Macrolactonizations in the Total Synthesis of Natural Products

A. Parenty,[†] X. Moreau,[†] and J.-M. Campagne*[,†,‡]

Institut de Chimie des Substances Naturelles, Avenue de la Terrasse, F-91198 Gif sur Yvette, France, and Ecole Nationale Supérieure de Chimie, 8 rue de l'Ecole Normale, F-34296 Montpellier, France

Received January 19, 2005

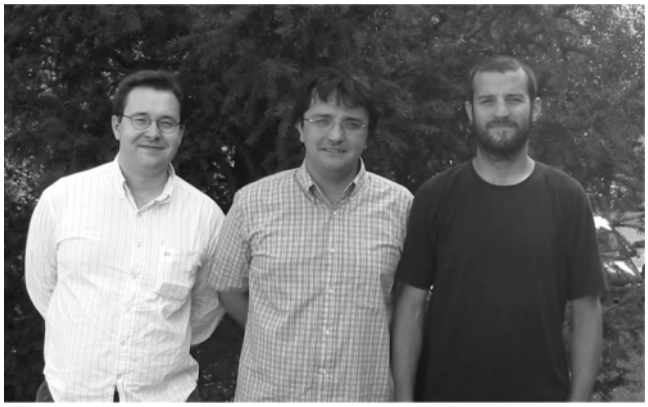
Contents

* To whom correspondence should be addressed. Current address: Ecole Nationale Supérieure de Chimie de Montpellier. Phone: 33 4 67 14 72 21. E-mail: jean-marc.campagne@enscm.fr.
[†] Institut de Chimie des Substances Naturelles, Gif-sur-Yvette.
[‡] Ecole Nationale Supérieure de Chimie de Montpellier.

1. Introduction

Ever since the first isolation of Exaltolide **1** (Figure 1) in 1927 by Kerschbaum,[1] interest in macrocyclic lactones, defined as lactones with more than 8 atoms in the ring, has been increasing. Indeed, natural macrocyclic lactones (the term macrolide[2] has been for years a synonym for "macrolactone glycoside antibiotics" and thus will not be used herein) present a large spectrum of interesting properties from perfumery, to phytotoxicity, to pheromone or insecticide activity, to medicinal (antibiotic, cytotoxic, antiangiogenesis) properties and a wide range of structures from 8-membered ones such as octalactins[3] **2** to the 60-membered quinolidomicins **3**. From their first isolation in the 50s, macrolide antibiotics, such as erythromycin (**4**),[5] were widely used to treat bacterial infections, and because of their safety and efficacy, they are still the preferred therapeutic agents for treatment of respiratory infections. Another important class of macrolactones with a wide range of biological activities is the cyclodepsipeptides[6,7] such as, for example, FK228 (**5**), which is currently in phase II clinical trials as an anticancer drug and which acts as a prodrug that undergoes disulfide reduction within the cell to release a zinc-binding thiol. The biopesticide Spinosad, a mixture of Spinosyn A and D (**6**), is currently marketed for use against a wide variety of insects. Of the more than 200 polyene macrolactones known, some, such as roxaticine (**7**), are currently used in the treatment of systemic fungal infections.[8] The 20-membered Apoptolidin (**8**) selectively induces apoptosis in rat glia cells transformed with adenovirus E1A oncogen in the presence of normal cells and inhibits the mithochondrial F_0F_1-ATPase. Actin-binding marine macrocyclic lactones (see for example mycalolide **9**) are also a large class of natural products possessing potent antitumor activity.[9,10] Epothilones **10**, with a mode of action similar to that of taxol and the potential to overcome known mechanisms of drug resistance, are considered to be promising anticancer drugs.[11] Macrocyclic glycolipids[12] and benzolactone enamides[13] with antibiotic and cytotoxic activity are also worthy of note. Even though many other efficient macrocyclization methods such as the RCM, intramolecular cross-coupling, Noxaki−Hiyama−Kishi, and HWE methods have been developed over the years, the lactonization of seco-acids still appears to be one of the more frequently used

10.1021/cr0301402 CCC: $59.00
Published on Web 01/25/2006



Arnaud Parenty (left) graduated from the Ecole Nationale Supérieure de Chimie de Montpellier in 2000. He then carried out his Ph.D. research at the ICSN—Gif sur Yvette working on the total synthesis of Dolastatin 14. After a postdoctoral experience in marine natural product extraction (IRD, New Caledonia), he is currently working in bioactive natural product isolation (Libragen, Toulouse, France). Jean-Marc Campagne (center) was born in Pau, France, in 1967. After studies at the Ecole Nationale Supérieure de Chimie de Montpellier, he received his Ph.D at the University of Montpellier in 1994. After postdoctoral trainings with Prof B. Trost (Stanford University, CA) and Prof. L. Ghosez (Université Catholique de Louvain), he was appointed in 1998 CNRS Researcher at the Institut de Chimie des Substances Naturelles in Gif sur Yvette. His current interests concern the development of catalytic asymmetric transformations and their application to the total synthesis of natural products. Xavier Moreau (right) studied Chemistry at the University of Tours—France. He obtained his B.S. degree in Chemistry from University of Paris-XI—Orsay and then carried out his Ph.D. research at the ICSN—Gif sur Yvette working on total synthesis.

approaches to obtain macrocyclic lactones. Due to entropic and enthalpic factors (*vide infra*), direct cyclization is generally not possible without activation of either the alcohol or the carboxylic acid terminal group. The aim of this review is to describe all macrolactonization reactions involving the activation of one or the other extremity of the seco-acid. This topic has been previously covered in part by several reviews at the end of the 1970s and in the mid 1990s; however, to the best of our knowledge no recent coverage has appeared in the literature.[14−20] The literature is surveyed until mid-2004.

After some general comments, this review will be organized into two main parts. The first of these two parts covers, broadly interpreted, activation of the acid (Scheme 1, path a), while the second covers, in a similarly broad sense, activation of the alcohol (Scheme 1, path b). Biosynthetic pathways[21−25] and industrial procedures, particularly in the synthesis of macrocylic musks,[26] are both beyond the scope of this review and have also both been recently reviewed. Those areas will thus not be covered here.

2. Basics of Macrolactonization

2.1. Introduction

Factors controlling the macrolactonization of ω-bromo alkanoic acids, $Br-(CH_2)_{n-2}CO_2H$, have been studied in detail by Illuminati and Mandolini,[27,28] and their results have been interpreted in terms of activation energy, related to the strain energy in the ring being formed, and in terms of entropy, related to the probability of end-to-end encounters as required for reaction. In medium ring lactones the entropic factor is outweighed by the enthalpic factor from strain energy in the ring being formed, but for the intramolecular reaction in the large ring lactones the entropic factor is increased while the enthalpic factor has decreased since the rings formed are almost strain free. These results are summarized in the reactivity profile described in Figure 2. From these studies, cyclizations of medium ring lactones with $n = 8-11$ appear to be the more difficult cases due to both enthalpic and entropic factors (Figure 2).

The same conclusions were drawn in 1935 by Stoll and Rouvé[29] when they determined the approximate rate constant for the lactonization of ω-hydroxy alkanoic acids $HO-(CH_2)_{n-2}CO_2H$ (Table 1).[29] These values can be compared with, for example, the yields obtained in these macrolactonizations using the Corey−Nicolaou reagent[30] (*vide infra*).

As illustrated in Table 1, the main problem arising in the macrolactonization is the competition between intra- and intermolecular reactions leading to the formation of diolide and oligomers (Scheme 2).[31] The principal method for favoring intramolecular reactions in this competition is to use a "high dilution technique" first introduced by Ruggli and Ziegler where the substrate is slowly added using a syringe pump over many hours to a large volume of solvent.[31,32]

To avoid high dilution techniques, alternatives for either decreasing intermolecular processes or for increasing intramolecular processes have been developed. The utility of decreasing intermolecular processes has been demonstrated using a "pseudo-high dilution technique" by immobilizing the seco-acid, or an activated intermediate, on a solid support.[33−36] On the other hand, acceleration of intramolecular processes[12,37−42] has been demonstrated with "template" syntheses using a metal ion. Solid−liquid phase transfer catalysis, and reactions in microemulsions, in inverse micelles, and in zeolites, all of which are methods of simulating high dilution conditions, have also been described for the synthesis of macrolactones.[43−46]

2.2. Influence of Conformation and Stereochemistry

As previously shown by Illuminati and Mandolini, eight-membered cycles are probably about the most difficult substrates to cyclize, but once again this argument needs to be counterbalanced by the influence of the substituents on the seco-acid and their conformational effects. Indeed, in the cyclizations of differently substituted eight-membered seco-acids derived from octalactins (Scheme 3), Andrus has shown that substituents play an essential role in the cyclization: a pathway involving a chair−boat conformation with the substituents in a pseudoequatorial position has been advocated to account for these results.[47,48]

The influence of stereochemistry on macrolactonization was recognized early by Woodward in the synthesis of erythronolides (see compound **4**). Among 17 differently protected seco-acids, only one gives the 9-dihydroerythronolide in good yield: in particular, the 9-(*S*) configuration appears to be crucial. In the cyclization of **11a** (Scheme 4), Stork and Rychnovsky[49] have shown that a favorable chair dioxane ring in the C9−C11 positions plays an essential role in the cyclization giving the dihydroerythronolide derivative in 64% yield, whereas in seco-acids **11b** and **11c** no

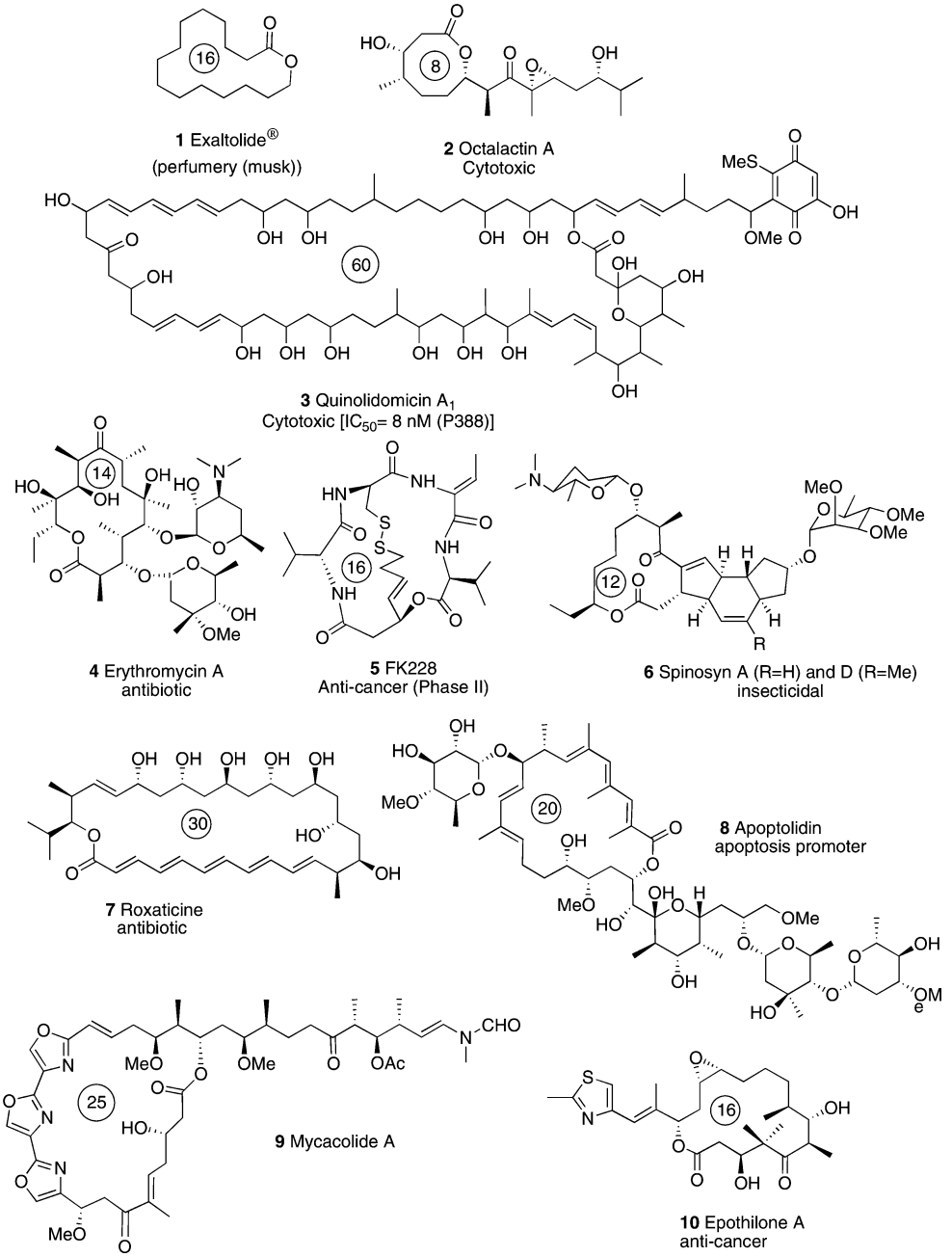
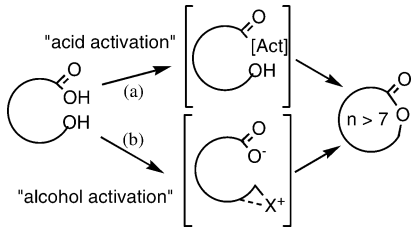


Figure 1. Some representative examples of natural macrocyclic lactones.

Scheme 1



lactonization occurs due to an unfavorable twist−boat conformation (see also ref 50). However, more recently, Martin,[51] in an abiotic strategy where one sugar moiety is introduced before the macrolactonization step, has shown that more flexible seco-acids can also be considered as valuable substrates.

From these observations, it appears that macrolactonizations should not be interpreted in terms of ring size but rather in terms of whether the reactive conformation can be easily adopted.[52] Indeed, conformationally constrained seco-acids

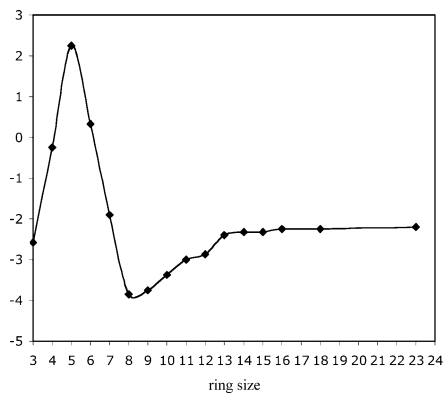


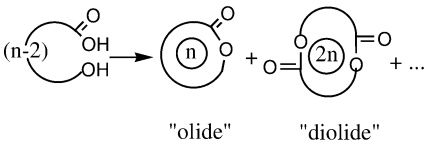
Figure 2. Reactivity profile for lactone formation. (Reproduced with permission from ref 27. Copyright 1981 American Chemical Society.)

Table 1. Approximate Rate Constants for the Lactonization of ω-Hydroxyalkanoic Acids HO−$(CH_2)_{n-2}$COOH and Yields Obtained Using the Corey−Nicolaou Reagent (Adapted with Permission from Ref 29)

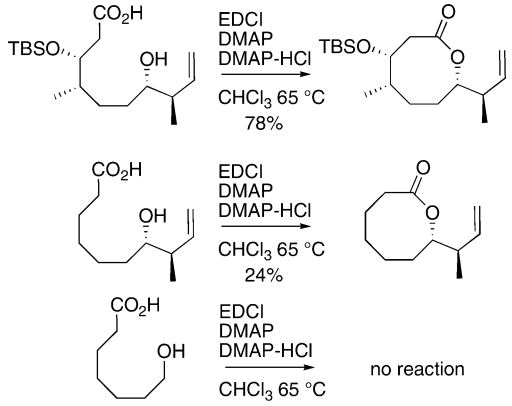
n	approximate rate constants	experimental yields obtained with the Corey−Nicolaou reagent[a]
5	>0.5	
7	2.8×10^{-3}	71 (7)
8	nd	
9	8×10^{-6}	8 (41)
10	1×10^{-5}	nd
11	2.8×10^{-5}	nd
12	1.4×10^{-4}	47 (30)
13	2.6×10^{-4}	66 (7)
14	1.3×10^{-3}	68 (6)
15	2.3×10^{-3}	nd
16	3.8×10^{-3}	80 (5)
17	4.4×10^{-3}	nd
18	6.0×10^{-3}	nd
19	4.9×10^{-3}	nd
24	3.4×10^{-3}	nd

[a] Diolide yields in parentheses.

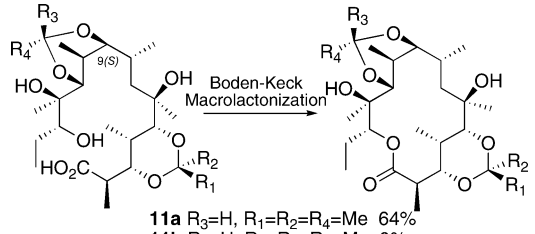
Scheme 2



Scheme 3

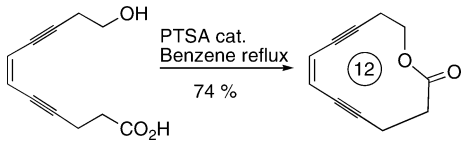


Scheme 4



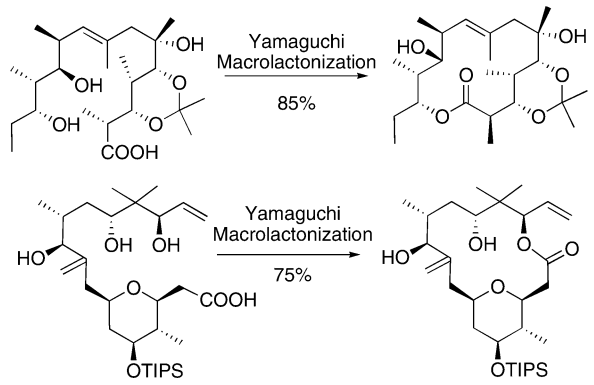
can be directly lactonized using PTSA as illustrated in Scheme 5.[53]

Scheme 5



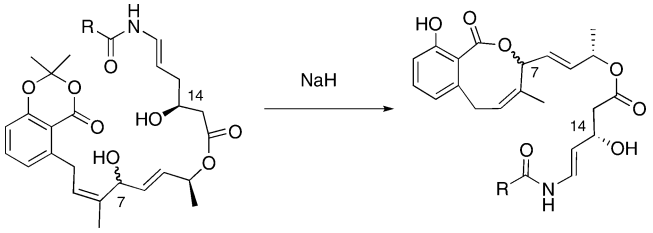
More recently, computer-assisted design of "easily cyclizable" seco-acids has also been reported in the total synthesis of lankanolide.[54,55] As a consequence of the above considerations, ring selective macrolactonizations have been observed, and thus, it is not always necessary to protect all hydroxy groups. For example, Mulzer and White have described selective macrolactonization where three nonprotected hydroxy groups are present on the seco-acid as illustrated in the syntheses of erythronolide[56] and polycavernoside,[57] respectively (Scheme 6).

Scheme 6



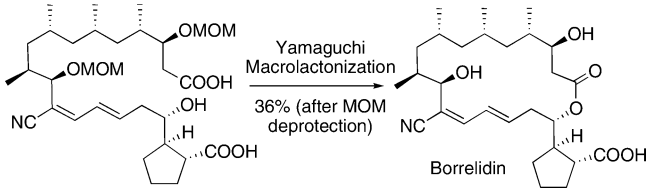
Similar ring-size selectivities have been described in the syntheses of bafilomycin[58] (16 vs 18), oleandolide[59] (14 vs 12), bryostatin[60] (25 vs 26), apoptolidinone[61,62] (20 vs 21 and 17), gloesporone[63] (14 vs 8), apicularen A[64] (12 vs 10), spongistatin/altohyrtin[65] (42 vs 44), and deoxytedanolide[66] (18 on a primary alcohol vs 16 and an alternative 18-membered lactone on secondary alcohols). Some other examples will be illustrated later in the text. When a mixture of two lactones is obtained, transesterifications can usually be performed by taking advantage of thermodynamic preferences using $Ti(OiPr)_4$, as is illustrated in the total syntheses of aplyronine A[67,68] and scytophycin.[69] Size selectivities are sometimes more surprising, as was illustrated by Porco in an approach to lobatamide C: The 8- rather than the 15-membered lactone was selectively obtained in a Boeckman type (*vide infra*) macrolactonization, and any efforts to translactonize were unsuccessful (Scheme 7).[70] A selective

Scheme 7



macrolactonization on a diacid has also been recently described by Morken in the total synthesis of borrelidin (Scheme 8).[71]

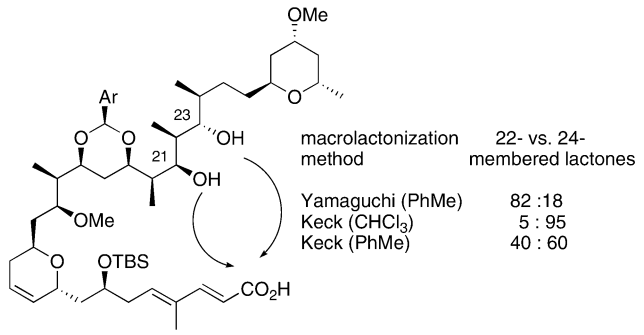
Scheme 8



Very interestingly, Paterson has shown in the total syntheses of swinholide and hemiswinholide that the ring-size selectivity may be different depending on the macro-

lactonization reagent and solvent (Scheme 9).[72]

Scheme 9



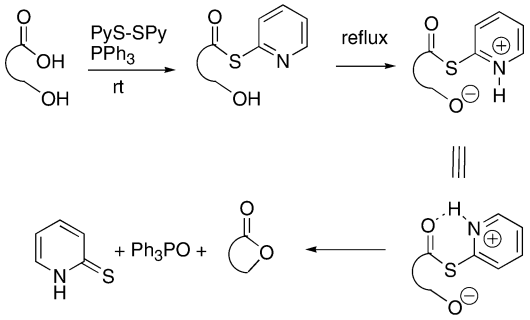
3. Macrolactonizations through "Acid" Activation.

3.1. Macrolactonizations through Thioesters

3.1.1. Corey (Nicolaou, Brunelle) and Gerlach Reactions

The macrolactonization of thioesters is the biosynthetic pathway for the formation of macrolides.[22−26] It is therefore not surprising that this strategy has also been one of the most popular chemical ways to obtain such macrolactones. The most famous reaction involving a thioester is the "double activation" method described in 1974 by Corey and Nicolaou.[30] The mechanism involves the initial formation of a 2-pyridine thioester of the ω-hydroxy acid via a Mukaiyama oxidation−reduction condensation with PySSPy and triphenylphosphine.[73] Internal proton transfer then affords an intermediate in which both the carbonyl and the hydroxy group have been activated, leading to the "electrostatically driven" macrolactonization (Scheme 10). This "double

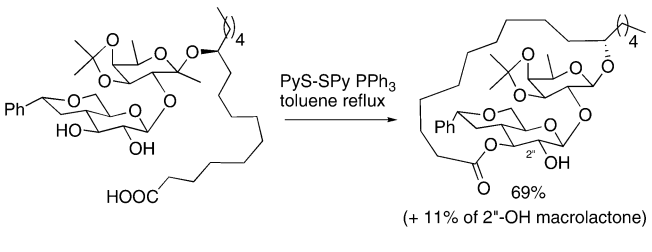
Scheme 10



activation" has been confirmed, and a mechanism involving ketene formation was ruled out by deuterium labeling and kinetic studies.[74,75]

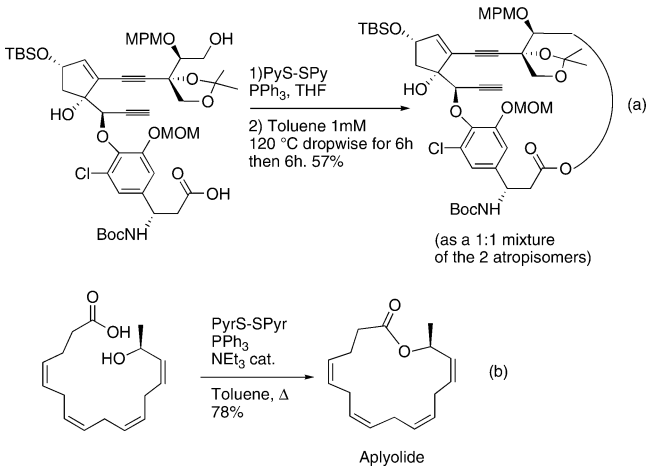
The "classical" Corey−Nicolaou method has been used in a large number of total syntheses and synthetic applications: zearalenone,[30] brefeldin,[76−78] tylonolide,[79,80] tricolorin A,[81] prostaglandin lactones,,[82,83] erythronolides,[84,85] vertalin,[86] macrolactones derived from monensin,[42,87] pyrrolizidine alkaloids,[88] and oxa-crown ethers (Scheme 11).[89] More

Scheme 11



recently, the Corey−Nicolaou method has shown its great potential in the total syntheses of an ene-diyne derivative[90] (equation a, Scheme 12) and aplyolide A[91] (equation b,

Scheme 12



Scheme 12) where other methods failed. It is worthy of note that, in the total synthesis of aplyolide A, addition of a catalytic amount of triethylamine to decrease the amount of diolide and polymeric byproducts was found to be essential and led to aplyolide in a 78% yield.

To avoid dimer formation, the reaction is usually carried out in a one-pot, two-step process: the thioester is first formed at room temperature overnight, then diluted, and finally slowly added by syringe pump to a large amount of refluxing solution of xylene or toluene.

Since the elimination of the thiopyridone and triphenylphosphine oxide byproducts resulting from the PySSPy/PPh_3 activation may be difficult in some circumstances, Corey and Clark[92] developed a variant of this reaction in which the thioester is synthesized first using thionylchloroformate (**13**) (Figure 3).

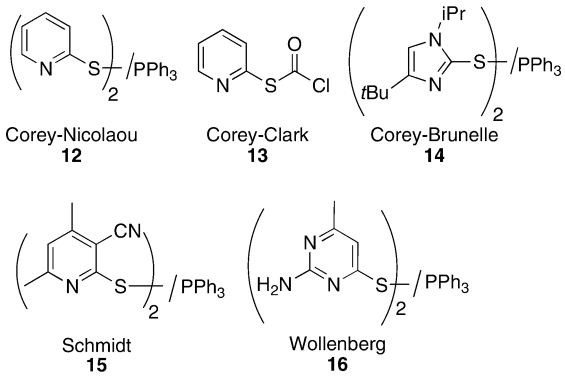


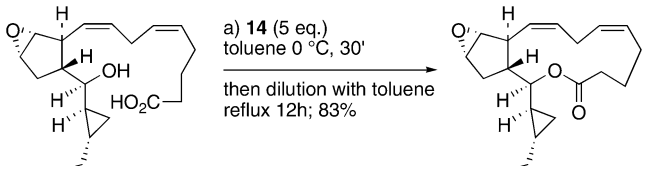
Figure 3.

