<http://www.diva-portal.org>

Postprint

This is the accepted version of a paper published in *Natural product reports (Print)*. This paper has been peer-reviewed but does not include the final publisher proof-corrections or journal pagination.

Citation for the original published paper (version of record):

Silva, L., Olofsson, B. (2011)

Hypervalent iodine reagents in the total synthesis of natural products.

Natural product reports (Print), 28(10): 1722-1754

<http://dx.doi.org/10.1039/c1np00028d>

Access to the published version may require subscription.

N.B. When citing this work, cite the original published paper.

Permanent link to this version:

<http://urn.kb.se/resolve?urn=urn:nbn:se:su:diva-66849>

Hypervalent Iodine Reagents in the Total Synthesis of Natural Products[†]

Luiz F. Silva, Jr. ^{‡*} and Berit Olofsson[#]

[‡] Departamento de Química Fundamental, Instituto de Química, Universidade de São Paulo, CP 26077, CEP 05513-970 São Paulo SP, Brazil

[#] *Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-106 91 Stockholm, Sweden*

e-mail: luizfsjr@iq.usp.br

Tel: +5511-3091-2388

Fax: +5511-3815-5579

Keywords: total synthesis, hypervalent iodine, oxidation, natural products

---

[†] Dedicated with deep respect to Prof. Dr. R. A. Pilli.

Contents

1. INTRODUCTION	3
1.1. STRUCTURE AND REACTIVITY OF HYPERVALENT IODINE REAGENTS	4
2. OXIDATION OF ALCOHOLS	5
2.1. OXIDATIONS USING DMP	5
2.2. OXIDATIONS USING IBX	16
2.3. OXIDATIONS USING DIB/NITROXYL RADICAL.....	23
3. REACTIONS OF PHENOLS AND PHENOL ETHERS	29
3.1. OXIDATIVE DEAROMATIZATION OF PHENOLS	29
3.2. OXIDATIVE COUPLING REACTIONS	37
3.3. OXIDATIVE TRANSFORMATIONS OF PHENOL ETHERS	40
4. TRANSFORMATION OF CARBONYL COMPOUNDS	42
4.1. DEHYDROGENATION OF KETONES	42
4.2. α -FUNCTIONALIZATION OF CARBONYL COMPOUNDS	46
5. TRANSFORMATION OF OTHER FUNCTIONAL GROUPS.....	50
5.1. TRANSFORMATIONS OF NITROGEN-CONTAINING COMPOUNDS	50
5.2. DEPROTECTION OF DITHIANES	56
5.3. OXIDATIONS VIA OXYGEN RADICALS	62
5.4. OXIDATION OF BENZYL BROMIDES	64
6. REARRANGEMENTS AND FRAGMENTATIONS.....	65
6.1. HOFMANN-TYPE REARRANGEMENT.....	65
6.2. REARRANGEMENT OF ALKENES.....	68
6.3. FRAGMENTATIONS.....	71
7. REACTIONS WITH IODONIUM SALTS.....	73
7.1. α -ARYLATION WITH DIARYLIODONIUM SALTS.....	73
7.2. ARYLATION OF PHENOLS WITH DIARYLIODONIUM SALTS.....	75
7.3. TRANSFORMATIONS WITH ALKYNILIODONIUM SALTS	76
8. CONCLUSIONS	78
ACKNOWLEDGMENT	79
REFERENCES AND NOTES	79

1. Introduction

The total synthesis of biologically active natural products has a central role in science.¹⁻²⁰ Presently, nearly any highly complex target can be obtained through chemical synthesis, providing enough resources are available. However, many advances are still necessary to furnish the required molecule in the desired quantity and short time without generation of toxic waste.^{2,5-8,11,14,18,21} Hypervalent iodine reagents are particularly important in this scenario, as they are efficient alternatives to toxic and expensive heavy metals for a large range of transformations.

Iodine(V) reagents, e.g. Dess-Martin periodinane (DMP) and 2-iodoxybenzoic acid (IBX), mediate the oxidation of alcohols to aldehydes under mild conditions, as well as various oxidative transformations of other functional groups (Figure 1). Iodine(III) compounds with two heteroatom ligands, e.g. (diacetoxyiodo)benzene (DIB) and hydroxy(tosyloxy)iodo]benzene (HTIB), react with alkenes and phenols, and are also employed in α -functionalization of carbonyl compounds and several rearrangement reactions. Iodine(III) reagents with two carbon ligands, e.g. diaryliodonium salts, are mainly employed in C-C bond formation reactions by transfer of one of the carbon ligands.

Hypervalent Iodine(V) Reagents:

Dess-Martin Periodinane
DMP

2-Iodoxybenzoic acid
IBX

Hypervalent Iodine(III) Reagents:

(Diacetoxy)iodobenzene
Phenyliodine(III) diacetate
DIB, PIDA, BAIB

[Bis(trifluoroacetoxy)]iodobenzene
Phenyliodine(III) bis(trifluoroacetate)
BTI, PIFA

[Hydroxy(tosyloxy)iodo]benzene
HTIB, HTI, Koser's Reagent

Diaryl-I³-iodane
Diaryliodonium salt

Figure 1. Commonly used hypervalent iodine reagents and their acronyms.²²

The chemistry of hypervalent iodine compounds has been reviewed several times in the last years.²³⁻⁶⁸ However, there is no broad and recent review on applications in the total synthesis of natural products.⁶⁹ This review aims to illustrate recent applications of hypervalent iodine compounds in the total synthesis of natural products, giving a panorama of the most important reactions in this area. Due to the vast amount of literature available on this topic, the review is not comprehensive, and focuses mainly on syntheses published in 2008-2010.

1.1. Structure and Reactivity of Hypervalent Iodine Reagents

Hypervalent iodine(III) compounds have a T-shaped structure, where the aryl group and the two free electron pairs are in equatorial positions. The two ligands have apical positions (Figure 2a) and share a hypervalent bond (3 center-4 electron bond) with the iodine. Iodine(V) compounds have four ligands and two orthogonal hypervalent bonds (Figure 2b). The non-bonding orbital of the hypervalent bond has a node on iodine (Figure 2c), which distributes the electrons to the ligands and renders the iodine electrophilic.²³

Figure 2. Shape of hypervalent iodine reagents and orbitals in the hypervalent bond.

Thus, hypervalent iodine reagents generally react with various nucleophiles by initial Nu-I bond formation with release of one of the ligands (Scheme 1). Subsequent reductive elimination by ligand coupling, or nucleophilic substitution by the free ligand anion, yields the product Nu-L and

releases ArI. The mechanism for this process depends on the nucleophile, the nature of the ligand and the reaction conditions.²³ Hypervalent iodine reagents are also good one electron acceptors, and SET mechanisms are observed under certain reaction conditions.²³

Scheme 1

Hypervalent iodine reagents are very reactive due to their highly electron deficient nature and the facile reductive transformations involved in their reactions with nucleophiles ($\text{Ar-IL}_2 \rightarrow \text{ArI}$ or $\text{Ar-IL}_4 \rightarrow \text{Ar-IL}_2$). The leaving group ability of iodine(III) compounds is 10^6 times higher than that of triflate, and they can be therefore classified as hypernucleofuges.²³

2. Oxidation of Alcohols

The oxidation of alcohols to aldehydes or ketones is a pivotal transformation in organic chemistry and hypervalent iodine reagents play an important role in this reaction.^{49,67} The iodine(V) reagents DMP and IBX are among the best reagents for this functional group transformation in complex molecules. The combination of the iodine(III) reagent DIB and a nitroxyl radical is also a powerful method.

2.1. Oxidations using DMP

DMP is the most common hypervalent reagent for the oxidation of alcohols.⁷⁰⁻⁷³ It is moisture sensitive and should be handled and stored under anhydrous atmosphere.⁷⁰ DMP does not appear to be impact sensitive but explodes violently when heated, thus limiting its use to small scale reactions.⁷⁴ The first step in DMP-oxidations is the displacement of an acetate group by the

alcohol. The α -proton of the alcohol is subsequently removed by acetate (internal or external) to form the desired carbonyl compound together with an iodine(III) side product (**Scheme 2**).

Scheme 2

Oxidations using DMP are typically performed in dichloromethane. NaHCO_3 or pyridine is often added to trap the acid released in the oxidation. This reaction tolerates a wide range of functional and protecting groups (**Table 1** and **Table 2**). During the synthesis of (–)-biyouyanagin A, the oxidation of an alcohol bearing an α -diazo- β -ketoester moiety was reported (**Scheme 3**).^{75,76} Another example is the oxidation of an alcohol possessing an enol ether functionality, as described by Deslommchamps in the total synthesis of (+)-cassaine (**Scheme 4**).^{77,78} The oxidation of a complex substrate bearing a primary alcohol has been described by Hiram and co-workers (**Scheme 5**).⁷⁹

Table 1. Examples of Functional Groups in Oxidations with DMP.

Entry	Conditions	Functional Groups
1	DMP, CH_2Cl_2	alkenes, ⁸⁰⁻⁹⁸ dienes, ^{91,92,97,99-103} alkynes, ^{87,96,104,105} ethers, ^{90,92,94,98,101,106-} ¹¹⁴ secondary allylic alcohols, ¹¹⁵ tertiary alcohols, ^{83,94,106,116-120} ketones, ^{107,111} esters, ^{94,95,101,112,113,117,120-122} carbamates, ^{88,123} lactones, ^{84,87,109,119,124} α,β -unsaturated ketones, ^{92,125,126} α,β -

		unsaturated esters, ^{90-92,117,119,126} α,β -unsaturated lactones, ^{85,87,89,102,103} lactams, ¹²⁷ <i>t</i> -butyl thioesters, ¹²⁸ α -diazo- β -ketoesters, ^{75,76} boronic esters, ¹²⁹ halides (aliphatic, ^{88,94} vinylic, ^{78,89,91,114,121,122} and aryl ¹⁰⁸), azides, ^{105,112,113,130} tertiary amines, ^{86,112,120} furanes, ⁸⁷ phosphonates, ^{91,110} acetals, ^{77,80,81,85,100,105,106,109,116,130-134} epoxides, ^{79,104,116,119,135-139} sulfoxides, ^{107,140} enol ethers ⁹⁰ (OTf, ^{77,78} OTBS, ¹⁴¹ and OTIPS ¹⁴²), indoles, ¹²⁰ and guanidines. ¹²³
2	DMP, CH ₂ Cl ₂ , NaHCO ₃	alkenes, ¹⁴³⁻¹⁴⁹ dienes, ^{144,145} alkynes, ^{105,145} ethers, ^{143,146,147,150,151} secondary ¹⁵¹ and tertiary ¹⁵² alcohols, phenols, ¹⁵³ tertiary iodides, ¹⁵⁴ vinyl iodides, ^{143,145} vinyl chlorides, ¹⁴³ ketones, ¹⁵³ α,β -unsaturated ketones, ^{150,153} esters, ¹⁴³⁻¹⁴⁵ α,β -unsaturated esters, ¹⁴⁵ lactones, ^{143,147,148} epoxides, ^{79,155-157} acetals, ^{105,146,155,158,159} and oxazolidinones. ¹⁴⁹
3	DMP, CH ₂ Cl ₂ , pyr	alkenes, ^{81,84,92,106,160-165} dienes, ^{92,166} alkynes, ¹⁶⁰ tertiary alcohols, ¹⁰⁶ ethers, ^{92,94,161,162,164,166,167} aldehydes, ⁹² α,β -unsaturated ketones, ⁹² esters, ^{98,166} α -hydroxy esters, ¹⁶⁸ amides, ¹⁶⁶ lactones, ¹⁶¹ α,β - unsaturated lactones, ^{92,165} macrolactones, ¹¹⁴ lactams, ¹⁶⁸ carbamates, ⁹⁸ amines, ¹⁶⁸ alkyl halides, ⁹⁴ phosphates, ¹⁶⁵ azides, ¹⁶⁵ acetals, ^{81,88,106,160} sulfides, ⁸¹ and epoxides. ⁸⁴

Table 2. Examples of Protecting Groups in Oxidations with DMP.

Entry	Conditions	Protecting Groups
1	DMP, CH ₂ Cl ₂	ROTBS, ^{77,83,85,89-93,96,97,100,101,103,104,112,121,122,125,126,133,134,139,158,169-177} ROTES, ^{95,101,104,170,178} ROTIPS, ^{87,90,94,106,111,114,132,179-182} ROBDPS, ^{78,101,104,114,116,183} ROAc, ^{95,113,115,138,173,184} ROiPr, ^{90,93,185} ROBz, ^{90,94,123,170} ROCO ₂ Me, ¹⁸⁶ ROCONH ₂ , ¹⁷⁶ ROMOM, ^{78,105,107,169,183,187} ROMEM, ⁸³

		ROPMB, ^{77,85,90,91,94,96,97,104,110,132,137,187-190} ROEE, ⁹³ ROBOM, ^{111,182} ROMPM, ^{114,115,118,183} ROBn, ^{80,90,104,106,110,124,191,192} ROTr, ¹⁸⁰ ROME, ^{94,101,107,113,192} RONPhth, ⁸⁸ RON=CMe ₂ , ⁸⁸ ArOAllyl, ¹⁹³ ArOMe, ^{108,130,131,192,194,195} ArOBn, ^{127,131} ArOTBS, ¹⁷⁴ R ₂ NBoc, ^{174,194-197} R ₂ NFmoc, ¹⁷⁴ R ₂ NCO ₂ Me, ^{86,198} R ₂ NPMB, ⁸⁰ R ₂ N- Teoc, ⁸¹ and R ₂ NNNs. ¹²⁷
2	DMP, CH ₂ Cl ₂ , NaHCO ₃	ROTBS, ^{79,84,105,143,145-147,152,155,157-159,172,175,179,199,200} ROTES, ^{79,84,142,147,159,200} ROTBDPS, ^{105,142,145,147} ROTIPS, ^{146,158,179,180,201,202} ROPMB, ^{77,142,145,149,152,156,158,159,200} ROME, ^{84,146,159,200} ROBn, ^{150,159,199} ROAllyl, ²⁰¹ ROMOM, ^{79,82,105,144,145,203} ROAc, ^{143,204} RODMPM, ⁸⁴ ROSEM, ^{84,146} ROCONH ₂ , ^{144,145} ArOMe, ^{105,205-} ²⁰⁷ ArOBn, ¹⁹⁹ ArOMOM, ²⁰⁶ R ₂ NBoc, ^{82,148,204} and R ₂ NTs. ¹⁴¹
3	DMP, CH ₂ Cl ₂ , pyr	ROTMS, ^{165,167} ROTBS, ^{84,94,160,166} ROTES, ^{81,84,160,166} ROTBDPS, ^{81,84,94,160} ROTIPS, ^{81,94,165} ROME, ^{84,166} ArOMe, ¹⁶⁸ ROBn, ^{106,160} ROPMB, ^{81,84,165} ROAlloc, ⁸⁴ ROBec, ⁸⁴ ROMOM, ^{106,168} silyl acetal, ¹⁶⁷ and R ₂ NBoc. ⁹⁸

Bec: 2-bromoethyl carbonate, EE: ethoxyethyl acetal

Scheme 3

Scheme 4

Scheme 5

Although DMP tolerates several functional groups, Grieco and Piñeiro-Nuñez reported that the oxidation of a hydroxy carboxylate intermediate (formed by ring opening the corresponding lactone) was best performed with the less popular fluorinated iodine(V) compound.²⁰⁸ This IBX analogue generates only water during the oxidation, while DMP releases acetic acid. When DMP was applied the required keto ester was obtained in only 60%, with 40% of the starting lactone recovered (**Scheme 6**).

