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NEW GENERAL SYNTHETIC METHODS INVOLVING π-ALLYLPALLADIUM COMPLEXES AS INTERMEDIATES AND NEUTRAL REACTION CONDITIONS

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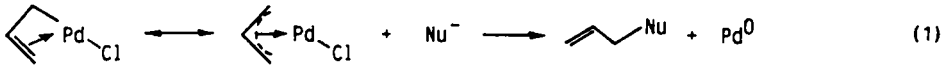
1. INTRODUCTION

We have reported in 1965 that π-allylpalladium chloride (**1**) reacts with C-nucleophiles such as malonates, acetoacetates, and enamines (Eq. 1), and shown that the reaction offers a new method of carbon–carbon bond formation.[1] On the other hand, π-allylnickel complexes **2** which have structures similar to π-allylpalladium complexes, react with electrophiles (Eq. 2).[2] Also allyl Grignard reagents react with electrophiles (Eq. 3). Since our discovery[1] of the reaction of π-allylpalladium



(1)

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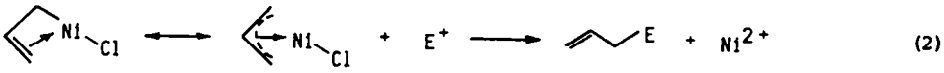

(2)

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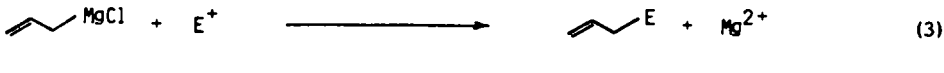
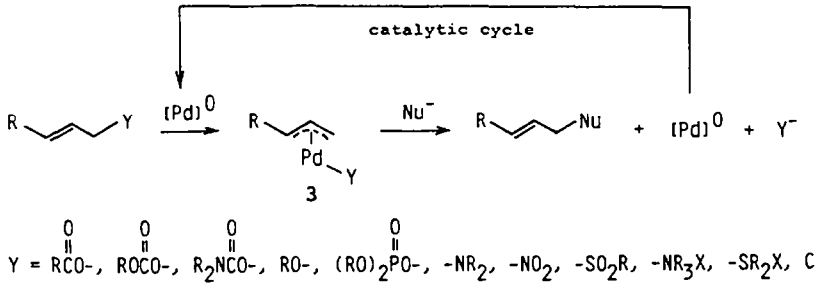


(3)

E = Electrophile Nu = Nucleophile

complexes with C-nucleophiles, the organic chemistry of π-allylpalladium complexes has attracted attention as a useful synthetic method. π-Allylpalladium complexes are formed by the reaction of various allylic compounds with Pd(0). (This is called the oxidative addition reaction.) In addition to allylic halides, some other allylic compounds such as allylic esters react with Pd(0) complexes to form π-allylpalladium complexes **3** *in situ* as intermediates, which, without being isolated, react with C-nucleophiles.[3,4] After these reactions, Pd(0) is regenerated, and this makes the whole process a catalytic cycle. This catalytic process is now widely used (Eq. 4).



Remarkable progress has been made in the organic chemistry of π-allylpalladium complexes and their application to organic synthesis in the last 15 years. A number of review articles have been published on π-allylpalladium chemistry.[5–13] In this report, new aspects of π-allylpalladium chemistry, particularly new catalytic reactions of allylic compounds such as allylic and propargyl carbonates, allyl β-keto carboxylates, and ene oxides, and their application to organic synthesis, which have been developed in our laboratories in the last five years are summarized. One characteristic feature is that these reactions proceed under mild neutral conditions. Achievements made in other laboratories are cited only when they are very closely related to our work. In these catalytic reactions, $Pd(PPh_3)_4$ can be used as a Pd(0) species, but it is unstable in the air. Stable $Pd_2(DBA)_3CHCl_3$, or $Pd_3(TBAA)_3CHCl_3$ is used with PPh_3.[14] More conveniently stable Pd^{2+} compounds such as $Pd(acac)_2$ or $Pd(OAc)_2$ are used with PPh_3, which are reduced and converted to a Pd(0) complex in the reaction medium.†

2. CATALYTIC ALLYLATION REACTIONS OF C-NUCLEOPHILES WITH VARIOUS ALLYLIC COMPOUNDS

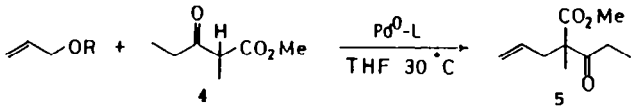
2.1. *Allylation with allylic carbonates under neutral conditions*

Many allylic compounds are used for the palladium-catalyzed allylation reactions as shown in Eq. (4). Allylic alcohols, esters, ethers, and phosphates[15] react with Pd(0) by C—O bond cleavage. With allylic amines, ammonium salts,[16] and allylic nitro compounds C—N bond cleavage takes place.[17,18] Also C—S bond cleavage is observed with allylic sulfones.[19] Allylic chlorides react with carbanions without a catalyst. But the reaction is remarkably accelerated by a palladium catalyst.[20–22] These allylic compounds have various reactivities toward Pd(0). For example, allylic chlorides are more reactive than allylic acetates in the presence of the palladium catalyst. Allylic alcohols and alkyl ethers are poor reagents. The most widely used ones are allylic esters, particularly allylic acetates. Allylic acetates are reactive, but for smooth reaction, bases such as NaH or amines must be added to the reaction medium, otherwise the reaction is very slow.

Allylic carbonates and allylic carbamates were found to be very reactive substrates, reacting with C-nucleophiles without addition of bases at room temperature.[23–25] In other words, C—C bond formation is possible under neutral conditions. In Table 1, reactivities of various allylic compounds with the β-keto ester **4** as a nucleophile are compared. The allylation reaction proceeds under neutral conditions at room temperature smoothly only with allyl carbonate (**6**) and allyl carbamate **7**. In the absence of bases, almost no reaction takes place with allyl acetate (**8**) and phosphate **10**, which react rapidly on the addition of bases. Formation of allyl alkyl ethers by the palladium-catalyzed reaction of allyl alkyl carbonates is known,[26] but the reaction of π-allylpalladium with C-nucleophiles is much faster than with alkoxide, thus no allyl alkyl ether formation takes place in the presence of C-nucleophiles. Allyl phenyl ether (**9**) reacts under neutral conditions, but heating is necessary.

†The following abbreviations are used in this report: DBA, dibenzylideneacetone; TBAA, tribenzylideneacetylacetone; dppe, bis(diphenylphosphino)ethane; acac, acetylacetone.

Table 1. Palladium-catalyzed allylation of β-keto ester with various allylic compounds

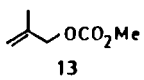
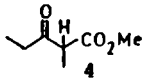
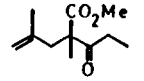
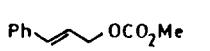
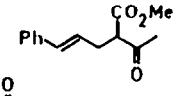
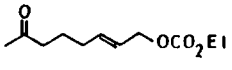
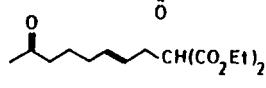
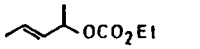
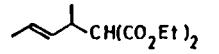
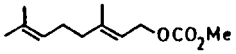
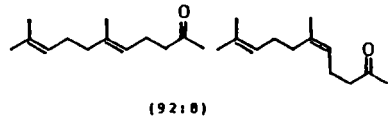
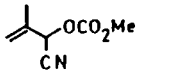
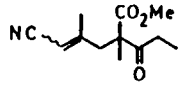
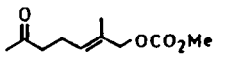
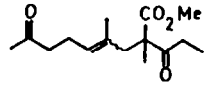


4 5

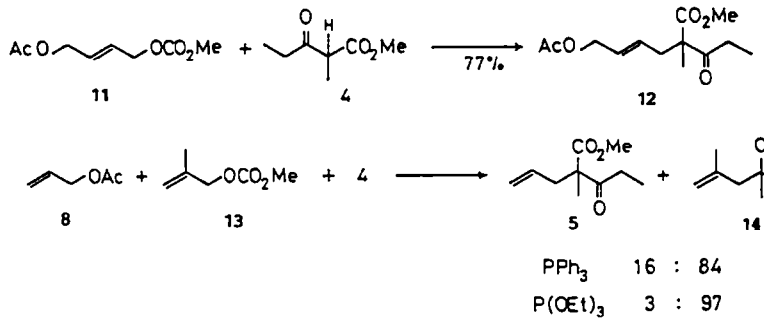
Run	Allylic compounds	Base	Ligand	Time	Yields (%)
1	$(CH_2{-}CHCH_2)O_2CO$ (**6**)	—	PPh_3	10 min	98
2	,,	—	$P(OEt)_3$	3.5 h	94
3	,, (50°)	—	$P(OPh)_3$	23 h	19
4	$CH_2{=}CHCH_2OCON(i\text{-}Pr)_2$ (**7**)	—	PPh_3	10 min	100
5	$CH_2{=}CHCH_2OAc$ (**8**)	—	PPh_3	22 h	24
6	,,	NaH	PPh_3	30 min	95
7	,,	—	$P(OEt)_3$	24 h	5
8	,,	NaH	$P(OEt)_3$	7 h	95
9	$CH_2{=}CHCH_2OPh$ (**9**)	—	PPh_3	19 h	0
10	,, (65°)	—	PPh_3	7.5 h	62
11	,,	NaH	PPh_3	4 h	5
12	$CH_2{=}CHCH_2OPO(OEt)_2$ (**10**)	—	PPh_3	24 h	6
13	,,	NaH	PPh_3	1.5 h	96

The higher reactivity of allyl carbonates with respect to acetates is clearly shown by the chemoselective reaction of 4-acetoxy-2-butenyl methyl carbonate (**11**) with β-keto ester **4**. The reaction takes place only with the allylic carbonate group to give **12** without attacking allylic acetate group under neutral conditions. Thus stepwise allylation with **11** is possible under neutral conditions first and then basic conditions (Eq. 5). As another example, in a competitive reaction of allyl acetate (**8**) and methallyl methyl carbonate (**13**) with the β-keto ester **4**, the carbonate reacted predominantly when PPh_3 was used as the ligand, but the selectivity of the carbonate became higher by using $P(OEt)_3$ as a ligand (Eq. 6).[24,27] Some other examples of the reactions of various carbonates with malonate and acetoacetates are shown in Table 2. Facile allylation of dimedone (5,5-dimethyl-1,3-

Table 2. Allylation of malonates and β-keto esters with allylic carbonates under neutral conditions

Allylic compounds	Nucleophiles	Ligands	Temp (°)	Time (h)	Products	Yields (%)
 13	 4	PPh_3	30	0.2		92
	$CH_3COCH_2CO_2Me$	PPh_3	25	1		90
	$CH_2(CO_2Et)_2$	dppe	30	0.5		91
	$CH_2(CO_2Et)_2$	PPh_3	30	2		86
	$CH_3COCH_3CO_2Me$	dppe	50	3	 (92:8)	74
 CN	4	PPh_3	65	5		93
	4	dppe	65	2		99

cyclohexanedione), or N-hydroxysuccinimide with allyl carbamates, derived by the reaction of amino acids or peptides with allyl chloroformate, under mild conditions is useful for the protection and deprotection of amino groups.[28,29]



The reason why the palladium-catalyzed allylation with allyl carbonates can be carried out under neutral conditions is explained by the following mechanism (Fig. 1). At first the oxidative addition of allyl carbonates gives the π-allylpalladium carbonate **15**, which undergoes decarboxylation to form π-allylpalladium alkoxide **16**. The alkoxide anion formed *in situ* then abstracts active hydrogen from an active methylene compound to generate a carbanion. The *in situ* formation of the carbanion in this way explains why the allylation reaction with allyl carbonates can be carried out without the addition of bases. Finally the carbanion attacks the π-allylpalladium complex to form the allylated product with regeneration of the Pd(0) species, making the whole reaction catalytic.

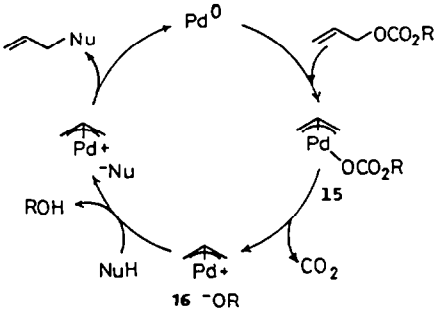
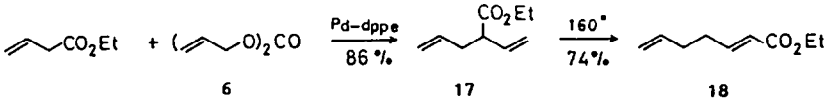
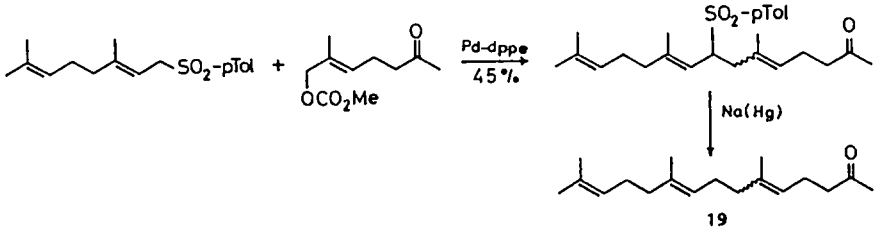


Fig. 1.

The allylation of active methylene compounds, which have one electron-withdrawing group and hence are less acidic than malonates and acetoacetates, is carried out with allylic carbonates under neutral conditions in boiling THF (Table 3). In these reactions dppe is a better ligand than PPh_3. The allylated products were obtained in high yields from allyl sulfones, benzyl sulfone, nitro compounds, β,γ-unsaturated nitriles, and β,γ-unsaturated carbonyl compounds.

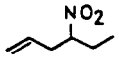
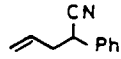
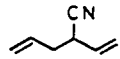
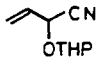
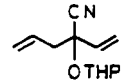
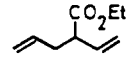
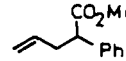
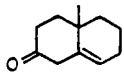
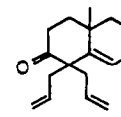
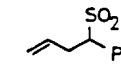
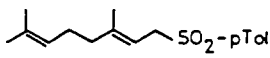
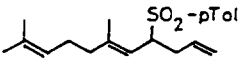
By these reactions, unsymmetrical 1,5-dienes **17** with functional groups such as ester, nitrile, or sulfone at C-3 can be prepared (Eq. 7). These compounds are converted to 1,5-dienes **18** with the





functional groups at C-1 by the Cope rearrangement. Chemoselective allylation of the allyl sulfone group is possible without attacking a ketone group present in the same molecules. Based on this

Table 3. Allylation reactions with diallyl carbonate in boiling THF with $Pd_2(DBA)_3CHCl_3$–dppe

Nucleophiles	Products	Yields (%)
$CH_3CH_2CH_2NO_2$		76
$PhCH_2CN$		91
$CH_2{=}CHCH_2CN$		73
		66
$CH_2{=}CHCH_2CO_2Et$		86
$PhCH_2CO_2Me$		91
		70
$PhCH_2SO_2$—*p*-Tol		92
		72

chemoselectivity, farnesylacetone (**19**) was synthesized by the allylation with allyl carbonate (Eq. 8).

The facile reaction of allyl sulfones and β,γ-unsaturated nitriles under neutral conditions with allyl carbonates suggests the following type of cycloaddition reaction to form cyclopentane rings.[30] As shown in Fig. 2, the allylic carbonates **20** which have an electron-withdrawing group at the methallylic position undergo decarboxylation by the reaction of Pd(0) to form **21**. This is followed by intramolecular deprotonation of the activated methylene group in the same molecule to form

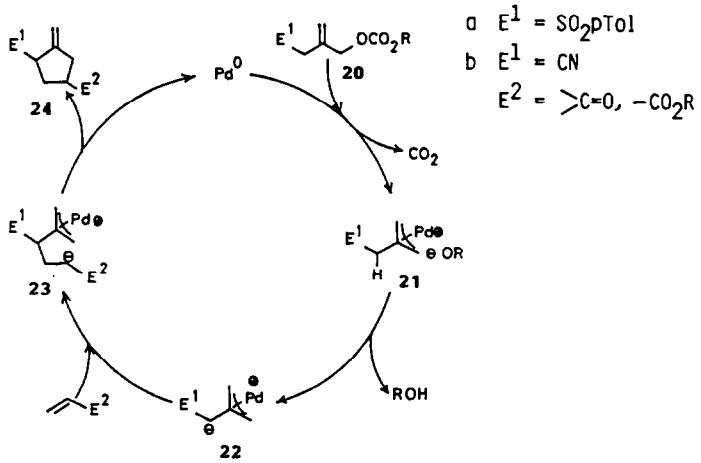
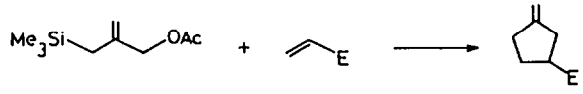


Fig. 2.

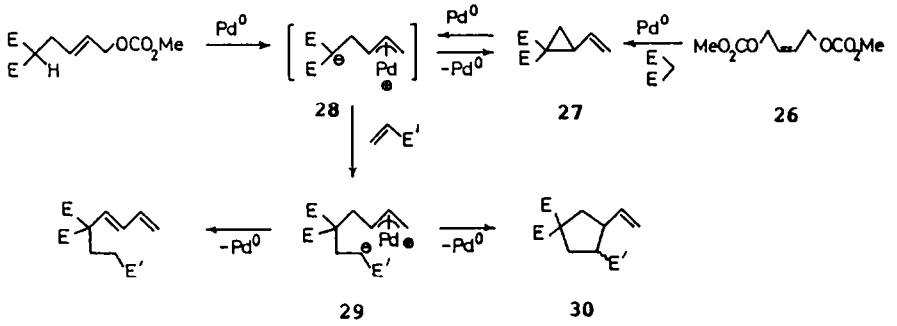
the π-allylpalladium complexes **22**. Carbanion **22** undergoes a Michael addition reaction with olefins with electron-withdrawing groups generating carbanions **23**, which then attack the π-allylpalladium system intramolecularly. Thus, [3+2]cycloaddition occurs forming five-membered compounds **24** with an exomethylene group.

The results of the reaction of allylic carbonates with various electron-deficient olefins are shown in Table 4. With nitrile **20b**, the exomethylene double bond isomerized to the endo position. The bicyclo[3.3.0]octane system can be synthesized by the reaction with cyclopentenone. By this palladium-catalyzed cycloaddition reaction, various five-membered rings with functional groups can be synthesized, which undergo further transformation. For example, allyl sulfone **25** undergoes palladium-catalyzed allylation with elimination of the sulfone, rearrangement, and desulfonylation (Fig. 3). As a related reaction, Trost and Chan reported the following [3+2]cycloaddition based on the generation of the carbanion by desilylation (Eq. 9).[31-34]



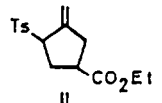
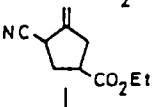
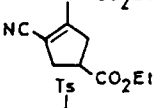
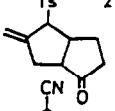
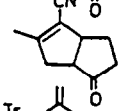
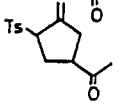
(9)

Vinylcyclopropanes **27** with two electron-withdrawing groups E, which are prepared by the palladium-catalyzed reaction of the biscarbonate of 2-butenediol (**26**), undergo the palladium-catalyzed cycloaddition reaction with electron-deficient olefins to form vinylcyclopentanes (Eq. 10).[35] The reaction proceeds by the formation of π-allylpalladium complexes **28** with a carbanionoid



(10)

Table 4. Palladium catalyzed [3+2] cycloaddition

Run	Allyl carbonate	Olefin	Time (h)	Products	Isolated yields (%)
1	**20a**	CO_2Et	20		77
2	**20b**	"	2		66
3	**20b**	"	20		72
4	**20a**		10		65
5	**20b**	"	18		71
6	**20a**		1		89

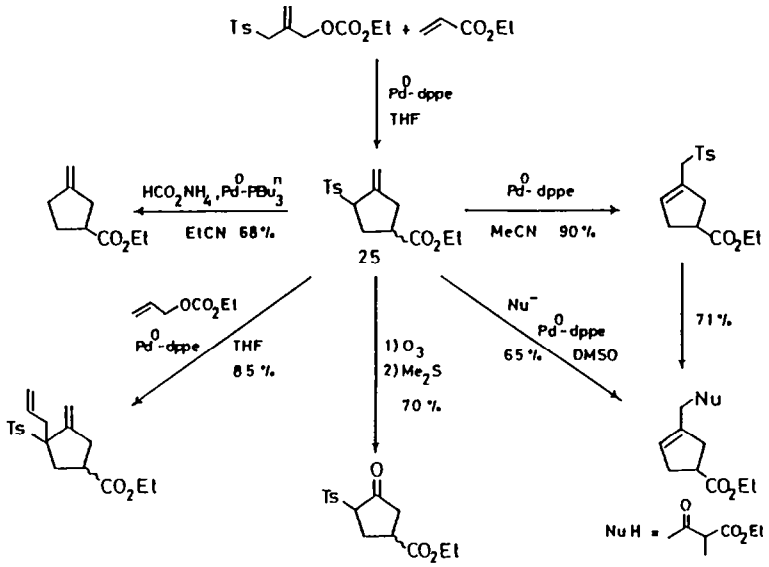
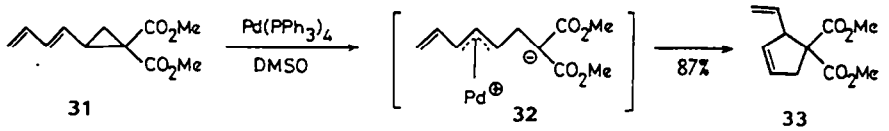


Fig. 3.