After a classical workup and drying, the thioester is then pure enough to be used in the thermolysis step. This modification has been used in some synthetic applications including grahamimycin A1,[93] thromboxane A2,[94] brefeldin,[95] and erythronolide.[96,97]

After a survey of different sulfides, Corey and Brunelle[98] concluded that diimidazoylsulfide (**14**) gives macrolactones under milder conditions and in better yields: the presence of the *tert*-butyl group on the 4 position is essential to prevent the formation of the undesired N-acyl intermediate. The Corey−Brunelle conditions have also found numerous

synthetic applications in the total syntheses of erythronolides A and B,[99−101] hybridalactone[102] (Scheme 13), enterobac-

Scheme 13



tin,[103,104] and mycaminosyltylonolide.[105] Two other very reactive disulfides, **15** and **16**, have been described by Schmidt[106] and Wollenberg.[107]

A substantial increase in the rate of cyclization in the presence of metal ions (Ag, Hg, Cu) has been described by several groups.[74,108−111] As illustrated in Figure 4, several explanations have been proposed to account for the role of these metals in increasing the thioester electrophilicity. Among these are chelation of the metal to the pyridine (structure A), chelation of the metal to the sulfur (structure B), and, finally, formation of a chelated complex containing a six-membered ring (structure C).

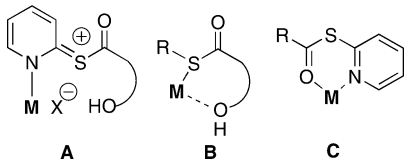


Figure 4.

Several thioesters with different chelation modes have been tested using mercury and other metal salts[74] (Figure 5). The rate of the macrolactonization is greatly enhanced using the bidentate intermediate **17a**, thus suggesting a pathway involving intermediate **B**.

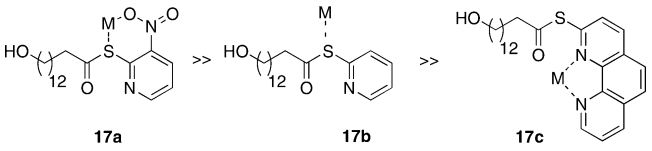


Figure 5.

Gerlach's modification introduced in 1974 is probably the most popular one. It uses silver salts ($AgClO_4$, $AgBF_4$, AgOTf) and allows some reactions to be carried out at room temperature.[108] Indeed tuckolide,[112] various 12-membered lactones with antiartherosclerosis activity,[113] octalactin,[114,115] and various eight-membered lactones,[48,116] muscone,[117] brefeldin,[118] phoracantholide,[119−122] lasiodiplodin,[122−126] nonactin,[127] and antimycin A_{3b},[128] have been synthesized using Gerlach's conditions. One of the more recent examples is the total synthesis of macrosphelide A[129] (Scheme 14) where other

Scheme 14

classical methods (Yamaguchi, Keck, and Mitsunobu reactions) had failed due to β-elimination. Using the classical Mukaiyama−Corey protocol, the lactone was obtained in low yield, but that was increased to 40% by adding AgOTf at room temperature.

Is it true then that Gerlach's modification is the "universal " method for performing such macrolactonizations? It is quite difficult to draw any such clear conclusion about the best conditions to realize these Corey−Nicolaou, Casey−Brunelle, and Gerlach type macrolactonizations. As previously noted by Woodward[84] and illustrated in the total syntheses of ferrulactones I and II (Figure 6),[130−132] the benefit of using silver salts depends strongly on the seco-acid structure.

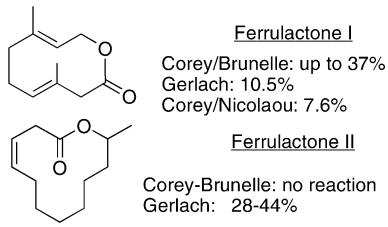
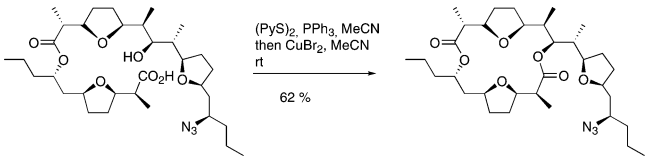


Figure 6.

The use of copper salts ($CuBr_2$, $CuCl_2$) has also been shown to be beneficial in these reactions. $CuBr_2$ was successfully used in the total synthesis (Scheme 15) of

Scheme 15



pamamycin[133] and in the synthesis[134] of macrocyclic oligomers derived from enantiomerically pure 3-hydroxybutyric acid. In the latter case, up to an $n = 128$ macrolactone was obtained in a 3% yield for the macrolactonization step.

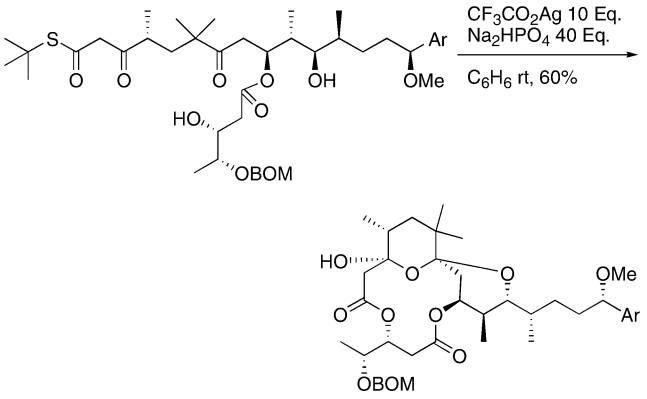
The use of DMAP has also been described by Yonemitsu,[135−137] although, in some instances, the activated species is too active and leads to the formation of the diolide.[90]

3.1.2. Masamune Reaction

Although it is not within the scope of this review (i.e., the cyclization of seco-acids), it appears necessary to add in this section a discussion of the reactivity of various "isolated" thioesters which are independently synthesized and then play successively the role of a carboxylic-protecting group during the synthesis followed by the role of the activating group during the macrolactonization step. Such macrolactonization reactions, usually known as the Masamune reaction,[18] are most often carried out using independently prepared benzyl or *tert*-butyl thioesters in the presence of a thiophilic metal salt such as mercury,[138,139] silver,[109] or copper[140−143] salts. For example, using silver trifluoroacetate in buffered benzene[144,145] (Scheme 16), this methodology was particularly useful in the aplysiatoxin[144] total synthesis, which involves a sensitive substrate prone to crotonization under basic conditions.

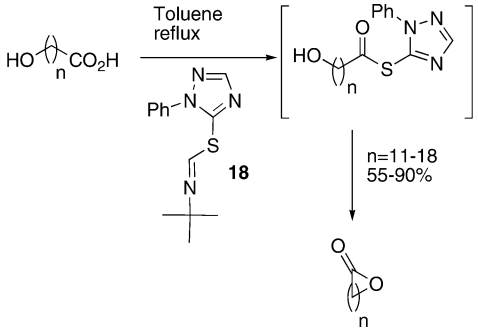
Several other syntheses have been reported: methynolide with $(CF_3CO_2)_2Hg$;[138] carbomycin/josamycin,[146] cytochalasins,[109] lactone antibiotic A26771B,[147] and chlorothricolide[148] with CF_3CO_2Ag; deoxyerythronolide[142] and crobarbatine acetate[149] with CuOTf−benzene complex; and tylonolide[150] with $(CF_3CO_2)_2Hg$. Nonmetallic additives such as NBS[151,152] and *p*-TsOH[73] proved to be useful in these reactions. The

Scheme 16



use of *p*-TsOH (previously described by Mukaiyama[73] in the macrolactonization of 6-phenyl-2-pyridyl esters) has been described in the total synthesis of nonactin using disulfide **15**.[153,154] It is worthy of note that the cyclization of polymer-supported thioesters[35] and template-driven macrolactonizations[39] have also been described.

Scheme 17



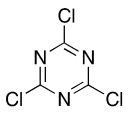
3.1.3. Miscellaneous Reactions

Schmidt[155] also has described formation of activated thioesters using **18**, which was made *in situ* by mixing *tert*-butyl isocyanide and 1-phenyl-2-tetrazoline-5-thione, and which lead in good yield to the macrolactonization of *ω*-hydroxy acids (Scheme 17).

The use of phenyl and mesityl sulfonyl chlorides,[156−158] $SOCl_2$,[159] $SOCl_2$-DMF,[160] and dithiocarbonates[161] has also been reported. The use of a ketene dithioacetal as a latent thioester has also been described in a pyrrolizidine alkaloid synthesis in which the macrolactonization was performed in the presence of silver acetate.[162]

3.2. Cyanuric Chloride

The use of cyanuric chloride (CC, **19**) (Figure 7) in



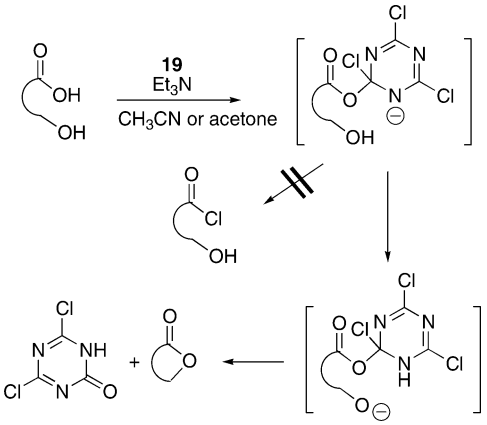
19

Cyanuric Chloride
(C.C.)

Figure 7.

macrolactonizations was introduced by Venkataraman[163] in 1980. The mechanism of this reaction, closely related to the mechanism invoked in the Corey−Nicolaou macrolactonizations, involves a double-activation mechanism (Scheme 18). An alternative pathway through an acyl chloride has been ruled out by the same authors.[164]

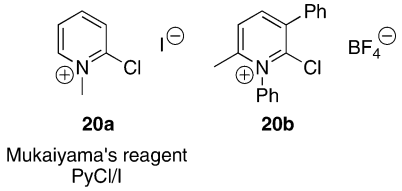
Scheme 18



Although CC (**19**) is a cheap commercially available reagent, this methodology has not found wide synthetic use and has been applied to only a few total syntheses: isoambrettolide,[163] exaltolide,[165] phoracantholide,[165,166] pentadecanolide,[166] and patutolide.[167]

3.3. Mukaiyama's Salt and Related Methods

The use of 1-methyl-2-chloropyridinium iodide (**20a**) (Figure 8) as an efficient agent for the macrolactonization of



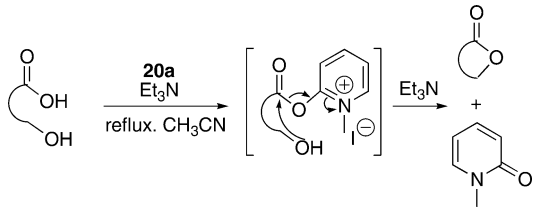
20a **20b**

Mukaiyama's reagent
PyCl/I

Figure 8.

ω-hydroxy acids was introduced by Mukaiyama in 1976.[168] The mechanism involves (Scheme 19) chloride substitution

Scheme 19

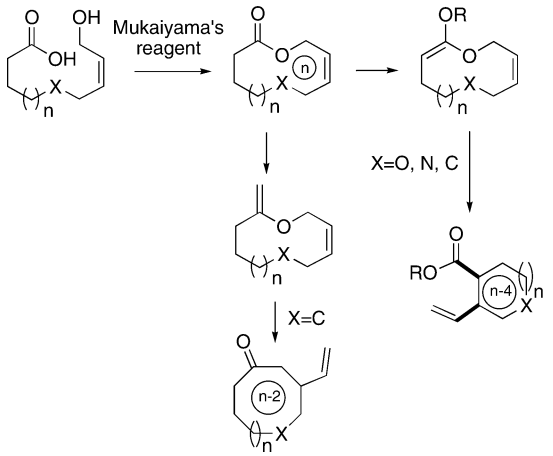


by the carboxylate ion to give a highly activated acyloxypyridinium species which then undergoes macrolactonizaton.

Mukaiyama has described further development of this reagent to suppress under the cyclization conditions the decomposition of the pyridinium salts by attack of triethylamine either on the 1-methyl group to form 2-chloropyridine or on the pyridinium ring to form ammoniopyridinium salts. The same group[73,169] synthesized a new pyridinium salt, 2-chloro-6-methyl-1,3-diphenylpyridinium tetrafluoroborate (**20b**), to avoid these side reactions. Indeed, in the presence of benzyltriethylammonium chloride and a hindered nonnucleophilic base such as a 2,6-disubstituted pyridine, this reagent gave better yields in the macrolactonization of unsubstituted seco-acids with lower diolide formation. (For example, 12 and 14 membered lactones were obtained in 85

and 99% yields, respectively, while the original reagent **20a** gave macrolactone yields of 69 and 84%, respectively.) This new reagent was further applied by the same authors in the total syntheses of prostaglandin $F_{2\alpha}$-1,15 and ricinelaidic lactones. Another drawback pointed out by Funk is the possible decomposition of the acyloxypyridinium intermediate to form the corresponding ketene which can undergo various side reactions such as [2+2] cycloadditions.[170,171] Nevertheless, this reagent has been successfully used in a number of total and formal syntheses and various other synthetic applications. This methodology has proved to be particularly useful in the synthesis of various unsaturated carbo, aza, and oxo macrocyclic lactones (Scheme 20) used in 2-

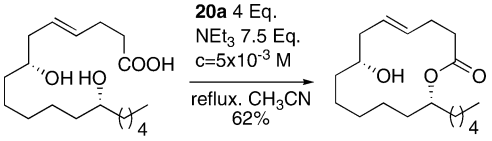
Scheme 20



and 4-ring contractions mediated by Claisen rearrangements;[172−174] the total syntheses of benzoylmeroquinene[175] and kainic acid;[171] formal synthesis, through an eight-membered lactone, of (±)-quadrone;[176] and approaches to the syntheses of the (B−C−D)-rings of ingenol,[177] of (±)-samin,[178] and of the cembranoids skeleton.[172]

Meinwald has also described the efficient synthesis of various aza (such as (*S*)-epilachnene) and polyaza macrocyclic lactones, obtaining, for example, a 98-membered ring in an impressive 48% yield for the lactonization step.[179,180] Syntheses using this methodology of various other macrolactones have also been described. Among them are the 34-membered ionophoric antibiotics aplasmomycin and boromycin synthesized by White,[181,182] gloeosporone,[183,184] in which the 14-membered macrolactone is formed (Scheme 21) rather than the eight-membered ring alternative (*vide*

Scheme 21



supra), various aggregation pheromones,[185−187] and nine-membered ascidiatrienolide[188] and jatrophone analogues.[189] Also worthy of note is Villemin's work,[190] in which in 1980-(!) the unsaturated seco-acid was constructed using a cross-metathesis and finally lactonized using Mukaiyama's reagent. This methodology has also been used to obtain bridged and constrained analogues of taxol,[191] sandostatin,[192] and thiazolinium salts.[193]

The Mukaiyama macrolactonization is usually carried out under high dilution conditions ($c = 10^{-3}$ M) with the slow addition of the hydroxy acid into a refluxing acetonitrile solution containing an excess of the pyridinium salt and triethylamine. The use of DMAP was also described by Armstrong in the total synthesis of the cyclodepsipeptide hapalosin,[194,195] and very recently, a polymer-supported reagent[196] was developed by Tye.

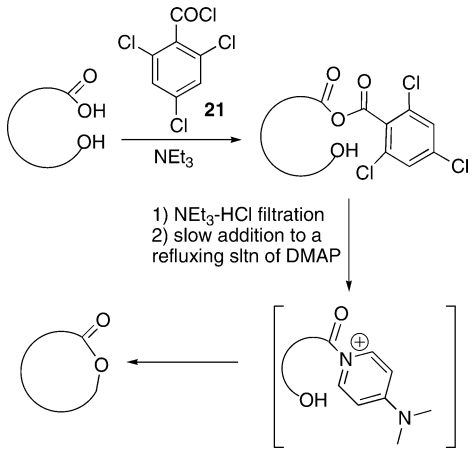
3.4. Macrolactonization through the Formation of a Mixed Anhydride Intermediate

From the seminal use of acetic and trifluoroacetic anhydrides, macrolactonizations through the formation of mixed anhydride intermediates have been increasingly used either under traditional basic conditions or, more recently, under acidic conditions.

3.4.1. Mixed Anhydrides and Basic Activation

3.4.1.1. Yamaguchi−Yonemitsu Conditions. With more than 200 papers using this methodology, the Yamaguchi reagent, 2,4,6-trichlorobenzoyl chloride (**21**), is probably the most popular method for performing macrolactonizations.[197] In the classical procedure (Scheme 22), the mixed anhydride

Scheme 22



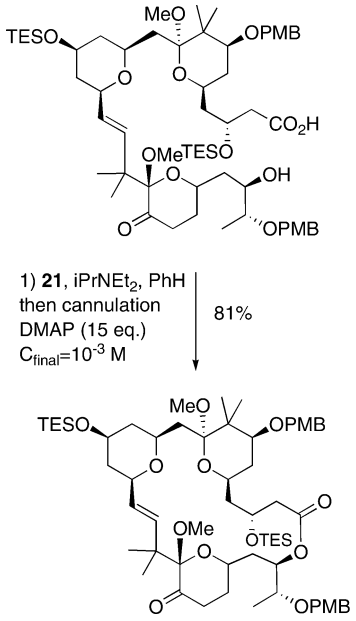
is preformed in THF in the presence of triethylamine. After filtration of the NEt_3-HCl salt and evaporation, the mixed anhydride is diluted in toluene and slowly added by syringe pump to a highly diluted solution of DMAP (2−5 equiv) at high temperature (80 °C or reflux). To the best of our knowledge, the formation of a symmetric anhydride in these reactions has been observed only in a single instance, that being in the total synthesis of hygrolidin.[198] Generally, filtration of the NEt_3-HCl salt is not crucial, but Evans has shown in the synthesis of roxaticin that it was essential to prevent the acid-promoted decomposition of the polyene unit of roxaticin.[199] The use of the 2,6-dichloro derivative with no alteration in the reactivity was also described before the Yamaguchi reagent (**21**) was commercially available.

Regarding DMAP, the use of pyrolidinopyridine[207−209] has also been described (for an excellent highlight of these additives, see ref 210). More recently, a polymer-supported DMAP reagent has been reported[211] in the total synthesis of epothilone C using a multistep application of immobilized reagents and scavengers.

There have been many variations and modifications of the original Yamaguchi procedure. Two major modifications have been developed by Yonemitsu in several papers[135,136,157] dedicated to the total synthesis of erythonolide derivatives. In the first of these two modifications, known as the "modified Yamaguchi conditions", Yonemitsu identified the ben-

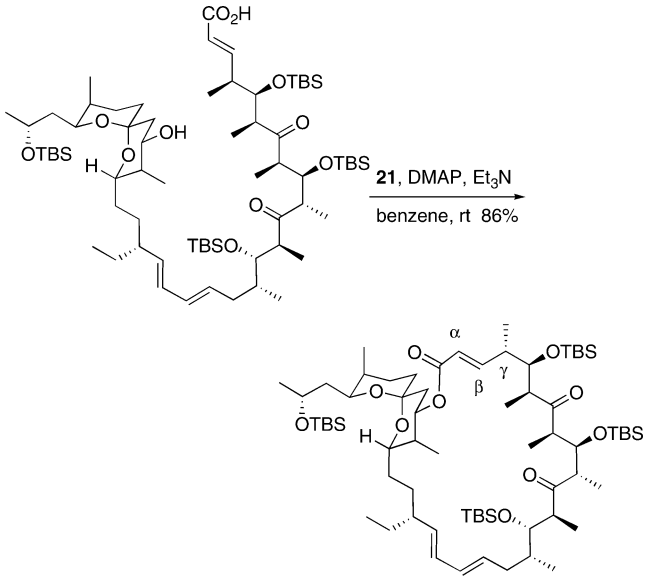
eficial effect of the direct addition of a large amount of DMAP to the preformed mixed anhydride, generally at room temperature and without the need for slow dilution. See, for example, the syntheses of oleandolide[59,212] and bryostatin 2[213] (Scheme 23).

Scheme 23



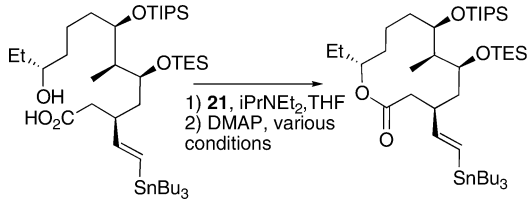
In the second of Yonemitsu's two modifications, known as the "Yonemitsu conditions", the mixed anhydride is not preformed and DMAP is directly introduced at room temperature from the beginning. These less basic conditions have proved to be highly efficient in, for example, the total synthesis of rutamycin B,[214] where the Keck, Mukaiyama, and Corey procedures gave mainly the deconjugated β/γ lactone as the major product and the classical Yamaguchi procedure gave a 1:1 mixture of the β/γ and α/β lactones (Scheme 24).

Scheme 24



Since macrolactonizations are usually carried out on very advanced substrates and consequently methodological studies are rather difficult and rare, there is still no rule about the best conditions to realize a Yamaguchi macrolactonization on a particular substrate. The general trend, however, seems to be use of the Yonemitsu conditions on rather large macrocycles (for example, the Yonemitsu conditions failed in the synthesis of the callipeltoside aglycon[215]) and classical conditions on medium ring lactones (to prevent the formation of diolides and oligomers). Indeed, the Yamaguchi reagent has also been used in the dimerization of seco-acids to form natural diolides, as illustrated in the syntheses of elaiophylin,[207,216,217] colletodiol,[218] and verbalactone.[219] Evans has shown the influence of the temperature and rate of addition in reducing diolide formation and destannylation in the macrolactonization of a sensitive lepicidin precursor (Scheme 25).[220]

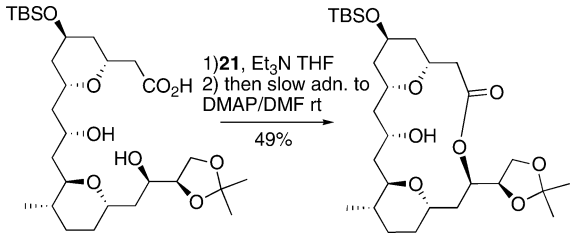
Scheme 25



T (°C)	addn time (h)	lactone (%)	destannylated S.M. (%)	dimer (%)
25	0.5	13	--	33
70	0.5	63	7	10
110	10	10	63	1
110	1	78	3	3

In the total synthesis of leucascandrolide, Carreira[221] has shown that the lactonization of the seco-acid (Scheme 26)

Scheme 26



under the usual conditions leads mainly to oligomerization, probably due to unfavorable hydrogen bonds. To disrupt these interactions, the reaction was carried out in DMF, giving the 14-membered lactone in 49% yield and none of the 8-membered lactone.

The main drawback of the Yamaguchi procedure is the use of the highly basic DMAP and high temperature. These factors sometimes lead to undesireable side reactions such as α/β to β/γ isomerization of conjugated double bonds *(vide supra)*, epimerization of sensitive chiral centers,[222] and *Z*/*E* isomerization of conjugated double bonds.[223−227] The latter problem is usually solved (Scheme 27) by performing the macrolactonization on the ynoic seco-acid and then reducing the triple bond, as illustrated in the synthesis of laulimalide.[227]

To date, the Yamaguchi protocol and variations have been used in more than 200 synthetic applications, including eight-membered lactones;[228,229] nine-membered halicholactone[230,231] and a nine-membered intermediate to laurencin;[232] 10-membered didemninlactone,[233] decarestricine,[234] mueggelone,[235,236] hebarumin,[237] and ascidiatrienolide;[238] epothilones A, B, D, E, and F and congeners;[211,239−268] macrolactin A;[269] erythronolides and analogues;[51,56,135,136,157,270−274] oleandolide;[59,212,270,275] lankanolide;[55] deoxytedanolide;[66] mycinolide;[276] brefeldin;[277−282]

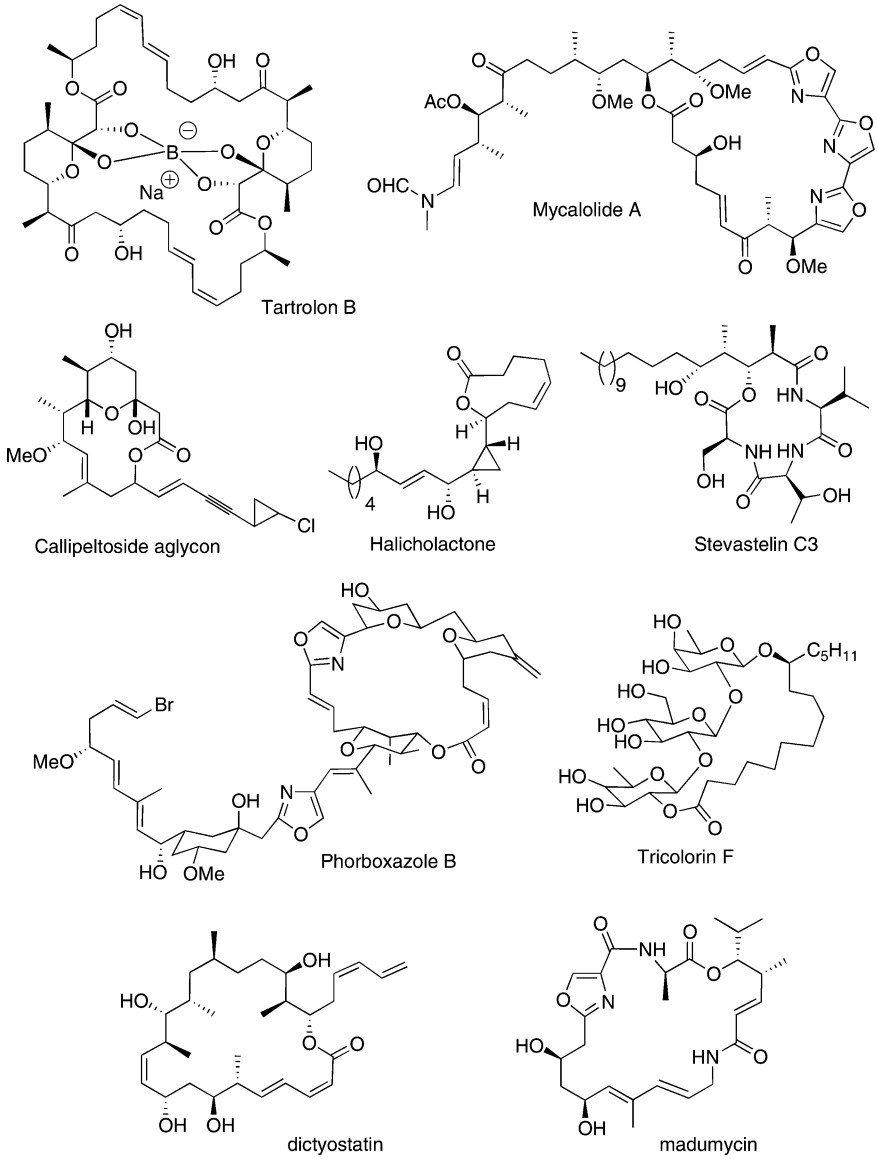
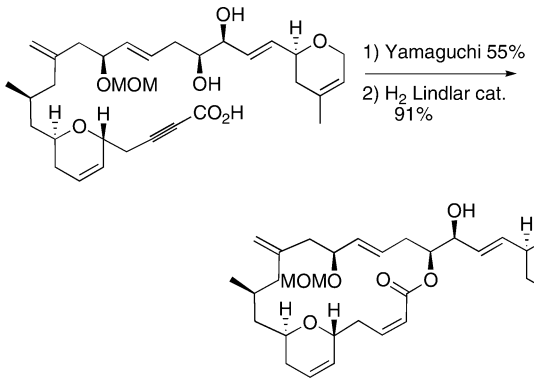


Figure 9. Representative examples of natural product syntheses using the Yamaguchi macrolactonization.