Scheme 6

In the inspiring review by Nicolaou and Baran about the synthesis of CP molecules, examples of DMP oxidations are discussed.²⁰⁹ A key issue in this synthesis was the preparation of a γ -hydroxylactol, which could only be performed under relatively harsh conditions, i.e. with 5 equiv of DMP in benzene at 80 °C (**Scheme 7**).^{210,211}

Scheme 7

An important feature of DMP oxidations using is the possibility to prepare aldehydes and ketones bearing an α -stereocenter without epimerization or racemization (DMP/CH₂Cl₂,^{91,93,97,98,103,114,121,123,132,137,159,174,184,185,188,192,195,198} DMP/CH₂Cl₂/NaHCO₃,^{142,146,147,149,152,159} and DMP/CH₂Cl₂/pyridine^{88,94,102,161,165,166,212}). This was exemplified in the oxidation of a diol to the corresponding dicarbonylic derivative in the synthesis of (+)-peloruside A (**Scheme 8**).²¹² Another example was reported by Dai and co-workers, who formed a ketone bearing stereocenters on both α -carbonyl positions in the synthesis of amphidinolide T2 (**Scheme 9**).¹⁴⁷ Analogous examples have been reported in the synthesis of (–)-callystatin A¹⁰² and nakiterpiosin. In the latter case the reaction was performed in the presence of H₂O (**Scheme 10**).^{213,214} Water has also been used in other total syntheses using DMP in CH₂Cl₂,^{97,121,122,215} because it accelerates the reaction.⁷³

Scheme 8

Scheme 9

Scheme 10

Treatment of diols with excess DMP leads to the corresponding dicarbonylic derivatives, as reported in the synthesis of (+)-clavolonine (3 equiv DMP, CH₂Cl₂, rt, 2 h),¹¹³ auriopyrones A and B (4 equiv DMP, CH₂Cl₂, rt, 20 min),¹²⁶ echinopines A and B (4 equiv DMP, 16 equiv NaHCO₃, CH₂Cl₂, 25 °C, 2 h),¹⁵² and cylindrocyclophane A (5 equiv DMP, 10 equiv NaHCO₃, CH₂Cl₂, 23 °C, 1 h).²⁰⁷ However, the oxidation of substrates bearing two or more alcohol moieties can be performed chemoselectively. Some recent examples reported in the context of total synthesis are shown herein. In one of the last steps of the total synthesis of (+)-azaspiracid-1, the chemoselective oxidation of a primary alcohol in the presence of a secondary was performed at 0 °C with a large excess of oxidant (**Scheme 11**). The low temperature is critical in this transformation, because at room temperature the C20 secondary alcohol is also oxidized.⁸¹ Another selective oxidation of a primary alcohol is given in studies toward the synthesis of azithromycin (**Scheme 12**).¹⁸⁶ During the synthesis of (–)-englerin A, the chemoselective oxidation of a secondary alcohol was achieved in the presence of a more hindered one (**Scheme 13**).¹⁵¹

Scheme 11

Scheme 12

Scheme 13

2.2. Oxidations using IBX

IBX is another hypervalent iodine reagent highly used in the oxidation of alcohols.⁶⁶ The first step in these oxidation reactions is a fast pre-equilibrium, which can be formally considered as a ligand exchange process (hydroxy $\pm$ alkyloxy) on the iodine atom. A hypervalent twist, which is considered the rate limiting step, then takes place. Finally, the intermediate disproportionates to the carbonyl derivative and the iodosoarene IBA (**Scheme 14**).^{67,216} The preparation and application of polymer-supported IBX in oxidation reactions has been described.^{217,218} IBX immobilized in the ionic liquid [bmim][Br] was used in the oxidation of alcohols and in the dehydrogenation of ketones (cf. section 4.1).²¹⁹

Scheme 14

Although IBX was first synthesized in 1893, its use in synthetic organic chemistry has intensified only in the last two decades.²²⁰⁻²²³ IBX is cheaper and more stable than DMP, but it is explosive (on heating > 200 °C and on impact)^{66,224} and light-sensitive.²²⁵ Several functional and protecting groups are tolerated in IBX oxidations (**Table 3**). However, during the total synthesis of baconipyrone C, the elimination of a pivaloate protecting group and hydrolysis of an acetal has been observed (cf. **Scheme 80**).²²⁶

Table 3. Examples of Functional and Protecting Groups in IBX-Oxidations.

Functional Groups	alkenes, ^{92,151,172,194,227-238} alkynes, ¹⁵¹ dienes, ¹⁷¹ secondary ²¹⁵ and tertiary ^{227,229} alcohols, phenols, ²³⁹ ethers, ^{92,227,231} acetals, ^{172,226,227,231,234,239} sulfides, ²²⁶ dithianes, ²²⁶ azides, ²⁴⁰ aliphatic and aromatic halides, ^{131,240} vinylic halides, ²¹⁵ guanidines, ²⁴⁰ ketones bearing an α -stereocenter, ²²⁶ enones, ²²⁶ esters, ^{241,242} lactones, ^{232,236} lactams, ²⁴³ and heterocyclic aromatic rings. ²³³
Protecting Groups	ROTBS, ^{125,171,172,194,231} ROTIPS, ^{231,238} ROTES, ²²⁶ ROBn, ^{226,231,242,244} ROTHp, ¹⁷¹ ROMOM, ^{226,239} ROPMB, ^{172,229} ROAc, ²¹⁵ ROPiv, ^{92,226} ArOMe, ^{194,230,232,233,236,239,241,242} ArOBn, ^{131,242} ArOAllyl, ¹²⁵ ArOMOM, ^{131,233} ArOAc, ²³² methylenedioxy ^{131,242} ArOEOM, ²⁴¹ and R ₂ NBoc. ^{194,229,243}

EOM: ethoxymethyl

IBX is not soluble in many organic solvents and the typical oxidation takes place in DMSO at room temperature.²²⁰⁻²²³ However, the oxidation of alcohols with IBX has been described using other procedures. Some examples in the total synthesis of natural products are:

i) The oxidation of a chiral primary alcohol with IBX in DMSO in the presence of 4Å molecular sieves at room temperature gave an aldehyde bearing an α -stereocenter,²⁴⁵

ii) Ethyl acetate is an alternative solvent for IBX oxidations when reactions are performed at reflux. The oxidation of a primary alcohol has been described using 2 equivalents of IBX in EtOAc at reflux for 2 h.¹⁷² In the synthesis of pluraflavin A by Danishefsky and his group, a secondary alcohol was also oxidized with 3.5 equivalents of IBX in EtOAc; the mixture was capped under argon and heated at 90 °C for 6 h.²³⁹ The preparation of a dialdehyde was achieved by the reaction of a *bis*-benzylic alcohol with 8.5 equivalents of IBX in EtOAc at reflux.²⁴² In the synthesis of all stereoisomers of phenetic acid B, the oxidation of a secondary alcohol was accomplished with 2 equivalents of IBX in refluxing EtOAc for 20 h.²³⁶ In the formal synthesis of palmerolide A, primary alcohols were oxidized to the corresponding aldehydes using 1.3 to 1.5 equiv of IBX at reflux in EtOAc for 6 h. The crude aldehydes were used in Wittig or Horner-Wadsworth-Emmons

reactions.²⁴⁶ The oxidation of a primary allylic alcohol was reported using 2.5 equiv of IBX in refluxing EtOAc for 4 h during the total synthesis of (–)-englerin A.¹⁵¹

iii) A mixture of DMSO with another solvent was used in some examples. A 1:1 mixture of DMSO/THF was employed in the synthesis of (–)-amphidinolide K (**Scheme 15**).¹⁷¹ Another possible mixture is DMSO/CH₂Cl₂ (1:1), which was used in the oxidation of a secondary alcohol in the synthesis of ciguatoxin.²³¹ In the synthesis of (–)-erinacine E, a 1:4 mixture of DMSO/CH₂Cl₂ was employed.²²⁷ The oxidation of an allylic alcohol to the corresponding enone was performed with IBX in a 2:1 mixture of toluene/DMSO during the synthesis of (+)-chamaecypanone C by Porco.²³⁰

iv) The oxidation of an alcohol with IBX has been performed in refluxing benzene in a sealed pressure tube. In this case, an intramolecular conjugate addition took place after the formation of the enone moiety (**Scheme 16**).²⁴⁰

v) The transformation of a diol into the corresponding dialdehyde has been performed using 2.4 equiv of IBX in MeCN at 80 °C in the total synthesis of baconipyronone A, baconipyronone C, and siphonarin B (**Scheme 16**).²²⁶

Scheme 15

Scheme 16

Scheme 17

Like DMP, IBX has been used in the oxidation of chiral primary alcohols, which delivered aldehydes bearing an α -stereocenter without epimerization problems^{171,194,226,235,244} (**Scheme 15** and **Scheme 18**).²³⁴

Scheme 18

The oxidation of a secondary alcohol and an anisole moiety to the desired keto quinoide derivative has been described in 66% yield by Nicolaou, Chen and co-workers using excess of IBX in DMSO during the synthesis of (–)-hopeahainol A and (–)-hopeanol (**Scheme 19**).^{232,247} Reagents unable to perform this transformation included DMP, PCC, $\text{SO}_3 \cdot \text{py}$, DDQ, and CAN.²⁴⁷

Scheme 19

A popular way to prepare carboxylic acids from primary alcohols is the oxidation with DMP¹⁸⁹ or IBX^{171,172,233} to the corresponding aldehyde, which is then oxidized to the acid using NaClO₂ (Pinnick oxidation), as exemplified in the synthesis of (+)-azaspiracid-1 (**Scheme 11**) and (–)-penifulvin A (**Scheme 20**).²³⁵

Scheme 20

The oxidation of alcohols with IBX can be chemoselective. For example, after deprotection of an acetonide, an allylic alcohol was selectively oxidized with the unactivated alcohol untouched, giving the corresponding enone as product (**Scheme 21**).²¹⁵

Scheme 21

The oxidation of a diol to the corresponding diketone can be difficult. One recent example of this transformation has been described by Nicolaou and his group in studies toward the synthesis of vannusals A and B (cf. **Scheme 25**). Among the oxidants tested under different conditions (PCC, DMP and TPAP-NMO), only IBX in DMSO promoted the desired oxidation (**Scheme 22**).²⁴⁸

Scheme 22

The handling of IBX and of DMP requires caution, because these compounds and their derivatives may explode. Quideau and co-workers developed a formulation consisting of benzoic acid (22%), isophthalic acid (29%), and IBX (49%). This non-explosive white power formulation was denominated SIBX (Stabilized IBX) and is a safe alternative to IBX.²⁴⁹ During the total synthesis of wasabidenone B₁ (cf. **Scheme 40**), the same research group applied this commercially available reagent in the oxidation of a secondary alcohol, affording the desired optically active ketone without epimerization (**Scheme 23**).²⁵⁰

Scheme 23

In the presence of oxygen nucleophiles, the oxidation of primary alcohols with IBX can go until the carboxylic acid oxidation level.²⁵¹⁻²⁵³ This reaction has been performed with an benzaldehyde derivative and IBX in the presence of *N*-hydroxysuccinimide as nucleophile.²⁵⁴ However, this protocol was not successful in the synthesis of erythronolide A.²⁵⁵

2.3. Oxidations using DIB/nitroxyl radical

Besides the highly popular iodine(V) reagents DMP and IBX, the combination of the iodine(III) reagent DIB and a nitroxyl radical is a powerful method for the oxidation of alcohols.²⁵⁶⁻²⁵⁸ In the total synthesis of natural products, the most common nitroxyl radical is TEMPO,^{228,257,259-262} but AZADO²⁵⁸ and 1-Me-AZADO²⁵⁸ have also been employed (**Figure 3**). The function of DIB in this transformation is to oxidize the nitroxyl radical to the more reactive oxoammonium salt, which is the species that oxidizes the alcohol moiety. Additionally, DIB regenerates the *N*-hydroxylamine formed in the reaction back to the oxoammonium salt (**Scheme 24**).²⁵⁸

Figure 3. Structure of *N*-Oxides used in Oxidations with DIB.

Scheme 24

Considering that the main actor in the oxidation of DIB/TEMPO is the *N*-oxide, only a few examples of this reaction will be discussed herein. In the total synthesis of natural products, the most important application of the combination DIB/nitroxyl radical is the chemoselective oxidation of a primary alcohol in the presence of a secondary. This transformation was performed by the

Nicolaou group in the synthesis and structure revision of vannusals A and B.^{248,263} The oxidation was performed with DIB and three different nitroxyl radicals: a) 2 equiv of DIB, 0.1 equiv of AZADO, CH₂Cl₂; b) 2 equiv of DIB, 0.2 equiv of 1-Me-AZADO, CH₂Cl₂ (**Scheme 25**); c) 4 equiv of DIB, 2.0 equiv of TEMPO, CH₂Cl₂.^{264,265} Other recent examples of chemoselective oxidations using DIB/TEMPO were reported in the total synthesis of neopeltolide,²⁶⁶ brevetoxin A,^{90,267} spirastrellolide A methyl ester,¹⁵⁹ (+)-branimycin,²⁶⁸ monorhizopodin,¹⁰¹ pteridic acids A and B,²⁶⁹ and studies toward maitotoxin.¹⁰⁴

Scheme 25

A chemoselective oxidation of three secondary alcohols to the corresponding keto diol has been performed using DIB/TEMPO in the synthesis of bafilomycin A₁ reported by Kleinbeck and Carreira²⁷⁰ (**Scheme 26**). According to the authors, this is the first example of such remarkable transformation.

Scheme 26

The combination DIB/TEMPO is efficient in the transformation of diols into the corresponding lactones,²⁷¹ as illustrated in the total synthesis of brevetoxin A by Crimmins.^{90,267} The diol moiety is oxidized to the lactone, an aldehyde is formed from a primary alcohol, and the secondary alcohol is kept untouched (**Scheme 27**). Another example was reported during studies toward maitotoxin by Nicolaou.^{104,110} Furthermore, the oxidation system TEMPO/DIB was employed in the oxidative cyclization of a pair of diol epimers to the corresponding lactones in the synthesis of (–)-cyclopamine (**Scheme 28**).²⁷²

Scheme 27

Scheme 28

The combination of TEMPO/DIB has been used in the transformation of a primary alcohol to the corresponding carboxylic acid during the total synthesis of tryprostatins A and B (**Scheme 29**).²⁷³ TEMPO/DIB can also be employed in the oxidation of aldehydes to carboxylic acids (cf.

Scheme 104)

Scheme 29

3. Reactions of Phenols and Phenol Ethers

3.1. Oxidative Dearomatization of Phenols

Oxidative dearomatization of phenols is a powerful strategy in the synthesis of natural products, and hypervalent iodine reagents are frequently employed in this transformation. The reaction of 2- or 4-substituted phenols with DIB or PIFA in the presence of a nucleophile gives cyclohexadienones. Depending on the substitution pattern of the phenol and whether the nucleophilic attack occurs intra- or intermolecularly, 2,4- and 2,5-cyclohexadienones can be selectively obtained. The mechanistic possibilities for this transformation are depicted in **Scheme 30**, starting with the electrophilic attack of the iodine(III) on the phenolic oxygen. The intermediate iodane can either undergo dissociative formation of a stabilized cation before nucleophilic attack (a), be directly attacked by the nucleophile (b) or have the nucleophile internally delivered via ligand exchange and subsequent reductive elimination (c). Both substrate and reaction conditions will influence which of these paths will operate.²⁸

Scheme 30

There is a detailed review by Quideau and co-workers dedicated to the use of hypervalent iodine reagents in oxidative dearomatization of phenols in natural product synthesis,²⁸ and this topic is also covered in other articles.^{37,250,274-276} Thus, only a few recent applications illustrating the rich chemistry available, with intra- and intermolecular nucleophilic attack by heteroatom (O, N) and carbon (olefinic and aromatic) nucleophiles, will be given here.

In the synthesis of isotarins E and F, Pettus and co-workers utilized a PIFA-mediated spirocyclization to reach the requested lactone intermediate with modest diastereoselectivity, which could be improved to 12:1 by treatment with DBU (**Scheme 31**).²⁷⁷ The same group also described the oxidative ipso-cyclization of a nitro group toward the synthesis of spironitronates,²⁷⁸ and scyphostatin analogues.²⁷⁹

Scheme 31

Myers and co-workers recently reported the synthesis of cortistatins A, J, K, and L (cf. **Scheme 53**) from a common precursor, the oxabicyclic core of which was prepared by PIFA-mediated oxidative dearomatization of a phenol derivative. In this one-pot three-step process, an internal hydroxyl group acted as nucleophile (**Scheme 32**).¹¹² This strategy has previously been

employed in synthetic efforts towards the cortistatin family^{28,275} (cf. **Scheme 69** for another example).

