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Selective deprotection of silyl ethers

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1. Introduction

Protection/deprotection sequences are common components in modern organic synthesis and methods for protecting and deprotecting hydroxyl groups have become important elements in synthetic strategies.[1,2] Among the many protecting groups available for rendering hydroxyl groups temporarily inert, silyl groups have earned a place of prominence. Some common silyl protecting groups and their abbreviations are illustrated in Fig. 1.[3,4]

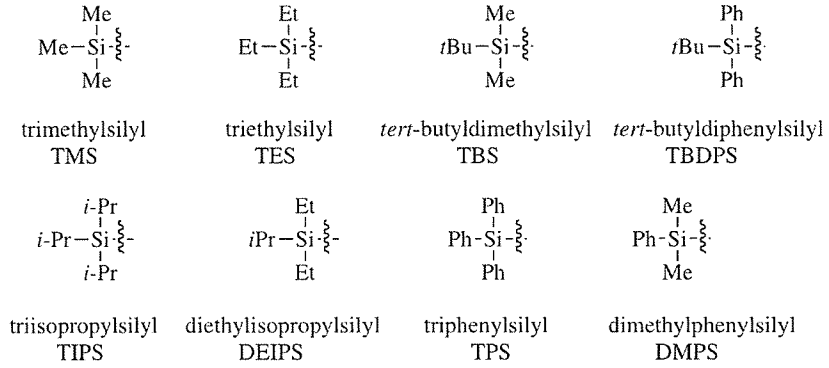


Fig. 1. Some commonly used silyl protecting groups.

As the complexity of synthetic targets has increased, the ability to protect multiple alcohol groups in the same molecule and then sequentially deprotect them allows individual alcohols in a polyhydroxylated compound to be modified. Silyl ether stability—and therefore the ease of deprotection—can be adjusted by altering the substituents on the silicon atom.[5,6] In most, but not all, cases, the effect is steric.[7] As a result, multiple hydroxyl groups in a single molecule can be protected *as the same functional group* but with different reactivities[3,4] and sequential selective desilylation allows each alcohol group to be released when it needs to be manipulated. This strategy is common in natural product syntheses and, although a comprehensive list of too long to be included here, some recent examples include such diverse natural products as Brevenal,[8–12] (−)-Sarain A,[13,14] Amphidinolide H[15] and G,[16] Leucascandrolide A,[17] Psymberin,[18–21] and Kendomycin.[22–25]

In recent years, protecting group-free synthetic strategies have been reported with increasing frequency.[26–34] Although such approaches will undoubtedly become part of the planning of synthetic routes in the future, the development of functional protecting groups such as fluorous[35,36] and magnetic[37] silyl groups that enhance product isolation, improved protocols for desilylation,[38,39] and enantioselective silylation techniques[40–45] point toward the continued importance of silyl protecting groups in organic synthesis. And, thus, selective deprotection reactions for silyl-protected polyhydroxy compounds will continue to be important tools in synthetic chemistry.

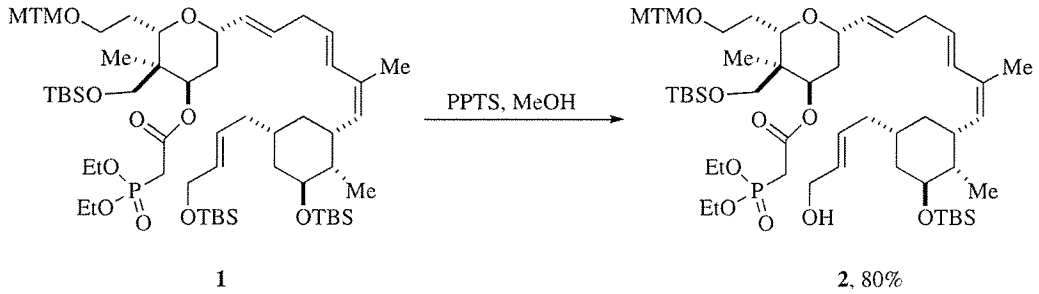
This paper follows two earlier reviews[3,4] on selective desilylation reactions and compiles examples from 2004 to the end of 2011. As was the case in the previous reviews, the focus is on reactions that cleave an oxygen–silicon bond and, thus, protection with groups involving a carbon–silicon bond such as the 2-(trimethylsilyl)ethoxymethyl (SEM) group are not included. This review is organized according to the type of silyl-protected alcohol (1°, 2°, etc.) that undergoes deprotection in the presence of another silyl-protected alcohol (1°, 2°, etc.), which remains intact with subcategories for acidic, basic, and miscellaneous reaction conditions. The text focuses on new and noteworthy examples with applications of more established methods included in the tabular summary. Although every effort has been made to be comprehensive, many examples of selective desilylation reactions are but one step in a multi-step synthetic scheme and typically not abstracted as a deprotection reaction.

2. Structure and selectivity

In predicting selectivity in silyl deprotection reactions, focus is often on the substituents on the silicon and on the parent alcohol's carbon. The role of steric and electronic effects in silyl deprotection reactions has been described elsewhere.[1,3–6,46] But, in general, silyl substituents that are bulky tend to slow the rate of silyl ether cleavage under acidic or basic conditions.[5,46] Similarly, an increase in steric bulk at the parent alcohol carbon decreases reactivity. Electron-withdrawing groups on the silicon atom decrease the rate of hydrolysis of silyl ethers under acidic conditions while electron donating substituents on silicon decrease the rate of base-mediated silyl ether cleavage.

Although this paper is organized according to the type of alcohol being released upon deprotection in the presence of another silyl ether, the entirety of the carbon framework plays a role in determining silyl ether stability and, thus, the rate of deprotection.[1] Through-bond

orbital interactions, for example, can have long range effects on the rates of desilylation reactions.[47] But, more typically, steric effects of the carbon backbone play an important role in determining selectivity. For example, although the steric differences between 1° and 2° silyl ethers would predict that, upon treatment with PPTS, the 1° TBS ethers in compound **1** would undergo selective cleavage in the presence of the 2° TBS ether, the selective desilylation of the 1° allylic TBS ether in the presence of another 1° TBS ether can best be ascribed to steric differences imposed by the surrounding carbon backbone[48] (Scheme 1).



Scheme 1. Ref. 48.

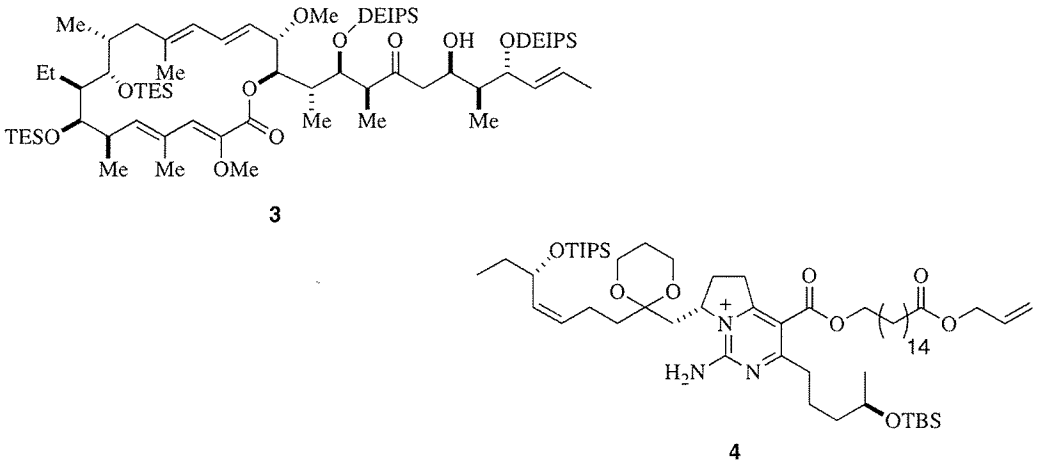
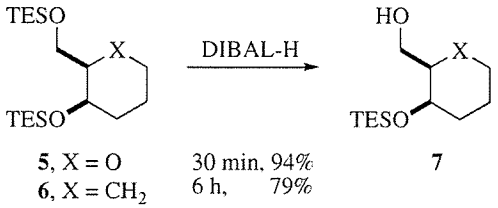


Fig. 2. Examples of the influence of substrate backbone.

The normal selectivity predicted by the steric influence of the silyl substituents alone can be reversed by the added steric effects of the backbone of the substrate.[1] For example, in the synthesis of (+)-Concanamycin F, two 2° DEIPS ethers in intermediate **3** were cleaved in the presence of two 2° TES ethers using TAS-F.[49] Typically, a DEIPS ether is considered to be more stable due to greater steric encumberance around the silicon atom. But, the two 2° TES ethers also proved to be surprisingly resistant to cleavage by TBAF and, ultimately, acidic conditions were employed to remove these protecting groups. In the total synthesis of (−)-Crambidine, a 2° allylic TIPS ether in intermediate **4** was shown to undergo deprotection in the presence of a 2° TBS ether using TBAF.[50] The selectivity in both of these examples can be ascribed to differences in the steric encumbrance of the substrate framework.

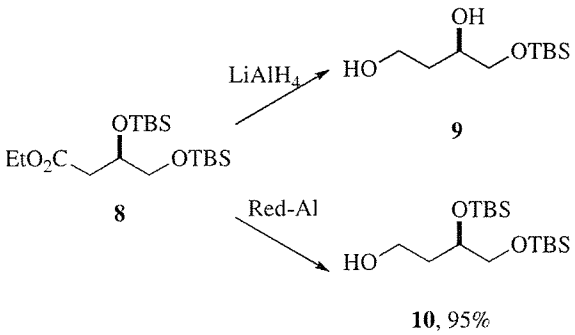
Neighboring group effects can also play a role in selective desilylation reactions but are often very substrate dependent. In the absence of direction by the required neighboring group, selectivity is not observed and, in some cases, deprotection is not effected. $LiAlH_4$, for example, has been shown to selectively deprotect TBS ethers that are near polar groups such as alcohols, esters, and amines.[51] The proposed mechanism involved reaction of $LiAlH_4$ to leave AlH_3 coordinated to the resulting anion. The proximity of the coordinated AlH_3 to the silyl ether allowed selective cleavage via hydride delivery to the silicon atom. Silyl ethers remote from the AlH_3–anion complex were inert.

A recent report described the importance of a neighboring ether on rate differences of selective deprotection using DIBAL-H.[52] An oxygen atom in cyclic ether **5** coordinated DIBAL-H and greatly accelerated deprotection of a nearby silyl ether (Scheme 2). But, substrate **6** lacked the ether and required a much longer reaction time to achieve a comparable yield of alcohol.



Scheme 2. Ref. 52.

Reduction of carbonyl groups resulting in the formation of an alkoxide can, ultimately, lead to selective cleavage of a neighboring silyl ether. For example, when ester **8** was treated with $LiAlH_4$, diol **9** was isolated (Scheme 3).[53] Interestingly, both TBS ethers remained intact when the reducing agent was Red-Al, producing alcohol **10** in high yield. When a longer carbon chain separated the 2° TBS ether and the ester, reduction of the ester could be accomplished with $LiAlH_4$ without silyl deprotection, illustrating the importance of the proximity of the neighboring group and the silyl ether. Although the selectivity of this example appears to be based on coordination of a hydride containing species to an alkoxide, the



Scheme 3. Ref. 53.

migration of a TBDPS group from a protected 2° alcohol to a 1° alkoxide has been reported in a reduction of an aldehyde near a 2° TBDPS ether.[54]

An even more unusual example of selective deprotection under reductive conditions was reported in the total synthesis of the proposed structure of Iriomoteolide-1a.[55] Reduction of the acetate group in intermediate **11** resulted in selective cleavage of the vicinal 3° TES ether without affecting the more remote 2° TES ethers. The proposed mechanism required that the silyl group undergoing deprotection be near the acetate as it underwent reduction (Scheme 4). Again, it is important to note that, although they represent selective desilylation reactions, examples such as these are very substrate specific.

