7.2
Oxidative Rearrangement Reactions

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7.2.1 INTRODUCTION

Oxidative rearrangements comprise a highly diverse group of reactions, some of which enjoy broad usage in synthesis, while others remain curiosities. This chapter necessarily reflects this heterogeneity. The designation 'oxidative rearrangement' is not used uniformly in the literature; the discussion in this chapter is limited to reactions which alter the connectivity in one or more carbon–carbon π- or σ-bonds in the substrate, and in which the molecule undergoes a net oxidation. Most often these changes will occur simultaneously, forming part of a single transformation, and the rearrangement is frequently driven by the oxidation. For the sake of brevity, the scope is further narrowed by excluding oxidative rearrangements of heterocyclic rings such as furans, pyrans, pyrroles and indoles; these reactions in themselves are numerous enough to fill a chapter. The overall emphasis is on selectivity and synthetic utility.

The organization is by type of reacting bond. The first section deals with functional group rearrangements — connectivity changes in carbon–carbon π-bonds and of bonds to heteroatoms which do not alter the carbon skeleton. The second section covers the skeletal rearrangements — connectivity changes in the carbon–carbon σ-bond framework with the concomitant functional group changes. Within each of these sections the discussion is divided according to the functional group undergoing oxidation.[1,2] The strained rings of cyclopropanes[3] and cyclobutanes[4] are treated as functional groups, and the oxidative rearrangements of these small rings which have no counterpart in the chemistry of larger rings are covered separately. Perhaps arbitrarily, oxidative cleavages of small rings are considered with the functional group rearrangements, while other structural reorganizations are covered with the skeletal rearrangements.

Several factors may cause an oxidation to take place with rearrangement. Conformational features of the substrate play an important role; steric crowding at the reaction site may favor strain relief through rearrangement over the normal mode of oxidation, or favorable overlap of the reacting bond with an allylic or an isolated but proximate double bond may cause a rearrangement. The first-formed products or intermediates of oxidation, such as an epoxide[5] or an alkylthallium(III) adduct,[6a] may be unstable and the pathway to a more stable species will involve a rearrangement. Many oxidative rearrangements follow a predictable pattern, and thus constitute reliable synthetic methods. Others are highly substrate dependent, and their utility in synthesis requires a careful conformational analysis of the substrate, or a good measure of luck.[7]

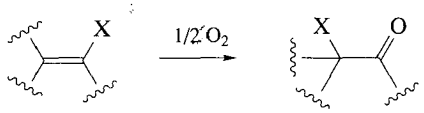
The examples presented here were selected to represent the variety of transformations which have been uncovered, from the heavily used to the seemingly unique cases. The aim is to acquaint practitioners with the more established methods, and to pique the interest in some reactions which could become useful tools with further development.

7.2.2 OXIDATIVE REARRANGEMENT OF FUNCTIONAL GROUPS

The discussion in this section is divided according to the functional group undergoing oxidative rearrangement: alkenes and enols, allylic alcohols, cyclopropanes and cyclobutanes, and miscellaneous functional group rearrangements. For the cyclopropanes and cyclobutanes, the scope is limited to the oxidative cleavages of the small rings which do not have counterparts in the chemistry of larger ring compounds. The major oxidants used commonly for these reactions include chromium(VI),[1,2b,8] lead(IV),[1,2c,9] and singlet oxygen ($^1O_2$).[10] From among the functional group rearrangements, the strongest contributors to synthetic methodology are the allylic oxidations of alkenes (including the singlet oxygen ene reaction), and the 1,3-ketone transposition resulting from the oxidative rearrangement of allylic tertiary carbinols.

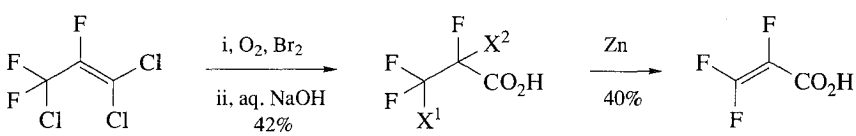
7.2.2.1 Alkenes and Enols

The reaction of oxygen with vinyl halides gives acyl derivatives,[11] as shown in equation (1). These reactions proceed in moderate to good yield, and follow a radical chain mechanism. The migratory preference is Br > Cl > F when mixed polyhaloalkenes are used. This reaction has found particular utility in the preparation of functionalized fluorocarbons, as shown in Scheme 1 for the example of perfluoroacrylic acid (**1**). Vinyl sulfides also undergo this oxidative rearrangement to give α-thio acyl derivatives.



(1)

X = halogen



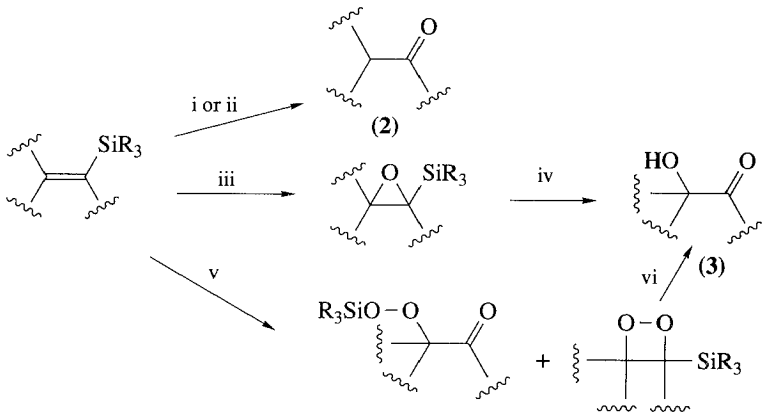
(**1**)

X^1, X^2 = Br, Cl; Cl, Br

Scheme 1

Vinylsilanes follow a similar course on oxidation with peroxy acid or with ozone.[6b,12] Depending upon the conditions of oxidation they can be converted either to a carbonyl compound (**2**) or to the α-hydroxycarbonyl compound (**3**), as in Scheme 2.[12,13] Vinyl silanes are useful synthetic intermediates, and this oxidation rearrangement procedure is an important component in their spectrum of reactivity.

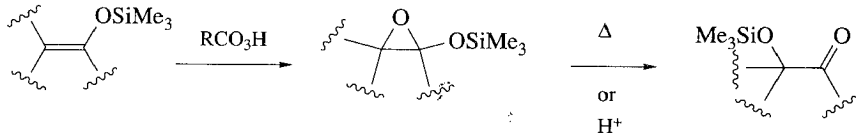
Enol ethers, and in particular silylated enols (see Volume 2, Chapter 2.3), react with peroxy acid reagents to give initially a silyloxy epoxide, which rearranges with silyl migration to yield an α-silyloxy ketone,[12,14] as in Scheme 3. The net result is that a ketone is converted to a protected α-hydroxy ketone, and the stereochemistry is determined by the least hindered approach of the peroxy acid to the enol.



i, MCPBA, KHF_2, DMF; ii, 30% H_2O_2, $NaHCO_3$, MeOH, THF; iii, MCPBA, CH_2Cl_2; iv, 30% H_2O_2, KHF_2, $KHCO_3$, MeOH, THF; v, O_3; vi, [H]

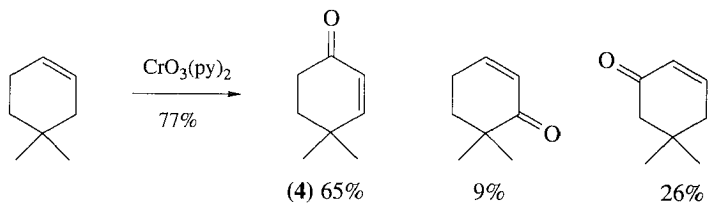
Scheme 2

Although peroxy acid is the reagent of choice, under the proper conditions simple double bonds survive this reaction.



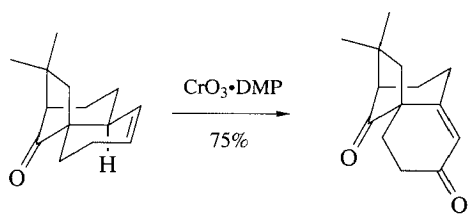
Scheme 3

Allylic oxidation (which is discussed in Chapter 2.1, this volume) takes place with rearrangement in certain substrates, the driving force being either a lower activation energy barrier for the chromate insertion into the C—H bond with rearrangement and/or a greater stability for the transposed enone product. Moderate selectivity is obtained in the case of 4,4-dimethylcyclohexene which serves to demonstrate,[8] as seen in equation (2). The oxidant shows a three-fold preference for hydrogen abstraction at C-3 over C-6 in order to avoid a 1,3-diaxial interaction with one of the methyl groups. The abstraction at C-3 leads mainly to the rearranged enone (**4**) for either steric or stereoelectronic reasons.

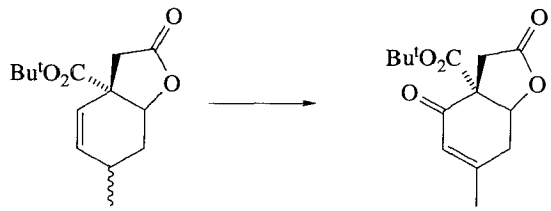


(2)

Two independent syntheses of quadrone employed an allylic oxidation with rearrangement, as shown in equation (3),[8] where the chromium trioxide·(3,5-dimethylpyrazole) reagent (CrO_3·DMP) was used. In some cases, the success of the reaction strongly depends on the nature of the oxidant, as shown in an approach to (–)-upial (equation 4). Here the chromium trioxide–heterocycle reagents, which are weaker oxidants, are quite inferior compared to the Fieser reagent.[15]



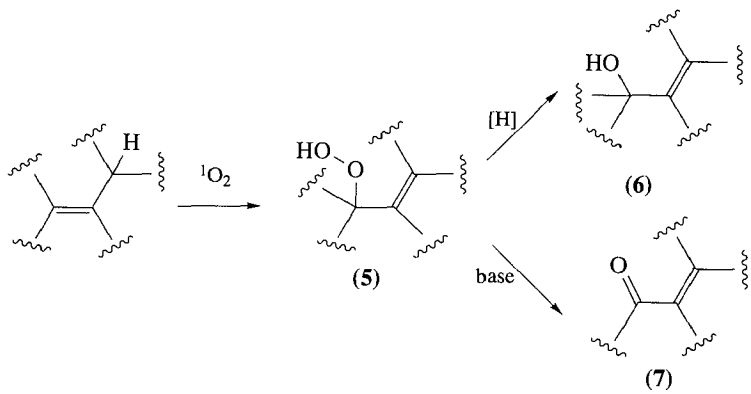
(3)



(4)

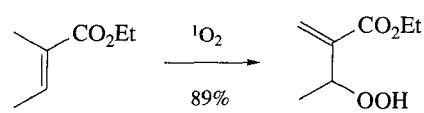
$CrO_3(py)_2$	0%
CrO_3•DMP	18%
CrO_3/HOAc/Ac_2O	67%

The allylic oxidation of alkenes by $^1O_2$ involves an ene reaction, and proceeds with rearrangement[10] as in Scheme 4. The intermediate allylic hydroperoxide (**5**) can be reduced to yield an allylic alcohol (**6**), or be treated with base to give an unsaturated carbonyl compound (**7**). The reaction works best on tri- or tetra-substituted alkenes, and the relative preference for attack is Me ≈ CH_2 >> CH. The $^1O_2$ allylic oxidation has been used in the synthesis of a large number of natural products, including some naturally occurring allylic hydroperoxides. It is possible that $^1O_2$ reactions of this type are involved in biosynthetic processes.