Scheme 27

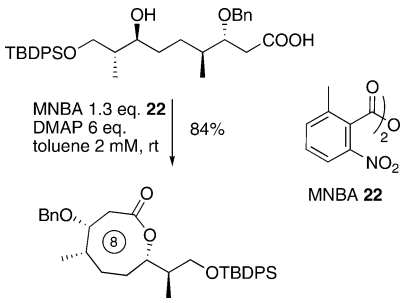


mycotycin;[283] roxaticin;[199,284,285] colletol;[286,287] colletallol;[204] cladospolide;[288,289] patulolides;[223,224,290−293] various insect pheromones;[294,295] antiobiotic A26771B;[296] spiruchostatin;[297] formamicinone;[298] callipeltoside;[215,299] borrelidin;[71,300,301] dictyostatin;[302−304] rutamycin;[214] spongisatins;[65,305−311] lepicidin;[220] halichondrin;[312,313] jasmine ketolactone;[314] *ent*-Haterumalide methyl ester;[315] myxovirescine;[316] grahamimycin;[317,318] auriside;[319] bryostatins;[213,320,321] apicularen;[64] madumycin;[322] mycacolide;[323] hydroxybutanoic acid, hydroxylenic acid, dihydropyrans (up to a 72-membered macrocycle), and quinine oligomers;[324−328] pamamycin 607;[222,329,330] phorboxazole;[226] recifeiolide;[331] amphidinolides;[332−334] cineromycin;[335] tartrolon B;[336,337] spinosyn A;[338] leucascandrolide;[221,339−341] cyclodepsipeptides such as geodiamolide,[342] globomycin,[343] and stevastelin;[344] nonactin[345−348] aspicilin;[293,349−352] 44-membered swhinholide;[72,353−355] acutiphycin;[356,357] scytophycin;[69,358,359] aplyronine A;[67,360−362] aplyolide;[363,364] hygrolidin;[198] nargenicin and dinemycin A precursors;[365,366] bafilomycin, where the Mukaiyama, Keck, and Palomo protocols failed;[367] apoptolidinone;[61,62,368,369] conglobatin;[209] and macrocyclic glycolipids,[12] such as tricolorins,[370,371] macrosphelides,[372−379] concanolide,[380] polycavernoside A,[57,381,382] laulimalide,[208,227,383−388] the clonostachydiol epimer,[389] and epilachnene and congeners.[390] Some of these applications are illustrated in Figure 9.

3.4.1.2. MNBA. The use of 2-methyl-6-nitrobenzoic anhydride (MNBA, **22)** has been described recently by Shiina.[391] The reaction can be carried out at room temperature in dichloromethane with limited diolide formation in the presence of an excess of DMAP. It can also be done in the presence of triethylamine with 20% of (dimethylamino)-pyridine oxide. These are illustrated in the syntheses of

aleuritic acid lactone, [391] octalactin[392,393] (Scheme 28), and

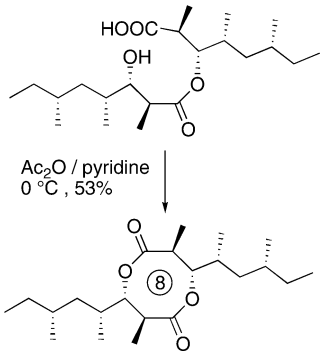
Scheme 28



patutolide C[394] and in an atropselective macrolactonization[395] in the synthesis of the C-1027 chromophore. (See also eq a in Scheme 12.)

3.4.1.3. Miscellaneous Mixed Anhydrides. Several other mixed anhydrides, obtained from pivaloyl chloride,[396,397] trifluoroacetic anhydride,[398,399] acetic anhydride[400,401] (Scheme 29), and Boc_2O[402−404] have also been described, but with only

Scheme 29



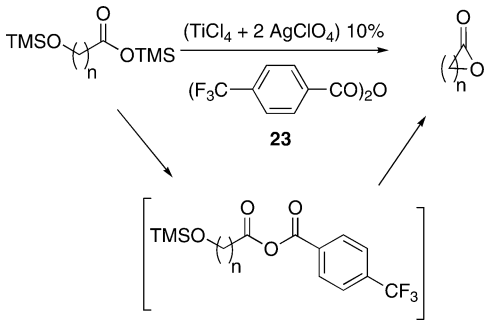
limited synthetic development.

Macrolactonizations through the formation of mixed carbon−phosphorus and carbon−sulfur anhydrides are discussed in sections 3.5 and 3.1.3.

3.4.2. Macrolactonizations Using Mixed Anhydrides under Lewis Acid Activation

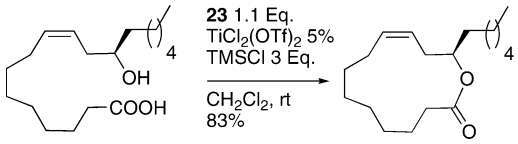
3.4.2.1. Mukaiyama−Shiina Catalysts. In 1993 Shiina and Mukaiyama described the macrolactonization of silyl *ω*-siloxycarboxylates at room temperature in the presence of *p*-trifluoromethylbenzoic anhydride (TFBA, **23**) and 0.10 equiv of a Ti(IV) catalyst made *in situ* by mixing $TiCl_4$ and $AgClO_4$ (Scheme 30).[405]

Scheme 30



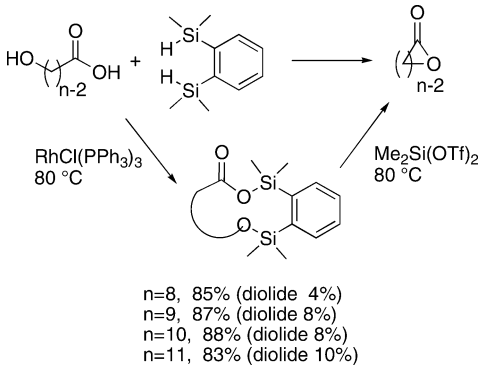
The use of silyl derivatives of seco-acids is required to prevent deactivation of the titanium catalysts. With that precaution, the same authors have described direct macrolactonizations of seco-acids in the presence of TMSCl (3 equiv) and $TiCl_2(OTf)_2$ (1−5%) in refluxing dichloromethane in good yields for macrolactones from 13 to 17 members. This procedure was further applied to the syntheses of (*R*)-ricinelaidic and (*R*)-ricinoleic acid lactones (Scheme 31).[406]

Scheme 31



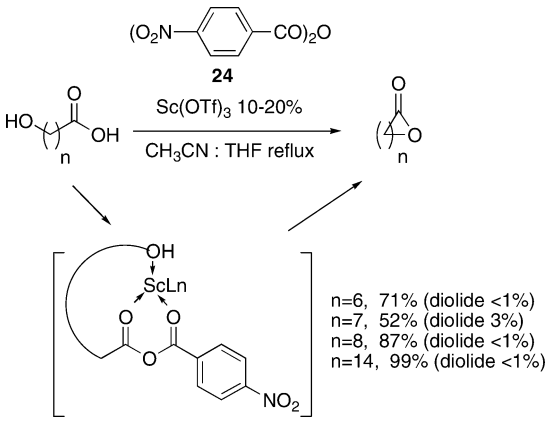
Since the yields for medium ring macrolactones are usually low, Shiina and Mukaiyama have developed an alternative strategy[407] based on the Rh-catalyzed formation of a cyclic silyl siloxycarboxylate intermediate which is, in turn, treated with $Me_2Si(OTf)_2$ to give the corresponding lactones in high yields (Scheme 32).

Scheme 32



3.4.2.2. Yamamoto Catalyst. The use of Lewis acid catalysts in the macrolactonization of mixed anhydrides has been independently investigated by Yamamoto et al.[408] Using a catalytic amount (10−20%) of $Sc(OTf)_3$, *ω*-hydroxycarboxylic acids are lactonized in the presence of *p*-nitrobenzoic anhydride (**24**) to give the correponding lactones in high yield. Results are particularly impressive for medium ring lactones ($n = 8-10$; Scheme 33), which usually provide the

Scheme 33

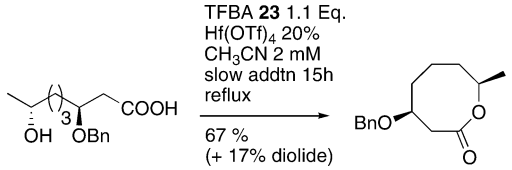


diolide as the major product. An intermediate in which scandium is coordinated with the mixed anhydride and with the hydroxyl group has been postulated by Yamamoto.

As far as we know, this promising methodology has not been widely used yet in total syntheses. In the synthesis of

cephalosporolide D, Shiina has described the use of $Hf(OTf)_4$ to give the eight-membered lactone in 67% yield. The yield in the presence of $Sc(Otf)_3$ was 44%, and the original procedure with TMSCl and Ti(IV) catalysts was unsuccessful (Scheme 34).

Scheme 34



3.5. Phosphorus-Based Reagents

Phosphorus-based reagents (Figure 10), widely used in the

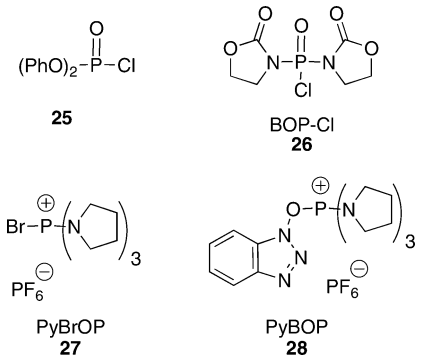
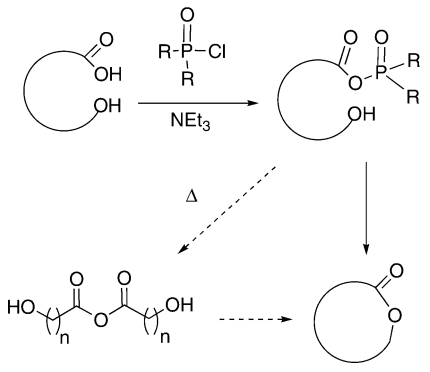


Figure 10.

synthesis of peptides, cyclodepsipeptides, and peptidomimetics, have also found some applications in macrolactonizations.

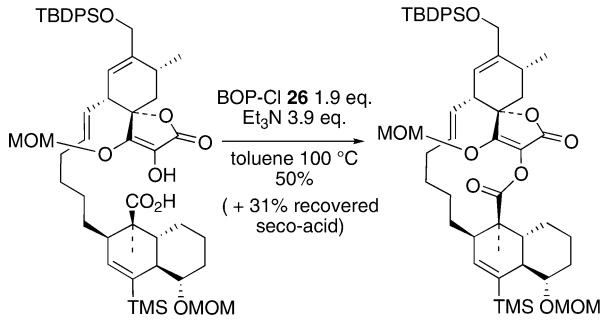
Masamune[409] and Corey[410] were the first to recognize the potential of mixed carbon−phosphorus anhydrides in the synthesis of macrolactones. Masamune[409] faced some difficulties in the thiophilic metal cation assisted cyclization of a thiol ester during the total synthesis of narbonolide (see section 3.1.2) and thus described the macrolactonization as done by the formation of a mixed anhydride using diphenylchlorophosphate (**25**) as the activating agent. The same methodology was applied in the syntheses of vertaline,[86] nonactin,[411] and a zearlenone derivative,[409] as well as in the dimerization−lactonization to form the diolide vermiculine.[412] Because mixed carbon−phosphorus anhydrides tend to give symmetrical anhydrides under heating[409(note 15),413] (Scheme 35), Masamune recognized the need to perform the

Scheme 35



macrolactonizations at a temperature below 80 °C. In 1982, Corey also described the use of Palomo's reagent BOP-Cl[414] (**26**) in the synthesis of aplasmomycin.[410] This methodology was then used in a synthetic approach to enetetraynes[415] and in the total synthesis of (−)-chlorothricolide by Roush (Scheme 36), where Yamaguchi−Yonemitsu and Boden−

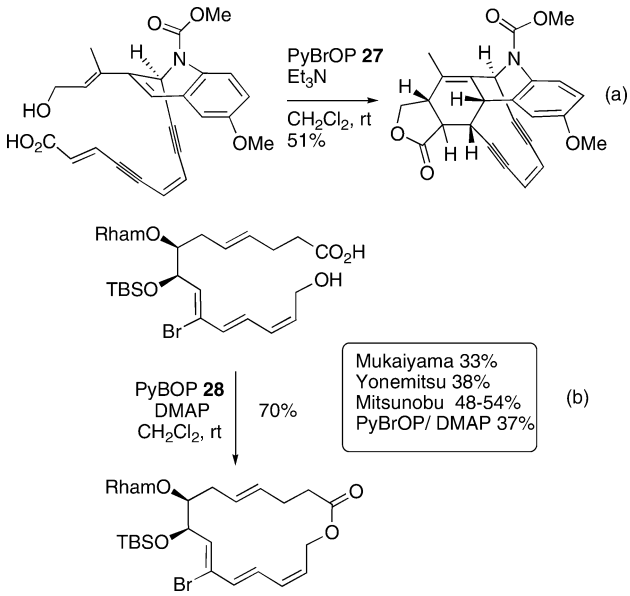
Scheme 36



Keck protocols gave very low yields.[416]

Peptide-coupling reagents PyBroP[417] (**27**) and PyBOP[418] (**28**) have also been successfully used in the synthesis of macrolactones. The enediyne-bridged tricyclic core of dynemicin A[419] was obtained in 51% yield using a PyBroP-mediated macrolactonization followed by a transannular Diels−Alder reaction at room temperature (eq a in Scheme 37). PyBOP was used during synthetic studies on (−)-

Scheme 37



spinosyn A[420] (eq b in Scheme 37) and for the synthesis of eight-membered bicyclic peptidomimetics,[421] of the 11-residue peptide lactone gelatinase biosynthesis-activating pheromone GBAP,[422] and of kahalalide B.[423] Although no mechanistic details are given in these studies, macrolactonizations probably proceed initially through the formation of an acyl-oxy-phosphonium intermediate.[424]

3.6. Carbodiimides and Related Reagents (Steglich and Boden−Keck)

Dicyclohexylcarbodiimide (DCC, **29a**) (Figure 11) in the presence of pyridine, though long known as an esterification reagent, was first used in a lactonization reaction by Woodward en route to reserpine.[425]

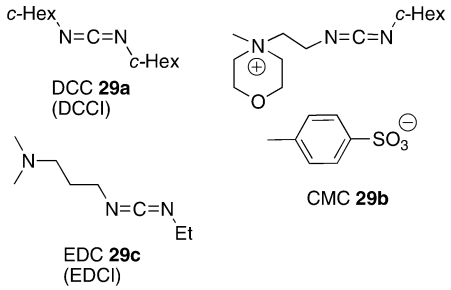
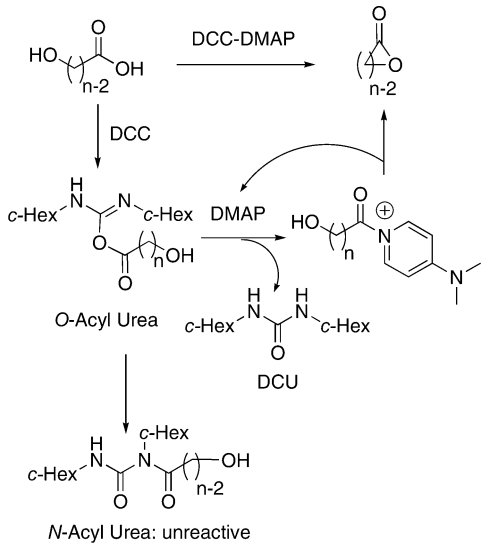


Figure 11.

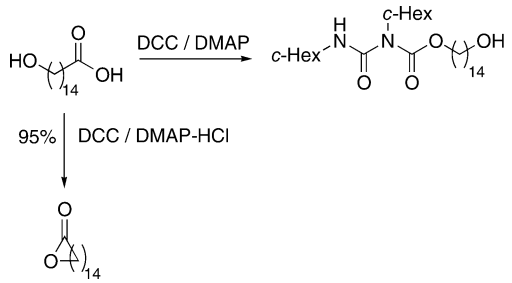
Steglich and Litivenko have independently demonstrated the superior reactivity of 4-*N*,*N*-dimethylaminopyridine (DMAP) and pyrrolidinopyridine in these reactions. For an excellent highlight on these additives, see ref 210, and for some examples, see the syntheses of benzolactone V8,[426] of renin peptidomimetics inhibitors,[427] of milbemycin E,[428] and of sanglifehrin.[429] Nevertheless, this DCC−DMAP protocol has been used rarely in macrolactonizations, mostly because of formation of an unreactive *N*-acyl urea byproduct (Scheme 38).

Scheme 38



Indeed, the major product in the macrolactonization of 15-hydroxypentadecanoic acid is the *N*-acyl urea byproduct, and the hexadecanolide is only isolated in 4% yield.[430] In synthetic studies toward the synthesis of colletodiol, Keck and Boden have shown the crucial role of the proton-transfer step, using DMAP−HCl and other amine hydrochloride salts to prevent the formation of the undesired byproduct and obtaining the hexadecanolide in 95% yield[430] (Scheme 39).

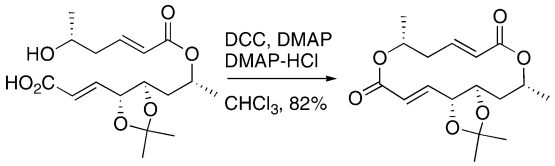
Scheme 39



The beneficial use of a catalytic amount of *p*-TSA in esterification reactions has also been previously described in 1979 by Holmberg.[431]

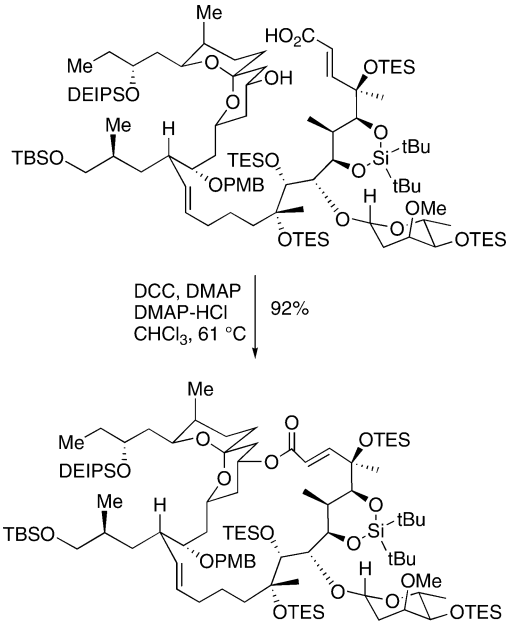
Keck et al. have applied this procedure in the syntheses of (−)-colletodiol[432] and colletol[433] (Scheme 40). The

Scheme 40



potential of this so-called Boden−Keck procedure was rapidly recognized and used in a great number of total syntheses, including those of cytovaricin[434] (where Mukaiyama's reagent failed) (Scheme 41), aplysiatoxin,[435] swhinolide

Scheme 41



and hemiswhinolide (*vide supra*),[72] colletodiol, colletol, and grahamimycin A,[436] epothilone derivatives,[437] and various olfactive alkynolides,[438] formal synthesis of apicularen[439] and diazonamide,[440] and synthetic studies of ingenane.[441] This procedure has also been used in the trimerization of a seco-acid to obtain the triolide arthrobacilin.[442]

Several other proton sources have been used in Boden−Keck type macrolactonizations, such as DMAP−TFA,[49,443−450] TsOH,[451] and camphorsulfonic acid (CSA).[452−454]

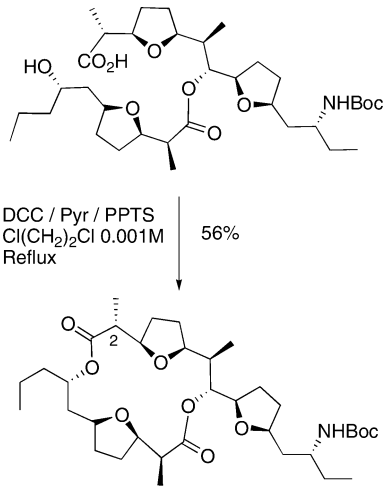
The main drawback associated with DCC, which is usually used in excess and "quenched" by methanol in acetic acid, is the tricky removal by flash chromatography of the corresponding urea byproduct, DCU. Several modifications of the esterification reagent have therefore appeared, being mainly water soluble ureas and supported reagents. Kocienski has used CMC (*N*-cyclohexyl-*N*′-(*b*-[*N*-methylmorpholino]-ethyl)carbodiimide *p*-toluenesulfonate, **29b**) in the presence of DMAP−TFA in the total synthesis of the cyclodepsipeptide jaspamide.[450] However, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC, **29c**), which is usually sold as its hydrochloride salt, is more widely used in, for example, the syntheses of bridged cyclosporins,[455] epothilones B and D,[456] sialyl Lewis X mimics,[457] bafilomycin,[458] octalactin,[47] sanglifehrin,[429] various oligopeptides macrocycles,[459] vancomy-

cin fragment,[460] nine-membered obtusenyne,[461] and an FK-506 analogue.[462]

More recently, Keck has described the use of a supported DCC reagent with no loss in the macrolactonization yield. (The supported DCU is easily eliminated by a simple filtration.[463])

The highly basic DMAP is sometimes detrimental to the macrolactonization. For example, in the total synthesis of bryostatin 7,[60] the use of DMAP led to an intractable mixture whereas the use of pyridine in the presence of PPTS[222,464,465] led to the macrolactone in good yield. In the synthesis of pamamycin 607, this DCC−pyridine−PPTS protocol was the only one to give the macrodiolide in good yield (Scheme 42): Corey−Nicolaou−Gerlach, Mukaiyama, and Yamaguchi−Yonemistu procedures yielded no lactone, whereas the "regular" Yamaguchi protocol resulted in complete epimerization at the C2 carbon.[222,465] As previously mentioned for Yamaguchi macrolactonizations, the use of DMAP may also result in epimerizations of sensitive chiral centers[446,453] as well as *Z*/*E* isomerizations.[454]

Scheme 42



The peptide coupling reagent DCC−HOBt−NEt_3 has also been described in rather rare examples of macrolactonizations.[466−468]

3.7. Chloroimidazolinium and Chloroformamidinium Chlorides

The dehydrating reagents 1,3-dimethyl-2-chloroimidazolium chloride (DMC,[469,470] **30**) and *N*,*N*,*N*′,*N*′-tetramethylchloroformamidinium[469] chloride (**31**) have been used in macrolactonizations (Figure 12). These reagents are usually synthesized *in situ* by heating a 1,2-dichloroethane solution of the corresponding urea with oxalyl chloride (Scheme 43). After evaporation of the solvent and of excess oxalyl chloride, the residue is dissolved in acetonitrile and an acetonitrile−ether solution of collidine and seco-acid is slowly added at room temperature to give the corresponding lactone.

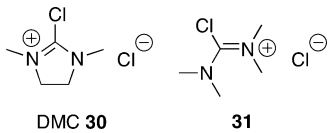
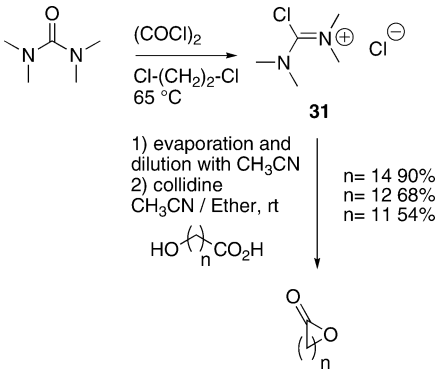


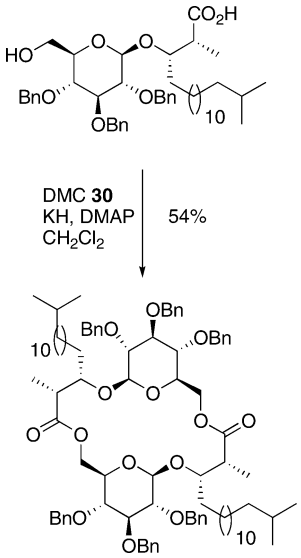
Figure 12.

Scheme 43



DMC (**30**) has found application in the selective dimerization of seco-acids in the synthesis of cyclic glycolipids such as cycloviracins, fattivaricins, glucolipsins, and macroviracins.[471−476] The use of an added metal cation (potassium[473−477] or sodium[471]) is crucial for the selectivity, and in this case the macrodilactonization is believed to proceed in a template-directed manner (Scheme 44).

Scheme 44

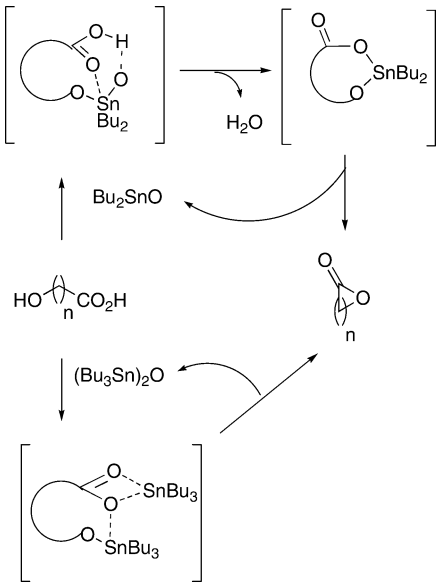


3.8. Tin-Based Reagents

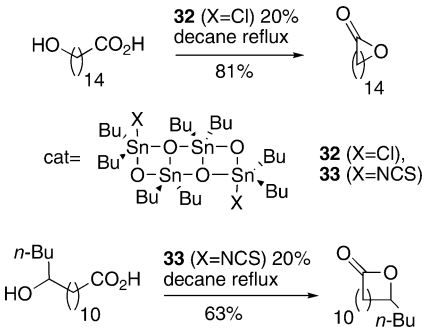
The use of tin reagents in macrolactonizations stems from the use of tin oxides to cleave esters.[478] In the 1980s, Hanessian and Steliou[479,480] showed that this reaction is an equilibrium, and they developed a macrolactonization (and esterification) method by elimination of the water produced. The use of Bu_2SnO and $(Bu_3Sn)_2O$ has been described, involving, however, two different pathways (Scheme 45), each with a double activation.The same authors have used this method, i.e., 10% Bu_2SnO in refluxing mesitylene (165 °C) with a Dean−Stark apparatus, in the syntheses of several 13- to 17-membered macrolactones.[480]

The use of distannoxanes **32** (X = Cl) and **33** (X = NCS) has been described by Otera[40] (Scheme 46). Interestingly, in contrast to Bu_2SnO-catalyzed reactions, the process is virtually irreversible so that a Dean−Stark apparatus is not required[40] and the reaction can be carried out under moderate dilution conditions.