Scheme 32

In studies toward the lomaiviticins A and B, the Nicloaou group synthesized the monomeric aglycon unit of the lomaivictins using two hypervalent iodine oxidation steps. First, a phenol moiety was oxidized with PIFA to the corresponding *p*-quinone. Then, three oxidations were performed in a single step using DMP: the secondary alcohol was oxidized to the corresponding ketone, the hydrazone was transformed into a diazo derivative, and the *bis*-(SEM)-protected aromatic system gave the quinine moiety (**Scheme 33**).²⁸⁰ The same group has employed PIFA with PMBOH as external nucleophile in an oxidative dearomatization toward (+)-sporolide B.¹⁹⁹ The preparation of 4-hydroxy dienones with DIB in MeCN/water has been reported in the synthesis of cleroidicins C, D, F²⁸¹ and in the formal synthesis of cortistatins.²⁸² Another example with an external oxygen nucleophile is given in **Scheme 54**, where a naphthol is transformed to the corresponding naphthoquinone ketal.²⁸³ A paraquinone is also formed as an intermediate in the synthesis of rubioncolin B reported by Trauner and co-workers.²⁸⁴ The use of DIB or PIFA in methanol results in formation of a 4,4-dimethoxycyclohexa-2,5-dienone. This transformation was utilized in the synthesis of starting material towards (–)-harveynone²⁸⁵ and the core structure of maoecrystal V.²³⁸

Scheme 33

Oxidative dearomatization with nitrogen nucleophiles has been more difficult to realize.³⁷ Ciufolini and co-workers found that sulfonamides and oxazolines could be employed in this transformation, which has been applied to the total synthesis of several natural products.^{286,287} A tandem oxidative amidation/intramolecular Diels-Alder reaction was devised for an approach to the himandrine core (**Scheme 34**).²⁸⁸

Scheme 34

Kita and co-workers have developed the intramolecular PIFA-mediated spirocyclization with carbon nucleophiles and applied it to several syntheses of the discorhabdin natural product family.^{289,290} A recent application is shown in **Scheme 35**, where PIFA is activated by montmorillonite K10 and the reaction is performed in 2,2,2-trifluoroethanol (TFE). The obtained spirocyclohexadienones were converted to oxa analogues of discorhabdin A.²⁹¹

Scheme 35

Solid-supported iodine(III) reagents have been developed to simplify removal of the PhI formed as a side product.^{31,56} In an elegant total synthesis of both enantiomers of plicamine, Ley and co-workers used solid-supported reagents in all the steps.^{292,293} Polymer-supported DIB (PS-DIB) in TFE was employed in the oxidative coupling of a phenol using an internal aryl nucleophile (**Scheme 36**).^{293,294}

Scheme 36

A formal total synthesis of (–)-platensimycin was described by Canesi's group, where the key transformation is a tandem Prins-pinacol process. This reaction took place upon treatment of an unsaturated phenol with DIB, and the oxonium intermediate was captured with H_2O_2 to yield the hydroperoxyketal shown in **Scheme 37**.²⁹⁵ Another oxidative Prins transformation was reported with an alkyne substituent, leading to the core structure of hispidospermidin.²⁹⁶

Scheme 37

The use of an external carbon nucleophile in dearomatization of phenols was developed by Quideau's group; both allyl silanes and silyl enol ethers could be employed.²⁹⁷ This reaction has

been applied in the total synthesis of ($\pm$)-aspidospermidine,²⁹⁸ and an intramolecular version was utilized in the synthesis of platensimycin.²⁹⁹

Oxidative functionalization of phenols in the *ortho* position leads to 2,4-cyclohexadienones, which are often employed in subsequent Diels-Alder reactions.²⁸ In the racemic synthesis of subereamollines A and B, Ley and co-workers used DIB to create a spiroisoxazoline from the corresponding oxime, as depicted in **Scheme 38**.³⁰⁰ An intramolecular *ortho*-functionalization was achieved with PIFA in TFE in Moon's racemic synthesis of the cripowellin skeleton.³⁰¹

Scheme 38

Phenols can be oxidized to the corresponding *o*-quinones using IBX,³⁰² and phenols carrying an *o*-methoxy substituent deliver *o*-quinones by oxidative demethylation.^{249,303} This reaction has been employed in Lee's synthesis of kendomycin (**Scheme 39**), and later also in Miltzer's synthesis of the same target.²³³

Scheme 39

When the phenol is otherwise ortho-substituted, treatment with IBX leads to hydroxylative dearomatization. This is exemplified using SIBX (see section 2.2) in the synthesis of wasabidenone **B₁** (Scheme 40).²⁵⁰

Scheme 40

In the synthesis of azaphilones, Porco and co-workers developed an elegant cycloisomerization-oxidation sequence of *o*-alkynylbenzaldehydes. Gold(III) acetate was employed as Lewis acid in a very fast cyclization to the intermediate 2-benzopyrylium salt, which was oxidized

with IBX under phase-transfer conditions to the azaphilone (**Scheme 41**).³⁰⁴ This methodology was later employed in Boger's synthesis of clorofusin and its seven chromophore diastereomers.³⁰⁵

Scheme 41

3.2. Oxidative Coupling Reactions

The reactions discussed in this section are mechanistically similar to the oxidative dearomatization of phenols. When the nucleophilic attack on the iodine(III) intermediate occurs at an unsubstituted carbon of the phenol moiety (**Scheme 30**) subsequent prototropic rearomatization takes place and the dearomatization is thus only temporary.²⁸

Harran and co-workers employed this type of transformation as key step in their synthesis of (–)-diazonamide A. The advanced intermediate depicted in **Scheme 42**, containing both a phenol and an indole moiety, was cyclized by treatment with DIB and LiOAc in TFE. Following reaction of the phenol with DIB, intramolecular attack by the indole gave an iminium ion that subsequently acted as electrophile in the final oxacyclization to give the product in moderate yield as a 3:1 diastereomeric mixture.³⁰⁶

Scheme 42

Nicolaou and Chen performed an intermolecular version of this type of coupling with PIFA in the synthesis of (+)-haplophytine (**Scheme 43**).^{307,308} Although the reaction was low-yielding, excellent diastereoselectivity was observed and the starting material could be recycled and successively transformed into product. This type of indole coupling was also studied towards the synthesis of phalarine,³⁰⁹ and a similar indole-aniline coupling was investigated with HTIB in the synthesis of psychotrimine, although other reagents were chosen to complete the synthesis.³¹⁰

Scheme 43

In the formal synthesis of both enantiomers of phalarine, Chen and co-workers developed an oxidative double cyclization with PIFA. In this reaction, the phenol oxygen reacts with PIFA in the usual manner, followed by attack by the alkene onto the oxygen to form the cationic intermediate depicted in **Scheme 44**, and subsequent cyclization by the amide leads to the product.³¹¹

Scheme 44

3.3. Oxidative Transformations of Phenol Ethers

Iodine(III) reagents are good single electron transfer (SET) oxidants for electron-rich arenes in fluoroalcoholic solvents like TFE and HFIP (1,1,1,3,3,3-hexafluoro-2-propanol).^{312,313} Kita and co-workers studied the *ortho*-substitution of *para*-substituted phenol ethers with a range of nucleophiles, the mechanism of which proceeds via cation radicals (**Scheme 45**).³¹⁴

Scheme 45

PIFA was employed to dihydroxylate a phenol ether in the total synthesis of hypocrellin A (**Scheme 46**).³¹⁵ An analogous procedure was used in the synthesis of related natural products, where the authors pointed out that the reaction was sensitive to changes in the oxidation potential, thereby needing reoptimization for each substrate.²⁴²

Scheme 46

Arenes can also act as nucleophiles in this reaction, resulting in an oxidative biaryl coupling. This was demonstrated in the synthesis of *N*-acetylcolchinel by Kocienski and co-workers, where the coupling was followed by TBS deprotection in the workup (**Scheme 47**).³¹⁶ The reaction mechanism was thus suggested to proceed via a cation radical rather than through the oxidative coupling mechanism described in Section 2.4. In a synthesis of 1-dearyllamellarin D, Iwao and co-workers reported that a key PIFA-mediated cyclization of a pyrrole-containing phenol ether failed, and instead resulted in a decarbonylative cyclization.³¹⁷

Scheme 47

4. Transformation of Carbonyl Compounds

4.1. Dehydrogenation of Ketones

Nicolaou and co-workers described that IBX can be used in the formation of α,β -unsaturated carbonyl compounds by dehydrogenation of the corresponding carbonyl derivatives,^{318,319} probably through a single electron transfer (SET) mechanism.³¹⁹ This transformation has been applied in the total synthesis of many natural products, such as (+)-lepadin B (**Scheme 48**),³²⁰ (–)-minfiensine (**Scheme 49**),⁸⁶ oidiolendrolides,¹¹⁹ alkaloids (–)-GB 13 and (+)-GB 16,¹⁴⁸ and (–)-mersicarpine.³²¹ The reaction is usually performed with an excess of IBX in a mixture of toluene and DMSO, and is selective for ketones in the presence of lactones.¹⁴⁸

Scheme 48

Scheme 49

Toward the synthesis of pallavicinolide A, Dong and Wong performed the oxidation of a ketone to the corresponding enone using IBX in DMSO in the presence of PPTS³²² The enone thus formed participated in a Diels-Alder reaction giving the tetracyclic structure of the target molecule (**Scheme 50**). In the synthesis of (–)-anominine, Tosic acid was used with IBX in DMSO to promote the dehydrogenation of a cyclohexanone derivative.⁹⁵ A dehydrogenation has been described using IBX in MeCN in the presence of triflic acid in the route toward baconipyronone A, baconipyronone C, and siphonarin B.²²⁶

Scheme 50

During the total synthesis of ceratamines A and B, Coleman and his group described the application of IBX in the presence of pyridine for a double dehydrogenation, which led to the formation of an α,β -unsaturated lactam (**Scheme 51**).³²³ Treatment of tetrahydro- β -carboline with IBX in the presence of tetrabutylammonium bromide at room temperature resulted in aromatization. This reaction was applied in the total synthesis of eudistomin U.³²⁴

Scheme 51

The reactivity of IBX can be enhanced by complexation with *N*-oxides such as MPO (4-methoxypyridine-*N*-oxide) and, consequently, the dehydrogenation of carbonyl compounds can be performed at room temperature.²²⁵ Moreover, the same transformation can be achieved through a two step procedure, where a silyl enol ether is first obtained and subsequently oxidized with the

complex IBX•MPO (**Scheme 52**).³²⁵ An example of this reaction in an architecturally complex substrate has been reported in the total synthesis of (+)-cortistatin A (**Scheme 53**).^{155,157} Additionally, this methodology was applied in studies toward platensimycin,^{283,326,327} platencin,²³⁷ and cylindramide.²³⁷ When two isomeric α,β -unsaturated compounds can be formed, a mixture of isomers is usually obtained (**Scheme 54** and **Scheme 55**).^{219,237,283} Furthermore, there are reports describing that this reaction did not afford the desired unsaturated product.^{118,328}

Scheme 52

Scheme 53

Scheme 54

Scheme 55

4.2. α -Functionalization of Carbonyl Compounds

A series of papers from Moriarty and co-workers^{47,62,329-331} described that ketones can be converted into the corresponding α -hydroxy derivative by iodine(III). This transformation is sometimes called Moriarty's α -hydroxylation, and the most used conditions are DIB in KOH/MeOH.^{47,62,329} The mechanism is illustrated in **Scheme 56**. The reaction occurs by attack of an enolate to (dimethoxyiodo)benzene, which is formed *in situ* from DIB and MeOH, giving a hypervalent iodine intermediate. This reacts with methoxide, followed by intramolecular displacement of the iodine(III) to give an oxirane and PhI. Finally, ring opening by methoxide delivers an α -hydroxy ketal, which can be isolated or treated with acid to yield an α -hydroxy-ketone.

Scheme 56

Examples include the synthesis of (+)-bakkenolide A (**Scheme 73**)³³² and rubrolone aglycon.³³³ This α -hydroxylation can be stereoselective, as described in the synthesis of nakiterpiosinone (**Scheme 57**),²¹⁴ seragakinone A,³³⁴ (–)-7-deoxydaunomycinone,³³⁵ and formal total synthesis of (–)-cephalotaxine (**Scheme 58**).³³⁶

Scheme 57

Scheme 58

During the total synthesis of (±)-gelsemine, Overman and his group tried to α -oxidize a ketone using DIB under basic conditions, but the reaction led to unidentifiable products.^{337,338} Instead, they utilized a two step protocol also developed by Moriarty and co-workers,^{339,340} where a silyl enol ether was prepared and treated with iodine(III) in the presence of a Lewis acid in methanol to give the α -oxidized product (**Scheme 59**). An analogous protocol can be used to promote a α -sulfonyloxylation,³⁴¹ as reported in the synthesis of (+)-duloxetine.³⁴²

Scheme 59

Nagasawa and co-workers have developed an IBX-mediated α -hydroxylation of α -amino carbonyl compounds, which proceeds through formation of an enol-IBX intermediate that delivers the hydroxyl group intramolecularly, assisted by the nitrogen (**Scheme 60**).³⁴³ When this reaction was applied as the key step in the synthesis of (–)-decarbamyloxysaxitoxin,³⁴³ preparation of the starting ketone was performed by Swern oxidation, as a one-pot reaction with 4 equiv IBX gave the dehydrogenated ketone as by-product. The methodology was later applied also in the synthesis of (+)-dibromophakellin (**Scheme 61**).³⁴⁴

Scheme 60

Scheme 61

5. Transformation of Other Functional Groups

5.1. Transformations of Nitrogen-containing Compounds

Aziridinations and C-H aminations have been used in the total synthesis of several natural products.^{345,346} Although this reaction can be performed in several ways using iodine(III),^{51,347-349} the most used protocol in recent total synthesis is with a Rh(II) catalyst and the iodine(III) reagent DIB as oxidant. Under these conditions, a nitrene intermediate is formed.

In the synthesis of (–)-agelastatin by Wehn and Du Bois, the key aziridination step was performed with a dimeric Rh(II) catalyst (bis[rhodium($\alpha,\alpha,\alpha',\alpha'$ -tetramethyl-1,3-benzenedipropionic acid)]), Rh₂(esp)₂ in the presence of DIB (**Scheme 62**).³⁵⁰ Similar conditions have been used in the enantioselective synthesis of the core of banyaside, suomilide, and spumigin HKVV.³⁵¹ In the latter case, the aziridination was followed by ring opening mediated by a sulfonamide to construct the oxazolidinone ring (**Scheme 63**).³⁵¹ An analogous sequence was reported by Wardrop and co-workers in the synthesis of (+)-castanospermine, where a piperidine ring was obtained by the cyclization of an unsaturated amide promoted by PIFA in TFE/CHCl₃.³⁵² In the synthesis of (–)-oseltamivir,^{353,354} which is used in the treatment of influenza, Trost and Zhang^{355,356} used an aziridination step that was investigated in detail. The catalyst used was also Rh₂(esp)₂, however the best yield was obtained using PhI(OCO t -Bu)₂ as oxidant in chlorobenzene (**Scheme 64**).

Scheme 62

Scheme 63

Scheme 64

The amination of a pyrrole derivative under conditions analogous to those utilized in the aziridination allowed the construction of the cyclic guanidine moiety of (+)-gonyautoxin 3 (**Scheme 65**).¹²³ The enantioselective amination of silyl enol ethers using a chiral rhodium(II) catalyst has

been developed³⁵⁷ and applied in the formal total synthesis of (–)-metazocine³⁵⁸ and in the synthesis of (–)-ritodrine³⁵⁹ by Hashimoto and co-workers.

Scheme 65

The stereospecific C-H insertion of guanidines using DIB and Rh(II) has been investigated by Du Bois and co-workers,³⁶⁰⁻³⁶² including the application in the total synthesis of (–)-manzacidin A,³⁶³ (+)-manzacidin C,³⁶³ and (–)-tetradotoxin.³⁶⁴ The key step in the synthesis of (+)-phakellin and (+)-monobromophakellin is a C-H insertion of a guanidine derivative, which was performed also using DIB and MgO. However, the best result was obtained without the presence of a Rh(II) catalyst.³⁶⁵ An important feature in the mechanism suggested by Wang and Romo is the generation of an acyliminium ion, which is intramolecularly attacked by guanidine (**Scheme 66**).