3. Selective deprotection of 1° silyl ethers

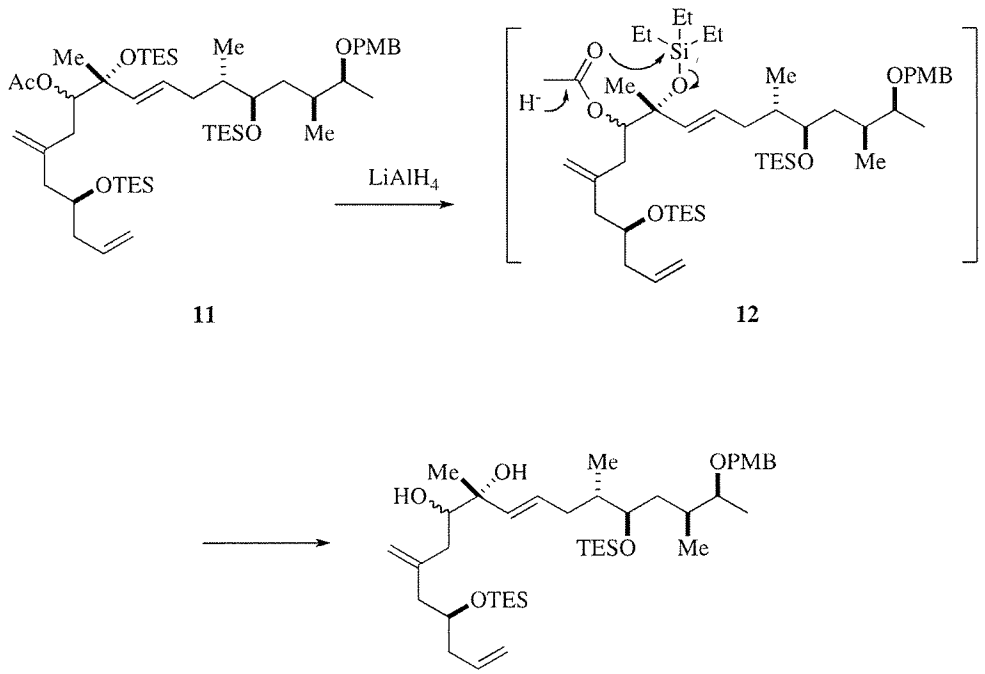
3.1. In the presence of 1° silyl ethers

3.1.1. Under acidic conditions. Since the steric difference between carbinol carbons of two 1° silyl ethers is not significant, steric and electronic effects of the substituents on silicon determine whether desilylation can occur in a selective fashion. Typically, a 1° TES or TBS ether is deprotected in the presence of a 1° TBDPS ether. For example, in two different total syntheses of Brevenal, a 1° TES ether was cleaved in the presence of a 1° TBDPS ether using PPTS[8,9] and a 1° TBS ether was cleaved in the presence of a 1° TBDPS ether using CSA.[11] Similarly, a 1° TES ether underwent desilylation in the presence of a 1° TBS ether using PPTS.[11]

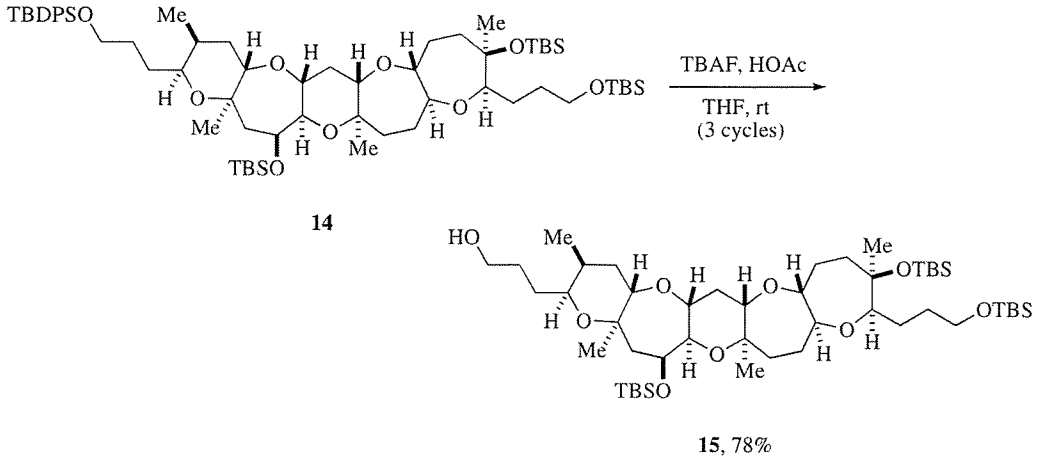
Although typically, a 1° TES or TBS ether undergoes deprotection in the presence of a 1° TBDPS ether under acidic conditions, TBAF buffered with HOAc was reported to deprotect a 1° TBDPS ether in the presence of a 1° TBS ether in intermediate **14** as part of a total synthesis of Brevenal (Scheme 5).[8,9] Note that 2° and 3° TBS ethers survived these conditions. However, three cycles of the reaction were required to achieve the reported yield.

Another example illustrates the unexpected difficulties sometimes encountered in trying to effect selective desilylation reactions. During the synthesis of an analog of Neplanocin A, bis-silyl ether **16** needed to be converted to monosilyl ether **17** (Scheme 6).[56] But selective cleavage of the 1° TBS ether proved surprisingly challenging using PPTS and other reagents known to effect selective desilylation of 1° TBS ethers in the presence of 1° TBDPS ethers. However, treatment of **16** with PPTS *and* TsOH in ethanol resulted in acceptable yields with no evidence of TBDPS ether cleavage. Although the difficulty in cleaving the TBS ether was ascribed to the 1° allylic TBDPS ether, the expected cleavage of the TBDPS ether in the presence of the TBS ether was not observed and it seems more likely that the steric crowding—a neopentyl-like alcoholic carbon—around the TBS ether inhibited its reactivity.

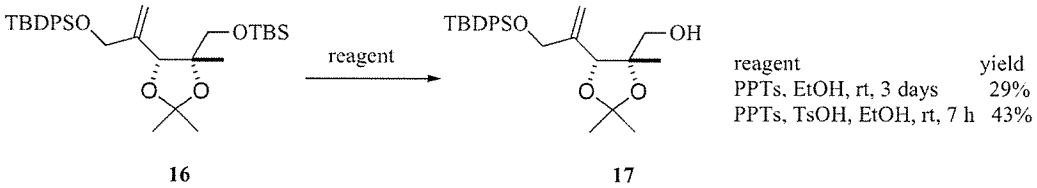
A number of other acids including HCl,[57] PPTS,[16,58–65] CSA,[11,25,66–72] TsOH,[73,74] and a mixture of TFA and HOAc[75] have been shown to effect deprotection of a 1° TBS ether in the presence of a TBDPS-protected 1° alcohol. Less-traditional acids such as high-loading sulfonic acid on nanoporous silica have been demonstrated to cleave 1° TBS ether **18a** but not 1° TBDPS ether **18b** (Scheme 7).[76]



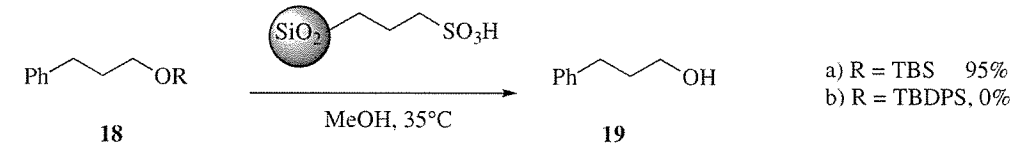
Scheme 4. Ref. 55.



Scheme 5. Refs. 8,9.



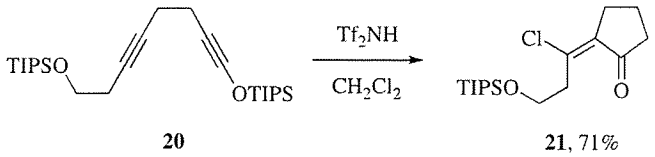
Scheme 6. Ref. 56.



Scheme 7. Ref. 76.

Phosphomolybdic acid on silica gel has also been reported to effect deprotection of a 1° TBS ether in the presence of a 1° TBDPS ether.[77]

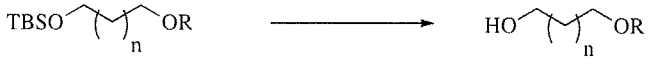
Another less-traditional acid, trifluoromethanesulfonimide, $HNTf_2$, was employed to desilylate a TIPS-protected alkynol in the presence of another 1° TIPS ether in bis-silyl ether **20** to form cyclopentanone **21** (Scheme 8).[78]

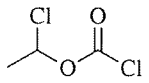
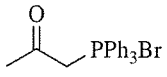
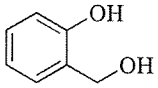


Scheme 8. Ref. 78.

Other systems employ reagents that generate acid in situ, effecting desilylation. 1-Chloroethyl chloroformate (**22**)[79] and acetonyltriphenylphosphonium bromide (**23**)[80] have been shown to generate HCl and HBr, respectively, upon reaction with methanol and *o*-hydroxybenzyl alcohol (**24**)[81] becomes more acidic upon irradiation with ultraviolet light. Each of these has been used to effect selective desilylation and some of the results are summarized in Table 1. It is noteworthy that chloroformate **22** has also been used to selectively deprotect 1° TES ethers in the presence of 1° TBS, TIPS, and TBDPS ethers and, in addition to requiring catalytic quantities of acid, the reaction times are considerably shorter than comparable acid-mediated reactions

Table 1
Selective deprotection of 1° TBS ethers via in situ generated acid



R	*n*	Reagent	Conditions	Yield (%)	Ref.
TIPS	4	 **22**	MeOH, rt, 15 min	86	79
TBDPS	4	**22**	MeOH, rt, <7 min	92	79
TBDPS	6	 **23**	MeOH, rt, 12 min	81	80
TBDPS	2	 **24**	hν, EtOH/H_2O, 10 h	95	81

in aqueous alcohol.[79] Selective deprotection of a 1° TES ether in the presence of a 1° TBS or TIPS ether has also been demonstrated with *o*-hydroxybenzyl alcohol (**24**).[81] Although this reaction requires long reaction times, the catalyst is recoverable and reusable.

A recent report describes the in situ generation of aqueous HF by the reaction of $KF{\cdot}H_2O$ and TMS-Cl in acetonitrile and this system has been used to effect selective cleavage of a 1° TBS ether in the presence of a 1° TBDPS ether.[82]

A number of metal salts have been used to effect selective desilylation reactions. Typically, these reactions involve the cleavage of a 1° TBS ether in the presence of a 1° TBDPS ether,[83–88] although instances of 1° TES deprotection in the presence of 1° TBS,[89] TIPS,[89] and TBDPS[86] and deprotection of a 1° TBS ether in the presence of a 1° TIPS ether have been reported.[89] Examples of desilylation of 1° TBS ethers in the presence of a 1° TBDPS ether are summarized in Table 2.

Table 2
Deprotection of 1° TBS ethers in the presence of 1° TBDPS ethers with metal salts

n	Metal salt	Conditions	Yield (%)	Ref.
2	Sulfated SnO_2	MeOH, rt, 15 min	98	83
3	$CuBr_2$	MeCN, rt, 24 h	60	84
6	$NiCl_2{\cdot}6H_2O/HSCH_2CH_2SH$	CH_2Cl_2/MeOH, rt, 15 min	83	85
3	$Fe(OTs)_3{\cdot}6H_2O$	MeOH, rt, 100 min	80	86
1	$SnCl_2{\cdot}2H_2O$	EtOH/H_2O, rt, 2.8 h	77	87

$SbCl_3$ in acetonitrile has been used to deprotect a 1° TBS ether in the presence of a 1° TBDPS ether in high yield.[88] Catalytic quantities of $FeCl_3$ in methanol have been reported to effect deprotection of 1° TES ethers in the presence of TBS-, TIPS-, or TBDPS-protected 1° alcohols and the cleavage of 1° TBS ethers in the presence of 1° TIPS or TBDPS ethers.[89]

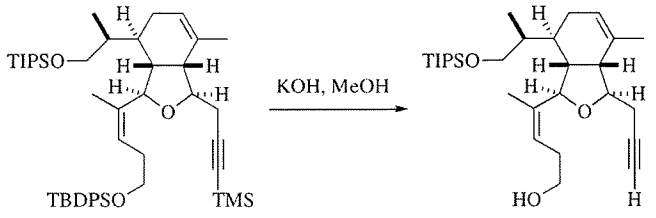
The mechanism by which these salts effect desilylation is not always clear and it is likely that a single mechanism does not explain all of these reactions. Some are ascribed to the generation of protic acid in situ.[83,85] Deprotection with $Fe(OTs)_3$, for example, was attempted in the presence of proton sponge and no desilylation was observed.[86] But, $FeCl_3$-catalyzed desilylation is thought to proceed via a single electron transfer mechanism.[89]

$CuBr_2$ has also been used to effect the conversion of silyl ethers to a variety of bisarylmethyl ethers in a mechanism that points to Lewis acid activity.[90] This reaction selectively converts 1° TES, TBS, and TIPS ethers to bis(methoxyphenyl)methyl ethers much more rapidly than TBDPS ethers.

