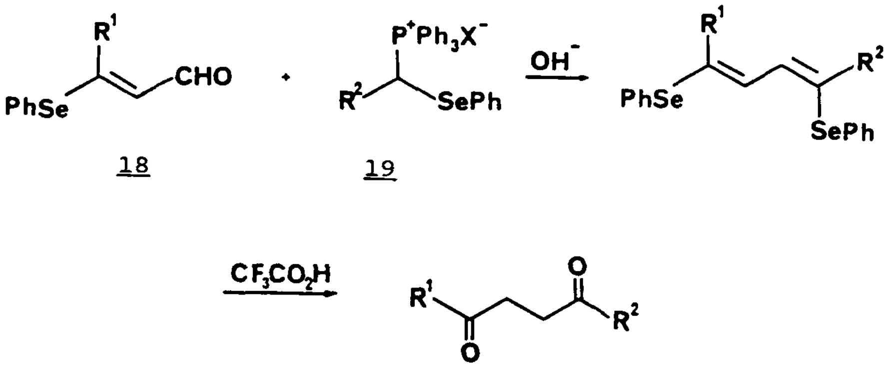


17, e.g., γ-valerolactone,[42] ethyl levulinate ethylene acetal.[42,43] Using this method, Umani-Ronchi[42] and Yoshida[43] synthesized *cis*-jasmone and dihydrojasmone, and Yoshida[43] prepared methyl jasmonate and γ-jasmolactone.



16 17

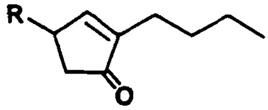
3-(Phenylseleno)-2-alkenal 18 reacts with Wittig reagents 19 in excellent yields. Hydrolysis with trifluoroacetic acid in benzene yields 1,4-diketones, which are transformed to jasmone[44] using described methodologies.



18 19

1

This approch can be extended to the substituted cyclopentenones of the type 20.



20 R = OH, OR, NH_2

C. Organometallic Reagents

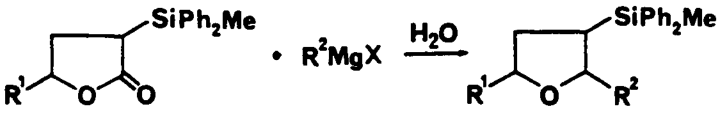
The α-silylated lactones 21a derived from γ-butyrolactone and γ-valerolactone react with a single equivalent of Grignard reagent to give a 2-substituted 4,5-dihydrofuran 22, which can be hydrolyzed and oxidized to 1,4-diketones.[45] Some results are shown in Table 3.

TABLE 3. 1,4-Diketones from α-(Diphenylmethylsilyl)γ-valerolactones

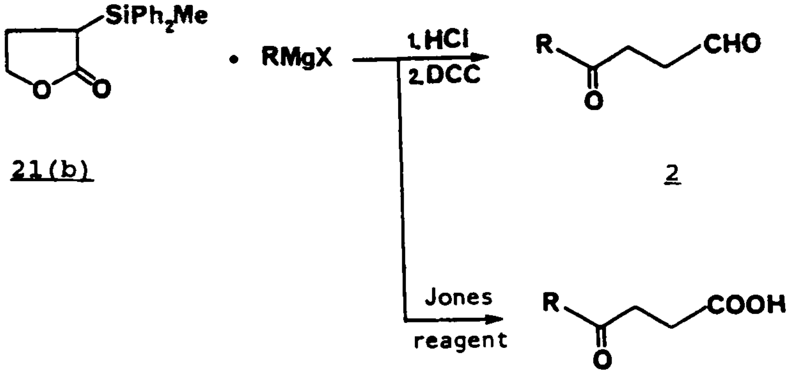
Grignard Reagent (RMgX) R	Product R^1	R^2	Yield (%)
CH_3	CH_3	CH_3	52
$n\text{-}C_6H_{13}$	CH_3	$n\text{-}C_6H_{13}$	75
$n\text{-}C_8H_{17}$	CH_3	$n\text{-}C_8H_{17}$	89
$n\text{-}C_9H_{19}$	CH_3	$n\text{-}C_9H_{19}$	98
$i\text{-}C_4H_9$	CH_3	$i\text{-}C_4H_9$	62
$CH_2{=}CH$	CH_3	$CH_2CH_2CH{=}CH_2$	42
$n\text{-}C_3H_7C{\equiv}C$	CH_3	$n\text{-}C_3H_7C{\equiv}C$	46
$PhCH_2$	CH_3	$PhCH_2$	49
Ph	CH_3	Ph	63

The application of this same procedure to the preparation of 4-oxoalkanals and 4-oxocarboxylic acids from α-silyl γ-lactones 21b gave similar results as can be seen from Table 4. The reaction with hexylmagnesium bromide provides the precursor to dihydrojasmone in 75% yield.

The reaction of γ-lactone 23 with an organometallic reagent gave the diol 24, and no 4-hydroxy ketone was obtained. The key to the synthesis of 4-hydroxy ketones from γ-lactones and Grignard reagents is to prevent the opening of intermediate to 4-hydroxyketone, which could then react with second equivalent of Grignard reagent.



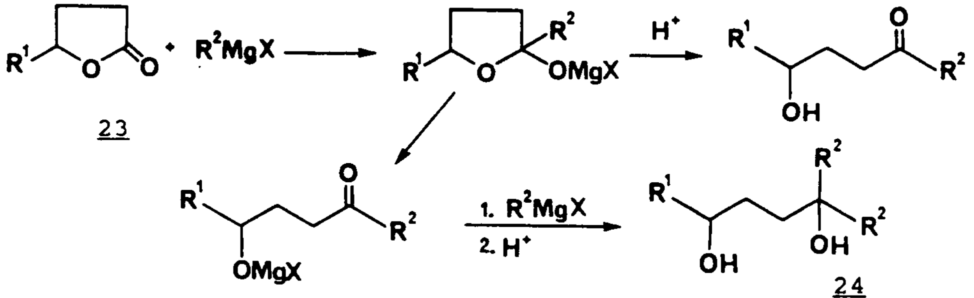
21(a) 22



21(b) 2 3

TABLE 4. 4-Oxocarboxylic Acid and 4-oxoaldehydes from α-(Diphenylmethylsilyl)γ-butyrolactone

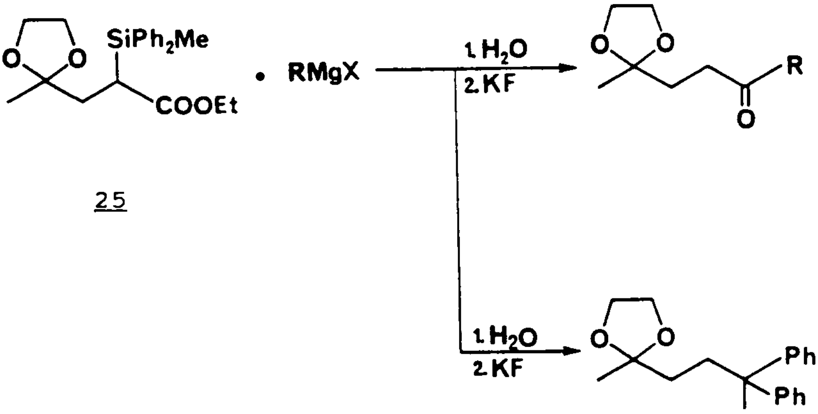
Grignard Reagent	Product	Yield (%)
RMgBr		
CH_3MgI	$CH_3CO(CH_2)_2COOH$	71
CH_3CH_2MgBr	$CH_3CH_2CO(CH_2)_2COOH$	73
n-$C_5H_{11}MgBr$	n-$C_5H_{11}CO(CH_2)_2COOH$	83
PhMgBr	$PhCO(CH_2)_2COOH$	75
$(CH_3)_2CHCH_2MgBr$	$(CH_3)_2CHCH_2CO(CH_2)_2COOH$	25
c-$C_6H_{11}MgBr$	c-$C_6H_{11}CO(CH_2)_2COOH$	50
n-$C_6H_{13}MgBr$	n-$C_6H_{13}CO(CH_2)_2CHO$	53
n-$C_9H_{19}MgBr$	n-$C_9H_{19}CO(CH_2)_2CHO$	66
$PhCH_2MgCl$	$PhCH_2CO(CH_2)_2COOH$	78
i-C_4H_9MgBr	i-$C_4H_9CO(CH_2)_2CHO$	49



23

24

The reaction of ethy-2-(diphenyl methyl silyl)levulinate ethylene ketal 25 with phenylmagnesium bromide produces the carbinol 26 *via* addition to form the α-hydroxy silane, which then undergoes desilylation. However, 25 reacts with primary Grignard reagents to give the mono protected diketones in good yield.[46] The results are shown in Table 5.



25

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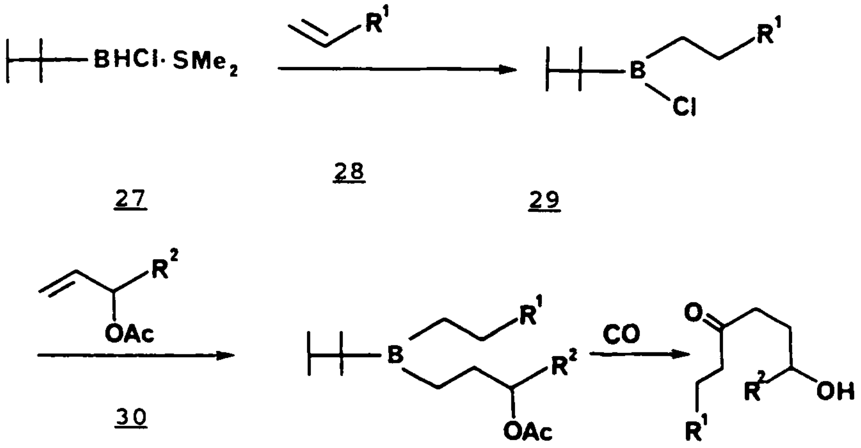
Reaction of the alkylthexylchloroborane 29 with olefin acetate 30 may be used to prepare compounds which are structurally related to the 1,4-diketones.[47] The key to the synthetic approach is the utilization of an olefin containing the acetoxy group, which could be appropriately chosen depending upon the diketone that needs to be synthesized. The hydroboration of an olefin 28 with thexylchloroborane/dimethyl sulfide

TABLE 5. The Reaction of Ester Ketal 25 with Grignard Reagents

RCH_2MgBr	Mono-protected Diketones
R	Yield (%)
Et	83
n-C_5H_{11}	66
n-C_8H_{17}	73
n-$C_{12}H_{23}$	76
C_3H_5	62

27 gives the alkylthexylchloroborane 29, which, upon hydridation in the presence of the second olefin (containing the acetoxy group) 30 by potassium triisopropoxyborohydride, affords the trialkylborane. High pressure carbonylation of the trialkylborane, followed by alkaline hydrogen peroxide oxidation, produces the ketol, converted by pyridinum chlorochromate to the 1,4-diketones 1 in 77-85% yield. Table 6 summarizes these results in the exploration of this procedure.