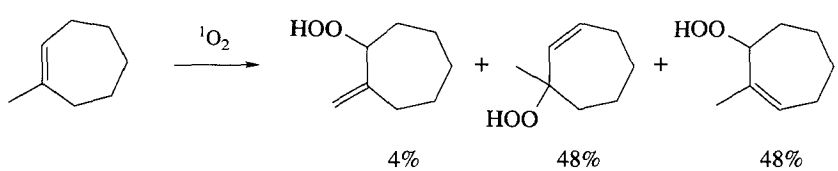


Scheme 4

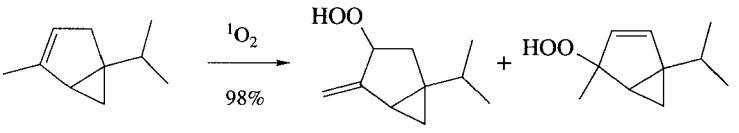
This oxidation is applicable to a wide variety of both electron-rich and electron-poor alkenes; for example a number of tiglic acid derivatives undergo this reaction in moderate to excellent yield,[16] as in equation (5). In cases where there are several nonequivalent allylic sites the course of this reaction is highly substrate dependent, and the yields and selectivity vary from excellent to mediocre. In trisubstituted alkenes (except for most 1-alkylcyclohexenes), a reactivity pattern has emerged which has been termed a preference for *syn* ene attack (or 'PSEA').[17] This means that $^1O_2$ will preferentially attack one of the two allylic carbons which are *cis* to each other. In practical terms, this still translates into relatively low product selectivity in most cases such as in equation (6), although some notable exceptions are known (equations 7 and 8).



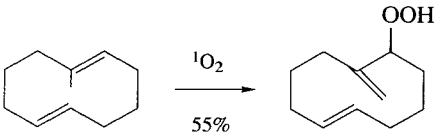
(5)



(6)



(7)

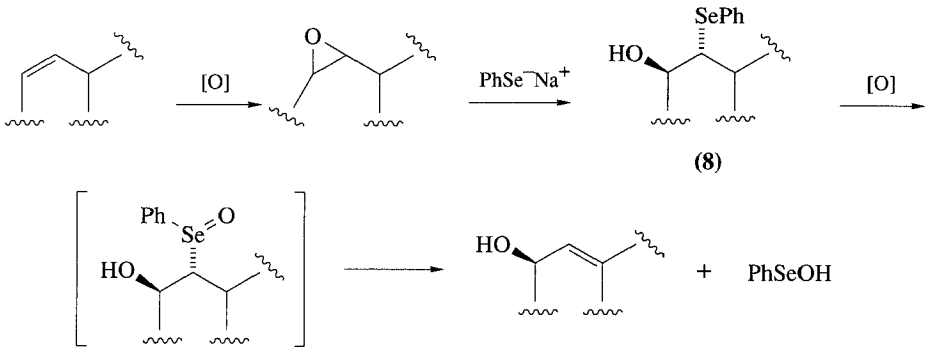


(8)

A procedure for the large-scale conversion of alkenes to unsaturated carbonyl compounds using singlet oxygen has been published,[18] whereby the conversion of cyclopentene to cyclopentenone can be carried out on a molar scale in 60% yield.

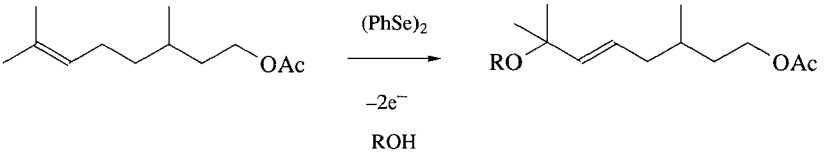
Another variant on this chemistry is the use of triphenyl phosphite ozonide as a source of singlet oxygen.[19] This reagent mimics singlet oxygen in many of its reactions, and is easier to quantify.

A further alternative to the singlet oxygen allylic oxidation method involves selenium chemistry.[20] This route involves epoxidation of the alkene, followed by nucleophilic opening of the epoxide with phenyl selenide anion, and finally oxidation to the selenoxide, which eliminates spontaneously to produce an allylic alcohol,[21] as described in Scheme 5. The β-hydroxy phenyl selenide (**8**) need not be isolated but can be oxidized *in situ*. The regioselectivity of this conversion depends on the degree of substitution on the alkene and the conformation of the β-hydrogens. The phenyl selenide anion will attack the least hindered carbon of the corresponding epoxide, and the geometry of the resulting double bond depends on the alignment of the hydrogens allylic to the original double bond; the elimination of the selenoxide is *syn*, and the transition state for elimination may require a rotation. If a ring fusion or conformational restrictions prevent the proper orbital overlap, the elimination may fail, or may give an enol if the hydroxy-bearing carbon is secondary.



Scheme 5

An electrochemical synthetic process (see Chapter 7.1, this volume) has been reported which requires only a catalytic amount of the selenating agent, and converts an alkene to the allylic alcohol in an aqueous cell, or to the allylic methyl ether if the electrolysis is run in methanol, as in equation (9).[22]

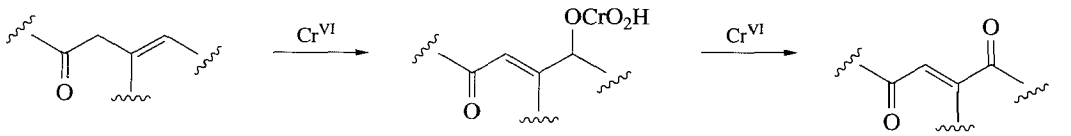


(9)

R = Me, 82%; R = H, 80%

A special case of allylic oxidation with rearrangement occurs in the action of chromium(VI) agents on 3,4-unsaturated ketones (**9**), and this is shown in Scheme 6. Hydrogen abstraction by the oxidant takes

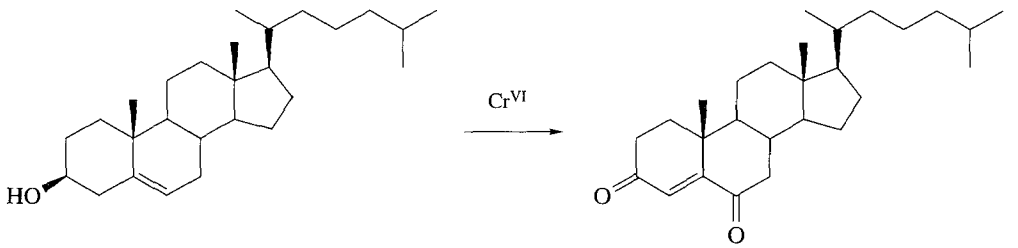
place at the doubly activated C-2 position of (**9**), and ultimate oxidation occurs at C-4 to give an enedione (**10**). This reaction is driven by the lability of the C-2 hydrogen, and by conjugation of the double bond with the carbonyl group; oxidation of the 3,4-unsaturated ketones is far more rapid than oxidation of their 2,3-unsaturated isomers. This reaction may have a broad scope, but the only examples to date involve six-membered ring-fused polycyclic and acyclic substrates.



(**9**) (**10**)

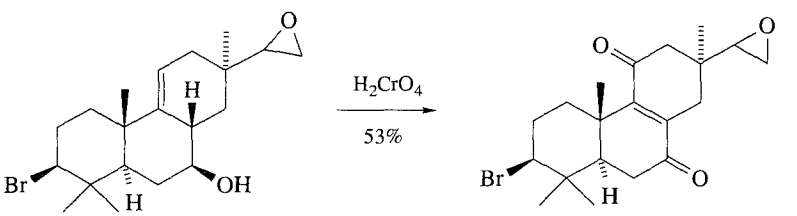
Scheme 6

The formation of a second carbonyl is not required, and where C-4 is fully substituted a 4-hydroxy-2-en-1-one is obtained.[23] The original carbonyl group may arise by oxidation of an alcohol, the classic example being the oxidation of cholesterol (**11**) to cholest-4-en-3,6-dione (**12**) with chromium(VI) reagents, in which a yield as high as 85% can be obtained, as in equation (10).[24] In degradation work on isopimarenes isolated from the mollusc *Aplysia kurodai*, Jones reagent serves to convert a β-hydroxyalkene (**13**) into the enedione (**14**) in moderate yield, as shown in equation (11).[25]



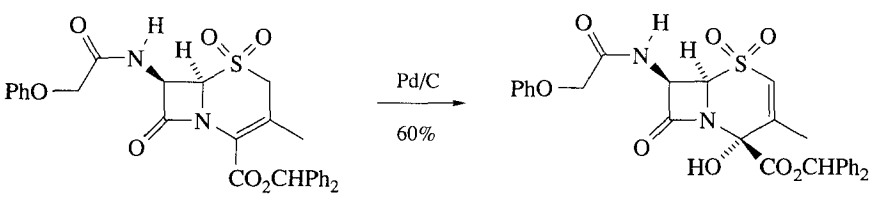
(**11**) (**12**) (10)

$Na_2Cr_2O_7$, AcOH, 40%; $CrO_3(py)_2$, AcOH, 85%



(**13**) (**14**) (11)

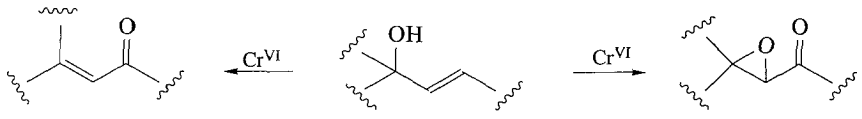
A related oxidative rearrangement of cephem dioxides has been reported[26] in which an alkene is oxidized stereospecifically with rearrangement to the allylic alcohol in good yield by simple exposure to a palladium/carbon catalyst, as depicted in equation (12). Adventitious oxygen preadsorbed on the catalyst seems the likely oxidant. The reaction fails on the parent cephem or its monoxide, or on the free acid of the dioxide. This reaction would seem to hold some promise for further utility in the cephem field and other related systems.



(12)

7.2.2.2 Allylic Alcohols

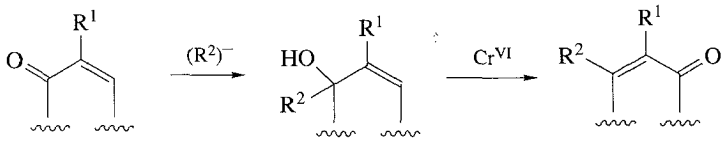
The oxidative rearrangement of allylic alcohols to α,β-unsaturated ketones or aldehydes is one of the most widely used synthetic reactions in this group, and forms part of a 1,3-carbonyl transposition sequence.[8] Scheme 7 shows this reaction and the related conversion of the allylic alcohol to an α,β-epoxy carbonyl compound. Chromate reagents induce some allylic alcohol substrates to undergo a directed epoxidation of the alkene without rearrangement, but this reaction is beyond the scope of the present discussion.



Scheme 7

The mechanism for this transformation, and the partitioning between unsaturated carbonyl and epoxycarbonyl products has been the subject of several studies.[27] The production of epoxycarbonyl compounds seems to be correlated with the nature of the chromate reagents used, although substrate structure also helps to determine this preference.

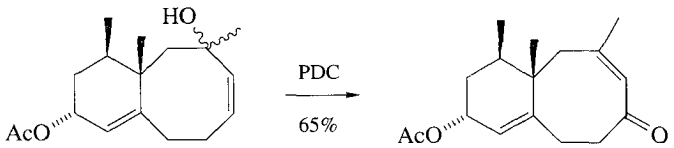
However, the conversion to the transposed α,β-unsaturated carbonyl compound is by far the more useful reaction. The full sequence serves both to form carbon–carbon bonds as well as to adjust the functional group array in the synthetic intermediate. Thus, starting with the enone (**15**), organometallic addition generates a tertiary allylic alcohol (**16**) and oxidative rearrangement yields a β-alkyl-α,β-enone (**17**), as shown in Scheme 8.