3.1.2. Under basic/nucleophilic conditions. Basic conditions tend to favor desilylation of 1° TBDPS ethers in the presence of 1° TBS ethers. An example is found in the total synthesis of Briarellins E and F in which, upon treatment with methanolic KOH, intermediate **25** undergoes selective cleavage of a TBDPS-protected 1° alcohol in the presence of a 1° TIPS ether, with concomitant protiodesilylation of a TMS-protected terminal alkyne (Scheme 9).[91]

Treatment of intermediate **27** with TBAF in THF allowed the selective cleavage of one 1° TBS ether in the presence of *another* 1° TBS ether (Scheme 10).[48] However, a closer look at the results illustrates the challenge of attempting to selectively discriminate between two like silyl ethers. Although desired product **28** was isolated in 40% yield, unreacted starting material **27** was recovered in 32% yield and 24% yield of the doubly deprotected diol **29** was isolated.

A more typical, and more successful, example of TBAF-mediated deprotection is illustrated by the selective cleavage of one 1° silyl



25 **26**, >55%

Scheme 9. Ref. 91.

ether in the presence of another in the formal total synthesis of (+)-Pinnatoxin.[92] Differentially silyl-protected intermediate **30** underwent desilylation of a 1° TBS and a 2° TES ether in the presence of a 1° TIPS ether in quantitative yield (Scheme 11).

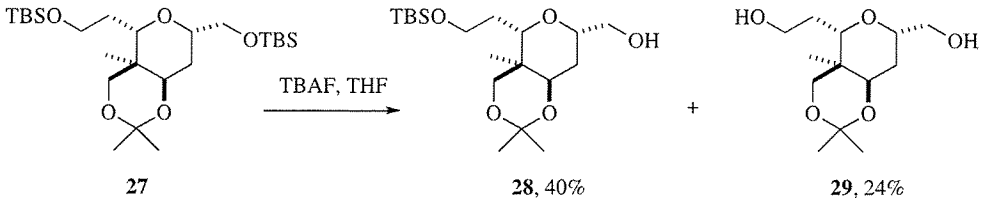
Although successful applications of TBAF to selective deprotection reactions have been reported,[3,4] more often than not, TBAF is employed when selectivity is not a concern such as in global desilylation reactions. Drawbacks to the use of TBAF include the need for stoichiometric quantities of reagent and the basicity of resultant solutions due to the inevitable presence of water.[93] Although the basicity can be addressed by buffering with HOAc, near stoichiometric quantities of TBAF are still required. Thus, the recent report of the use of *catalytic* quantities of TBAF at near neutral conditions[94] is a potentially important advance. Commercially available TBAF was dissolved in anhydrous THF and mixed with a small quantity of aqueous K_2HPO_4 to buffer the reaction mixture at pH 7.1. Relative rates of deprotection of 1° silyl ethers indicate that 1° TES ethers can be desilylated in the presence of 1° TBS, TIPS, and TBDPS ethers (Table 3).[94]

A fluorous version of TBAF has recently been reported to mediate selective desilylation reactions.[39] Although designed to allow easier removal of silyl by-products from deprotection reaction mixtures, this reagent was shown to selectively cleave 1° TES ethers in the presence of 1° TBS and TIPS ethers in good to excellent yields. Fluorous TBAF is somewhat less-reactive in silyl deprotections than its non-fluorous counterpart, a difference that has been attributed to the presence of the electron-withdrawing perfluoro chain.

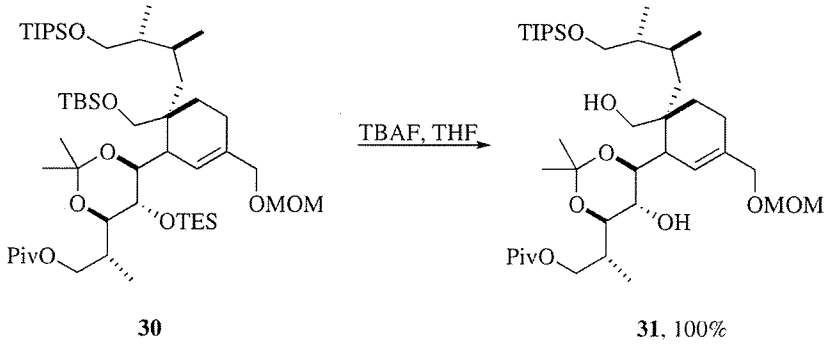
3.1.3. Under miscellaneous conditions. A recent report describes the use of an ionic liquid *in the absence of any catalyst* to effect the selective cleavage of 1° benzyl TMS ethers in the presence of other 1° TMS ethers.[95] TMS-protected 1° benzylic alcohols underwent deprotection upon stirring in 1-butyl-3-methylimidazolium chloride, [bmim]Cl, at room temperature. But other TMS-protected alcohols were inert, even after prolonged exposure to the reaction conditions. Evaluation of other silyl groups was not reported.

Reductive conditions have been successfully applied to selective desilylation reactions. Hydrogenation with catalytic Pd/C in methanol has been used to effect cleavage of 1° TES, TBS, and TPS ethers while 1° TIPS or TBDPS ethers are inert with especially high yielding desilylations of TES-protected 1° alcohols in the presence 1° TIPS and TBDPS ethers.[96] Catechol borane and Wilkinson's catalyst were used to deprotect 1° TES ethers in the presence of 1° TBS and TIPS ethers.[97] Interestingly, a TIPS-protected 1° alcohol was selectively deprotected in the presence of a TBS-protected 1° alcohol in differentially protected diol **32** (Scheme 12). A mechanism has not yet been proposed to explain this selectivity.

Lithium metal and naphthalene in dry THF have been shown to effect deprotection of 1° alcohols protected with silyl groups bearing at least one phenyl substituent.[98] But, if a bulky *tert*-butyl group was also a substituent, deprotection was so slow that selective cleavage of silyl ethers was possible. Some examples of attempted deprotection of silyl ether **34** to form alcohol **35** are illustrated in Scheme 13. Interestingly, 1° TBDPS ether **34d** was successfully

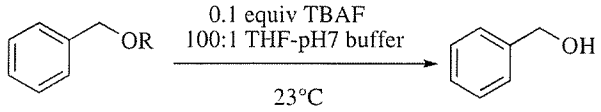


Scheme 10. Ref. 48.

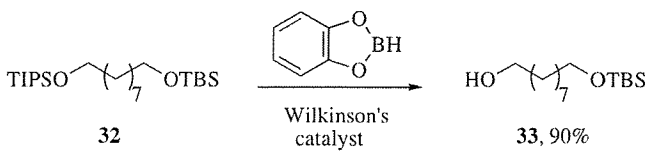


Scheme 11. Ref. 92.

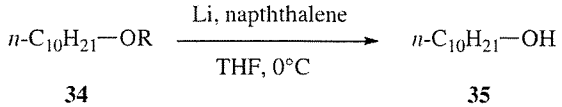
Table 3
Deprotection of 1° silyl ethers with buffered, catalytic TBAF[94]



R	Conversion (%)	Time
TES	95	30 min
TBS	94	42 h
TIPS	96	24 h
TBDPS	94	75 h



Scheme 12. Ref. 97.

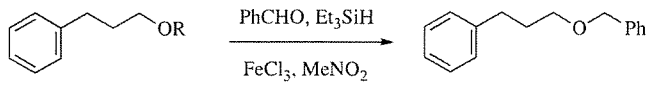


	time	yield
a) R = TMS	3 days	0%
b) DMPS	2 h	>99%
c) TPS	4.5 h	>99%
d) TBDPS	8 h	0%

Scheme 13. Ref. 98.

desilylated in 85% yield over four days when naphthalene was replaced with 4,4′-di-*tert*-butylbiphenyl (DTBB).[98]

In another reductive process, 1° TES and TBS ethers (**36a,b**) were readily converted into benzyl alkyl ethers (**37a,b**) upon treatment of benzaldehyde, triethylsilane, and catalytic $FeCl_3$.[99] But, under the same conditions, 1° TIPS and TBDPS ethers (**36c,d**) were very slow to react, indicating selective conversion of silyl ethers to benzyl ethers is possible (Scheme 14).

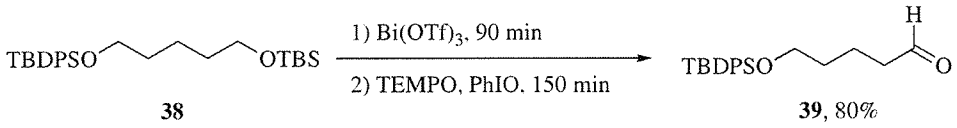


	time	yield
a) R = TES	2 h	100%
b) TBS	10 min	100%
c) TIPS	24 h	71%
d) TBDPS	24 h	37%

Scheme 14. Ref. 99.

Oxidative conditions have also been applied to selectively cleave one 1° silyl ether in the presence of another. Catalytic quantities of a single electron transfer agent, tris(4-bromophenyl)aminium hexachloroantimonate ($TBPA^+ \cdot SbCl_6^-$), were shown to effect selective desilylation of a 1° TBS ether in the presence of a 1° TBDPS ether.[100]

Oxidation of alcohols freed by silyl deprotection is a common synthetic strategy and oxidative deprotection of silyl ethers has been previously reviewed.[101] A one-pot, two-step deprotection/oxidation process has been reported to allow the conversion of 1° TBS ethers to aldehydes without reaction of 1° TBDPS ethers.[102] Thus, differentially protected bis-silyl ether **38** underwent selective deprotection and oxidation to form aldehyde **39** with survival of the TBDPS ether (Scheme 15). Other triflate salts such as $Sc(OTf)_3$ and $La(OTf)_3$ were also used to achieve deprotection and



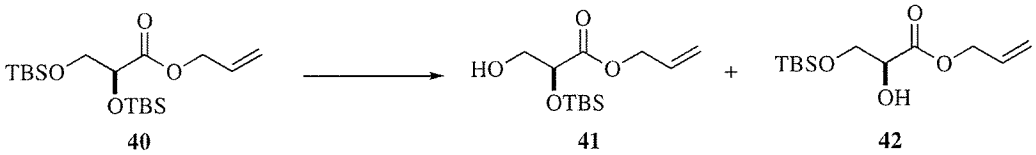
38 39, 80%

Scheme 15. Ref. 102.

oxidation. However, the reaction *must* be performed sequentially; when the Lewis acid and oxidant were added in a single step, the desired reaction was not observed. $Bi(OTf)_3$ has been reported to generate trifilic acid in situ after first binding with oxygenated substrates[103] and it seems likely that acid-catalyzed deprotection is the first step in this two-step sequence.