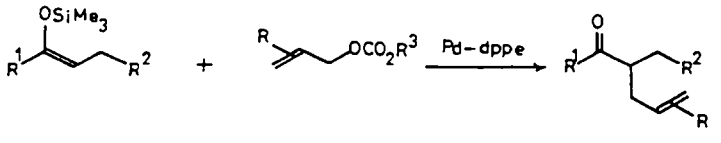
residue which undergoes Michael type addition to electron-deficient olefins. The generated carbanion **29** then attacks the π-allylpalladium group forming cyclopentane **30**. Results are shown in Table 5. 1,3-Butadienylcyclopropanes **31** activated by two electron-withdrawing groups smoothly rearrange to vinylcyclopentenes **33** via π-allylpalladium complex **32** by ring opening (Eq. 11).[36,37]



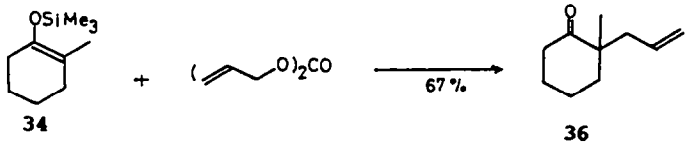
(11)

Simple ketones cannot be allylated satisfactorily with allylic carbonates. Recently allylation of ketones with O-allylisoureas under neutral conditions has been reported,[38] but the reaction gives a mixture of mono- and diallylated products. Also palladium-catalyzed allylations of ketones via their lithium,[39] boron,[40] and tin[41] enolates have been reported.

Ketones and aldehydes can be monoallylated cleanly with allyl carbonates via their silyl enol ethers.[42] Silyl enol ethers are useful intermediates for organic synthesis and are used frequently with Lewis acids such as $TiCl_4$, or the fluoride anion.[43] The intramolecular reaction of an allylic acetate with a silyl enol ether promoted by an organoaluminum reagent has also been reported.[44] The palladium-catalyzed reaction of silyl enol ethers with allyl carbonates proceeds smoothly without using Lewis acids, or bases (Eq. 12), whereas the attempted palladium-catalyzed allylation of silyl enol ethers with either allyl acetate or allyl ammonium salts gave poor results.[41,45] Only allylic carbonates are satisfactory allylating agents. Using the reaction with allyl carbonates, mono-allylation at the α-position of ketones and aldehydes is possible. The reaction is regioselective. For example, the two isomeric silyl enol ethers **34** and **35** are prepared from 2-methylcyclohexanone via thermodynamic and kinetic enolates. Their allylation gave regioselectively 2-allyl-2-methyl-



(12)



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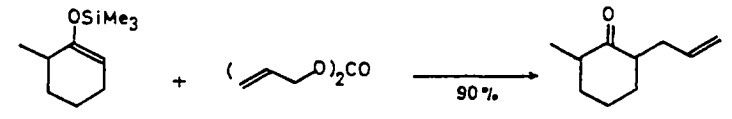
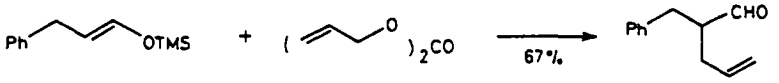


35 37 (14)

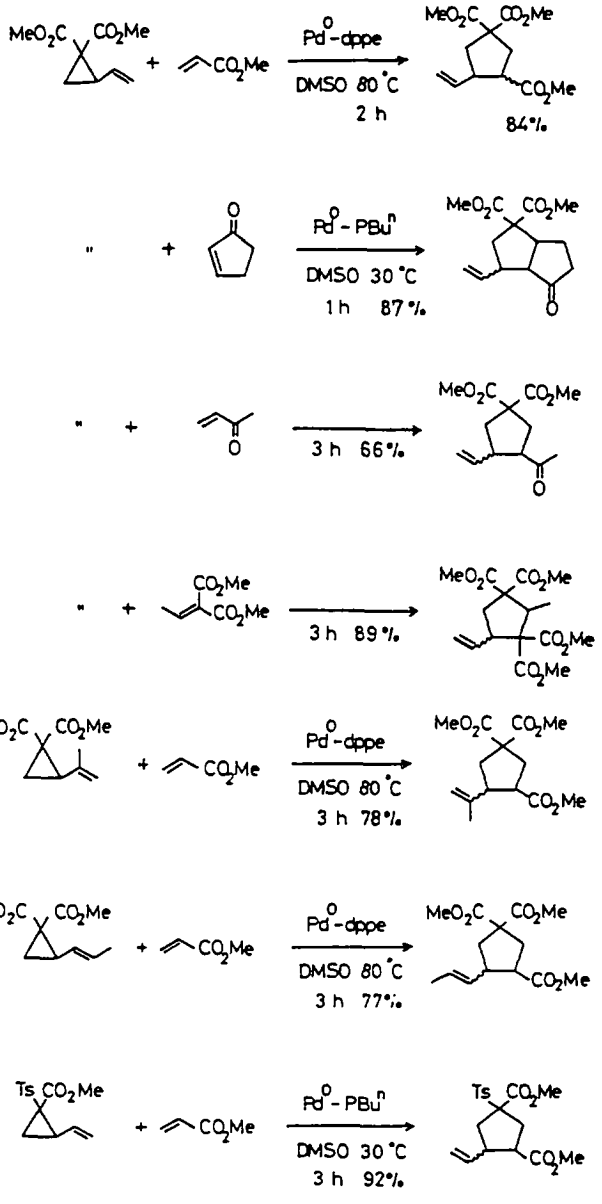


(15)

cyclohexanone (**36**) and 2-methyl-6-allylcyclohexanone (**37**), respectively, without forming a mixture of these isomers (Eqs 13 and 14). Clearly the reaction proceeds without proton transfer. Allylation of aldehydes via silyl enol ethers is also possible (Eq. 15). For this reaction, dppe is a more suitable ligand than PPh_3.

This reaction can be explained by the mechanism shown in Fig. 4. At first the oxidative addition

Table 5



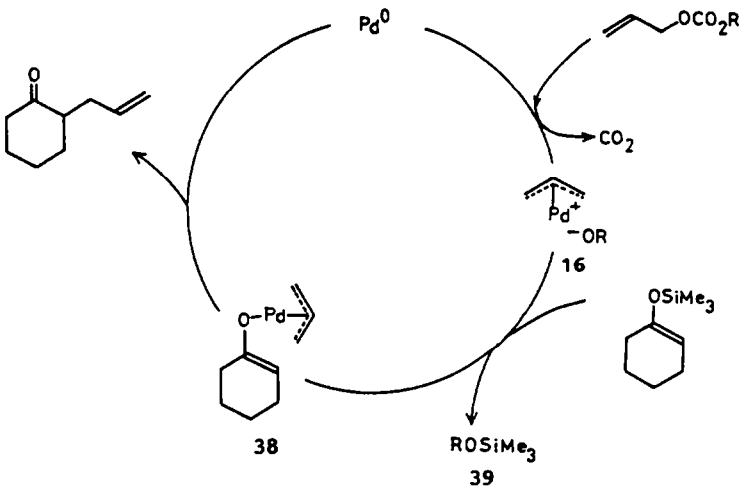
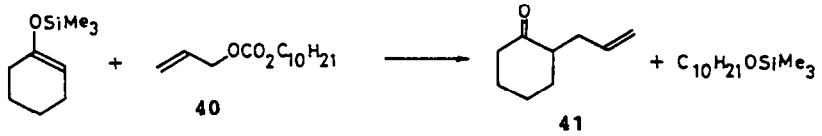


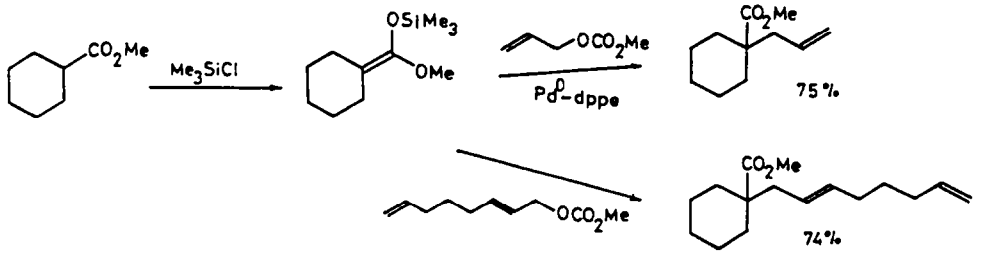
Fig. 4.

of allyl carbonates to Pd(0) occurs and this is followed by decarboxylation giving π-allylpalladium alkoxide **16**, which undergoes transmetalation with silyl enol ethers giving π-allylpalladium enolate **38** and alkoxysilane **39**. Finally reductive elimination gives the α-allylated ketones with the regeneration of Pd(0) species, which then starts a new catalytic cycle again. In support of this mechanism, the allylation reaction with allyl decyl carbonate (**40**) gave decyl silyl ether (**41**) (Eq. 16).



(16)

Ketene silyl acetals are prepared by the silylation of ester enolates. Unlike silyl enol ethers which are used extensively in organic synthesis, ketene silyl acetals have a rather limited use, because they are more sensitive to various reagents. Ketene silyl acetals were found to react with allyl carbonates with Pd–PPh_3 as catalyst to give α-allylated esters in high yields (Eq.17).[46] The allylation can be carried out simply by refluxing a solution of ketene silyl acetals, allylic carbonate, and catalytic amounts of Pd and dppe. The reaction can also be applied to the allylation of lactones (Eq. 18). This is a useful method for α-monoallylation of esters and lactones.



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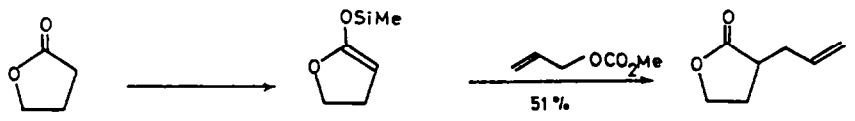
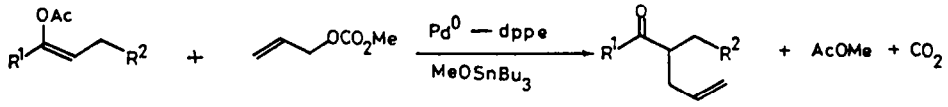


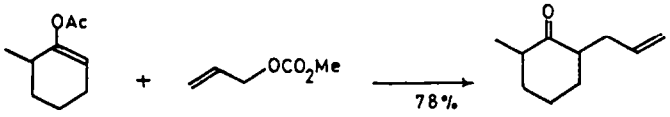
(18)

Enol acetates are enolate equivalents which are easily prepared from ketones. However, they are relatively stable and few reactions of enol acetates are known. Enol acetates can be allylated with allyl carbonates by using Pd and Sn compounds as bimetallic catalysts (Eq. 19).[47] When enol acetates are treated with allyl carbonates in the presence of catalytic amounts of Pd–PPh_3 and tributyltin

methoxide, α-allyl ketones are obtained in high yields. For this reaction, dppe is the most suitable ligand. The allylation is regioselective as shown by Eqs (20) and (21).



(19)



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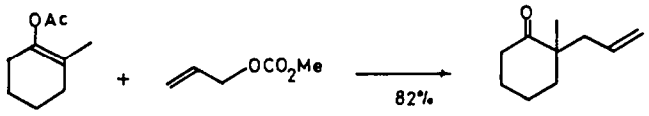
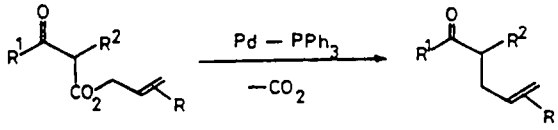


(21)

This unique bimetallic catalysis can be rationalized by the mechanism shown in Fig. 5. The *in situ* formation of tin enolates **42** by the reaction of enol acetates with tributyltin methoxide **43** is known.[48] The transmetalation of tin enolates **42** with the π-allylpalladium alkoxide complex **44**, formed by the oxidative addition of allyl carbonates to the Pd(0) complex and subsequently decarboxylation, gives the π-allylpalladium enolates **38**, which undergo reductive elimination giving the α-allyl ketones. Regeneration of the tributyltin alkoxide **43** and Pd(0) makes the reaction catalytic. The *in situ* formation of tin enolates by the reaction of tin methoxide with enol acetates, followed by the palladium-catalyzed reaction with alkenyl and aryl halides to give 2-alkenyl or 2-aryl ketones has been reported.[49,50] However, in these cases, stoichiometric amounts of tin methoxide are consumed.

2.2. *Allylation via allyl β-keto carboxylates and allyl alkenyl carbonates*

Thermal rearrangement of allyl β-keto carboxylates with decarboxylation to give α-allyl ketones is known as the Carroll rearrangement (170–200°).[51] The reaction is useful for terpene synthesis. The same rearrangement is expected to be promoted by using Pd catalyst via π-allylpalladium complex formation. The smooth rearrangement proceeds in boiling THF or even at room temperature by using Pd–PPh_3 as catalyst (Eq. 22).[52,53] Geranylacetone (**46**) was obtained from geranyl acetoacetate (**45**) in high yield with retention of configuration of the double bond in boiling THF (Eq. 23). From linalyl acetoacetate (**47**), a mixture of geranylacetone and nerylacetone was obtained in a ratio of 3 : 2 (Eq. 24).



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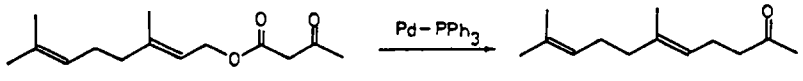
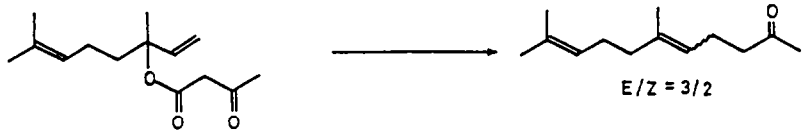


45 46

(23)



47

(24)

The palladium-catalyzed Carroll rearrangement can be explained by the mechanism shown in Fig. 6. Oxidative addition of the allylic ester is followed by facile decarboxylation to give the π-

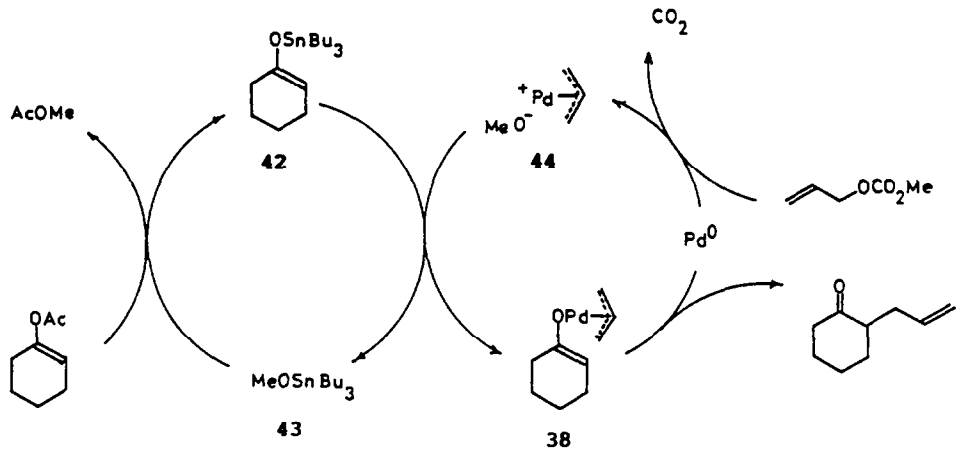
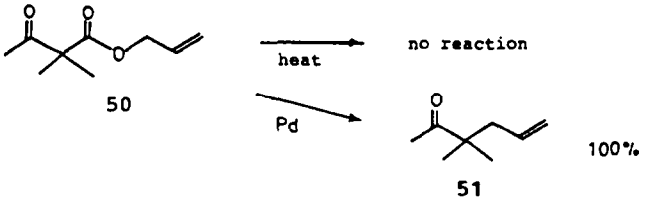


Fig. 5.

allylpalladium enolate **48**, which then undergoes reductive elimination to give allyl ketones. This mechanism is completely different from the thermal rearrangement mechanism, which proceeds by a [3,3]sigmatropic rearrangement of an enol form **49** of allyl β-keto ester. In order to prove the difference between the mechanisms, the reaction of the allylic ester **50**, which has no hydrogen at the α-position, and hence enolization is impossible, was carried out. No thermal reaction took place. On the other hand, smooth palladium-catalyzed reaction proceeded to give allyl ketone **51** in nearly quantitative yield. The reaction was regioselective and the allyl group was introduced at the more crowded carbon (Eq. 25). Thus this reaction also offers a good method for the monoallylation of ketones.