(15) **(16)** **(17)**

Scheme 8

Applications are found in acyclic as well as five-, six-, seven- and eight-membered ring cyclic substrates, and yields are generally in the range of 50–90%. The best substrate is one in which the C—O bond of the alcohol is (or can easily become) parallel with the *p*-orbitals of the alkene double bond, as the transition state is believed to involve a 3,3-sigmatropic rearrangement of the chromate ester. Isolated double bonds, esters, lactones and silyl ethers, and a number of other functional groups, survive these conditions. Protected carbohydrates undergo degradation which limits the application to such substrates. Examples are found in equations (13)–(15).[28–30]



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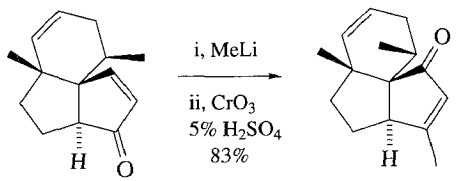
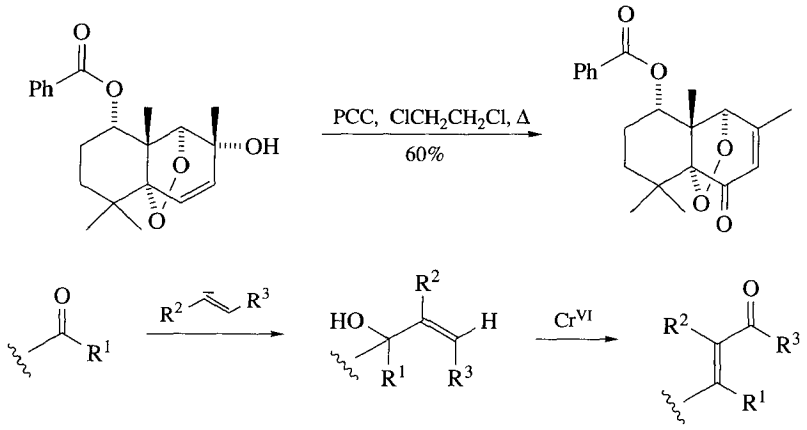


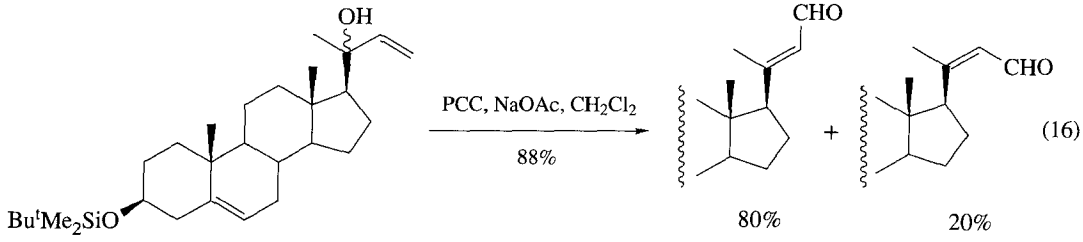
(14)

Ketones can be homologated to unsaturated ketones or aldehydes by addition of the appropriate vinyl nucleophile followed by oxidative rearrangement, as shown in Scheme 9. The use of this transformation in a synthetic approach to steroids with unsaturated side chains is shown in equation (16).[31]



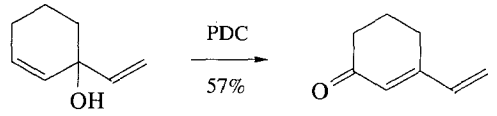
(15)

Scheme 9

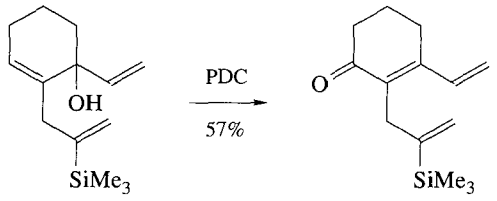


(16)

The regioselectivity of these reactions has been studied in cases where two allylic rearrangements would be possible. In one report tertiary alcohols which were both allylic and propargylic were found to rearrange solely over the allylic system where the alkene is contained in a five- or six-membered ring.[32] In a cyclic system where the alcohol is equatorial, and in acyclic systems, the yield of rearrangement is poor and oxidative cleavage becomes important. In a particularly interesting study a series of bis-allylic alcohols were examined.[33] Vinylic cyclohexenols and cyclopentenols rearrange exclusively within the ring to give 57–80% yields of the β-vinylic cyclohexenone or cyclopentenone, as shown in equation (17). The bis-allylic alcohol (**18**; equation 18), which contains an allylsilane substituent, undergoes clean oxidative rearrangement to the dienone (**19**). This example helps to clarify the mechanism of the rearrangement, since a discreet carbonium ion intermediate would doubtless be trapped through cyclization with the allylsilane moiety; the absence of such cyclization products argues against a cationic intermediate and in favor of the 3,3-sigmatropic mechanism. The fact that the mildly nucleophilic allylsilanes (see Volume 2, Chapter 2.2) survive this reaction is important for its synthetic utility.



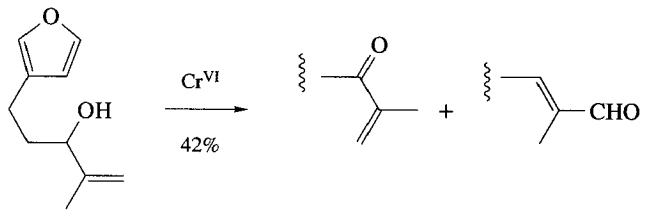
(17)



(18)

(18) **(19)**

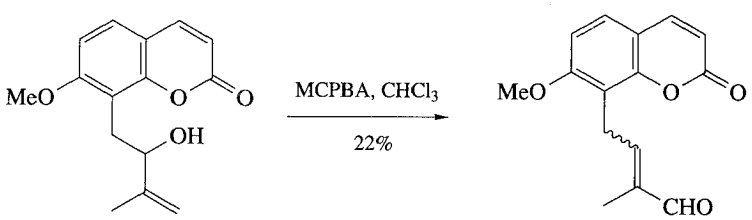
Where the allylic alcohol is in a secondary position, conformational effects or the character of the oxidant can still favor an oxidative rearrangement over simple oxidation to the ketone (equation 19).[34]



(19)

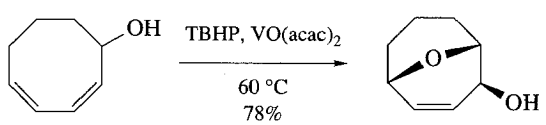
PCC	100%	
PCC, TsOH	17%	83%

An oxidative rearrangement took place during the MCPBA epoxidation of the secondary allylic alcohol auraptenol, leading to the enal shown in equation (20). This reaction has been used in an approach to casegravol and in a synthesis of arnottinin.[35] The reason why the intermediate epoxy alcohol undergoes rearrangement in this case is not known beyond the possibility that the *m*-chlorobenzoic acid by-product could act as an acidic catalyst.



(20)

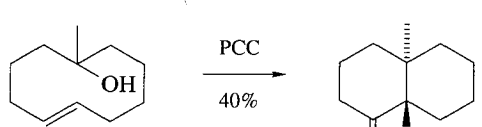
The peculiar oxidative rearrangement of cycloocta-2,4-dien-1-ol (**20**) shown in equation (21), involves a highly selective *cis* epoxidation (*cis*:*trans* = 20:1) followed by transannular S_N2' attack by the hydroxy group on the allylic epoxide to give the *exo*-β-hydroxy cyclic ether (**21**).[36] This rearrangement is stereospecific in that the *trans*-epoxy alcohol, available by treatment of the cyclooctadienol with MCPBA, does not give a rearranged product. A similar example with a cycloheptadienol was also reported. The pure *cis*-epoxy alcohol rearranges to the bicyclic alcohol at 156 °C, but does so far more rapidly in the presence of the vanadium catalyst at 60 °C.



(21)

(20) **(21)**

The cyclodecenol substrate (**22**; equation 22), undergoes a transannular oxidative rearrangement to yield the decalone (**23**) in moderate yield.[37] Although not strictly a simple functional group rearrangement, this reaction can be thought of as the through-space version of the oxidative rearrangement of allylic alcohols. In this case it is quite likely that the reaction proceeds through attack by the alkene on the carbon bearing a preformed chromate ester, which behaves as a leaving group. The intermediate decalinyl carbonium ion is captured by additional chromate and eliminates to the observed product (**23**).

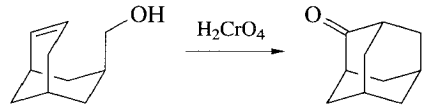


(22)

(22) **(23)**

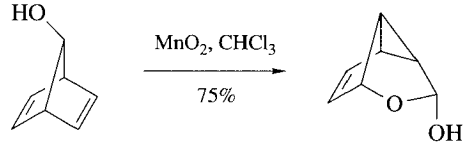
A related example occurs in the adamantane field, as seen in equation (23).[38] It is surprising that a primary alcohol undergoes ring closure instead of the standard oxidation to an aldehyde or acid under the influence of chromate. The chromate ester of this *endo*-oriented alcohol would undoubtedly experience severe crowding, and direct oxidation is probably inhibited for steric reasons.[39] In both of these cases the

proximity of the alkene to the carbinol carbon seems to drive the rearrangement, and there is precedent for a related type of oxidative cyclization.[8] In a further example, the norbornadienol (**25**; equation 24) is oxidized by MnO_2 with rearrangement to give the hemiacetal (**26**).[40] This reaction is believed to involve a displacement of the Mn^{4+} ester by the alkene, followed by oxidation of the resulting carbonium ion and cleavage.



(23)

(24)



(24)

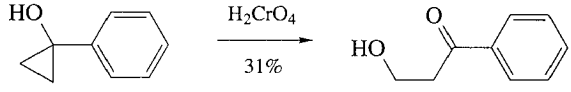
(25) (26)

7.2.2.3 Cyclopropanes and Cyclobutanes

The strained rings of cyclopropanes[3] and cyclobutanes[4] can be considered as functional groups, since these molecules react in ways which are not characteristic of other cycloalkanes. The chemical behavior of cyclopropanes in particular has many analogies to that of alkenes. For the purposes of this discussion the oxidative ring cleavage reactions of cyclopropanes and cyclobutanes which do not have counterparts in the chemistry of larger rings are considered as functional group rearrangements.

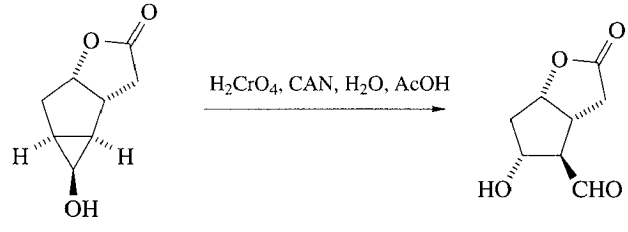
Oxidative cleavage of cyclopropanes has been studied mostly with lead(IV),[2c,9] thallium(III)[6] and chromium(VI) reagents.[2b,8] The oxidative cleavage of cyclobutanols has been explored mainly with chromium(VI) reagents,[2b,8] although other oxidants have been studied.[4]

Cyclopropanols undergo oxidative cleavage with a variety of oxidants to give β-functionalized propanal derivatives. Even secondary cyclopropanols give moderate yields of ring-opened products. The activation barrier on the pathway to cyclopropanone is steep, and the alternative pathway of rearrangement is driven by relief of ring strain. The example given in equation (25) shows the use of chromic acid.[8] These oxidations are much faster than the oxidation of a normal secondary alcohol.



(25)

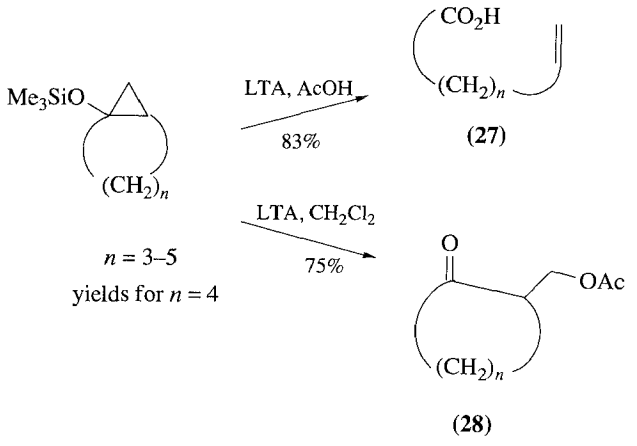
An approach to a prostaglandin intermediate employed a cyclopropanol oxidation with a mixed chromate/cerate reagent shown in equation (26), but the yield was unacceptably low.[41] Although no information on the selectivity is available, the *trans* stereochemistry of oxidative cleavage in the reported product is of note. In these more complex substrates, side reactions and low yields plague the reaction, which will see only limited use in synthesis unless a better reagent system is developed.