Scheme 45



Scheme 46

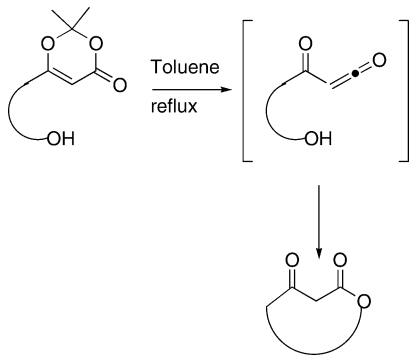


Tin oxides have also been described as efficient transesterification reagents[481] and used in a number of macrolactonizations (see section 3.10.3.5).[482]

3.9. Boeckman's Method

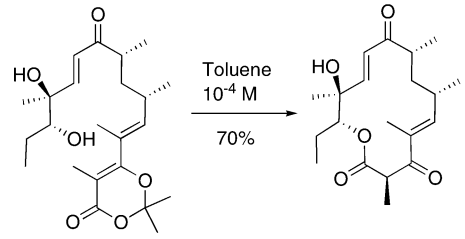
Dioxolenone thermolysis is a known process for obtaining β-acetylketene derivatives under relatively mild conditions (refluxing toluene).[483] The ketene intermediate can also be trapped intramolecularly by oxygen and nitrogen nucleophiles to give the corresponding macrolactone or macrolactam through a cycloreversion/macrocyclization process (Scheme 47).

Scheme 47



This methodology has been used by Boeckman to develop an efficient macrolactonization method illustrated in the syntheses of the 10-membered diploalide A and the 14-membered kromacyn, which was obtained with excellent regio- and diastereoselectivities (Scheme 48).[484]

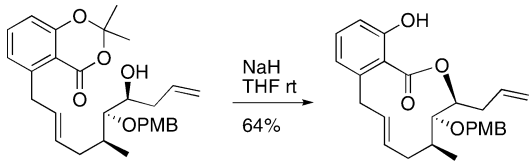
Scheme 48



This methodology has found synthetic applications in the syntheses of various eight-membered lactones[485] and of deschlorocallipeltoside A/callipeltoside A.[486−488] However, in further synthetic studies, Kurth et al.[489,490] have shown that, using unsubstituted chains, oligomeric products are obtained. It is also worthy of note that the acyl-ketene intermediate can be generated photochemically (see section 3.12).

A related but mechanistically different process has been independently decribed by De Brabander,[491,492] and Rizzacasa,[493,494] in the synthesis of benzolactone apicularens. This methodology has also been used in the synthesis of salicylihalamides A and B[495] (Scheme 49). During the synthesis

Scheme 49



of lobotamide, a surprising size-selectivity (8- rather than 15-membered lactone) has been observed in a Boeckman type macrolactonization (no lactonization occurs under various conditions (basic or photochemical) with a TBS-protected alcohol) (Scheme 7).[70]

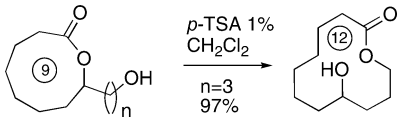
3.10. Macrolactonizations through the Formation of an "Activated" Ester: Transesterification and Translactonization Methods

Transesterification methods are well-known processes in the modern organic synthesis tool box,[482,496] and numerous industrial applications of them have been developed, particularly in musk synthesis.[21]

3.10.1. Translactonizations

Acid-catalyzed thermodynamically driven translactonizations were studied by Corey and Nicolaou in 1977.[497] These translactonizations proceed in high yields for n= 1, 2, and 3, as illustrated in Scheme 50. The interconversion rate

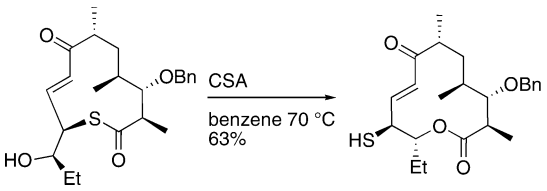
Scheme 50



usually decreases within increasing n because larger ring sizes are formed in the transition state. A "7 + 3" strategy has been successfully applied in the total syntheses of erythronolides A and B.[100,498]

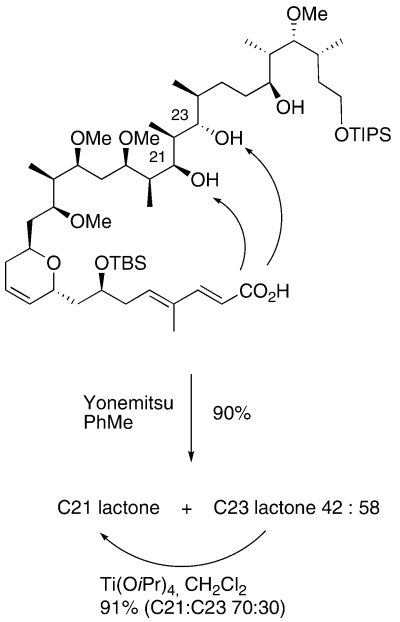
A related process which proceeds through a thiolactone also affords various 8-, 9-, and 10-membered lactones[499] in good yields. This process was used in the synthesis of phoracantholide[499] and of methynolide[500,501] (Scheme 51).

Scheme 51



Lewis acid-mediated translactonizations have also been used in a number of total syntheses in which macrolactonizations without size selectivity have been observed. By taking advantage of the thermodynamic preferences, the undesired lactones can usually be isomerized as illustrated in Scheme 52.[9] It is also worthy of note that there is one

Scheme 52



example where an eight-membered lactone could not be isomerized, under various conditions, to the corresponding 15-membered lactone.[70]

Basic and acidic translactonizations have also been observed in several ring contractions of natural products.[502]

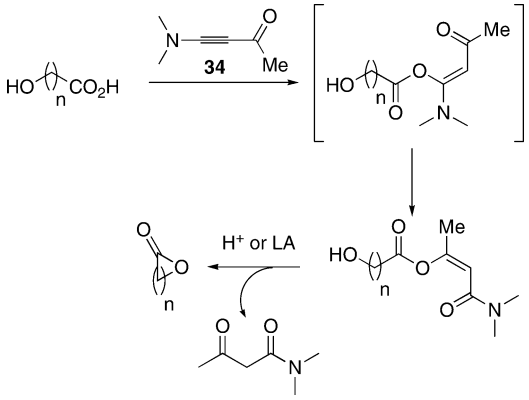
3.10.2. Macrolactonizations through the Formation of a Vinylic Ester

The Gais and Trost methodologies are two-step processes based on the synthesis of a vinylic ester followed by an acid-catalyzed macrolactonization.

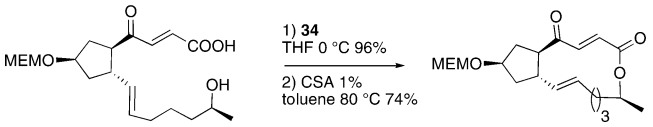
3.10.2.1. Gais Vinylic Esters. In the Gais methodology, the vinylic ester is formed in a very elegant push−pull reaction of the carboxylic acid with 4-(dimethylamino)but-3-yn-2-one (**34**). The vinylic ester is then treated in the presence of CSA (1−5%) to give the corresponding lactone (Scheme 53).[503] A mercury salt or magnesium bromide is sometimes used in place of the CSA.

This methodology has been used in the syntheses of various 13-, 14-, and 16-membered lactones and brefeldin A (Scheme 54).[503,504] The main drawback of the reaction,

Scheme 53



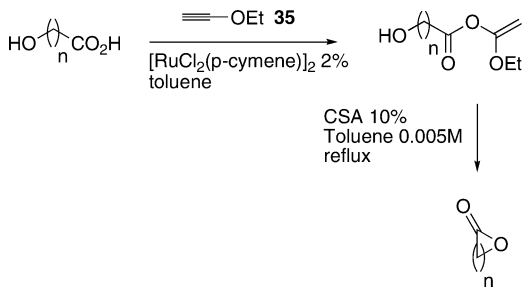
Scheme 54



which is catalytic in CSA and very mild, is the synthesis of the sensitive 4-(dimethylamino)but-3-yn-2-one.

3.10.2.2. Trost Vinylic Esters. In the Trost macrolactonization, the vinylic ester is formed through a ruthenium-catalyzed reaction[505,506] of the carboxylic acid with commercialy available ethoxyacetylene (**35**) (Scheme 55). The

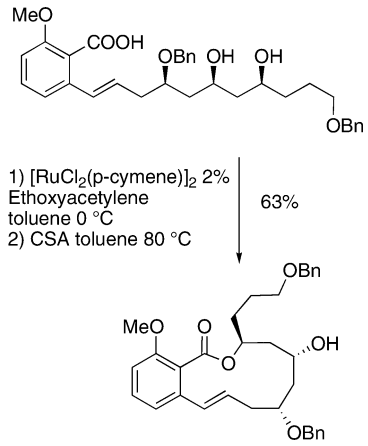
Scheme 55



vinylic ester, which can be isolated by chromatography, can then be lactonized under acidic conditions (CSA 10%).[507]

This methodology has been used in the macrolactonizations of various 14-, 15-, 16-, 17-, and 22-membered macrolactones, and it has more recently been illustrated by Maier in the size-selective synthesis of apicularen A (Scheme 56).[508]

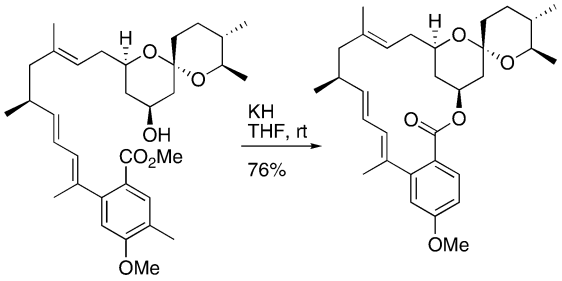
Scheme 56



3.10.3. Transesterifications of "Activated" Esters and Amides

The use of "unactivated" alkyl esters in basic transesterifications has been described in rather rare examples[166,509,510] of macrolactonizations (see, for an example, Scheme 57).

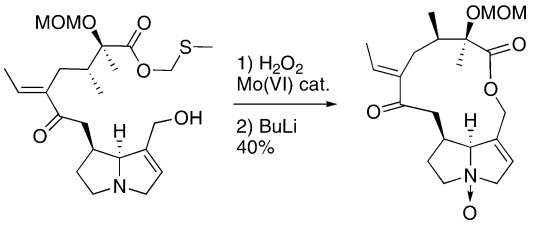
Scheme 57



Derivatives of "activated" esters and amides have been developed by several groups.

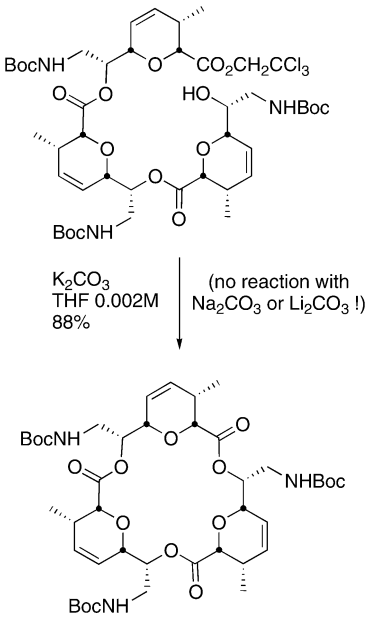
3.10.3.1. Narasaka's Ester. Narasaka has described the use of (methylthio)methyl ester in macrolactonizations. The ester is "activated" by oxidation, and then the alcohol is deprotonated to yield the corresponding macrolactone, as illustrated in the synthesis of integerrimine (Scheme 58).[511]

Scheme 58



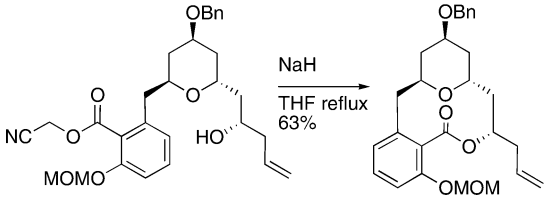
3.10.3.2. Burke's Ester. Burke has developed the use of trichloroethyl esters in the presence of a base in the synthesis of hydropyranic macrolactones. The use of potassium salts is, however, essential to promote the macrolactonization; in the presence of sodium carbonate or lithium carbonate, no reaction occurs (Scheme 59).[37] More recently, Burke has also described the transesterification of tribromomethyl esters in the presence of phosphines with, however, limited success in macrolactonizations.[512]

Scheme 59



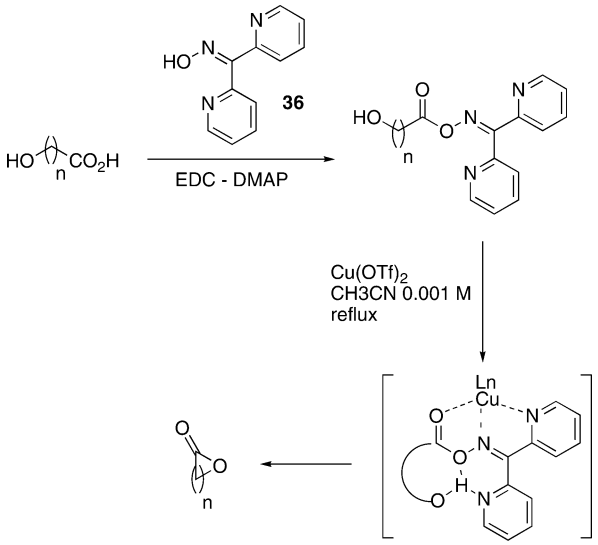
3.10.3.3. Panek−Porco's Ester. A cyanomethyl ester previously described in intermolecular transesterifications[513] has been used by Panek in the synthesis of apicularen (Scheme 60).[514]

Scheme 60



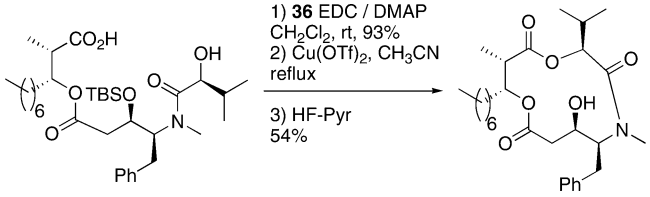
3.10.3.4. Palomo's Reagent. In the synthesis of the cyclodepsipeptide hapalosin, Palomo et al. used a di-2-pyridyl ketone oxime ester which was previously described by them as a peptide coupling reagent.[515] The di-2-pyridyl ketone oxime ester is prepared from the seco-acid by treatment with di-2-pyridyl ketone oxime **36** and EDC in dichloromethane in the presence of a catalytic amount of DMAP (Scheme 61).[111]

Scheme 61



This ester is stable, and no lactonization occurs without activation. The oxime ester cleanly converts into the lactone through a double activation in the presence of a copper salt (see also section 3.1.1), as is illustrated in the synthesis of hapalosin (Scheme 62).[111]

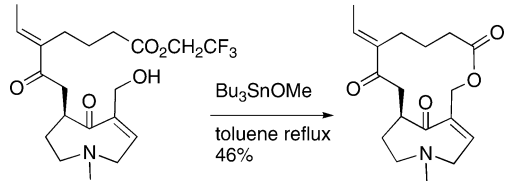
Scheme 62



3.10.3.5. Tin-Mediated Transesterifications. As previously stated (see section 3.8), tin oxides are efficient transesterification reagents[481,482] and have been applied intramolecularly to perform macrolactonizations. In 1992,

Shimizu described the transesterification of an ethyl ester to obtain a 13-membered lactone in a route to jasmine ketolactone.[516] Shortly after, White described the efficient transesterifications of trifluoroethyl esters in the presence of Bu_3SnOMe.[517] This reaction is thermodynamically driven by the elimination of trifluoroethanol and has been used by Yamada in a total synthesis of otenicin (Scheme 63).[518] More

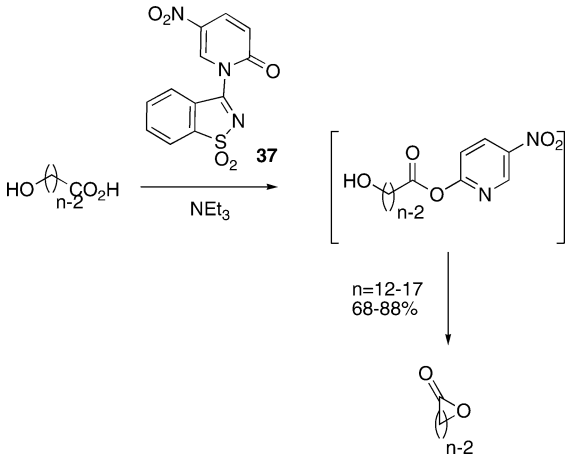
Scheme 63



recently, Porco and Panek[519] have described the selective cyclodimerizations (including heterodimerizations) of hydroxyesters using distannoxanes **32** and **33**.

3.10.3.6. Kinoshita Reagent. The peptide-coupling reagent BID-Npy (**37**) has also been used in macrolactonization of various ω-hydroxy acids in good yields through the formation of an activated ester (Scheme 64).[520]

Scheme 64

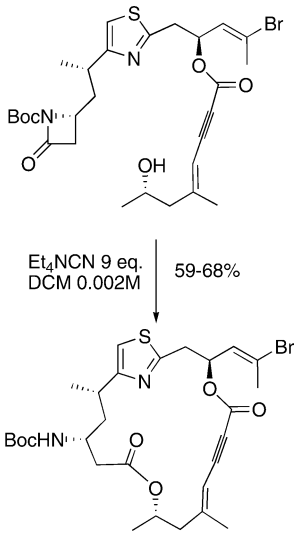


3.10.3.7. Macrolactones from β-Lactams. β-Lactam alcoholysis is known to yield the corresponding β-aminoesters, as illustrated, for example, in the taxol side-chain synthesis.[521] This strategy has been used intramolecularly by Romo in the total synthesis of the 25-membered pateamine.[522,523] The original conditions, NaHMDS in THF, were too basic and thus were changed to Palomo's milder conditions,[524] DCM with Et_4NCN as a soluble cyanide source, to give the corresponding macrolactone in 59−68% yield through an acyl-cyanide intermediate (Scheme 65). Georg[525,526] has recently applied the same strategy in the total synthesis of arenastatin.

3.10.3.8. Activated Amides. Macrolactonizations through the formation of activated amides have been described in several total syntheses using Staab's carbonyldiimidazole methodology,[156,527−529] and a diacyl-activated amide has been used by Wasserman[530] in a total synthesis of antimycin A3.

3.10.3.9. Enzymatic Reactions. Using a *Pseudomonas* lipase at 40 °C in apolar solvents, the transesterification of $HO(CH_2)_nCO_2Me$ for $n = 12$, 13, 14, and 15 with yields of 38, 64, 78, and 80%, respectively, has been accomplished.[531,532] An irreversible reaction starting from a vinylic ester has also been shown to improve the transesterification

Scheme 65

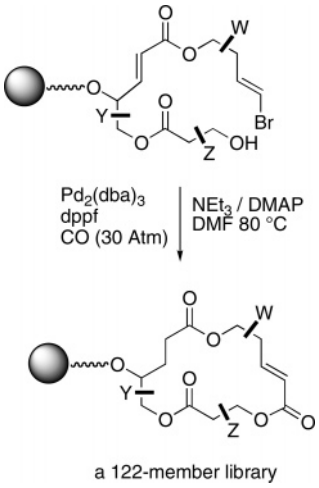


yields.[533] Direct conversion of seco-acids to macrolactones using *Lucor miehi* lipase has been described.[534] A monoclonal antibody raised against a macrocyclic phosphonate transition state has been reported to catalyze an intramolecular transesterification of a *p*-nitrophenyl ester to give the corresponding 14-membered lactone.[535]

3.11. Carbonylative Macrolactonizations

Despite the extensive development of palladium-catalyzed carbonylations, this strategy has rarely been used in macrolactonizations. In 1995, the carbonylative macrolactonization of terminal acetylenes in moderate yields was described.[536] More recently, a 122-member macrosphelide library was produced based on a polymer-supported palladium-catalyzed cyclocarbonylation (Scheme 66).[36]

Scheme 66



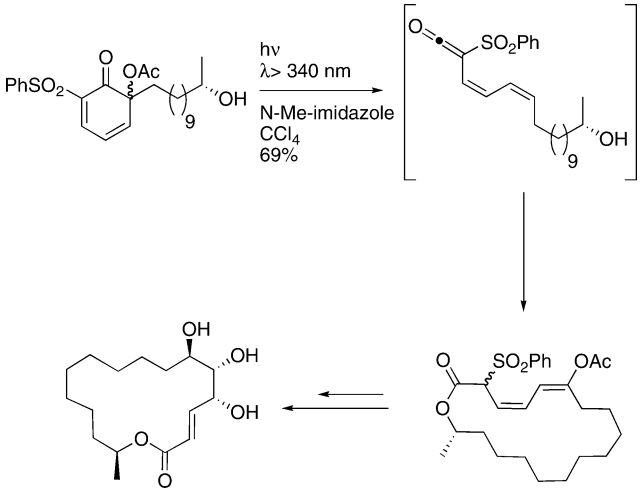
Two examples of ruthenium-catalyzed cyclocarbonylation of allenyl alcohols to give eight-membered lactones in good yield have been published.[537]

3.12. Photochemistry

Quinkert and collaborators have described an original way to obtain macrolactones in good yield by using photolactonization of *o*-quinol acetates, which passes through a diene

ketene intermediate. This method is illustrated in the total synthesis of (+)-aspicilin (Scheme 67).[538−542]

Scheme 67

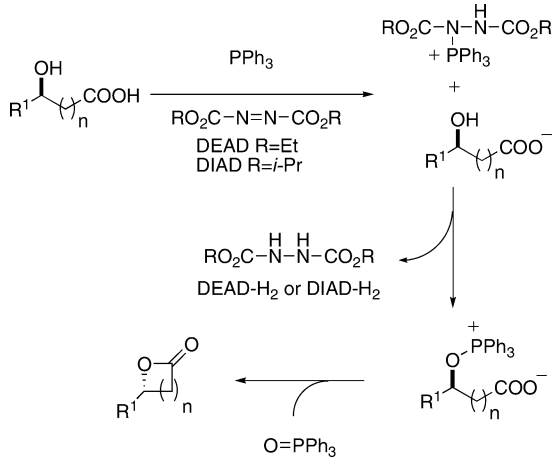


4. Macrolactonizations by "Alcohol" Activation

4.1. Mitsunobu Reactions

In 1976 Mitsunobu described a macrolactonization protocol to obtain medium and large macrolactones. This methodology is based on the activation of the seco-acid alcohol using diethyl azodicarboxylate (DEAD) and triphenylphosphine.[543−546] Initially, diolides were usually obtained as the major products for medium ring lactones,[317,547−549] and the Mitsunobu reaction has long been considered as a selective method to obtain diolides. A modification was introduced by Steglich in 1991 during the synthesis of combrestatin analogues.[550] Using the classical Mitsunobu protocol, the diolide was obtained as the major product (diolide 40%, macrolactone 2%), but with slow addition of the seco-acid to DEAD−triphenylphosphine, the macrolactone was the major product (macrolactone 59% yield, diolide trace yield) (Scheme 68). In the reaction mechanism, the key

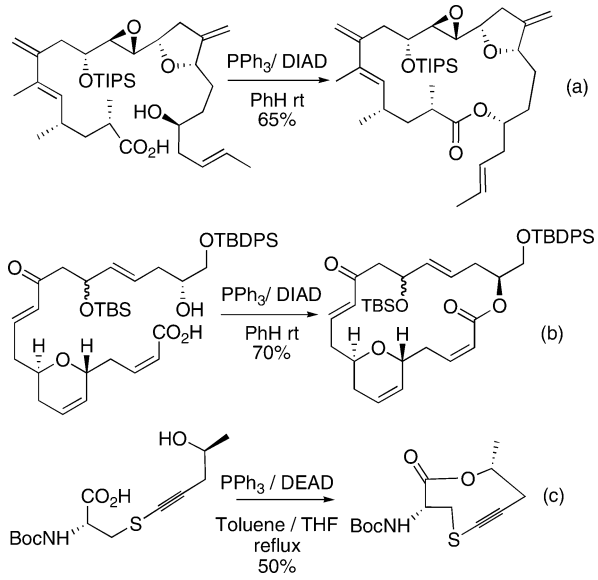
Scheme 68



intermediate is an alkoxyphosphonium salt produced *in situ*, and the macrolactonization proceeds via an intramolecular S_N2 reaction and with inversion of the alcohol configuration.