Other oxidative deprotections have exploited the enhanced reactivity of TMS-protected alcohols toward desilylation. Bromine/polyvinylpolypyrrolidine (Br_2/PVPP) has been reported to effect deprotection of 1° TMS ethers more rapidly and in higher yield than 1° TES or TBS ethers.[104] When the substrate was a silyl-protected benzylic alcohol, oxidized product predominated; for other silyl-ether in the presence of a 2° TBS ether does not involve fluorine, the most frequently used acids are HOAc,[106–113] PPTS,[48,114–126] TsOH,[74,127] and CSA.[11,24,71,72,128–143]

With such well-established precedent, selective removal of a TBS protecting group from a 1° silyl ether in the presence of a 2° TBS ether would seem to be a trivial transformation. However, examples can be found in which, a seemingly simple selective deprotection is considerably more complicated than expected. For example, as part of the total synthesis of Micropeptin T-20, the selective cleavage of a 1° TBS ether in the presence of a 2° TBS ether in protected diol **40** was found to be surprisingly difficult to accomplish in high yield (Scheme 16).[144] Treatment with HF·pyr



40 41 42

	yield of **41**
a) HF•pyr, THF, rt	complex mixture
b) HOAc, THF, H_2O, rt - 40°C	28%
c) TFA, H_2O, THF, 0°C - rt	54%
d) Oxone, MeOH, H_2O, rt	trace
e) $CeCl_3$•$7H_2O$, NaI, MeCN, rt-reflux	62%

Scheme 16. Ref. 144.

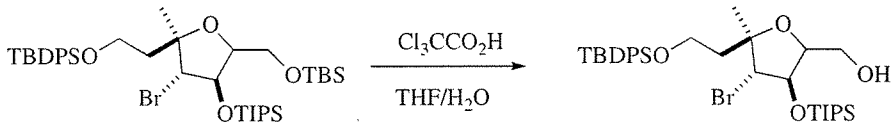
protected alcohols, the freed alcohol was predominant. Allyltriphenylphosphonium peroxodisulfate has been reported to effect deprotection and oxidation of TMS-protected 1° benzylic alcohols to aldehyde.[105] But, most other TMS-protected 1° alcohols failed to react, indicating that selective deprotection/oxidation of 1° benzylic TMS ethers in the presence of another 1° TMS ether is possible.

3.2. In the presence of 2° silyl ethers

The oldest and most widely employed selective desilylation reactions involve cleavage of a 1° silyl ether in the presence of a 2° silyl ether. The differences in the steric environment around the carbinol carbons is often enough to drive chemoselectivity. But, in some instances, the use of different silyl groups on the two alcohols can further bias the outcome in favor of the desired product.

3.2.1. Under acidic conditions. By far, the most common selective deprotection of a 1° silyl ether in the presence of a 2° silyl ether is when both are TBS ethers. When selective desilylation of a 1° TBS ether in the presence of a 2° TBS ether included using HOAc, TFA, and oxone. But the best result was achieved using $CeCl_3 \cdot 7H_2O$ and NaI.[144]

Use of a less-reactive, bulkier silyl group to protect the 2° alcohol can improve the selectivity of deprotection. For example, the 1° alcohols in intermediate **43** en route to Leiodolide B were protected as TBS and TBDPS ethers while a 2° alcohol was protected as a TIPS ether.[145] Selective deprotection of the 1° TBS ether without cleavage of either the 1° TBDPS ether or the TIPS-protected 2° alcohol was achieved using Cl_3CCO_2H in THF and water (Scheme 17).



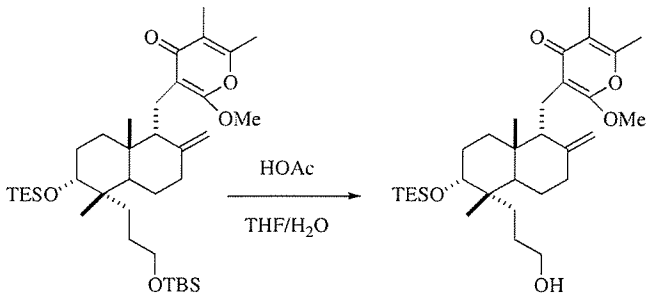
43 44, 86%

Scheme 17. Ref. 145.

Selective deprotection of a 1° TBS ether in the presence of a 2° fluorous TIPS ether was achieved using acetyl chloride and methanol.[146]

Examples in which less hindered silyl groups protecting 2° alcohols have been found to be stable while permitting deprotection of a 1° silyl ether has been reported. For example, differentially silyl-protected diol **45** underwent selective desilylation of the 1° TBS

ether in the presence of the 2° TES ether with acetic acid/water/THF (Scheme 18).[147] It is likely that steric crowding at the carbon adjacent to the protected 2° alcohol hindered hydrolysis of the TES ether.



45 46, 84%

Scheme 18. Ref. 147.

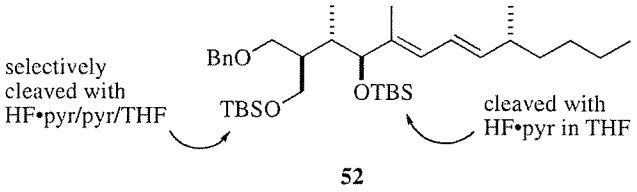
Acid catalysis is, of course, also employed in other important reactions and a tandem selective desilylation/transesterification/ketal formation was reported as part of the total synthesis of Bryostatin B.[148,149] Thus, protected triol **47** was treated with catalytic CSA in methanol at 0 °C and transesterification of the lactone and mixed ketal formation to yield intermediate **48** was accompanied by selective desilylation of the 1° TBS ether in the presence of the less-reactive 2° TBDPS ether (Scheme 19).

reaction was applied to a different substrate, selective acetylation of the 1° TMS ether in the presence of a 2° TMS ether was observed.

Selective deprotection of 1° TBS ethers in the presence of 2° TBS ethers has been most frequently achieved using HF·pyr.[140,152–183] Aqueous HF, generated in situ, has also been shown to effect desilylation of 1° TBS ethers in the presence of 2° TBS ethers.[82] And, HF·pyr has been used to selectively deprotect a 1° TBS ether in the presence of a fluorous TIPS-protected 2° alcohol.[184]

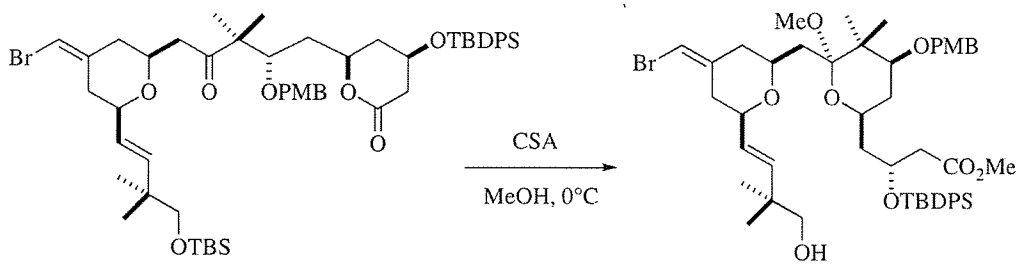
HF·pyr has been used less frequently with other silyl groups but examples of selective deprotection include cleavage of a 1° TBDPS in the presence of a 2° TES,[185] a 2° TBS,[185] a 2° TIPS,[145,186] or a 2° TBDPS ether.[21,187,188] Similarly, a TIPS-protected 1° alcohol was cleaved in the presence of a 2° TIPS ether using HF·pyr.[189]

Reaction conditions, however, can have a major effect on the chemoselectivity of desilylation reactions. For example, when HF·pyr was used in a THF–pyridine mixture, selective removal of the 1° TBS ether in protected triol **52** was achieved in 84% yield (Fig. 3).[160] Subsequently, the 2° TBS ether was cleaved using HF·pyr



52

Fig. 3. Example of the effect of reaction conditions.[160]



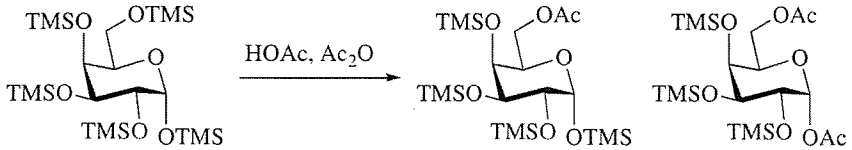
47 48, 93-96%

Scheme 19. Refs. 148,149.

Methods for the direct chemoselective conversion of silyl ethers to acetate esters have been reported. Perchloric acid absorbed on silica gel ($HClO_4$–SiO_2) was used with Ac_2O to effect the selective replacement of a TBS group with an acetyl group on a 1° alcohol without reacting at a 2° TBS ether.[150] A similar outcome was achieved using HOAc and Ac_2O to acetylate only the 1° TMS ether of per-*O*-TMS-protected galactoside **49**.[151] When the reaction was performed at room temperature, the major product was monoacetate **50**. The use of microwave irradiation to accelerate the reaction produced diacetate **51** as the predominant product (Scheme 20). However, when the microwave version of this

in THF without excess pyridine. Similarly, adjustment of the amount of pyridine added to an HF·pyr-mediated deprotection of a molecule containing 1° TES and 2° TBS ethers allowed selective deprotection of the 1° TES ether or global silyl removal.[190]

Although a 1° TBDPS ether was cleaved using HF·pyr without reaction of a cyclic siloxane that protected a 2° alcohol in the total synthesis of (−)-7-Demethylpiericidin A_1,[191] TBAF buffered with HOAc is typically used for the selective deprotection of TBDPS-protected 1° alcohols in the presence of 2° TBS ethers.[8–11,63,70,192–201] For example, in the synthesis of the spiroketal fragment of Spirangien A, a 1° TBDPS ether underwent desilylation

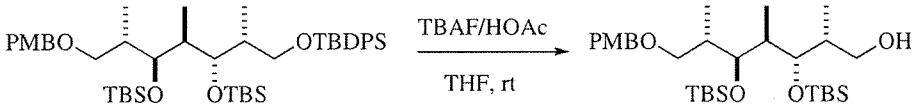


49 50 51

	50	51
room temp, 48 h	90%	7%
microwave, 3 x 25 min	22%	52%

Scheme 20. Ref. 151.

in the presence of two 2° TBS ethers and a PMB-protected 1° alcohol in intermediate **53** (Scheme 21).[200] This same report describes an unusually recalcitrant attempt at global desilylation of 1° and 2° TBS ethers to form a spiroketal, ultimately forcing the synthetic route to be revised.

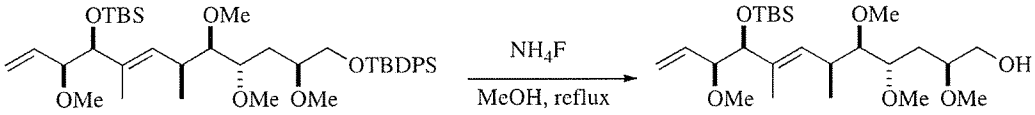


53 **54**, 68%

Scheme 21. Ref. 200.

A common means of effecting selective deprotection of a 1° TBS ether in the presence of a 2° TBS ether employs NH_4F.[17,116,202–208] NH_4F also allows selective deprotection of 1° TBDPS ethers in the presence of 2° TBS ethers.[205,209–214] For example, NH_4F in methanol allowed selective cleavage of a 1° TBDPS ether without deblocking of a 2° TBS ether in protected diol **55** (Scheme 22).[211]

A recent report describes the selective desilylation of a 1° TBS ether in the presence of a 2° TBDPS ether using TBAF in THF at room temperature,[221] illustrating the competing roles of the electronic nature of the silyl protecting group and the steric environment of the alcoholic carbon. TBAF has also been used in the selective deprotection of 1° TIPS ethers in the presence of 2° TBS ethers.[222,223]



55 **56**, 82%

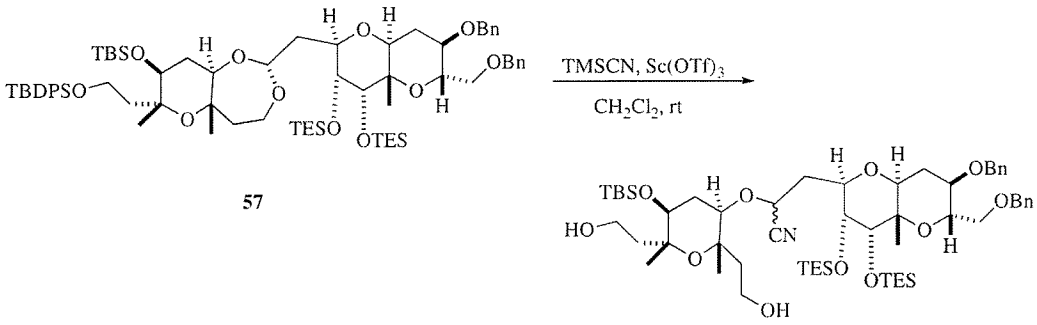
Scheme 22. Ref. 211.