(26)

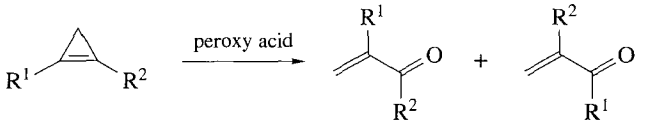
The lead tetraacetate oxidation of tertiary cyclopropanol silyl ethers does show some promise.[42] As shown in Scheme 10, a two-bond oxidative cleavage of the three-membered ring takes place in acetic acid solvent to yield the alkenoic acid (**27**); a carboxy group is produced from the original carbinol carbon and the alkene is derived from the other two ring carbons. The yields for this transformation are from 65–88%, and with a substituent on the methylene bridge the fragmentation is highly stereoselective for

alkene geometries. In methylene chloride, a one-bond cleavage takes place to give the acetoxymethylcycloalkanone (**28**). Both types of reaction are useful, and as the starting cyclopropanols are available through Simmons–Smith methylenation of the corresponding silylated enol (see Volume 4, Chapter 4.7), these methods have good synthetic potential.



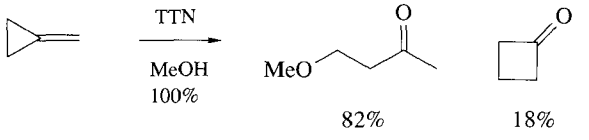
Scheme 10

Cyclopropenes undergo an oxidative cleavage to yield substituted enones, as shown in equation (27).[43] The reaction is believed to proceed through the unstable epoxide. The regioselectivity is generally low if $R^1 \neq R^2$, but if one of the substituents is trimethylsilyl a highly selective conversion to the α-silyl enone takes place. There is one report of a similar oxidative cleavage that takes place with thallium(III).[6]



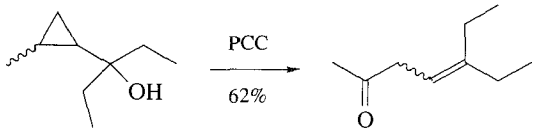
(27)

Methylenecyclopropane undergoes oxidative cleavage and ring expansion with thallium trinitrate in methanol to furnish in quantitative yield a mixture of the ring cleavage product 1-methoxybutan-3-one and cyclobutanone in the ratio of 4:1, as in equation (28).[44]



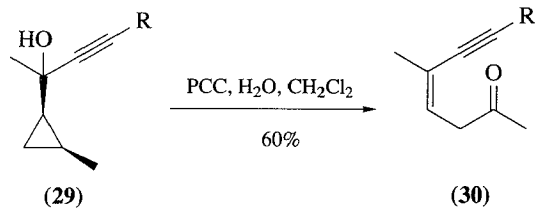
(28)

The oxidative rearrangement of tertiary cyclopropylcarbinols to 3,4-unsaturated carbonyl compounds is analogous (or homologous) to the reaction of allylic alcohols, and is shown in the example in equation (29).[8] This reaction has been shown to proceed stereospecifically in the conversion of the *cis*-substituted cyclopropylcarbinol (**29**) to the (*Z*)-enynone (**30**) shown in equation (30).[45] The substrates with R = H, Me and TMS all gave comparable yields.



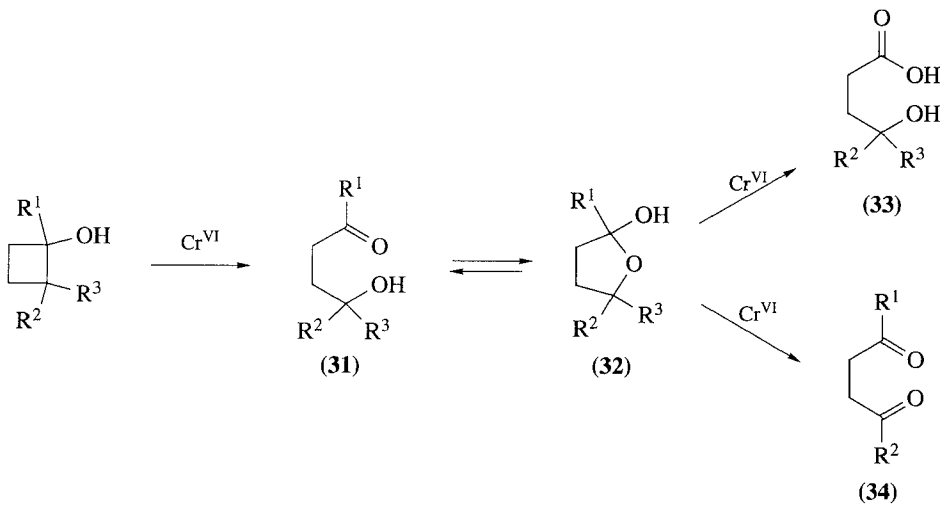
(29)

Cyclobutanols oxidize with ring cleavage to 4-hydroxy ketones, 4-hydroxy acids, or 1,4-diones under the influence of chromium(VI) reagents (Scheme 11).[8] The first formed product is a 4-hydroxycarbonyl compound (**31**) which exists as the five-membered ring hemiacetal (**32**). This form will persist in the absence of excess reagent under nonforcing conditions; otherwise further oxidation takes place to give a



(29) (30) (30)

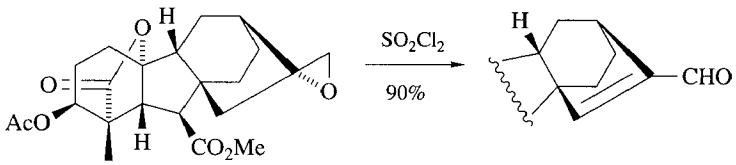
4-hydroxy acid (**33**; if R^1 = H) or a 1,4-dione (**34**; if R^3 = H). In unsymmetrical cyclobutanes the bond cleaved is the one between the carbinol carbon and the more highly substituted β-carbon, and the yields are generally good. With a quaternary β-carbon (R^2 and R^3 = alkyl) some of the 3,4- or 4,5-unsaturated carbonyl product arises.



Scheme 11

7.2.2.4 Miscellaneous Functional Group Rearrangements

Treatment of 1,1-disubstituted epoxides of the gibberellin family with sulfuryl chloride results in the formation of the corresponding α,β-enal in good yield, as shown in equation (31).[46] Four examples were reported in which alcohols, esters, lactones and alkenes survive. The postulated mechanism involves an electrophilic opening of the epoxide with elimination, followed by oxidation of the primary chlorosulfate ester. A steroidal 3-spirooxirane also undergoes this reaction, but the yield is poor and several products are obtained, suggesting that the overall scope of this reaction may be limited.

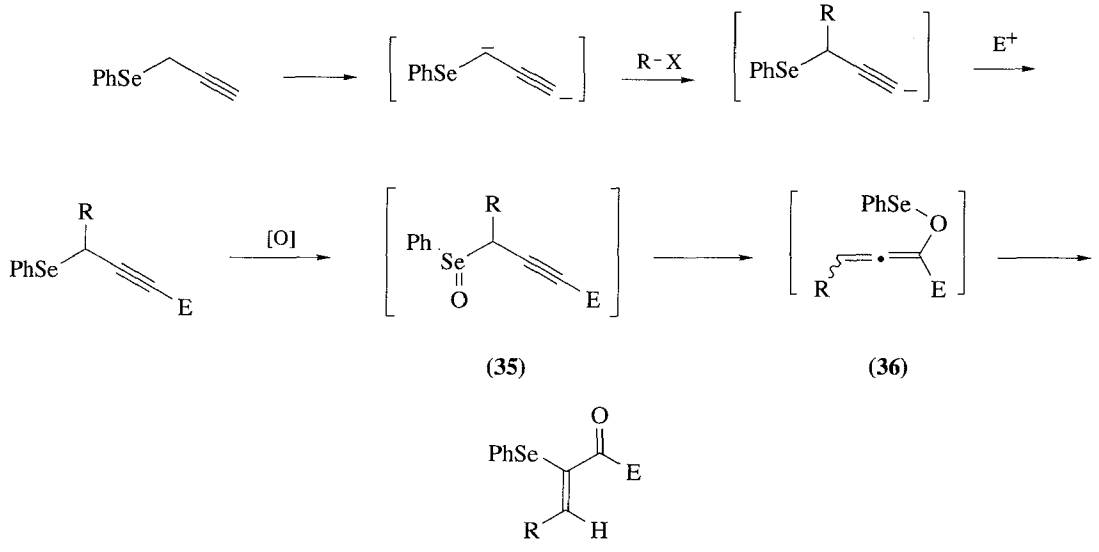


(31)

The Pummerer rearrangement (which is discussed in Volume 6, Chapter 4.7) is a type of oxidative rearrangement, as is the related 2,3-sigmatropic rearrangement of 2,3-unsaturated sulfoxides. Two related examples are presented here from selenium chemistry.[20] These reactions enhance the attractiveness of sulfur- and selenium-based synthetic methods, in that after being used to forge new carbon–carbon bonds, the heteroatom moiety can be exploited for a further functional group interchange.

Propargyl phenyl selenide is a versatile multifunctional acrylate synthon, as shown in Scheme 12.[47] The dianion is prepared and reacted successively with an alkylating agent (R—X) and an electrophile (E^+). The oxidative rearrangement of the propargylic selenoxide (**35**) to an allenic selenenate (**36**), and thence to the α-phenylselenoenone (**37**), forms the keystone of this synthetic method, and overall yields from propargyl phenyl selenide are in the range of 38–68%. Further elaboration of (**37**) is possible

through conjugate additions, deselenation or another oxidative rearrangement. This method was used in a synthesis of 7-hydroxymyoporone.[47]

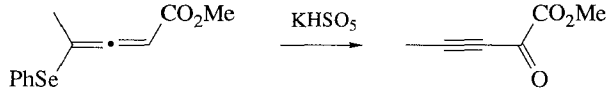


(35) (36)

(37)

Scheme 12

Equation (32) shows another example of this type of rearrangement, in which a phenylselenoallenic ester is converted to an α-keto alkynic ester in quantitative yield.[48]



(32)

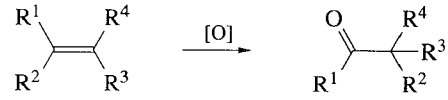
7.2.3 OXIDATIVE SKELETAL REARRANGEMENT

The discussion in this section is divided according to the functional group undergoing oxidative rearrangement: alkenes and enols, dienes, alkynes, cyclopropanes and cyclobutanes, and miscellaneous skeletal rearrangements. In view of the voluminous body of work on alkenes and enols, this area has been subdivided according to particular substrates: arylalkenes, aryl ketones, chalcones and cinnamyl compounds, and cyclic alkenes and ketones. Chalcones and cinnamyl compounds are treated as a special case of arylalkenes because of the extensive synthetic use of the chalcone to isoflavone transformation. In order to focus on the application to ring expansion and ring contraction reactions, cyclic alkenes and ketones are treated as a separate case, and methylenecycloalkanes are discussed with cycloalkenes. For the cyclopropanes and cyclobutanes, the scope is limited to the skeletal rearrangements of the small rings which do not have counterparts in the chemistry of larger ring compounds. The oxidants which have played the largest role in these transformations are thallium(III),[6a] lead(IV)[2c,9] and iodine.[49] The best reagents appear to be lead tetraacetate and thallium trinitrate, although on a larger scale cost is a concern for the latter, and toxicity is a problem for both. The newer hypervalent iodine reagents may prove more amenable in view of these factors.

Three highly useful synthetic transformations are presented in this section: the synthesis of isoflavones from chalcones, the synthesis of α-arylalkanones from arylalkenes, and the synthesis of α-arylalkanoic acids from aryl ketones. Two others are potentially useful methods, but are not as yet widely used: the preparation of α-branched carboxylic acids from alkynes, and the ring expansion and ring contraction of cyclic alkenes and ketones.