This reaction has been used in a number of 11- to 16-membered macrolactones,[186,225,551−554] in the total syntheses of natural products such as (+)-amphidinolide K[555] (eq a in Scheme 69), 19-epi-avermectin B_1,[556] (+)-brefeldin C,[557]

Scheme 69



citreofuran,[558] antibiotics derived from erythromycin,[559,560] (+)-gloeosporone,[561−563] hypothemycin,[564] cyclothialidine,[565] lasiodiplodin,[123] lobotamide C,[70,513,566] latrunculins A and B,[567−571] laulimalide,[572−574] where Yamaguchi and Keck methodologies result in *Z*/*E* isomerization of the conjugated double bond (eq b in Scheme 69), leucascandrolide A,[575−577] (+)-milbemycin β_3,[578,579] (+)-patulolide,[580] suspensolide,[581,582] diolides UK-2A and UK-3A,[583,584] verrucarin A,[585] zearalane,[586] and aplyronine A analogues,[361] in the total synthesis of griseoviridin,[587] and in several approaches to its thiolactone core,[588−592] where, in particular, a highly strained nine-membered lactone has been obtained by Pancrazi[588] (see eq c in Scheme 69). This methodology has also been successfully used in the syntheses of various cyclodepsipeptides as illustrated in Scheme 70.[457,565,593−597]

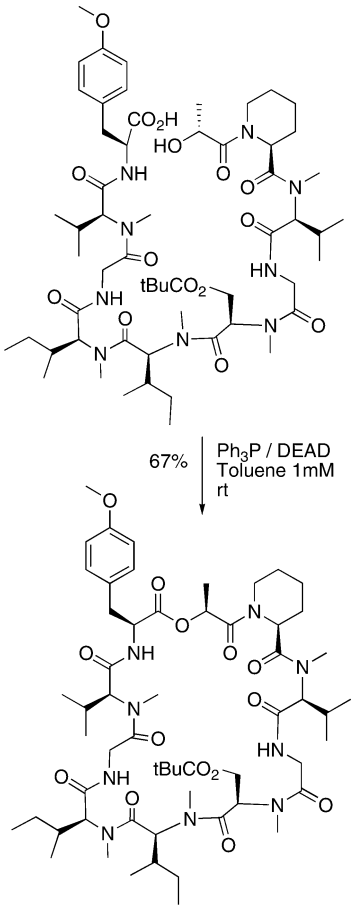
Classical conditions (i.e., PPh_3−DEAD in benzene, toluene, or THF at room temperature) may, however, suffer from some drawbacks such as the formation of hydrazide byproducts.[545] Evans encountered this problem in the total synthesis of lonomycin A (Scheme 71) and solved it by using the more hindered DIAD in the nonpolar solvent toluene.[598]

The same problem was recently faced by Roush in the total synthesis of spinosyn, but unfortunately in this case the amount of byproduct could not be minimized using DIAD. However, the lactonization was finally carried out using PyBOP (Scheme 37).[420]

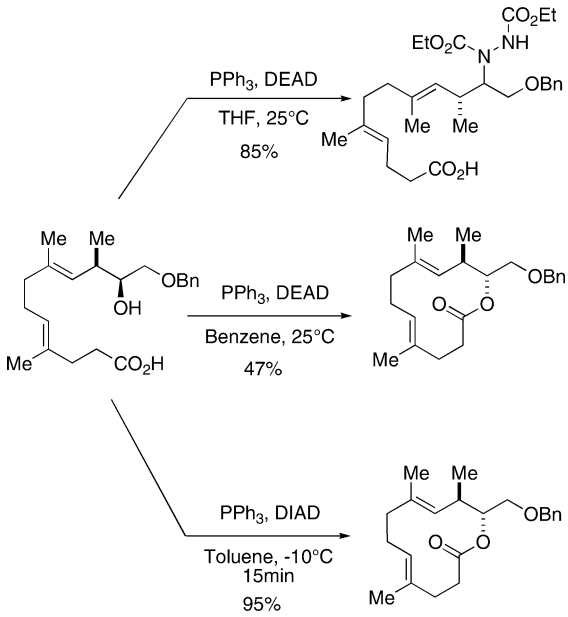
Another drawback in Mitsunobu reactions is the tedious removal of DEAD-H_2 or DIAD-H_2 and Ph_3PO byproducts by flash chromatography. In the synthesis of the nine-membered thio-lactone core of griseoviridin, PPh_2Py and di-*tert*-butyldiazodicarboxylate (DTBAD) were used: $Ph_2(Py)$-PO is water-soluble and can be eliminated by an acidic workup, and DTBAD-H_2 decomposes spontaneously into isoprene and CO_2 (Scheme 72).[599]

The use of polymer-supported reagents which provide pseudo-high dilution conditions and the easy removal of byproducts by filtration has also been described. A supported alkyl diazocarboxylate has been reported in a total synthesis of Zeralenone with a 42% yield for the lactonization key step as compared to an 8% yield for lactonization under

Scheme 70



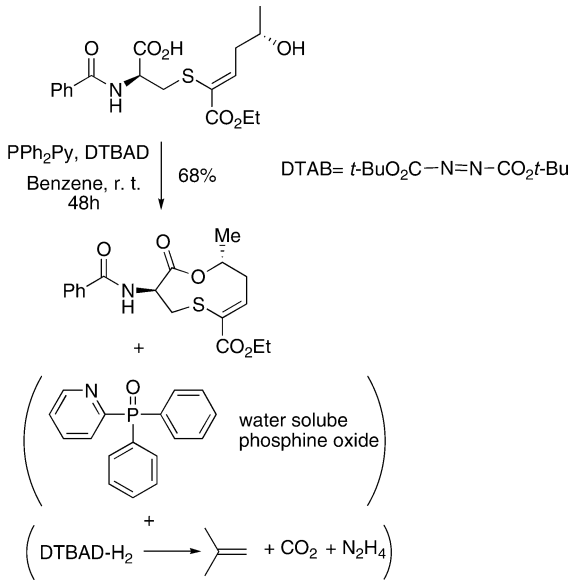
Scheme 71



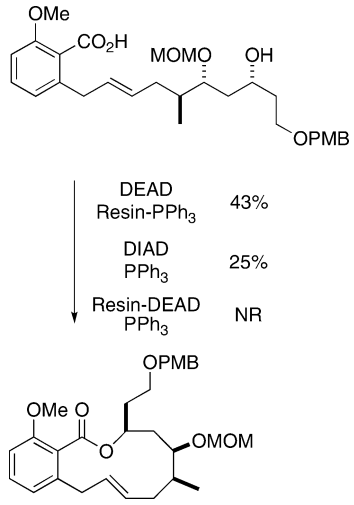
classical conditions.[600] Supported triphenylphosphine has been reported to effect the closure of a 13-membered lactone in a low yield (10%) but was recently more successful in the formal synthesis of salicylihalamides A and B (Scheme 73).[601]

Many other phosphine/diazo pairs and solutions to purification problems have been used in intermolecular reactions (for recent reviews, see refs 602 and 603).

Scheme 72



Scheme 73



The use of allylic alcohols in Mitsunobu macrolactonizations is tricky and deserves some comments. Problems with allylic alcohols were first observed in the syntheses of combretastatin D1 and D2 (Figure 13).

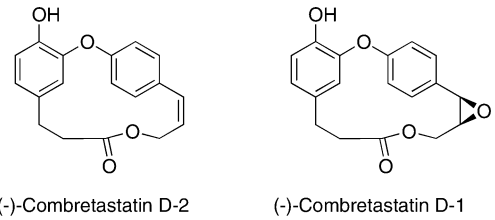
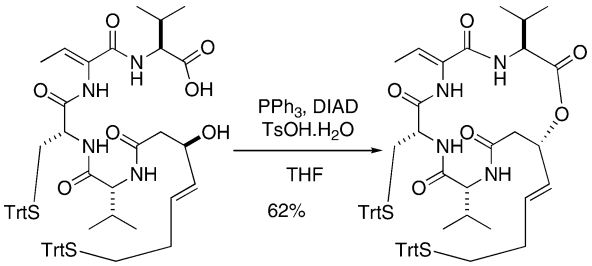


Figure 13.

These problems were initially thought to be related to the highly strained structure of the seco-acids,[604−606] but Rychnovsky[607] has suggested as an alternative explanation the possibility of S_N1 side reactions. Indeed, starting from the saturated seco-acid, the macrolactone is obtained in good yield. The same type of problem with allylic alcohols has been observed in the syntheses of cyclodepsipeptides FR-901228[608] (Scheme 74) and the related R-901375,[609] where addition of TsOH was crucial to prevent the elimination of

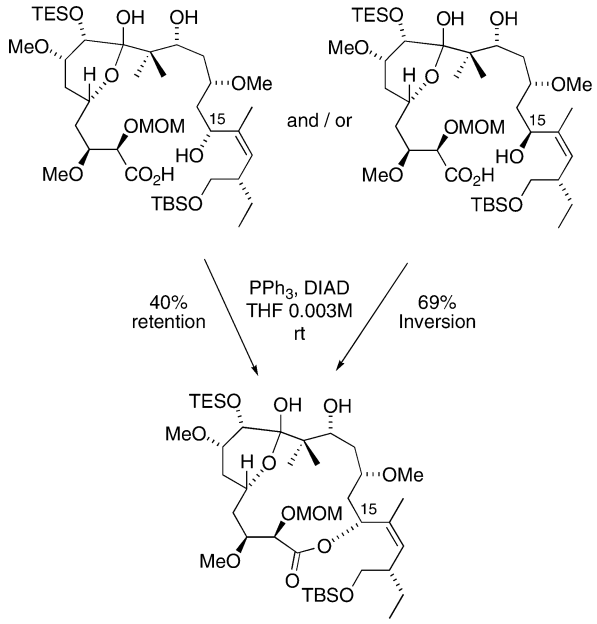
Scheme 74



the activated allylic alcohol (a 5% yield was obtained using the Boden−Keck methodology).

De Brabander obtained the same macrolactone from two epimers of a seco-acid during the total synthesis of peloruside A.[610] The authors explained the retention of configuration by the formation of an acyloxyphosphonium derivative,[611−613] because of conformational constraints preventing the formation of the C15 epimeric lactone (Scheme 75).

Scheme 75



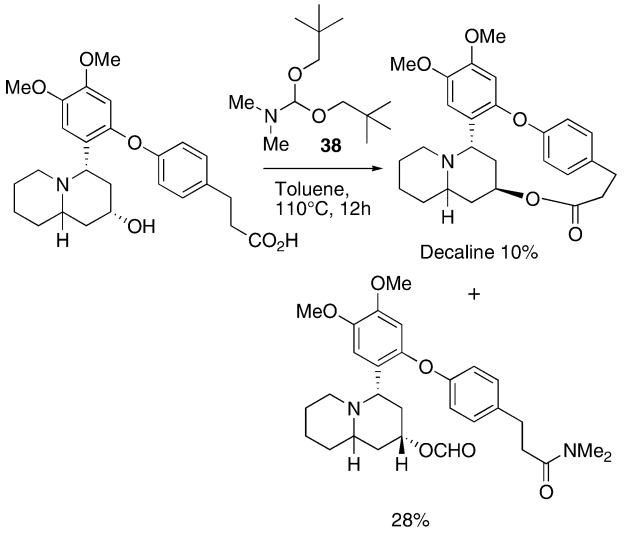
4.2. Eschenmoser Reagent

The use of the Eschenmoser esterification reagent, DMF dineopentylacetal (**38**),[614] has been described in the macrolactonizations of two ω-hydroxy acids to give the corresponding 13- and 17-membered lactones in moderate yields of 49% and 40%, respectively. To our knowledge, only one synthetic application in the total synthesis of a quinolizidine gave low yield (10%) in those cases in which the Kellogg and Mitsunobu reactions failed. (Scheme 76).[86,615]

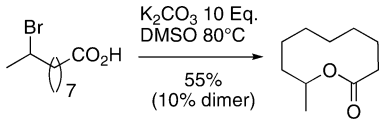
4.3. Macrolactonizations through Alkylhalides, Mesylates, and Sulfoniums

Macrolactonizations of bromocarboxylic acids $Br-(CH_2)_n-CO_2H$ in the presence of potassium carbonate were first described in 1947 by Hunsdiecker and Erlbach[616] and gave good yields for 9- to 17-membered macrolactones. This methodology using chloro- and iodocarboxylic acids as well as the bromo-acids has subsequently been widely studied,[617,618] including several kinetic studies.[28,619] Several bases have been tested, including potassium hydroxide in a water−isopropanol−toluene microemulsion[44] and under PTC conditions.[43] In the presence of cesium carbonate, a "cesium effect" was advocated to explain the selectivity in the macrolactonization/oligomerization process[44] but was then ruled out by Galli and Mandolini,[620] who demonstrated that there is no particular difference between cesium and other alkaline cations in this application. Quaternary ammonium salts derived from 2-pyrrolidone are also effective in obtaining 12- to 16-membered lactones in 66−84% yields.[621] The usual conditions for these reactions are cesium or potassium carbonates in DMF or DMSO. This methodology has been applied to various syntheses of fluorolactones,[622] ilalactones,[623] keto-lactones,[624,625] 13−15-membered olfactive lactones,[626] cyclodepsipeptides,[627] exaltolide and ambrettolide,[628,629] taxanes A−B cycles,[630] and the hemisynthesis[631] of myxovirescine. It is also worthy of note that this procedure (potassium carbonate in DMSO) was found in a comparative study with other alcohol and acid activation methods to be the most efficient methodology to obtain a 10-membered lactone model (Scheme 77).[632]

Scheme 76

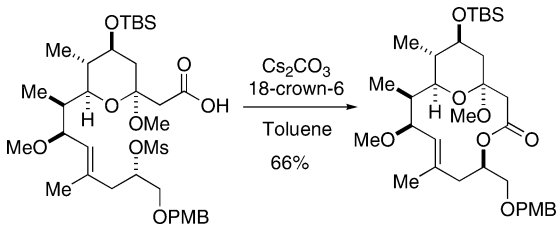


Scheme 77



Activation of alcohols as mesylates and macrolactonization in the presence of cesium carbonate was first developed by Kellogg and illustrated in the syntheses of ricinelaidic acid lactone and zearalenone with a clean S_N2 inversion.[617] This methodology has recently been applied successfully in a callipeltoside A total synthesis in which a Mitsunobu reaction failed (Scheme 78).[633]

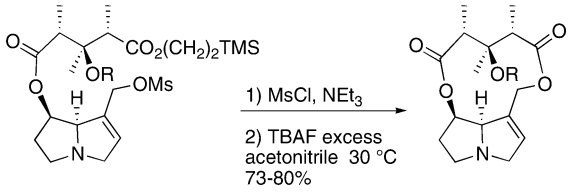
Scheme 78



A related approach has been illustrated by Vedejs in the syntheses of fulvine and crispatine where deprotection of

the ester in the presence of TBAF is followed in the same pot by the macrolactonization on a mesylate (Scheme 79).[634]

Scheme 79



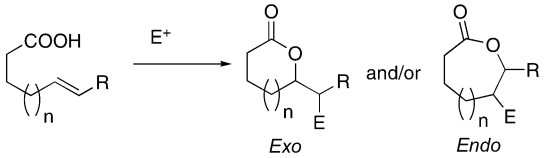
However, White has shown in the same approach to integerrimine and usaramine[635] that the activated intermediate is the allylic chloride and not the mesylate. In addition, sulfonium salts obtained from the corresponding halides or alcohols can be efficiently lactonized using potassium carbonate in refluxing acetone.[636]

4.4. Iodo- (Bromo- and Seleno-) Lactonizations

Although it is not strictly within the scope of this review (the macrolactonization of seco-acids), a discussion is given in the next two sections of iodo-, bromo-, and selenolactonizations as well as epoxide ring-opening.

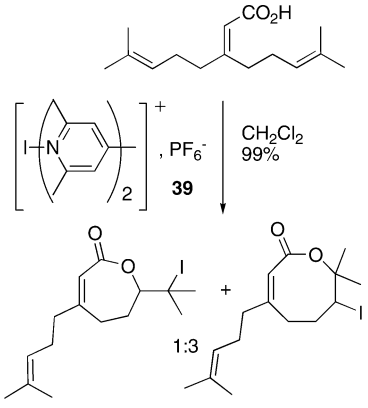
Iodolactonization reactions are well-known processes for obtaining small cycles,[637] but because of their slower reaction rates[638] they have rarely been used for medium and large macrolactones. Moreover, a lack of regioselectivity dependent on the chain size and substituents is also observed due to competitive *endo*/*exo* cyclization modes (Scheme 80).[639−641]

Scheme 80



Eight- to twenty-membered macrolactones have, however, been obtained in moderate to excellent yields using bis-collidine-iodine(I) hexafluorophosphate (**39)** (Scheme 81).[642−644]

Scheme 81

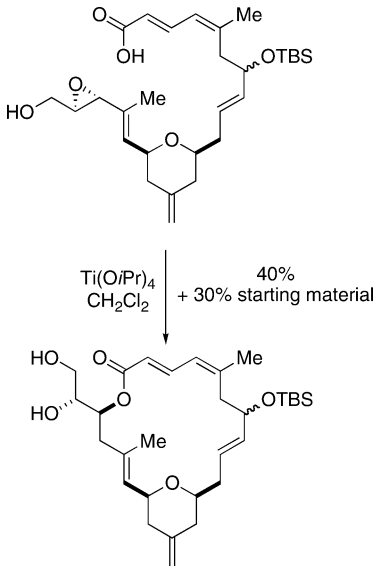


Bromolactonizations using the corresponding bromide reagent have also been described with lower regioselectivities.[643] Finally, other electrophiles such as *N*-phenylselenophthalimide have also been used in the syntheses of 14- to 16-membered macrolactones.[645,646]

4.5. Epoxide Ring-Opening

A clever example of an epoxide ring-opening macrolactonization has been reported by Hoye in the total synthesis of (−)-dactylolide.[647] When carried out according to the intermolecular Sharpless methodology,[648] the $Ti(OiPr)_4$-mediated regioselective epoxide ring-opening is observed to give the corresponding macrolactone in 40% yield (Scheme 82).

Scheme 82



5. Conclusion

The objective of this review has been to present an overview of the macrolactonization of seco-acids in the total synthesis of natural products. The need for macrolactonizations has inspired many clever solutions either by activation of the alcohol or activation of the acid moiety. Among future challenges will be further developments of enantio-, atrop- and diastereoselective macrolactonizations and the development of a truly atom-economic macrolactonization method under moderate dilution conditions.

6. Acknowledgments

We are grateful to the CNRS for financial support and the MENRT for a grant (X. M.). Dr. Y. Six and Prof. Y. Stenstrom are warmly acknowledged for helpful discussions.

7. References

(1) Kerschbaum, M. *Chem. Ber.* **1927**, *60*, 907.
(2) According to IUPAC (rule C-472.2), lactones formed from aliphatic acids are named by adding "-olide" to the name of the (nonhydroxylated) hydrocarbon with the same number of carbon atoms.
(3) Tapiolas, D. M.; Roman, M.; Fenical, W.; Stout, T. J.; Clardy, J. *J. Am. Chem. Soc.* **1991**, *113*, 4682.
(4) Hayakawa, Y.; Shinya, K.; Furihata, K.; Seto, H. *J. Am. Chem. Soc.* **1993**, *115*, 3014.
(5) Henninger, T. C. *Expert Opin. Ther. Pat.* **2003**, *13*, 787.
(6) Davies, J. S. *J. Peptide Sci.* **2003**, *9*, 471.
(7) Cyclodepsipeptides are usually cyclized using macrolactamization reactions, but several examples using a macrolactonization reaction have also been described.
(8) Rychnovsky, S. D. *Chem. Rev.* **1995**, *95*, 2021.
(9) Yeung, K. S.; Paterson, I. *Angew. Chem., Int. Ed. Engl.* **2002**, *41*, 4632.
(10) Norcross, R. D.; Paterson, I. *Chem. Rev.* **1995**, *95*, 2041.
(11) Nicolaou, K. C.; Ritzen, A.; Namoto, K. *Chem. Commun.* **2001**, 1523.
(12) Fürstner, A. *Eur. J. Org. Chem.* **2004**, 943.
(13) Yet, L. *Chem. Rev.* **2003**, *103*, 4283.
(14) Rousseau, G. *Tetrahedron* **1995**, *51*, 2777.
(15) Back, T. G. *Tetrahedron* **1977**, *33*, 3041.
(16) Haslam, E. *Tetrahedron* **1980**, *36*, 2409.

(17) Boeckman, R. K., Jr; Goldstein, S. W. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1988; Vol. 7.
(18) Masamune, S.; Bates, G. S.; Corcoran, J. W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 585.
(19) Nicolaou, K. C. *Tetrahedron* **1977**, *33*, 683.
(20) Meng, Q.; Hesse, M. *Top. Curr. Chem.* **1991**, *161*, 107.
(21) Kohli, R. M.; Walsh, C. T. *Chem. Commun.* **2003**, 297.
(22) Katz, L. *Chem. Rev.* **1997**, *97*, 2557.
(23) Khosla, C. *Chem. Rev.* **1997**, *97*, 2577.
(24) Staunton, J.; Weissman, K. J. *Nat. Prod. Rep.* **2001**, *18*, 380.
(25) Aparicio, J. F.; Mendes, M. V.; Anton, N.; Recio, E.; Martin, J. F. *Curr. Med. Chem.* **2004**, *11*, 1645.
(26) Williams, A. S. *Synthesis* **1999**, 1707.
(27) Illuminati, G.; Mandolini, L. *Acc. Chem. Res.* **1981**, *14*, 95.
(28) Galli, C.; Giovannelli, G.; Illuminati, G.; Mandolini, L. *J. Org. Chem.* **1979**, *44*, 1258.
(29) Stoll, M.; Rouvé, A. *Helv. Chim. Acta* **1935**, *18*, 1087.
(30) Corey, E. J.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1974**, *96*, 5614.
(31) Galli, C.; Mandolini, L. *J. Chem. Soc., Chem. Commun.* **1982**, 251.
(32) Rossa, L.; Vogtle, F. *Top. Curr. Chem.* **1983**, *113*, 1.
(33) Regen, S. L.; Kimura, A. *J. Am. Chem. Soc.* **1982**, *104*, 2064.
(34) Amos, R. A.; Emblidge, R. W.; Havens, N. *J. Org. Chem.* **1983**, *48*, 3598.
(35) Mohanraj, S.; Ford, W. T. *J. Org. Chem.* **1985**, *50*, 1616.
(36) Takahashi, T.; Kusaka, S.-i.; Doi, T.; Sunazuka, T.; Omura, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 5230.
(37) Burke, S. D.; McDermott, T. S.; O'Donnell, C. J. *J. Org. Chem.* **1998**, *63*, 2715.
(38) Brady, P. A.; Sanders, J. K. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3237.
(39) Rastetter, W. H.; Phillion, D. P. *J. Org. Chem.* **1981**, *46*, 3209.
(40) Otera, J.; Yano, T.; Himeno, Y.; Nozaki, H. *Tetrahedron Lett.* **1986**, *27*, 4501.
(41) Carrillo, R.; Martin, V. S.; Martin, T. *Tetrahedron Lett.* **2004**, *45*, 5215.
(42) Nakamura, A.; Nagai, S.; Ueda, T.; Murakami, N.; Sakakibara, J.; Shibuya, H.; Kitagawa, I. *Chem. Pharm. Bull.* **1991**, *39*, 1726.
(43) Kimura, Y.; Regen, S. L. *J. Org. Chem.* **1983**, *48*, 1533.
(44) Gonzalez, A.; Holt, S. L. *J. Org. Chem.* **1981**, *46*, 2594.
(45) Jaeger, D. A.; Ippoliti, J. T. *J. Org. Chem.* **1981**, *46*, 4964.
(46) Tatsumi, T.; Sakashita, H.; Asano, K. *Chem. Commun.* **1993**, 1264.
(47) Andrus, M. B.; Argade, A. B. *Tetrahedron Lett.* **1996**, *37*, 5049.
(48) Buszek, K. R.; Jeong, Y.; Sato, N.; Still, P. C.; Muino, P. L.; Ghosh, I. *Synth. Commun.* **2001**, *31*, 1781.
(49) Stork, G.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1987**, *109*, 1565.
(50) Paterson, I.; Laffan, D. D. P.; Rawson, D. J. *Tetrahedron Lett.* **1988**, *29*, 1461.
(51) Hergenrother, P. J.; Hodgson, A.; Judd, A. S.; Lee, W.-C.; Martin, S. F. *Angew. Chem., Int. Ed.* **2003**, *42*, 3278.
(52) Blankenstein, J.; Zhu, J. *Eur. J. Org. Chem.* **2005**, *10*, 1949.
(53) Guillerm, D.; Linstrumelle, G. *Tetrahedron Lett.* **1985**, *26*, 3811.
(54) Hamada, T.; Kobayashi, Y.; Kiyokawa, M.; Yonemitsu, O. *Tetrahedron Lett.* **2003**, *44*, 4343.
(55) Hamada, T.; Kobayashi, Y. *Tetrahedron Lett.* **2003**, *44*, 4347.
(56) Mulzer, J.; Kirstein, H. M.; Buschmann, J.; Lehmann, C.; Luger, P. *J. Am. Chem. Soc.* **1991**, *113*, 910.
(57) White, J. D.; Blakemore, P. R.; Browder, C. C.; Hong, J.; Lincoln, C. M.; Nagornyy, P. A.; Robarge, L. A.; Wardrop, D. J. *J. Am. Chem. Soc.* **2001**, *123*, 8593.
(58) Hanessian, S.; Ma, J.; Wang, W.; Gai, Y. *J. Am. Chem. Soc.* **2001**, *123*, 10200.
(59) Hu, T.; Takenaka, N.; Panek, J. S. *J. Am. Chem. Soc.* **2002**, *124*, 12806.
(60) Kageyama, M.; Tamura, T.; Nantz, M. H.; Roberts, J. C.; Somfai, P.; Whritenour, D. C.; Masamune, S. *J. Am. Chem. Soc.* **1990**, *112*, 7407.
(61) Schuppan, J.; Wehlan, H.; Keiper, S.; Koert, U. *Angew. Chem., Int. Ed.* **2001**, *40*, 2063.
(62) Wehlan, H.; Dauber, M.; Mujica Fernaud, M. T.; Schuppan, J.; Mahrwald, R.; Ziemer, B.; Juarez Garciz, M. E.; Koert, U. *Angew. Chem., Int. Ed.* **2004**, *43*, 4597.
(63) Schreiber, S. L.; Kelly, S. E.; Porco, J. A.; Sammakia, T.; Suh, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 6210.
(64) Kuehnert, S. M.; Maier, M. E. *Org. Lett.* **2002**, *4*, 643.
(65) Evans, D. A.; Trotter, B. W.; Coleman, P. J.; Cote, B.; Dias, L. C.; Rajapakse, H. A.; Tyler, A. N. *Tetrahedron* **1999**, *55*, 8671.
(66) Smith, A. B.; Adams, C. M.; Barbosa, S. A. L.; Degan, A. P. *J. Am. Chem. Soc.* **2003**, *125*, 350.
(67) Paterson, I.; Woodrow, M. D.; Cowden, C. J. *Tetrahedron Lett.* **1998**, *39*, 6041.
(68) Kigoshi, H.; Ojika, M.; Ishigaki, T.; Suenaga, K.; Mutou, T.; Sakakura, A.; Ogawa, T.; Yamada, K. *J. Am. Chem. Soc.* **1994**, *116*, 7443.
(69) Paterson, I.; Watson, C.; Yeung, K.-S.; Wallace, P. A.; Ward, R. A. *J. Org. Chem.* **1997**, *62*, 452.
(70) Shen, R.; Lin, C. T.; Bowman, E. J.; Bowman, B. J.; Porco, J. A., Jr. *J. Am. Chem. Soc.* **2003**, *125*, 7889.
(71) Duffey, M. O.; LeTiran, A.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 1458.
(72) Paterson, I.; Yeung, K.-S.; Ward, R. A.; Smith, J. D.; Cumming, J. G.; Lamboley, S. *Tetrahedron* **1995**, *51*, 9467.
(73) Mukaiyama, T. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 707.
(74) Wollenberg, R. H.; Nimitz, J. S.; Gokcek, D. Y. *Tetrahedron Lett.* **1980**, *21*, 2791.
(75) Corey, E. J.; Brunelle, D. J.; Stork, P. J. *Tetrahedron Lett.* **1976**, *17*, 3405.
(76) Kitahara, T.; Mori, K. *Tetrahedron* **1984**, *40*, 2935.
(77) Taber, D. F.; Silverberg, L. J.; Robinson, E. D. *J. Am. Chem. Soc.* **1991**, *113*, 6639.
(78) Corey, E. J.; Carpino, P. *Tetrahedron Lett.* **1990**, *31*, 7555.
(79) Tatsuta, K.; Amemiya, Y.; Kanemura, Y.; Kinoshita, M. *Tetrahedron Lett.* **1981**, *22*, 3997.
(80) Grieco, P. A.; Inanaga, J.; Lin, N. H.; Yanami, T. *J. Am. Chem. Soc.* **1982**, *104*, 5781.
(81) Lu, S.-F.; O'Yang, Q.; Guo, Z.-W.; Yu, B.; Hui, Y.-Z. *J. Org. Chem.* **1997**, *62*, 8400.
(82) Bundy, G. L.; Peterson, D. C.; Cornette, J. C.; Miller, W. L.; Spilman, C. H.; Wilks, J. W. *J. Med. Chem.* **1983**, *26*, 1089.
(83) Corey, E. J.; Nicolaou, K. C.; Melvin, L. S. *J. Am. Chem. Soc.* **1975**, *97*, 653.
(84) Woodward, R. B.; Au−Yeung, B. W.; Balaram, P.; Browne, L. J.; Ward, D. E.; Card, P. J.; Chen, C. H. *J. Am. Chem. Soc.* **1981**, *103*, 3213.
(85) Nakata, M.; Arai, M.; Tomooka, K.; Ohsawa, N.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2618.
(86) Shishido, K.; Tanaka, K.; Fukumoto, K.; Kametani, T. *Tetrahedron Lett.* **1983**, *24*, 2783.
(87) Maruyama, K.; Sohmiya, H.; Tsukube, H. *Tetrahedron* **1992**, *48*, 805.
(88) Barbour, R. H.; Robins, D. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1923.
(89) Janssen, H. M.; Peeters, E.; van Zundert, M. F.; van Genderen, M. H. P.; Meijer, E. W. *Angew. Chem., Int. Ed.* **1997**, *36*, 122.
(90) Sasaki, T.; Inoue, M.; Hirama, M. *Tetrahedron Lett.* **2001**, *42*, 5299.
(91) Hansen, T. V.; Stenstrom, Y. *Tetrahedron: Asymmetry* **2001**, *12*, 1407.
(92) Corey, E. J.; Clark, D. A. *Tetrahedron Lett.* **1979**, 2875.
(93) Hillis, L. R.; Ronald, R. C. *J. Org. Chem.* **1985**, *50*, 470.
(94) Bhagwat, S. S.; Hamann, P. R.; Still, W. C. *J. Am. Chem. Soc.* **1985**, *107*, 6372.
(95) Le Drian, C.; Greene, A. E. *J. Am. Chem. Soc.* **1982**, *104*, 5473.
(96) Woodward, R. B.; Au−Yeung, B. W.; Balaram, P.; Browne, L. J.; Ward, D. E.; Card, P. J.; Chen, C. H. *J. Am. Chem. Soc.* **1981**, *103*, 3213.
(97) Kinoshita, M.; Arai, M.; Ohsawa, M.; Nakata, M. *Tetrahedron Lett.* **1986**, *27*, 1815.
(98) Corey, E. J.; Brunelle, D. J. *Tetrahedron Lett.* **1976**, 3409.
(99) Sviridov, A. F.; Ermolenko, M. S.; Yashunskii, D. V.; Borodkin, V. S.; Kochetkov, N. K. *Tetrahedron Lett.* **1987**, *28*, 3835.
(100) Corey, E. J.; Hopkins, P. B.; Kim, S.; Yoo, S.-E.; Nambiar, K. P.; Falck, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 7131.
(101) Kochetkov, N. K.; Sviridov, A. F.; Ermolenko, M. S.; Yashunsky, D. V.; Borodkin, V. S. *Tetrahedron* **1989**, *45*, 5109.
(102) Corey, E. J.; De, B. *J. Am. Chem. Soc.* **1984**, *106*, 2735.
(103) Rastetter, W. H.; Erickson, T. J.; Venuti, M. C. *J. Org. Chem.* **1981**, *46*, 3579.
(104) Rastetter, W. H.; Erickson, T. J.; Venuti, M. C. *J. Org. Chem.* **1980**, *45*, 5011.
(105) Tanaka, A.; Watanabe, A.; Kobayashi, R.; Tsuchiya, T.; Umezawa, S. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3837.
(106) Schmidt, U.; Heermann, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 308.
(107) Nimitz, J. S.; Wollenberg, R. H. *Tetrahedron Lett.* **1978**, *19*, 3523.
(108) Gerlach, H.; Thalmann, A. *Helv. Chim. Acta* **1974**, *57*, 2661.
(109) Masamune, S.; Hayase, Y.; Schilling, W.; Chan, W. K.; Bates, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 6756.
(110) Kim, S.; Lee, J. I. *J. Org. Chem.* **1984**, *49*, 1712.
(111) Palomo, C.; Oiarbide, M.; Garcia, J. M.; Gonzalez, A.; Pazos, R.; Odriozola, J. M.; Banuelos, P.; Tello, M.; Linden, A. *J. Org. Chem.* **2004**, *69*, 4126.
(112) Andrus, M. B.; Shih, T.-L. *J. Org. Chem.* **1996**, *61*, 8780.