(25)

Allyl carbonates are very reactive allylating agents of β-keto esters under mild conditions, and allyl β-keto carboxylates undergo smooth decarboxylation. It is therefore of interest to determine which reacts faster when allyl β-keto carboxylate is treated with allyl carbonate. It was found that the allylation with allyl carbonate is faster than the Carroll rearrangement of allyl β-keto carboxylate.[54] Based on this difference of reactivity, it is possible to introduce two allylic groups at the α-position of ketones. The regioselective introduction of two alkyl groups at the α-position of ketones is generally rather difficult, but this can be done in principle by regioselective consecutive alkylation. However, the regioselective generation of an anion at the same carbon after the first alkylation is difficult. One-pot tandem allylation of ketones is possible based on the palladium-catalyzed reaction

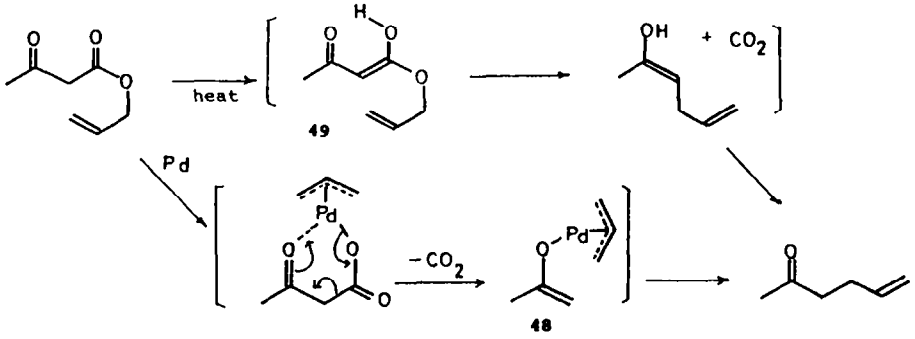
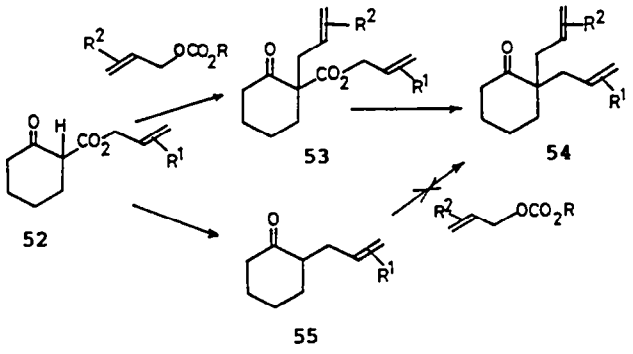


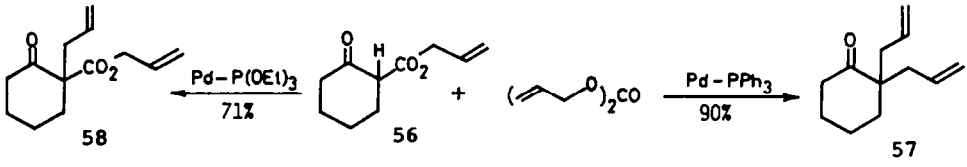
Fig. 6.

of allyl β-keto carboxylates with allylic carbonates under neutral conditions. In other words, the regioselective α,α-diallylation of ketones is possible. The first step is the allylation of β-keto carboxylate **52** with allyl carbonates to afford **53** and this is then followed by the decarboxylation–allylation (Carroll rearrangement) of **53** which gives the α,α-diallylated ketones **54**. If the Carroll reaction is faster, then simple allylation takes place to give **55** without forming the diallylated product (Eq. 26). Reaction of allyl 2-oxocyclohexanecarboxylate (**56**) and diallyl carbonate with



(26)

Pd–PPh_3 in THF gave 2,2-diallylcyclohexanone (**57**) in 81–90% yields with small amounts of allyl 1-allyl-2-oxocyclohexanecarboxylate (**58**) and 2-allylcyclohexanone. When the reaction was carried out using $P(OEt)_3$, instead of PPH_3, the allylated ester **58** was obtained as the main product and the diallyl ketone **57** was hardly obtained showing that the phosphite ligand is active only for the allylation of the β-keto ester, but not for Carroll rearrangement (Eq. 27). α,α,α-Triallylacetone was



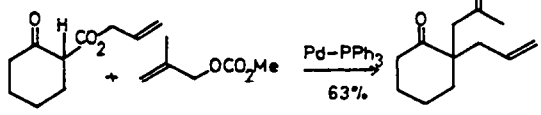
(27)

similarly obtained by the reaction of allyl acetoacetate with diallyl carbonate in 93% yield (Eq. 28).

Different allyl groups can be introduced using appropriate allyl β-keto esters and allylic carbon-

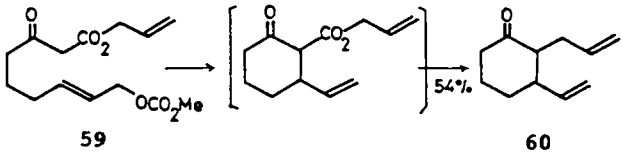
(28)

ates. 2-Allyl-2-methallylcyclohexanone was obtained in 63% yield by the reaction of allyl 2-cyclohexanonecarboxylate with methallyl methyl carbonate (Eq. 29). Intramolecular reaction offers an



(29)

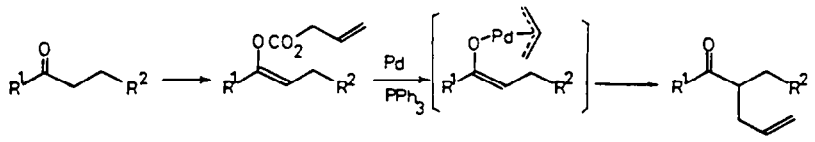
interesting synthetic method for α,β-disubstituted cyclic ketones. The reaction of β-keto ester carbonate **59** at 80° afforded 2-allyl-3-vinylcyclohexanone (**60**) in 54% yield after chromatographic purification. At first cyclization takes place by intramolecular allylation. The second step is the decarboxylation–allylation of the allyl β-keto ester (Eq. 30). The overall transformation of β-keto



(30)

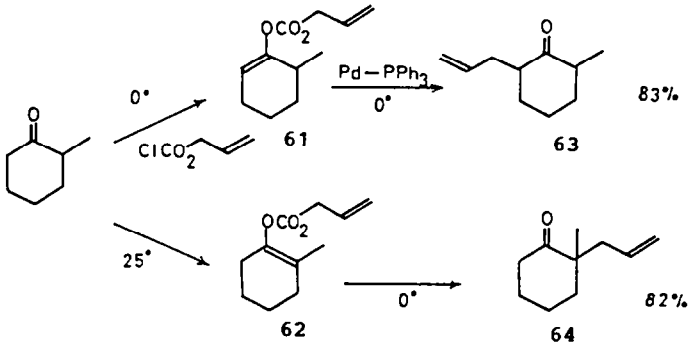
esters to diallyl ketones is a one-pot reaction but it may be regarded as the generation of the α,α-dianion equivalent and its stepwise quenching with two alkyl groups. The palladium-catalyzed tandem diallylation under neutral conditions is very useful, because this transformation is difficult to carry out by the usual alkylation methods.

Allyl enol carbonates (allyl alkenyl carbonates), undergo facile palladium-catalyzed rearrangement to give allyl ketones in high yields.[55] Alkenyl allyl carbonates can be prepared easily by the reaction of allyl chloroformates with enolates of ketones or aldehydes. Allyl enol carbonates are more reactive than allyl β-keto carboxylates and the reaction proceeds even at 0° by using Pd–PPh_3 as catalyst (Eq. 31). Allyl alkenyl carbonates prepared from cyclopentanone and cyclohex-



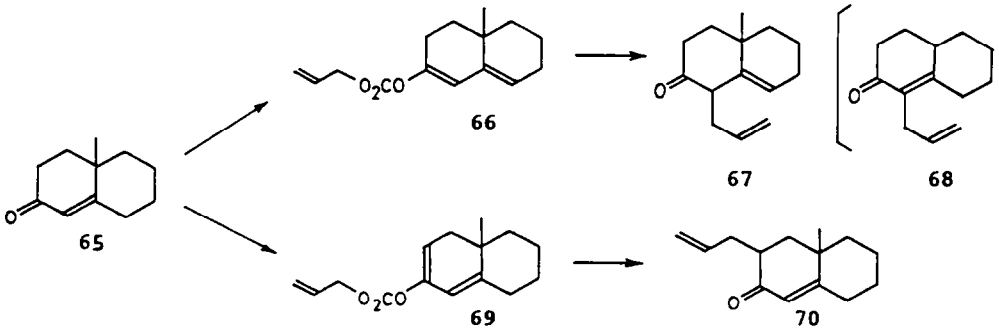
(31)

anecarboaldehyde were converted to 2-allylcyclopentanone (82%) and α-allylated aldehyde (64%). High regioselectivity was confirmed by the reaction of 2-methylcyclohexanone. The enol carbonate was prepared by quenching the thermodynamically stable potassium enolate at 25° with allyl chloroformate as a 93 : 7 mixture of **62** and **61**. The reaction of **62**, without separation of **61**, gave a mixture of 2-allyl-2-methylcyclohexanone (**64**) and 6-methyl-2-allylcyclohexanone (**63**) in 82% yield (**64** : **63** = 95 : 5). On the other hand, the allyl alkenyl carbonate **61**, prepared from kinetically generated potassium enolate at 0° (99 : 1 mixture of 61 : 62), was converted to **63** (**63** : **64** = 98 : 2) in 83% yield (Eq. 32). The dienyl carbonate **66**, prepared from the thermodynamically stable potassium



(32)

enolate of 10-methyl-$\Delta^{1,9}$-2-octalone (**65**), was converted to the 1-allylated octalone **67** as the sole product in 78% yield. The olefin was deconjugated and no isomerization to form **68** took place. On the other hand, the thermodynamically generated dienyl carbonate **69** was converted to the 3-allylated octalone **70** in 80% yield (Eq. 33). In this reaction, oxidative addition and decarboxylation

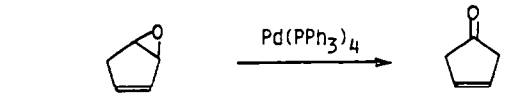


(33)

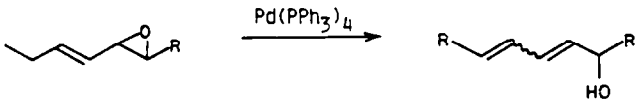
give the π-allylpalladium enolate **48**, which is the same intermediate formed by the reaction of allyl-β-keto carboxylates with Pd(0) (Fig. 6). The decarboxylative allylation of allyl β-keto carboxylates and allyl alkenyl carbonates is also catalyzed by molybdenum, nickel, and rhodium complexes.[56]

2.3. *Regio- and stereoselective reaction of ene oxides*

2.3.1. *Reactions with C-nucleophiles under neutral conditions.* Noyori and co-workers reported the palladium-catalyzed rearrangement of diene monoepoxide (ene oxides) to β,γ-unsaturated ketones and dienols (Eqs 34 and 35).[57] Ene oxides are one kind of allylic ethers and it is possible to

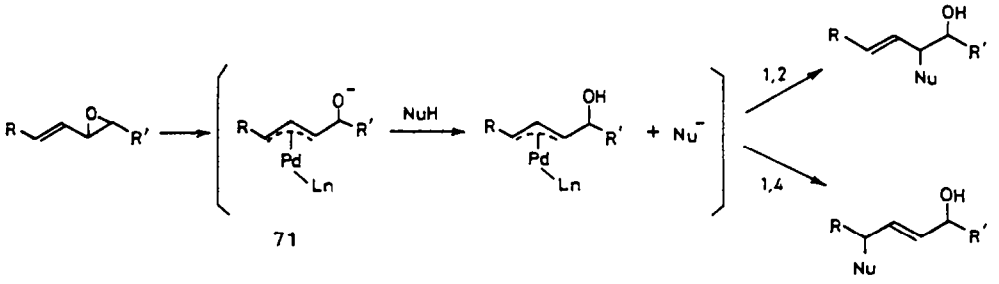


(34)



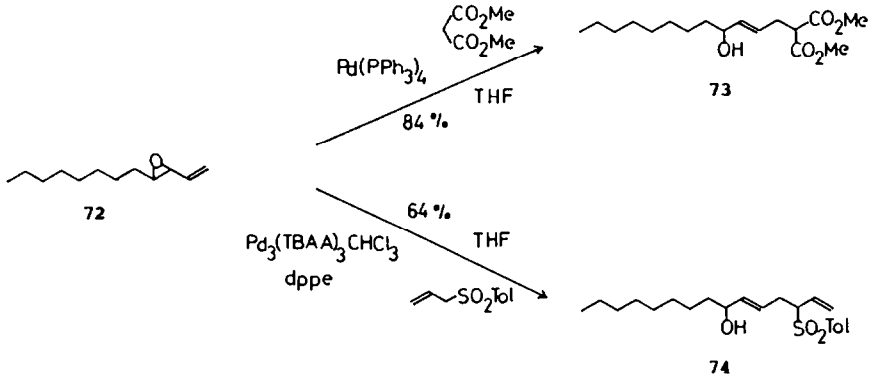
(35)

form π-allylpalladium complexes **71** with Pd(0). Reaction of common allyl alkyl ethers with Pd(0) is very slow, but ene oxides are highly reactive due to steric effects. Once π-allylpalladium complex formation takes place, then it reacts with C-nucleophiles. In addition, in π-allylpalladium complex **71**, an alkoxide ion is generated. Thus as in the reaction of allylic carbonates, the reaction with C-nucleophiles should proceed smoothly under neutral conditions.[58,59] In the reaction of ene oxides, how to achieve this high regio- and stereoselectivity is a problem (Eq. 36).



(36)

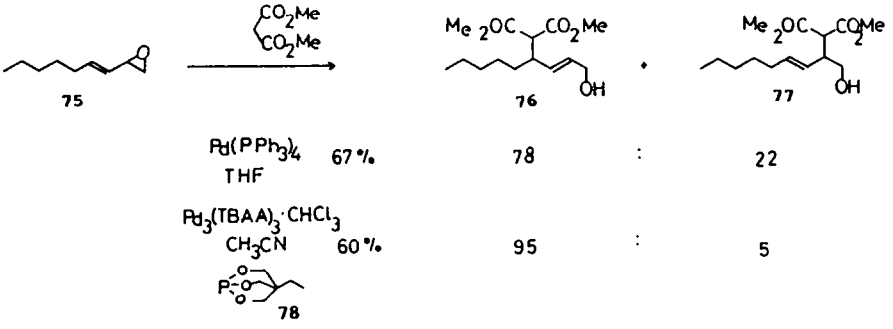
Regioselective 1,4-addition was observed in the reaction of ene oxide **72** with malonate to give (*E*)-allyl alcohol **73** without giving any 1,2-addition product. Such regioselectivity can not be observed in the uncatalyzed reactions of various nucleophiles. Similarly allyl sulfone reacted with the ene oxide under neutral conditions giving the 1,4-adduct **74** cleanly (Eqs 37 and 38). However,



(37)

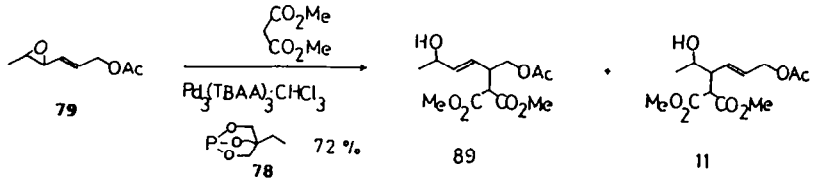
(38)

the reaction of ene oxide **75** which has a terminal oxide structure is not completely regioselective. Although the 1,4-adduct **76** is the main product, a considerable amount of the 1,2-adduct **77** was obtained. But regioselectivity for 1,4-addition becomes higher by using polar solvents such as DMSO or CH_3CN. Also the ratio of the 1,4-adduct becomes higher by using the cyclic phosphite **78** rather than PPh_3 (Eq. 39). In addition to high regioselectivity, the reaction shows high chemoselectivity.



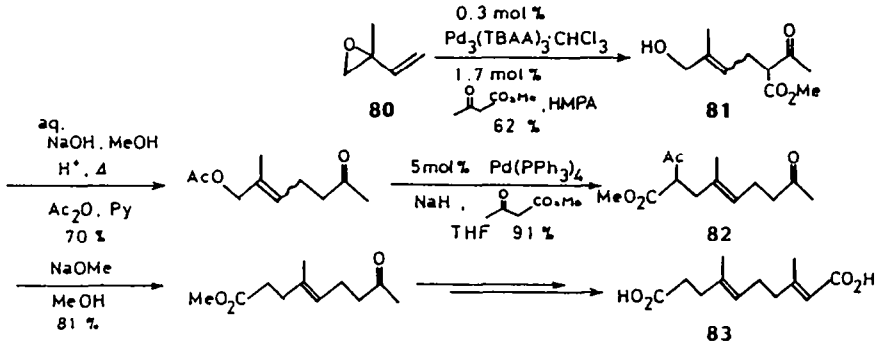
(39)

Ene oxide **79** also has an allylic acetate grouping in the same molecule, but the reaction took place cleanly with the ene oxide group giving 1,4-adduct selectively. No reaction takes place with the allylic acetate group, because of neutral reaction conditions (Eq. 40).



(40)

The regioselective 1,4-addition reaction gives allylic alcohols, which can then be used for the palladium-catalyzed reaction again after acetylation or carbonation. In other words, it is possible to introduce two different nucleophiles on both sides of the ene oxide using palladium catalyst. As an example, Monarch butterfly pheromone **83** was synthesized from isoprene monoepoxide **80**. First the acetoacetate group was introduced selectively giving the allylic alcohol **81**. After modification of the acetoacetate group, the alcohol was then acetylated. The second palladium-catalyzed reaction with acetoacetate afforded product **82** with *E*-olefin in high selectivity. Conversion of **82** to pheromone **83** is known (Eq. 41). The highly regioselective cyclization of ene oxides has been applied to the syntheses of macrocyclic compounds.[60]



(41)

2.3.2. *Application to syntheses of steroids and prostaglandins.* The introduction of a side chain to steroids by applying the highly regioselective and stereoselective palladium-catalyzed reactions of ene oxides has been achieved (Fig. 7).[61,62] First enone **85** was prepared by the palladium-catalyzed dehydrogenation reaction of enol acetate **84** described in Section 5.3. The epoxidation, followed by Wittig reaction afforded the desired ene oxides **86** and **89**. The palladium-catalyzed reaction of **86** with malonate afforded **87** and the reaction of **89** with β-keto ester **90** afforded product **91** in high yields. In these reactions, no isomers of **87** and **91** were formed, and the diastereoselectivity was higher than 95% in both cases. The absolute stereochemistry of C-20 was determined by converting **87** to 15-hydroxycholesterol **88**, and **91** to 20-isocholesterol **92**. Thus the introduction of 15-hydroxy and 20-methyl or alkyl groups based on the palladium-catalyzed reaction of ene oxides offers a useful method for the synthesis of oogoniol **93** and pavoninin **94**, naturally occurring steroids with a 15-hydroxy group.