Scheme 66

Feldman's group has developed an oxidative cyclization of an imidazole derivative using PhI(CN)OTf. The suggested mechanism is an extension of the Pummerer reaction, with initial oxidation of the sulfide followed by two cyclizations (**Scheme 67**). The reaction, which did not work with DIB or PIFA, was employed in the synthesis of (±)-dibromophakellstatin and (±)-dibromophakellin.^{366,367} In a different approach to the same target molecule, Austin and co-workers used hypervalent iodine in a diazidation reaction to introduce the vicinal nitrogen moiety as a diazide.³⁶⁸

54

Scheme 68

Ciufolini and co-workers recently developed the DIB-mediated oxidation of oximes to nitrile oxides, which were trapped *in situ* by alkenes.³⁷¹ This enabled a tandem oxidative phenol dearomatization (see section 3.1) and cycloaddition sequence,³⁷¹ which was applied in Sorensen's synthesis of the cortistatin core structure. The sequence started by intramolecular oxidative ether formation followed by oxidation to the nitrile oxide and [3+2] dipolar cycloaddition (**Scheme 69**).³⁷²

Scheme 69

One of the key steps in the synthesis of (+)-cephalostatin involves a selective allylic oxidation, where a methyl group is oxidized in the presence of three other allylic hydrogens. The reaction sequence starts by treatment with 4-phenyl-1,2,4-triazoline-3,5-dione, which selectively functionalizes the methyl group with the substituent shown in blue (**Scheme 70**). This group is oxidatively removed with DIB via N=N formation, tautomerization and hydrolysis, yielding the aldehyde.³⁷³

Scheme 70

5.2. Deprotection of Dithianes

Dithianes are highly used protecting groups for carbonyl compounds. In addition, these sulfur-containing compounds can be used in alkylation reactions. For many years, the deprotection of dithianes relied on the use of mercury(II) reagents. However, in 1989 Stork and Zhao³⁷⁴ reported that PIFA can be used in this transformation. This iodine(III) reagent has been used in an efficient manner during the total synthesis of several natural products, including cembranes (**Scheme 71**),²⁴⁵ (±)-uleine (**Scheme 72**),³⁷⁵ lyngbouilloside macrolactone core,³⁷⁶ peribysin E,³⁷⁷ (+)-bakkenolide A (**Scheme 73**),³³² and rapamycin.¹⁶⁶ The deprotection using PIFA can also be performed using an alcohol as solvent, directly delivering an acetal.³⁷⁴ This protocol has been used in studies toward brevetoxin A, using MeOH as solvent (**Scheme 74**).^{90,267}

Scheme 71

Scheme 72

Scheme 73

Scheme 74

In the total synthesis of (+)-aculeatin D, several reactions took place in the same operation using PIFA: oxidative dearomatization of the phenol, deprotection of the dithiane, and cyclization (**Scheme 74**).³⁷⁸

Scheme 75

In complex substrates, the acidic medium of the reaction using PIFA can lead to additional transformations. For example, in the synthesis of (–)-2-*epi*-peloruside A, the deprotection using PIFA led to the hydrolysis of the 1,3-dithiane, as well as deprotection of the isopropylidene group, giving eventually a hemiketal as final product (**Scheme 76**).³⁷⁹ In addition, the dethioacetalization mediated by PIFA gave low yield of the desired products in the synthesis of (+)-tedanolide (**Scheme 77**)¹⁴⁶ and on studies toward hexacyclinic acid (**Scheme 78**).⁸⁹ In the latter case, the transformation was accomplished using MeI/Ag₂CO₃ instead.

Scheme 76

Scheme 77

Scheme 78

In the early 2000's, Wu³⁸⁰ and Panek³⁸¹ described, respectively, that the iodine(V) reagents IBX and DMP can be used for the deprotection of dithianes. The IBX reaction was latter investigated in detail by Nicolaou,^{382,383} including an application in the synthesis of cortistatins.^{155,157} Using these reagents, the reaction medium is less acidic, which can be advantageous in certain

applications. For example, in the total synthesis of leucascandrolide A, Panek and co-workers observed the formation of alkene isomerization using PIFA, which did not take place using DMP (**Scheme 79**).^{384,385} However, in studies toward (+)-rimocidin, these iodine(V) reagents were not effective in the deprotection of dithianes.³⁸⁶ During the total synthesis of baconipyronone C, a mixture of aldol products was oxidized with IBX in DMSO, giving the corresponding diketone derivative. This was again treated with IBX, but in MeCN and in the presence of triflic acid to remove the dithiane and promote the formation of the pyrone ring. However, the undesired elimination of the pivaloate and hydrolysis of the acetal group was also observed (**Scheme 80**).²²⁶

Scheme 79

Scheme 80

For the IBX-mediated deprotection of dithianes, a mechanism has been suggested by Nicolaou and co-workers.³⁸³ The first step would be the reaction of the dithiane with IBX, leading to a sulfonium intermediate. From this intermediate, two pathways were proposed according to the structure of the sulfonium intermediate. For those without an α -hydrogen adjacent to the sulfonium cation, formation of a mixed thioacetal leads to the desired unmasked carbonyl compound. Alternatively, tautomerization could take place in the sulfonium intermediate when an α -hydrogen adjacent is present, subsequently giving the free carbonyl compound (**Scheme 81**). A different mechanism has been proposed for hindered dithianes lacking α -hydrogen.³⁸³

Scheme 81

5.3. Oxidations via Oxygen Radicals

Suárez and co-workers have developed several hypervalent iodine-mediated transformations of carbohydrates and other compounds that proceed via alkoxy radicals.^{387,388} Treatment of an alcohol with DIB and iodine or bromine under irradiation yields an alkyl hypohalite

intermediate, which upon homolysis gives an alkoxy radical (**Scheme 82**). Subsequent 1,5-hydrogen transfer delivers a carbon radical that is trapped to yield the halogenated alcohol or the corresponding ether.³⁸⁹

Scheme 82

The DIB/iodine reaction was applied to construct a tetrahydrofuranyl ether in the synthesis of theopederin D by Floreancig and co-workers.³⁹⁰ The bromination methodology has been applied as the key step in the synthesis of (+)-cortistatin A (cf. **Scheme 53**) by Baran and co-workers.³⁹¹ This impressive reaction, which is the first example of an alcohol-directed geminal dibromination of an unactivated methyl group, delivered the product in 57% yield after trapping the alcohol with TMSCl to avoid ether formation (**Scheme 83**).

Scheme 83

Amino acids can be decarboxylated by treatment with DIB and iodine via a radical mechanism similar to that in **Scheme 82**. After formation of a carboxyl radical, carbon dioxide is lost

and the corresponding carbon radical is oxidized to an *N*-acyliminium ion, which can be trapped by various nucleophiles.³⁹² A decarboxylation step in Danishefsky's synthesis of (–)-phalarine proved challenging, and several variants of radical-based decarboxylation were attempted. The most successful conditions employed DIB/I₂ with reduction of the *N*-acyliminium intermediate with NaCNBH₃ (**Scheme 84**).³⁹³

Scheme 84

5.4. Oxidation of Benzyl Bromides

IBX in DMSO promotes the oxidation of benzyl bromides to the corresponding carbonyl compound.³⁹⁴ According to the proposed mechanism, this transformation resembles the oxidation of alcohols. The first step is a nucleophilic substitution that releases HBr and a hypervalent intermediate (**Scheme 85**), which subsequently gives IBA and the desired carbonyl compound, as previously discussed (**Scheme 14**).

Scheme 85

This transformation was not successful in the synthesis of cyclo-mumbaistatin.³⁹⁵ However, Trauner and co-workers described the oxidation of an allylic bromide to the corresponding aldehyde upon heating with IBX in DMSO during the biomimetic synthesis of (+)-shimalactone A (**Scheme 86**).³⁹⁶

Scheme 86

6. Rearrangements and Fragmentations

6.1. Hofmann-Type Rearrangement

The treatment of aliphatic amides with iodine(III) gives the corresponding amines in a Hofmann-type rearrangement. This transformation has been described with DIB,³⁹⁷ PIFA,^{398,399} and HTIB.⁴⁰⁰ An important feature of this rearrangement is the retention of configuration of the migrating carbon. An analogous reaction was also reported for aromatic amides using DIB.⁴⁰¹ The procedure described by Loudon and co-workers using PIFA in aqueous acetonitrile appears to be the most commonly employed in total synthesis of natural products.³⁹⁸ Examples of applications are (±)-2-*epi*-validamine (**Scheme 87**),⁴⁰² pantocin B,^{403,404} and (–)-platensimide A (**Scheme 88**).²⁹⁹ An

application of this rearrangement in large scale has been reported using DIB. A lower yield was obtained when PIFA/pyridine was used (**Scheme 89**).³⁹⁷

Scheme 87

Scheme 88

Scheme 89

The following mechanism has been suggested for the PIFA-mediated Hofmann-type rearrangement.³⁹⁹ The first step is the formation of a dimer of PIFA (although the reaction could also take place by PIFA itself), on which the amide displaces one of the ligands to give a mixed dimer. Migration of the R group to the electron-deficient nitrogen then delivers an isocyanate, which gives the amine as a salt after hydrolysis (**Scheme 90**).

Scheme 90

Moriarty and co-workers developed a protocol where the amide is treated with DIB and KOH in methanol. Under these conditions, the intermediate isocyanate reacts with methanol, giving a methyl carbamate.⁴⁰⁵ This procedure has been applied in the total synthesis of (–)-epinephrine⁴⁰⁶ and of isoprekinamycin (**Scheme 91**).⁴⁰⁷ The reaction can also be performed in the presence of other alcohols than methanol. For example, allyl alcohol was used in the synthesis of (–)-oseltamivir phosphate (Tamiflu®) (**Scheme 92**).^{353,354,408,409} Furthermore, the intermediate isocyanate can be trapped by an internal hydroxyl group giving an oxazolidinone ring, as described in the synthesis of (–)-myriocin.⁴¹⁰

Scheme 91

Scheme 92

6.2. Rearrangement of Alkenes

Ring contraction is an important method to increase molecular complexity in a single step. Although the number of carbon-carbon bonds remain the same in these rearrangements, the reorganization of the bonds may occur with a high level of selectivity, affording products not easily accessible by other approaches.^{42,411,412} Ring contraction reactions can be effected by acids, bases, oxidants or by photochemical means.⁴¹² The ring contraction of 1-alkyl-1,2-dihydronaphthalenes mediated by iodine(III) is an efficient method to obtain *trans*-1,3-disubstituted indanes,^{413,414} representing an alternative to the analogous transformation mediated by thallium(III).⁴¹⁵⁻⁴¹⁷ The exclusive formation of *trans*-1,3-disubstituted indanes in the ring contractions in methanol can be explained by the mechanism detailed in **Scheme 93**. The electrophilic addition of HTIB to the double bond leads to an iodine(III) intermediate through a cyclic organoiodine. The approach of the electrophile occurs opposite to the remote methyl group,^{418,419} explaining the stereoselectivity of this ring contraction. The iodine(III) intermediate equilibrates to its more stable conformation, in which the required *anti*-periplanarity for the rearrangement is achieved. Migration of the aryl group (carbon 8a) displaces PhI to give an oxonium ion, which furnishes the *trans*-indane after addition of MeOH.

Scheme 93

This reaction has been applied in the total synthesis of (–)- and (+)-mutisianthol (**Scheme 94**)⁴²⁰ and (±)-indatraline (**Scheme 95**).⁴¹³ The synthesis of the latter target also features a Hofmann-type rearrangement. Iodine(III) was tested without success in the ring contraction step of the synthesis (±)-*trans*-trikentrin A. Eventually, the required rearrangement was performed using thallium(III).⁴²¹ Although in low yield and diastereoselectivity, an iodine(III)-promoted ring contraction of an optically octalone was mentioned in the total synthesis of (+)-bakkenolide A (cf. **Scheme 73**).³³²

Scheme 94

Scheme 95

Chalcones can undergo oxidative rearrangement in the presence of iodine(III) reagents. The reaction starts by addition of HTIB and MeOH to the alkene, followed by 1,2-aryl migration (**Scheme 96**).⁴²² This transformation has been employed as key step in the synthesis of (±)-pterocarpin,⁴²³ wightone and other isoflavone natural products,⁴²⁴ and using unprotected carbohydrate-substituted chalcones in the synthesis of genistein and orobol (**Scheme 97**).⁴²⁵

Scheme 96

Scheme 97

6.3. Fragmentations

Kita's group has reported a PIFA-mediated domino reaction of 2,3-epoxy alcohols, which leads to lactols by oxidative fragmentation and subsequent ring closure (**Scheme 98**). This reaction was applied in the synthesis of (+)-tanikolide.^{426,427}

Scheme 98

Kita and co-workers have developed an efficient synthesis of *N,O*-acetals by oxidative fragmentation of α -amino acids or β -amino alcohols. The reaction is believed to proceed via a five membered ring intermediate that fragments into an iminium ion.⁴²⁸ This methodology was applied in the total synthesis of both enantiomers of discorhabdin A, which also involved a PIFA-mediated spirodiene formation (**Scheme 99**).⁴²⁹

Scheme 99

Oxidative fragmentations have also been used in the synthesis of medium ring lactones,^{430,431} as demonstrated by Posner in the synthesis of (–)-phoracantholide J (**Scheme 72**).⁴³⁰

Scheme 100

7. Reactions with Iodonium Salts

Iodonium salts are iodine(III) compounds with two carbon ligands, one of which is a vinyl, alkynyl or aryl moiety and the other is usually a phenyl group (Figure 1). In reactions with nucleophiles, they transfer one of the carbon ligands through mechanisms that vary both with the type of salt and with the nucleophile.^{25,33,63}

7.1. α -Arylation with Diaryliodonium Salts

α -Arylated carbonyl subunits are commonly occurring in biologically active molecules. Introduction of aryl moieties to the α -position of carbonyl compounds usually involves Pd-catalyzed couplings at elevated temperature for prolonged reaction times, whereas methodology for asymmetric α -arylation is scarce.³³ Diaryliodonium salts have successfully been used in metal-free or metal-mediated α -arylations of various carbonyl compounds, including asymmetric transformations.^{33,432} The reaction entails nucleophilic attack of an enolate onto the iodonium salt, with subsequent transfer of one aryl moiety and elimination of PhI. The mechanistic studies of this reaction have recently been reviewed.²⁵

Gao and Portoghese utilized this methodology in the synthesis of 7-arylmorphinans to be tested on opioid receptors.⁴³³ Arylation of a highly substituted ketone using diphenyliodonium iodide

and LiHMDS diastereoselectively delivered the monophenylated product without scrambling of the existing α -stereocenter (**Scheme 101**).^{433,434}

Scheme 101

In the synthesis of tabersonine, Kozmin and Rawal arylated a silylenol ether in excellent yield using (2-nitrophenyl)phenyliodonium fluoride (**Scheme 102**).⁴³⁵ The electron deficient 2-nitrophenyl group was chemoselectively transferred in this mild and base-free arylation.

Scheme 102

In the first total synthesis employing an asymmetric α -arylation with diaryliodonium salts. Aggarwal and Olofsson used a chiral base to desymmetrize a 4-substituted cyclohexanone prior to arylation in a short synthesis of (–)-epibatidine (**Scheme 103**).⁴³⁶

Scheme 103

MacMillan and co workers recently combined the use of organocatalysis and diaryliodonium salts to obtain a highly enantioselective α -arylation of aldehydes.⁴³² The efficiency of this transformation was demonstrated in the rapid synthesis of (S)-ketoprofen, which also involved the TEMPO/DIB oxidation of the aldehyde to the corresponding carboxylic acid (**Scheme 104**).

Scheme 104

7.2. Arylation of Phenols with Diaryliodonium Salts

Diaryl ethers are common structures in natural products, and there are several methods available for their synthesis.⁴³⁷ Diaryliodonium salts are powerful electrophiles for a variety of heteroatom nucleophiles, including phenoxides.³³ The application to natural product synthesis has been hampered by harsh reaction conditions, but it was recently demonstrated that the reaction can be performed at room temperature without racemization of sensitive α -amino acid derivatives.⁴³⁸

Couladouros and co-workers have employed diaryliodonium salts in the synthesis of several bastadins. Both diaryl ether moieties in the target molecules were created using the same iodonium salt, and the couplings proceeded in good to excellent yields (**Scheme 105**).⁴³⁹ Similar diaryliodonium salts have been used in the synthesis of glycopeptide antibiotics.^{440,441}

Scheme 105

7.3. Transformations with Alkynyliodonium Salts

Alkynyl(aryl)iodonium salts are structurally related to diaryliodonium salts, but are less stable and react with nucleophiles through different mechanisms, usually with formation of an alkylidenecarbene intermediate that undergoes further transformations.^{53,63} Cossy's group

alkynylated an amide by sequential treatment with KHMDS and an alkynyliodonium triflate in the synthesis of (±)-lennoxamine (**Scheme 103**).⁴⁴²

Scheme 106

Wardrop and Fritz generated an alkynyliodonium salt from the corresponding alkynyl stannane and $\text{PhI}(\text{CN})\text{OTf}$, which was directly treated with sodium benzene sulfinate to generate an alkylidenecarbene. This intermediate underwent [1,5] C-H insertion to form a dihydrofuran, which was transformed into (±)-magnofargesin (**Scheme 107**).⁴⁴³

Scheme 107

Feldman *et al* have utilized alkynyliodonium salts in the synthesis of (–)-agelastatin A, B⁴⁴⁴ and pareitropone.⁴⁴⁵ In the latter synthesis, an unusual addition of the carbene to an aromatic ring leads to a ring-expanded product (**Scheme 108**).

Scheme 108

8. Conclusions

The examples described in this review show that hypervalent iodine compounds have been used intensively in the total synthesis of natural products. Good isolated yields and chemoselective reactions can be achieved even for highly functionalized molecules. Additionally, tandem transformations could be accomplished in many circumstances. Based on these features, hypervalent iodine reagents have become an essential tool in synthetic organic chemistry.

Many outstanding reactions mediated by hypervalent iodine have recently been developed. They will probably be used in the near future in stereoselective key steps of the total synthesis of

complex natural products, more often including transformations involving carbon-carbon bond formations.

Acknowledgment

The authors thank CNPq, STINT, The Swedish Research Council, and FAPESP for continuous financial support.