(113) Baldazzi, C.; Calderoni, F.; Marotta, E.; Piani, S.; Righi, P.; Rosini, G.; Saguatti, S.; Tiozzo, R.; Calandra, S.; Venturelli, F. *Bioorg. Med. Chem.* **1999**, *7*, 411.
(114) Buszek, K. R.; Sato, N.; Jeong, Y. *J. Am. Chem. Soc.* **1994**, *116*, 5511.
(115) Bach, J.; Garcia, J. *Tetrahedron Lett.* **1998**, *39*, 6761.
(116) Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Kim, B. H.; Ogilvie, W. W.; Yiannikouros, G.; Prasad, C. V. C.; Veale, C. A.; Hark, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 6263.
(117) Brunner, R. K.; Broschberg, H.-J. *Helv. Chim. Acta* **1983**, *66*, 2608.
(118) Ohta, T.; Sunagawa, M.; Nishimaki, K.; Nozoe, S. *Heterocycles* **1983**, *20*, 1567.
(119) Naoshima, Y.; Hasegawa, H. *Chem. Lett.* **1987**, 2379.
(120) Naoshima, Y.; Hasegawa, H.; Nishiyama, T.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 608.
(121) Jones, G. B.; Chapman, B. J.; Huber, R. S.; Beaty, R. *Tetrahedron: Asymmetry* **1994**, *5*, 1199.
(122) Jones, G. B.; Huber, R. S.; Chapman, B. J. *Tetrahedron: Asymmetry* **1997**, *8*, 1797.
(123) Bracher, F.; Schulte, B. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2619.
(124) Gerlach, H.; Thalmann, A. *Helv. Chim. Acta* **1977**, *60*, 2866.
(125) Solladie, G.; Rubio, A.; Carreno, M. C.; Garcia Ruano, J. L. *Tetrahedron: Asymmetry* **1990**, *1*, 187.
(126) Braun, M.; Mahler, U.; Houben, S. *Liebigs Ann. Chem.* **1990**, 513.
(127) Gerlach, H.; Oertle, K.; Thalmann, A.; Servi, S. *Helv. Chim. Acta* **1975**, *58*, 2036.
(128) Tsunoda, T.; Nishii, T.; Yoshizuka, M.; Yamasaki, C.; Suzuki, T.; Ito, S. *Tetrahedron Lett.* **2000**, *41*, 7667.
(129) Kusaka, S.-i.; Dohi, S.; Doi, T.; Takahashi, T. *Tetrahedron Lett.* **2003**, *44*, 8857.
(130) Mori, K.; Tomioka, H. *Liebigs Ann. Chem.* **1992**, 1011.
(131) Keinan, E.; Sinha, S. C.; Singh, S. P. *Tetrahedron* **1991**, *47*, 4631.
(132) Oehlschlager, A. C.; Wong, J. W.; Verigin, V. G.; Pierce, H. D. *J. Org. Chem.* **1983**, *48*, 5009.
(133) Kang, S. H.; Jeong, J. W.; Hwang, Y. S.; Lee, S. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 1392.
(134) Lengweiler, U. D.; Fritz, M. G.; Seebach, D. *Helv. Chim. Acta* **1996**, *79*, 670.
(135) Hikota, M.; Tone, H.; Horita, K.; Yonemitsu, O. *J. Org. Chem.* **1990**, *55*, 7.
(136) Tone, H.; Nishi, T.; Oikawa, Y.; Hikota, M.; Yonemitsu, O. *Tetrahedron Lett.* **1987**, *28*, 4569.
(137) Hikota, M.; Tone, H.; Horita, K.; Yonemitsu, O. *Tetrahedron* **1990**, *46*, 4613.
(138) Masamune, S.; Yamamoto, H.; Kamata, S.; Fukuzawa, A. *J. Am. Chem. Soc.* **1975**, *97*, 3513.
(139) Masamune, S.; Kamata, S.; Schilling, W. *J. Am. Chem. Soc.* **1975**, *97*, 3515.
(140) Fox, C. M. J.; Ley, S. V.; Slawin, A. M. Z.; Williams, D. J. *Chem. Commun.* **1985**, 1805.
(141) Booth, P. M.; Broughton, H. B.; Ford, M. J.; Fox, C. M. J.; Ley, S. V.; et al. *Tetrahedron* **1989**, *45*, 7565.
(142) Masamune, S.; Hirama, M.; Mori, S.; Ali, S. A.; Garvey, D. S. *J. Am. Chem. Soc.* **1981**, *103*, 1568.
(143) Ley, S. V.; Woodward, P. R. *Tetrahedron Lett.* **1987**, *28*, 345.
(144) Park, P. U.; Broka, C. A.; Johnson, B. F.; Kishi, Y. *J. Am. Chem. Soc.* **1987**, *109*, 6205.
(145) Toshima, H.; Suzuki, T.; Nishiyama, S.; Yamamura, S. *Tetrahedron Lett.* **1989**, *30*, 6725.
(146) Tatsuta, K.; Amemiya, Y.; Maniwa, S.; Kinoshita, M. *Tetrahedron Lett.* **1980**, *21*, 2837.
(147) Tatsuta, K.; Nakagawa, A.; Maniwa, S.; Kinoshita, M. *Tetrahedron Lett.* **1980**, *21*, 1479.
(148) Ireland, R. E.; Varney, M. D. *J. Org. Chem.* **1986**, *51*, 635.
(149) Huang, J.; Meinwald, J. *J. Am. Chem. Soc.* **1981**, *103*, 861.
(150) Masamune, S.; Lu, L. D. L.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *J. Am. Chem. Soc.* **1982**, *104*, 5523.
(151) Trost, B. M.; McDougal, P. G. *J. Org. Chem.* **1984**, *49*, 458.
(152) Kumamoto, T.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2111.
(153) Schmidt, U.; Werner, J. *J. Chem. Soc., Chem. Commun.* **1986**, 996.
(154) Schmidt, U.; Werner, J. *Synthesis* **1986**, 986.
(155) Schmidt, U.; Dietsche, M. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 771.
(156) White, J. D.; Lodwig, S. N.; Trammell, G. L.; Fleming, M. P. *Tetrahedron Lett.* **1974**, *15*, 3263.
(157) Hikota, M.; Sakurai, Y.; Horita, K.; Yonemitsu, O. *Tetrahedron Lett.* **1990**, *31*, 6367.
(158) White, J. D.; Johnson, A. T. *J. Org. Chem.* **1990**, *55*, 5938.
(159) Wróbel, J. T.; Gobiewsk, W. M. *Tetrahedron Lett.* **1973**, *14*, 4293.
(160) Arrieta, A.; Aizpurua, J. M.; Palomo, C. *Tetrahedron Lett.* **1984**, *25*, 3365.
(161) Takeda, K.; Tsuboyama, K.; Takayanagi, H.; Ogura, H. *Synthesis* **1987**, 560.
(162) Chou, W.-C.; Fang, J.-M. *J. Org. Chem.* **1996**, *61*, 1473.
(163) Venkataraman, K.; Wagle, D. R. *Tetrahedron Lett.* **1980**, *21*, 1893.
(164) Venkataraman, K.; Wagle, D. R. *Tetrahedron Lett.* **1979**, *20*, 3037.
(165) Cossy, J.; Pete, J. P. *Tetrahedron Lett.* **1986**, *27*, 2369.
(166) Cossy, J.; Pete, J.-P. *Bull. Soc. Chim. Fr.* **1988**, 989.
(167) Ayyangar, N. R.; Chanda, B.; Wakharkar, R. D.; Kasar, R. A. *Synth. Commun.* **1988**, *18*, 2103.
(168) Mukaiyama, T.; Usui, M.; Saigo, K. *Chem. Lett.* **1976**, 49.
(169) Narasaka, K.; Maruyama, K.; Mukaiyama, T. *Chem. Lett.* **1978**, 885.
(170) Funk, R. L.; Abelman, M. M.; Jellison, K. M. *Synlett* **1989**, 36.
(171) Cooper, J.; Knight, D. W.; Gallagher, P. T. *J. Chem. Soc., Perkin Trans. 1* **1992**, 553.
(172) Petasis, N. A.; Bzowej, E. I. *Tetrahedron Lett.* **1993**, *34*, 1721.
(173) Abelman, M. M.; Funk, R. L.; Munger, J. D. *J. Am. Chem. Soc.* **1982**, *104*, 4030.
(174) Funk, R. L.; Abelman, M., M.; Munger, J. D. *Tetrahedron* **1986**, *42*, 2831.
(175) Funk, R. L.; Munger, J. D., Jr. *J. Org. Chem.* **1984**, *49*, 4319.
(176) Funk, R. L.; Abelman, M. M. *J. Org. Chem.* **1986**, *51*, 3247.
(177) Funk, L.; Olmstead, T. A.; Parvez, M. *J. Am. Chem. Soc.* **1988**, *110*, 3298.
(178) Hull, H. M.; Jones, e. G.; Knight, D. W. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1779.
(179) Garcia-Rubio, S.; Meinwald, J. *J. Org. Chem.* **2001**, *66*, 1082.
(180) Farmer, J. J.; Schroeder, F. C.; Meinwald, J. *Helv. Chim. Acta* **2000**, *83*, 2594.
(181) White, J. D.; Avery, M. A.; Choudhry, S. C.; Dhingra, O. P.; Gray, B. D.; Kang, M. C.; Kuo, S. C.; Whittle, A. J. *J. Am. Chem. Soc.* **1989**, *111*, 790.
(182) White, J. D.; Vedananda, T. R.; Kang, M. C.; Choudhry, S. C. *J. Am. Chem. Soc.* **1986**, *108*, 8105.
(183) Schreiber, S. L.; Kelly, S. E.; Porco, J. A., Jr.; Sammakia, T.; Suh, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 6210.
(184) Matsushita, M.; Yoshida, M.; Zhang, Y.; Miyashita, M.; Irie, H.; Ueno, T.; Tsurushima, T. *Chem. Pharm. Bull.* **1992**, *40*, 524.
(185) Naoshima, Y.; Nakamura, A.; Munakata, Y. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1263.
(186) Boden, C. D. J.; Chambers, J.; Stevens, I. D. R. *Synthesis* **1993**, 411.
(187) Millar, J. G.; Oehlschlager, A. C. *J. Org. Chem.* **1984**, *49*, 2332.
(188) McNaughton-Smith, G. A.; Taylor, R. J. K. *Tetrahedron* **1996**, *52*, 2113.
(189) Smith, A. B.; Malamas, M. S. *J. Org. Chem.* **1982**, *47*, 3442.
(190) Villemin, D. *Tetrahedron Lett.* **1980**, *21*, 1715.
(191) Yuan, H.; Kingston, D. G. I.; Sackett, D. L.; Hamel, E. *Tetrahedron* **1999**, *55*, 9707.
(192) Damour, D.; Doerflinger, G.; Pantel, G.; Labaudiniere, R.; Leconte, J.-P.; Sable, S.; Vuilhorgne, M.; Mignani, S. *Synlett* **1999**, 189.
(193) Leeper, F. J.; Smith, D. H. C. *J. Chem. Soc., Perkin Trans. 1* **1995**, 861.
(194) Dinh, T. Q.; Du, X.; Armstrong, R. W. *J. Org. Chem.* **1996**, *61*, 6606.
(195) Dinh, T. Q.; Armstrong, R. W. *J. Org. Chem.* **1995**, *60*, 8118.
(196) Convers, E.; Tye, H.; Whittaker, M. *Tetrahedron Lett.* **2004**, *45*, 3401.
(197) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989.
(198) Makino, K.; Nakajima, N.; Hashimoto, S.-i.; Yonemitsu, O. *Tetrahedron Lett.* **1996**, *37*, 9077.
(199) Evans, D. A.; Connell, B. T. *J. Am. Chem. Soc.* **2003**, *125*, 10899.
(200) Waanders, P. P.; Thijs, L.; Zwanenburg, B. *Tetrahedron Lett.* **1987**, *28*, 2409.
(201) Solladie, G.; Fernandez, I.; Maestro, C. *Tetrahedron: Asymmetry* **1991**, *2*, 801.
(202) Thijs, L.; Egenberger, D. M.; Zwanenburg, B. *Tetrahedron Lett.* **1989**, *30*, 2153.
(203) Plattner, D. A.; Brunner, A.; Dobler, M.; Mueller, H.-M.; Petter, W.; et al. *Helv. Chim. Acta* **1993**, *76*, 2004.
(204) Dommerholt, F. J.; Thijs, L.; Zwanenburg, B. *Tetrahedron Lett.* **1991**, *32*, 1495.
(205) Dommerholt, F. J.; Thijs, L.; B., Z. *Tetrahedron Lett.* **1991**, *32*, 1499.
(206) Seebach, D.; Hoffmann, T.; Kuehnle, F. N. M.; Lengweiler, U. D. *Helv. Chim. Acta* **1994**, *77*, 2007.
(207) Jackson, R. F. W.; Sutter, M. A.; Seebach, D. *Liebigs Ann. Chem.* **1985**, 2313.
(208) Nelson, S. G.; Cheung, W. S.; Kassick, A. J.; Hilfiker, M. A. *J. Am. Chem. Soc.* **2002**, *124*, 13654.
(209) Schregenberger, C.; Seebach, D. *Liebigs Ann. Chem.* **1986**, 2081.
(210) Spivey, A. C.; Arseniyadis, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 5436.
(211) Storer, R. I.; Takemoto, T.; Jackson, P. S.; Brown, D. S.; Baxendale, I. R.; Ley, S. V. *Chem.—Eur. J.* **2004**, *10*, 2529.
(212) Evans, D. A.; Kim, A. S. *J. Am. Chem. Soc.* **1996**, *118*, 11323.
(213) Evans, D. A.; Carter, P. H.; Carreira, E. M.; Charette, A. B.; Prunet, J. A.; Lautens, M. *J. Am. Chem. Soc.* **1999**, *121*, 7540.

(214) Evans, D. A.; Ng, H. P.; Rieger, D. L. *J. Am. Chem. Soc.* **1993**, *115*, 11446.
(215) Paterson, I.; Davies, R. D. M.; Marquez, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 603.
(216) Evans, D. A.; Fitch, D. M. *J. Org. Chem.* **1997**, *62*, 454.
(217) Toshima, K.; Tatsuta, K.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2369.
(218) Schnurrenberger, P.; Hungerbuehler, E.; Seebach, D. *Liebigs Ann. Chem.* **1987**, 733.
(219) Gogoi, S.; Barua, N. C.; Kalita, B. *Tetrahedron Lett.* **2004**, *45*, 5577.
(220) Evans, D. A.; Black, W. C. *J. Am. Chem. Soc.* **1993**, *115*, 4497.
(221) Fettes, A.; Carreira, E. M. *J. Org. Chem.* **2003**, *68*, 9274.
(222) Jeong, E. J.; Kang, E. J.; Sung, L. T.; Hong, S. K.; Lee, E. *J. Am. Chem. Soc.* **2002**, *124*, 14655.
(223) Mori, K.; Sakai, T. *Liebigs Ann. Chem.* **1988**, 13.
(224) Leemhuis, F. M. C.; Thijs, L.; Zwanenburg, B. *J. Org. Chem.* **1993**, *58*, 7170.
(225) Kaisalo, L.; Koskimies, J.; Hase, T. *Synthesis* **1996**, 1122.
(226) Evans, D. A.; Fitch, D. M.; Smith, T. E.; Cee, V. J. *J. Am. Chem. Soc.* **2000**, *122*, 10033.
(227) Enev, V. S.; Kaehlig, H.; Mulzer, J. *J. Am. Chem. Soc.* **2001**, *123*, 10764.
(228) Takao, K.-i.; Saegusa, H.; Watanabe, G.; Tadano, K.-i. *Tetrahedron: Asymmetry* **2000**, *11*, 453.
(229) Sasaki, M.; Ishikawa, M.; Fuwa, H.; Tachibana, K. *Tetrahedron* **2002**, *58*, 1889.
(230) Critcher, D. J.; Connolly, S.; Mahon, M. F.; Wills, M. *Chem. Commun.* **1995**, 139.
(231) Critcher, D. J.; Connolly, S.; Wills, M. *J. Org. Chem.* **1997**, *62*, 6638.
(232) Burton, J. W.; Clark, J. S.; Derrer, S.; Stork, T. C.; Bendall, J. G.; Holmes, A. B. *J. Am. Chem. Soc.* **1997**, *119*, 7483.
(233) Niwa, H.; Watanabe, M.; Inagaki, H.; Yamada, K. *Tetrahedron* **1994**, *50*, 7385.
(234) Arai, M.; Morita, N.; Aoyagi, S.; Kibayashi, C. *Tetrahedron Lett.* **2000**, *41*, 1199.
(235) Motoyoshi, H.; Ishigami, K.; Kitahara, T. *Tetrahedron* **2001**, *57*, 3899.
(236) Ishigami, K.; Motoyoshi, H.; Kitahara, T. *Tetrahedron Lett.* **2000**, *41*, 8897.
(237) Sabino, A. A.; Pilli, R. A. *Tetrahedron Lett.* **2002**, *43*, 2819.
(238) Congreve, M. S.; Holmes, A. B.; Hughes, A. B.; Looney, M. G. *J. Am. Chem. Soc.* **1993**, *115*, 5815.
(239) Nicolaou, K. C.; Sarabia, F.; Finlay, M. R. V.; Ninkovic, S.; King, N. P.; et al. *Chem.—Eur. J.* **1997**, *3*, 1971.
(240) Nicolaou, K. C.; Ninkovic, S.; Sarabia, F.; Vourloumis, D.; He, Y.; Vallberg, H.; Finlay, M. R. V.; Yang, Z. *J. Am. Chem. Soc.* **1997**, *119*, 7974.
(241) Nicolaou, K. C.; Sarabia, F.; Ninkovic, S.; Yang, Z. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 525.
(242) Nicolaou, K. C.; Finlay, M. R. V.; Ninkovic, S.; Sarabia, F. *Tetrahedron* **1998**, *54*, 7127.
(243) Martin, N.; Thomas, E. J. *Tetrahedron Lett.* **2001**, *42*, 8373.
(244) Taylor, R. E.; Chen, Y. *Org. Lett.* **2001**, *3*, 2221.
(245) Sawada, D.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 10521.
(246) Martin, H. J.; Pojarliev, P.; Kaehlig, H.; Mulzer, J. *Chem.—Eur. J.* **2001**, *7*, 2261.
(247) Martin, H. J.; Drescher, M.; Mulzer, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 581.
(248) Harris, C. R.; Kuduk, S. D.; Balog, A.; Savin, K.; Glunz, P. W.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1999**, *121*, 7050.
(249) Glunz, P. W.; He, L.; Horwitz, S. B.; Chakravarty, S.; Ojima, I.; Chuo, T.-C.; Danishefsky, S. J. *Tetrahedron Lett.* **1999**, *40*, 6895.
(250) Nicolaou, K. C.; King, N. P.; Finlay, M. R.; He, Y.; Roschangar, F.; Vourloumis, D.; Vallberg, H.; Sarabia, F.; Ninkovic, S.; Hepworth, D. *Bioorg. Med. Chem.* **1999**, *7*, 665.
(251) Balog, A.; Harris, C.; Savin, K.; Zhang, X.-G.; Chou, T. C.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 2675.
(252) White, J. D.; Carter, R. G.; Sundermann, K. F. *J. Org. Chem.* **1999**, *64*, 684.
(253) White, J. D.; Carter, R. G.; Sundermann, K. F.; Wartmann, M. *J. Am. Chem. Soc.* **2001**, *123*, 5407.
(254) Ermolenko, M. S.; Potier, P. *Tetrahedron Lett.* **2002**, *43*, 2895.
(255) Nicolaou, K. C.; Namoto, K.; Ritzen, A.; Ulven, T.; Shoji, M.; Li, J.; D′Amico, G.; Liotta, D.; French, C. T.; Wartmann, M.; Altmann, K.-H.; Giannakakou, P. *J. Am. Chem. Soc.* **2001**, *123*, 9313.
(256) Lee, C. B.; Wu, Z.; Zhang, F.; Chappell, M. D.; Stachel, S. J.; Chou, T.-C.; Guan, Y.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2001**, *123*, 5249.
(257) Chappell, M. D.; Harris, C. R.; Kuduk, S. D.; Balog, A.; Wu, Z.; Zhang, F.; Lee, C. B.; Stachel, S. J.; Danishefsky, S. J.; Chou, T.-C.; Guan, Y. *J. Org. Chem.* **2002**, *67*, 7730.
(258) Altmann, K.-H.; Bold, G.; Caravatti, G.; Denni, D.; Floersheimer, A.; Schmidt, A.; Rihs, G.; Wartmann, M. *Helv. Chim. Acta* **2002**, *85*, 4086.
(259) Nicolaou, K. C.; Ritzen, A.; Namoto, K.; Buey, R. M.; Diaz, J. F.; Andreu, J. M.; Wartmann, M.; Altmann, K.-H.; O'Brate, A.; Giannakakou, P. *Tetrahedron* **2002**, *58*, 6413.
(260) Hindupur, R. M.; Panicker, B.; Valluri, M.; Avery, M. A. *Tetrahedron Lett.* **2001**, *42*, 7341.
(261) Bode, J. W.; Carreira, E. M. *J. Am. Chem. Soc.* **2001**, *123*, 3611.
(262) Bode, J. W.; Carreira, E. M. *J. Org. Chem.* **2001**, *66*, 6410.
(263) Zhu, B.; Panek, J. S. *Eur. J. Org. Chem.* **2001**, 1701.
(264) Zhu, B.; Panek, J. S. *Org. Lett.* **2000**, *2*, 2575.
(265) Lee, C. B.; Chou, T.-C.; Zhang, X.-G.; Wang, Z.-G.; Kuduk, S. D.; Chappell, M. D.; Stachel, S. J.; Danishefsky, S. J. *J. Org. Chem.* **2000**, *65*, 6525.
(266) Schinzer, D.; Bourguet, E.; Ducki, S. *Chem.—Eur. J.* **2004**, *10*, 3217.
(267) Ganesh, T.; Schilling, J. K.; Palakodety, R. K.; Ravindra, R.; Shanker, N.; Bane, S.; Kingston, D. G. I. *Tetrahedron* **2003**, *59*, 9979.
(268) Mulzer, J.; Karig, G.; Pojarliev, P. *Tetrahedron Lett.* **2000**, *41*, 7635.
(269) Marino, J. P.; McClure, M. S.; Holub, D. P.; Cornasseto, J. V.; Tucci, F. C. *J. Am. Chem. Soc.* **2002**, *124*, 1664.
(270) Evans, D. A.; Kim, A. S.; Metternich, R.; Novack, V. J. *J. Am. Chem. Soc.* **1998**, *120*, 5921.
(271) Myles, D. C.; Danishefsky, S. J.; Schulte, G. *J. Org. Chem.* **1990**, *55*, 1636.
(272) Peng, Z.-H.; Woerpel, K. A. *J. Am. Chem. Soc.* **2003**, *125*, 6018.
(273) Gerber-Lemaire, S.; Ainge, S. W.; Glanzmann, C.; Vogel, P. *Helv. Chim. Acta* **2002**, *85*, 417.
(274) Mulzer, J.; Mareski, P. A.; Buschmann, J.; Luger, P. *Synthesis* **1992**, 215.
(275) Paterson, I.; Norcross, R. D.; Ward, R. A.; Romea, P.; Lister, M. A. *J. Am. Chem. Soc.* **1994**, *116*, 11287.
(276) Hoffmann, R. W.; Ditrich, K. *Liebigs Ann. Chem.* **1990**, 23.
(277) Nokami, J.; Ohkura, M.; Dan-Oh, Y.; Sakamoto, Y. *Tetrahedron Lett.* **1991**, *32*, 2409.
(278) Casy, G.; Gorins, G.; McCague, R.; Olivo, H. F.; Roberts, S. M. *Chem. Commun.* **1994**, 1085.
(279) Solladie, G.; Lohse, O. *J. Org. Chem.* **1993**, *58*, 4555.
(280) Trost, B. M.; Crawley, M. L. *J. Am. Chem. Soc.* **2002**, *124*, 9328.
(281) Haynes, R. K.; Lam, W. W.-L.; Yeung, L.-L.; Williams, I. D.; Ridley, A. C.; et al. *J. Org. Chem.* **1997**, *62*, 4552.
(282) Suh, Y.-G.; Jung, J.-K.; Seo, S.-Y.; Min, K.-H.; Shin, D.-Y.; Lee, Y.-S.; Kim, S.-H.; Park, H.-J. *J. Org. Chem.* **2002**, *67*, 4127.
(283) Poss, C. S.; Rychnovsky, S. D.; Schreiber, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 3360.
(284) Mori, Y.; Asai, M.; Kawade, J.-i.; Okumura, A.; Furukawa, H. *Tetrahedron Lett.* **1994**, *35*, 6503.
(285) Mori, Y.; Asai, M.; Kawade, J.-i.; Furukawa, H. *Tetrahedron* **1995**, *51*, 5315.
(286) Sharma, G. V. M.; Rao, A. V. S. R.; Murthy, V. S. *Tetrahedron Lett.* **1995**, *36*, 4117.
(287) Shimizu, I.; Omura, T. *Chem. Lett.* **1993**, 1759.
(288) Solladie, G.; Almario, A. *Tetrahedron: Asymmetry* **1995**, *6*, 559.
(289) Banwell, M. G.; Jolliffe, K. A.; Loong, D. T. J.; McRae, K. J.; Vounatsos, F. *J. Chem. Soc., Perkin Trans. 1* **2002**, 22.
(290) Yang, H.; Kuroda, H.; Miyashita, M.; Irie, H. *Chem. Pharm. Bull.* **1992**, *40*, 1616.
(291) Sharma, A.; Sankaranarayanan, S.; Chattopadhyay, S. *J. Org. Chem.* **1996**, *61*, 1814.
(292) Kalita, D.; Khan, A. T.; Barua, N. C.; Bez, G. *Tetrahedron* **1999**, *55*, 5177.
(293) Kobayashi, Y.; Nakano, M.; Kumar, G. B.; Kishihara, K. *J. Org. Chem.* **1998**, *63*, 7505.
(294) Hamada, T.; Daikai, K.; Irie, R.; Katsuki, T. *Tetrahedron: Asymmetry* **1995**, *6*, 2441.
(295) Mori, K.; Tomioka, H. *Liebigs Ann. Chem.* **1992**, 1011.
(296) Fujisawa, T.; Okada, N.; Takeuchi, M.; Sato, T. *Chem. Lett.* **1983**, 1271.
(297) Yurek-George, A.; Habens, F.; Brimmell, M.; Packham, G.; Ganesan, A. *J. Am. Chem. Soc.* **2004**, *126*, 1030.
(298) Savall, B. M.; Blanchard, N.; Roush, W. R. *Org. Lett.* **2003**, *5*, 377.
(299) Paterson, I.; Davies, R. D. M.; Heimann, A. C.; Marquez, R.; Meyer, A. *Org. Lett.* **2003**, *5*, 4477.
(300) Hanessian, S.; Yang, Y.; Giroux, S.; Mascitti, V.; Ma, J.; Raeppel, F. *J. Am. Chem. Soc.* **2003**, *125*, 13784.
(301) Vong, B. G.; Kim, S. H.; Abraham, S.; Theodorakis, E. A. *Angew. Chem., Int. Ed.* **2004**, *43*, 3947.
(302) Shin, Y.; Choy, N.; Balachandran, R.; Madiraju, C.; Day, B. W.; Curran, D. P. *Org. Lett.* **2002**, *4*, 4443.
(303) Paterson, I.; Britton, R.; Delgado, O.; Meyer, A.; Poullennec, K. G. *Angew. Chem., Int. Ed.* **2004**, *43*, 4629.
(304) Shin, Y.; Fournier, J.-H.; Fukui, Y.; Brueckner, A. M.; Curran, D. P. *Angew. Chem., Int. Ed.* **2004**, *43*, 4634.