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29

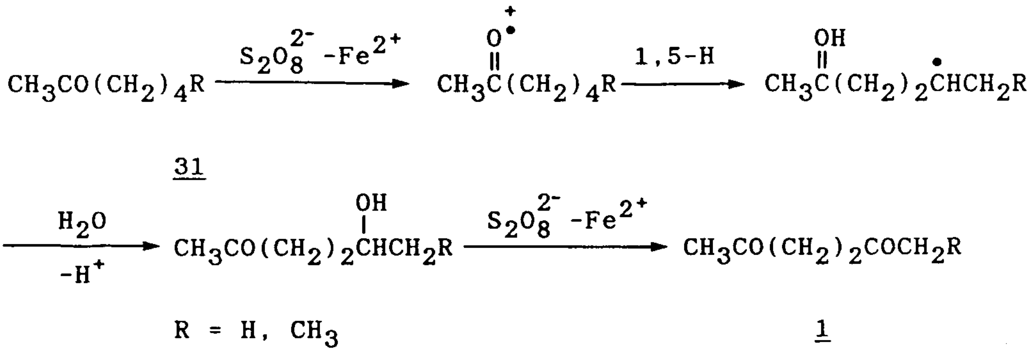
30

TABLE 6. Synthesis of 1,4-Diketones *via* Organoboranes

R^1	R^2	1,4-Diketones Yield (%)
$t-C_4H_9$	$n-C_4H_9$	80
$n-C_8H_{17}$	CH_3	78
$n-C_9H_{19}$	CH_3	85
$n-C_4H_9$	CH_3	82
C_6H_5	CH_3	77
$n-C_9H_{19}$	CH_3	80

D. Misecllaneous Preparations

1,4-diketones are also obtainable by oxidative coupling. Aliphatic linear and cyclic ketones 31 are converted into 1,4-diketones 1 in a one pot oxidation reaction on treatment with $Na_2S_2O_8$ in presence of Fe(II) ions. Thus, 2-hexanone is converted on heating with $Na_2S_2O_8$-$FeSO_4$ into 2,5-hexanedione in 50% yield.[48] The mechanism of the reaction involves initial generation of O-centered cation radicals that undergo 1,5-H shift to C-centered cation radicals. Further oxidation of these cation radicals *via* ω-hydroxyketone leads to 1,4-diketones 1.



$$CH_3CO(CH_2)_4R \xrightarrow{S_2O_8^{2-}\ -Fe^{2+}} CH_3\overset{\overset{+}{O^{\bullet}}}{\overset{\|}{C}}(CH_2)_4R \xrightarrow{1,5\text{-}H} CH_3\overset{OH}{\overset{\|}{C}}(CH_2)_2\overset{\bullet}{C}HCH_2R$$

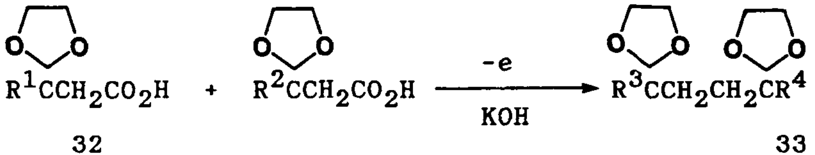
31

$$\xrightarrow[-H^+]{H_2O} CH_3CO(CH_2)_2\overset{OH}{\overset{|}{C}}HCH_2R \xrightarrow{S_2O_8^{2-}\ -Fe^{2+}} CH_3CO(CH_2)_2COCH_2R$$

R = H, CH_3

1

The anodic oxidation of some dioxolanes of β-ketoacids 32 gives symmetrical 1,4-bisdioxolanes 33 by dimerization of an intermediate Kolbe's radical.[49] A series of unsymmetrical 1,4-bisdioxolanes has been prepared by a mixed coupling of the Kolbe's radicals obtained by anodic oxidation of mixture of two dioxolanes of β-keto acids. The hydrolysis of the unsymmetrical 1,4-bisdioxolanes leads with 80-95% yields to the unsymmetrical 1,4-diketones 1. This technique has been applied to the production of dihydrojasmone.[49] The palladium-catalyzed oxidation of the terminal olefins to methyl ketones is an important synthetic method for 1,4-diketones.[50]



32

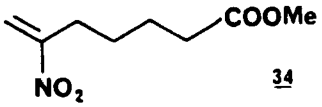
33

A : $R^3 = R^1$, $R^4 = R^1$
B : $R^3 = R^1$, $R^4 = R^2$
C : $R^3 = R^2$, $R^4 = R^2$

E. Synthetic Applications

1,4-Diketones are highly important, versatile substrates in organic synthesis. The main reaction of 1,4-diketones is their cyclization to cyclopentenones via aldol condensation and dehydration under mild basic conditions.[10] Many of these reactions have been used to make cis-jasmone and its side-chain dehydro analogues. Reaction of 1,4-diketones with hydrogen sulphide gives 2,5-disubstituted thiophenes, ammonia derivatives give pyrroles, and direct dehydration gives furans by the Paal-Knorr reaction. Excellent results in the furan synthesis are given by slow distillation from a sulphonic acid ion-exchange resin.[10]

In a recent approach aimed at prostanoids was devised a very short synthesis of 6-oxo-PGE$_1$ 36 and -PGF$_1$ by Tanaka,[51] starting from nitro olefins 34 and α,β-unsaturated enones 35.



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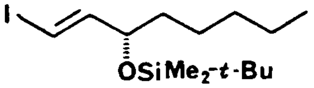

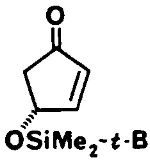

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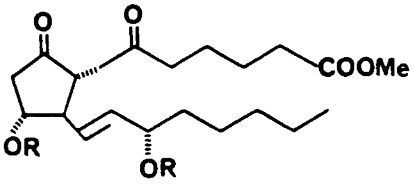

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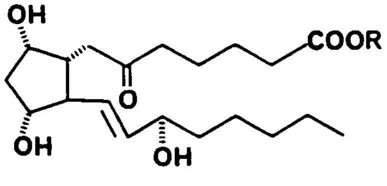

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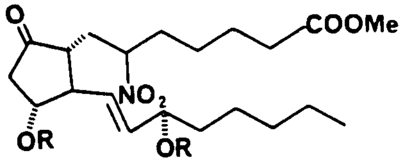


6-nitroprostaglandin E$_1$ methyl ester

6-Oxo-PEG$_1$ methyl ester 36 was proposed in a single pot synthesis from (R)-4-t-butyldimethylsiloxy-2-cyclopentenone 35 by organocopper conjugate addition with an side-chain unit, trapping of the resulting enolate with 6-methoxycarbonyl-2-nitrohex-1-ene 34 and treatment with aqueous titanium(III) trichloride (66% yield). Hydrolysis of the methyl ester was accomplished by porcine liver esterase (89% yield). 6-Oxo-PGF$_1$ 37 gave 6-nitro-prostaglandin E$_1$ methyl ester in four steps.

The recently disclosed procedures for the preparation of cis-jasmone[52] and dihydrojasmone using organometallic reagents are of interest in that they provide the possibility for the construction of a wide range of functionalized carbon chains which can be further elaborated.

An easy synthetic route to 1,4-diketone derivatives starting from the thiazolium salt catalyzed addition of aldehydes to methyl vinyl ketone has been developed by Stetter (Table 7).[53] This procedure represents an efficient and elegant method for the synthesis of jasmine fragrances, γ-lactones and 1,4-diketones.[53f]

$$\mathrm{RCHO} + \mathrm{CH_2{=}CHCOCH_3} \xrightarrow{\text{Thiazolium salt/base}} \underset{\underline{1}}{\mathrm{RCOCH_2CH_2COCH_3}}$$

II. PREPARATION OF 4-OXOALKANALS

4-Oxoalkanals are an important class of compounds especially as intermediates for the preparation of cyclopentenones. The available routes to 4-oxoalkanals include ring opening of substituted furans,[54] radical addition of an aldehyde to acrolein diethyl acetal,[55] oxidative cleavage of olefins,[56] alkylation of 2,4,4,6-tetramethyldihydrooxazine with 2-iodomethyl-1,3-dioxolane,[57] alkylation of 2-ethoxyallyl vinyl sulfide followed by thio-Claisen rearrangement,[58] condensation of γ-oxosulfone acetals with esters, and the reaction of Grignard reagents derived from γ-halo ketals or γ-siloxy allylsilanes with acid chlorides.[59] Many 4-oxoalkanals can be made by the reaction of an enamine with the monoxide of ketene dimethylthioacetal.[60]

A. Rearrangement Routes

The three-membered rings in 2-ethythoxycyclopropyl ketones 38 are easily opened by treatment with dilute hydrochloric acid to form 4-oxoalkanals 2 and their hydrated forms.[61] After dehydration of the latter in the presence of p-toluenesulfonic

TABLE 7. Synthesis of 1,4-Diketones from Thiazolium Salt Catalyzed Addition of Aldehydes to α,β-Unsaturated Ketones

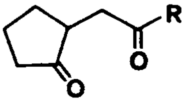
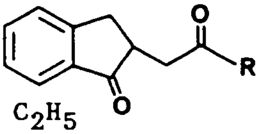
Aldehyde	α,β-Unsaturated Ketone	Cat.	Product	Yield (%)	Ref.
$CH_3CH=CHCHO$	$CH_2=CHCOCH_3$	A	6-Octen-2,5-dione	28	53a)
Citral		A	7,11-Dimethyl-6,10-dodecadien-2,5-dione	65	
Citronellal		A	7,11-Dimethyl-10-dodecen-2,5-dione	80	
RCHO	5-NB-$COCH=CH_2$	A	5-NB-$COCH_2CH_2COR$		53b)
			$R = C_2H_5$	72	
			$R = CH_3(CH_2)_2$	46	
			$R = (CH_3)_3CH$	63	
5-NB-CHO	5-NB-$COCH=CH_2$	A	5-NB-$COCH_2CH_2CO$-NB-5	61	53b)
RCHO	2-Methylene-1-cyclopentanone				53c)
		A	$R = C_2H_5$	67	
			$R = CH_3(CH_2)_2$	63	
		B	$R = C_4H_3S$	60	
			$R = C_6H_5$	44	
RCHO	2-Methylene-1-indanone				53c)
		A	$R = C_2H_5$	74	
			$R = CH_3(CH_2)_2$	76	
		B	$R = C_4H_3O$	69	
			$R = C_6H_5$	51	
	$CH_2=CHCOR$	A	$RCOCH_2CH_2COR$		53d)
			$R = CH_3$	37	
			$R = C_2H_5$	36	
			$R = C_6H_5$	56	
			$R = CH_2OAc$	43	