Very efficient chirality transfer observed in these reactions can be explained by the mechanism shown in Fig. 8. First Pd(0) attacks the epoxide from the backside to form the π-allylpalladium complex **95**. Then the nucleophile attacks from the opposite side of the palladium to give product **96** by an overall *syn*-S_N2 reaction. Marino *et al.* carried out the reaction of similar steroidal ene oxides with alkyl copper reagents. The reaction with the copper reagent was *anti*-S_N2 type. Also in addition to the 1,4-addition product **97**, a considerable amount of 1,2-adduct **98** was obtained depending on the alkyl copper reagents (Fig. 8).[63] The regioselective reaction of ene oxide was applied to the synthesis of digitoxigenin by Wicha and Kabat, but stereoselectivity was not a problem in this synthesis.[64]

Aiming at the stereoselective synthesis of prostaglandins, the palladium-catalyzed cyclization of ene oxides **99** and **104** was attempted (Fig. 9).[65] The reaction gave regioselectively the six-membered lactone and produced the appropriate relative stereochemistry at positions 12 and 15 as well as the (*E*)-

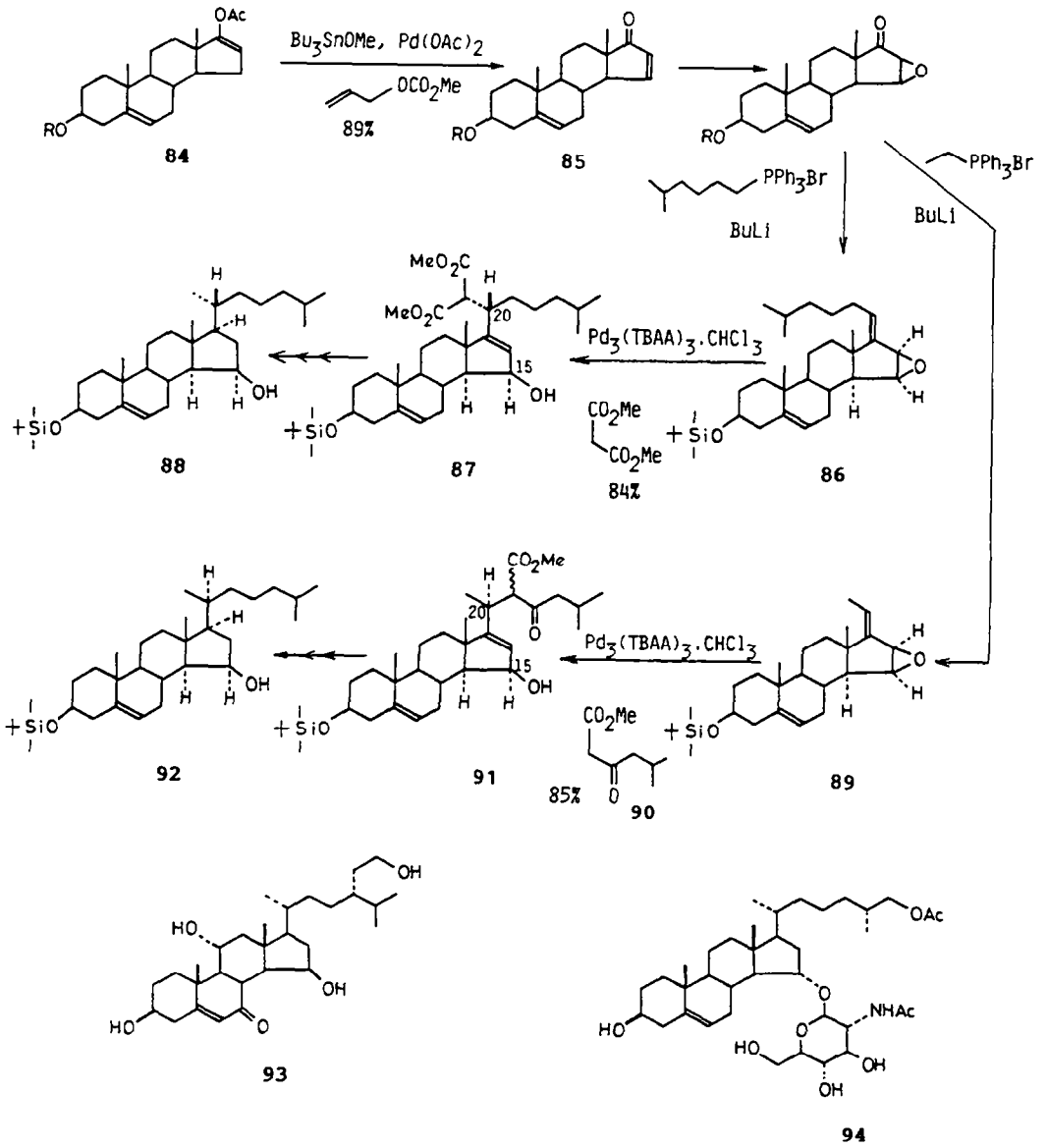
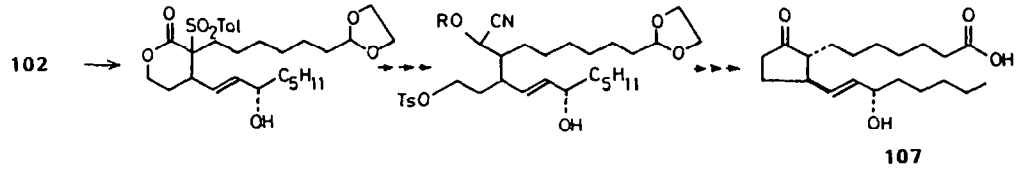


Fig. 7.

double bond. The palladium-catalyzed cyclization of ene oxide **99**, which has a *Z*-double bond and an *E*-epoxide, afforded the six-membered lactones **102** and **106** in a ratio of 92:8. Similarly ene oxide **104**, which has an *E*-double bond and epoxide afforded the same lactones in a ratio of 5:95. That lactones **102** and **106** are diastereoisomers differing in the stereochemistry at C-5 was confirmed by the oxidation of the allylic alcohol **102** to enone **103**, which by non-selective reduction gave **102** and **106**. In these cyclizations, formation of the eight-membered lactone and the *Z*-double bond was not observed. Lactone **102** was converted to 11-deoxyprostaglandin E_1 (**107**) and its structure was confirmed by comparing it with an authentic sample (Eq. 42). By this way, the relative stereo-



(42)

chemistry at C-12 and C-15 in **102** and **106** was established. The high stereoselectivity observed in these cyclization reactions can be explained by the following mechanism. In the reaction of **99**,

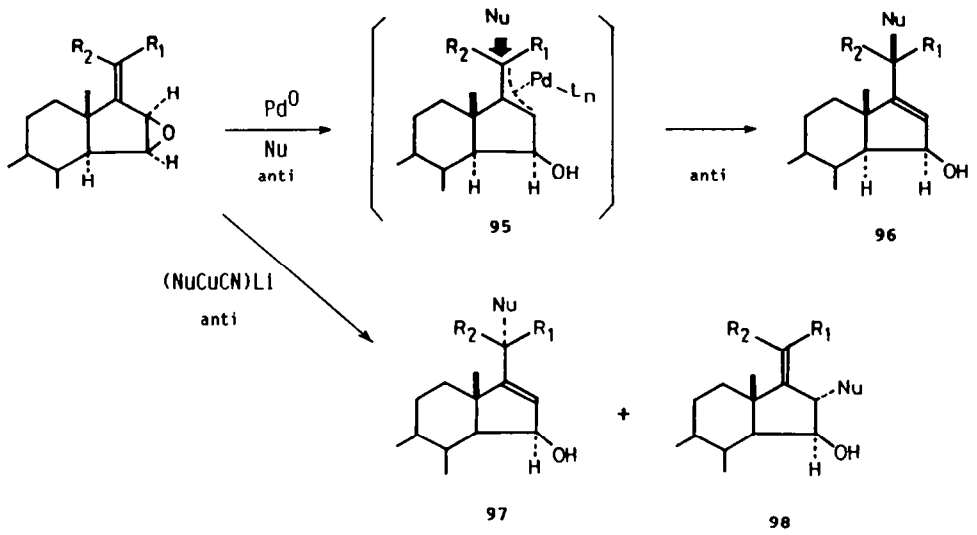


Fig. 8.

Pd(0) attacks from the backside of the epoxide to form the rather unstable *anti,syn*-complex **100**, which isomerizes to stable *syn,syn*-complex **101**. The attack of the C-nucleophile takes place towards the face remote from the palladium giving lactone **102**. In the case of **104**, the cyclization proceeds via *syn,syn*-complex **105** to give lactone **106** directly (Fig. 9).

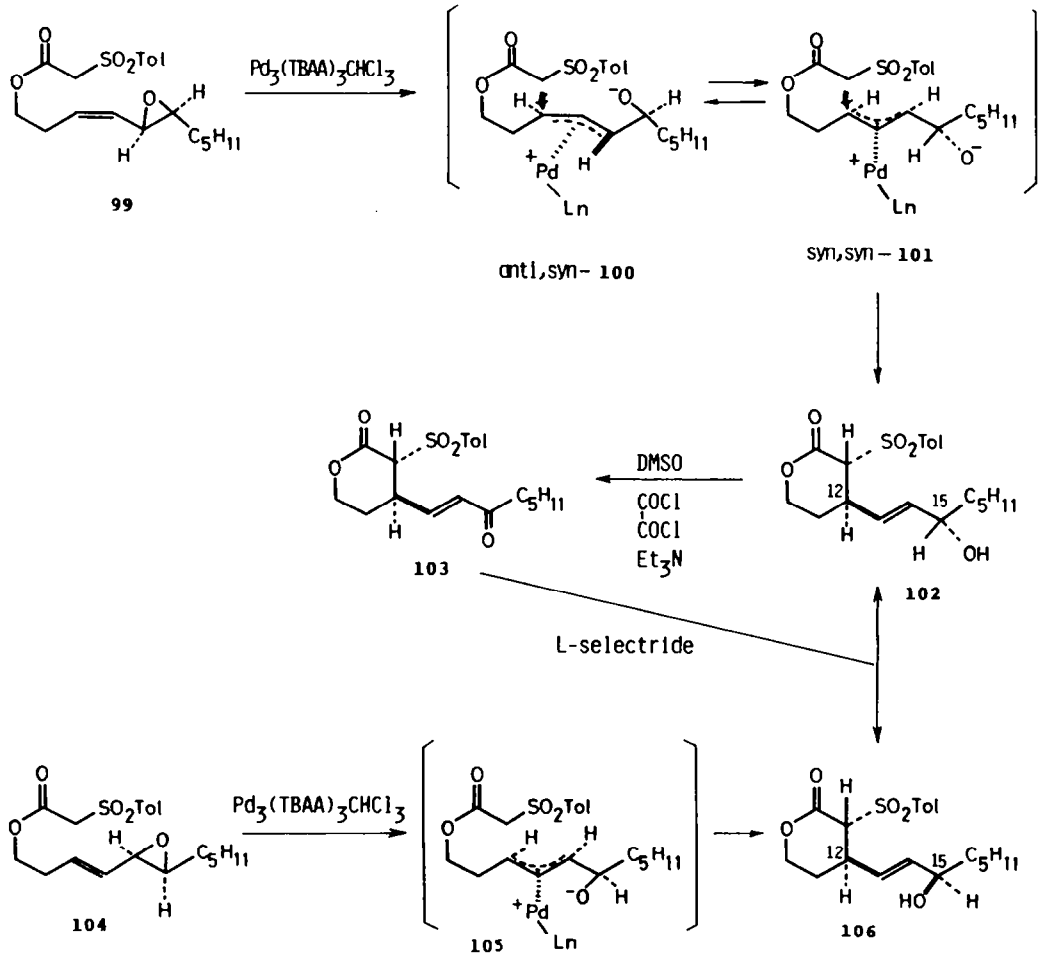
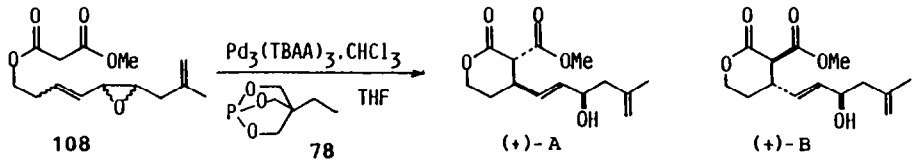


Fig. 9.

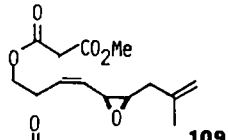
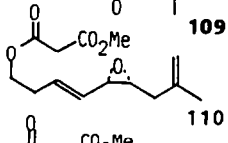
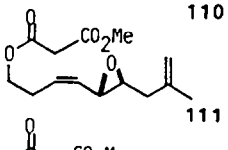
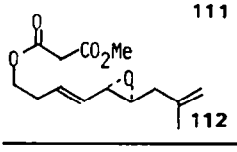
Further studies on the stereo- and regioselective cyclization of ene oxide **108** was also carried out (Eq. 43). Four possible isomers **109–112** derived from the combination of the *Z* and *E* con-



108 78 (+)-A (+)-B (43)

figurations of the double bond and the epoxide have been synthesized in optically active forms, and subjected to palladium-catalyzed cyclization under neutral conditions using bicyclic phosphite **78** as ligand.[66] The cyclization proceeded regioselectively giving the six-membered lactones. Furthermore, the reaction was apparently stereospecific and only one isomer was obtained from each ene oxide as shown in Table 6.

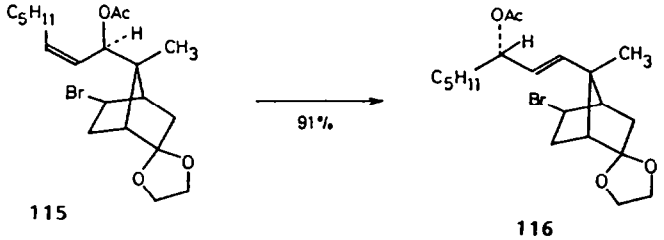
Table 6

	Time (h)	Ratio
 **109**	0.5	100:0 [(+)-A:(+)-B]
 **110**	1.5	0:100 [(+)-A:(+)-B]
 **111**	4	6:94 [(−)-A:(−)-B]
 **112**	4	100:0 [(−)-A:(−)-B]

The palladium-catalyzed highly regio- and stereoselective reaction of ene oxides under mild neutral conditions results in efficient chirality transfer. This is very useful for the construction of natural products with unstable functional groups. Particularly, since optically active ene oxides can be synthesized by the well-known asymmetric epoxidation of allylic alcohols, asymmetric reduction of acetylenic ketones, and modification of naturally occurring sugars. The reaction has obvious potential for the syntheses of many natural products in optically active forms.

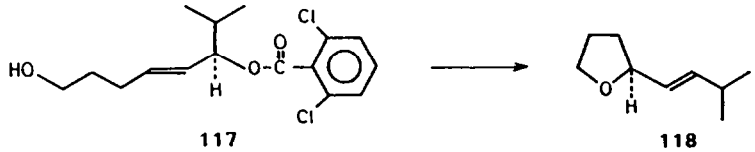
2.4. *Chirality transfer in allylic systems*

Very high diastereoselective chirality transfer was observed in the palladium-catalyzed reaction of chiral ene oxides. The chirality transfer is an important method for asymmetric synthesis, and extensive studies have been carried out. Very efficient palladium-catalyzed chirality transfer has been observed recently with some allylic systems.[67] These studies are summarized in this section. Complete C—O to C—O chirality transfer was observed in the allylic rearrangement of allylic acetate **115** catalyzed by $PdCl_2(MeCN)_2$ at 25°. Only a single product **116** was obtained in this reaction in a high yield (Eq. 44).[68] This highly diastereoselective rearrangement was applied to



115 116 (44)

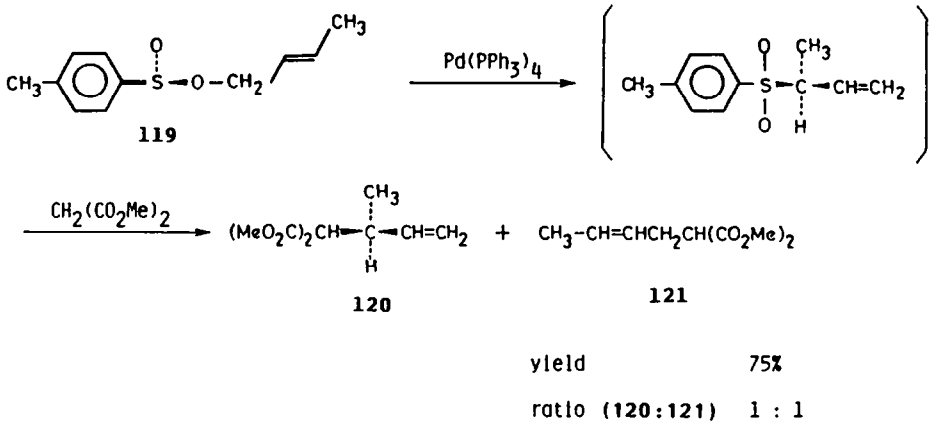
stereocontrolled syntheses of prostaglandins possessing either the C-15(*S*) or C-15(*R*) configuration. Efficient C—O to C—O chirality transfer was achieved in the cyclization reaction of (*R*) allylic dichlorobenzoate **117** catalyzed by $Pd(PPh_3)_4$ at 35° to give (*S*)-2-(3-methyl-1-(*E*)-butenyl)-tetrahydrofuran (**118**) in 95% yield.[69] A slight loss of efficiency (5–10%) was observed in a similar cyclization of the *Z*-form of the allylic ester (Eq. 45). On the other hand, the attempted cyclization to pyrrolidines gave poor transfer of chirality.



(45)

117 **118**

The C—S to C—C chirality transfer was observed in the palladium-catalyzed rearrangement of chiral allylic sulfinates to allylic sulfones, followed by the reaction with malonate.[70] The reaction of *trans*-2-butenyl-(*S*)-(−)-*p*-toluenesulfinate (**119**) with sodiomalonate in the presence of $Pd(PPh_3)_4$ and PPh_3 in boiling THF proceeded to give two products **120** and **121**. Dimethyl (*S*)-(+)-1-butenyl-3-ylmalonate (**120**) was obtained as one product, in an optically active form with 83% chirality transfer (Eq. 46). With the Z-form of the allylic sulfinate, the efficiency was 78%. The optically



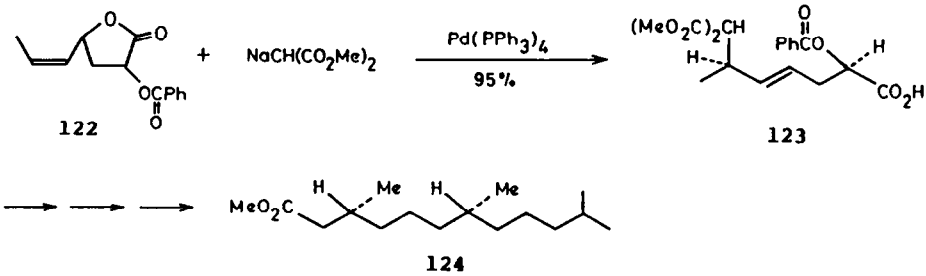
(46)

119 **120** **121**

yield 75%

ratio (120:121) 1 : 1

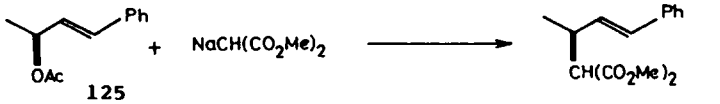
active allylic lactone **122** was prepared from glucose and subjected to the $Pd(PPh_3)_4$ catalyzed reaction with sodiomalonate in THF to give acid **123** in 95% yield.[71] The chirality transfer was stereospecific. This acid **123** was converted to the side chain of vitamin K (**124**) (Eq. 47). Another



(47)

122 **123** **124**

example of complete C—O to C—C chirality transfer is the reaction of (*S*)-(*E*)-3-acetoxy-1-phenyl-1-butene (**125**) with sodiomalonate to give (*S*)-dimethyl 1-((*E*)-styryl)ethyl malonate in high yield (Eq. 48).[72]

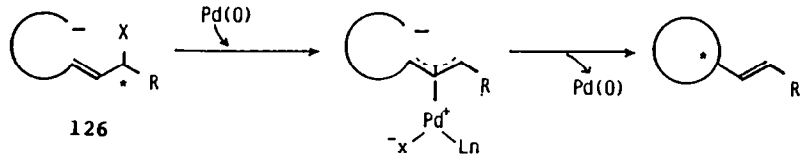


(48)

125

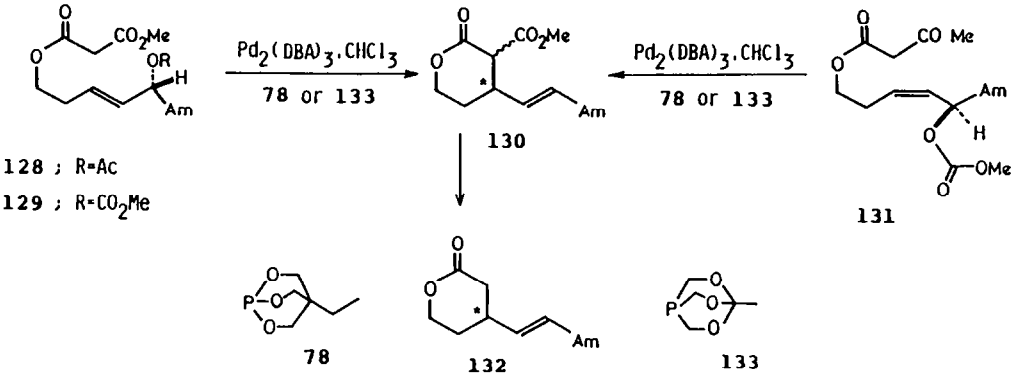
Thus several examples of complete chirality transfer have been reported. Also it has been shown by NMR studies that the isolated 1,3-unsymmetrically substituted π-allylpalladium systems such as

128 never racemize and only undergo epimerization via a π–σ–π mechanism.[73-76] However, racemization or poor chirality transfer has been observed in some cases. Equation (49) shows the mechanism of racemization during the cyclization of **126** via π-allylpalladium **127**.[77]



(49)

Efficient chirality transfer was observed in the palladium-catalyzed cyclization of methyl (5*R*)-methoxycarbonyloxy-(3*E*)-decenyl malonate (**129**) and its (*Z*)-isomer **131** (Eq. 50). The former gave (*R*)-lactone **130** and the (*Z*)-isomer gave the (*S*)-lactone selectively. The degree of chirality transfer was determined by converting **130** to lactone **132** by decarboxylation. The cyclization proceeded smoothly using the cyclic phosphine **133** and phosphite **78** as a ligand. No cyclization took place with PPh_3. Although the cyclization proceeds under neutral conditions, the higher rate and chirality transfer were observed by prior formation of carbanion by the addition of NaH.