Metal salts have also been used to deprotect silyl-protected 1° alcohols in the presence of silyl-protected 2° alcohols. Rate differences in the cleavage of 1° TES and 2° TBS ethers using $Fe(OTs)_3$ as a catalyst indicate selective deprotection is possible.[86] $SnCl_2 \cdot 2H_2O$[87] and $SbCl_3$[88] have been shown to allow deprotection of 1° TBS ethers in the presence of 2° TBS ethers. Treatment of polyether **57** with $Sc(OTf)_3$ and TMSCN resulted in the opening of the cyclic acetal with concomitant cleavage of the 1° TBDPS ether in the presence of 2° TES and TBS ethers (Scheme 23).[215]

3.2.2. Under basic/nucleophilic conditions. Under basic conditions, the most common selective deprotection of 1° silyl ethers in the presence of 2° silyl ethers also occurs when TBS groups protect both alcohols and the most common reagent for effecting this transformation is TBAF.[216–220] Fluorous TBAF has been reported to allow selective cleavage of a 1° TBS ether in the presence of a 2° TBS ether in high yield.[39]

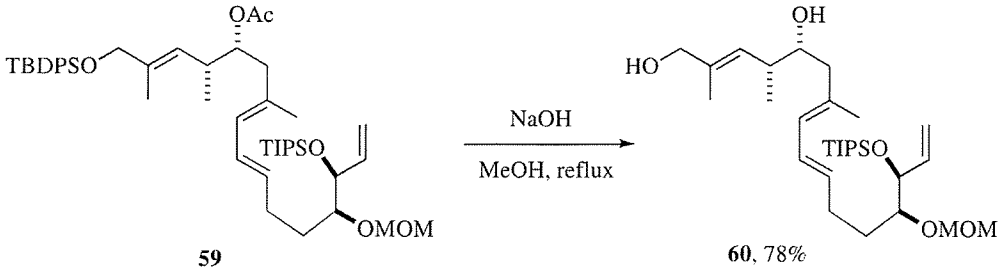
NaOH in methanol[224] and KOH in THF with 18-crown-6[225] have been used to effect selective desilylation of a 1° TBDPS ether in the presence of a 2° TBS ether. Similarly, when subjected to refluxing methanolic NaOH, bis-silyl ether **59** underwent deprotection of the 1° TBDPS ether without cleavage of the 2° TIPS ether, although an acetate group was hydrolyzed (Scheme 24).[226]

DIBAL-H has also been reported to effect selective deprotection of a variety of 1° silyl ethers in the presence of 2° silyl ethers.[52] So, 1° TBS ethers were cleaved with excess DIBAL-H at −40 °C in the presence of 2° TBS ethers. Similarly, 1° TES, TBS, and TBDPS ethers of bis-silyl ether **61a–c** underwent selective desilylation in the presence of a 2° TES ether (Scheme 25). Other protecting groups such as benzyl ethers and benzylidene acetals survive these reaction



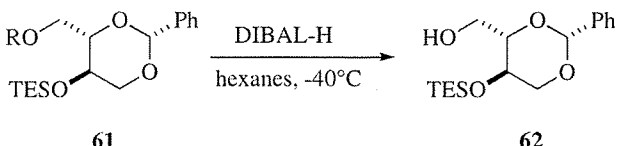
57 **58**, 83%

Scheme 23. Ref. 215.



59 60, 78%

Scheme 24. Ref. 226.



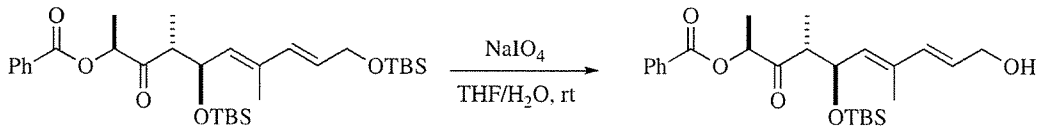
61 62

a) R = TES, 80%
b) R = TBS, 87%
c) R = TBDPS, 81%

Scheme 25. Ref. 52.

conditions. Of particular note, though, is the observation that ether groups, near the silyl group being removed, accelerate desilylation.

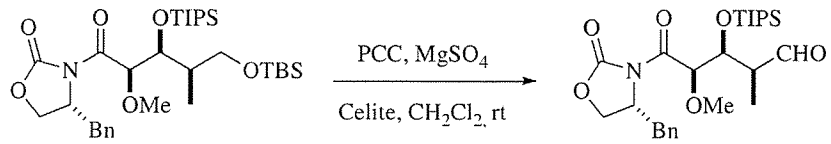
3.2.3. Under miscellaneous conditions. An excess of $NaIO_4$ in a THF–water mixture at room temperature has been shown to effect the selective deprotection of 1° TBS ethers in the presence of 2° TBS ethers.[227,228] The reaction conditions were sufficiently mild to permit application to substrates that exhibit acid- or base-sensitivity. Thus, the differentially protected triol **63** underwent selective cleavage of the 1° TBS ether in the presence of a 2° TBS ether and a benzoyl ester to yield monosilyl ether **64** (Scheme 26).[227]



63 64, 94%

Scheme 26. Ref. 227.

A common subsequent fate of 1° alcohols produced in deprotection reactions is oxidation. Appropriate selection of oxidizing conditions, however, can permit a one-pot selective deprotection/oxidation sequence to occur. For example, PCC on Celite was used to selectively deprotect and oxidize the alcohol in bis-silyl ether **65** to the resultant aldehyde **66** without cleavage of the 2° TIPS ether (Scheme 27).[229]



65 66, 82%

Scheme 27. Ref. 229.

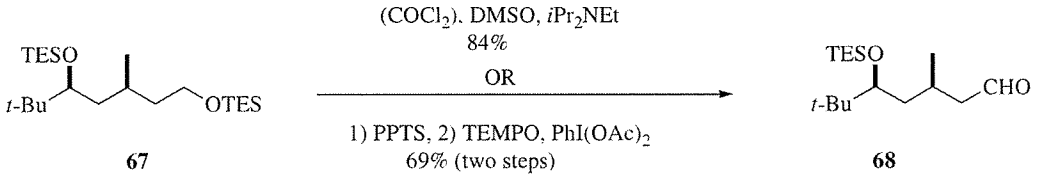
More typically, though, Swern conditions have been used in the selective deprotection and oxidation of 1° silyl ethers in the presence of 2° silyl ethers. Examples include selective cleavage of a 1° TMS ether in the presence of a 2° TMS ether,[230] a 1° TES ether in the presence of a 2° TES ether,[231–235] and a 1° TES ether in the presence of a 2° TBS ether.[236–238] An example of the efficiency of the one-pot selective deprotection/oxidation versus the two-step procedure was described as part of the total synthesis of Apratoxin A.[231] Bis-silyl ether **67** was exposed to Swern conditions to desilylate and oxidize the 1° alcohol without reaction of the 2° TES ether, yielding aldehyde **68** in 84% yield (Scheme 28). But a two-step sequence involving selective deprotection of the 1° TES ether in bis-silyl ether **67** with PPTS followed by TEMPO mediated oxidation yielded aldehyde **68** in 69% overall yield.

A one-pot, two-step process uses $Bi(OTf)_3$, then TEMPO, and co-oxidants in the selective deprotection/oxidation of a 1° TBS ethers to form an aldehyde in the presence of a 2° TBS ether.[102]

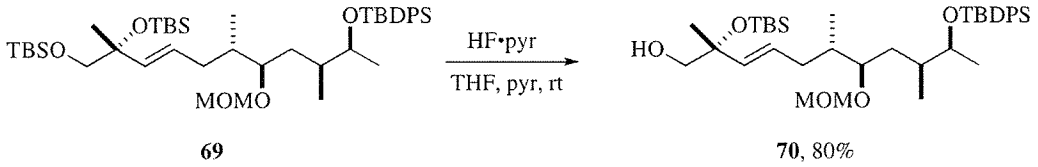
3.3. In the presence of 3° silyl ethers

3.3.1. Under acidic conditions. Selective desilylation of silyl-protected 1° alcohols in the presence of 3° silyl ethers is encountered with less frequency than cleavage of 1° silyl ethers in the presence of 1° or 2° silyl ethers and no single acidic reagent stands out as the preferred method. Protic acids such as PPTS have been used to deprotect 1° TES ethers in the presence of 3° TES[8,9] or 3° TBS[11] ethers. Similarly, CSA has been used to desilylate a 1° TBS ether in the presence of a 3° TBS ether.[11,69] The Lewis acid, $BF_3 \cdot OEt_2$, afforded selective deprotection of a 1° TBS ether in the presence of a 3° TBS ether.[239]

HF·pyr has been used on a number of occasions to deprotect 1° silyl ethers in the presence of 3° silyl ethers. Tris-silyl ether **69** was treated with HF·pyr in THF and pyridine to deblock a 1° TBS ether in the presence of 3° TBS and 2° TBDPS ethers (Scheme 29).[240] Subsequent oxidation of the newly released alcohol was followed by cleavage of the 3° TBS ether using TBAF in THF. HF·pyr has also been used to desilylate a TBS-protected 1° alcohol in the presence of a 3° TES ether.[241,242]



Scheme 28. Ref. 231.



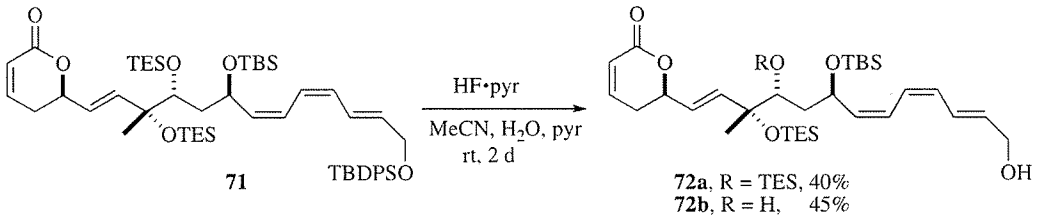
Scheme 29. Ref. 240.

Selective deprotection of a 1° TBDPS ether in the presence of a 3° TES ether using HF·pyr has also been reported. Treatment of compound **71** with HF·pyr in a mixture of 9:1:2 CH_3CN/H_2O/pyridine resulted in removal of the TBDPS group protecting the 1° alcohol without deblocking the 3° TES ether (Scheme 30).[185] Although a 2° TBS ether survived these conditions, partial deprotection of the 2° TES ether was observed. Subsequent re-exposure to the same reaction conditions resulted in complete removal of the 2° TES ether. The stability of the 3° TES ether to the prolonged desilylation conditions is illustrative of the general stability of 3° silyl ethers to acidic conditions.

Later in the reaction pathway, exposure of the remaining 3° TES ether to TBAF in THF for 6 h resulted in desilylation in 80% yield. TBAF has also been shown to deprotect a 1° TBS ether in the presence of a 3° TBS ether.[158]

Difference in the rate of desilylation of 1° TES and 3° TES ethers indicates that selective deprotection of 1° TES ethers in the presence of 3° TES ethers is possible using 1.5 equiv of KF in tetraethylene glycol.[246]

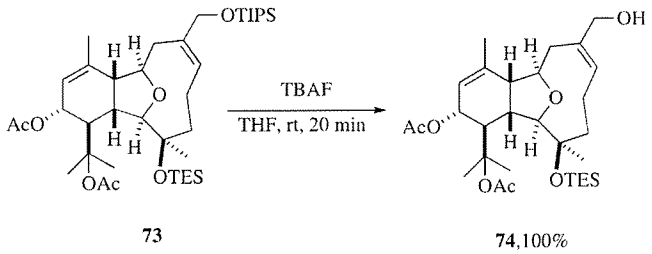
3.3.3. Under miscellaneous conditions. Swern oxidation conditions have been demonstrated to allow selective deprotection/oxidation



Scheme 30. Ref. 185.