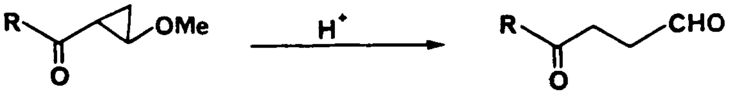
TABLE 7 (Cont'd)

Aldehyde	α,β-Unsaturated Ketone	Cat.	Product	Yield (%)	Ref.
$R^1O(CH_2)_nCHO$	$CH_2=CHCOR^2$	A	$R^1O(CH_2)_nCOCH_2CH_2COR^2$		53d)
			n R^1 R^2		
			3 CH_3 CH_3	68	
			4 CH_3 CH_3	67	
			5 CH_3CO CH_3	52	
RCHO	$CH_2=CHCO(CH_2)_nCOCH_3$		$RCO(CH_2)_2CO(CH_2)_nCOCH_3$		53e)
		A	$n = 3$ $R = C_2H_5$	71	
			$n = 3$ $R = C_5H_{11}$	75	
		B	$n = 3$ $R = C_6H_5$	67	
			$n = 4$ $R = C_6H_5$	80	
R^1CHO	$R^2CH=CHCOR^3$		$R^1COR^2(CH_2)_2COR^3$		53f)
		A	$R^1 = CH_3(CH_2)_2$, $R^2 = R^3 = C_6H_5$	70	
		C	$R^1 = C_4H_3O$, $R^2 = C_6H_5$, $R^3 = CH_3$	80	
		C	$R^1 = C_4H_3O$, $R^2 = CH_3$, $R^3 = CH_3$	34	
$n-C_6H_{13}CHO$	$CH_2=CHCN$	D	$n-C_6H_{13}COCH_2CH_2CN$	61	53g)
	$CH_2=CHCO_2C_2H_5$	D	$n-C_6H_{13}COCH_2CH_2CO_2H_5$	59	

Abbreviations: A: 3-Benzyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium chloride; B: 5-(2-Hydroxyethyl)-3,4-dimethyl-1,3-thiazolium iodide; C: 3-Ethyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium bromide; D: 3-(2-Ethoxyethyl)-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium bromide; NB: Norbornen ring.

acid, 4-oxoalkanals 2 are isolated. 2-Ethyoxycyclopropyl ketones 38 were prepared from starting acid chlorides and allyl chloride proceeding *via* alkyl 2,3-dichloropropyl ketones, alkyl 3-chloropropenyl ketones, and alkyl 3-chloro-2-methoxypropyl ketones. The reaction of 3,4-dicholoroketones with triethylamine, and then with methanol under acidic conditions gives 3-chloro-2-methoxypropyl ketones in 60-65% yields. The

4-oxoalkanals 2 prepared by this procedure are outlined in Table 8.[61]



38 2

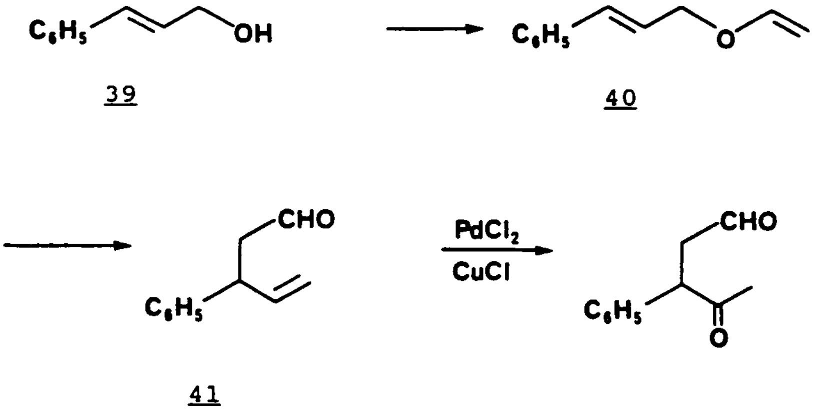
TABLE 8. 4-Oxoalkanals 2 Prepared from Alkyl 3-Chloro-2-Methoxypropyl Ketones 38

4-Oxoalkanal ($RCOCH_2CH_2CHO$)	Yield (%)
R: CH_3	60
C_2H_5	63
$n\text{-}C_3H_7$	64
$n\text{-}C_4H_9$	68
$n\text{-}C_5H_{11}$	65
$n\text{-}C_6H_{13}$	67

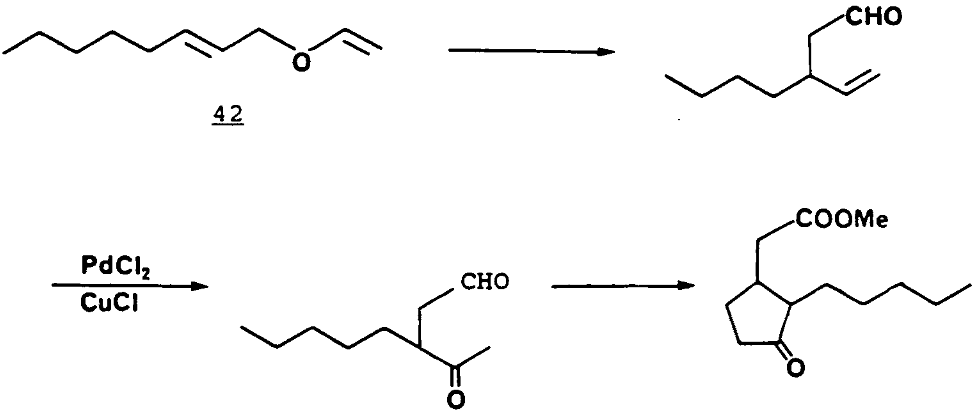
B. Oxidation

Many 4-oxoalkanals 2 can be made by cleavage of the olefinic group of appropriate 4-olefinic ketones. The palladium-catalyzed oxidation of the terminal olefins to methyl ketones is an important synthetic method for 1,4-dicarbonyl compounds.[50] A simple synthetic method was based on the allylation of carbonyl compounds with allyl halide as a C_3 component, followed by the palladium-catalyzed oxidation of the terminal olefins to carbonyl compounds. This is a good annellation method for cyclopentenones.[62] There are many examples of the palladium-catalyzed oxidation of olefins to ketones.[62] 4-Oxopentanals are synthesized from allyl alcohols by [3,3]sigmatropic rearrangement of their vinyl ethers, and subsequent oxidation of the terminal double bond.

Cinnamyl alcohol 39 was converted to the allyl vinyl ether 40, which was subjected to Claisen rearrangement to give 3-phenyl-4-pentenal 41 in 50% yield. Oxidation of the terminal double bond of 41 using palladium(II) chloride/copper(I) chloride gave 3-phenyl-4-oxopentanal in 76% yield.



Syntheses of methyl dihydro jasmonate and dihydrojasmone were carried out starting from 2-octenol, which was easily prepared by palladium-catalyzed dimerization of butadiene and selective hydrogenation with tris[triphenylphosphine]ruthenium(II) chloride.[63] 2-Octenol was converted to 2-octenyl vinyl ether. The [3,3]sigmatropic rearrangement of 2-octenyl vinyl ether, afforded 3-vinyloctanal 42 in 79% yield. The terminal double bond was converted to the methyl ketone 43 in 90% yield. Methyl jasmonate 44 was synthesized from this ketoaldehyde 43 via the aldol condensation and the double bond migration. Similarly, the synthesis of dihydrojasmone was carried out. Rearrangement of 2-octenyl allyl ether gave the aldehyde in 60% yield. By the same oxidation procedure as above, dihydro-



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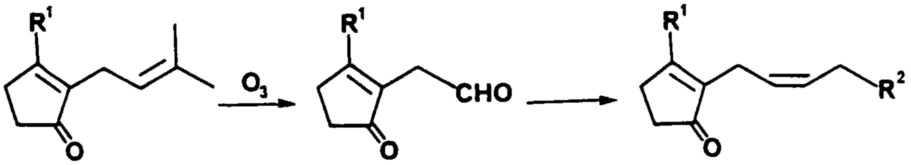
jasmone was synthesized. 2-(3-Methylbut-2-enyl)cyclopenten-3-one 45 undergoes selective ozonolysis in dichloromethane using Fat Red 7B as indicator to produce the 2-(formylmethyl)-cyclopenten-3-one 46 in 61% yield. This compound has synthetic utility in the prostanoid field, and 11-deoxyprostanoids of intermediate was obtained from this compound 46 by treatment with carboxybutylidene triphenylphosphorane, compound 46 has been converted into cis-jasmone by treatment with propylidene triphenylphosphorane.[64]



45

46

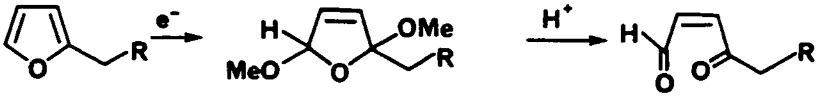
47

R^1 = H, CH_3

R^2 = CH_2CH_3, $(CH_2)_3CO_2H$

C. Approaches by Use of Furans

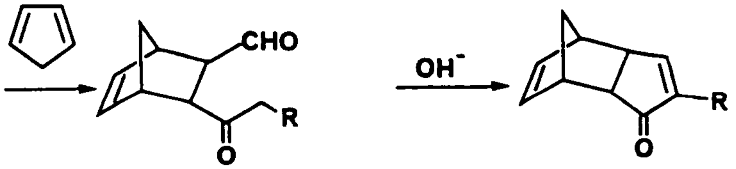
Electrolysis of alkylfurans 48 in methanol in the presence of NH_4Br led quantitatively to dihydrodimethoxyalkylfurans 49,



48 49 50

R=H, CH_3, C_5H_{11}, SCH_3, $CO_2C_2H_5$, CH_2OH, CH_2OCH_3, CH_2OAc

50



which on hydrolysis gave cis enedione 50.[65] These enediones reacted in a Diels-Alder reaction with cyclopentadiene to afford the endo-cis-norbornene adduct in quantitative yields. Subsequent intermolecular aldol condensation with base gave a mixture of exo- and endo-tricyclodecenones in overall yields ranging from 59-90%. Chemical transformation of the remaining enone system in tricyclo[5.2.1.$0^{2,6}$]decane followed by thermal cycloreversion regenerates the double bond and produces a functionalized cyclopentenone. The result of this sequence is actually a selective transformation of one of the olefinic bonds on cyclopentadienone. Cyclopentenoids such as pentenomycin and analogs can be prepared from funtionalized tricyclodecenone.[65]

D. Routes Based on Michael Addition

4-Oxoalkanals 2 are prepared from the reaction of nitroalkane 8 with acrolein catalyzed by a tertiary phosphine such as tributylphosphine, followed by Nef reaction of the resulting 4-nitro aldehyde ethyleneacetals 51.[66-68] In the reaction of nitroalkanes with acrolein, 4-nitro ethylene acetals 51 were obtained in 62-70% yields. These were subjected to an electrochemical oxidative Nef reaction to give 4-oxoaldehydes 2. Some results are shown in Table 9.