(50)

Results are summarized in Table 7 which suggest the following characteristics.

(1) In the presence of NaH, cyclizations of (*E*)-allylic carbonate **129** and (*Z*)-isomer **131** proceed with higher than 94% chirality transfer, regardless of ligand (Nos. 5, 7, 9 and 11).

(2) In the absence of NaH, cyclizations of (*E*)-allylic carbonate **129** and (*Z*)-isomer **131** give generally a lower degree of chirality transfer than in the presence of NaH (No. 3 vs 5, 6 vs 7, 8 vs 9, 10 vs 11).

(3) The cyclization of allylic carbonate **129** was faster and gave a higher chirality transfer than that of the corresponding allylic acetate **128** in the presence of NaH (No. 1 vs 5).

(4) The degree of chirality transfer depends on the concentration of palladium; the higher the concentration the lower the optical yield (Nos. 2–4).

Table 7

No.	Substrate	Ligand, Base	Time	Pd(0) mol %	Yield of **130** (%)	$[\alpha]_D^{25}$ of **132**	Chirality transfer (%)
1	**128**	**78**, NaH	3 h	10	72	+9.4 (*R*)	75
2	**129**	,, , —	20 min	20	71	+5.4 (*R*)	41
3	,,	,, , —	30 min	10	62	+7.7 (*R*)	58
4	,,	,, , —	70 min	3	88	+10.4 (*R*)	78
5	,,	,, , NaH	10 min	10	53	+12.8 (*R*)	96
6	,,	,, , —	3 h	10	65	+12.0 (*R*)	90
7	,,	**133**, NaH	90 min	10	65	+13.3 (*R*)	100
8	**131**	**78**, —	30 min	10	67	−7.3 (*S*)	55
9	,,	,, , NaH	10 min	10	63	−12.5 (*S*)	94
10	,,	**133**, —	3 h	10	73	−7.3 (*S*)	65
11	,,	,, , NaH	90 min	10	68	−13.3 (*S*)	99

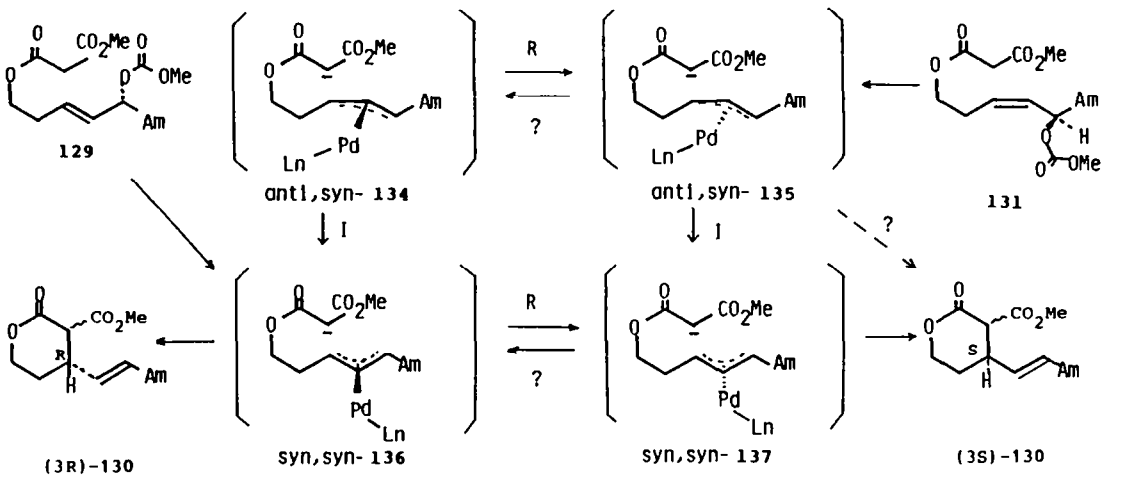


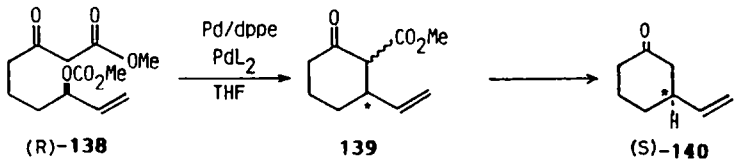
Fig. 10.

These observations can be rationalized by the mechanism shown in Fig. 10. The stable *syn,syn* complex **136** with phosphine **133** as ligand, formed from (*E*)-**129** with inversion by oxidative addition, is quite stable and the following alkylation proceeds from the opposite side of palladium to give (3*R*)-**130** (No. 6). The same complex **136** having phosphite **78** instead of phosphine **133**, however, partially racemizes to *syn,syn*-**137** to give a mixture of (3*R*)- and (3*S*)-**130** in the absence of NaH (No. 3). Similarly in the absence of NaH, the less stable *anti,syn*-**135** with phosphine or phosphite as ligand, generated from (*Z*)-**131**, partially racemizes to the stable *syn,syn*-**136** via complex **134** or **137** (Nos. 8 and 10). On the other hand, in the presence of NaH *syn,syn*-**136** and *anti,syn*-**135** were alkylated, regardless of ligand, with less racemization to give (3*R*)-**130** and (3*S*)-**130**, respectively (Nos. 5, 7, 9 and 11). The extent of racemization during the reaction is markedly dependent upon the order in which the two reactions are carried out:

(a) the carbanion is generated before π-allylpalladium complex formation, or
(b) the carbanion is generated after π-allylpalladium complex formation.

One rational explanation for the racemization of **136** to **137** or **135** to **134** is that π-allylpalladium is displaced from the opposite side of the complex by Pd(0) present in the reaction medium, as a strong nucleophile, with inversion of stereochemistry. Thus the higher concentration of Pd(0) lowers the efficiency of the chirality transfer (Nos. 2–4). The fact that acetate **128** gave a lower degree of chiral transfer than that of carbonate **129** under the same conditions means the racemization takes place by attack of the acetate anion to the allyl group from the same side of palladium.[72,78,79] Faller *et al.*[73] and Bosnich *et al.*[74] have proposed the rapid epimerization, but without racemization, of the less stable *anti,syn* π-allylpalladium complexes such as **134** and **135** to the corresponding stable *syn,syn* complexes **136** and **137** via π–σ–π interconversion. But this may not always be so. The difference in optical yield in cyclizations of (*E*)-**129** and (*Z*)-**131** in the presence of the phosphite (Nos. 6 and 10) indicates that the π–σ–π isomerization is not always faster than the nucleophilic attack to the π-allylpalladium complex by Pd(0) or C-nucleophile. Bosnich *et al.* proposed the rapid racemization and epimerization of monosubstituted π-allylpalladium systems via the π–σ–π mechanism, and suggested the difficulty in asymmetric allylation in these simple systems.[74] However, this is not always the case as shown by the following example. Catalytic cyclization of methyl (*R*)-3-oxo-7-(methoxycarbonyloxy)-8-nonenoate (**138**) using $Pd(OAc)_2$-dppe in THF at 25° (without addition of NaH) gave selectively the six-membered ring compound, 3-vinyl-2-methoxycarbonylcyclohexanone (**139**), in 80% yield.[80] But complete racemization took place. However, the cyclization of **138** in the presence of NaH proceeded very rapidly even at 0° in THF, yielding optically active **139**, which was decarboxylated to give (*S*)-3-vinylcyclohexanone (**140**) (Eq. 51). The chirality transfer was stereospecific. This means that, contrary to the proposal by Bosnich *et al.*, the

cyclization of **138** is faster than π–σ–π conversion (**143** ⇋ **141** ⇋ **142**), and the contribution of achiral σ-allyl form **142** is almost negligible (Eq. 52).



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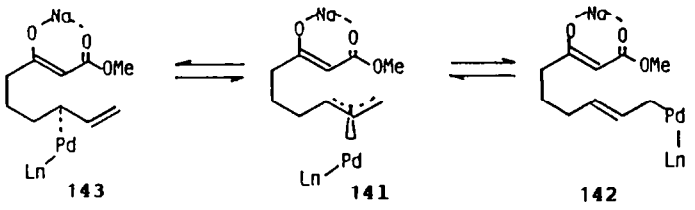


(52)

The interesting features of the cyclization of (*R*)-**138** are given below.

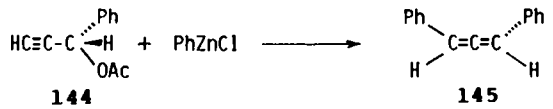
(1) As far as a preformed resonance-stabilized carbanion is available, it attacks intramolecularly the chiral monosubstituted π-allylpalladium group which is formed by oxidative addition of the catalyst with inversion of the chiral center, from the opposite side of the palladium to form (*R*)-**139**; the cyclization proceeds with complete overall retention of the original chiral center.

(2) On the other hand, while the chiral π-allylpalladium **141** retains its configurational integrity at least around 0°, the methoxide ion formed from carbonate *in situ* at 25° in THF, in the absence of NaH, can only abstract an active hydrogen at a rate comparative to racemization of the monosubstituted π-allylpalladium.

The results of the cyclization cleanly demonstrate that the racemization is not always very fast even in monosubstituted π-allyl systems, especially in the case of an intramolecular catalytic allylation. Similarly a high degree of chirality transfer (83%) by the palladium-catalyzed alkylation of chiral monosubstituted allylic sulfinates was found even in refluxing THF as described above (Eq. 46).[70]

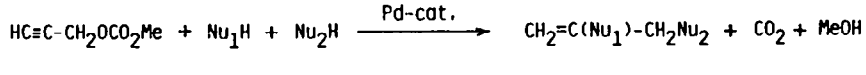
3. REACTIONS OF PROPARGYL CARBONATES WITH C-NUCLEOPHILES UNDER NEUTRAL CONDITIONS

In contrast to the extensive studies on the palladium-catalyzed reactions of allylic compounds, very few studies have been carried out on the palladium-catalyzed reactions of propargyl compounds. Conversion of propargyl esters to 1,2-dienes by the reaction of hard C-nucleophiles such as organomagnesium[81] and zinc compounds[82] has been reported. For example, the acetate of (*R*)-(−)-1-phenyl-2-propyn-1-ol (**144**) was converted to (*R*)-1,3-diphenylpropadiene (**145**) by 1,3-addition of phenylzinc chloride catalyzed by $Pd(PPh_3)_4$ (Eq. 53).[83] Propargyl carbonates **146** react with soft C-



(53)

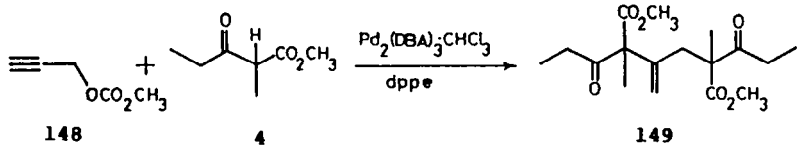
nucleophiles to give 2,3-disubstituted propenes **147** under neutral conditions via the formation of π-allylpalladium complexes (Eq. 54).[84]



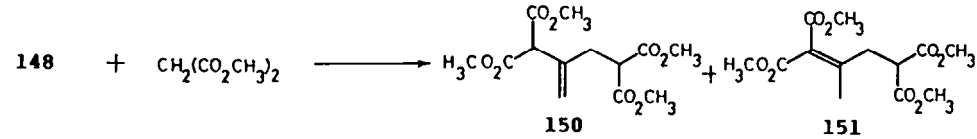
(54)

Reaction of methyl propargyl carbonate (**148**) with two equivalents of methyl 2-methyl-3-oxopentanoate (**4**) in boiling THF for 2 h in the presence of $Pd_2(DBA)_3CHCl_3$ and dppe

(Pd/dppe = 1/2, 5 mol%) gave adduct **149** in 69% yield. Reaction of dimethyl malonate with **148** also afforded a 1 : 1 mixture of adducts **150** and **151** in 49% yield in boiling THF for 2 h. In boiling dioxane for 9 h **151** was obtained in 69% yield (Eqs 55 and 56).

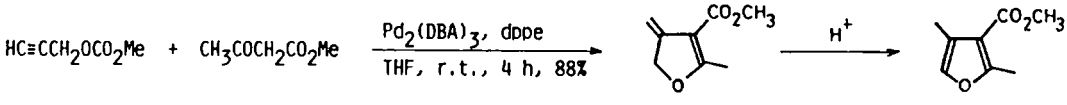


148 **4** **149** (55)

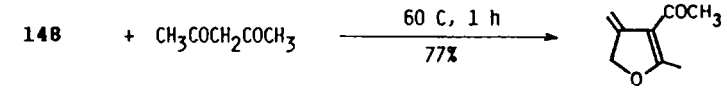


150 **151** (56)

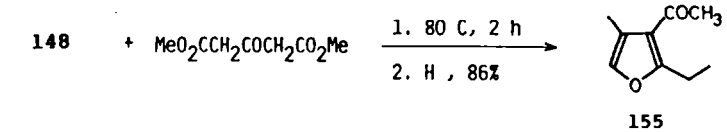
β-Keto esters and β-diketones bearing two active hydrogens react with propargyl carbonates in a 1 : 1 ratio. In other words, both C- and O-alkylations take place with these compounds to give 4-methylene-4,5-dihydrofurans and 4-methylfurans. Reaction of **148** with methyl acetoacetate in THF at room temperature for 2 h in the presence of Pd–dppe catalyst (5 mol%) gave 3-methoxycarbonyl-2-methyl-4-methylene-4,5-dihydrofuran (**152**) in 88% yield. This smooth cyclization proceeds under completely neutral conditions. Methylenefuran **152** is unstable and isomerizes to the stable furan **153** quantitatively under acidic conditions (Eq. 57). Acetylacetone, dimethyl 3-oxoglutarate, and 1,3-cyclohexanedione reacted similarly with **148** to give the corresponding furans, **154**–**156** (Eqs 58–60). Reactions of both methyl 2-butynyl carbonate (**157**) and methyl 1-methylpropargyl carbonate (**158**) with acetacetate gave the same methylidene furan **159** selectively without forming the ethylidene furan (Eqs 61 and 62). Reaction of methyl 1-methyl-2-butynyl carbonate (**160**) gave (*E*)-2,5-dimethyl-3-ethylidenefuran (**161**) in 94% yield (Eq. 63).



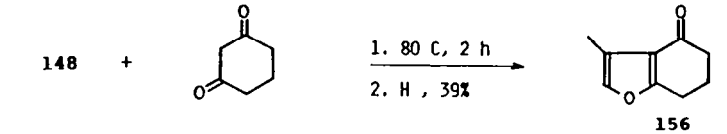
152 **153** (57)



154 (58)

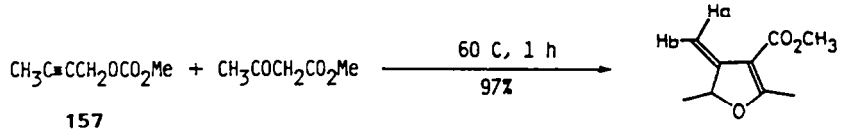


155 (59)



156 (60)

The reaction of **157** with methyl α,α-bisdeuterioacetoacetate (**162**) gave the 5-deuteriofuran **163** (97%) as the sole product, but the reaction of **158** afforded furan **164** deuterated at the methylene carbon (1 : 1 *E*/*Z* mixture, 67%). One deuterium from **162** was transferred to **157** or **158** at a different



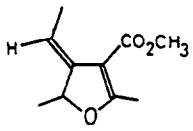
157 **159** (61)

$$HC{\equiv}CCH(CH_3)OCO_2Me + CH_3COCH_2CO_2Me \xrightarrow[79\%]{60\ C,\ 1\ h} \mathbf{159} \qquad (62)$$

158

$$CH_3C{\equiv}CCH(CH_3)OCO_2Me + CH_3COCH_2CO_2Me \xrightarrow[94\%]{60\ C,\ 1\ h} \qquad (63)$$

160



161

carbon. These results can be explained by the following mechanism shown in Fig. 11. At first, S_N2'-type reaction of propargyl carbonate with palladium phosphine complex takes place to give 1,2-propadienylpalladium carbonate **165**. Then the palladium carbonate **165** undergoes decarboxylation to give a methoxide anion, which picks up an acidic hydrogen (or deuterium) from active methylene compound **162** to give complex **166**. Then the enolate anion attacks the sp-carbon of the 1,2-propadienyl moiety to form the palladium carbene complex **167**, which isomerizes to π-allyl-palladium complex **168** by intramolecular proton (or deuterium) transfer. Finally, π-allyl complex **168** undergoes intramolecular O-alkylation with the carbonyl oxygen at the more substituted side of the π-allyl system to give the exomethylenefurans.

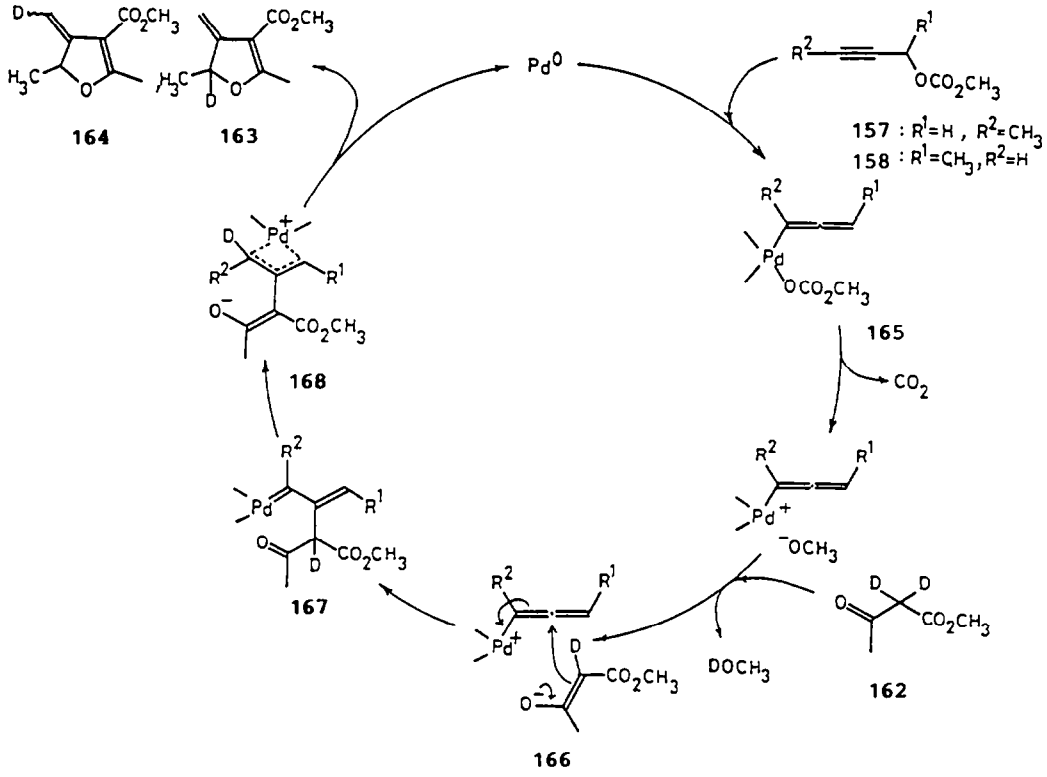
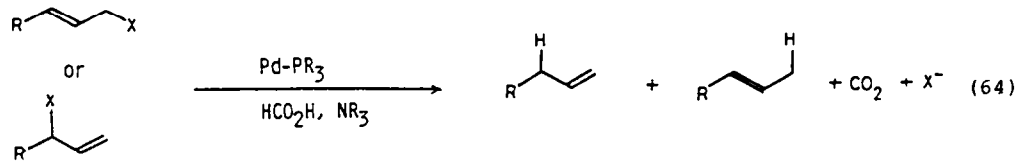


Fig. 11.