References and Notes

- (1) This theme was discussed in the editorial of the JACS virtue issue regarding the total synthesis of natural products: W. R. Roush, *J. Am. Chem. Soc.*, 2008, **130**, 6654.
- (2) T. Hudlicky and J. W. Reed *The Way of Synthesis*; Wiley-VCH: Germany, 2007.
- (3) S. Danishefsky, *Nat. Prod. Rep.*, 2010, **27**, 1114.
- (4) H. Ledford, *Nature*, 2010, **468**, 608.
- (5) S. V. Ley, *Tetrahedron*, 2010, **66**, 6270.
- (6) T. Gaich and P. S. Baran, *J. Org. Chem.*, 2010, **75**, 4657.
- (7) I. S. Young and P. S. Baran, *Nature Chem.*, 2009, **1**, 193.
- (8) P. A. Wender and B. L. Miller, *Nature*, 2009, **460**, 197.
- (9) S. J. Miller, *Nature Chem.*, 2009, **1**, 261.
- (10) K. Kumar and H. Waldmann, *Angew. Chem. Int. Ed.*, 2009, **48**, 3224.
- (11) K. C. Nicolaou, *J. Org. Chem.*, 2009, **74**, 951.
- (12) K. C. Nicolaou, J. S. Chen and S. M. Dalby, *Bioorg. Med. Chem.*, 2009, **17**, 2290.
- (13) R. A. Shenvi, D. P. O'Malley and P. S. Baran, *Acc. Chem. Res.*, 2009, **42**, 530.
- (14) N. Z. Burns, P. S. Baran and R. W. Hoffmann, *Angew. Chem. Int. Ed.*, 2009, **48**, 2854.
- (15) G. M. Cragg, P. G. Grothaus and D. J. Newman, *Chem. Rev.*, 2009, **109**, 3012.
- (16) T. E. Nielsen and S. L. Schreiber, *Angew. Chem. Int. Ed.*, 2008, **47**, 48.
- (17) R. M. Wilson and S. J. Danishefsky, *Chem. Soc. Rev.*, 2007, **36**, 1207.
- (18) P. S. Baran, T. J. Maimone and J. M. Richter, *Nature*, 2007, **446**, 404.
- (19) R. M. Wilson and S. J. Danishefsky, *J. Org. Chem.*, 2006, **71**, 8329.
- (20) K. C. Nicolaou, D. Vourloumis, N. Winssinger and P. S. Baran, *Angew. Chem. Int. Ed.*, 2000, **39**, 44.
- (21) E. Roulland, *Angew. Chem. Int. Ed.*, 2011, **50**, 1226.

- (22) Different acronyms are used in the literature for iodine(III) reagents. Unfortunately, there is no consensus even among the specialists. The most employed in the literature (DIB, PIFA, and HTIB) are used in the review.
- (23) T. Wirth *Hypervalent iodine chemistry - Modern developments in organic synthesis*; Springer: Berlin, 2003; Vol. 224.
- (24) A. Varvoglis *Hypervalent Iodine in Organic Synthesis*; Academic Press, Inc: San Diego, 1997.
- (25) E. A. Merritt and B. Olofsson, *Synthesis*, 2011, 517.
- (26) J. P. Brand, D. F. Gonzalez, S. Nicolai and J. Waser, *Chem. Commun.*, 2011, **47**, 102.
- (27) V. V. Zhdankin, *J. Org. Chem.*, 2011, **76**, 1185.
- (28) L. Pouysegue, D. Deffieux and S. Quideau, *Tetrahedron*, 2010, **66**, 2235.
- (29) M. Ochiai, K. Miyamoto, S. Hayashi and W. Nakanishi, *Chem. Commun.*, 2010, **46**, 511.
- (30) M. Ngatimin and D. W. Lupton, *Aust. J. Chem.*, 2010, **63**, 653.
- (31) M. S. Yusubov and V. V. Zhdankin, *Mendeleev Commun.*, 2010, **20**, 185.
- (32) V. V. Zhdankin, *Arkivoc*, 2009, 1.
- (33) E. A. Merritt and B. Olofsson, *Angew. Chem. Int. Ed.*, 2009, **48**, 9052.
- (34) E. Malamidoli-Xenikaki and S. Spyroudis, *Synlett*, 2008, 2725.
- (35) S. Quideau, L. Pouysegue and D. Deffieux, *Synlett*, 2008, 467.
- (36) V. V. Zhdankin and P. J. Stang, *Chem. Rev.*, 2008, **108**, 5299.
- (37) M. A. Ciufolini, N. A. Braun, S. Canesi, M. Ousmer, J. Chang and D. Chai, *Synthesis*, 2007, 3759.
- (38) M. Ochiai, *Chem. Record*, 2007, **7**, 12.
- (39) U. Ladziata and V. V. Zhdankin, *Synlett*, 2007, 527.
- (40) N. R. Deprez and M. S. Sanford, *Inorg. Chem.*, 2007, **46**, 1924.
- (41) R. D. Richardson and T. Wirth, *Angew. Chem. Int. Ed.*, 2006, **45**, 4402.
- (42) L. F. Silva, Jr., *Molecules*, 2006, **11**, 421.
- (43) E. D. Matveeva, M. V. Proskurnina and N. S. Zefirov, *Heteroatom Chem.*, 2006, **17**, 595.
- (44) U. Ladziata and V. V. Zhdankin, *Arkivoc*, 2006, 26.
- (45) M. Ochiai, *Coord. Chem. Rev.*, 2006, **250**, 2771.
- (46) T. Wirth, *Angew. Chem. Int. Ed.*, 2005, **44**, 3656.
- (47) R. M. Moriarty, *J. Org. Chem.*, 2005, **70**, 2893.
- (48) V. V. Zhdankin, *Curr. Org. Synth.*, 2005, **2**, 121.
- (49) H. Tohma and Y. Kita, *Adv. Synth. Cat.*, 2004, **346**, 111.
- (50) G. F. Koser In *Advances in Heterocyclic Chemistry, Vol 86* 2004; Vol. 86, p 225.
- (51) P. Dauban and R. H. Dodd, *Synlett*, 2003, 1571.
- (52) P. J. Stang, *J. Org. Chem.*, 2003, **68**, 2997.
- (53) K. S. Feldman, *Arkivoc*, 2003, 179.

- (54) I. Moreno, I. Tellitu, M. T. Herrero, R. SanMartin and E. Dominguez, *Curr. Org. Chem.*, 2002, **6**, 1433.
- (55) T. Okuyama, *Acc. Chem. Res.*, 2002, **35**, 12.
- (56) H. Togo and K. Sakuratani, *Synlett*, 2002, 1966.
- (57) V. V. Zhdankin and P. J. Stang, *Chem. Rev.*, 2002, **102**, 2523.
- (58) G. F. Koser, *Aldrichim. Acta*, 2001, **34**, 89.
- (59) T. Wirth, *Angew. Chem. Int. Ed.*, 2001, **40**, 2812.
- (60) M. Ochiai, *J. Organomet. Chem.*, 2000, **611**, 494.
- (61) T. Wirth and U. H. Hirt, *Synthesis*, 1999, 1271.
- (62) R. M. Moriarty and O. Prakash, *Org. React.*, 1999, **54**, 273.
- (63) V. V. Zhdankin and P. J. Stang, *Tetrahedron*, 1998, **54**, 10927.
- (64) A. Kirschning, *Eur. J. Org. Chem.*, 1998, 2267.
- (65) A. Varvoglis, *Tetrahedron*, 1997, **53**, 1179.
- (66) V. Satam, A. Harad, R. Rajule and H. Pati, *Tetrahedron*, 2010, **66**, 7659.
- (67) M. Uyanik and K. Ishihara, *Chem. Commun.*, 2009, 2086.
- (68) A. Duschek and S. F. Kirsch, *Angew. Chem. Int. Ed.*, 2011, **50**, 1524.
- (69) The chapter "Synthetic Applications (Total Synthesis and Natural Product Synthesis)" by Tohma and Kita in ref. 23 published in 2003 describes several applications. Reference 28 describes applications of the phenol dearomatization in the total synthesis of natural products. Reference 49 does the same for the oxidation of alcohols.
- (70) D. B. Dess and J. C. Martin, *J. Org. Chem.*, 1983, **48**, 4155.
- (71) D. B. Dess and J. C. Martin, *J. Am. Chem. Soc.*, 1991, **113**, 7277.
- (72) R. E. Ireland and L. B. Liu, *J. Org. Chem.*, 1993, **58**, 2899.
- (73) S. D. Meyer and S. L. Schreiber, *J. Org. Chem.*, 1994, **59**, 7549.
- (74) P. Caron, R. W. Dugger, S. G. Ruggeri, J. A. Ragan and D. H. B. Ripin, *Chem. Rev.*, 2006, **106**, 2943.
- (75) C. Du, L. Q. Li, Y. Li and Z. X. Xie, *Angew. Chem. Int. Ed.*, 2009, **48**, 7853.
- (76) C. Du, L. Li, Y. Li and Z. X. Xie, *Angew. Chem. Int. Ed.*, 2009, **48**, 9211.
- (77) G. W. O'Neil, J. Ceccon, S. Benson, M.-P. Collin, B. Fasching and A. Furstner, *Angew. Chem. Int. Ed.*, 2009, **48**, 9940.
- (78) S. Phoenix, M. S. Reddy and P. Deslongchamps, *J. Am. Chem. Soc.*, 2008, **130**, 13989.
- (79) K. Ogawa, Y. Koyama, I. Ohashi, I. Sato and M. Hirama, *Angew. Chem. Int. Ed.*, 2009, **48**, 1110.
- (80) K. Takahashi, M. Midori, K. Kawano, J. Ishihara and S. Hatakeyama, *Angew. Chem. Int. Ed.*, 2008, **47**, 6244.
- (81) D. A. Evans, L. Kvaerno, T. B. Dunn, A. Beauchemin, B. Raymer, J. A. Mulder, E. J. Olhava, M. Juhl, K. Kagechika and D. A. Favor, *J. Am. Chem. Soc.*, 2008, **130**, 16295.

- (82) P. Liu, S. Hong and S. M. Weinreb, *J. Am. Chem. Soc.*, 2008, **130**, 7562.
- (83) H. M. Lee, C. Nieto-Oberhuber and M. D. Shair, *J. Am. Chem. Soc.*, 2008, **130**, 16864.
- (84) J. R. Dunetz, L. D. Julian, J. S. Newcom and W. R. Roush, *J. Am. Chem. Soc.*, 2008, **130**, 16407.
- (85) B. M. Trost and B. M. O'Boyle, *J. Am. Chem. Soc.*, 2008, **130**, 16190.
- (86) A. B. Dounay, P. G. Humphreys, L. E. Overman and A. D. Wroblewski, *J. Am. Chem. Soc.*, 2008, **130**, 5368.
- (87) W. He, J. Huang, X. F. Sun and A. J. Frontier, *J. Am. Chem. Soc.*, 2008, **130**, 300.
- (88) S. E. Reisman, J. M. Ready, M. M. Weiss, A. Hasuoka, M. Hirata, K. Tamaki, T. V. Ovaska, C. J. Smith and J. L. Wood, *J. Am. Chem. Soc.*, 2008, **130**, 2087.
- (89) P. A. Clarke, A. P. Cridland, G. A. Rolla, M. Iqbal, N. P. Bainbridge, A. C. Whitwood and C. Wilson, *J. Org. Chem.*, 2009, **74**, 7812.
- (90) M. T. Crimmins, J. L. Zuccarello, J. M. Ellis, P. J. McDougall, P. A. Haile, J. D. Parrish and K. A. Emmitte, *Org. Lett.*, 2009, **11**, 489.
- (91) W. Zhu, M. Jiménez, W.-H. Jung, D. P. Camarco, R. Balachandran, A. Vogt, B. W. Day and D. P. Curran, *J. Am. Chem. Soc.*, 2010, **132**, 9175.
- (92) S. Y. Yun, E. C. Hansen, I. Volchkov, E. J. Cho, W. Y. Lo and D. Lee, *Angew. Chem. Int. Ed.*, 2010, **49**, 4261.
- (93) C. P. Burke, M. R. Swingle, R. E. Honkanen and D. L. Boger, *J. Org. Chem.*, 2010, **75**, 7505.
- (94) A. Larivée, J. B. Unger, M. Thomas, C. Wirtz, C. Dubost, S. Handa and A. Furstner, *Angew. Chem. Int. Ed.*, 2011, **50**, 304.
- (95) B. Bradshaw, G. Etxebarria-Jardí and J. Bonjoch, *J. Am. Chem. Soc.*, 2010, **132**, 5966.
- (96) S. K. Woo and E. Lee, *J. Am. Chem. Soc.*, 2010, **132**, 4564.
- (97) I. R. Correa and R. A. Pilli, *Angew. Chem. Int. Ed.*, 2003, **42**, 3017.
- (98) L. C. Dias, L. G. de Oliveira, J. D. Vilcachagua and F. Nigsch, *J. Org. Chem.*, 2005, **70**, 2225.
- (99) M. Tortosa, N. A. Yakelis and W. R. Roush, *J. Org. Chem.*, 2008, **73**, 9657.
- (100) S. Bonazzi, O. Eidam, S. Güttinger, J.-Y. Wach, I. Zemp, U. Kutay and K. Gademann, *J. Am. Chem. Soc.*, 2010, **132**, 1432.
- (101) K. C. Nicolaou, X. Jiang, P. J. Lindsay-Scott, A. Corbu, S. Yamashiro, A. Bacconi and V. M. Fowler, *Angew. Chem. Int. Ed.*, 2011, **50**, 1139.
- (102) L. C. Dias and P. R. R. Meira, *J. Org. Chem.*, 2005, **70**, 4762.
- (103) S. Bonazzi, S. Guttinger, I. Zemp, U. Kutay and K. Gademann, *Angew. Chem. Int. Ed.*, 2007, **46**, 8707.
- (104) K. C. Nicolaou, M. O. Frederick, A. C. B. Burtoloso, R. M. Denton, F. Rivas, K. P. Cole, R. J. Aversa, R. Gibe, T. Umezawa and T. Suzuki, *J. Am. Chem. Soc.*, 2008, **130**, 7466.

- (105) K. Komano, S. Shimamura, M. Inoue and M. Hirama, *J. Am. Chem. Soc.*, 2007, **129**, 14184.
- (106) C. E. Stivala and A. Zakarian, *J. Am. Chem. Soc.*, 2008, **130**, 3774.
- (107) Y. Shimizu, S.-L. Shi, H. Usuda, M. Kanai and M. Shibasaki, *Angew. Chem. Int. Ed.*, 2010, **49**, 1103.
- (108) N. Slavov, J. Cvengros, J.-M. Neudorfl and H.-G. Schmalz, *Angew. Chem. Int. Ed.*, 2010, **49**, 7588.
- (109) X.-G. Xie, X.-W. Wu, H.-K. Lee, X.-S. Peng and H. N. C. Wong, *Chem. Eur. J.*, 2010, **16**, 6933.
- (110) K. C. Nicolaou, R. J. Aversa, J. Jin and F. Rivas, *J. Am. Chem. Soc.*, 2010, **132**, 6855.
- (111) M. Fleck and T. Bach, *Chem. Eur. J.*, 2010, **16**, 6015.
- (112) A. N. Flyer, C. Si and A. G. Myers, *Nature Chem.*, 2010, **2**, 886.
- (113) K. M. Laemmerhold and B. Breit, *Angew. Chem. Int. Ed.*, 2010, **49**, 2367.
- (114) H. Fuwa, T. Suzuki, H. Kubo, T. Yamori and M. Sasaki, *Chem. Eur. J.*, 2011, **17**, 2678.
- (115) E. Roulland, *Angew. Chem. Int. Ed.*, 2008, **47**, 3762.
- (116) X. Wan and M. M. Joullie, *J. Am. Chem. Soc.*, 2008, **130**, 17236.
- (117) B. M. Trost, J. Waser and A. Meyer, *J. Am. Chem. Soc.*, 2008, **130**, 16424.
- (118) M. Takano, A. Umino and M. Nakada, *Org. Lett.*, 2004, **6**, 4897.
- (119) S. Hanessian, N. Boyer, G. J. Reddy and B. Deschênes-Simard, *Org. Lett.*, 2009, **11**, 4640.
- (120) P. Va, E. L. Campbell, W. M. Robertson and D. L. Boger, *J. Am. Chem. Soc.*, 2010, **132**, 8489.
- (121) R. A. Pilli, M. M. Victor and A. de Meijere, *J. Org. Chem.*, 2000, **65**, 5910.
- (122) R. A. Pilli and M. M. Victor, *Tetrahedron Lett.*, 1998, **39**, 4421.
- (123) J. V. Mulcahy and J. Du Bois, *J. Am. Chem. Soc.*, 2008, **130**, 12630.
- (124) K. C. Nicolaou, T. R. Wu, D. Sarlah, D. M. Shaw, E. Rowcliffe and D. R. Burton, *J. Am. Chem. Soc.*, 2008, **130**, 11114.
- (125) K. C. Nicolaou and A. Li, *Angew. Chem. Int. Ed.*, 2008, **47**, 6579.
- (126) I. Hayakawa, T. Takemura, E. Fukasawa, Y. Ebihara, N. Sato, T. Nakamura, K. Suenaga and H. Kigoshi, *Angew. Chem. Int. Ed.*, 2010, **49**, 2401.
- (127) P. X. Li, C. D. Evans, Y. Z. Wu, B. Cao, E. Hamel and M. M. Joullie, *J. Am. Chem. Soc.*, 2008, **130**, 2351.
- (128) C. H. Kim, K. P. Jang, S. Y. Choi, Y. K. Chung and E. Lee, *Angew. Chem. Int. Ed.*, 2008, **47**, 4009.
- (129) K. K. Larson and R. Sarpong, *J. Am. Chem. Soc.*, 2009, **131**, 13244.
- (130) S. Krishnan, J. T. Bagdanoff, D. C. Ebner, Y. K. Ramtohul, U. K. Tambar and B. M. Stoltz, *J. Am. Chem. Soc.*, 2008, **130**, 13745.