7.2.3.1 Alkenes and Enols

The oxidative rearrangement most widely used in synthesis is the oxidative 1,2-shift of an alkene or enol, which is shown in the formal sense in equation (33). The alkene may be electron deficient such as an unsaturated ketone, or electron rich such as an enol, enol ether or enamine.

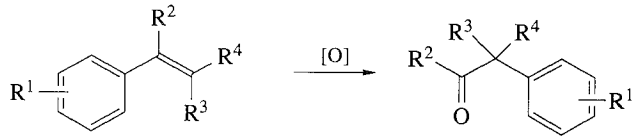


(33)

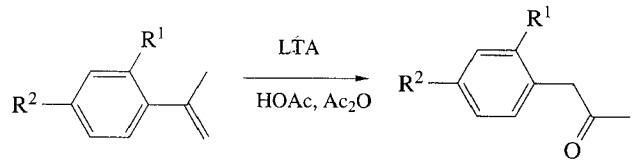
If R^2 and R^3 are connected then a ring contraction results. If R^1 and R^2 are connected, a ring expansion takes place. The reagents used to carry out this transformation are strongly electrophilic oxidants, or an oxidant used together with a Lewis acid. Hypervalent main group oxidants such as thallium(III), lead(IV) and iodine(III) have played the largest role in this area. The substrates have been divided into four major groups by compound class: arylalkenes, aryl ketones, chalcones and cinnamyl compounds, and cyclic alkenes and ketones in ring expansion and ring contraction reactions.

7.2.3.1.1 Arylalkenes

Arylalkenes undergo oxidation with 1,2-rearrangement of the aryl group to give α-arylcarbonyl compounds, and this reaction is shown in the formal sense in equation (34). Useful reagents for this transformation include lead(IV),[50] thallium(III),[51] iodine(III),[52] and palladium.[53] The yields for this reaction are moderate to excellent, and there is a reasonable tolerance of functional groups on the aromatic ring (R^1) such as halogen, methyl or methoxy. At least one *ortho* substituent is permissible with no loss in yield. If R^2 = H, the product is an α-aryl aldehyde, and if R^2 = alkyl an α-aryl ketone is obtained. The rearrangement of 2-propenylbenzenes to the 1-arylpropan-2-ones is important due to the interest in the latter compounds as pharmaceutical intermediates, as in equation (35).[50b]



(34)

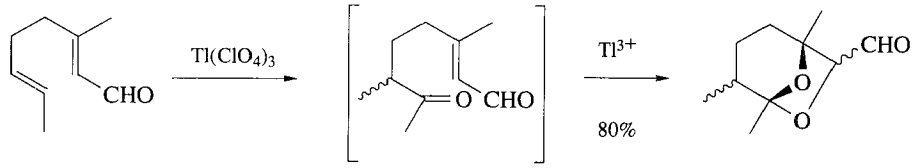


(35)

R^1 = OMe; R^2 = Me; 52%

R^1 = H; R^2 = OMe; 80%

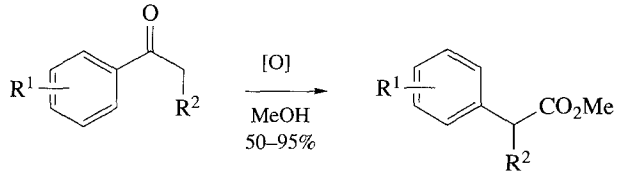
The interesting sequence depicted in Scheme 13 for a sequential oxidative rearrangement and hydroxylation of citral shows some potential for this reaction in nonaromatic alkenes. This transformation affords an elegant, single-step approach to the 6,8-dioxabicyclo[3.2.1]octane skeleton, although the stereoselectivity for the two induced centers is poor.[54]



Scheme 13

7.2.3.1.2 Aryl ketones

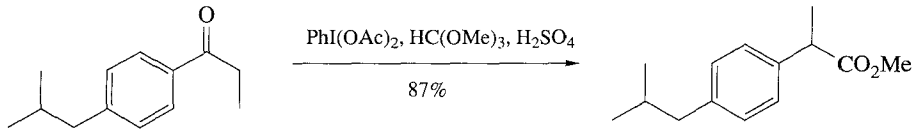
Aryl ketones undergo oxidative rearrangement with hypervalent main group oxidants such as thallium(III), lead(IV) and iodine(III) to give α-arylalkanoic acids in good to excellent yield,[55] and the general transformation is shown in equation (36).[6a,56] This reaction is related to the Willgerodt–Kindler reaction,[57] and has drawn considerable attention due to the antiinflammatory properties of the product α-arylalkanoic acids. A Friedel–Crafts acylation of an aromatic precursor followed by this oxidative rearrangement forms the synthetic sequence of choice for these compounds. At least a dozen patents have been issued on applications of this method, including one which describes a process catalytic in thallium.



(36)

The best results are obtained with the above-named oxidants in a mixed solvent of methanol and trimethyl orthoformate in the presence of a strong acid; these conditions presumably ensure rapid acetalization of the carbonyl to prevent α-oxidation. This side reaction is more serious when R^2 is alkyl and the orthoformate is omitted, or if ethyl carbonate or acetonitrile is used as solvent. Preformed enol ethers and enamines give the desired oxidative rearrangement in high yield.

A wide variety of substituents are tolerated. The group R^1 can be alkyl, halogen, alkoxy, *N*-amido, azidomethyl, ester, aryl, aryloxy and aryloyl, and at least one *ortho* substituent is permissible with no loss in yield. The aromatic ring can also be 2-naphthyl, 9,10-dihydro-2-phenanthryl, 3-pyridyl, thiophen-2-yl or pyrrol-3-yl. The group R^2 can be hydrogen, alkyl, acyl or acetic acid. Beyond the antiinflammatory targets, successful reaction substrates include the methyl ketones of a binaphthyl crown ether, a morphinane and a polyaromatic hydrocarbon. The preparation of ibuprofen methyl ester (**38**) is shown in equation (37) as a typical example.[56c]



(37)

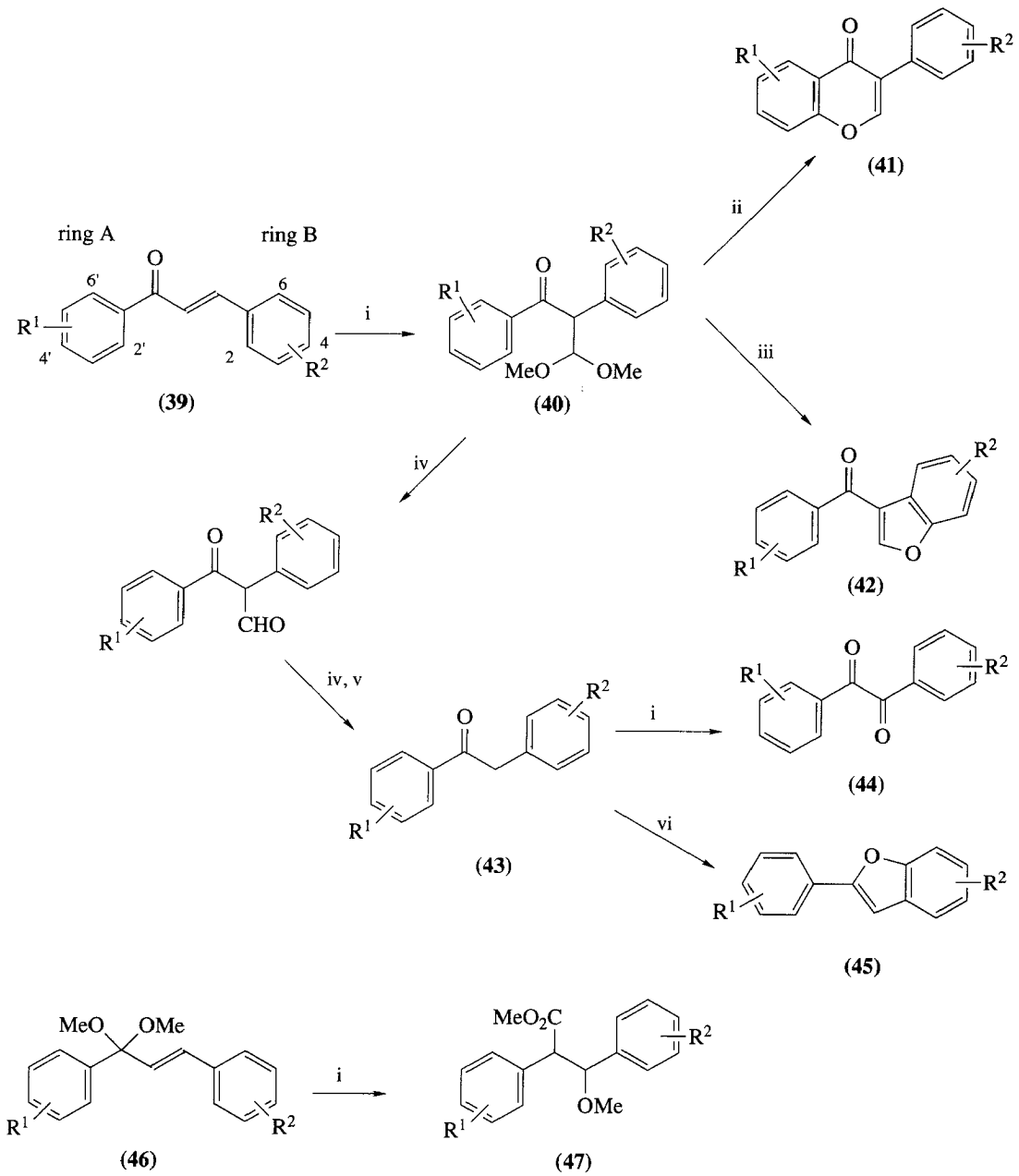
(**38**)

Dialkyl ketones have been little studied as precursors in this reaction. Selenium dioxide with hydrogen peroxide and *t*-butyl alcohol effects a similar reaction with these substrates to give 35–40% yield of the corresponding carboxylic acid. In methyl alkyl ketones, the regioselectivity is of the order of 5:1 in favor of methyl migration.[58]

7.2.3.1.3 Chalcones and cinnamyl compounds

While following the reactivity patterns of arylalkenes, the extensive use in synthesis that has been made of the chalcone to isoflavone conversion and related sequences warrants a separate treatment. Chalcones (**39**) oxidize with thallium(III)[6a,59] and iodine(III)[52a] under rearrangement of the aromatic B-ring to give 3,3-dimethoxy-1,2-diarylpropan-1-ones (**40**) in yields from 30–90%, as shown in Scheme 14. This intermediate can be hydrolyzed in aqueous acid, and will cyclize to give an isoflavone (**41**) if a hydroxy group is present at C-2′ in the A-ring, or to give a benzoyl benzofuran (**42**) if a hydroxy group is present at C-2 in the B-ring. If the oxidation is carried out in acidic aqueous glyme, deformylation of this intermediate takes place *in situ* to furnish a substituted benzyl phenyl ketone (**43**), which undergoes further oxidation to the benzil (**44**). The isolated dimethyl acetal can be hydrolyzed, deformylated and cyclized to the corresponding phenylbenzofuran (**45**).[60] A preformed chalcone acetal (**46**) undergoes oxidation with migration of the A-ring phenyl to give 3-methoxy-1,2-diarylpropionates (**47**).