4. HYDROGENOLYSIS OF ALLYLIC COMPOUNDS WITH AMMONIUM FORMATES

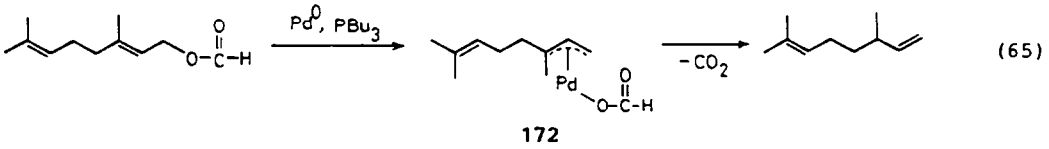
Formic acid is a cheap reducing agent, and in the presence of palladium catalyst, behaves as a hydride source. Allyl acetate was converted to propylene by the palladium-catalyzed reaction of formic acid.[85] Dienes, acetylenes, and α,β-unsaturated carbonyl compounds,[86,87] nitro compounds,[88] and aromatic halides[88,89] can be hydrogenated by using palladium–phosphine complex or palladium on carbon as catalysts. The extensive studies on palladium-catalyzed hydrogenolysis of various allylic compounds, particularly terminal allylic compounds, from which the formation of either 1-

or 2-olefins is expected, with ammonium formate has been carried out in order to prepare more useful terminal olefins selectively (Eq. 64).



From this viewpoint, the effects of ligands and solvents on the regiochemistry was studied.[90] As shown in Table 8, ligands show a remarkable effect on the regiochemistry of the hydrogenolysis. Phosphites are not good ligands for the formation of 1-olefins. Higher regioselectivity was observed by using PPh_3. Depending on the structure of the allylic compounds, terminal olefins were obtained in 80–90% selectivity. However, the highest selectivity was observed by using alkyl phosphines, such as $P(n\text{-}Bu)_3$.[91] In most cases, nearly complete formation of 1-olefins was observed by using PBu_3. The same 1-olefin was obtained with the same regioselectivity from isomeric allylic compounds (Nos. 1–11 and 13–16). For the reaction of allylic chloride, sodium formate, rather than ammonium formate gave better results (No. 12). Ene oxides are converted to homoallylic alcohols cleanly (Nos. 22 and 23). Thus this is a very good synthetic method for 1-olefins from various terminal allylic compounds. The reaction is carried out in boiling dioxane, but N,N-dimethylimidazolone (DMI) is the better solvent, and the reaction proceeds at room temperature (Nos. 7 and 23).

The palladium-catalyzed hydrogenolysis can be explained by the following mechanism shown in Fig. 12. The first step is the formation of π-allylpalladium complexes **169** from allylic compounds and Pd(0). The complex reacts with formate to give π-allylpalladium formate **170**, which undergoes decarboxylation to form the palladium hydride complex (**171**). Hydride attack on the allylic group, or reductive elimination, affords the olefin. When $P(n\text{-}Bu)_3$ is used as the ligand, the hydride attacks the more substituted side of the allylic group preferentially to give 1-olefins. To support this mechanism, the reaction of allylic formate, which forms π-allylpalladium formate **172** directly, proceeds without addition of ammonium formate (Eq. 65).



172

The palladium-catalyzed hydrogenolysis of various allylic compounds is also possible by using different hydride sources, such as tin hydrides,[92] hydrosilanes,[93] sodium borohydride,[94] organozinc,[95]

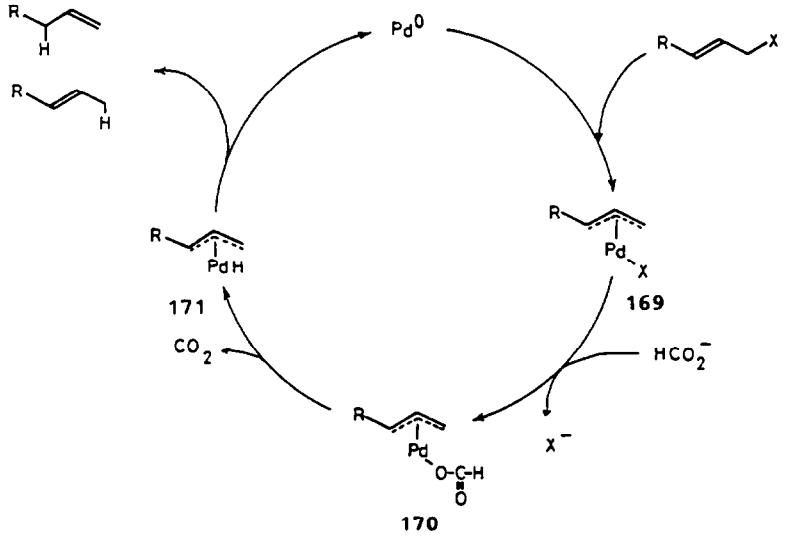
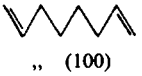
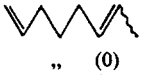
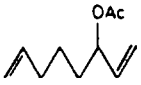
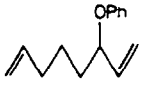
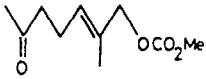
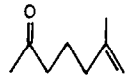
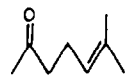


Fig. 12.

Table 8. Palladium-catalyzed hydrogenolyses of allylic compounds with ammonium formate[a]

No.	Allylic compounds	Catalysts	Products (selectivity/%)[b]	
1		$Pd_2(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$		
			,, (100)	,, (0)
2	,,	$PdCl_2$–$P(n\text{-}Bu)_3$	,, (100)	,, (0)
3	,,	$Pd(PPh_3)_4$–$P(n\text{-}Bu)_3$	,, (100)	,, (0)
4	,,	$Pd(OAc)_2$–$P(n\text{-}Bu)_3$	,, (94)	,, (6)
5	,,	$Pd_2(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$	,, (93)	,, (7)
6	,,	$Pd(PPh_3)_4$	,, (70)	,, (30)
7	,,	$Pd(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$, DMI, 30°[c]	,, (99)	,, (1)
8		$Pd_2(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$	,, (96)	,, (4)
9		$Pd_2(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$	,, (98)	,, (2)
10		$Pd_2(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$	,, (99)	,, (1)
11		$Pd_2(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$	,, (99)	,, (1)
12		$Pd_2(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$, HCO_2Na	,, (100)	,, (0)
13		$Pd_2(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$		
			,, (100)	,, (0)
14	,,	$Pd(OAc)_2$–PPh_3	,, (94)	,, (6)
15	,,	$Pd(OAc)_2$–$P(OEt)_3$	,, (51)	,, (49)
16		$Pd_2(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$	,, (100)	,, (0)
17		$Pd(OAc)_2$–$P(n\text{-}Bu)_3$		
			,, (99)	,, (1)
18	,,	$PdCl_2[P(C_6H_5)_3]_2$	,, (93)	,, (7)
19	,,	$PdCl_2(PPh_3)_2$–PPh_3	,, (90)	,, (10)
20	,,	$PdCl_2$–$P(o\text{-}Tol)_3$	,, (34)	,, (66)
21		$Pd_2(dba)_3CHCl_3$–$P(n\text{-}Bu)_3$		12 (100)[c]
22		$Pd_2(DBA)_3CHCl_3$–$P(n\text{-}Bu)_3$, DMI, 30°		97% yield

[a] All reactions were carried out using allylic compound (1 mmol), palladium catalyst (0.025–0.05 mmol, Pd : P = 1 : 4) and ammonium formate (2 mmol) in boiling dioxane (3 cm^3) for 0.5–2 h.

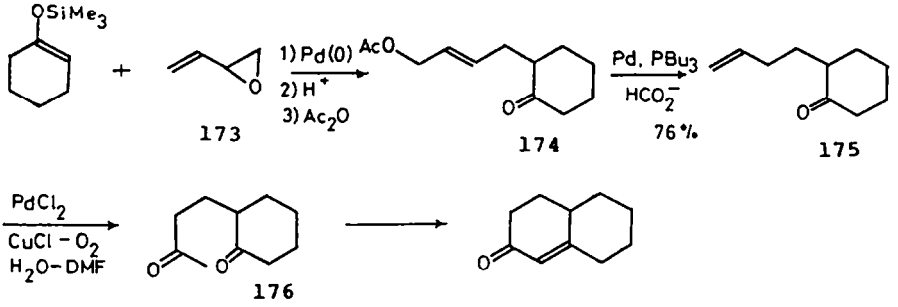
[b] GLC analysis.

[c] The vinyl epoxide (15%) was recovered.

and dihydropyridines.[96] But with these hydrides, the main product of the hydrogenolysis is 2-olefin. Thus the reaction with ammonium formate is the most useful from a synthetic viewpoint.

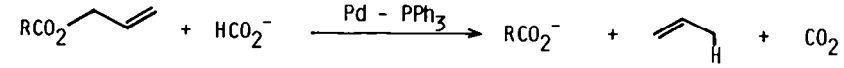
The regioselective hydrogenolysis has a considerable synthetic value. For example, the palladium-catalyzed reaction of ene oxide **173** with silyl enol ether gives allylic acetate **174** after acetylation, which is converted to terminal olefin **175** with ammonium formate. Oxidation of the terminal double

bond catalyzed by $PdCl_2$–CuCl gives 1,5-diketone **176**, which can be cyclized (Eq. 66).[97] This is a new annelation method. Usually, the direct butenylation of ketone is not easy (Eq. 66).

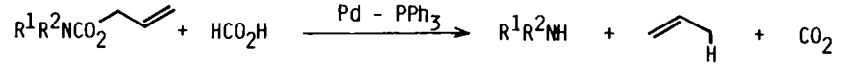


(66)

Based on the palladium-catalyzed facile hydrogenolysis of allylic esters, allylic esters can be used as a protecting group of carboxylic acids, which can be removed under mild conditions without using acids or bases (Eq. 67).[90] Amines can be protected as carbamates and deprotected by the palladium-catalyzed reaction of formic acid. The method is applicable to amino acids without racemization (Eq. 68).[25]

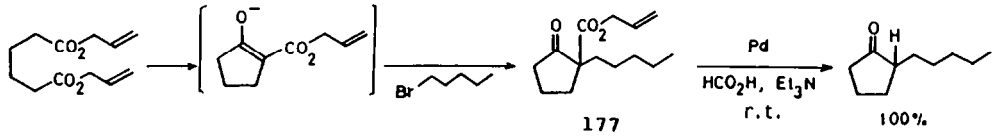


(67)



(68)

As described in Section 5, allylic esters of β-keto carboxylates undergo facile palladium-catalyzed decarboxylation. When the palladium-catalyzed decarboxylation of allyl β-keto carboxylates **177** and **178** is carried out in the presence of triethylammonium formate, removal of the carboxyl group is possible under nearly neutral conditions at room temperature without attacking other labile functional groups.[98] Thus the palladium-catalyzed hydrogenolysis is a better method of removing carboxyl groups from β-keto esters than a common method via base-catalyzed hydrolysis, followed by thermal decarboxylation (Eqs 69 and 70). The method can be applied also to malonates.



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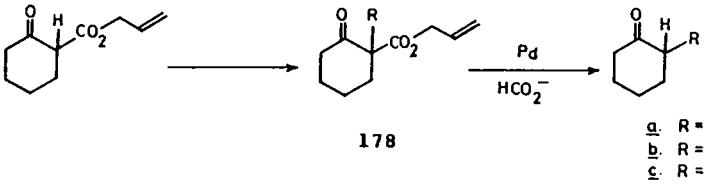
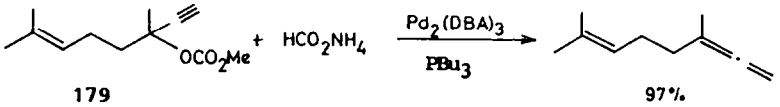


(70)

Propargyl carbonates **179** and **180** are converted to 1,2-dienes by the palladium-catalyzed reaction of ammonium formate in DMF (Eqs 71 and 72).[99]



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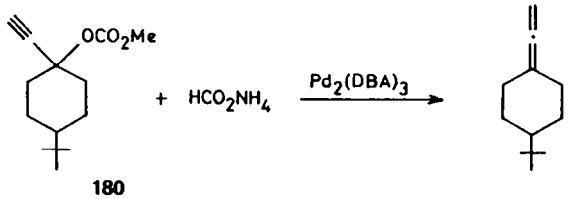


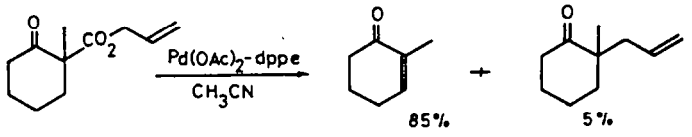
(72)

5. PREPARATION OF α,β-UNSATURATED CARBONYL COMPOUNDS BY THE PALLADIUM-CATALYZED DECARBOXYLATION–DEHYDROGENATION

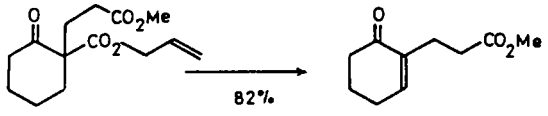
5.1. *Reactions of allyl β-keto carboxylates and allyl alkenyl carbonates*

Efficient conversion of saturated carbonyl compounds to α,β-unsaturated carbonyl compounds is an important synthetic method. This can be done usually by introducing heteroatoms (X) such as S, Se, or halogens at the α-position, followed by elimination of HX. Also direct dehydrogenation with DDQ is known.

In Section 2, the decarboxylation–allylation reaction of allyl β-keto carboxylates is described. The reaction proceeds by the formation of palladium enolate complexes, which exist as keto **181** and enol forms **182**, and their equilibrium is controlled by ligands and solvents. In the palladium-catalyzed reaction of allyl β-keto carboxylates, interesting effects of solvents and ligands on the course of the reaction were found. The selective enone formation occurs by carrying out the reaction in CH_3CN and using dppe or PPh_3 as the ligand (Fig. 13).[100] In a typical example, allyl 2-methylcyclohexanone-2-carboxylate (1 mmol) in CH_3CN was refluxed for 30 min in the presence of $Pd(OAc)_2$ (0.05 mmol) and dppe (0.05 mmol). GLC analysis showed the formation of 2-methyl-2-cyclohexenone in 85%yield. In this reaction, choice of solvent is crucial. Aprotic polar solvents such as CH_3CN and DMF are the best for enone formation. On the other hand, in acetone or t-butyl alcohol, the allylated products are the main products even when dppe is used. In addition, the presence of a substituent or the absence of active hydrogen at the α-position is essential for selective enone formation. For example, the reaction of allyl cyclohexanone-2-carboxylate is not selective and produced a mixture of cyclohexenone, 2-allyl- and 2,2-diallylcyclohexanone with the Pd–dppe catalyst. Some examples are shown in Eqs (73)–(77).



(73)



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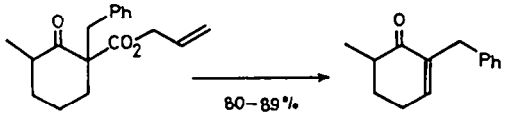

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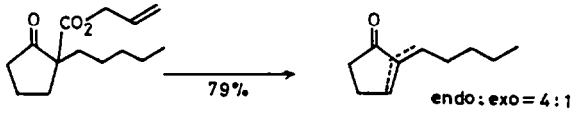
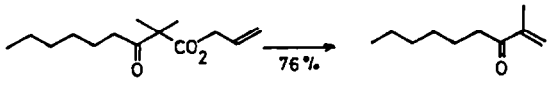


(76)



(77)

The enone formation can be explained by the mechanism shown in Fig. 14. The oxidative addition of allyl ester **178** to Pd(0) species, formed *in situ* from $Pd(OAc)_2$, affords allylpalladium β-keto carboxylate **183**, which undergoes decarboxylation to produce the allylpalladium enolate complex **184**, which is in equilibrium with the C-bonded complex **185**. Then enone **186** is formed by the elimination of PdH from **185**. Finally reductive elimination of the allylpalladium hydride complex **187** produces propene and regenerates the Pd(0) species. This reductive elimination step was confirmed by the fact that a 1 : 1 mixture of enone **189** and 1-phenylpropene (**190**) was obtained

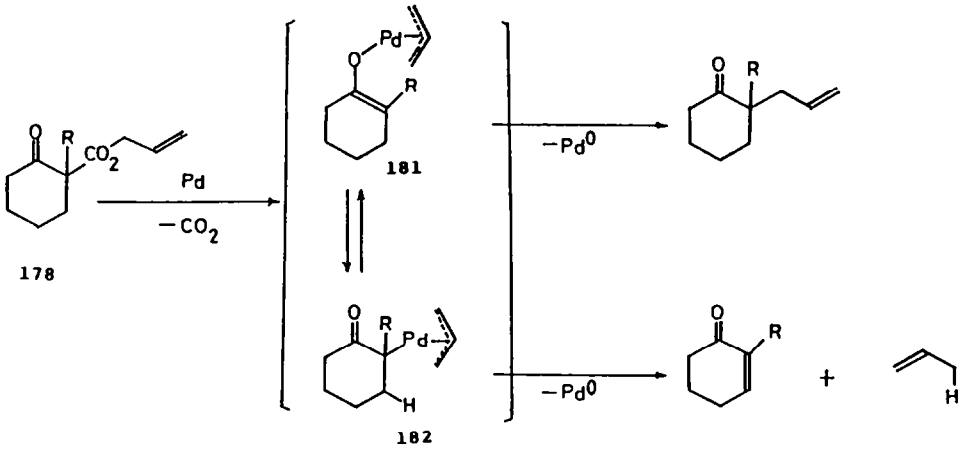
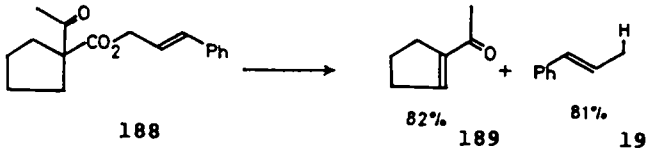


Fig. 13.

from the cinnamyl ester of α,α-cyclopentanoacetoacetic acid (**188**) (Eq. 78). In other words, the allyl group is the hydrogen acceptor in this dehydrogenation reaction.



(78)

The enone formation is also possible by the palladium-catalyzed reaction of allyl alkenyl carbonates (allyl enol carbonates).[101] The enones are obtained selectively when the reaction is carried out at 80° in CH_3CN in the presence of $Pd(OAc)_2$ and dppe. When the reaction is carried out at 20°, allylation takes place to give allyl ketone, rather than enone. By this method, not only ketones, but also aldehydes can be converted to α,β-unsaturated aldehydes (Eq. 79). The reaction of allyl enol carbonates of unsymmetrical ketones is regioselective. The reaction of allyl enol carbonate obtained from the thermodynamic enolate **191** of 2-methylcyclohexanone gave 2-methyl-2-cyclohex-

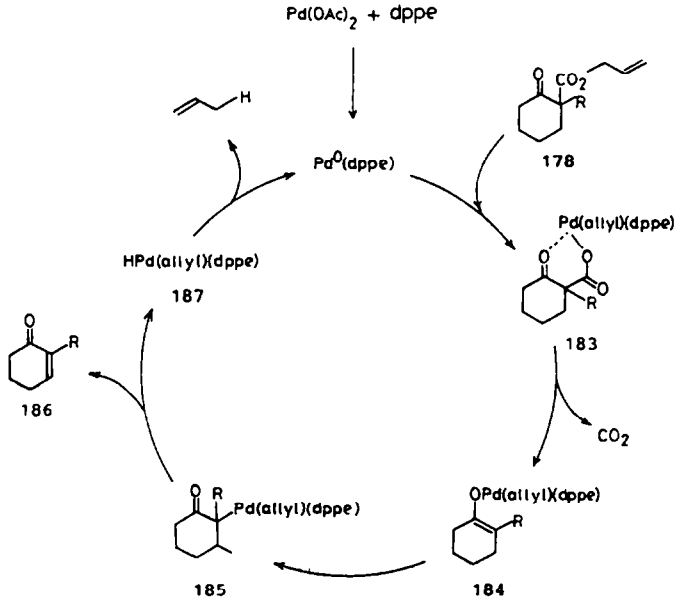
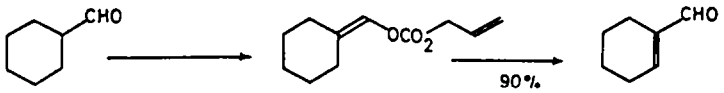


Fig. 14.

enone (**193**) selectively. On the other hand, the allyl enol carbonate from kinetically generated enolate **192** gave 6-methyl-2-cyclohexenone (**194**) in 81% yield (Eq. 80).