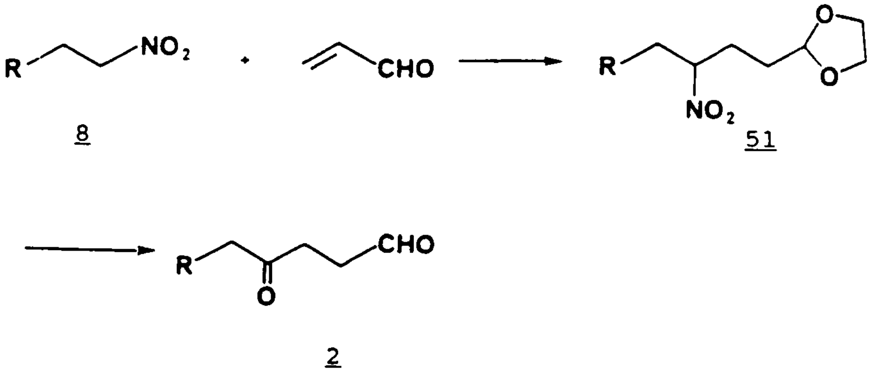
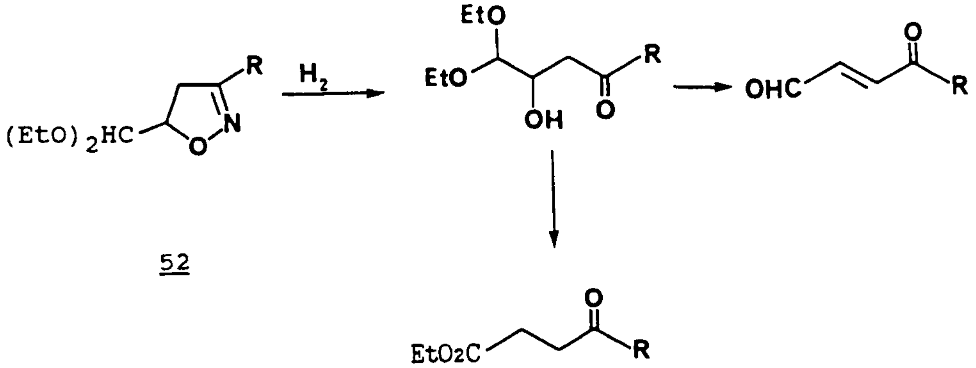


TABLE 9. 4-Oxoalkanals 2 Prepared from 4-Nitro Ethylene Acetals 51

4-Oxoalkanal ($RCOCH_2CH_2CHO$)	Yield (%)	Ref.
R: CH_3	54	68
C_2H_5	75	68
n-C_3H_7	80	68
i-C_3H_7	84	68
n-C_4H_9	82	68
i-C_4H_9	85	68
i-C_5H_{11}	89	68
n-C_6H_{13}	89	66
n-C_9H_{19}	81	67
n-$C_{10}H_{21}$	85	67

The reaction of acrolein diethyl acetal with nitroalkane, triethylchlorosilane, and triethylamine in acetonitrile/benzene produced the isooxazolidine 52. The reduction of acetal with titanous ions to the expected 2-hydroxy-4-oxoaldehyde was unsuccessful. Cleavage of the C^5-O bond occurred and 4-oxoalkanal was obtained. Catalytic hydrogenation over Raney-Ni in methanol cleaved the N-O bond smoothly and 4-oxo-2-hydroxyacetals were formed quantitativly. 4-Oxo-2-hydroxyacetals were converted into 4-oxo esters, α,β-unsaturated 4-oxoaldehydes, and acetals.[69]



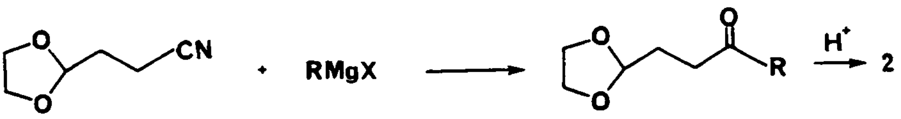
52

3

$R = CH_3, C_6H_{13}, (CH_2)_7CO_2CH_3$

E. Use of Grignard Reagents

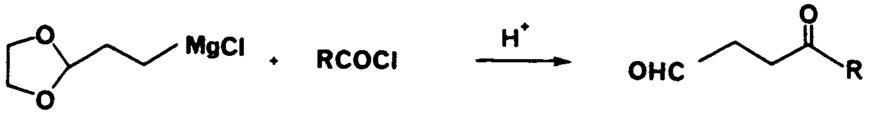
The treatment of β-chloropropyldioxolane with sodium cyanide gave the cyanodioxolane derivative 53. Reaction of 53 with alkylmagnesium bromide was followed by selective hydrolysis with 1N aqueous HCl to afford oxodioxolanes 54. Hydrolysis of 54 with 5% aqueous H_2SO_4 gave 4-oxoalkanals 2.[70]



53 54

The reaction of 3-cyano-1,1-dimethoxypropane with cis-3-hexenylmagnesium bromide in THF gave 1,1-dimethoxy-cis-7-decen-4-

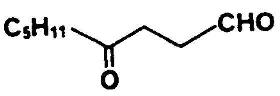
one in 54% yield. Deacetalization of the keto acetal followed by cyclization afforded 2-(cis-2-pentenyl)-2-cyclopenten-1-one. Methyl jasmonate was obtained from 54 (R = n-3-cis-C_6H_{11}).[71] The prostaglandin intermediate methyl 9,12-dioxydodecanoate 56 can be made by the reaction of 2-(1,3-dioxolan-2-yl)ethylmagnesium chloride with nonanoyl chloride 55, followed by cleavage of the dioxolane ring of the ketone.[72,73]

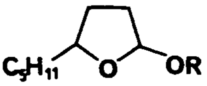


55 56

F. Synthetic Applications

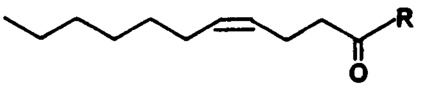
Recently, Yajima[72] investigated the flavor components of watermelon essential oil which were obtained by steam distillation under reduced pressure. They used the glass capillary GLC procedure, and isolated five new characteristic minor components which were determined to be 4-oxononanal, 2-hydroxy-5-pentyltetrahyrofuran and three alkyl derivatives from GC-MS and IR data. Syntheses of five characteristic flavor components of watermelon essential oil were carried out starting from 53 with Grignard reaction.[70]





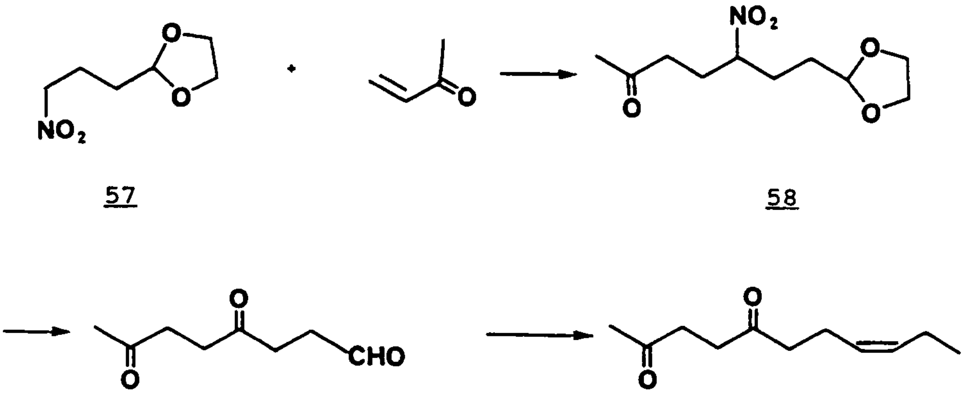
R = H, n-C_6H_{13},
Z-$CH_3(CH_2)_4CH{=}CH(CH_2)_2$,
Z,Z-$C_2H_5CH{=}CHCH_2CH{=}CH(CH_2)_7$

It is known that Z-13-eicosen-10-one 60a and Z-12-nonadecen-9-one 60b are the pheromones of the Japanese peach fruit moth (Carposia niponensis Walshingham), and that a mixture of the ratio of 20:1 has the strongest biological activity. These pheromones were synthesized *via* 4-oxodecanal and 4-oxododecanal with Wittig reagents.[67,74]



R = C_8H_{17}, C_7H_{15}

The Michael addition of acrolein to nitromethane catalyzed by tributylphosphine in benzene followed by acetalization gave 1,1-ethylenedioxy-4-nitrobutane 57. The method was applied to the synthesis of *cis*-Jasmone. The Michael reaction of nitro acetal to 3-butene-2-one gave 1,1-ethylenedioxy-4-nitrooctane 58 in good yield. 4,7-Dioxyoctanal 59 was obtained from the nitro ketone by oxidation with H_2O_2-K_2CO_3 and subsequently hydrolysis in 85% yield. The Wittig reaction between the aldehyde and propylidene triphenylphosphorane in benzene gave *cis*-8-undecene-2,5-dione in 60% yield. *Cis*-jasmone was formed from the 1,4-diketone under basic conditions in 83% yield.[23]



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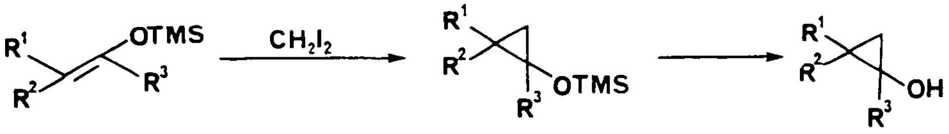
59

III. PREPARATION OF 4-OXO ESTERS, 4-OXOCARBOXYLIC ACIDS AND 4-OXONITRILES

4-Oxoalkanoic acids and related compounds represent an interesting class of organic compounds. They can be used to prepare cyclic products such as lactones, γ-lactam antibiotics, isoquinolines and lactonic sex pheromones. They are also used without further transformation. Several methods to prepare 4-oxoalkanoic acids have been developed.