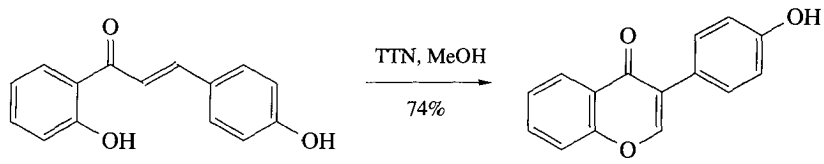
By far the most used pathway is that leading to the isoflavones, and literally scores of natural products have been prepared in this way. The yields for these cyclizations vary from 10–90%. Good solubility in methanol is the key to a successful reaction. The oxidation may be carried out with an unprotected C-2′ hydroxy with TTN/methanol, as long as the C-5′ position is unsubstituted; substrates of the latter type



i, TTN, MeOH; ii, HCl (2'-hydroxy); iii, HCl (2-hydroxy); iv, HCl, H_2O; v, heat; vi, heat (2-hydroxy); R^1 and R^2 can be alkyl, alkoxy, single or multiple

Scheme 14

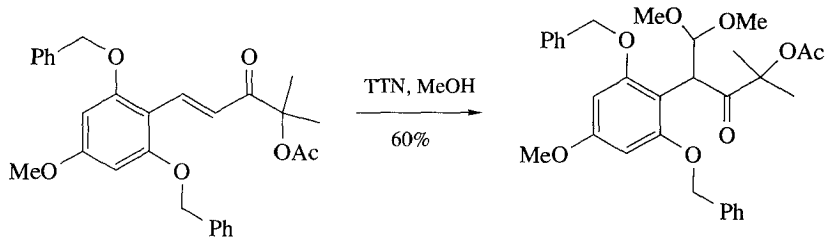
will oxidize to quinone-type products. Aside from this exception, the tolerance for substitution in both rings is rather broad. R^1 and R^2 can be alkyl, alkoxy, halogen, acetoxy, methylenedioxy and pentaacetyl-β-glycosyl. Attempted oxidative rearrangement of a unprotected C-3′-β-glucosyl chalcone in a synthesis of 7,4′-di-*O*-methylpuerarin gave a low yield, but this was attributed to low solubility and separation problems; the protected glucosyl derivative gave a 90% yield of the target.[61] A dihydropyran ring may be fused to either of the aromatic rings, but some degradation does occur with a similarly fused pyran ring. A free hydroxy group in the B-ring has been used, as in the example found in equation (38), but yields are somewhat better if it is protected as the acetate or the methoxymethyl ether. Ring B can tolerate at least one *ortho* substituent, but ring A can be fully substituted with little loss in yield.



(38)

The ready availability of chalcones, from aldol condensation of acetophenones and benzaldehydes, makes this oxidative rearrangement a useful synthetic entry to isoflavone targets. The isoflavone products may be further elaborated to isoflavanones, isoflavans, pterocarpans and coumestones, broadening the scope of this method.

Cinnamyl compounds rearrange in a similar fashion under the influence of thallium(III), as shown in equation (39); this reaction was used in a synthetic approach to the polystachins.[62] Cinnamaldehydes and cinnamate esters react likewise to give the corresponding α-aryl-substituted malondialdehyde bisacetals and β,β-dimethoxypropionates, respectively.

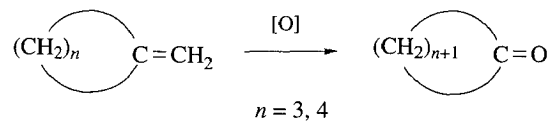


(39)

7.2.3.1.4 Cyclic alkenes and cyclic ketones: ring expansion and ring contraction

The oxidative rearrangement of cyclic alkenes and ketones often leads to ring expansion[63] or ring contraction reactions. The reagents generally used for this purpose are hypervalent main group oxidants such as thallium(III), lead(IV), iodine(III) and selenium(IV), although palladium(II) has been used as well.

Methylenecycloalkanes undergo ring expansion to the next higher homologous cycloalkanone, as shown in equation (40). The yields are good to excellent for four- and five-membered rings, and for six-membered rings if fused to an aromatic ring. The example given in equation (41) comes from a synthetic route to dopamine receptor stimulating compounds.[64] Simple methylenecyclohexanes give hydroxylation products, and the reaction does not appear to have been tried in larger rings. Thallium(III),[6a] lead(IV)[65] and palladium(II)[66] reagents have been used for this transformation, which is related to the pinacol rearrangement and the Demjanov rearrangement (Volume 3, Chapters 3.2 and 3.3 respectively).



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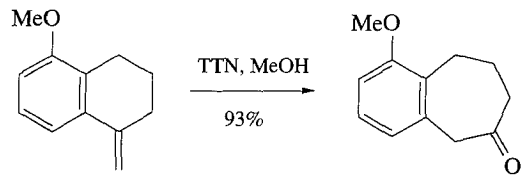
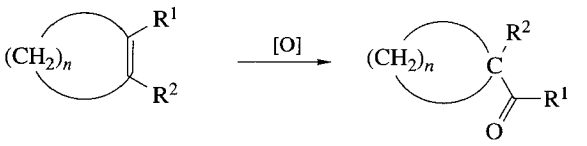


(41)

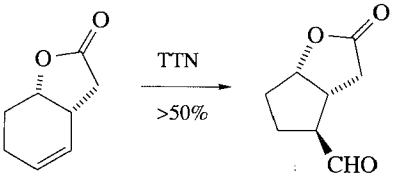
Cycloalkenes give ring contraction products, as shown in equation (42). This reaction is related to the Favorskii rearrangement and the Wolff rearrangement of ketones (Volume 3, Chapters 3.7 and 3.9, respectively). Moderate to good yields are obtained from four- to seven-membered ring cycloalkene substrates, although cyclopentenes give lower yields in favor of hydroxylation. Dihydropyrans yield the corresponding tetrahydrofuranyl aldehydes. This type of reaction was used in the stereospecific preparation of a key prostaglandin intermediate, as shown in equation (43).[67] Thallium(III)[6a] and lead(IV)/BF_3·Et_2O[68] are the reagents of choice for this transformation.

Cycloalkanones of ring size from four to six oxidize with ring contraction to give the cycloalkanecarboxylic acid of the next smaller ring size with thallium(III), as shown in equation (44). This reaction



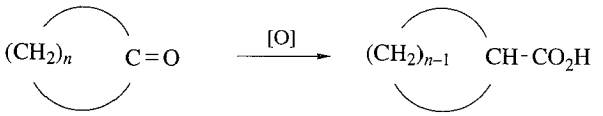
(42)

R^1 = H, alkyl, amino; R^2 = H, alkyl; n = 2–5



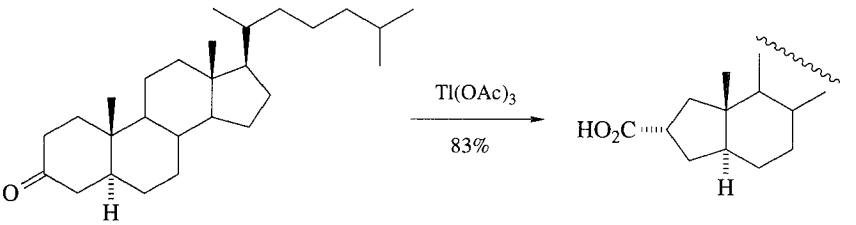
(43)

goes through the enol form, and requires acid, since in base cycloalkanones undergo α-hydroxylation. Cyclohexenones are converted in moderate to good yield to the cyclopentene-3-carboxylic esters by TTN/methanol.[69] Good yields of ring contraction products are obtained from 3-keto steroids, as shown in equation (45),[6a] but ketones at other positions are much less selective in this reaction. Selenium dioxide has been used in this reaction with five-, six-, seven- and twelve-membered ring ketones.[70] This reagent does not tolerate α-branching in the substrate, which leads to Baeyer–Villiger-type reaction.



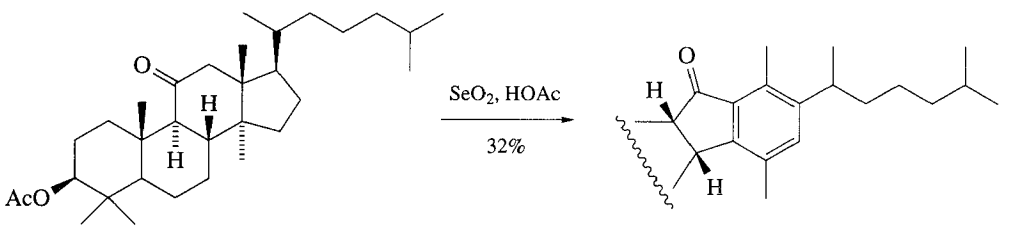
(44)

n = 3–5



(45)

With some polycyclic substrates, a tandem ring expansion and ring contraction can take place under conditions of oxidative rearrangement. The 11-oxolanostanyl acetate (**48**; equation 46) undergoes such a reaction, in which ring C is contracted and ring D is expanded and aromatized.[71] The yield is poor though, and such a transformation would seem to have limited synthetic potential.



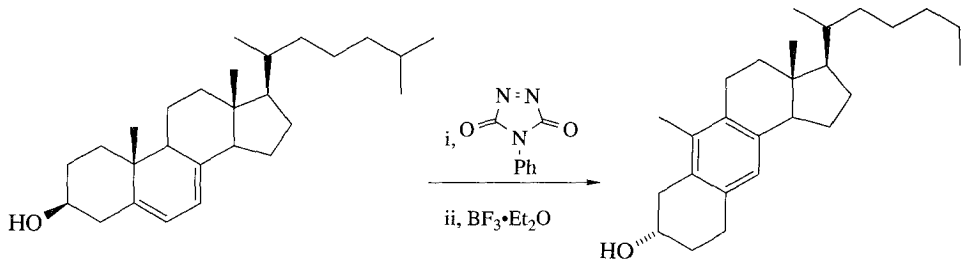
(46)

(48)

7.2.3.2 Dienes

Oxidative rearrangements of dienes are related to the dienone/phenol rearrangement, which is discussed in Volume 3, Chapter 3.5. The examples discussed here are limited to cyclohexadienes, and the driving force for the rearrangement is aromatization.

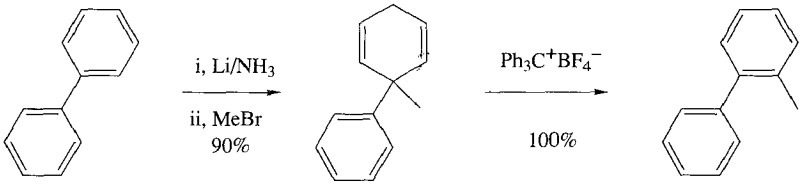
A novel route to the ring B aromatic anthrasteroids (**49**) from 5,7-dienes (**50**) proceeds in two steps and uses 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) as the oxidant, as is shown in equation (47).[72] Addition of PTAD to the steroidal 5,7-diene gives an adduct which, when treated with boron trifluoride etherate, rearranges to the anthrasteroid in generally greater than 90% yield. This reaction presumably proceeds through a spirocyclohexa-1,4-diene.



(47)

(**50**) (**49**)

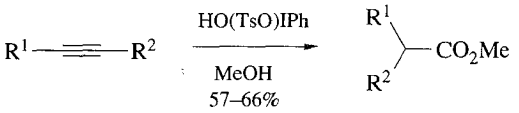
Scheme 15 depicts a high yield, general method for specific *ortho* alkylation of polycyclic aromatic hydrocarbons.[73] In this example, biphenyl is subjected to reductive methylation followed by oxidative rearrangement with trityl tetrafluoroborate to give 2-methylbiphenyl. In unsymmetrical substrates the regioselectivity is poor; phenanthrene gives a 3:2 mixture of 4-methyl- and 1-methyl-phenanthrene.



Scheme 15

7.2.3.3 Alkynes

Disubstituted alkynes will undergo oxidation with a concomitant 1,2-alkyl shift under the right conditions, to yield α-branched carboxylic acid derivatives. A variety of oxidants will effect this transformation, including nitrous oxide,[74] peracetic acid,[75] thallium trinitrate (TTN)[6a] and [hydroxy (tosyloxy)iodo]benzene (HTIB).[76] Yields are moderate to good, as shown in equation (48) for the use of HTIB, where R^1 is alkyl and R^2 may be alkyl or aromatic. The TTN procedure is limited to arylalkylalkynes, as diarylalkynes will oxidize to α-diones and dialkylalkynes yield α-methoxy ketones. The TTN and HTIB reactions proceed through a solvometallation intermediate. The peroxy acid and N_2O reactions are believed to proceed through cycloaddition and rearrangement to a ketene; diphenylacetylene is converted to methyl diphenylacetate by N_2O in methanol.