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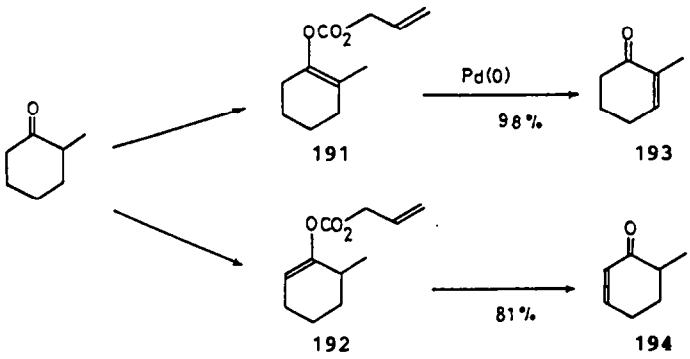
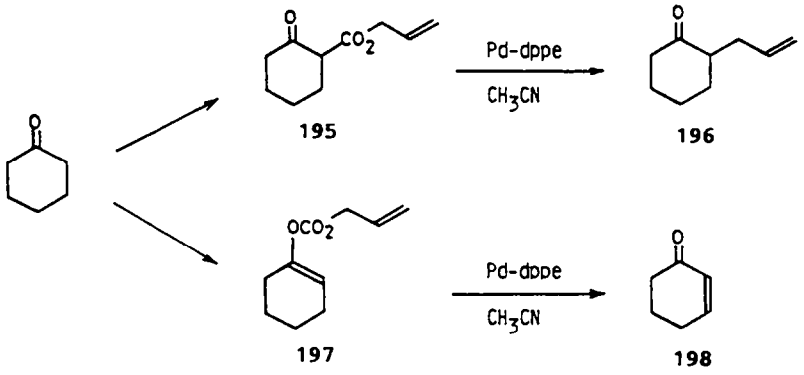


(80)

2-Methyl-2-cyclohexenone is obtained from both allyl 1-methyl-2-cyclohexanone carboxylate and the corresponding allyl enol carbonate. But allyl 2-cyclohexanonecarboxylate (**195**) which possesses an active hydrogen was converted to 2-allylcyclohexanones (**196**) as a major product and 2-cyclohexenone as a minor product even when the reaction was carried out in CH_3CN (Eq. 81). On the other hand, allyl enol carbonate **197** prepared from cyclohexanone was converted to 2-cyclohexenone (**198**) in 92% yield (Eq. 82). Thus the allyl enol carbonate method can be applied to α-unsubstituted ketones more satisfactorily than allyl β-keto carboxylates.



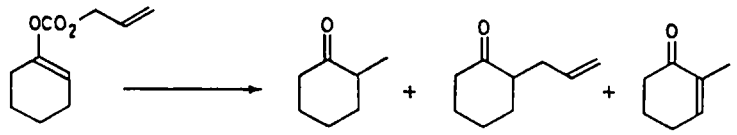
(81)

(82)

The reactions of allyl β-keto esters and allyl enol carbonates are versatile, but unsatisfactory selectivity is obtained with some carbonyl compounds, particularly five-membered cyclic ketones, even when dppe is used in CH_3CN. Saturated ketones or allylated ketones are formed in these cases. But more careful studies on the effects of solvents and ligands solved the problem for the selective formation of enones.[102] As shown in Table 9, enone formation is possible by using not only dppe, but also PPh_3. However, the ratio of Pd : ligand is crucial. If the ratio of the ligand to palladium is large, the allylation becomes predominant even when CH_3CN is used as solvent. Furthermore, enone formation proceeds even in the absence of the ligand. Thus for five-membered ketones, ligand-free palladium catalyst is good for the selective enone formation.

Enone formation from allyl β-keto carboxylates and allyl enol carbonates is very useful for organic synthesis. One example is the facile synthesis of 2-methyl-2-cyclopentenone (**199**),[103] which is a useful intermediate for various cyclopentanoids. Many synthetic methods for this rather simple compound are known,[104] but none of them is satisfactory. Thus the Dieckmann condensation of allyl adipate (**200**), followed by methylation gives allyl 2-methyl-2-cyclopentanonecarboxylate (**201**) in 87% yield. This compound was subjected to the palladium-catalyzed decarboxylation–dehydrogenation to give 2-methyl-2-cyclopentenone (**199**) in 79% yield using ligand-free $Pd(OAc)_2$ (Eq. 83).

Table 9. Effect of solvent and ligand[a]

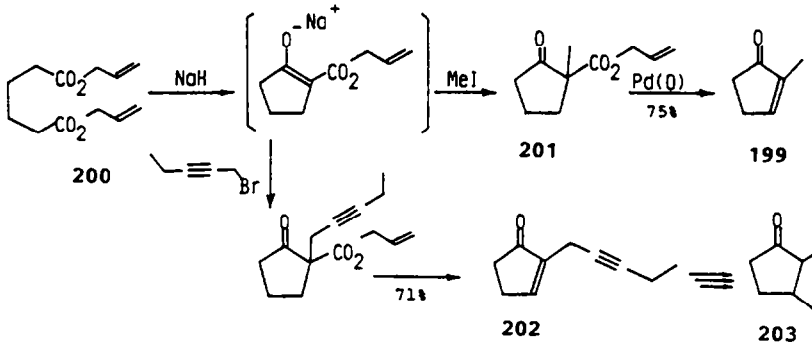


197 A B C

Run	Catalyst	Phosphine	Phosphine/palladium molar ratio	Solvent	Yield[b]/% A	B	C
1[c]	$Pd(OAc)_2$	None	—	THF	0	0	0
2	,,	,,	,,	MeCN	1	0	98
3	$Pd_2(DBA)_3$	,,	,,	,,	3	0	97
4	$Pd(OAc)_2$	PPh_3	0.54/1	,,	1	0	98
5	,,	,,	1.30/1	,,	0	5	95
6	,,	,,	1.70/1	,,	3	63	34
7	,,	dppe	0.5/1	,,	2	0	86
8	,,	,,	1/1	,,	1	0	99
9	,,	,,	2/1	,,	4	57	38

[a] Pd catalyst (0.1 mmol), 197 (1.0 mmol), dry solvent (5 cm^3) at 80° under argon.
[b] GLC analyses.
[c] Reaction at 65°.

Methyl jasmonate (**203**) was prepared similarly. The alkylation with 2-pentynyl bromide, followed by decarboxylation affords an important intermediate **202** for jasmonate synthesis (Eq. 84). Methyl jasmonate is now produced in an industrial scale in Japan by this method.

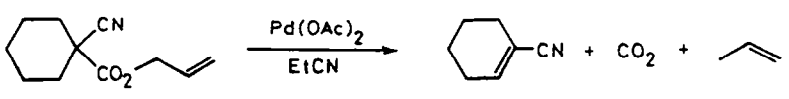


200 201 199 (83)

202 203 (84)

In preparative organic chemistry, β-keto esters are used for selective monoalkylation of ketones by removing the carboxylate by hydrolysis and decarboxylation after alkylation. Three palladium-catalyzed reactions of allyl β-keto carboxylates **178** have been discovered, namely, decarboxylation–allylation to form **204**, dehydrogenation to give enone **186**, and hydrogenolysis to form **205** by careful selection of reaction conditions. As summarized in Fig. 15, by these palladium-catalyzed reactions, the usefulness of β-keto carboxylates is greatly enhanced. Particularly the facile enone formation has a high synthetic value, which is difficult to achieve by other means.

Allyl alkylcyanoacetates **206** also undergo the palladium-catalyzed decarboxylation–dehydrogenation to give α,β-unsaturated nitriles in propionitrile (Eq. 85).[105]



206 207 92% (85)

5.2. *Reactions of silyl enol ethers and ketene silyl acetals with allyl carbonates*

In Section 2.1, the allylation reaction of silyl enol ethers with allyl carbonates to give allyl ketones or allyl aldehydes is described. The reaction proceeds via the formation of π-allylpalladium enolates.

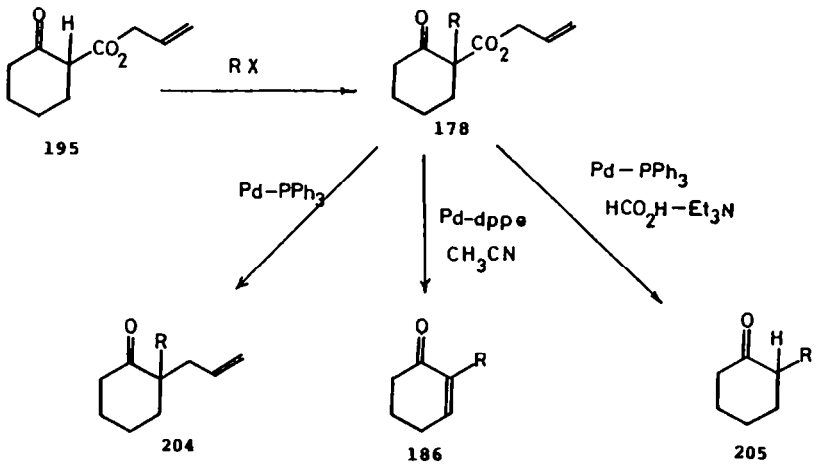
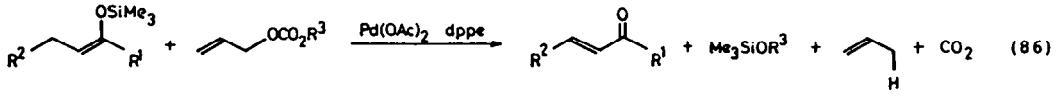


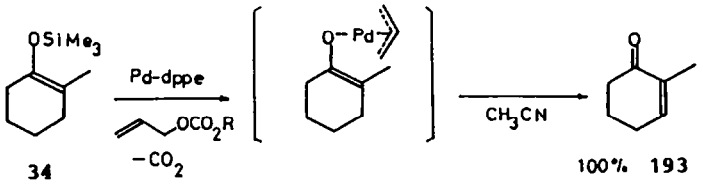
Fig. 15.

Silyl enol ethers can be converted in one step in good yields to α,β-unsaturated carbonyl compounds by the reaction of allyl carbonates in CH_3CN using palladium complex as a catalyst (Eq. 86).[106,107]



(86)

Enone and enal formation proceeds satisfactorily only in nitriles, and CH_3CN is used most conveniently. A solution of $Pd(OAc)_2$ (0.05 mmol) and dppe (0.05 mmol) in dry CH_3CN (1 ml) is heated under argon. As soon as the solution begins to reflux, a mixture of silyl enol ethers (1 mmol) and diallyl carbonate (2 mmol) in CH_3CN (4 ml) is added in one portion. The mixture is refluxed for 1 h. From 2-methylcyclohexanone, the kinetic and thermodynamic silyl enolates **34** and **35** were prepared, and subjected to palladium-catalyzed dehydrogenation to give 2-methyl-2-cyclohexenone (**193**) from **34**, and 6-methyl-2-cyclohexenone (**194**) from **35** regioselectively.



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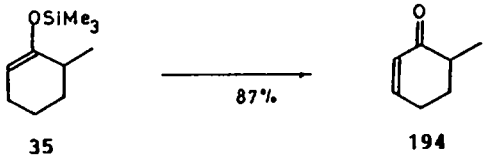
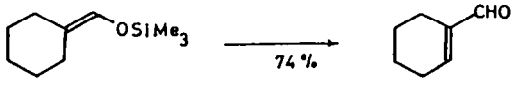


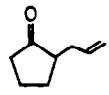
(88)



(89)

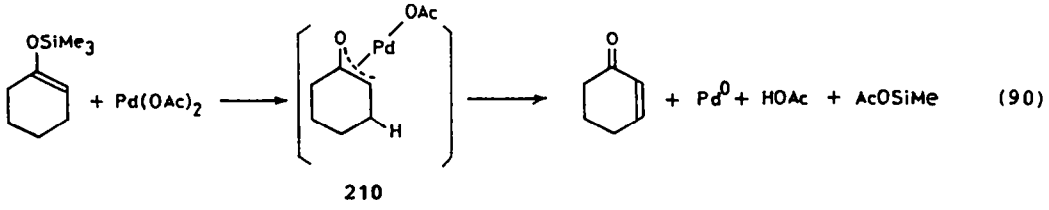
The reaction is applicable to both ketones and aldehydes. But unsatisfactory results are obtained with five-membered ketones. For example, the reaction of silyl enol ether derived from cyclopentanone with allyl carbonate and Pd–dppe catalyst in CH_3CN affords cyclopentanone as the main product and a considerable amount of 2-allylcyclopentanone. In benzonitrile, a somewhat better result is obtained. The desired cyclopentenone was obtained in 81% yield by using a phosphine-free palladium catalyst in CH_3CN. Again in this case, too, a phosphine-free palladium catalyst gives the best results for the selective dehydrogenation (Table 10).[102]

Table 10

OTMS						
	$Pd(OAc)_2$–dppe	1:1	MeCN	12	72	16
,,	,, ,,		PhCN	69	0	31
,,	$Pd(OAc)_2$		MeCN	81	12	0

As in the palladium-catalyzed allylation of silyl enol ethers with allyl carbonates (Fig. 4), allylpalladium enolate **208** is formed by the transmetalation between Pd and Si as the common intermediate, which is in equilibrium with the C-bonded complex **209**. The enone is formed by the elimination of PdH from **209**. Finally reductive elimination of the allylpalladium hydride complex produces propene and regenerates the Pd(0) species (Fig. 16). The last part of this mechanism is closely related to that of the palladium-catalyzed enone formation from allyl β-keto carboxylates and allyl enol carbonates.

Also enone formation is carried out regioselectively by the reaction of silyl enol ethers with $Pd(OAc_2)$.[108] In this reaction, palladium enolate **210** is formed as an intermediate by the transmetalation of silyl enol ethers with Pd^{2+} and then decomposed to enones and Pd(0). The reaction requires a cocatalyst such as benzoquinone or $CuCl_2$ to reoxidize Pd(0) for making the reaction catalytic (Eq. 90).



210

The palladium-catalyzed dehydrogenation can be applied also to ketene silyl acetals derived from saturated esters and lactones.[46] The dehydrogenation of ketene silyl acetals can be carried out most satisfactorily in boiling CH_3CN by using $Pd(OAc)_2$ without using phosphine ligand. In the presence of phosphine ligand, the allylation reaction proceeds in a considerable extent. Thus this is a very useful method for the conversion of saturated esters and lactones into α,β-unsaturated ones,

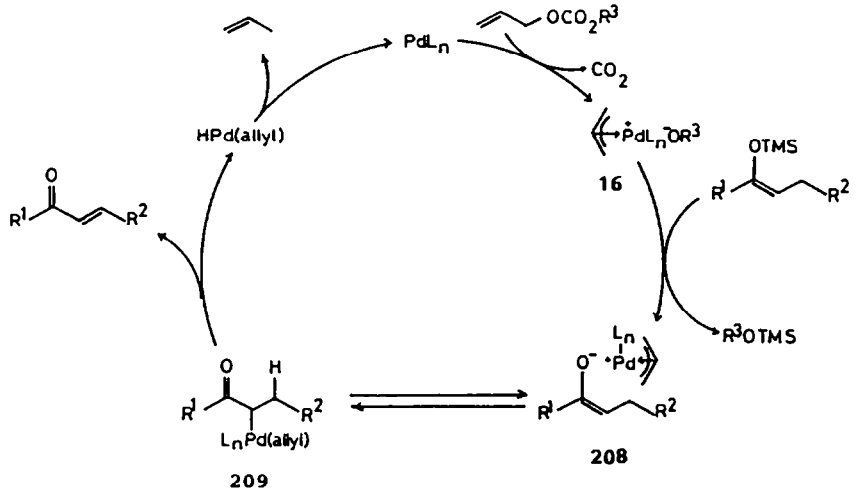
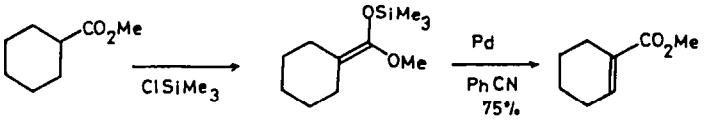
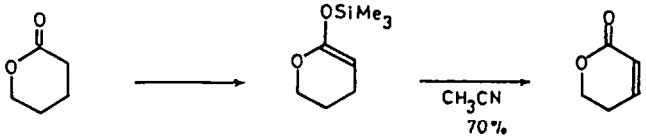


Fig. 16.

because there is no good method for converting saturated esters to α,β-unsaturated esters (Eqs 91 and 92).



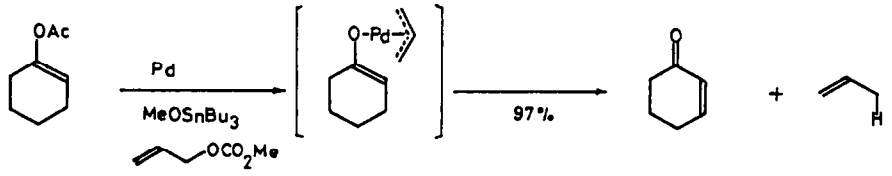
(91)



(92)

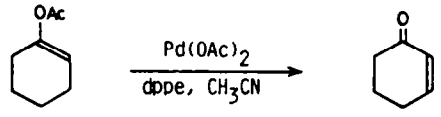
5.3. *Reactions of enol acetates with allyl carbonates*

As described before enol acetates are allylated by the Pd–Sn catalyzed reaction of allylic carbonates. In this reaction, solvents have a crucial effect. When the reaction is carried out in CH_3CN, enol acetates are converted to enones selectively (Eq. 93).[107,109]



(93)

A solution of enol acetate (1 mmol), allyl methyl carbonate (2 mmol), $Pd(OAc)_2$ (0.05 mmol), and dppe (0.05 mmol) in dry CH_3CN (5 ml) is stirred at room temperature for 10 min under argon. Then tributyltin methoxide (0.2 mmol) is added and the mixture is refluxed for 10 h. Somewhat poor results are obtained with five- and eight-membered ketones, and α-substituted ketones by using Pd–Sn–dppe catalyst. But in these cases the enone formation takes place satisfactorily with the phosphine-free palladium catalyst. For example, cyclooctenone was obtained in 20% yield (cyclooctanone was recovered in 80% yield) by using Pd–Sn–dppe as catalyst. But the enone was obtained in 73% yield by using the phosphine-free Pd–Sn catalyst. Similarly, 2-methyl-2-cyclohexenone was obtained in 90% yield from the enol acetate of 2-methylcyclohexanone without using the phosphine ligand (Eqs 98 and 99). From α,β-unsaturated steroidal ketone **211**, two enol acetates **212** and **213**



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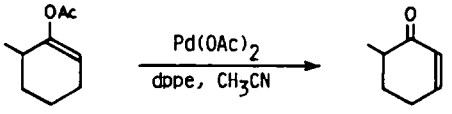
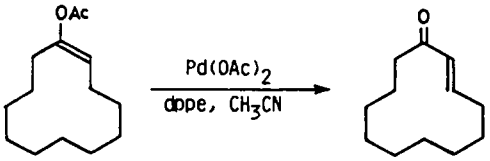
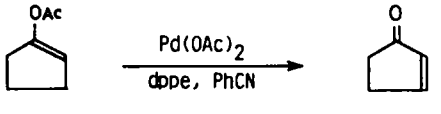


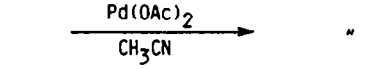
(95)

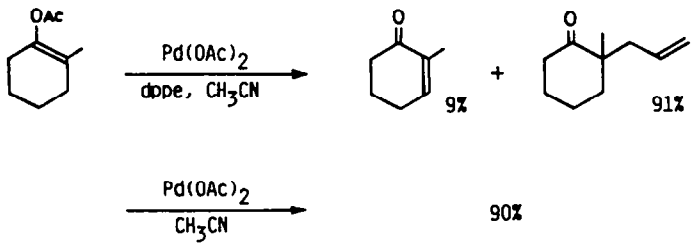


(96)



(97)

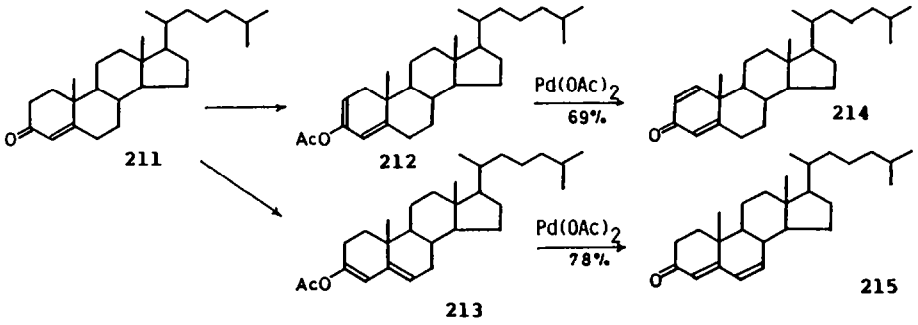




(98)

(99)

were prepared, and the dehydrogenation took place at the direction of the enolization regioselectively to give different dienones **214** and **215** cleanly (Eq. 100).[102]



(100)

As for the mechanism of the dehydrogenation, the π-allylpalladium enolate is formed by transmetalation, and elimination of PdH proceeds in nitrile to form enones.