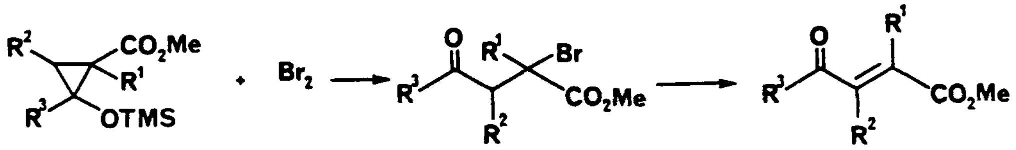
A. Ring Cleavage Routes

Cyclopropanation of silyl enol ethers 60 by the Simmons-Smith reaction or modified versions is a very common reaction.[75a] Much of the development of this process is due to Conia, who has revealed early work.[75b] Recent improvements include the use of zinc-silver couple or diethylzinc instead of zinc-copper couple. Alcoholysis of the initially formed siloxy cyclopropanes 61 gives cyclopropanols 62, but many other interesting transformations have been noted.[76]

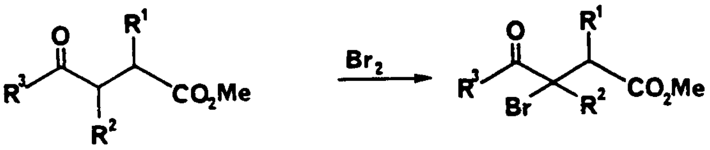


60 61 62

Some of these ring opening reactions are shown below. Most involve cleavage of one of the bonds of the cyclopropane ring next to the oxygen substituent, with concomitant loss of the silyl group. Silyloxycyclopropane esters 63 undergo ring opening on reaction with bromine to provide the 2-bromo-4-oxo-alkanoates 64. Subsequent treatment with triethylamine gives the 4-oxo-2-alkenoates 65. In the case of $R^3 = t\text{-}C_4H_9$ the alternative pathway via 4-oxoalkanonates 66 and 3-bromo-4-oxo-alkanonates 67 leads to the 4-oxoalkenonates 65.[77] Cyclopropanation of ethyl 3-trimethylsilyloxy-2-alkenoates 68 with

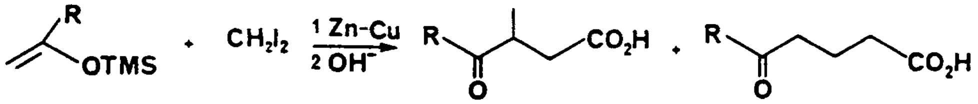


63 64 65



66 67

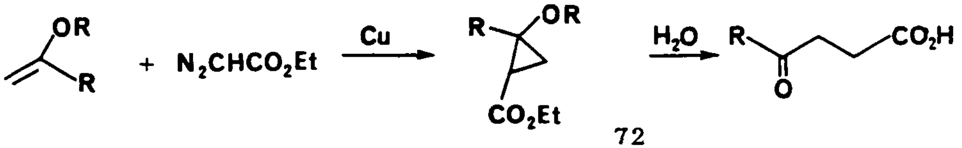
diiodomethane in the presence of zinc-copper couple, followed by treatment with an alkali solution, gave the corresponding 3-methyl-4-oxoalkanoic acids 69 and 5-oxoalkanoic acids 70 (69a, b and c; 39, 68 and 54% yields, respectively). None of them was found to be 4-oxo-4-alkyl butanoic acid which could be produced by ring cleavage.[78]



68 69 70

R = Rh (a), Me_2CHCH_2 (b), $PhCH_2CH_2$ (c)

Enol ethers 71 react with ethyl diazoacetate to give mixtures of stereoisomeric 2-alkoxycyclopropanecarboxylic esters 72. Saponification of these compounds affords the corrresponding carboxylic acids, which are quantitatively transformed into the 4-oxoalkanoic acids by heating in methanol/water.[79]

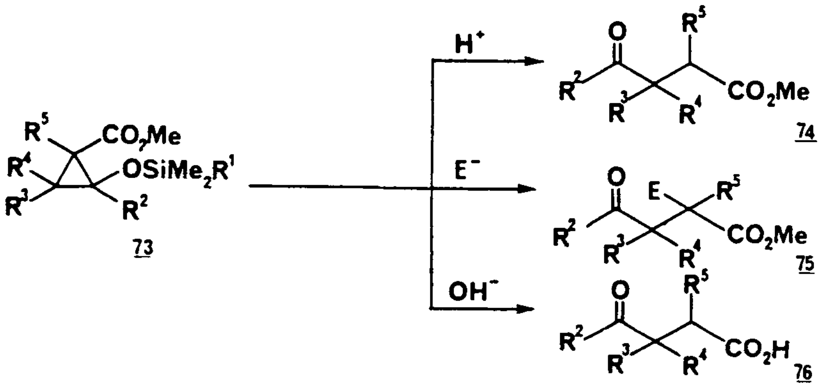


72

71

R = i-C_3H_7, t-C_4H_9, C_6H_5, Veratryl

Methyl 2-(trialkylsilyloxy)cyclopropanecarboxylates 73 can be cleaved under various conditions to give 4-oxoalkanoic acid derivatives. The especially mild fluoride ion-induced ring opening reaction gives high yields of 4-oxoalkanoates 74. *In situ* quenching of the intermediate ester-enolate carbanion by electrophiles allows the preparation of 2-substituted 4-oxo-alkanonates 75. Further, suitable reaction conditions afford the free acid or the 4-oxoalkanoic acid dervatives 76 by one-pot reactions.[80]



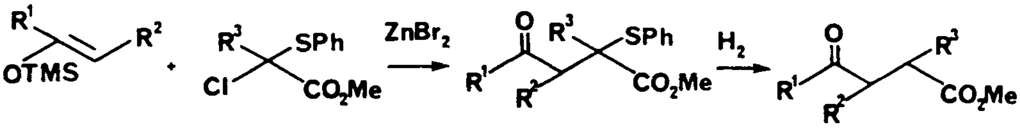
R^1 = CH_3, t-C_4H_9 R^2 = H, CH_3, i-C_3H_7, t-C_4H_9, CH_2=CH, Ph

R^3 = H, CH_3 R^4 = H, CH_3, OTMS

R^5 = H, CH_3, n-C_4H_9, CH_2=$CHCH_2$, Bzl

B. Alkylative Assemblage

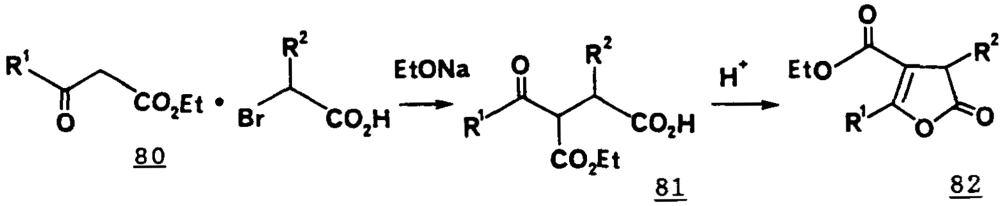
Silyl enol ethers 77 react with α-chloro-α-phenylthioesters 78 in the presence of a Lewis acid regioselectively to give α-phenylthio keto esters 79 in 69 - 90% yields. Reductive de-



77 78 79 80

R^1 = Ph, Et, EtO R^2 = H, Me R^3 = H, Me, Et sulfurisation with Raney nickel leads to the saturated 4-oxo esters, whereas oxidative elimination affords the unsaturated 4-oxoalkenoates in 73 - 93% yields.[81]

Keto diacid derivatives were prepared from the β-keto esters 80 and α-bromoacids in the presence of sodium ethoxide. Phosphorus pentoxide/phosphoric acid mixture in dichloromethane solution proved to be the most effective and general reagent for cyclization to give lactones 82. The ester function of compounds 82 can not be hydrolysed either in an acidic medium or a basic medium.[82]

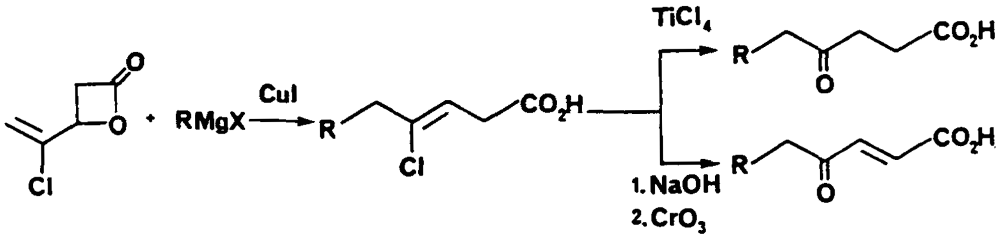


R^1 = CH_3, n-C_3H_7, n-C_5H_{11}, i-C_3H_7, c-C_6H_{11}, Ph

R^2 = H, CH_3, C_2H_5, i-C_3H_7, Ph

C. Use of Grignard Reagents

4-Chloro-3-alkenoic acids 83 may be obtained in a regioselective ring-opening reaction from β-(1-chlorovinyl)-β-propiolactone with Grignard or organo-copper reagents. With diphenyl-, divinyl-, and diallyl-cuprates, higher yields of acids were obtained than with the corresponding Grignard



83

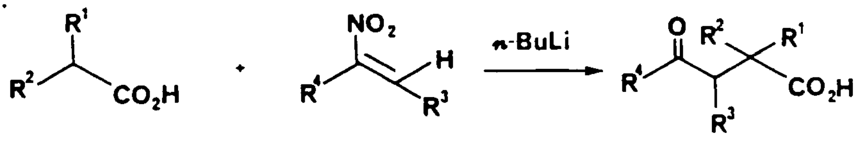
reagents. 4-Chloro-3-alkenoic acids 83 can be transformed either into 4-oxoalkanoic acids by treatment with titanium(IV) chloride in aqueous methanol or into 4-oxo-(E)-2-alkenoic acids by hydrolysis with sodium hydroxide followed by Jones oxidation.[83] Some results are shown in Table 10.