- (131) R. Masuo, K. Ohmori, L. Hintermann, S. Yoshida and K. Suzuki, *Angew. Chem. Int. Ed.*, 2009, **48**, 3462.
- (132) M. Penner, V. Rauniyar, L. T. Kaspar and D. G. Hall, *J. Am. Chem. Soc.*, 2009, **131**, 14216.
- (133) S. Benson, M.-P. Collin, G. W. O'Neil, J. Ceccon, B. Fasching, M. D. B. Fenster, C. Godbout, K. Radkowski, R. Goddard and A. Furstner, *Angew. Chem. Int. Ed.*, 2009, **48**, 9946.
- (134) A. M. Szpilman, D. M. Cereghetti, N. R. Wurtz, J. M. Manthorpe and E. M. Carreira, *Angew. Chem. Int. Ed.*, 2008, **47**, 4335.
- (135) R. Cribiu, C. Jager and C. Nevado, *Angew. Chem. Int. Ed.*, 2009, **48**, 8780.
- (136) Z. Wang, S. J. Min and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2009, **131**, 10848.
- (137) A. T. Radosevich, V. S. Chan, H. W. Shih and F. D. Toste, *Angew. Chem. Int. Ed.*, 2008, **47**, 3755.
- (138) N. A. McGrath, C. A. Lee, H. A. Raki, M. Brichacek and J. T. Njardarson, *Angew. Chem. Int. Ed.*, 2008, **47**, 9450.
- (139) J. Burghart and R. Bruckner, *Angew. Chem. Int. Ed.*, 2008, **47**, 7664.
- (140) J. H. Jung and E. Lee, *Angew. Chem. Int. Ed.*, 2009, **48**, 5698.
- (141) K. Kong, D. Romo and C. Lee, *Angew. Chem. Int. Ed.*, 2009, **48**, 7402.
- (142) M. E. Jung and R. Salehi-Rad, *Angew. Chem. Int. Ed.*, 2009, **48**, 8766.
- (143) J. M. Schomaker and B. Borhan, *J. Am. Chem. Soc.*, 2008, **130**, 12228.
- (144) K. C. Nicolaou, G. Y. C. Leung, D. H. Dethe, R. Guduru, Y. P. Sun, C. S. Lim and D. Y. K. Chen, *J. Am. Chem. Soc.*, 2008, **130**, 10019.
- (145) K. C. Nicolaou, Y. P. Sun, R. Guduru, B. Banerji and D. Y. K. Chen, *J. Am. Chem. Soc.*, 2008, **130**, 3633.
- (146) A. B. Smith and D. J. Lee, *J. Am. Chem. Soc.*, 2007, **129**, 10957.
- (147) H. Li, J. Wu, J. Luo and W.-M. Dai, *Chem. Eur. J.*, 2010, **16**, 11530.
- (148) W. Zi, S. Yu and D. Ma, *Angew. Chem. Int. Ed.*, 2010, **49**, 5887.
- (149) T. Anderl, L. Nicolas, J. Munkemer, A. Baro, F. Sasse, H. Steinmetz, R. Jansen, G. Hofle, R. E. Taylor and S. Laschat, *Angew. Chem. Int. Ed.*, 2011, **50**, 942.
- (150) K. C. Nicolaou, Q. Kang, S. Y. Ng and D. Y.-K. Chen, *J. Am. Chem. Soc.*, 2010, 8219.
- (151) Q. Zhou, X. Chen and D. Ma, *Angew. Chem. Int. Ed.*, 2010, **49**, 3513.
- (152) K. C. Nicolaou, H. Ding, J.-A. Richard and D. Y.-K. Chen, *J. Am. Chem. Soc.*, 2010, **132**, 3815.
- (153) S. A. Snyder, T. C. Sherwood and A. G. Ross, *Angew. Chem. Int. Ed.*, 2010, **49**, 5146.
- (154) D. C. Beshore and A. B. Smith, *J. Am. Chem. Soc.*, 2008, **130**, 13778.
- (155) K. C. Nicolaou, X. S. Peng, Y. P. Sun, D. Polet, B. Zou, C. S. Lim and D. Y. K. Chen, *J. Am. Chem. Soc.*, 2009, **131**, 10587.
- (156) L. Tan and D. W. Ma, *Angew. Chem. Int. Ed.*, 2008, **47**, 3614.

- (157) K. C. Nicolaou, Y. P. Sun, X. S. Peng, D. Polet and D. Y. K. Chen, *Angew. Chem. Int. Ed.*, 2008, **47**, 7310.
- (158) K. L. Jackson, J. A. Henderson, H. Motoyoshi and A. L. Phillips, *Angew. Chem. Int. Ed.*, 2009, **48**, 2346.
- (159) I. Paterson, E. A. Anderson, S. M. Dalby, J. H. Lim, J. Genovino, P. Maltas and C. Moessner, *Angew. Chem. Int. Ed.*, 2008, **47**, 3016.
- (160) S. Nakamura, F. Kikitchi and S. Hashimoto, *Angew. Chem. Int. Ed.*, 2008, **47**, 7091.
- (161) A. B. Smith, T. Bosanac and K. Basu, *J. Am. Chem. Soc.*, 2009, **131**, 2348.
- (162) D. R. Williams, M. J. Walsh and N. A. Miller, *J. Am. Chem. Soc.*, 2009, **131**, 9038.
- (163) K. C. Nicolaou, G. S. Tria, D. J. Edmonds and M. Kar, *J. Am. Chem. Soc.*, 2009, **131**, 15909.
- (164) J. S. Clark, R. Berger, S. T. Hayes, L. H. Thomas, A. J. Morrison and L. Gobbi, *Angew. Chem. Int. Ed.*, 2010, **49**, 9867.
- (165) B. Gebhardt, C. M. König, C. Schleth, M. Dauber and U. Koert, *Chem. Eur. J.*, 2010, **16**, 5934.
- (166) S. V. Ley, M. N. Tackett, M. L. Maddess, J. C. Anderson, P. E. Brennan, M. W. Cappi, J. P. Heer, C. Helgen, M. Kori, C. Kouklovsky, S. P. Marsden, J. Norman, D. P. Osborn, M. A. Palomero, J. B. J. Pavey, C. Pinel, L. A. Robinson, J. Schnaubelt, J. S. Scott, C. D. Spilling, H. Watanabe, K. E. Wesson and M. C. Willis, *Chem. Eur. J.*, 2009, **15**, 2874.
- (167) H. Furuta, Y. Hasegawa, M. Hase and Y. Mori, *Chem. Eur. J.*, 2010, **16**, 7586.
- (168) D. Kato, Y. Sasaki and D. L. Boger, *J. Am. Chem. Soc.*, 2010, **132**, 3685.
- (169) Y. Murata, D. Yamashita, K. Kitahara, Y. Minasako, A. Nakazaki and S. Kobayashi, *Angew. Chem. Int. Ed.*, 2009, **48**, 1400.
- (170) H. Fuwa, A. Saito, S. Naito, K. Konoki, M. Yotsu-Yamashita and M. Sasaki, *Chem. Eur. J.*, 2009, **15**, 12807.
- (171) H. M. Ko, C. W. Lee, H. K. Kwon, H. S. Chung, S. Y. Choi, Y. K. Chung and E. Lee, *Angew. Chem. Int. Ed.*, 2009, **48**, 2364.
- (172) K. Prantz and J. Mulzer, *Angew. Chem. Int. Ed.*, 2009, **48**, 5030.
- (173) M. D. Helm, M. Da Silva, D. Sucunza, T. K. Findley and D. J. Procter, *Angew. Chem. Int. Ed.*, 2009, **48**, 9315.
- (174) W. Xie, D. Ding, W. Zi, G. Li and D. Ma, *Angew. Chem. Int. Ed.*, 2008, **47**, 2844.
- (175) P. F. Li, J. Li, F. Arian, W. Ahlbrecht, M. Dieckmann and D. Menche, *J. Am. Chem. Soc.*, 2009, **131**, 11678.
- (176) S. J. Mickel, D. Niederer, R. Daeffler, A. Osmani, E. Kuesters, E. Schmid, K. Schaer, R. Gamboni, W. C. Chen, E. Loeser, F. R. Kinder, K. Königsberger, K. Prasad, T. M. Ramsey, J. Repic, R. M. Wang, G. Florence, I. Lyothier and I. Paterson, *Org. Proc. Res. Dev.*, 2004, **8**, 122.

- (177) T. J. Maimone, A. F. Voica and P. S. Baran, *Angew. Chem. Int. Ed.*, 2008, **47**, 3054.
- (178) S. M. Canham, D. J. France and L. E. Overman, *J. Am. Chem. Soc.*, 2010, **132**, 7876.
- (179) N. Tanaka, T. Suzuki, T. Matsumura, Y. Hosoya and M. Nakada, *Angew. Chem. Int. Ed.*, 2009, **48**, 2580.
- (180) W. H. Jung, S. Guyenne, C. Riesco-Tagundo, J. Mancuso, S. Nakamura and D. P. Curran, *Angew. Chem. Int. Ed.*, 2008, **47**, 1130.
- (181) J. Carpenter, A. B. Northrup, D. Chung, J. J. M. Wiener, S. G. Kim and D. W. C. MacMillan, *Angew. Chem. Int. Ed.*, 2008, **47**, 3568.
- (182) M. Fleck and T. Bach, *Angew. Chem. Int. Ed.*, 2008, **47**, 6189.
- (183) K. I. Takao, N. Hayakawa, R. Yamada, T. Yamaguchi, U. Morita, S. Kawasaki and K. I. Tadano, *Angew. Chem. Int. Ed.*, 2008, **47**, 3426.
- (184) H. X. Zhang, M. S. Reddy, S. Phoenix and P. Deslongchamps, *Angew. Chem. Int. Ed.*, 2008, **47**, 1272.
- (185) J. A. Henderson and A. J. Phillips, *Angew. Chem. Int. Ed.*, 2008, **47**, 8499.
- (186) H. C. Kim and S. H. Kang, *Angew. Chem. Int. Ed.*, 2009, **48**, 1827.
- (187) B. M. Trost, D. Amans, W. M. Seganish and C. K. Chung, *J. Am. Chem. Soc.*, 2009, **131**, 17087.
- (188) N. Rahn and M. Kalesse, *Angew. Chem. Int. Ed.*, 2008, **47**, 597.
- (189) S. K. Woo, M. S. Kwon and E. Lee, *Angew. Chem. Int. Ed.*, 2008, **47**, 3242.
- (190) C. Hamel, E. V. Prusov, J. Gertsch, W. B. Schweizer and K. H. Altmann, *Angew. Chem. Int. Ed.*, 2008, **47**, 10081.
- (191) M. S. Kwon, S. K. Woo, S. W. Na and E. Lee, *Angew. Chem. Int. Ed.*, 2008, **47**, 1733.
- (192) J. K. Belardi and G. C. Micalizio, *Angew. Chem. Int. Ed.*, 2008, **47**, 4005.
- (193) X. X. Wu, J. Y. Zhou and B. B. Snider, *Angew. Chem. Int. Ed.*, 2009, **48**, 1283.
- (194) M. Zhang, X. P. Huang, L. Q. Shen and Y. Qin, *J. Am. Chem. Soc.*, 2009, **131**, 6013.
- (195) J. Garfinkle, F. S. Kimball, J. D. Trzupek, S. Takizawa, H. Shimamura, M. Tomishima and D. L. Boger, *J. Am. Chem. Soc.*, 2009, **131**, 16036.
- (196) L. Q. Shen, M. Zhang, T. Wu and Y. Qin, *Angew. Chem. Int. Ed.*, 2008, **47**, 3618.
- (197) M. Amat, R. Grier, R. Tabregat, E. Molins and J. Bosch, *Angew. Chem. Int. Ed.*, 2008, **47**, 3348.
- (198) Y. Ni, R. M. Kassab, M. V. Chevliakov and J. Montgomery, *J. Am. Chem. Soc.*, 2009, **131**, 17714.
- (199) K. C. Nicolaou, Y. F. Tang and J. H. Wang, *Angew. Chem. Int. Ed.*, 2009, **48**, 3449.
- (200) I. Paterson, E. A. Anderson, S. M. Dalby, J. H. Lim, J. Genovino, P. Maltas and C. Moessner, *Angew. Chem. Int. Ed.*, 2008, **47**, 3021.
- (201) T. J. Donohoe, A. Flores, C. J. R. Bataille and F. Churrua, *Angew. Chem. Int. Ed.*, 2009, **48**, 6507.

- (202) J. Liu and J. K. De Brabander, *J. Am. Chem. Soc.*, 2009, **131**, 12562.
- (203) A. B. Smith, S. Z. Dong, J. B. Brennen and R. J. Fox, *J. Am. Chem. Soc.*, 2009, **131**, 12109.
- (204) D. Lefranc and M. A. Ciufolini, *Angew. Chem. Int. Ed.*, 2009, **48**, 4198.
- (205) S. A. Snyder, S. P. Breazzano, A. G. Ross, Y. Q. Lin and A. L. Zografos, *J. Am. Chem. Soc.*, 2009, **131**, 1753.
- (206) S. A. Snyder, Z. Y. Tang and R. Gupta, *J. Am. Chem. Soc.*, 2009, **131**, 5744.
- (207) K. C. Nicolaou, Y.-P. Sun, H. Korman and D. Sarlah, *Angew. Chem. Int. Ed.*, 2010, **49**, 5875.
- (208) P. A. Grieco and M. M. Piñeiro-Nuñez, *J. Am. Chem. Soc.*, 1994, **116**, 7606.
- (209) K. C. Nicolaou and P. S. Baran, *Angew. Chem. Int. Ed.*, 2002, **41**, 2678.
- (210) K. C. Nicolaou, P. S. Baran, Y. L. Zhong, K. C. Fong and K. S. Choi, *J. Am. Chem. Soc.*, 2002, **124**, 2190.
- (211) K. C. Nicolaou, Y. L. Zhong, P. S. Baran, J. Jung, H. S. Choi and W. H. Yoon, *J. Am. Chem. Soc.*, 2002, **124**, 2202.
- (212) D. A. Evans, D. S. Welch, A. W. H. Speed, G. A. Moniz, A. Reichelt and S. Ho, *J. Am. Chem. Soc.*, 2009, **131**, 3840.
- (213) S. H. Gao, O. L. Wang and C. Chen, *J. Am. Chem. Soc.*, 2009, **131**, 1410.
- (214) S. H. Gao, O. L. Wang, L. J.-S. Huang, L. Lum and C. Chen, *J. Am. Chem. Soc.*, 2010, **132**, 371.
- (215) T. K. Macklin and G. C. Micalizio, *J. Am. Chem. Soc.*, 2009, **131**, 1392.
- (216) J. T. Su and W. A. Goddard, *J. Am. Chem. Soc.*, 2005, **127**, 14146.
- (217) M. Mulbaier and A. Giannis, *Arkivoc*, 2003, 228.
- (218) M. Mulbaier and A. Giannis, *Angew. Chem. Int. Ed.*, 2001, **40**, 4393.
- (219) B. S. Chhikara, R. Chandra and V. Tandon, *Tetrahedron Lett.*, 2004, **45**, 7585.
- (220) M. Frigerio and M. Santagostino, *Tetrahedron Lett.*, 1994, **35**, 8019.
- (221) M. Frigerio, M. Santagostino, S. Sputore and G. Palmisano, *J. Org. Chem.*, 1995, **60**, 7272.
- (222) M. Frigerio, M. Santagostino and S. Sputore, *J. Org. Chem.*, 1999, **64**, 4537.
- (223) E. J. Corey and A. Palani, *Tetrahedron Lett.*, 1995, **36**, 7945.
- (224) J. B. Plumb and D. J. Harper, *Chem. Eng. News*, 1990, **68**, 3.
- (225) K. C. Nicolaou, T. Montagnon and P. S. Baran, *Angew. Chem. Int. Ed.*, 2002, **41**, 993.
- (226) G. E. Beye and D. E. Ward, *J. Am. Chem. Soc.*, 2010, **132**, 7210.
- (227) H. Watanabe and M. Nakada, *J. Am. Chem. Soc.*, 2008, **130**, 1150.
- (228) K. C. Nicolaou, H. Zhang, A. Ortiz and P. Dagneau, *Angew. Chem. Int. Ed.*, 2008, **47**, 8605.
- (229) A. B. Leduc and M. A. Kerr, *Angew. Chem. Int. Ed.*, 2008, **47**, 7945.
- (230) S. W. Dong, E. Hamel, R. L. Bai, D. G. Covell, J. A. Beutler and J. A. Porco, *Angew. Chem. Int. Ed.*, 2009, **48**, 1494.