(305) Smith, A. B., III.; Zhu, W.; Shirakami, S.; Sfouggatakis, C.; Doughty, V. A.; Bennett, C. S.; Sakamoto, Y. *Org. Lett.* **2003**, *5*, 761.
(306) Paterson, I.; Chen, D. Y. K.; Coster, M. J.; Acena, J. L.; Bach, J.; Gibson, K. R.; Keown, L. E.; Oballa, R. M.; Trieselmann, T.; Wallace, D. J.; Hodgson, A. P.; Norcross, R. D. *Angew. Chem., Int. Ed.* **2001**, *40*, 4055.
(307) Heathcock, C. H.; McLaughlin, M.; Medina, J.; Hubbs, J. L.; Wallace, G. A.; Scott, R.; Claffey, M. M.; Hayes, C. J.; Ott, G. R. *J. Am. Chem. Soc.* **2003**, *125*, 12844.
(308) Guo, J.; Duffy, K. J.; Stevens, K. L.; Dalko, P. I.; Roth, R. M.; Hayward, M. M.; Kishi, Y. *Angew. Chem., Int. Ed.* **1998**, *37*, 187.
(309) Hayward, M. M.; Roth, R. M.; Duffy, K. J.; Dalko, P. I.; Stevens, K. L.; Guo, J.; Kishi, Y. *Angew. Chem., Int. Ed.* **1998**, *37*, 192.
(310) Smith, A. B., III.; Doughty, V. A.; Lin, Q.; Zhuang, L.; McBriar, M. D.; Boldi, A. M.; Moser, W. H.; Murase, N.; Nakayama, K.; Sobukawa, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 191.
(311) Smith, A. B., III.; Lin, Q.; Doughty, V. A.; Zhuang, L.; McBriar, M. D.; Kerns, J. K.; Brook, C. S.; Murase, N.; Nakayama, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 196.
(312) Horita, K.; Nagasawa, M.; Hachiya, S.-I.; Sakurai, Y.; Yamazaki, T.; Uenishi, J. i.; Yonemitsu, O. *Tetrahedron Lett.* **1997**, *38*, 8965.
(313) Aicher, T. D.; Buszek, K. R.; Fang, F. G.; Forsyth, C. J.; Jung, S. H.; Kishi, Y.; Matelich, M. C.; Scola, P. M.; Spero, D. M.; Yoon, S. K. *J. Am. Chem. Soc.* **1992**, *114*, 3162.
(314) Inoue, M.; Nishi, T.; Kitahara, T. *Biosci. Biotechnol. Biochem.* **1999**, *63*, 1122.
(315) Gu, Y.; Snider Barry, B. *Org. Lett.* **2003**, *5*, 4385.
(316) Maestro, M. A.; Sefkow, M.; Seebach, D. *Liebigs Ann. Chem.* **1994**, 731.
(317) Ohta, K.; Miyagawa, O.; Tsutsui, H.; Mitsunobu, O. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 523.
(318) Kobayashi, Y.; Matsuumi, M. *J. Org. Chem.* **2000**, *65*, 7221.
(319) Sone, H.; Suenaga, K.; Bessho, Y.; Kondo, T.; Kigoshi, H.; Yamada, K. *Chem. Lett.* **1998**, 85.
(320) Ohmori, K. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 875.
(321) Ohmori, K.; Ogawa, Y.; Obitsu, T.; Ishikawa, Y.; Nishiyama, S.; Yamamura, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 2290.
(322) Ghosh, A. K.; Liu, W. *J. Org. Chem.* **1997**, *62*, 7908.
(323) Panek, J. S.; Liu, P. *J. Am. Chem. Soc.* **2000**, *122*, 11090.
(324) Weibel, D. B.; Shevy, L. E.; Schroeder, F. C.; Meinwald, J. *J. Org. Chem.* **2002**, *67*, 5896.
(325) Rowan, S. J.; Brady, P. A.; Sanders, J. K. M. *Tetrahedron Lett.* **1996**, *37*, 6013.
(326) Rowan, S. J.; Sanders, J. K. M. *J. Org. Chem.* **1998**, *63*, 1536.
(327) Bachmann, B. M.; Seebach, D. *Helv. Chim. Acta* **1998**, *81*, 2430.
(328) Burke, S. D.; Zhao, Q. *J. Org. Chem.* **2000**, *65*, 1489.
(329) Wang, Y.; Bernsmann, H.; Gruner, M.; Metz, P. *Tetrahedron Lett.* **2001**, *42*, 7801.
(330) Germay, O.; Kumar, N.; Thomas, E. J. *Tetrahedron Lett.* **2001**, *42*, 4969.
(331) Okuma, K.; Hirabayashi, S.-i.; Ono, M.; Shioji, K.; Matsuyama, H.; Bestmann, H. J. *Tetrahedron* **1998**, *54*, 4243.
(332) Williams, D. R.; Kissel, W. S. *J. Am. Chem. Soc.* **1998**, *120*, 11198.
(333) Ghosh, A. K.; Liu, C. *J. Am. Chem. Soc.* **2003**, *125*, 2374.
(334) Ghosh, A. K.; Gong, G. *J. Am. Chem. Soc.* **2004**, *126*, 3704.
(335) Takahashi, T.; Watanabe, H.; Kitahara, T. *Tetrahedron Lett.* **2003**, *44*, 9219.
(336) Berger, M.; Mulzer, J. *J. Am. Chem. Soc.* **1999**, *121*, 8393.
(337) Mulzer, J.; Berger, M. *J. Org. Chem.* **2004**, *69*, 891.
(338) Paquette, L. A.; Collado, I.; Purdie, M. *J. Am. Chem. Soc.* **1998**, *120*, 2553.
(339) Fettes, A.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 4098.
(340) Hornberger, K. R.; Hamblett, C. L.; Leighton, J. L. *J. Am. Chem. Soc.* **2000**, *122*, 12894.
(341) Williams, D. R.; Plummer, S. V.; Patnaik, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 3934.
(342) Hirai, Y.; Yakota, K.; Yamazaki, T.; Momose, T. *Heterocycles* **1990**, *30*, 1101.
(343) Kiho, T.; Nakayama, M.; Kogen, H. *Tetrahedron* **2003**, *59*, 1685.
(344) Sarabia, F.; Chammaa, S.; Lopez-Herrera, F. J. *Tetrahedron Lett.* **2002**, *43*, 2961.
(345) Fleming, I.; Ghosh, S. K. *Chem. Commun.* **1994**, 2287.
(346) Lee, J. Y.; Kim, B. H. *Tetrahedron Lett.* **1995**, *36*, 3361.
(347) Lee, J. Y.; Kim, B. H. *Tetrahedron* **1996**, *52*, 571.
(348) Fleming, I.; Ghosh, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2733.
(349) Sinha, S. C.; Keinan, E. *J. Org. Chem.* **1994**, *59*, 949.
(350) Sinha, S. C.; Keinan, E. *J. Org. Chem.* **1997**, *62*, 377.
(351) Enders, D.; Prokopenko, O. F. *Liebigs Ann. Org. Bioorg. Chem.* **1995**, 1185.
(352) Quinkert, G.; Fernholz, E.; Eckes, P.; Neumann, D.; Duerner, G. *Helv. Chim. Acta* **1989**, *72*, 1753.
(353) Kobayashi, M.; Kawazoe, K.; Okamoto, T.; Sasaki, T.; Kitagawa, I. *Chem. Pharm. Bull.* **1994**, *42*, 19.
(354) Nicolaou, K. C.; Patron, A. P.; Ajito, K.; Richter, P. K.; Khatuya, H. *Chem.—Eur. J.* **1996**, *2*, 847.
(355) Paterson, I.; Yeung, K.-S.; Ward, R. A.; Cumming, J. G.; Smith, J. D. *J. Am. Chem. Soc.* **1994**, *116*, 9391.
(356) Smith, A. B.; Chen, S. S.-Y.; Nelson, F. C.; Reichert, J. M.; Salvatore, B. A. *J. Am. Chem. Soc.* **1997**, *119*, 10935.
(357) Smith, A. B.; Chen, S. S.-Y.; Nelson, F. C.; Reichert, J. M.; Salvatore, B. A. *J. Am. Chem. Soc.* **1995**, *117*, 12013.
(358) Paterson, I.; Watson, C.; Yeung, K.-S.; Ward, R. A.; Wallace, P. A. *Tetrahedron* **1998**, *54*, 11955.
(359) Nakamura, R.; Tanino, K.; Miyashita, M. *Org. Lett.* **2003**, *5*, 3583.
(360) Kigoshi, H.; Suenaga, K.; Mutou, T.; Ishigaki, T.; Atsumi, T.; Ishiwata, H.; Sakakura, A.; Ogawa, T.; Ojika, M.; Yamada, K. *J. Org. Chem.* **1996**, *61*, 5326.
(361) Kigoshi, H.; Suenaga, K.; Takagi, M.; Akao, A.; Kanematsu, K.; Kamei, N.; Okugawa, Y.; Yamada, K. *Tetrahedron* **2002**, *58*, 1075.
(362) Suenaga, K.; Kamei, N.; Okugawa, Y.; Takagi, M.; Akao, A.; Kigoshi, H.; Yamada, K. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 269.
(363) Spinella, A.; Caruso, T.; Coluccini, C. *Tetrahedron Lett.* **2002**, *43*, 1681.
(364) Caruso, T.; Spinella, A. *Tetrahedron: Asymmetry* **2002**, *13*, 2071.
(365) Roush, W. R.; Koyama, K.; Curtin, M. L.; Moriarty, K. J. *J. Am. Chem. Soc.* **1996**, *118*, 7502.
(366) Porco, J. A., Jr.; Schoenen, F. J.; Stout, T. J.; Clardy, J.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 7410.
(367) Toshima, K.; Jyojima, T.; Yamaguchi, H.; Noguchi, Y.; Yoshida, T.; Murase, H.; Nakata, M.; Matsumura, S. *J. Org. Chem.* **1997**, *62*, 3271.
(368) Nicolaou, K. C.; Li, Y.; Weyershausen, B.; Wei, H. *Chem. Commun.* **2000**, 307.
(369) Nicolaou, K. C.; Fylaktakidou, K. C.; Monenschein, H.; Li, Y.; Weyershausen, B.; Mitchell, H. J.; Wei, H.-X.; Guntupalli, P.; Hepworth, D.; Sugita, K. *J. Am. Chem. Soc.* **2003**, *125*, 15433.
(370) Brito-Arias, M.; Pereda-Miranda, R.; Heathcock, C. H. *J. Org. Chem.* **2004**, *69*, 4567.
(371) Larson, D. P.; Heathcock, C. H. *J. Org. Chem.* **1997**, *62*, 8406.
(372) Sunazuka, T.; Hirose, T.; Harigaya, Y.; Takamatsu, S.; Hayashi, M.; Komiyama, K.; Omura, S.; Sprengeler, P. A.; Smith, A. B., III. *J. Am. Chem. Soc.* **1997**, *119*, 10247.
(373) Kobayashi, Y.; Kumar, G. B.; Kurachi, T.; Acharya, H. P.; Yamazaki, T.; Kitazume, T. *J. Org. Chem.* **2001**, *66*, 2011.
(374) Kobayashi, Y.; Acharya, H. P. *Tetrahedron Lett.* **2001**, *42*, 2817.
(375) Matsuya, Y.; Kawaguchi, T.; Nemoto, H.; Nozaki, H.; Hamada, H. *Heterocycles* **2003**, *59*, 481.
(376) Sharma, G. V. M.; Mouli, C. C. *Tetrahedron Lett.* **2002**, *43*, 9159.
(377) Nakamura, H.; Ono, M.; Shida, Y.; Akita, H. *Tetrahedron: Asymmetry* **2002**, *13*, 705.
(378) Ono, M.; Nakamura, H.; Arakawa, S.; Honda, N.; Akita, H. *Chem. Pharm. Bull.* **2002**, *50*, 692.
(379) Sharma, G. V. M.; Mouli, C. C. *Tetrahedron Lett.* **2003**, *44*, 8161.
(380) Toshima, K.; Jyojima, T.; Miyamoto, N.; Katohno, M.; Nakata, M.; Matsumura, S. *J. Org. Chem.* **2001**, *66*, 1708.
(381) Fujiwara, K.; Murai, A.; Yotsu-Yamashita, M.; Yasumoto, T. *J. Am. Chem. Soc.* **1998**, *120*, 10770.
(382) Paquette, L. A.; Barriault, L.; Pissarnitski, D.; Johnston, J. N. *J. Am. Chem. Soc.* **2000**, *122*, 619.
(383) Wender, P. A.; Hegde, S. G.; Hubbard, R. D.; Zhang, L. *J. Am. Chem. Soc.* **2002**, *124*, 4956.
(384) Mulzer, J.; Hanbauer, M. *Tetrahedron Lett.* **2002**, *43*, 3381.
(385) Ghosh, A. K.; Wang, Y.; Kim, J. T. *J. Org. Chem.* **2001**, *66*, 8973.
(386) Ghosh, A. K.; Wang, Y. *Tetrahedron Lett.* **2001**, *42*, 3399.
(387) Paterson, I.; Savi, C. D.; Tudge, M. *Org. Lett.* **2001**, *3*, 213.
(388) Ahmed, A.; Hoegenauer, E. K.; Enev, V. S.; Hanbauer, M.; Kaehlig, H.; Oehler, E.; Mulzer, J. *J. Org. Chem.* **2003**, *68*, 3026.
(389) Rao, A. V. R.; Murthy, V. S.; Sharma, G. V. M. *Tetrahedron Lett.* **1995**, *36*, 139.
(390) Rao, B. V.; Kumar, V. S. *Tetrahedron Lett.* **1995**, *36*, 147.
(391) Shiina, I.; Kubota, M.; Ibuka, R. *Tetrahedron Lett.* **2002**, *43*, 7535.
(392) Shiina, I.; Oshiumi, H.; Hashizume, M.; Yamai, Y.-s.; Ibuka, R. *Tetrahedron Lett.* **2004**, *45*, 543.
(393) Shiina, I.; Kubota, M.; Oshiumi, H.; Hashizume, M. *J. Org. Chem.* **2004**, *69*, 1822.
(394) Tian, J.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *Org. Lett.* **2003**, *5*, 3021.
(395) Inoue, M.; Sasaki, T.; Hatano, S.; Hirama, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 6500.
(396) Roush, W. R.; Blizzard, T. A. *J. Org. Chem.* **1984**, *49*, 4332.
(397) Jeker, N.; Tamm, C. *Helv. Chim. Acta* **1988**, *71*, 1895.
(398) Kinoshita, M.; Aburaki, S.; Wada, M.; Umezawa, S. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1279.
(399) Taub, D.; Girotra, N. N.; Hoffsommer, R. D.; Kuo, C. H.; Slates, H. L.; Weber, N. L.; Wendler, N. L. *Tetrahedron* **1968**, *24*, 2443.
(400) White, J. D.; Johnson, A. T. *J. Org. Chem.* **1994**, *59*, 3347.

(401) Bodo, B. *Bull. Mus. Hist. Nat.* **1975**, *6*, 97.
(402) Nagarajan, M.; Kumar, V. S.; Rao, V. V. *Tetrahedron* **1999**, *55*, 12349.
(403) Nagarajan, M. *Tetrahedron Lett.* **1999**, *40*, 1207.
(404) Nagarajan, M.; Kumar, V. S.; Rao, B. V. *Tetrahedron Lett.* **1997**, *38*, 5835.
(405) Mukaiyama, T.; Izumi, J.; Miyashita, M.; Shiina, I. *Chem. Lett.* **1993**, 907.
(406) Shiina, I. *Tetrahedron* **2004**, *60*, 1587.
(407) Mukaiyama, T.; Izumi, J.; Shiina, I. *Chem. Lett.* **1997**, 187.
(408) Ishihara, K.; Kubota, M.; Kurihara, H.; Yamamoto, H. *J. Org. Chem.* **1996**, *61*, 4560.
(409) Kaiho, T.; Masamune, S.; Toyoda, T. *J. Org. Chem.* **1982**, *47*, 1612.
(410) Corey, E. J.; Hua, D. H.; Pan, B. C.; Seitz, S. P. *J. Am. Chem. Soc.* **1982**, *104*, 6818.
(411) Bartlett, P. A.; Meadows, J. D.; Ottow, E. *J. Am. Chem. Soc.* **1984**, *106*, 5304.
(412) Wakamatsu, T.; Yamada, S.; Ban, Y. *Heterocycles* **1986**, *24*, 309.
(413) Arrieta, A.; Garcia, T.; Lago, J. M.; Palomo, C. *Synth. Commun.* **1983**, *13*, 471.
(414) Diago-Meseguer, J.; Palomo-Coll, A. L.; Fernandez-Lizarbe, J. R.; Zugaza-Bilbao, A. *Synthesis* **1980**, 547.
(415) Elbaum, D.; Nguyen, T. B.; Jorgensen, W. L.; Schreiber, S. L. *Tetrahedron* **1994**, *50*, 1503.
(416) Roush, W. R.; Sciotti, R. J. *J. Am. Chem. Soc.* **1998**, *120*, 7411.
(417) Coste, J.; Frerot, E.; Jouin, P.; Castro, B. *Tetrahedron Lett.* **1991**, *32*, 1967.
(418) Frerot, E.; Coste, J.; Pantaloni, A.; Dufour, M. N.; Jouin, P. *Tetrahedron* **1991**, *47*, 259.
(419) Wood, J. L.; Porco, J. A., Jr.; Taunton, J.; Lee, A. Y.; Clardy, J.; Schreiber, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 5898.
(420) Frank, S. A.; Roush, W. R. *J. Org. Chem.* **2002**, *67*, 4316.
(421) Banfi, L.; Basso, A.; Guanti, G.; Riva, R. *Tetrahedron Lett.* **2004**, *45*, 6637.
(422) Nakayama, J.; Cao, Y.; Horii, T.; Sakuda, S.; Nagasawa, H. *Biosci. Biotechnol. Biochem.* **2001**, *65*, 2322.
(423) López-Macià, A.; Jiménez, J. C.; Royo, M.; Giralt, E.; Albericio, F. *Tetrahedron Lett.* **2000**, *41*, 9765.
(424) Coste, J.; Frerot, E.; Jouin, P. *J. Org. Chem.* **1994**, *59*, 2437.
(425) Woodward, R. B.; Bader, F. E.; Bickel, H.; Frey, A. J.; Kierstead, R. W. *Tetrahedron* **1958**, *2*, 1.
(426) Nakagawa, Y.; Irie, K.; Yamanaka, N.; Ohigashi, H.; Tsuda, K.-i. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3015.
(427) Wittenberger, S. J.; Baker, W. R.; Donner, B. G.; Hutchins, C. W. *Tetrahedron Lett.* **1991**, *32*, 7655.
(428) Parmee, E. R.; Steel, P. G.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1989**, 1250.
(429) Paquette, L. A.; Duan, M.; Konetzki, I.; Kempmann, C. *J. Am. Chem. Soc.* **2002**, *124*, 4257.
(430) Boden, E. P.; Keck, G. E. *J. Org. Chem.* **1985**, *50*, 2394.
(431) Holmberg, K.; Hansen, B. *Acta Chem. Scand.* **1979**, *33*, 410.
(432) Keck, G. E.; Boden, E. P.; Wiley: M. R. *J. Org. Chem.* **1989**, *54*, 896.
(433) Keck, G. E.; Murry, J. A. *J. Org. Chem.* **1991**, *56*, 6606.
(434) Evans, D. A.; Kaldor, S. W.; Jones, T. K.; Clardy, J.; Stout, T. J. *J. Am. Chem. Soc.* **1990**, *112*, 7001.
(435) Ireland, R. E.; Thaisrivongs, S.; Dussault, P. H. *J. Am. Chem. Soc.* **1988**, *110*, 5768.
(436) Hunter, T. J.; O'Doherty, G. A. *Org. Lett.* **2002**, *4*, 4447.
(437) Balog, A.; Betinato, P.; Su, D.-S.; Meng, D.; Sorensen, E.; Danishefsky, S. J.; Zheng, Y.-H.; Chou, T.-C.; He, L.; Horwitz, S. B. *Tetrahedron Lett.* **1997**, *38*, 4529.
(438) Lehmann, J.; Tochtermann, W. *Tetrahedron* **1999**, *55*, 2639.
(439) Lewis, A.; Stefanuti, I.; Swain, S. A.; Smith, S. A.; Taylor, R. J. K. *Org. Biomol. Chem* **2003**, *1*, 104.
(440) Feldman Ken, S.; Eastman Kyle, J.; Lessene, G. *Org. Lett.* **2002**, *4*, 3525.
(441) Funk, R. L.; Olmstead, T. A.; Parvez, M.; Stallman, J. B. *J. Org. Chem.* **1993**, *58*, 5873.
(442) Garcia, D. M.; Yamada, H.; Hatakeyama, S.; Nishizawa, M. *Tetrahedron Lett.* **1994**, *35*, 3325.
(443) Tanner, D.; Somfai, P. *Tetrahedron* **1987**, *43*, 4395.
(444) Grieco, P. A.; Perez-Medrano, A. *Tetrahedron Lett.* **1988**, *29*, 4225.
(445) White, J. D.; Amedio, J. C., Jr. *J. Org. Chem.* **1989**, *54*, 736.
(446) Boger, D. L.; Keim, H.; Oberhauser, B.; Schreiner, E. P.; Foster, C. A. *J. Am. Chem. Soc.* **1999**, *121*, 6197.
(447) Schulz, T.; Eicher, T. *Synthesis* **2003**, 1253.
(448) Stork, G.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1987**, *109*, 1565.
(449) Chu, K. S.; Negrete, G. R.; Konopelski, J. P. *J. Org. Chem.* **1991**, *56*, 5196.
(450) Ashworth, P.; Broadbelt, B.; Jankowski, P.; Kocienski, P.; Pimm, A.; Bell, R. *Synthesis* **1995**, 199.
(451) O'Neill, J. A.; Lindell, S. D.; Simpson, T. J.; Willis, C. L. *J. Chem. Soc., Perkin Trans. 1* **1996**, 637.
(452) Niwa, H.; Kunitani, K.; Nagoya, T.; Yamada, K. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 3094.
(453) Ishiwata, H.; Sone, H.; Kigoshi, H.; Yamada, K. *Tetrahedron* **1994**, *50*, 12853.
(454) Niwa, H.; Sakata, T.; Yamada, K. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1990.
(455) Eberle, M. K.; Nuninger, F. *J. Org. Chem.* **1995**, *60*, 4868.
(456) Mulzer, J.; Mantoulidis, A.; Oehler, E. *J. Org. Chem.* **2000**, *65*, 7456.
(457) Tsai, C. Y.; Huang, X.; Wong, C. H. *Tetrahedron Lett.* **2000**, *41*, 9499.
(458) Hanessian, S.; Ma, J.; Wang, W. *J. Am. Chem. Soc.* **2001**, *123*, 10200.
(459) Kataoka, H.; Katagi, T. *Tetrahedron* **1987**, *43*, 4519.
(460) Lamont, R. B.; Allen, D. G.; Clemens, I. R.; Newall, C. E.; Ramsay, M. V. J.; Rose, M.; Fortt, S.; Gallagher, T. *J. Chem. Soc., Chem. Commun.* **1992**, 1693.
(461) Fujiwara, K.; Awakura, D.; Tsunashima, M.; Nakamura, A.; Honma, T.; Murai, A. *J. Org. Chem.* **1999**, *64*, 2616.
(462) Stocks, M. J.; Harrison, R. P.; Teague, S. J. *Tetrahedron Lett.* **1995**, *36*, 6555.
(463) Keck, G. E.; Sanchez, C.; Wager, C. A. *Tetrahedron Lett.* **2000**, *41*, 8673.
(464) Magriotis, P. A.; Scott, M. E.; Kim, J. D. *Tetrahedron Lett.* **1991**, *32*, 6085.
(465) Lee, E.; Jeong, E. J.; Kang, E. J.; Sung, L. T.; Hong, S. K. *J. Am. Chem. Soc.* **2001**, *123*, 10131.
(466) Zhang, Y.; Boyer, R.; Sun, X.; Paschal, J.; Chen, S.-H. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 775.
(467) Nakagawa, Y.; Irie, K.; Nakamura, Y.; Ohigashi, H. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 723.
(468) Lamont, R. B.; Allen, D. G.; Clemens, I. R.; Newall, C. E.; Ramsay, M. V. J.; Rose, M.; Fortt, S.; Gallagher, T. *Chem. Commun.* **1992**, *22*, 1693.
(469) Fujisawa, T.; Mori, T.; Fukumoto, K.; Sato, T. *Chem. Lett.* **1982**, 1891.
(470) Isobe, T.; Ishikawa, T. *J. Org. Chem.* **1999**, *64*, 6984.
(471) Takahashi, S.; Souma, K.; Hashimoto, R.; Koshino, H.; Nakata, T. *J. Org. Chem.* **2004**, *69*, 4509.
(472) Fürstner, A.; Albert, M.; Mlynarski, J.; Matheu, M. *J. Am. Chem. Soc.* **2002**, *124*, 1168.
(473) Fürstner, A.; Mlynarski, J.; Albert, M. *J. Am. Chem. Soc.* **2002**, *124*, 10274.
(474) Fürstner, A.; Albert, M.; Mlynarski, J.; Matheu, M.; DeClercq, E. *J. Am. Chem. Soc.* **2003**, *125*, 13132.
(475) Fürstner, A.; Ruiz-Caro, J.; Prinz, H.; Waldmann, H. *J. Org. Chem.* **2004**, *69*, 459.
(476) Bailliez, V.; de Figueiredo, R. M.; Olesker, A.; Cleophax, J. *Tetrahedron Lett.* **2003**, *44*, 9151.
(477) Fürstner, A.; Albert, M.; Mlynarski, J.; Matheu, M. *J. Am. Chem. Soc.* **2002**, *124*, 1168.
(478) Davies, A. G.; Mitchell, T. N.; Symes, W. R. *J. Chem. Soc. (C)* **1966**, 1311.
(479) Steliou, K.; Szczygielska-Nowosielska, A.; Favre, A.; Poupart, M. A.; Hanessian, S. *J. Am. Chem. Soc.* **1980**, *102*, 7578.
(480) Steliou, K.; Poupart, M.-A. *J. Am. Chem. Soc.* **1983**, *105*, 7130.
(481) Otera, J. *Acc. Chem. Res.* **2004**, *37*, 288.
(482) Otera, J. *Chem. Rev.* **1993**, *93*, 1449.
(483) Hyatt, J. A.; Feldman, P. L.; Clemens, R. J. *J. Org. Chem.* **1984**, *49*, 5105.
(484) Boeckman, R. K., Jr; Pruitt, J. R. *J. Am. Chem. Soc.* **1989**, *111*, 8286.
(485) Petasis, N. A.; Patane, M. A. *J. Chem. Soc., Chem. Commun.* **1990**, 836.
(486) Trost, B. M.; Gunzner, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 9449.
(487) Trost, B. M.; Gunzner, J. L.; Dirat, O.; Rhee, Y. H. *J. Am. Chem. Soc.* **2002**, *124*, 10396.
(488) Trost, B. M.; Dirat, O.; Gunzner, J. L. *Angew. Chem., Int. Ed.* **2002**, *41*, 841.
(489) Eisenberg, S. W. E.; Chen, C.; Wu, J.; Lebrilla, C.; Kurth, M. J. *Tetrahedron Lett.* **1996**, *37*, 7683.
(490) Chen, C.; Quinn, E. K.; Olmstead, M. M.; Kurth, M. J. *J. Org. Chem.* **1993**, *58*, 5011.
(491) Bhattacharjee, A.; De Brabander, J. K. *Tetrahedron Lett.* **2000**, *41*, 8069.
(492) Bhattacharjee, A.; Seguil, O. R.; De Brabander, J. K. *Tetrahedron Lett.* **2001**, *42*, 1217.
(493) Hilli, F.; White, J. M.; Rizzacasa, M. A. *Tetrahedron Lett.* **2002**, *43*, 8507.
(494) Hilli, F.; White Jonathan, M.; Rizzacasa Mark, A. *Org. Lett.* **2004**, *6*, 1289.
(495) Holloway Georgina, A.; Hugel Helmut, M.; Rizzacasa Mark, A. *J. Org. Chem.* **2003**, *68*, 2200.
(496) Grasa, G. A.; Singh, R.; Nolan, S. P. *Synthesis* **2004**, 971.