TABLE 10. Synthesis of 4-Oxoalkanoic Acids 3 via 4-Chloro-3-Alkenoic Acids 83

Grignard Reagent (RMgX) R	Yield (%) 4-Chloro-3-Alkenoic Acid 83	Yield (%) 4-Oxoalkanoic Acid 3
Me	81	66
Bu	81	82
s-Bu	85	77
t-Bu	76	71
Ph	73	71
CH_2=CH	51	0
CH_2=$CHCH_2$	25	5

D. Miscellaneous Preparations

Dilithiated carboxylic acids 84 react with nitroolefins 85 to give a variety of 4-oxoalkanoic acids 3, which were isolated as the methyl esters in good to moderate yields (Table 11).[84a] The use of α-(phenylthio) dervatives 84 allows the further elaboration of synthetically useful 4-oxo-2-alkenoates (Table 12).[84b]



84 85 3

TABLE 11. Oxoalkylation of Phenylacetic and Some Aliphatic Acid with Nitro Olefines

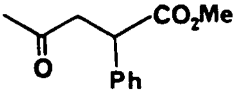
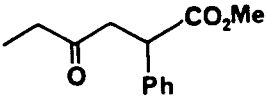
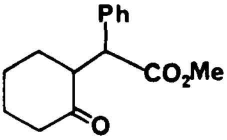
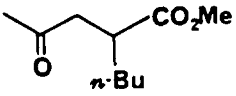
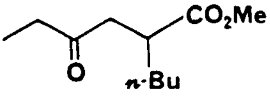
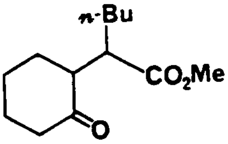
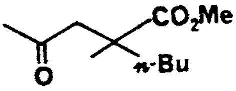
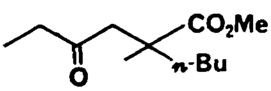
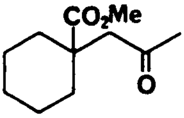
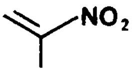
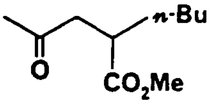
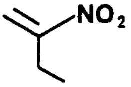
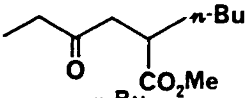
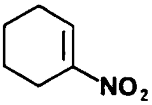
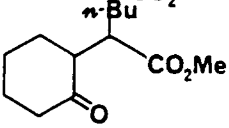
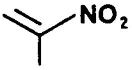
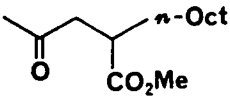
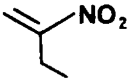
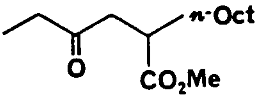
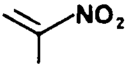
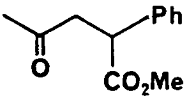
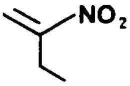
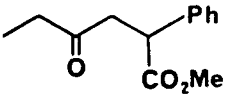
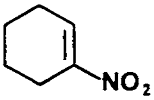
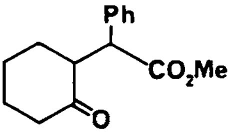
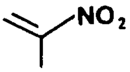
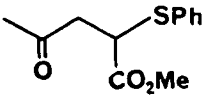
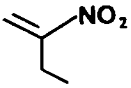
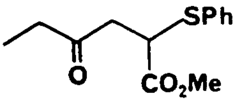
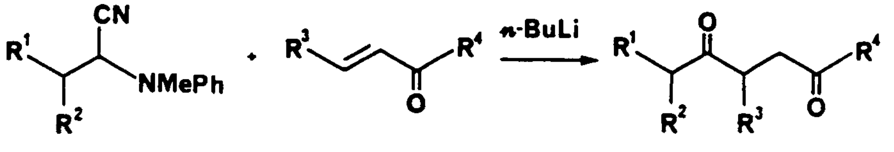
Carboxylic Acid		Nitro Olefin		Base	Product	Yield (%)
R^1	R^2	R^3	R^4			
Ph	H	H	CH_3	n-BuLi		88
Ph	H	H	CH_3CH_2	n-BuLi		73
Ph	H	$-(CH_2)_4-$		n-BuLi		72
$CH_3(CH_2)_3$	H	H	CH_3	LDA		65
$CH_3(CH_2)_3$	H	H	CH_3CH_2	LDA		55
$CH_3(CH_2)_3$	H	$-(CH_2)_4-$		LDA		24
$CH_3(CH_2)_3$	CH_3	H	CH_3	LDA		46
$CH_3(CH_2)_3$	CH_3	H	CH_3CH_2	LDA		38
$-(CH_2)_5-$		H	CH_3	LDA		37

TABLE 12. Synthesis of γ-Keto Esters from Conjugated Nitro Olefines and Ester Enolates

Ester	Nitro Olefin	Product	Yield (%)
$CH_3(CH_2)_4CO_2Me$			81
			56
			54
$CH_3(CH_2)_8CO_2Me$			61
			53
$C_6H_5CH_2CO_2Me$			79
			75
			61
$C_6H_5SCH_2CO_2Me$			65
			66



86

Michael reaction of amino nitrile 86 with α, β-unsaturated carbonyl compounds and various enolates gave the corresponding 4-oxocarbonyl compounds.[85]

One new method for the preparation of 4-oxoalkanoic acids consists of the conjugate addition of primary nitro compounds to acrolein on alumina surface in the absence of a solvent and oxidation of the 4-nitroalkanals thus obtained with hydrogen peroxide (Table 13).[86]

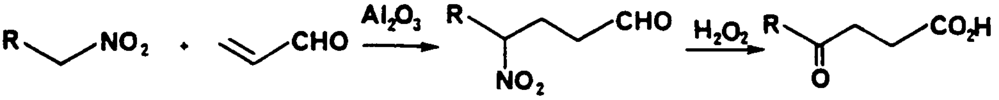


TABLE 13. Synthesis of 4-Oxoalkanoic Acids from Nitroalkanes and Acrolein

RCH_2NO_2 R	$RCOCH_2CH_2CO_2H$ Yield (%)
CH_3	62
C_2H_5	70
n-C_4H_9	78
n-C_5H_{11}	80
$CH_3C(OCH_2CH_2O)CH_2$	56
$HC(OCH_2CH_2O)CH_2$	57
$CH_3OOC(CH_2)_4$	40

In the presence of a catalytic amount of trityl salts, α,β-unsaturated orthoesters react with various silyl enol ethers to afford the corresponding Michael adducts as 5-oxo ester in good yields (Table 14).[87]

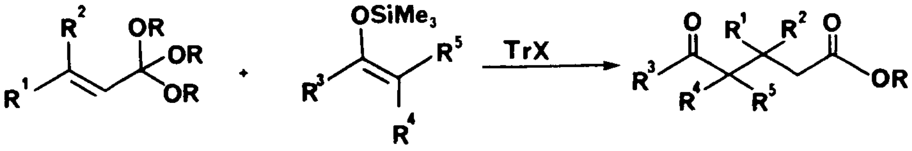
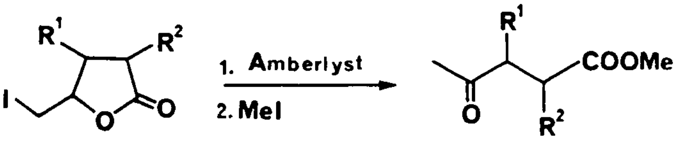


TABLE 14. The Reaction of α,β-Unsaturated Orthoesters with Silyl Enol Ethers

α,β-Unsaturated Orthoester			Silyl Enol Ether			Yield (%)
R^1	R^2	R	R^4	R^5	R^6	
Me	H	Et	MeO	H	Ph	73
Me	H	Et	MeO	Me	Me	75
Me	H	Et	Ph	H	H	67
Me	H	Et	Ph	H	Me	58
Me	H	Me	MeO	H	Ph	84
Me	H	Me	MeO	Me	Me	87
Me	H	Me	Ph	H	H	65
H	H	Et	MeO	H	Ph	61
H	H	Et	Ph	H	Me	70
Ph	H	Et	MeO	Me	Me	92
Me	Me	Me	MeO	Me	Me	90

γ-Lactones 87 are converted into methyl 4-oxoalkanoates by treatment with fluoride ion on polymeric support and subsequent hydrolysis, followed by methylation with methyl iodide,[88]

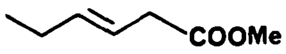
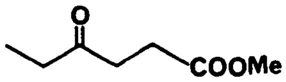
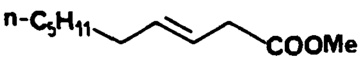
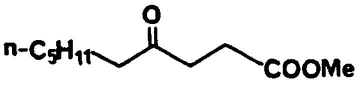
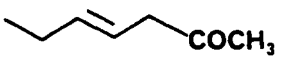
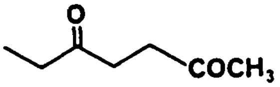
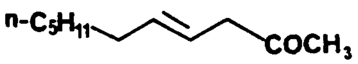
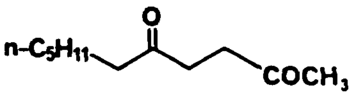


87 3 $R^1 = R^2 =$ H, Ph

affords the methyl 4-oxoalkanonates.

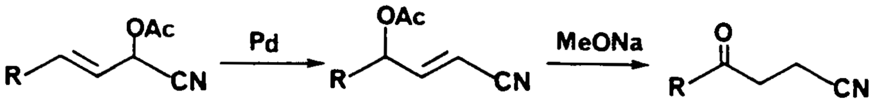
It is well-known that π-allylpalladium complexes are easily formed by the reaction of palladium(II) chloride with α,β-unsaturated esters. An attempted oxidation of α,β-unsaturated esters with the palladium(II) chloride/copper(I) chloride/oxygen catalyst system in aqueous dioxan or tetrahydrofuran led to 4-oxoalkanoates, with high regioselectivity.[89] Some results are shown in Table 15.