- (231) A. Hamajima and M. Isobe, *Angew. Chem. Int. Ed.*, 2009, **48**, 2941.
- (232) K. C. Nicolaou, T. R. Wu, Q. Kang and D. Y. K. Chen, *Angew. Chem. Int. Ed.*, 2009, **48**, 3440.
- (233) T. Magauer, H. J. Martin and J. Mulzer, *Angew. Chem. Int. Ed.*, 2009, **48**, 6032.
- (234) M. Willot, L. Radtke, D. Konning, R. Frohlich, V. H. Gessner, C. Strohmann and M. Christmann, *Angew. Chem. Int. Ed.*, 2009, **48**, 9105.
- (235) T. Gaich and J. Mulzer, *J. Am. Chem. Soc.*, 2009, **131**, 452.
- (236) R. A. Fernandes and A. K. Chowdhury, *J. Org. Chem.*, 2009, **74**, 8826.
- (237) K. A. B. Austin, M. G. Banwell and A. C. Willis, *Org. Lett.*, 2008, **10**, 4465.
- (238) K. C. Nicolaou, L. Dong, L. J. Deng, A. C. Talbot and D. Y. K. Chen, *Chem. Commun.*, 2010, **46**, 70.
- (239) B. J. D. Wright, J. Hartung, F. Peng, R. Van de Water, H. B. Liu, Q. H. Tan, T. C. Chou and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2008, **130**, 16786.
- (240) J. Yamaguchi, I. B. Seiple, I. S. Young, D. P. O'Malley, M. Maue and P. S. Baran, *Angew. Chem. Int. Ed.*, 2008, **47**, 3578.
- (241) D. C. K. Rathwell, S. H. Yang, K. Y. Tsang and M. A. Brimble, *Angew. Chem. Int. Ed.*, 2009, **48**, 7996.
- (242) B. J. Morgan, S. Dey, S. W. Johnson and M. C. Kozlowski, *J. Am. Chem. Soc.*, 2009, **131**, 9413.
- (243) P. Selig and T. Bach, *Angew. Chem. Int. Ed.*, 2008, **47**, 5082.
- (244) C. L. Pereira, Y. H. Chen and F. E. McDonald, *J. Am. Chem. Soc.*, 2009, **131**, 6066.
- (245) L. F. Tietze, C. C. Brazel, S. Holsken, J. Magull and A. Ringe, *Angew. Chem. Int. Ed.*, 2008, **47**, 5246.
- (246) P. Gowrisankar, S. A. Pujari and K. P. Kaliappan, *Chem. Eur. J.*, 2010, **16**, 5858.
- (247) K. C. Nicolaou, Q. Kang, T. R. Wu, C. S. Lim and D. Y.-K. Chen, *J. Am. Chem. Soc.*, 2010, **132**, 7540.
- (248) K. C. Nicolaou, A. Ortiz, H. Zhang, P. Dagneau, A. Lanver, M. P. Jennings, S. Arseniyadis, R. Faraoni and D. E. Lizos, *J. Am. Chem. Soc.*, 2010, **132**, 7138.
- (249) A. Ozanne, L. Pouysegue, D. Depernet, B. Francois and S. Quideau, *Org. Lett.*, 2003, **5**, 2903.
- (250) L. Pouysegue, M. Marguerit, J. Gagnepain, G. Lyvinec, A. J. Eatherton and S. Quideau, *Org. Lett.*, 2008, **10**, 5211.
- (251) A. Schulze and A. Giannis, *Adv. Synth. Catal.*, 2004, **346**, 252.
- (252) R. Mazitschek, M. Mulbaier and A. Giannis, *Angew. Chem. Int. Ed.*, 2002, **41**, 4059.
- (253) A. Schulze and A. Giannis, *Synthesis*, 2006, 257.
- (254) L. E. Brown, Y. R. Landaverry, J. R. Davies, K. A. Milinkevich, S. Ast, J. S. Carlson, A. G. Oliver and J. P. Konopelski, *J. Org. Chem.*, 2009, **74**, 5405.

- (255) D. Muri and E. M. Carreira, *J. Org. Chem.*, 2009, **74**, 8695.
- (256) A. DeMico, R. Margarita, L. Parlanti, A. Vescovi and G. Piancatelli, *J. Org. Chem.*, 1997, **62**, 6974.
- (257) W. Adam, C. R. Saha-Moller and P. A. Ganeshpure, *Chem. Rev.*, 2001, **101**, 3499.
- (258) M. Shibuya, M. Tomizawa, I. Suzuki and Y. Iwabuchi, *J. Am. Chem. Soc.*, 2006, **128**, 8412.
- (259) R. Ciriminna and M. Pagliaro, *Org. Proc. Res. Dev.*, 2010, **14**, 245.
- (260) T. Vogler and A. Studer, *Synthesis*, 2008, 1979.
- (261) R. A. Sheldon, I. Arends, G. J. Ten Brink and A. Dijkman, *Acc. Chem. Res.*, 2002, **35**, 774.
- (262) K. C. Nicolaou, D. Sarlah, T. R. Wu and W. Q. Zhan, *Angew. Chem. Int. Ed.*, 2009, **48**, 6870.
- (263) K. C. Nicolaou, A. Ortiz, H. Zhang and G. Guella, *J. Am. Chem. Soc.*, 2010, **132**, 7153.
- (264) K. C. Nicolaou, H. J. Zhang and A. Ortiz, *Angew. Chem. Int. Ed.*, 2009, **48**, 5642.
- (265) K. C. Nicolaou, A. Ortiz and H. J. Zhang, *Angew. Chem. Int. Ed.*, 2009, **48**, 5648.
- (266) D. W. Custer, T. P. Zabawa and K. A. Scheidt, *J. Am. Chem. Soc.*, 2008, **130**, 804.
- (267) M. T. Crimmins, J. L. Zuccarello, P. J. McDougall and J. M. Ellis, *Chem. Eur. J.*, 2009, **15**, 9235.
- (268) S. Marchart, A. Gromov and J. Mulzer, *Angew. Chem. Int. Ed.*, 2010, **49**, 2050.
- (269) L. C. Dias and A. G. Salles, *J. Org. Chem.*, 2009, **74**, 5584.
- (270) F. Kleinbeck and E. M. Carreira, *Angew. Chem. Int. Ed.*, 2009, **48**, 578.
- (271) T. M. Hansen, G. J. Florence, P. Lugo-Mas, J. H. Chen, J. N. Abrams and C. J. Forsyth, *Tetrahedron Lett.*, 2003, **44**, 57.
- (272) A. Giannis, P. Heretsch, V. Sarli and A. Stossel, *Angew. Chem. Int. Ed.*, 2009, **48**, 7911.
- (273) T. Yamakawa, E. Ideue, J. Shimokawa and T. Fukuyama, *Angew. Chem. Int. Ed.*, 2010, **49**, 9262.
- (274) D. Magdziak, S. J. Meek and T. R. R. Pettus, *Chem. Rev.*, 2004, **104**, 1383.
- (275) A. R. H. Narayan, E. M. Simmons and R. Sarpong, *Eur. J. Org. Chem.*, 2010, 3553.
- (276) K. C. Guerard, C. Sabot, M.-A. Beaulieu, M.-A. Giroux and S. Canesi, *Tetrahedron*, 2010, **66**, 5893.
- (277) J. Y. Cha, Y. D. Huang and T. R. R. Pettus, *Angew. Chem. Int. Ed.*, 2009, **48**, 9519.
- (278) M. A. Marsini, Y. D. Huang, R. W. V. De Water and T. R. R. Pettus, *Org. Lett.*, 2007, **9**, 3229.
- (279) J. Y. Cha, G. L. Burnett, IV, Y. Huang, J. B. Davidson and T. R. R. Pettus, *J. Org. Chem.*, 2011, **76**, 1361.
- (280) K. C. Nicolaou, A. L. Nold and H. M. Li, *Angew. Chem. Int. Ed.*, 2009, **48**, 5860.
- (281) Z. You, A. H. Hoveyda and M. L. Snapper, *Angew. Chem. Int. Ed.*, 2009, **48**, 547.
- (282) L. Fang, Y. Chen, J. Huang, L. Liu, J. Quan, C.-c. Li and Z. Yang, *J. Org. Chem.*, 2011, dx.doi.org/10.1021/jo102202t.

- (283) G. Lalic and E. J. Corey, *Org. Lett.*, 2007, **9**, 4921.
- (284) J. P. Lumb, K. C. Choong and D. Trauner, *J. Am. Chem. Soc.*, 2008, **130**, 9230.
- (285) D. R. Hookins and R. J. K. Taylor, *Tetrahedron Lett.*, 2010, **51**, 6619.
- (286) H. Liang and M. A. Ciufolini, *Chem. Eur. J.*, 2010, **16**, 13262.
- (287) H. Liang and M. A. Ciufolini, *Tetrahedron*, 2010, **66**, 5884.
- (288) H. Liang and M. A. Ciufolini, *Org. Lett.*, 2010, **12**, 1760.
- (289) H. Tohma, Y. Harayama, M. Hashizume, M. Iwata, M. Egi and Y. Kita, *Angew. Chem. Int. Ed.*, 2002, **41**, 348.
- (290) Y. Kita, H. Tohma, M. Inagaki, K. Hatanaka and T. Yakura, *J. Am. Chem. Soc.*, 1992, **114**, 2175.
- (291) Y. Wada, K. Otani, N. Endo, Y. Harayama, D. Kamimura, M. Yoshida, H. Fujioka and Y. Kita, *Org. Lett.*, 2009, **11**, 4048.
- (292) S. V. Ley, I. R. Baxendale, R. N. Bream, P. S. Jackson, A. G. Leach, D. A. Longbottom, M. Nesi, J. S. Scott, R. I. Storer and S. J. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 2000, 3815.
- (293) I. R. Baxendale, S. V. Ley, M. Nesi and C. Piutti, *Tetrahedron*, 2002, **58**, 6285.
- (294) I. R. Baxendale, S. V. Ley and C. Piutti, *Angew. Chem. Int. Ed.*, 2002, **41**, 2194.
- (295) M.-A. Beaulieu, C. Sabot, N. Achache, K. C. Guérard and S. Canesi, *Chem. Eur. J.*, 2010, **16**, 11224.
- (296) J.-C. Andrez, M.-A. Giroux, J. Lucien and S. Canesi, *Org. Lett.*, 2010, **12**, 4368.
- (297) S. Quideau, M. A. Looney and L. Pouysegue, *Org. Lett.*, 1999, **1**, 1651.
- (298) C. Sabot, K. C. Guerard and S. Canesi, *Chem. Commun.*, 2009, 2941.
- (299) K. C. Nicolaou, A. Li, D. J. Edmonds, G. S. Tria and S. P. Ellery, *J. Am. Chem. Soc.*, 2009, **131**, 16905.
- (300) J. W. Shearman, R. M. Myers, J. D. Brenton and S. V. Ley, *Org. Biomol. Chem.*, 2011, **9**, 62.
- (301) B. Moon, S. Han, Y. Yoon and H. Kwon, *Org. Lett.*, 2005, **7**, 1031.
- (302) D. Magdziak, A. A. Rodriguez, R. W. Van De Water and T. R. R. Pettus, *Org. Lett.*, 2002, **4**, 285.
- (303) L. Pouysegue, T. Sylla, T. Garnier, L. B. Rojas, J. Charris, D. Deffieux and S. Quideau, *Tetrahedron*, 2010, **66**, 5908.
- (304) J. Zhu, A. R. Germain and J. A. Porco, *Angew. Chem. Int. Ed.*, 2004, **43**, 1239.
- (305) R. C. Clark, S. Y. Lee and D. L. Boger, *J. Am. Chem. Soc.*, 2008, **130**, 12355.
- (306) A. W. G. Burgett, Q. Li, Q. Wei and P. G. Harran, *Angew. Chem. Int. Ed.*, 2003, **42**, 4961.
- (307) K. C. Nicolaou, S. M. Dalby, S. L. Li, T. Suzuki and D. Y. K. Chen, *Angew. Chem. Int. Ed.*, 2009, **48**, 7616.
- (308) K. C. Nicolaou, U. Majumder, S. P. Roche and D. Y. K. Chen, *Angew. Chem. Int. Ed.*, 2007, **46**, 4715.

- (309) C. Chan, C. Li, F. Zhang and S. J. Danishefsky, *Tetrahedron Lett.*, 2006, **47**, 4839.
- (310) T. Newhouse and P. S. Baran, *J. Am. Chem. Soc.*, 2008, **130**, 10886.
- (311) H. Ding and D. Y.-K. Chen, *Angew. Chem. Int. Ed.*, 2011, **50**, 676.
- (312) T. Dohi, N. Yamaoka and Y. Kita, *Tetrahedron* 2010, **66**, 5775.
- (313) T. Dohi, M. Ito, N. Yamaoka, K. Morimoto, H. Fujioka and Y. Kita, *Tetrahedron*, 2009, **65**, 10797.
- (314) Y. Kita, H. Tohma, K. Hatanaka, T. Takada, S. Fujita, S. Mitoh, H. Sakurai and S. Oka, *J. Am. Chem. Soc.*, 1994, **116**, 3684.
- (315) E. M. O'Brien, B. J. Morgan and M. C. Kozlowski, *Angew. Chem. Int. Ed.*, 2008, **47**, 6877.
- (316) G. Besong, K. Jarowicki, P. J. Kocienski, E. Sliwinski and F. T. Boyle, *Org. Biomol. Chem.*, 2006, **4**, 2193.
- (317) T. Ohta, T. Fukuda, F. Ishibashi and M. Iwao, *J. Org. Chem.*, 2009, **74**, 8143.
- (318) K. C. Nicolaou, Y. L. Zhong and P. S. Baran, *J. Am. Chem. Soc.*, 2000, **122**, 7596.
- (319) K. C. Nicolaou, T. Montagnon, P. S. Baran and Y. L. Zhong, *J. Am. Chem. Soc.*, 2002, **124**, 2245.
- (320) G. Barbe and A. B. Charette, *J. Am. Chem. Soc.*, 2008, **130**, 13873.
- (321) R. Nakajima, T. Ogino, S. Yokoshima and T. Fukuyama, *J. Am. Chem. Soc.*, 2010, **132**, 1236.
- (322) J. Q. Dong and H. N. C. Wong, *Angew. Chem. Int. Ed.*, 2009, **48**, 2351.
- (323) R. S. Coleman, E. L. Campbell and D. J. Carper, *Org. Lett.*, 2009, **11**, 2133.
- (324) J. D. Panarese and S. P. Waters, *Org. Lett.*, 2009, **11**, 5086.
- (325) K. C. Nicolaou, D. L. F. Gray, T. Montagnon and S. T. Harrison, *Angew. Chem. Int. Ed.*, 2002, **41**, 996.
- (326) K. C. Nicolaou, D. Pappo, K. Y. Tsang, R. Gibe and D. Y. K. Chen, *Angew. Chem. Int. Ed.*, 2008, **47**, 944.
- (327) K. C. Nicolaou, A. F. Stepan, T. Lister, A. Li, A. Montero, G. S. Tria, C. I. Turner, Y. F. Tang, J. H. Wang, R. M. Denton and D. J. Edmonds, *J. Am. Chem. Soc.*, 2008, **130**, 13110.
- (328) K. C. Nicolaou, T. Montagnon, G. Vassilikogiannakis and C. J. N. Mathison, *J. Am. Chem. Soc.*, 2005, **127**, 8872.
- (329) R. M. Moriarty, H. Hu and S. C. Gupta, *Tetrahedron Lett.*, 1981, **22**, 1283.
- (330) R. M. Moriarty and K. C. Hou, *Tetrahedron Lett.*, 1984, **25**, 691.
- (331) R. M. Moriarty, B. A. Berglund and R. Penmasta, *Tetrahedron Lett.*, 1992, **33**, 6065.
- (332) V. M. T. Carneiro, H. M. C. Ferraz, T. O. Vieira, E. E. Ishikawa and L. F. Silva, *J. Org. Chem.*, 2010, **75**, 2877.
- (333) D. L. Boger, S. Ichikawa and H. J. Jiang, *J. Am. Chem. Soc.*, 2000, **122**, 12169.
- (334) A. Takada, Y. Hashimoto, H. Takikawa, K. Hikita and K. Suzuki, *Angew. Chem. Int. Ed.*, 2011, **50**, 2297.