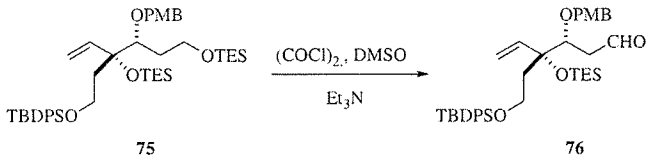
Other acidic fluoride sources have also been applied to selective removal of silyl groups protecting 1° alcohols in molecules that also contain a 3° silyl ether. TBAF buffered with HOAc was used to effect the desilylation of a 1° TBDPS ether in the presence of a 3° TBS ether.[10,11] NH_4F allowed deprotect of a 1° TBS ether in the presence of a 3° TBS ether.[243]

3.3.2. Under basic/nucleophilic conditions. TBAF has been used to cleave a 1° TBS ether in the presence of a 2° TBS ether and a 1° TIPS ether without deprotecting a 3° TES ether.[244,245] For example, in the synthesis of Astrogorgin, TBAF in THF effected quantitative conversion of intermediate **73** to alcohol **74**, selectively deprotecting the 1° TIPS ether without cleaving the 3° TES ether (Scheme 31).[244] Reaction time was critical; exposure of **73** to TBAF lasted 20 min.



Scheme 31. Ref. 244.

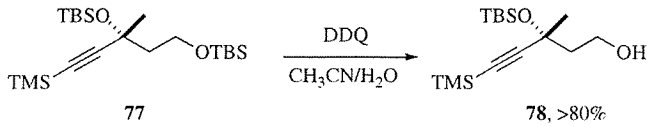
of 1° TMS ethers in the presence of 3° TMS ethers[247] and 1° TES ethers in the presence of 3° TES ethers.[248] As part of a synthesis of the central core of Phoslactomycin B, Swern conditions were used to selectively desilylate and oxidize the 1° TES ether of intermediate **75** without affecting a 1° TBDPS or a 3° TES ether to yield aldehyde **76** (Scheme 32).[248]



Scheme 32. Ref. 248.

Selective deprotection of a 1° TBS ether in the presence of a 3° TBS ether in bis-silyl ether **77** was effected using DDQ in CH_3CN (Scheme 33).[249] The resultant 1° alcohol was then oxidized to an aldehyde. It is noteworthy that these conditions do not result in protiodesilylation of the TMS-protected terminal alkyne.

Selective conversion of 1° TIPS ethers to bis(*p*-methoxyphenyl) methyl ethers without reaction at 3° TIPS ethers has been shown to be possible using catalytic $CuBr_2$ and bis(*p*-methoxyphenyl) methanol.[90]



77 78, >80%

Scheme 33. Ref. 249.

4. Selective deprotection of 2° silyl ethers

4.1. In the presence of 1° silyl ethers

In general, deprotection of a 2° silyl ether in the presence of a 1° silyl ether occurs when the less hindered 1° alcohol is protected using a bulkier silyl group or a silyl group with electronic characteristics that increase its stability under the reaction conditions.

4.1.1. Under acidic conditions. The most common acid-mediated selective deprotection of a 2° silyl ether in the presence of a 1° silyl ether occurs when the 2° alcohol is protected with a relatively small TES group and the 1° alcohol is protected with the larger and less acid sensitive TBDPS group. Methods for selective deprotection of 2° TES ethers in the presence of 1° TBDPS ethers without using fluoride sources include HCl,[8,9,250] HOAc,[251–253] CSA,[11,12,25,69,254] PPTS,[16,255–257] TsOH,[232,258–264] and TFA.[265–267] Some examples of this transformation involve a second reaction that occurs in tandem with selective desilylation. For example, TsOH was used to convert tris-silyl ether **79** into the spiroketal **80** via selective desilylation of two 2° TES ethers in the presence of a 1° TBDPS ether (Scheme 34).[261] Similar examples of this reaction have been reported[258,262] including an example in which two 2° TBS ethers were deprotected to form a spiroketal.[268]

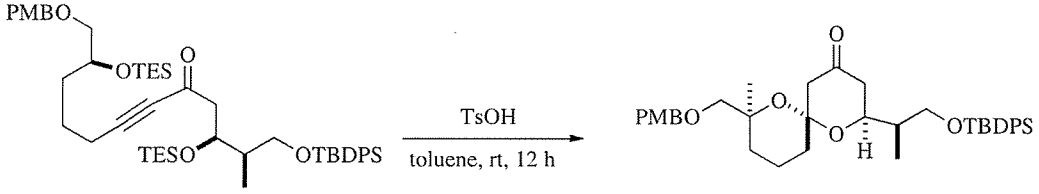
step process of sequential treatment with CSA followed by TsOH at room temperature afforded a satisfactorily useful mixture of spiroketals **82** and **83**, resulting from selective deprotection of two 2° TES ethers and subsequent conjugate addition of the resulting alcohols (Scheme 35). Note that the more sterically hindered 2° TES ether was not fully desilylated.

Though fewer in number, selective deprotection of 2° TES ethers in the presence of 1° TIPS ethers is also common and examples of acidic reagents used in this selective transformation include CSA,[270,271] PPTS,[186,256,272–274] TsOH,[275] and TFA.[276] For example, PPTS was used to selectively desilylate two 2° TES ethers in poly silyl ether **84** without cleavage of a 1° TIPS or a 2° TBS ether to yield spiroketal **85** (Scheme 36).[272]

Although less common, selective deprotection of 2° silyl ethers in the presence of 1° silyl ethers has also been effected using acidic fluoride sources. HF·pyr was used to selectively cleave a 2° TMS ether in the presence of 1° TBDPS ether,[277] a 2° TES ether in the presence of a 1° TBDPS ether,[278–280] and a 2° TES ether in the presence of a 1° TIPS ether.[274] Thus, as part of studies toward the total synthesis of Azaspiracid-1, bis-silyl ether **86** was treated with HF·pyr in a 1:1 mixture of pyridine and THF for 2 h at 0 °C to yield monosilyl ether **87** in 85% yield (Scheme 37).[278]

TBAF buffered with HOAc has been used to effect selective desilylation of a 2° TBS ether in the presence of a 1° TBDPS ether[281] and of a 2° TIPS enol ether in the presence of a 1° TIPS ether.[282] In another example of the importance of the molecular framework of the substrate, TBAF buffered with *o*-nitrophenol was used to selectively cleave a 2° DEIPS ether in the presence of a 1° DEIPS ether in the synthesis of the enediyne, N1999A2.[283]

TMS-OTf has been used as a Lewis acid to effect selective deprotection of a 2° TES ether in the presence of a 1° TBDPS ether in

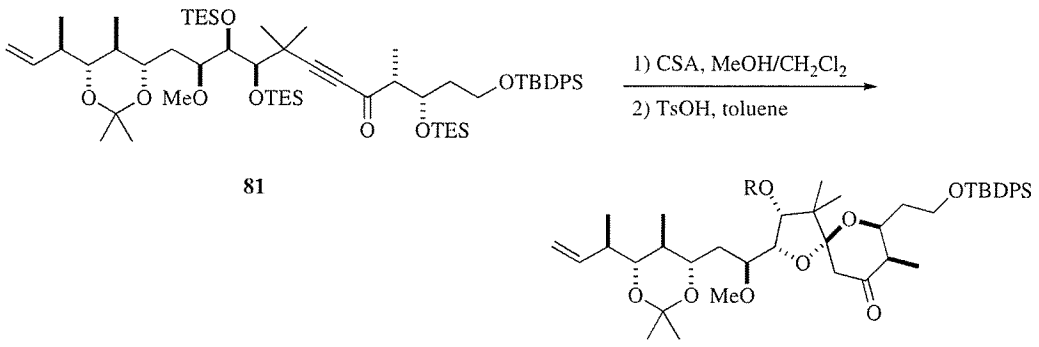


79 80, 87%

Scheme 34. Ref. 261.

A similar spiroketal formation via selective desilylation of 2° TES ethers illustrates the challenges presented by some systems. Attempts to convert intermediate **81** to spiroketal **82** using a variety of acids such as TsOH, CSA, and PPTS were unsuccessful.[269] But, a two-

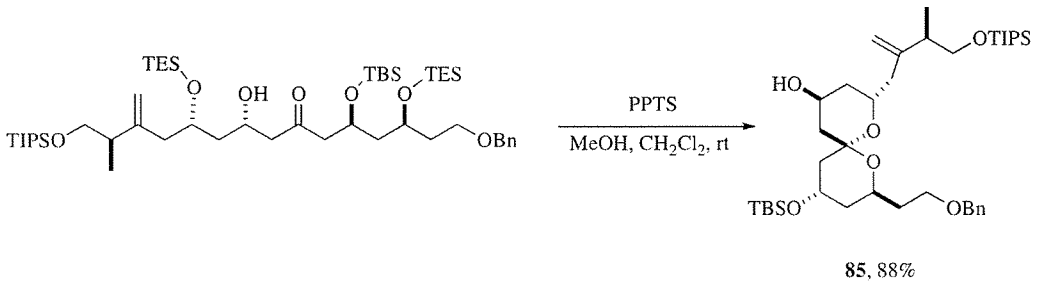
studies toward the total synthesis of Azaspiracid-1.[284,285] Thus, doubly silyl-protected intermediate **88** underwent selective cleavage of the 2° TES ether and concomitant cyclization to form the bis-spiroketal **89** in high yield and as a single stereoisomer



81

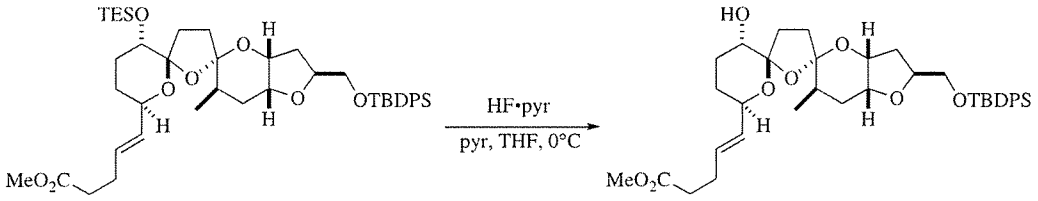
82, R = H 31%
83, R = TES, 47%

Scheme 35. Ref. 269.



85, 88%

Scheme 36. Ref. 272.



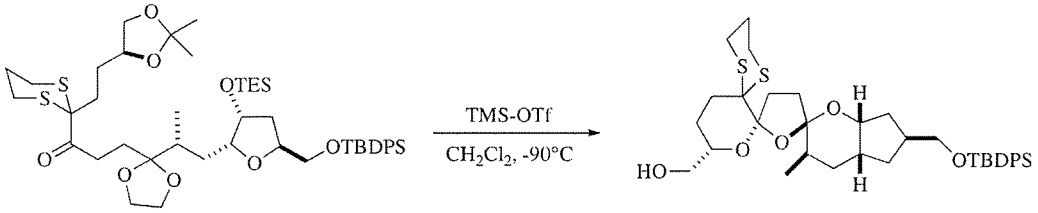
86 87, 85%

Scheme 37. Ref. 278.