TABLE 15. Pd(II)/Cu(I)/O_2 Oxidation of α,β-Unsaturated Esters and Ketones

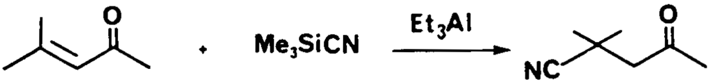
Olefin	Product	Yield (%)
		52
		61
		45
		61

A palladium-catalyzed isomerization of cyanohydrin acetates proceeded with nearly quantitative yield to give 4-acetoxy-2-alkenenitriles. Solvolysis of acetates gave the 4-hydroxy-2-alkenenitriles which were oxidized with oxalyl chloride/dimethyl sulfoxide under mild conditions to afford the

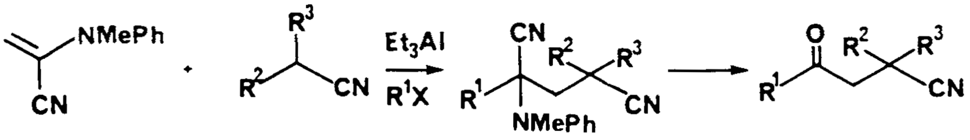
4-oxoalkenenitriles in good yields.[90]



α, β -Unsaturated ketones react with cyanotrimethylsilane in the presence of a Lewis acid to give almost quantitatively the 1,4-adducts. Subsequent hydrolysis affords the 4-cyano ketones in quantitative yield[91].



Michael addition of 2-(N-Methylanilino)acrylonitrile with lithio nitrile, followed by alkylation, affords the 4-oxo-alkanenitriles (Table 16).[92]



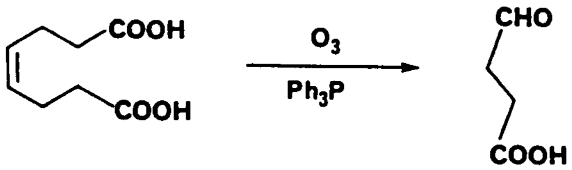
E. Synthetic Applications

Succinic semialdehyde is formed from 4-aminobutanoic acid by transamination in the brain and in microorganisms and is therefore of relevance in neurochemistry and in pharmacology. Succinic semialdehyde is rather unstable, since it easily polymerizes to the corresponding trioxane and is in equilibrium with the cyclic form of 5-hydroxy-4,5-dihydro-2(3H)-furanone. The equilibrium can be completely shifted to the lactone form in water at room temperature, although a hydrate structure cannot be excluded. 4-Octene-1,8-dioic acid was ozonized in ethyl acetate at -78°C.

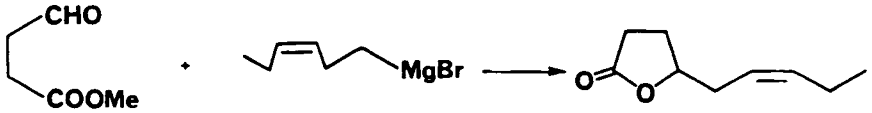
TABLE 16. 4-Oxoalkyl Nitrile from 2-(N-Methyanilino)acrylonitrile and Lithio Nitrile

R^1X	Product R^2	R^3	Bp (°C/torr)	Yield (%)
CH_3J	CH_3	H	100/1	40
C_2H_5J	CH_3	H	50/0.01	70
$C_6H_5CH_2Br$	CH_3	H	90/0.05	92
CH_3J	$n\text{-}C_4H_9$	H	50/0.01	94
C_2H_5J	$n\text{-}C_4H_9$	H	80/0.01	85
$C_6H_5CH_2Br$	$n\text{-}C_4H_9$	H	150/0.01	70
CH_3J	CH_3	CH_3	70/0.01	76
C_2H_5J	CH_3	CH_3	60/0.01	75
$C_6H_5CH_2Br$	CH_3	CH_3	mp 54	72
CH_3J	$-(CH_2)_5-$		100/0.01	84
C_2H_5J	$-(CH_2)_5-$		110/0.01	88
$C_6H_5CH_2Br$	$-(CH_2)_5-$		118/0.01	70

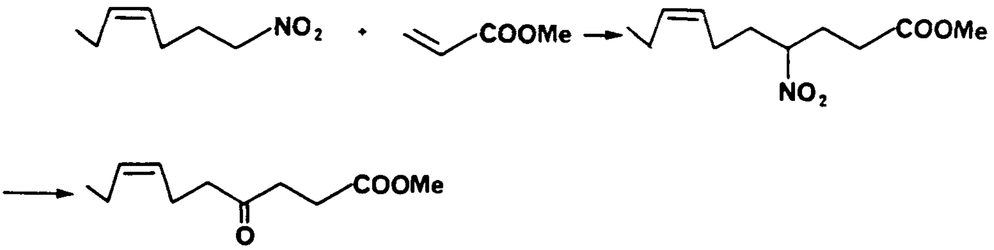
Treatment of the ozonide with a solution of triphenylphosphine in ethyl acetate at -78°C, followed by extraction with water, afforded an aqueous solution of succinic semialdehyde in 70% yield.[93]



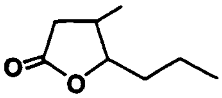
Methyl 4,4-dimethoxybutyrate was refluxed in water to afford methyl 4-oxobutyrate in 90% yield. γ-Jasmolactone was synthesized by a one-pot reaction of methyl 4-oxobutyrate with *cis*-3-hexenylmagnesium bromide in 69% yield.[71a]



From the reaction of acetylenic Grignard reagents with ethyl 4-oxobutanoate unsaturated γ-lactones were obtained *via* hydroxy carboxylates.[71b] γ-Jasmolactone was prepared by the Michael reaction of 1-nitro-*cis*-4-heptene with methyl acrylate, followed by Nef reaction and reduction of 4-oxoalkenoate.[94]



3-Methyl-4-octanolide, a γ-lactone known as a constituent of alcoholic beverages called Quercus lactone or Whisky lactone was synthesized by Michael addition of nitropenthane with methyl crotonate, followed by Nef electrochemical oxidation.[40]



Ethyl 3-methyl-4-oxooctanoate has been synthesized by reaction of pentanal with ethyl crotonate. Reduction with $NaBH_4$ and cyclization yields racemic *cis*/*trans*-Quercus lactone.[95] Optically pure stereo isomers of Quercus lactone have then been synthesized and separated by liquid chromatography.[95a]

REFERENCES

1. a) R. A. Ellison, Synthesis, 397 (1973).
   b) T.-L. Ho, Synth. Commun., *4*, 265 (1974).
   c) B.-T. Grobel and D. Seebach, ibid., *7*, 357 (1977).

d) T.-L. Ho, ibid., 7, 351 (1977).

2. a) U. Axen, J. E. Pike and W. P. Schneider, "The Total Synthesis of Natural Products", J. ApSimon Ed., Wiley, New York, 1973, Vol. 1, p. 81.
   b) J. S. Bindra, " The Total Synthesis of Natural Products", J. ApSimone Ed., Wiley, New York, 1981, Vol. 4, p. 353.
   c) J. S. Bindra and R. Bindra, "Prostaglandin Synthesis", Academic, New York, 1977.
   d) A. Mita, "The Synthesis of Prostaglandins", Wiley, New York, 1977, p. 233.

3. S. Bergstrom, Science, 157, 382 (1967).

4. a) L. Crombie and M. Elliot, Fortschr. Chem. Org. Naturstoffe, 19, 120 (1961).
   b) L. Crombie, P. Hemesley and G. Pattenden, J. Chem. Soc. [C], 1016 (1969).

5. G. Buchi and H. Wuest, J. Org. Chem., 31, 977 (1966).

6. W. S. Johnson, M. B. Gravestock and B. E. McCarry, J. Am. Chem. Soc., 93, 4332 (1971).

7. P. A. Grieco and C. S. Pogonowski, J. Org. Chem., 39, 732 (1974).

8. E. J. Corey and D. Enders, Terahedron Lett., 11 (1976).

9. F. Duus, Tetrahedron, 32, 2817 (1976).

10. D. H. R. Barton, "Comprehensive Organic Chemistry", Pergamon Press, Oxford, 1979, Vol. 1, 1062 and references cited therein.

11. a) D. Seebach, E. W. Colvin, F. Lehr and T. Weller, Chimia 33, 1 (1979).
    b) N. Ono and A. Kaji, Yuki Gosei Kagaku Kyokai Shi, 38, 115 (1980).

12. J. K. Rasmussen, Synthesis, 91 (1977).

13. a) M. Miyashita, T. Yamani and A. Yoshikoshi, J. Am. Chem. Soc., 98, 4679 (1976).
    b) M. Miyashita, T. Yamani, T. Kumazawa and A. Yoshikoshi, ibid., 106, 2149 (1984).

14. a) A. Yoshikoshi, Yuki Gosei Kagaku Kyokai Shi, 40, 427 (1982).
    b) Y. Kita, O. Tamura and Y. Tamura, ibid., 44, 1118 (1986).

15. G. P. Pollini, A. Barco and G. DeGiule, Synthesis, 44 (1972).

16. P. Bakuzis, M. L. Bakuzis and T. F. Weingartner, Tetrahedron Lett., 2371 (1978).

17. D. D. Miller, K. B. Moorthy and A. Hamada, ibid., 555 (1983).

18. R. V. Stevens and A. W. M. Lee, J. Chem. Soc., Chem. Commun., 102 (1982).

19. J. E. McMurry and J. Melton, J. Org. Chem., 38, 4367 (1973).

20. a) R. Walchli and M. Hesse, Helv. Chim. Acta., 65, 2299 (1982).
b) Y. Nakashita and M. Hesse, ibid., 845 (1983).
c) M. Wada, A. Tsuboi, K. Nishimura and T. Erabi, Nippon Kagaku Kaishi, 1284 (1987).

21. D. W. Chasar, Synthesis, 841 (1982).

22. T. Miyakoshi and S. Saito, Yukagaku, 31, 35 (1982).

23. T. Miyakoshi and S. Saito, ibid., 31, 231 (1982).

24. a) N. Ono, H. Miyake and A. Kaji, J. Chem. Soc., Chem. Commun., 873 (1983).
b) N. Ono, A. Kamimura, H. Miyake, I. Hamamoto and A. Kaji, J. Org. Chem., 50, 3692 (1985).
c) N. Ono and A. Kaji, Synthesis, 693 (1986).

25. N. Ono, A. Kamimura and A. Kaji, Synthesis, 226 (1984).

26. J. H. Clark, D. G. Cork and M. S. Robertson, Chem. Lett., 1145 (1983).

27. a) J. H. Clark and D. G. Cork, J. Chem. Soc., Chem Commun., 635 (1982).
b) J. H. Clark, D. G. Cork and H. W. Gibbs, J. Chem. Soc., Perkin Trans. I, 2253 (1983).

28. a) G. Rosini, E. Marotta, R. Ballini and M. Petrini, Synthesis, 237 (1986).
b) G. Rosini, R. Ballini, M. Petrini and E. Marotta, Angew. Chem. Int. Ed. Engl., 25, 941 (1986).
c) R. Ballini, M. Petrini and E. Marotta, Synth. Commun., 17, 543 (1987).