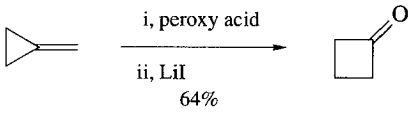
(48)

7.2.3.4 Cyclopropanes and Cyclobutanes

As was discussed in Section 7.2.2.3, cyclopropanes[3] and cyclobutanes[4] form a special group, with behavior distinct in many ways from that of other cycloalkanes. Several examples of oxidative skeletal rearrangements of these strained ring compounds are presented here.

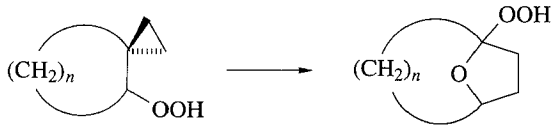
Methylenecyclopropanes undergo oxidative ring expansion in a two-step sequence; peroxy acid oxidation to an oxaspiropentane followed by lithium iodide induced rearrangement yields a cyclobutanone in moderate yield, as illustrated in equation (49).[77] Cyclobutanone is a minor product from the reaction of

methylenecyclopropane with thallium trinitrate, in contrast to the analogous reaction of the larger methylenecycloalkanes.



(49)

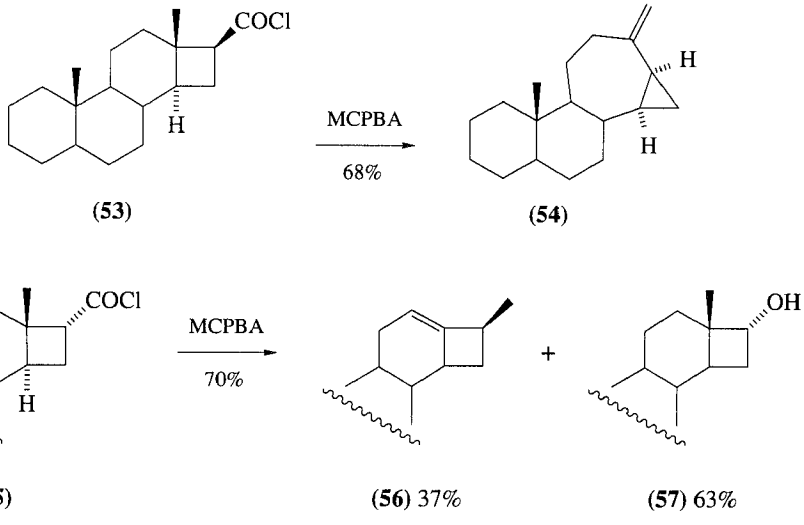
Spiro-fused cyclopropyl carbinols undergo solvolysis with hydrogen peroxide to give the corresponding hydroperoxides (**51**), which rearrange to the two carbon ring-expanded bicyclic hydroperoxy hemiacetals (**52**) in good yield, as in equation (50).[78] Yields range from 72–91% for a variety of ring size substrates, and the rearrangement is stereospecific in that the stereochemistry of the initial alcohol is reflected in the stereochemistry of the bridgehead carbon in those rings large enough to accommodate this feature.



(50)

(**51**) (**52**)

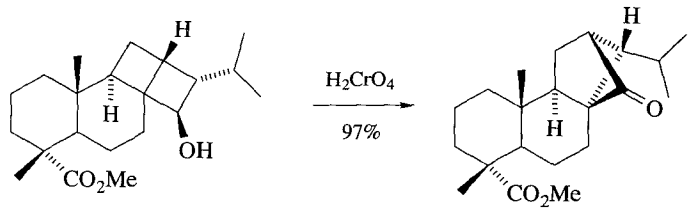
Ring D norsteroidal carboxylic acid chlorides do not follow the normal carboxy inversion reaction on treatment with MCPBA, as shown in Scheme 16.[79] The β-acid chloride (**53**) undergoes rearrangement to the allylic cyclopropane (**54**) in good yield, while the α-acid chloride (**55**) gives mostly the intended alcohol (**57**) and a lesser amount of the product of elimination with methyl migration (**56**). Conformational analysis of these substrates suggests that the stereochemistry of the acid chloride group guides the course of rearrangement, since the bond to the migrating group must be suitably disposed to participate in the decarboxylation.



Scheme 16

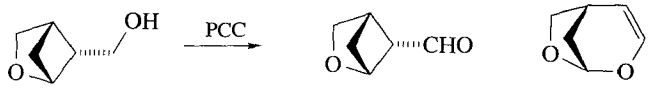
Bicyclo[2.2.0]hexan-2-ols oxidize with rearrangement to the isomeric bicyclo[2.1.1]hexan-2-ones. This takes place under Oppenauer oxidation conditions,[80] as well as with chromic acid,[81] and is illustrated for photolevopimarate and chromic acid in equation (51). The yield for this transformation is excellent, although the scope and synthetic potential are probably quite limited. The reaction is highly dependent on the nature of the oxidant, as the chromate/pyridine reagent gave only 15% of the product after several days, and most of the starting alcohol was recovered.

The oxidation of the cyclobutylcarbinol in equation (52) with buffered PCC proceeds with partial rearrangement; a 1:2 ratio of the expected aldehyde (**58**) to the ring-expanded cyclic enol ether (**59**) is ob-



(51)

tained.[82] This latter product is suggested to arise through a 1,3-rearrangement of the first-formed aldehyde, driven by relief of strain; the rearrangement of (**58**) to (**59**) goes to completion on standing.



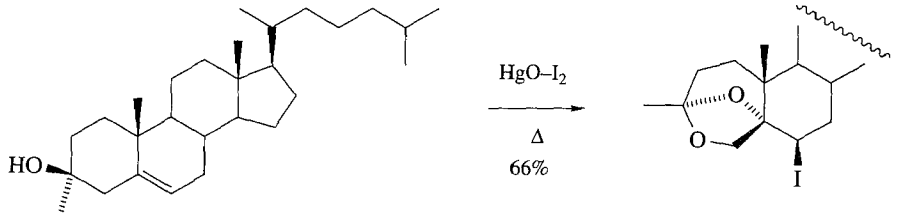
(52)

(**58**) 33% (**59**) 67%

7.2.3.5 Miscellaneous Skeletal Rearrangements

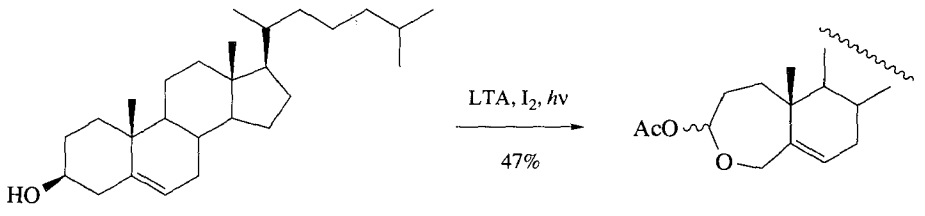
Into this group fall the named oxidation rearrangement reactions which proceed with carbon–carbon bond cleavage and 1,2-transfer of an alkyl group to a heteroatom, such as the Baeyer–Villiger reaction (discussed in Chapter 5.1, this volume) and the Beckmann reaction (found in Chapter 5.2, this volume) of ketones, as well as the Hofmann reaction/Schmidt reaction/Curtius rearrangement of carboxylic acid derivatives. The two examples discussed here involve related reactions of alcohols.

The oxidative cleavage of the alcohol (**60**; equation 53) by mercury(II) oxide and iodine leads to the iodoacetal (**61**) in good yield.[83] If cholesterol (**11**) is treated with lead tetraacetate and iodine under irradiation, the lactol acetate (**62**) is obtained in moderate yield, as seen in equation (54).[84] These reactions are both believed to go through the hypoiodite, which cleaves heterolytically to an oxygen radical. This intermediate fragments to an aldehyde and an allylic radical, and it is at this point that the mechanisms seem to diverge. In the mercury(II) cyclization the aldehyde adds IO·, and the resulting oxygen radical adds to the terminus of the allyl radical. The second oxygen of the acetal adds to the remaining alkene, and the penultimate intermediate carbon radical is trapped by iodine to give the observed product. In the lead(IV) cyclization the intermediate allyl radical is believed to add to the oxygen of the aldehyde to give an oxepanyl radical, which oxidizes to the lactol acetate. The scope of these reactions seems limited, since other similar substrates give poor selectivity and low yields in these reactions.



(53)

(**60**) (**61**)

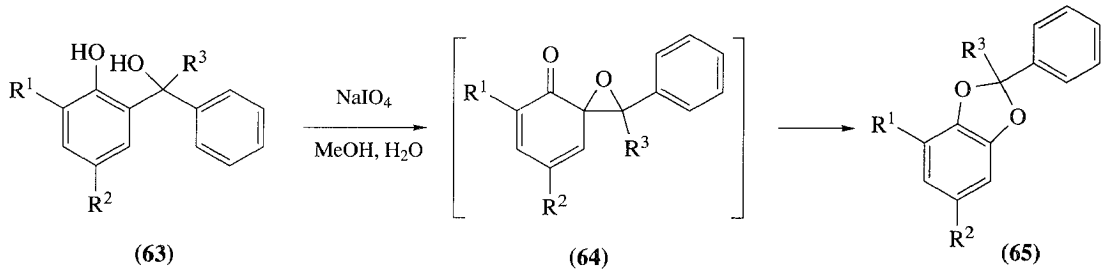


(54)

(**11**) (**62**)

Sodium periodate is known to oxidize 2-alkylphenols to the corresponding 2-hydroxycyclohexadienones. Phenolic benzhydrol-type compounds (**63**) follow a rearrangement pathway under these conditions, and the results are shown in Scheme 17.[85] The benzylic hydroxy group participates in the periodate

oxidation to give an intermediate spiroepoxycyclohexadienone (**64**), which suffers intramolecular attack with carbon–carbon bond cleavage by the ketone carbonyl to yield the benzaldehyde acetal (**65**). Yields for this reaction are in the range of 40–60%.



(63) (64) (65)