(Scheme 38). A 2° TBS ether was also subject to selective deprotection in the presence of a 1° TBDPS ether using TMS-OTf.[284,285]

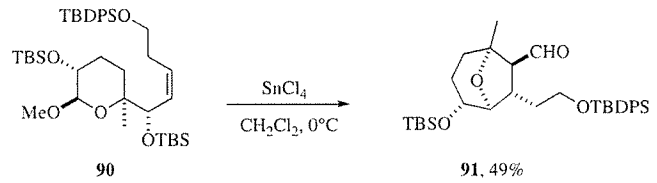
Other Lewis acids have been used to effect selective desilylation as one step in a more complex transformation. For example, as part of the total synthesis of (+)-Aspergillin PZ, tris-silyl ether **90** was treated with 0.5 equiv of $SnCl_4$ in CH_2Cl_2 at 0 °C to yield aldehyde **91** via deprotection of one 2° TBS ether in the presence of another 2° TBS ether and a 1° TBDPS ether followed by a tandem 2-oxonia [3,3]-sigmatropic rearrangement/aldol reaction (Scheme 39).[286] As part of the synthesis of Peribysin E, $TiCl_4$ was used to selectively cleave two 2° TES ethers in tris-silyl ether **92** with subsequent ring contraction to form silyl ether **93** (Scheme 40).[287]

A total synthesis of (−)-Brevenal provides yet another example of selective desilylation of 2° TES ethers as the first step in a tandem process.[8,9] $Zn(OTf)_2$ and ethanethiol were used to deprotect 2° TES ethers without affecting a 1° TBDPS or a 3° TBS ether and the newly liberated alcohol underwent cyclization with a nearby ketone to form a mixed thioketal and the C ring of Brevenal.



88 89, 89%

Scheme 38. Refs. 284,285.



90 91, 49%

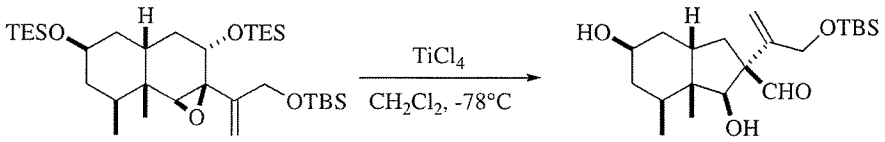
Scheme 39. Ref. 286.

Likewise, $BiBr_3$ was used in conjunction with the TMS enol ether of methyl α-bromopropionate to effect the deprotection and cyclization of bis-silyl ether **94** to yield the cyclic ether **95** in quantitative yield (Scheme 41).[288] $BiBr_3$ has been shown to generate HBr in situ as the acidic agent.[289]

4.1.2. Under basic/nucleophilic conditions. Surprisingly few examples have been reported in recent years of selective desilylation reactions of 2° silyl ethers in the presence of 1° silyl ethers. TBAF has been used to deprotect 2° TMS[92] or 2° TES ethers[92,290] in the presence of a 1° TIPS ether. Similarly, TBAF was used to selectively cleave 2° TES[290,291] or 2° TBS ethers[292,293] without affecting TBDPS-protected 1° alcohols. For example, upon treatment with TBAF in THF, bis-silyl ether **96** underwent selective desilylation of a 2° TES ether in the presence of a 1° TBDPS ether to generate 2° alcohol **97** in quantitative yield (Scheme 42).[291]

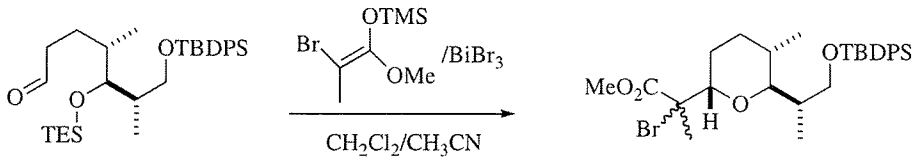
In an example of the effect of neighboring groups directing deprotection, reduction of an ester with $LiAlH_4$ resulted in selective cleavage of a nearby 2° TBS ether in the presence of a 1° TBS ether (see Scheme 3).[53] But, when the distance between the ester and 2° TBS ether was increased, ester reduction was achieved without deprotection of the silyl ether. Red-Al also allows ester reduction without effecting deprotection.

4.1.3. Under miscellaneous conditions. As part of studies directed toward the synthesis of Bryostatin 1, alcohol **98** was treated with 2-mercaptothiazole, PPh_3, and DIAD in an attempt to prepare the



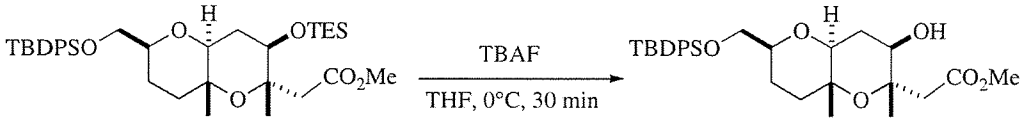
92 93, 50%

Scheme 40. Ref. 287.



94 95, 100%

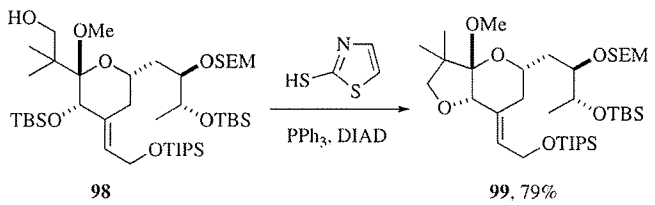
Scheme 41. Ref. 288.



96 97, 100%

Scheme 42. Ref. 291.

corresponding thiol.[273] However, selective deprotection of a 2° TBS ether in the presence of a 1° TIPS and a 2° TBS ether was observed with cyclization to the tetrahydrofuran **99** (Scheme 43).



98 99, 79%

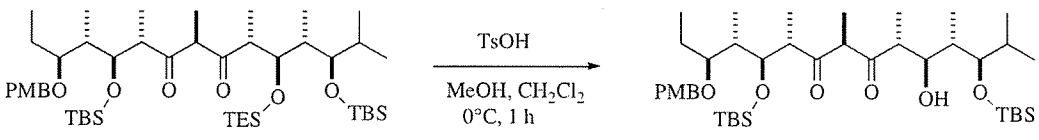
Scheme 43. Ref. 273.

Lithium powder and naphthalene have been shown to allow deprotection of 2° DMPS ethers while 1° TBDPS ethers are inert.[98] But, oxidizing conditions are more commonly used. Iodoxybenzoic acid and methoxypyridine-*N*-oxide were used to selectively cleave a 2° TMS enol ether in the presence of a 1° TBS ether.[294] DDQ in THF was used to selectively deprotect a 2° TES[295] and a 2° TBS ether[296,297] in the presence of a 1° TBDPS ether. CrO_3/H_5IO_6 has been shown to convert TBS-protected 2° benzylic alcohols into ketones while 1° TBDPS ethers are inert.[298]

4.2. In the presence of 2° silyl ethers

4.2.1. Under acidic conditions. Distinguishing one 2° silyl ether from another often relies on steric differences of the substituents on the silicon atoms. But the steric effect of the surrounding carbon framework also plays a role. Under acidic conditions, the most common strategy is for the 2° silyl ether, that is, to undergo deprotection to bear a TES group while the other bears a TBS group. Acids that have been employed to achieve the selective deprotection of a 2° TES ether in the presence of a 2° TBS ether include HOAc,[113,253,299–301] CSA,[11,143,302] PPTS,[16,22,23,53,174,233,255–257,272–274,303–309] TsOH,[260,264,275,310] TFA,[311] and HCO_2H.[312] For example, upon treatment with TsOH, the differentially protected polyol **100** underwent selective desilylation of a TES-protected 2° alcohol in the presence of two 2° TBS ethers to yield alcohol **101** in high yield (Scheme 44).[310]

Similarly, 2° TES ethers have been deprotected in the presence of 2° TIPS ethers using acids such as HOAc,[313] CSA, and PPTS[170,186,314] and 2° TBDPS ethers using HCl,[232] HOAc,[315,316] CSA,[317,318] and PPTS.[308,319] TBS-protected 2° alcohols have also been deprotected in the presence of 2° TBPDS ethers using HCl,[320] HOAc,[321] and CSA.[322–324] And, PPTS was employed to selectively deprotect a 2° DEIPS ether in the presence of a 2° TIPS ether with concomitant cleavage of an acetonide as part of the total synthesis of 13-deoxytedanolide.[325]



100 101, 95%

Scheme 44. Ref. 310.

In a study of the reactivities of fluorous versions of silyl groups, a 2° TES ether was cleaved without reaction of 2° alcohols protected with two versions of so-called fluorous TIPS groups (see Fig. 4) using PPTS or HOAc/H_2O/THF.[35] But when H_2SiF_6 was the desilylation agent, 2° fluorous TIPS ethers were susceptible to cleavage while 2° TIPS ethers were inert.[35] But, the real power of fluorous TIPS group lies in its use as a tool in separations.[146]

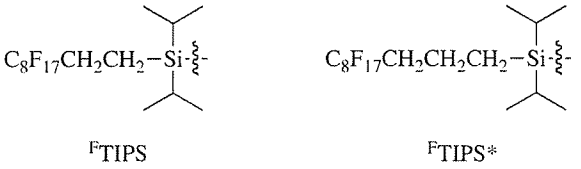
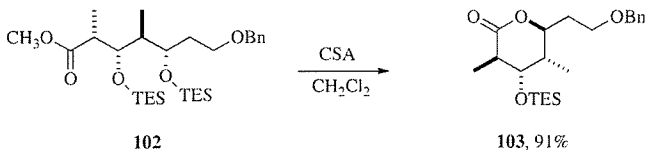


Fig. 4. Fluorous TIPS groups.[35]

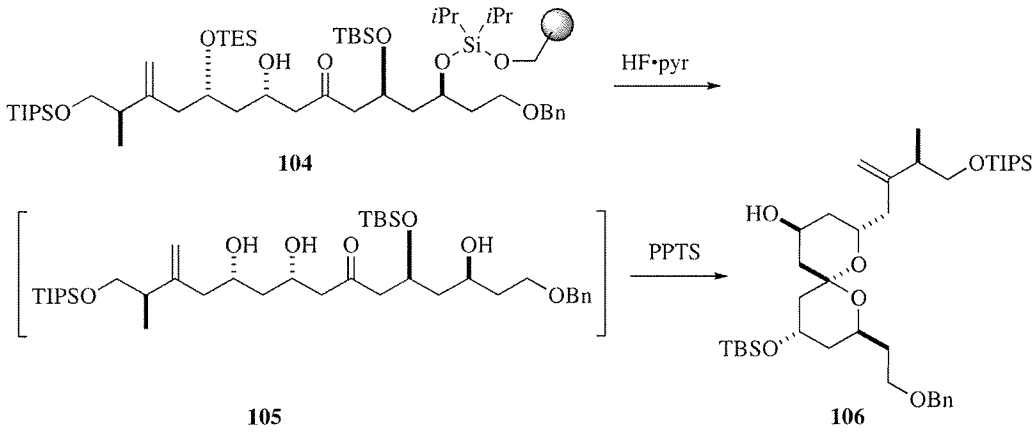
Differences in the steric environment near a 2° silyl ether can shield it from deprotection, allowing, for example, a 2° TES ether to be cleaved in the presence of another 2° TES ether.[141] As part of the total synthesis of (+)-Discodermolide, upon treatment with 1 equiv of CSA, bis-silyl ether **102** underwent successful selective deprotection and concomitant lactone formation to yield monosilyl ether **103** (Scheme 45).



102 **103**, 91%

Scheme 45. Ref. 141.

Selective deprotection of TES-protected 2° alcohols in the presence of 2° TBS ethers has also been accomplished using HF·pyr.[55,185,231,310,326–330] For example, one step in the synthesis of spongistatin on a solid supported employed HF·pyr in THF to deprotect a 2° TES ether on differentially protected polyol **104** in the presence of a 2° TBS ether and a 1° TIPS ether (Scheme 46).[326] Note that the silyl linker to the solid support was also cleaved under these conditions and subsequent cyclization to the desired spiroketal **106** required equilibration with PPTS.

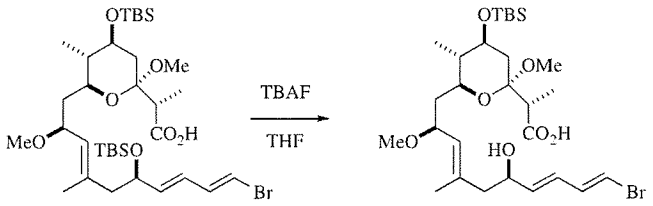


Scheme 46. Ref. 326.