29. W. E. Noland, Chem. Rev., 55, 137 (1955).

30. M. Langrenee, Compt. Rend. Acad. Sci. Ser., [C], 284, 153 (1977).

31. a) D. St. C. Black, Tetrahedron Lett., 1331 (1972).
b) H. Chikashita, Y. Morita and K. Itoh, Synth. Commun., 17, 677 (1987).

32. a) E. Keinan and Y. Mazur, J. Am. Chem. Soc., 99, 3861 (1977).
    b) P. S. Vankar, R. Rathore and S. Chandrasekaran, Synth. Commun., 17, 195 (1987).

33. J. E. McMurry and J. Melton, J. Am. Chem. Soc., 93, 5309 (1971).

34. A. H. Pagano and H. Shechter, J. Org. Chem., 35, 295 (1970).

35. G. A. Olah, M. Arvanaghi, Y. O. Vanker and G. K. S. Prakash, Synthesis, 662 (1980).

36. M. R. Galobardes and H. W. Pinnick, Tetrahedron Lett, 5235 (1981).

37. G. A. Olah and B. G. B. Gupta, Synthesis, 44 (1980).

38. J. Nogami, T. Sonoda and S. Wakabayashi, ibid., 763 (1983).

39. W. T. Monte, M. M. Baizer and R. D. Little, J.Org. Chem., 48, 803 (1983).

40. T. Miyakoshi and S. Saito, Yukagaku, 22, 749 (1983).

41. M. Mikolajczyk and P. Balczewski, Synthesis, 691 (1984).

42. M. C. Mussatto, D. Savoia, C. Trombini and A. U. Ronchi, J. Org. Chem., 45, 4002 (1980).

43. T. Yoshida and S. Saito, Yukagaku, 32, 82 (1983).

44. J. V. Comasseto and C. A. Brandt, Synthesis, 146 (1987).

45. R. M. B. Perez, L. M. Fuentes, G. L. Larson, C. L. Barnes and M.J.Heeg, J. Org. Chem., 51, 2039 (1986).

46. I. M. Cepero, A. Santiago and G. L. Larson, Synth. Commun., 16, 705 (1986).

47. H. C. Brown, U. S. Racherla and S. M. Singh, Synthesis, 922 (1984).

48. G. I. Nikishin, E. I. Troyansky and M. I. Lazareva, Terahedron Lett., 4987 (1984).

49. a) C. B. Einhorn, J-L. Soulier and D. Lelandais, Bull. Soc. Chim. Belg., 92, 305 (1983).
    b) J. Einhorn, J-L. Soulier, C. Bacquet and D. Lelandais, Can. J. Chem., 61, 584 (1983).

50. J. Tsuji, I. Shimizu and Y. Kobayashi, Israel J. Chem., 24, 153 (1984).

51. T. Tanaka, A. Hazato, K. Bannai, N. Okamura, S. Sugiura, K. Manabe, S. Kurozumi, M. Suzuki and R. Noyori, Tetrahedron Lett., 4947 (1984).

52. a) G. W. K. Cavill, B. S. Goodrich and D. G. Laing, Aust. J. Chem., 23, 83 (1970).
b) F. Ogura, T. Otsubo, T. Sakamoto and H. Yamaguchi, Bull. Chem. Soc. Jpn., 57, 1691 (1984).
c) M. Kosugi, T. Takano, M. Sakurai, H. Sano and T. Migita, Chem. Lett., 1221 (1984).
d) J. B. Hendrickson and P. S. Palumbo, J. Org. Chem., 50, 2110 (1985).
e) A. Furuhata, K. Onishi, A. Fujita and K. Kogami, Agric. Biol. Chem., 46, 1757 (1982).
f) R. T. Reddy and U. R. Nayak, Synth. Commun., 16, 713 (1986).
g) A. Chattapadhyay, Chem. Ind.(London), 471 (1986).
h) G. Rosini, R. Ballini and P. Sorrenti, Tetrahedron, 39, 4127 (1983).
i) M. Kawashima and T. Fujisawa, Chem. Lett., 1851 (1984).
j) M. Yamashita, K. Matsumiya, M. Tanabe and R. Suemitsu, Bull. Chem. Soc. Jpn., 58, 407 (1985).

53. a) H. Stetter, G. Hillboll and H. Kuhlmann, Chem. Ber., 112, 84 (1979).
b) H. Stetter and B. Jansen, ibid., 118, 4877 (1985).
c) H. Stetter and W. Haese, ibid., 117, 682 (1984).
d) H. Stetter and H. T. Leinen, ibid., 116, 254 (1983).
e) H. Stetter and A. Mertens, ibid., 114, 2479 (1981).
f) H. Stetter and H. Kuhlmann, ibid., 109, 2890 (1976).
g) H. Stetter, W. Basse and J. Nienhaus, ibid., 113, 690 (1980).
h) H. Kuhlmann and H. Stetter, Soap, Perfumery & Cosmetics, 97 (1981).

54. G. W. K. Cavill, B. S. Goodrich and D. G. Laing, Aust. J. Chem., 23, 83 (1970).

55. A. Mondon, Angew. Chem., 64, 224 (1952).

56. a) P. M. McCurry, Jr. and K. Abe, Tetrahedron Lett., 1387 (1974).
b) R. A. Ellison, E. R. Lukenbach and C-W. Chiu, ibid., 499 (1975).
c) E. Brown and A. Bonte, ibid., 2881 (1975).

57. A. I. Meyers and N. Nazarenko, J. Org. Chem., 38, 175 (1973).

58. K. Oshima, H. Yamamoto and H. Nozaki, J. Am. Chem. Soc., 95, 4446 (1973).

59. a) J. C. Stowell, J. Org. Chem., 41, 560 (1976).
b) S. A. Bal, A. Marfat and P. Helquist, ibid., 47, 5045 (1982).

c) C. Boga, D. Savoia, C. Trombini and A. U. Ronchi, Synthesis, 212 (1986).
d) A. Hosomi, H. Hashimoto and H. Sakurai, J. Org. Chem., 43, 2551 (1978) and references cited therein.

60. J. L. Herrmann, G. R. Kieczykowski, R. F. Romanet, P. J. Wepplo and R. H. Schlessinger, Tetrahedron Lett., 4711 (1973).

61. O. G. Kulinkovich, I. G. Tischenko and V. L. Sorokin, Synthesis, 1058 (1985).
62. a) J. Tsuji, I. Shimizu and Y. Kobayashi, Israel J. Chem., 24, 153 (1984).
b) J. Tsuji, Synthesis, 369 (1984).

63. J. Tsuji, Y. Kobayashi and I. Shimizu, Tetrahedron Lett., 39 (1979).

64. D. A. Armstead and J. Mann, Synth. Commun., 15, 1147 (1985).

65. J. M. J. Verlaak, A. J. H. Klunder and B. Zwanenburg, Terahedron Lett., 5463 (1982).

66. T. Miyakoshi and S. Saito, Yukagaku, 34, 115 (1985).

67. T. Miyakoshi, J. Jpn. Oil Chem. Soc., 35, 157 (1986).

68. T. Miyakoshi, Synthesis, 766 (1986).

69. K. K. Sharma and K. B. G. Torssell, Tetrahedron Lett., 1085 (1984).

70. M. Iwamoto, Y. Takagi, K. Kogami and K. Hayashi, Agric. Biol. Chem., 47, 115 (1983).

71. a) T. Yoshida, T. Miyakoshi and S. Saito, Yukagaku, 33, 628 (1984).
b) B. Maurer, A. Hauser, Helv. Chem. Acta., 65, 462 (1982).

72. I. Yajima, H. Sakakibara, J. Ida, T. Yazima and K. Hayashi, Agric. Biol. Chem., 49, 3145 (1985).

73. C. Boga, D. Savoia, C. Trombini and A. U-Ronchi, Synthesis, 212 (1986).

74. T. Yoshida and S. Saito, Bull. Chem. Soc. Jpn., 55, 3047 (1982).

75. a) P. Brownbridge, Synthesis, 1 (1983).
b) J. M. Conia, Pure Appl. Chem., 43, 317 (1975).

76. I. Ryu, Tetrahedron Lett., 4283 (1980).

77. R. Bohm and H.-U. Reissig, ibid., 2013 (1982).

78. a) K. Saigo, H. Kurihara, H. Miura, A. Hongu, N. Kubota, H. Nohira and M. Hasegawa, Synth. Commun., 14, 787 (1984).
b) K. Saigo, T. Yamashita and M. Hasegawa, ibid., 15, 715 (1985).

79. H. Kunz and M. Lindig, Chem. Ber., 116, 220 (1983).

80. E. Kunkel, I. Reichelt and H. U. Reissig, Justus Liebigs Ann. Chem., 802 (1984).

81. a) T. V. Lee and J. O. Okonkwo, Tetrahedron Lett., 323 (1983).
b) I. Fleming and J.Iqbal, ibid., 327 (1983).

82. F. G. Bardone, M. Mladenova and R. Couffignal, Synthesis, 1043 (1982).

83. M. Kawashima and T. Fujisawa, Chem. Lett., 1851 (1984).

84. a) M. Miyashita, R. Yamaguchi and A. Yoshikoshi, ibid., 1505 (1982).
b) M. Miyashita, R. Yamaguchi and A. Yoshikoshi, J. Org. Chem., 49, 2857 (1984).

85. a) H. Ahlbrecht and H. M. Kompter, Synthesis, 645 (1983).
b) H. Ahlbrecht and M. Dietz, ibid., 417 (1985).

86. R. Ballini and M. Petrini, ibid., 1024 (1986).

87. S. Kobayashi and T. Mukaiyama, Chem. Lett., 1183 (1987).

88. G. Cardillo, M. Orena, G. Porzi, S. Sandri and C. Tomasini, J. Org. Chem., 49, 701 (1984).

89. H. Nagashima, K. Sakai and J. Tsuji, Chem. Lett., 859 (1982).

90. E. Keinan, Synthesis, 687 (1982).

91. K. Utimoto, Y. Wakabayashi, T. Horiie, M. Inoue, Y. Shishiyama, M. Obayashi and H. Nozaki, Tetrahedron, 39, 967 (1983).

92. H. Ahlbrecht and M. Ibe, Synthesis, 421 (1985).

93. A. Manzocchi, F. Astori and E. Santaniello, ibide., 324 (1982).

94. T. Miyakoshi and S. Saito, Research Reports of the Faculty of Engineering Meiji University, 48, 221 (1985).

95. a) C. Gunther and A. Mosandl, Justus Liebigs Ann. Chem., 211 (1986).
b) H. Tsukasa, Yukagaku, 36, 51 (1987).

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