Scheme 17

7.2.4 REFERENCES

1. A. H. Haines, 'Methods for the Oxidation of Organic Compounds: Alkanes, Alkenes, Alkynes and Arenes', Academic Press, London, 1985.
2. (a) W. J. Mijs and C. R. H. I. de Jonge (eds.), 'Organic Synthesis by Oxidation with Metal Compounds', Plenum Press, New York, 1986; (b) F. Freeman, in 'Organic Synthesis by Oxidation with Metal Compounds', ed. W. J. Mijs and C. R. H. I. de Jonge, Plenum Press, New York, 1986, p. 41; (c) M. L. Mihailović, Ž. Čeković and L. Lorenc, in 'Organic Synthesis by Oxidation with Metal Compounds', ed. W. J. Mijs and C. R. H. I. de Jonge, Plenum Press, New York, 1986, p. 741.
3. For a review on cyclopropanes in synthesis see: H. N. C. Wong, M.-Y. Hon, C.-W. Tse, Y.-C. Yip, J. Tanko and T. Hudlicky, *Chem. Rev.*, 1989, **89**, 165.
4. For a review on cyclobutanes in synthesis see: H. N. C. Wong, K.-L. Lau and K.-F. Tam, *Top. Curr. Chem.*, 1986, **133**, 83.
5. N. Miyaura and J. K. Kochi, *J. Am. Chem. Soc.*, 1983, **105**, 2368.
6. (a) A. McKillop and E. C. Taylor, in 'Comprehensive Organometallic Chemistry', ed. G. Wilkinson, F. G. A. Stone and E. W. Abel, Pergamon Press, Oxford, 1982, vol. 7, p. 465; (b) P. D. Magnus, T. Sarkar and S. W. Djuric, in 'Comprehensive Organometallic Chemistry', ed. G. Wilkinson, F. G. A. Stone and E. W. Abel, Pergamon Press, Oxford, 1982, vol. 7, p. 515.
7. While trial and error still furnish the majority of advances in synthetic chemistry, efforts are underway to systematize predictive rationale, even for such a difficult area as oxidation reactions; see: G. D. Paderes and W. L. Jorgensen, *J. Org. Chem.*, 1989, **54**, 2058.
8. G. Cainelli and G. Cardillo, 'Chromium Oxidations in Organic Chemistry', Springer Verlag, New York, 1984.
9. G. M. Rubottom, in 'Oxidation in Organic Chemistry', ed. W. S. Trahanovsky, Academic Press, New York, 1978, vol. 5, part D, p. 1.
10. H. H. Wasserman and J. L. Ives, *Tetrahedron*, 1981, **37**, 1825; L. M. Stephenson, M. J. Grdina and M. Orfanopoulos, *Acc. Chem. Res.*, 1980, **13**, 419; A. A. Frimer, *Chem. Rev.*, 1979, **79**, 359; K. Gollnick and H. J. Kuhn, in 'Singlet Oxygen', ed. H. H. Wasserman, Academic Press, New York, 1979, p. 287; K. Gollnick and H. J. Kuhn, *J. Org. Chem.*, 1979, **40**, 287.
11. R. J. Steltenkamp and W. E. Truice, *Mech. Mol. Migr.*, 1969, **2**, 65.
12. E. Colvin, 'Silicon in Organic Synthesis', Butterworth, London, 1981.
13. K. Tamao and K. Maeda, *Tetrahedron Lett.*, 1986, **27**, 65.
14. For a review on the chemistry of silyl enol ethers see: J. K. Rasmussen, *Synthesis*, 1977, 91.
15. M. J. Taschner, University of Akron, private communication.
16. W. Adam and A. Griesbeck, *Synthesis*, 1986, 1050.
17. K. H. Schulte-Elte and V. Rautenstrauch, *J. Am. Chem. Soc.*, 1980, **102**, 1738, and references cited therein.
18. E. D. Mihelich and D. J. Eickhoff, *J. Org. Chem.*, 1983, **48**, 4135.
19. L. M. Stephenson and M. B. Zielinski, *J. Am. Chem. Soc.*, 1982, **104**, 5819.
20. H. J. Reich, in 'Oxidation in Organic Chemistry', ed. W. S. Trahanovsky, Academic Press, New York, 1978, vol. 5, part C, p. 1; D. L. J. Clive, *Tetrahedron*, 1978, **34**, 1049; D. Liotta, *Acc. Chem. Res.*, 1984, **17**, 28.
21. K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, 1973, **95**, 2697.
22. S. Torii, K. Uneyama, M. Ono and T. Bannou, *J. Am. Chem. Soc.*, 1981, **103**, 4606.
23. J. Iriarte, J. N. Shoolery and C. Djerassi, *J. Org. Chem.*, 1962, **27**, 1139.
24. L. F. Fieser, *Org. Synth., Coll. Vol.*, 1963, **4**, 189; K.-E. Stensiö, *Acta Chem. Scand.*, 1971, **25**, 1125.
25. A. G. González, J. F. Ciccio, A. P. Rivera and J. D. Martin, *J. Org. Chem.*, 1985, **50**, 1261.
26. G. D. S. Ananda, A. M. Z. Slawin, R. J. Stoodley and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1986, 165.
27. R. N. Warrener, T. S. Lee, R. A. Russell and M. N. Paddon-Row, *Aust. J. Chem.*, 1978, **31**, 1113, and references cited therein; P. Sundararaman and W. Herz, *J. Org. Chem.*, 1977, **42**, 813.
28. G. Majetich, University of Georgia, private communication.
29. C. Iwata, Y. Takemoto, M. Doi and T. Imanishi, *J. Org. Chem.*, 1988, **53**, 1623.
30. E. J. Corey, P. D. S. Jardine and J. C. Rohloff, *J. Am. Chem. Soc.*, 1988, **110**, 3672.

31. J. Drew, G. Gowda, P. Morand, P. Proulx, A. G. Szabo and D. Williamson, *J. Chem. Soc., Chem. Commun.*, 1985, 901.
32. D. Liotta, D. Braun, W. Hoekstra and R. Monahan, III, *Tetrahedron Lett.*, 1987, **28**, 1069.
33. G. Majetich, S. Condon, K. Hull and S. Ahmad, *Tetrahedron Lett.*, 1989, **30**, 1033.
34. P. Baekström, S. Okecha, N. DeSilva, D. Wijekoon and T. Norin, *Acta Chem. Scand., Ser. B*, 1982, **36**, 31.
35. J. Banerji, A. Chatterjee, N. Ghoshal, A. K. Das, S. Surkar, S. Bhattacharya and J. N. Shoolery, *J. Indian Chem. Soc.*, 1982, **59**, 145; J. Banerji, A. K. Das and B. Das, *Chem. Ind. (London)*, 1987, 395.
36. T. Itoh, K. Jitsukawa, K. Kaneda and S. Teranishi, *J. Am. Chem. Soc.*, 1979, **101**, 159, and previous papers in this series.
37. M. F. Schlecht and H.-J. Kim, unpublished results.
38. W. H. Stass and L. A. Spurlock, *J. Org. Chem.*, 1974, **39**, 3822.
39. E. J. Corey and L. S. Melvin, Jr., *Tetrahedron Lett.*, 1975, 929.
40. T. K. Hall and P. R. Storey, *J. Am. Chem. Soc.*, 1967, **89**, 6759.
41. E. J. Corey, Z. Arnold and J. Hutton, *Tetrahedron Lett.*, 1970, 307.
42. G. M. Rubottom, E. C. Beedle, C.-W. Kim and R. C. Mott, *J. Am. Chem. Soc.*, 1985, **107**, 4230.
43. M. S. Baird, *Top. Curr. Chem.*, 1988, **144**, 193.
44. J. Salaun, B. Gardnier and J. M. Conia, *Tetrahedron*, 1974, **30**, 1423.
45. W. Holweger and M. Hannack, *Chem. Ber.*, 1984, **117**, 3004.
46. C. L. Willis, *Tetrahedron Lett.*, 1987, **28**, 2175.
47. H. J. Reich, S. K. Shah, P. M. Gold and R. E. Olson, *J. Am. Chem. Soc.*, 1981, **103**, 3112.
48. R. F. C. Brown, K. J. Coulston, F. W. Eastward and M. P. Hill, *Aust. J. Chem.*, 1988, **41**, 215.
49. R. M. Moriarty and O. Prakash, *Acc. Chem. Res.*, 1986, **19**, 244.
50. (a) A. Lethbridge, R. O. C. Norman and C. B. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1973, 35; (b) K. J. Divakar and A. S. Rao, *Indian J. Chem., Sect. B*, 1976, **14**, 704.
51. A. McKillop, J. D. Hunt, F. Kienzle, E. Bigham and E. C. Taylor, *J. Am. Chem. Soc.*, 1973, **95**, 3635.
52. (a) R. M. Moriarty, J. S. Khosrowshahi and O. Prakash, *Tetrahedron Lett.*, 1985, **26**, 2961; (b) A. Citterio, M. Gandolfi, C. Giordano and G. Castaldi, *Tetrahedron Lett.*, 1985, **26**, 1665.
53. P. R. Stapp (Phillips Petroleum Co.), *US Pat.* 4 220 604 (1980) (*Chem. Abstr.*, 1980, **93**, 220 381).
54. Y. Tamada, H. Sanjoh and K. Iguchi, *Tetrahedron Lett.*, 1979, 423.
55. For a review on this and other methods to carry out the transformation see: C. Giordano, G. Castaldi and F. Uggeri, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 413.
56. (a) T. Yamauchi, K. Nakao and K. Fujii, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1255, and references cited therein; (b) T. Yamauchi, K. Nakao and K. Fujii, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1433, and references cited therein; (c) Y. Tamura, T. Yakura, Y. Shirouchi and J.-I. Haruta, *Chem. Pharm. Bull.*, 1985, **33**, 1097.
57. For a review on this named reaction see: E. V. Brown, *Synthesis*, 1975, 358.
58. N. Sonoda and S. Tsutsumi, *Bull. Chem. Soc. Jpn.*, 1959, **32**, 505.
59. E. C. Taylor, R. A. Conley, D. K. Johnson, A. McKillop and M. E. Ford, *J. Org. Chem.*, 1980, **45**, 3433, and references cited therein.
60. B. Vu, G. Mezey-Vándor and M. Nógrádi, *Liebigs Ann. Chem.*, 1984, 734.
61. R. A. Eade, F. J. McDonald and H.-P. Pham, *Aust. J. Chem.*, 1978, **31**, 2699.
62. S. Antus, F. Boross, M. Katjar-Peredy and M. Nógrádi, *Liebigs Ann. Chem.*, 1984, 1068.
63. H. Heimgartner, *Chimia*, 1980, **34**, 333 (*Chem. Abstr.*, 1981, **94**, 3285); G. R. Krow, *Tetrahedron*, 1987, **43**, 3.
64. U. Hacksell, L.-E. Arvidsson, U. Svensson, J. L. G. Nilsson, H. Wikström, P. Lindberg, D. Sanchez, S. Hjorth, A. Carlsson and L. Paalzow, *J. Med. Chem.*, 1981, **24**, 429.
65. G. Lenz, *J. Org. Chem.*, 1988, **53**, 5791.
66. P. Boontanonda and R. Grigg, *J. Chem. Soc., Chem. Commun.*, 1977, 583.
67. E. J. Corey and T. Ravindranathan, *Tetrahedron Lett.*, 1971, 4753.
68. Ž. Čeković, J. Bosnjak and M. Cvetković, *Tetrahedron Lett.*, 1980, **21**, 2675.
69. E. Mincione, P. Bovicelli, J. B. Gil and M. L. Forcellese, *Gazz. Chim. Ital.*, 1985, **115**, 37 (*Chem. Abstr.*, 1985, **103**, 22 833).
70. W. Dittmann, W. Kirchhof and W. Stumpf, *Justus Liebigs Ann. Chem.*, 1965, **681**, 30, and references cited therein.
71. W. Lawrie, W. Hamilton, J. McLean and J. Meney, *J. Chem. Soc., Perkin Trans. 1*, 1978, 471.
72. N. Bosworth, A. Emke, J. M. Midgley, C. J. Moore, W. B. Whalley, G. Ferguson and W. C. Marsh, *J. Chem. Soc., Perkin Trans. 1*, 1977, 805, and previous papers by this group.
73. D. F. Lindow and R. G. Harvey, *J. Am. Chem. Soc.*, 1971, **93**, 3786.
74. G. D. Buckley and W. J. Levy, *J. Chem. Soc.*, 1951, 3016.
75. V. Franzen, *Chem. Ber.*, 1954, **87**, 1219.
76. R. M. Moriarty, R. K. Vaid, M. P. Duncan and B. K. Vaid, *Tetrahedron Lett.*, 1987, **28**, 2845.
77. J. Salaun, B. Gardnier and J. M. Conia, *Tetrahedron*, 1974, **30**, 1413.
78. T. S. Lillie and R. C. Ronald, *J. Org. Chem.*, 1985, **50**, 5084.
79. H. Suginome and T. Uchida, *J. Chem. Soc., Perkin Trans. 1*, 1980, 943; H. Suginome, Y. Ohue and K. Orito, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1247.
80. R. N. McDonald and C. E. Reineke, *J. Org. Chem.*, 1967, **32**, 1888.
81. W. Herz, M. G. Nair and D. Prakash, *J. Org. Chem.*, 1975, **40**, 1017.
82. W. Kirmse and U. Mrotzeck, *Chem. Ber.*, 1988, **121**, 1013.
83. H. Suginome and N. Maeda, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 2621.
84. H. Suginome, H. Washiyama and S. Yamada, *Bull. Chem. Soc. Jpn.*, 1987, **60**, 1071.
85. H.-D. Becker and T. Bremholt, *Tetrahedron Lett.*, 1973, 197.