- (335) Y. Tamura, H. Annoura, H. Yamamoto, H. Kondo, Y. Kita and H. Fujioka, *Tetrahedron Lett.*, 1987, **28**, 5709.
- (336) W. D. Z. Li and Y. Q. Wang, *Org. Lett.*, 2003, **5**, 2931.
- (337) A. Madin, C. J. O'Donnell, T. Oh, D. W. Old, L. E. Overman and M. J. Sharp, *J. Am. Chem. Soc.*, 2005, **127**, 18054.
- (338) A. Madin, C. J. O'Donnell, T. B. Oh, D. W. Old, L. E. Overman and M. J. Sharp, *Angew. Chem. Int. Ed.*, 1999, **38**, 2934.
- (339) R. M. Moriarty, O. Prakash, M. P. Duncan, R. K. Vaid and H. A. Musallam, *J. Org. Chem.*, 1987, **52**, 150.
- (340) R. M. Moriarty, M. P. Duncan and O. Prakash, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1781.
- (341) R. M. Moriarty, R. Penmasta, A. K. Awasthi, W. R. Epa and I. Prakash, *J. Org. Chem.*, 1989, **54**, 1101.
- (342) S. H. Kwak, J. M. Seo and K. I. Lee, *Arkivoc*, 2010, 55.
- (343) O. Iwamoto, H. Koshino, D. Hashizume and K. Nagasawa, *Angew. Chem. Int. Ed.*, 2007, **46**, 8625.
- (344) T. Imaoka, O. Iwamoto, K. Noguchi and K. Nagasawa, *Angew. Chem. Int. Ed.*, 2009, **48**, 3799.
- (345) I. D. G. Watson, L. L. Yu and A. K. Yudin, *Acc. Chem. Res.*, 2006, **39**, 194.
- (346) T. B. Bisol and M. M. Sa, *Quim. Nova*, 2007, **30**, 106.
- (347) J. Y. Li, J. L. Liang, P. W. H. Chan and C. M. Che, *Tetrahedron Lett.*, 2004, **45**, 2685.
- (348) J. Y. Li, P. W. H. Chan and C. M. Che, *Org. Lett.*, 2005, **7**, 5801.
- (349) R. D. Richardson, M. Desai and T. Wirth, *Chem. Eur. J.*, 2007, **13**, 6745.
- (350) P. M. Wehn and J. Du Bois, *Angew. Chem. Int. Ed.*, 2009, **48**, 3802.
- (351) C. S. Schindler, C. R. J. Stephenson and E. M. Carreira, *Angew. Chem. Int. Ed.*, 2008, **47**, 8852.
- (352) E. G. Bowen and D. J. Wardrop, *Org. Lett.*, 2010, **12**, 5330.
- (353) J. Magano, *Chem. Rev.*, 2009, **109**, 4398.
- (354) M. Shibasaki and M. Kanai, *Eur. J. Org. Chem.*, 2008, 1839.
- (355) B. M. Trost and T. Zhang, *Angew. Chem. Int. Ed.*, 2008, **47**, 3759.
- (356) B. M. Trost and T. Zhang, *Chem. Eur. J.*, 2011, **17**, 3630.
- (357) M. Tanaka, Y. Kurosaki, T. Washio, M. Anada and S. Hashimoto, *Tetrahedron Lett.*, 2007, **48**, 8799.
- (358) M. Anada, M. Tanaka, T. Washio, M. Yamawaki, T. Abe and S. Hashimoto, *Org. Lett.*, 2007, **9**, 4559.
- (359) M. Tanaka, S. Nakamura, M. Anada and S. Hashimoto, *Heterocycles*, 2008, **76**, 1633.
- (360) M. Kim, J. V. Mulcahy, C. G. Espino and J. Du Bois, *Org. Lett.*, 2006, **8**, 1073.
- (361) C. G. Espino and J. Du Bois, *Angew. Chem. Int. Ed.*, 2001, **40**, 598.

- (362) C. G. Espino, P. M. Wehn, J. Chow and J. Du Bois, *J. Am. Chem. Soc.*, 2001, **123**, 6935.
- (363) P. M. Wehn and J. Du Bois, *J. Am. Chem. Soc.*, 2002, **124**, 12950.
- (364) A. Hinman and J. Du Bois, *J. Am. Chem. Soc.*, 2003, **125**, 11510.
- (365) S. H. Wang and D. Romo, *Angew. Chem. Int. Ed.*, 2008, **47**, 1284.
- (366) K. S. Feldman and A. P. Skoumbourdis, *Org. Lett.*, 2005, **7**, 929.
- (367) K. S. Feldman, A. P. Skoumbourdis and M. D. Fodor, *J. Org. Chem.*, 2007, **72**, 8076.
- (368) R. Chung, E. Yu, C. D. Incarvito and D. J. Austin, *Org Lett*, 2004, **6**, 3881.
- (369) A. Correa, I. Tellitu, E. Dominguez, I. Moreno and R. SanMartin, *J. Org. Chem.*, 2005, **70**, 2256.
- (370) D. Kajiyama, K. Inoue, Y. Ishikawa and S. Nishiyama, *Tetrahedron*, 2010, **66**, 9779.
- (371) B. A. Mendelsohn, S. Lee, S. Kim, F. Teyssier, V. S. Aulakh and M. A. Ciufolini, *Org. Lett.*, 2009, **11**, 1539.
- (372) J. L. Frie, C. S. Jeffrey and E. J. Sorensen, *Org. Lett.*, 2009, **11**, 5394.
- (373) K. C. Fortner, D. Kato, Y. Tanaka and M. D. Shair, *J. Am. Chem. Soc.*, 2010, **132**, 275.
- (374) G. Stork and K. Zhao, *Tetrahedron Lett.*, 1989, **30**, 287.
- (375) S. Patir and N. Uludag, *Tetrahedron*, 2009, **65**, 115.
- (376) D. Webb, A. van den Heuvel, M. Kogl and S. V. Ley, *Synlett*, 2009, 2320.
- (377) A. R. Angeles, D. C. Dorn, C. A. Kou, M. A. S. Moore and S. J. Danishefsky, *Angew. Chem. Int. Ed.*, 2007, **46**, 1451.
- (378) Z.-B. Zhen, J. Gao and Y. Wu, *J. Org. Chem.*, 2008, **73**, 7310.
- (379) A. B. Smith, J. M. Cox, N. Furuichi, C. S. Kenesky, J. Zheng, O. Atasoylu and W. M. Wuest, *Org. Lett.*, 2008, **10**, 5501.
- (380) Y. K. Wu, X. Shen, J. H. Huang, C. J. Tang, H. H. Liu and Q. Hu, *Tetrahedron Lett.*, 2002, **43**, 6443.
- (381) N. F. Langille, L. A. Dakin and J. S. Panek, *Org. Lett.*, 2003, **5**, 575.
- (382) K. C. Nicolaou, C. J. N. Mathison and T. Montagnon, *Angew. Chem. Int. Ed.*, 2003, **42**, 4077.
- (383) K. C. Nicolaou, C. J. N. Mathison and T. Montagnon, *J. Am. Chem. Soc.*, 2004, **126**, 5192.
- (384) Q. B. Su, L. A. Dakin and J. S. Panek, *J. Org. Chem.*, 2007, **72**, 2.
- (385) L. A. Dakin and J. S. Panek, *Org. Lett.*, 2003, **5**, 3995.
- (386) A. B. Smith, M. A. Foley, S. Z. Dong and A. Orbin, *J. Org. Chem.*, 2009, **74**, 5987.
- (387) P. de Armas, J. I. Concepcion, C. G. Francisco, R. Hernandez, J. A. Salazar and E. Suarez, *J. Chem. Soc., Perkin Trans. 1*, 1989, 405.
- (388) C. C. González, A. R. Kennedy, E. I. León, C. Riesco-Fagundo and E. Suárez, *Angew. Chem. Int. Ed.*, 2001, **40**, 2326.
- (389) Z. Cekovic, *Tetrahedron*, 2003, **59**, 8073.
- (390) M. E. Green, J. C. Rech and P. E. Floreancig, *Angew. Chem. Int. Ed.*, 2008, **47**, 7317.

- (391) R. A. Shenvi, C. A. Guerrero, J. Shi, C. C. Li and P. S. Baran, *J. Am. Chem. Soc.*, 2008, **130**, 7241.
- (392) A. Boto, R. Hernandez and E. Suarez, *J. Org. Chem.*, 2000, **65**, 4930.
- (393) J. D. Trzuppek, D. Lee, B. M. Crowley, V. M. Marathias and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2010, **132**, 8506.
- (394) J. N. Moorthy, N. Singhal and K. Senapati, *Tetrahedron Lett.*, 2006, **47**, 1757.
- (395) S. Neufeind, N. Hulsken, J.-M. Neudorfl, N. Schlörer and H.-G. Schmalz, *Chem. Eur. J.*, 2011, **17**, 2633.
- (396) V. Sofiyev, G. Navarro and D. Trauner, *Org. Lett.*, 2008, **10**, 149.
- (397) L. H. Zhang, J. C. Chung, T. D. Costello, I. Valvis, P. Ma, S. Kauffman and R. Ward, *J. Org. Chem.*, 1997, **62**, 2466.
- (398) G. M. Loudon, A. S. Radhakrishna, M. R. Almond, J. K. Blodgett and R. H. Boutin, *J. Org. Chem.*, 1984, **49**, 4272.
- (399) R. H. Boutin and G. M. Loudon, *J. Org. Chem.*, 1984, **49**, 4277.
- (400) I. M. Lazbin and G. F. Koser, *J. Org. Chem.*, 1986, **51**, 2669.
- (401) K. Swaminathan and N. Venkatasubramanian, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1161.
- (402) K. Afarinkia and F. Mahmood, *Tetrahedron*, 1999, **55**, 3129.
- (403) A. E. Sutton and J. Clardy, *Org. Lett.*, 2000, **2**, 319.
- (404) A. E. Sutton and J. Clardy, *J. Am. Chem. Soc.*, 2001, **123**, 9935.
- (405) R. M. Moriarty, C. J. Chany, R. K. Vaid, O. Prakash and S. M. Tuladhar, *J. Org. Chem.*, 1993, **58**, 2478.
- (406) R. A. Singer and E. M. Carreira, *Tetrahedron Lett.*, 1997, **38**, 927.
- (407) W. Liu, M. Buck, N. Chen, M. Shang, N. J. Taylor, J. Asoud, X. Wu, B. B. Hasinoff and G. I. Dmitrienko, *Org. Lett.*, 2007, **9**, 2915.
- (408) N. Satoh, T. Akiba, S. Yokoshima and T. Fukuyama, *Tetrahedron*, 2009, **65**, 3239.
- (409) N. Satoh, T. Akiba, S. Yokoshima and T. Fukuyama, *Angew. Chem. Int. Ed.*, 2007, **46**, 5734.
- (410) M. Inai, T. Goto, T. Furuta, T. Wakimoto and T. Kan, *Tetrahedron Asymm.*, 2008, **19**, 2771.
- (411) D. Redmore and C. D. Gutsche In *Advances in Alicyclic Chemistry* Hart, H., Karabastos, G. J., Eds.; Academic Press: New York and London, 1971; Vol. 3, p 1.
- (412) L. F. Silva, Jr., *Tetrahedron* 2002, **58**, 9137.
- (413) L. F. Silva, Jr., F. A. Siqueira, E. C. Pedrozo, F. Y. M. Vieira and A. C. Doriguetto, *Org. Lett.*, 2007, **9**, 1433.
- (414) H. M. C. Ferraz, A. M. Aguilar, L. F. Silva, Jr. and M. V. Craveiro, *Quim. Nova* 2005, **28**, 703.
- (415) L. F. Silva, Jr., R. M. F. Sousa, H. M. C. Ferraz and A. M. Aguilar, *J. Braz. Chem. Soc.*, 2005, **16**, 1160.

- (416) H. M. C. Ferraz, A. M. Aguilar and L. F. Silva, Jr., *Synthesis* 2003, **7**, 1031.
- (417) L. F. Silva, Jr. and V. M. T. Carneiro, *Synthesis*, 2010, 1059.
- (418) M. J. Lucero and K. N. Houk, *J. Org. Chem.*, 1998, **63**, 6973.
- (419) M. J. Martinelli, B. C. Peterson, V. V. Khau, D. R. Hutchison, M. R. Leanna, J. E. Audia, J. J. Droste, Y. D. Wu and K. N. Houk, *J. Org. Chem.*, 1994, **59**, 2204.
- (420) G. G. Bianco, H. M. C. Ferraz, A. M. Cost, L. V. Costa-Lotufo, C. Pessoa, M. O. de Moraes, M. G. Schrems, A. Pfaltz and L. F. Silva, *J. Org. Chem.*, 2009, **74**, 2561.
- (421) L. F. Silva and M. V. Craveiro, *Org. Lett.*, 2008, **10**, 5417.
- (422) R. M. Moriarty, J. S. Khosrowshahi and O. Prakash, *Tetrahedron Lett.*, 1985, **26**, 2961.
- (423) Y. Miki, R. Fujita and K.-i. Matsushita, *J. Chem. Soc., Perkin Trans. 1*, 1998, 2533.
- (424) M. M. Hossain, Y. Kawamura, K. Yamashita and M. Tsukayama, *Tetrahedron*, 2006, **62**, 8625.
- (425) S. Sato and H. Ishikawa, *Synthesis*, 2010, 3126.
- (426) H. Fujioka, S. Matsuda, M. Horai, E. Fujii, M. Morishita, N. Nishiguchi, K. Hata and Y. Kita, *Chem. Eur. J.*, 2007, **13**, 5238.
- (427) Y. Kita, S. Matsuda, E. Fujii, M. Horai, K. Hata and H. Fujioka, *Angew. Chem. Int. Ed.*, 2005, **44**, 5857.
- (428) Y. Harayama, M. Yoshida, D. Kamimura and Y. Kita, *Chem. Commun.*, 2005, 1764.
- (429) Y. Harayama, M. Yoshida, D. Kamimura, Y. Wada and Y. Kita, *Chem. Eur. J.*, 2006, **12**, 4893.
- (430) G. H. Posner, M. A. Hatcher and W. A. Maio, *Org. Lett.*, 2005, **7**, 4301.
- (431) W. A. Maio, S. Sinishtaj and G. H. Posner, *Org. Lett.*, 2007, **9**, 2673.
- (432) A. E. Allen and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2011, **133**, 4260.
- (433) P. Gao, D. L. Larson and P. S. Portoghese, *J. Med. Chem.*, 1998, **41**, 3091.
- (434) P. Gao and P. S. Portoghese, *J. Org. Chem.*, 1995, **60**, 2276.
- (435) S. A. Kozmin and V. H. Rawal, *J. Am. Chem. Soc.*, 1998, **120**, 13523.
- (436) V. K. Aggarwal and B. Olofsson, *Angew. Chem. Int. Ed.*, 2005, **44**, 5516.
- (437) E. N. Pitsinos, V. P. Vidali and E. A. Couladouros, *Eur. J. Org. Chem.*, 2011, **2011**, 1207.
- (438) N. Jalalian, E. E. Ishikawa, L. F. Silva, Jr. and B. Olofsson, *Org. Lett.*, 2011, **13**, 1552.
- (439) E. A. Couladouros, E. N. Pitsinos, V. I. Moutsos and G. Sarakinos, *Chem. Eur. J.*, 2005, **11**, 406.
- (440) T. K. Chakraborty and G. V. Reddy, *J. Org. Chem.*, 1992, **57**, 5462.
- (441) M. J. Crimmin and A. G. Brown, *Tetrahedron Lett.*, 1990, **31**, 2017.
- (442) S. Couty, B. Liegault, C. Meyer and J. Cossy, *Tetrahedron*, 2006, **62**, 3882.
- (443) D. J. Wardrop and J. Fritz, *Org. Lett.*, 2006, **8**, 3659.
- (444) K. S. Feldman, J. C. Saunders and M. L. Wroblewski, *J. Org. Chem.*, 2002, **67**, 7096.
- (445) K. S. Feldman, T. D. Cutarelli and R. Di Florio, *J. Org. Chem.*, 2002, **67**, 8528.