(497) Corey, E. J.; Brunelle, D. J.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1977**, *99*, 7359.
(498) Corey, E. J.; Kim, S.; Yoo, S.-E.; Nicolaou, K. C.; Melvin, L. S., Jr.; Brunelle, D. J.; Falck, J. R.; Trybulski, E. J.; Lett, R.; Sheldrake, P. W. *J. Am. Chem. Soc.* **1978**, *100*, 4620.
(499) Vedejs, E.; Powell, D. W. *J. Am. Chem. Soc.* **1982**, *104*, 2046.
(500) Vedejs, E.; Buchanan, R. A.; Conrad, P.; Meier, G. P.; Mullins, M. J.; Watanabe, Y. *J. Am. Chem. Soc.* **1987**, *109*, 5878.
(501) Vedejs, E.; Buchanan, R. A.; Watanabe, Y. *J. Am. Chem. Soc.* **1989**, *111*, 8430.
(502) Nagel, A. A.; Celmer, W. D.; Jefferson, M. T.; Vincent, L. A.; Whipple, E. B.; Schulte, G. *J. Org. Chem.* **1986**, *51*, 5397.
(503) Gais, H. J. *Tetrahedron Lett.* **1984**, *25*, 273.
(504) Gais, H. J.; Lied, T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 145.
(505) Ruppin, C.; Dixneuf, P. H. *Tetrahedron Lett.* **1986**, *27*, 6323.
(506) Kita, Y.; Maeda, H.; Omori, K.; Okuno, T.; Tamura, Y. *Synlett* **1993**, 273.
(507) Trost, B. M.; Chisholm, J. D. *Org. Lett.* **2002**, *4*, 3743.
(508) Petri, A. F.; Bayer, A.; Maier, M. E. *Angew. Chem., Int. Ed.* **2004**, *43*, 5821.
(509) Duret, P.; Figadère, B.; Hocquemiller, R.; Cavé, A. *Tetrahedron Lett.* **1997**, *38*, 8849.
(510) Vlattas, I.; Harrison, I. T.; Tokes, L.; Fried, J. H.; Cross, A. D. *J. Org. Chem.* **1968**, *33*, 4176.
(511) Narasaka, K.; Sakakura, T.; Uchimaru, T.; Guedin-Vuong, D. *J. Am. Chem. Soc.* **1984**, *106*, 4.
(512) Hans, J. J.; Driver, R. W.; Burke, S. D. *J. Org. Chem.* **2000**, *65*, 2114.
(513) Shen, R.; Lin, C. T.; Porco, J. A., Jr. *J. Am. Chem. Soc.* **2002**, *124*, 5650.
(514) Su, Q.; Panek, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 2425.
(515) Palomo, C.; Palomo, A. L.; Palomo, F.; Mielgo, A. *Org. Lett.* **2002**, *4*, 4005.
(516) Shimizu, I.; Nakagawa, H. *Tetrahedron Lett.* **1992**, *33*, 4957.
(517) White, J. D.; Green, N. J.; Fleming, F. F. *Tetrahedron Lett.* **1993**, *34*, 3515.
(518) Niwa, H.; Sakata, T.; Yamada, K. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2345.
(519) Su, Q.; Beeler, A. B.; Lobkovsky, E.; Porco, J. A.; Panek, J. S. *Org. Lett.* **2003**, *5*, 2149.
(520) Ahmed, A.; Taniguchi, N.; Fukuda, H.; Kinoshita, H.; Inomata, K.; Kotake, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 781.
(521) Ojima, I.; Sun, C. M.; Zucco, M.; Park, Y. H.; Duclos, O.; Kuduk, S. *Tetrahedron Lett.* **1993**, *34*, 4149.
(522) Romo, D.; Rzasa, R. M.; Shea, H. A.; Park, K.; Langenhan, J. M.; Sun, L.; Akhiezer, A.; Liu, J. O. *J. Am. Chem. Soc.* **1998**, *120*, 12237.
(523) Rzasa, R. M.; Shea, H. A.; Romo, D. *J. Am. Chem. Soc.* **1998**, *120*, 591.
(524) Palomo, C.; Aizpurua, J. M.; Cuevas, C.; Mielgo, A.; Galarza, R. *Tetrahedron Lett.* **1995**, *36*, 9027.
(525) Eggen, M.; Nair, S. K.; Georg, G. I. *Org. Lett.* **2001**, *3*, 1813.
(526) Vidya, R.; Eggen, M.; Nair, S. K.; Georg, G. I.; Himes, R. H. *J. Org. Chem.* **2003**, *68*, 9687.
(527) Colvin, E. W.; Purcell, T. A.; Raphael, R. A. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1718.
(528) Colvin, E. W.; Purcell, T. A.; Raphael, R. A. *J. Chem. Soc., Chem. Commun.* **1972**, 1031.
(529) Staab, H. A. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 351.
(530) Wasserman, H. H.; Gambale, R. J. *J. Am. Chem. Soc.* **1985**, *107*, 1423.
(531) Yamada, H.; Ohsawa, S.; Sugai, T.; Ohta, H.; Yoshikawa, S. *Chem. Lett.* **1989**, 1775.
(532) Makita, A.; Nihira, T.; Yamada, Y. *Tetrahedron Lett.* **1987**, *28*, 805.
(533) Lobell, M.; Schneider, M. P. *Tetrahedron: Asymmetry* **1993**, *4*, 1027.
(534) Zhi-Wei, G.; Sih, J. *J. Am. Chem. Soc.* **1988**, *110*, 1999.
(535) Pungente, M. D.; Weiler, L.; Ziltener, H. J. *Can. J. Chem.* **2002**, *80*, 1643.
(536) Setoh, M.; Yamada, O.; Ogasawara, K. *Heterocycles* **1995**, *40*, 539.
(537) Yoneda, E.; Zhang, S.; Onitsuka, K.; Takahashi, S. *Tetrahedron Lett.* **2001**, *42*, 5459.
(538) Quinkert, G.; Billhardt, U. M.; Jakob, H.; Fischer, G.; Glenneberg, J.; Nagler, P.; Autze, V.; Heim, N.; Wacker, M.; et al. *Helv. Chim. Acta* **1987**, *70*, 771.
(539) Quinkert, G.; Heim, N.; Glenneberg, J.; Doeller, U.; Eichhorn, M.; Billhardt, U. M.; Schwarz, C.; Zimmermann, G.; Bats, J. W.; Duerner, G. *Helv. Chim. Acta* **1988**, *71*, 1719.
(540) Quinkert, G.; Doeller, U.; Eichhorn, M.; Kueber, F.; Nestler, H. P.; Becker, H.; Bats, J. W.; Zimmermann, G.; Duerner, G. *Helv. Chim. Acta* **1990**, *73*, 1999.
(541) Quinkert, G.; Kueber, F.; Knauf, W.; Wacker, M.; Koch, U.; Becker, H.; Nestler, H. P.; Duerner, G.; Zimmermann, G.; et al. *Helv. Chim. Acta* **1991**, *74*, 1853.
(542) Quinkert, G.; Fischer, G.; Billhardt, U. M.; Glenneberg, J.; Hertz, U.; Duerner, G.; Paulus, E. F.; Bats, J. W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 430.
(543) Kurihara, T.; Nakajima, Y.; Mitsunobu, O. *Tetrahedron Lett.* **1976**, 2455.
(544) Mitsunobu, O. *Synthesis* **1981**, 1.
(545) Hughes, D. L. *Org. React.* **1992**, *42*, 335.
(546) Hughes, D. L. *Org. Prep. Proced. Int.* **1996**, *28*, 127.
(547) Ohta, K.; Mitsunobu, O. *Tetrahedron Lett.* **1991**, *32*, 517.
(548) Tsutsui, H.; Mitsunobu, O. *Tetrahedron Lett.* **1984**, *25*, 2163.
(549) Boger, D. L.; Sakya, S. M.; Yohannes, D. *J. Org. Chem.* **1991**, *56*, 4204.
(550) Justus, K.; Steglich, W. *Tetrahedron Lett.* **1991**, *32*, 5781.
(551) Noda, Y.; Kashin, H. *Heterocycles* **1998**, *48*, 5.
(552) Ghera, E.; Ramesh, N. G.; Laxer, A.; Hassner, A. *Tetrahedron Lett.* **1995**, *36*, 1333.
(553) Kuwahara, S.; Tsuruta, T.; Leal, W. S.; Kodama, O. *Biosci., Biotechnol., Biochem.* **1998**, *62*, 1261.
(554) Haviv, F.; Ratajczyk, J. D.; DeNet, R. W.; Martin, Y. C.; Dyer, R. D.; Carter, G. W. *J. Med. Chem.* **1987**, *30*, 254.
(555) Williams, D. R.; Meyer, K. G. *J. Am. Chem. Soc.* **2001**, *123*, 765.
(556) Blizzard, T.; Bostrom, L.; Margiatto, G.; Mrozik, H.; Fisher, M. *Tetrahedron Lett.* **1991**, *32*, 2723.
(557) Hatakeyama, S.; Osanai, K.; Numata, H.; Takano, S. *Tetrahedron Lett.* **1989**, *30*, 4845.
(558) Bracher, F.; Schulte, B. *Nat. Prod. Res.* **2003**, *17*, 293.
(559) Waddell, S. T.; Blizzard, T. A. *Tetrahedron Lett.* **1993**, *34*, 5385.
(560) Waddell, S. T.; Eckert, J. M.; Blizzard, T. A. *Heterocycles* **1996**, *43*, 2325.
(561) Adam, G.; Zibuck, R.; Seebach, D. *J. Am. Chem. Soc.* **1987**, *109*, 6176.
(562) Seebach, D.; Adam, G.; Zibuck, R.; Simon, W.; Rouilly, M.; Meyer, W. L.; Hinton, J. F.; Privett, T. A.; Templeton, G. E. *Liebigs Ann. Chem.* **1989**, 1233.
(563) Seebach, D.; Adam, G.; Von dem Bussche-Huennefeld, C.; Gisi, U.; Binder, H. *Liebigs Ann. Chem.* **1990**, 1007.
(564) Selles, P.; Lett, R. *Tetrahedron Lett.* **2002**, *43*, 4627.
(565) Goetschi, E.; Jenny, C. J.; Reindl, P.; Ricklin, F. *Helv. Chim. Acta* **1996**, *79*, 2219.
(566) Shen, R.; Lin, C. T.; Bowman, E. J.; Bowman, B. J.; Porco, J. A., Jr. *Org. Lett.* **2002**, *4*, 3103.
(567) Zibuck, R.; Liverton, N. J.; Smith, A. B., III. *J. Am. Chem. Soc.* **1986**, *108*, 2451.
(568) Smith, A. B., III.; Noda, I.; Remiszewski, S. W.; Liverton, N. J.; Zibuck, R. *J. Org. Chem.* **1990**, *55*, 3977.
(569) White, J. D.; Kawasaki, M. *J. Am. Chem. Soc.* **1990**, *112*, 4991.
(570) Smith, A. B., III.; Leahy, J. W.; Noda, I.; Remiszewski, S. W.; Liverton, N. J.; Zibuck, R. *J. Am. Chem. Soc.* **1992**, *114*, 2995.
(571) White, J. D.; Kawasaki, M. *J. Org. Chem.* **1992**, *57*, 5292.
(572) Paterson, I.; De Savi, C.; Tudge, M. *Org. Lett.* **2001**, *3*, 3149.
(573) Crimmins, M. T.; Stanton, M. G.; Allwein, S. P. *J. Am. Chem. Soc.* **2002**, *124*, 5958.
(574) Paterson, I.; de Savi, C.; Tudge, M. *Org. Lett.* **2001**, *3*, 213.
(575) Wipf, P.; Reeves, J. T. *Chem. Commun.* **2002**, 2066.
(576) Paterson, I.; Tudge, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 343.
(577) Paterson, I.; Tudge, M. *Tetrahedron* **2003**, *59*, 6833.
(578) Attwood, S. V.; Barrett, A. G. M.; Carr, R. A. E.; Richardson, G. *J. Chem. Soc., Chem. Commun.* **1986**, 479.
(579) Barrett, A. G. M.; Carr, R. A. E.; Attwood, S. V.; Richardson, G.; Walshe, N. D. A. *J. Org. Chem.* **1986**, *51*, 4840.
(580) Kaisalo, L.; Koskimies, J.; Hase, T. *Synth. Commun.* **1999**, *29*, 399.
(581) Mori, K.; Nakazono, Y. *Liebigs Ann. Chem.* **1988**, 167.
(582) Battiste, M. A.; Rocca, J. R.; Wydra, R. L.; Tumlinson, J. H., III.; Chuman, T. *Tetrahedron Lett.* **1988**, *29*, 6565.
(583) Shimano, M.; Shibata, T.; Kamei, N. *Tetrahedron Lett.* **1998**, *39*, 4363.
(584) Shimano, M.; Kamei, N.; Shibata, T.; Inoguchi, K.; Itoh, N.; Ikari, T.; Senda, H. *Tetrahedron* **1998**, *54*, 12745.
(585) Still, W. C.; Ohmizu, H. *J. Org. Chem.* **1981**, *46*, 5242.
(586) Bracher, F.; Krauss, J. *Eur. J. Org. Chem.* **2001**, 4701.
(587) Dvorak, C. A.; Schmitz, W. D.; Poon, D. J.; Pryde, D. C.; Lawson, J. P.; Amos, R. A.; Meyers, A. I. *Angew. Chem., Int. Ed.* **2000**, *39*, 1664.
(588) Kuligowski, C.; Bezzenine-Lafollee, S.; Chaume, G.; Mahuteau, J.; Barriere, J.-C.; Bacque, E.; Pancrazi, A.; Ardisson, J. *J. Org. Chem.* **2002**, *67*, 4565.
(589) Meyers, A. I.; Amos, R. A. *J. Am. Chem. Soc.* **1980**, *102*, 870.
(590) Butera, J.; Rini, J.; Helquist, P. *J. Org. Chem.* **1985**, *50*, 3676.
(591) Liu, L.; Tanke, R. S.; Miller, M. J. *J. Org. Chem.* **1986**, *51*, 5332.
(592) Moreau, X.; Campagne, J.-M. *J. Org. Chem.* **2003**, *68*, 5346.
(593) Emmer, G.; Grassberger, M. A.; Meingassner, J. G.; Schulz, G.; Schaude, M. *J. Med. Chem.* **1994**, *37*, 1908.

(594) Emmer, G.; Grassberger, M. A.; Schulz, G.; Boesch, D.; Gaveriaux, C.; Loor, F. *J. Med. Chem.* **1994**, *37*, 1918.
(595) Geiwiz, J.; Goetschi, E.; Hebeisen, P. *Synthesis* **2003**, 1699.
(596) Angehrn, P.; Buchmann, S.; Funk, C.; Goetschi, E.; Gmuender, H.; Hebeisen, P.; Kostrewa, D.; Link, H.; Luebbers, T.; Masciadri, R.; Nielsen, J.; Reindl, P.; Ricklin, F.; Schmitt-Hoffmann, A.; Theil, F.-P. *J. Med. Chem.* **2004**, *47*, 1487.
(597) Kuisle, O.; Quinoa, E.; Riguera, R. *Tetrahedron Lett.* **1999**, *40*, 1203.
(598) Evans, D. A.; Ratz, A. M.; Huff, B. E.; Sheppard, G. S. *J. Am. Chem. Soc.* **1995**, *117*, 3448.
(599) Marcantoni, E.; Massaccesi, M.; Petrini, M.; Bartoli, G.; Bellucci, M. C.; Bosco, M.; Sambri, L. *J. Org. Chem.* **2000**, *65*, 4553.
(600) Arnold, L. D.; Assil, H. I.; Vederas, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 3973.
(601) Herb, C.; Maier, M. E. *J. Org. Chem.* **2003**, *68*, 8129.
(602) Dandapani, S.; Curran, D. P. *Chem.—Eur. J.* **2004**, *10*, 3130.
(603) Dembinski, R. *Eur. J. Org. Chem.* **2004**, 2763.
(604) Couladouros, E. A.; Soufli, I. C. *Tetrahedron Lett.* **1994**, *35*, 4409.
(605) Couladouros, E. A.; Soufli, I. C. *Tetrahedron Lett.* **1995**, *36*, 9369.
(606) Couladouros, E. A.; Soufli, I. C.; Moutsos, V. I.; Chadha, R. K. *Chem.—Eur. J.* **1998**, *4*, 33.
(607) Rychnovsky, S. D.; Hwang, K. *J. Org. Chem.* **1994**, *59*, 5414.
(608) Li, K. W.; Wu, J.; Xing, W.; Simon, J. A. *J. Am. Chem. Soc.* **1996**, *118*, 7237.
(609) Chen, Y.; Gambs, C.; Abe, Y.; Wentworth, P., Jr.; Janda, K. D. *J. Org. Chem.* **2003**, *68*, 8902.
(610) Liao, X.; Wu, Y.; De Brabander, J. K. *Angew. Chem., Int. Ed.* **2003**, *42*, 1648.
(611) McNulty, J.; Capretta, A.; Laritchev, V.; Dyck, J.; Robertson, A. J. *J. Org. Chem.* **2003**, *68*, 1597.
(612) Ahn, C.; Correia, R.; DeShong, P. *J. Org. Chem.* **2002**, *67*, 1751.
(613) Camp, D.; Jenkins, I. D. *J. Org. Chem.* **1989**, *54*, 3049.
(614) Vorbrueggen, H.; Krolikiewicz, K. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 914.
(615) Shishido, K.; Tanaka, K.; Fukumoto, K.; Kametani, T. *Chem. Pharm. Bull.* **1985**, *33*, 532.
(616) Hunsdiecker, H.; Erlbach, H. *Chem. Ber.* **1947**, *80*, 129.
(617) Kruizinga, W. H.; Kellogg, R. M. *J. Am. Chem. Soc.* **1981**, *103*, 5183.
(618) Talma, A. G.; Jouin, P.; De Vries, J. G.; Troostwijk, C. B.; Buning, G. H. W.; Waninge, J. K.; Visscher, J.; Kellogg, R. M. *J. Am. Chem. Soc.* **1985**, *107*, 3981.
(619) Davies, A. G.; Davies, M.; Stoll, M. *Helv. Chim. Acta* **1954**, *37*, 1351.
(620) Galli, C.; Mandolini, L. *J. Org. Chem.* **1991**, *56*, 3045.
(621) Shono, T.; Ishige, O.; Uyama, H.; Kashimura, S. *J. Org. Chem.* **1986**, *51*, 546.
(622) Sattler, A.; Haufe, G. *Tetrahedron* **1996**, *52*, 5469.
(623) Mironov, V. F.; Fedotov, N. S. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1972**, *8*, 676.
(624) Karim, M. R.; Sampson, P. *Tetrahedron Lett.* **1988**, *29*, 6897.
(625) Karim, M. R.; Sampson, P. *J. Org. Chem.* **1990**, *55*, 598.
(626) Rodefeld, L.; Heinemann, I.; Tochtermann, W. *Tetrahedron* **1998**, *54*, 5265.
(627) Kruizinga, W. H.; Kingman, R.; Leegstra, L.; Rokaszewski, E.; Gruppen, G.; Kellogg, R. M. *J. Chem. Soc., Chem. Commun.* **1990**, 1647.
(628) Sato, T.; Kawara, T.; Kokubu, Y.; Fujisawa, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 945.
(629) Sanz, V.; Seoane, E. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1837.
(630) Chai, K. B.; Sampson, P. *J. Org. Chem.* **1993**, *58*, 6807.
(631) Borgschulte, K.; Trowitzsch-Kienast, W.; Hoefle, G. *Liebigs Ann. Chem.* **1990**, 69.
(632) Bartra, M.; Vilarrasa, J. *J. Org. Chem.* **1991**, *56*, 5132.
(633) Evans, D. A.; Hu, E.; Burch, J. D.; Jaeschke, G. *J. Am. Chem. Soc.* **2002**, *124*, 5654.
(634) Vedejs, E.; Larsen, S. D. *J. Am. Chem. Soc.* **1984**, *106*, 3030.
(635) White, J. D.; Amedio, J. C., Jr.; Gut, S.; Ohira, S.; Jayasinghe, L. R. *J. Org. Chem.* **1992**, *57*, 2270.
(636) Matsuyama, H.; Nakamura, T.; Kamigata, N. *J. Org. Chem.* **1989**, *54*, 5218.
(637) Ranganathan, S.; Muraleedharan, K. M.; Vaish, N. K.; Jayaraman, N. *Tetrahedron* **2004**, *60*, 5273.
(638) Rousseau, G.; Homsi, F. *Chem. Soc. Rev.* **1997**, *26*, 453.
(639) Simonot, B.; Rousseau, G. *Tetrahedron Lett.* **1993**, *34*, 4527.
(640) Simonot, B.; Rousseau, G. *J. Org. Chem.* **1994**, *59*, 5912.
(641) Roux, M.-C.; Paugam, R.; Rousseau, G. *J. Org. Chem.* **2001**, *66*, 4304.
(642) Simonot, B.; Rousseau, G. *J. Org. Chem.* **1993**, *58*, 4.
(643) Homsi, F.; Rousseau, G. *J. Org. Chem.* **1998**, *63*, 5255.
(644) Rousseau, G.; Strzalko, T.; Roux, M.-C. *Tetrahedron Lett.* **2004**, *45*, 4503.
(645) Nicolaou, K. C.; Seitz, S. P.; Sipio, W. J.; Blount, J. F. *J. Am. Chem. Soc.* **1979**, *101*, 3884.
(646) Nicolaou, K. C.; Claremon, D. A.; Barnette, W. E.; Seitz, S. P. *J. Am. Chem. Soc.* **1979**, *101*, 3704.
(647) Hoye, T. R.; Hu, M. *J. Am. Chem. Soc.* **2003**, *125*, 9576.
(648) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557.

CR0301402