Palladium-catalyzed dehydrogenation reactions from four different species have been explored. Intramolecular reaction takes place with allyl β-keto carboxylates and allyl alkenyl carbonates. Also intermolecular reaction of allyl carbonates with silyl enol ethers, ketene silyl acetals, and enol acetates is possible. In all these reactions, π-allylpalladium enolates are formed as common intermediates, which then undergo a dehydrogenation reaction in nitriles as solvents. All these reactions proceed with high selectivity under neutral conditions, and have high synthetic utility (Fig. 17).

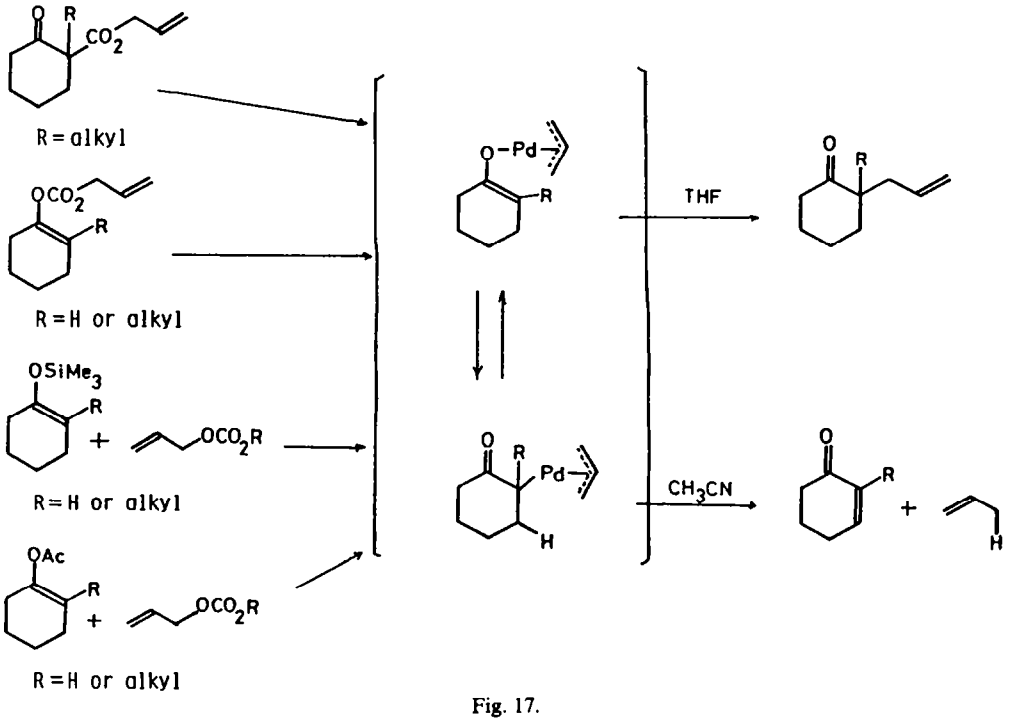
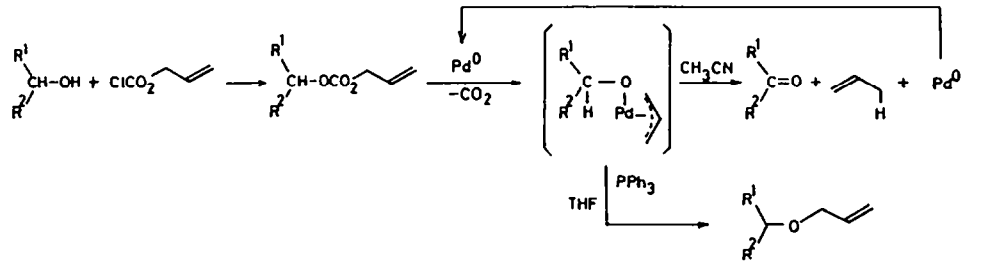


Fig. 17.

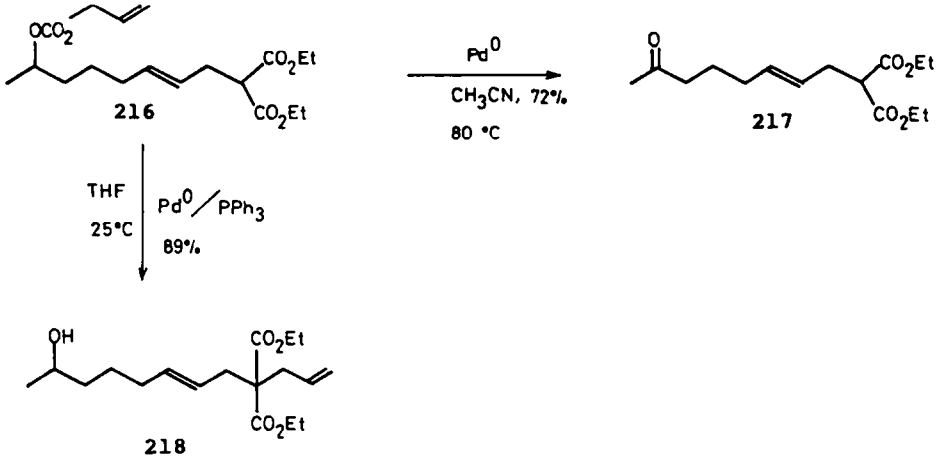
6. OXIDATION OF ALCOHOLS VIA THEIR ALLYL CARBONATES

Oxidation of alcohols is one of the most important synthetic methods, and a number of oxidation methods are known, mainly by using inorganic reagents, such as Cr or Mn salts. But separation of inorganic compounds after the oxidation is sometimes a problem. As described in the preceding section, facile palladium-catalyzed elimination of β-hydrogen proceeds in CH_3CN. Consideration of the mechanism of the elimination of β-hydrogen suggests the possibility of oxidation of alcohols via their allyl carbonates, and a new method of palladium-catalyzed oxidation of alcohols via their allyl carbonates, which are easily prepared by the reaction of alcohols with allyl chloroformate, has been found.[110,111] As expressed by Eq. (101), the reaction produces only carbon dioxide and propene as by-products, and hence the reaction is very clean.



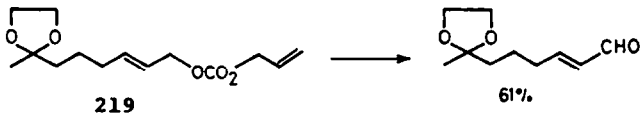
(101)

The phosphine-free palladium catalyst is active for this reaction. In the presence of PPh_3, the decarboxylation–ether formation takes place without undergoing oxidation.[26] High chemoselectivity was observed in the reaction of **216**. Use of the phosphine-free palladium catalyst afforded ketone **217**. On the other hand, simple allylation of the malonate took place without oxidation of alcohol to give **218** by using Pd–PPh_3 in THF (Eq. 102).



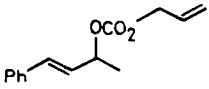
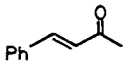
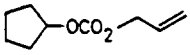
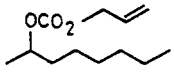
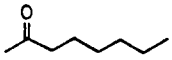
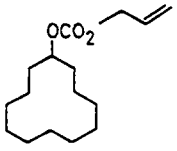
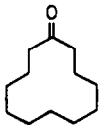
(102)

The selection of solvents is important, CH_3CN being the most suitable one. $Pd(OAc)_2$ as a catalyst is dissolved in CH_3CN, which is refluxed. To this refluxing solution, allylic carbonate is added slowly, and the oxidation proceeds rapidly with evolution of carbon dioxide and propene. At the end of the reaction, palladium precipitates on the surface of the flask as a black film. The separation of the product from the solvent can be done easily. As shown in Table 11, the reaction can be applied to various alcohols except simple primary alcohols, which give aldehydes in somewhat lower yields, and a considerable amount of alcohols is recovered (No. 4). But primary benzyl and allyl alcohols can be oxidized smoothly. When unsymmetrical biallylic carbonates are subjected to oxidation, the less hindered simple allyl alcohol is cleaved to form α,β-unsaturated ketones or aldehydes in high yields (Nos. 2, 3 and 5). This oxidation proceeds under neutral conditions without attacking functional groups. For example, acetal **219** stays intact during the oxidation (Eq. 103).



(103)

Table 11

No.	Alkyl allyl carbonate	Products	Yield (%)
1	$PhCH_2OCO_2CH{=}CH_2$	PhCHO	76
2	$n\text{-}C_3H_7CH{=}CHCH_2OCO_2CH_2CH{=}CH_2$	$n\text{-}C_3H_7CH{=}CHCHO$	95
3	$PhCH{=}CHCH_2OCO_2CH_2CH{=}CH_2$	$PhCH{=}CHCHO$	69
4	$n\text{-}C_{10}H_{21}OCO_2CH_2CH{=}CH_2$	$n\text{-}C_9H_9CHO$	27
		$n\text{-}C_{10}H_{21}OH$	73
5			88
6			76
7			96
8			77

The reaction can be explained by the mechanism shown in Fig. 18. The first step is the formation of π-allylpalladium carbonate by oxidative addition, which undergoes smooth decarboxylation to give π-allylpalladium alkoxide **220**. In nitrile solvent, the π-allylpalladium alkoxides undergo elimination of β-hydrogen to give carbonyl compounds.

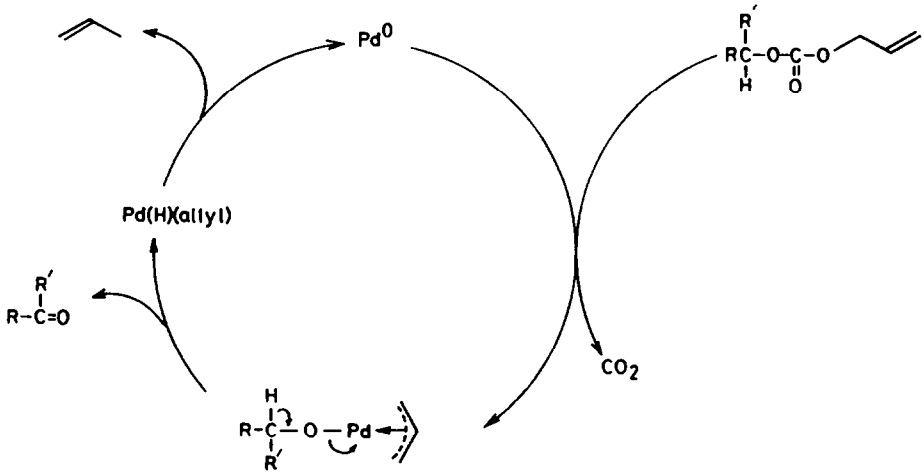
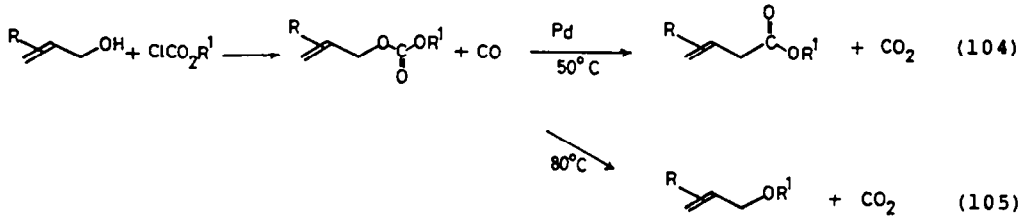


Fig. 18.

7. PALLADIUM-CATALYZED DECARBOXYLATION–CARBONYLATION OF ALLYLIC CARBONATES AND PROPARGYL CARBONATES

The stoichiometric carbonylation of π-allylpalladium chloride in alcohol to give 3-butenoate is known.[112] Also allyl chloride is carbonylated using $PdCl_2$ or π-allylpalladium chloride as catalyst to give the same ester.[113–115] However, a high carbon monoxide pressure (100 atm) is necessary. Also an attempt to carbonylate allyl acetate is unsuccessful. This result is explained from the fact that π-

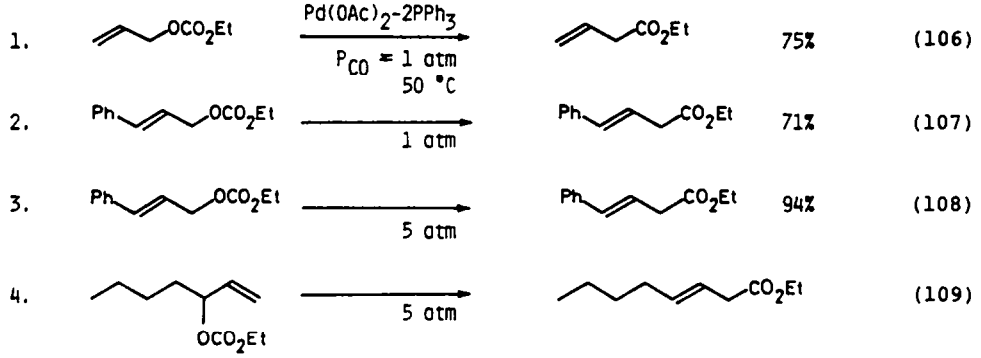
allylpalladium acetate is converted to allyl acetate by reductive elimination when the complex is treated with carbon monoxide.[116,117] On the other hand, allylic carbonates react with carbon monoxide under mild conditions.[118,119] Decarboxylation–carbonylation takes place to give β,γ-unsaturated esters in high yields (Eq. 104). In other words, the exchange reaction of carbon dioxide with carbon monoxide takes place. This is a very good method of preparing β,γ-unsaturated esters from allylic alcohols.



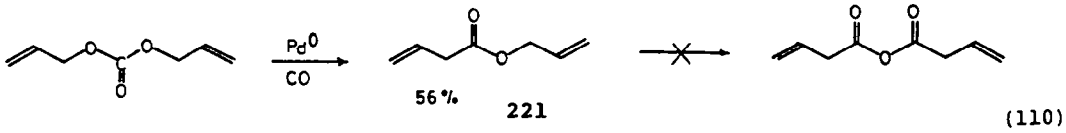
(104)

(105)

The reaction proceeds even under carbon monoxide at atmospheric pressure using a rubber balloon filled with carbon monoxide. The reaction is somewhat accelerated by increasing the pressure up to 10 atm. Selection of reaction temperature is important. At room temperature, almost no reaction takes place. At temperatures higher than 80°, simple decarboxylation takes place to give allylic ethers (Eq. 105). The optimum temperature for the carbonylation is about 50°. In a typical example, ethyl methallyl carbonate (3.6 g, 25 mmol), $Pd(OAc)_2$ (112 mg, 0.5 mmol), and PPh_3 (262 mg, 1.0 mmol) were placed in a small pressure bottle or a glass vessel and the reaction was carried out at 50° under 1 or 10 atm of carbon monoxide for 8 h. After the reaction, ethyl 3-methyl-3-butenoate was isolated by distillation (2.43 g, 76%). Some results of the carbonylation with several carbonates are shown in Eqs (106)–(109). Equation (110) shows the chemoselective carbonylation



of diallyl carbonate to give **221**. But no carbonylation of the allyl ester **221** was observed, showing that only allyl carbonate is carbonylated without attacking allyl carboxylate.



(110)

The decarboxylation–carbonylation can be explained by the following mechanism shown in Fig. 19. The first step is the oxidative addition of allyl carbonate to give π-allylpalladium alkoxide **16**.

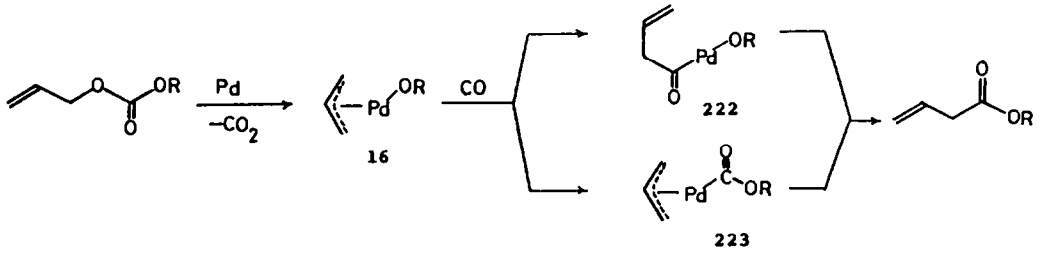
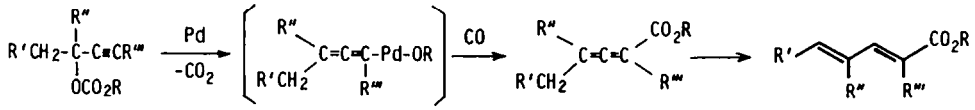


Fig. 19.

There are two possible reaction paths for carbon monoxide insertion. One possibility is the insertion of carbon monoxide to the π-allylpalladium bond to give 3-butenoylpalladium complex **222**. The other is the insertion into the palladium–alkoxide bond to give (carboalkoxy)(π-allyl)palladium complex **223**. There is no evidence yet which will discriminate between these two possibilities. The final step is the reductive elimination to give the β,γ-unsaturated ester. At the same time, the Pd(0) species is regenerated.

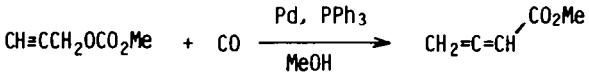
Propargyl carbonates are reactive substrates in the presence of palladium catalyst as shown in Section 3. The decarboxylation–carbonylation of propargyl carbonates **224** proceeds at 50° under 1–30 atm of carbon monoxide using Pd–PPh_3 complex as a catalyst to afford substituted 2,3-butadienoates **226** in high yields.[120] As shown in Eq. (111), the reaction proceeds by the formation



(111)

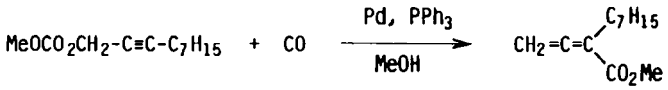
224 **225** **226** **227**

of allenylpalladium complex **225** and subsequent carbon monoxide insertion. In some solvents, isomerization of the 2,3-butadienoates to 2,4-pentadienoates **227** takes place. Thus these reactions offer good synthetic methods for 2,3- and 2,4-diene carboxylates. Some examples are shown in Eqs (112)–(114).



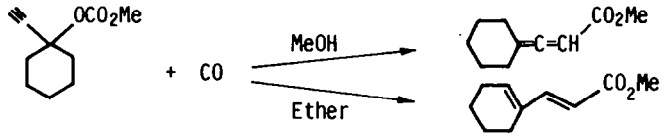
(112)

50%



(113)

82%



(114)

95%

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