Lewis acids have also been used to discriminate between 2° silyl ethers. BF_3·OEt_2 selectively deprotected a 2° TES ether in the presence of a 2° TBDPS ether in a substrate that underwent global desilylation when acidic methods or TBAF were used.[331] Similarly, $TiCl_4$–EtOAc complex converted a 2° TBS ether to an alcohol without reaction with a 2° TBDPS ether.[332] A 2° TES ether was cleaved in the presence of a 2° TIPS when treated with $Zn(OTf)_2$ and EtSH with concomitant reaction of the newly released alcohol to form a mixture of hemiketal and thioketal.[333]

4.2.2. Under basic/nucleophilic conditions. The most common selective deprotection of one 2° silyl ether in the presence of another 2° silyl ether occurs when TBAF is used to deprotect a 2° TES ether in the presence of a 2° TBS ether, relying on the steric effects of the silicon substituents.[280,334–337] TBAF has also been used to deprotect a 2° TES ether in the presence of a 2° TBDPS ether.[263,338]

When differences in the steric environment around the carbinol carbons are large enough, silyl ethers bearing like silyl groups can be distinguished from one another in TBAF-mediated deprotection reactions. Examples include the selective cleavage of a 2° TES ether in the presence of another 2° TES ether[334,335] and a 2° TBS ether in the presence of another 2° TBS ether.[20,304,307,339] For example, in the total synthesis of (+)-Dolastatin **19**, a 2° allylic TBS ether in intermediate **107** was cleaved in the presence of another 2° TBS ether using TBAF (Scheme 47).[304]



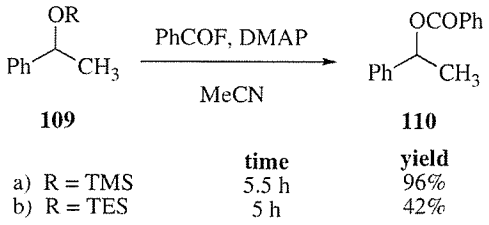
107 **108**, 98%

Scheme 47. Ref. 304.

If one 2° silyl ether is sterically encumbered by the carbon framework, a smaller silyl group can be preserved in selective deprotection reactions. For example, cleavage of a 2° allylic TIPS ether in the presence of a 2° TBS ether upon treatment with 2–3 equiv of TBAF has been reported in the total synthesis of (−)-Crambidine (see **4** in Fig. 2).[50] Larger amounts of TBAF, however, yielded the globally desilylated product.

TBAF at 0 °C was used to effect selective cleavage of a 2° TBDPS ether in the presence of a 2° TBS and a 3° TMS ether as part of the total synthesis of Lituarines B and C.[177] Similarly, selective deprotection of a 2° allylic DMPS ether using TBAF without affecting a 2° TBS ether has been reported.[340]

Benzoyl fluoride has been reported to convert silyl ethers into benzoate esters with modest selectivity for 2° TMS ethers **109a** over 2° TES ethers **109b** (Scheme 48).[341] Unlike acetyl chloride mediated desilylation reaction, the mechanism of this reaction does not appear to generate HF.



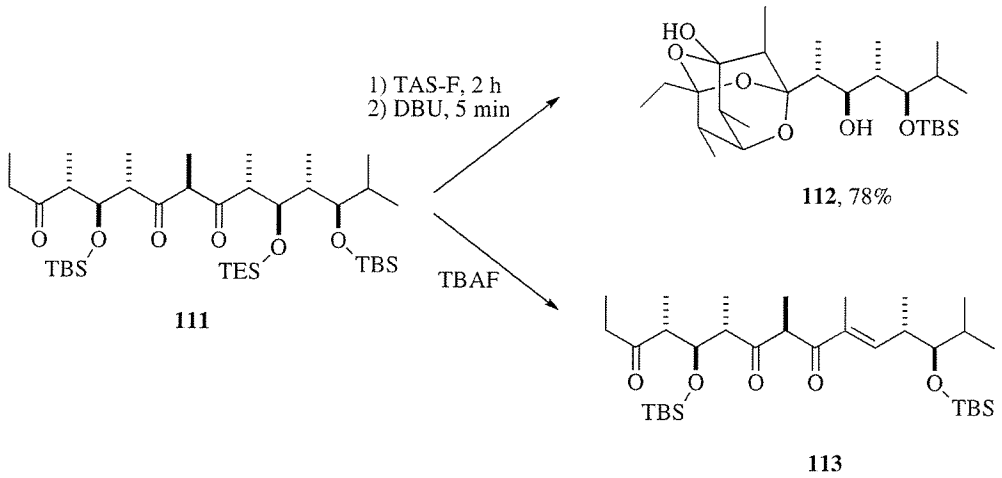
Scheme 48. Ref. 341.

TAS-F has been reported to effect the selective deprotection of a 2° TES and a 2° TBS ether in the presence of yet another 2° TBS ether in intermediate **111** to produce the complex trioxaadamantane **112** after brief exposure to DBU (Scheme 49).[310] The observation that treatment of intermediate **111** with TBAF yielded enone **113** illustrates the strongly basic nature of TBAF solutions, due to traces of water.

with enantiomerically pure binaphthols. The polyether fragments coordinate with K^+ while the hydroxyl groups coordinate with the F- and the silyl ether oxygen. The result is that one enantiomer of racemic 2° TMS ethers underwent selective desilylation without reaction of the other enantiomer. Thus, upon treatment with 0.7 equiv of KF and 20 mol% polyether **114**, racemic 2° TMS ether **115** is resolved to form **R-116**, leaving **S-115** intact (Scheme 50).

Reduction of an aldehyde has been reported to allow intramolecular silyl migration of one of two silyl groups, representing a selective desilylation of a 2° TBDPS ether in the presence of another 2° TBDPS ether. Bis-silyl ether **117** was thus treated with $NaBH_4$ to afford a 10:90 mixture of alcohols **118** and **119** (Scheme 51).[54] The remaining 1° alcohol **118** was converted into the desired 2° alcohol **119** by heating with DMAP in ethanol. This is another substrate-specific example in which the proximity of the newly formed alkoxide is crucial to silyl migration.

4.2.3. Under miscellaneous conditions. Oxidative conditions leading to selective cleavage of a 2° TBS ether in the presence of another 2° TBS ether include treatment with $NaIO_4$,[227] and a salen–Mn^{III} complex with PhIO.[343] Oxidative conditions that effect the selective desilylation of 2° TES ethers in the presence of 2° TBS ethers include $(NH_4)_6Mo_7O_{24}$ and H_2O_2,[344] DDQ,[345,346] and $PdCl_2/CuCl_2/O_2$.[347]



Scheme 49. Ref. 310.

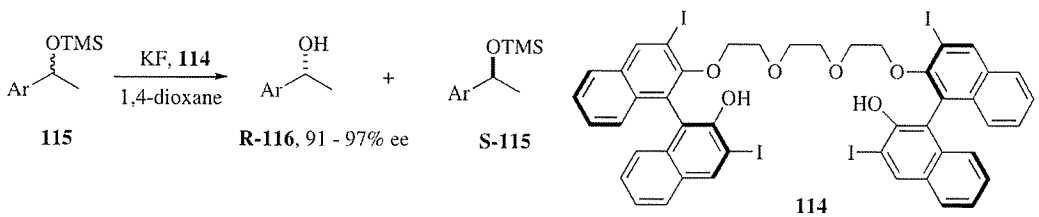
Taking advantage of subtle steric differences between the 2° alcohols from which the silyl ethers were made, selective cleavage of two 2° DEIPS ethers in the presence of two 2° TES ethers was achieved using TAS-F en route to the total synthesis of (+)-Concanamycin F (see **3** in Fig. 2).[49]

A recent report described the use of KF in the desilylative kinetic resolution of 2° TMS ethers.[342] This method relies on a polyether that resembles a potassium selective crown ether in size but, rather than a closed ring as in crown ethers, is capped

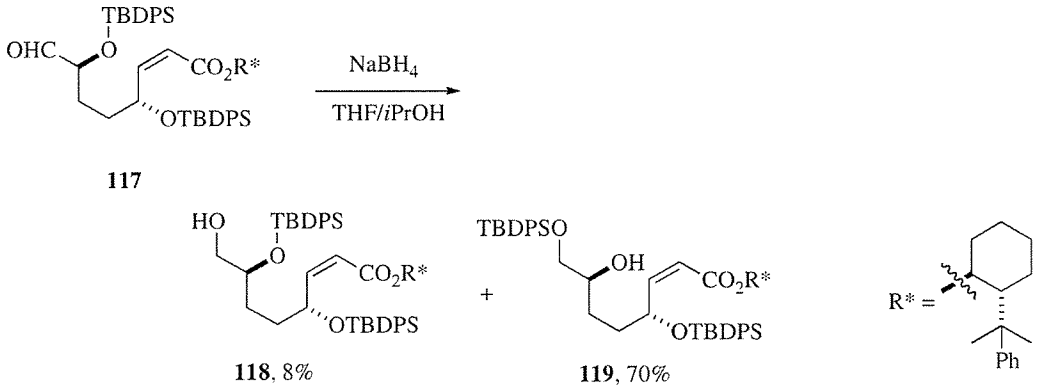
Other oxidative methods that effect selective deprotection of 2° TBS ethers in the presence of 2° TBDPS ethers include treatment with $NaIO_4$[227] and CrO_3/H_5IO_6.[298]

4.3. In the presence of 3° silyl ethers

4.3.1. Under acidic conditions. Examples of selective deprotection of 2° silyl ethers in the presence of 3° silyl ethers are relatively few in number. Reported examples include selective desilylation of a 2° TES



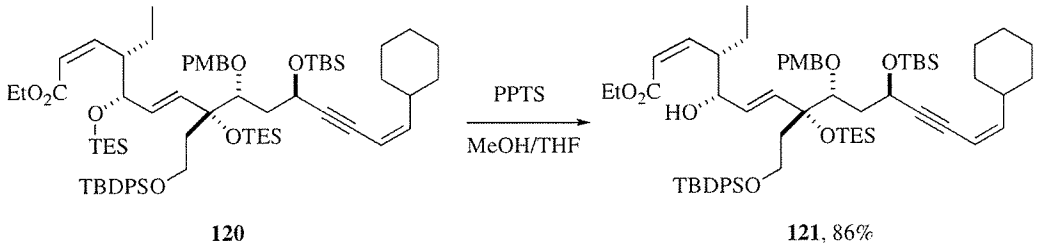
Scheme 50. Ref. 342.



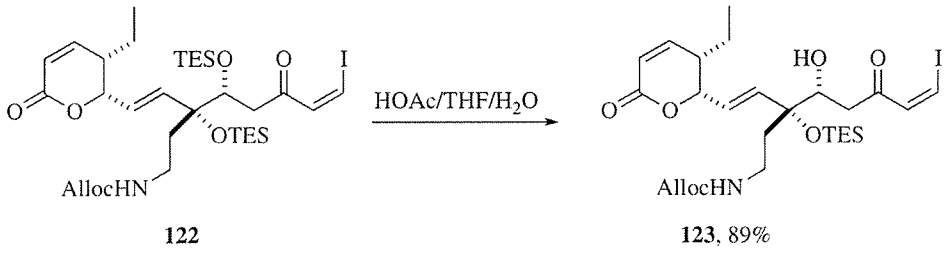
Scheme 51. Ref. 54.

ether in the presence of a 3° TES ether using HOAc[348] or PPTS[53,255,349] and a 2° TES ether in the presence of a 3° TBS ether using CSA.[11,12,69,271] Two examples from different approaches to the total synthesis of Phoslactmycin B are illustrative of these approaches. Upon exposure to PPTS, differentially protected intermediate **120** underwent selective deprotection of a 2° TES ether in the presence of a 3° TES ether, a 1° TBDPS, and a 2° TBS ether to yield alcohol **121** (Scheme 52).[255] In a similar fashion, bis-TES ether **122** underwent selective cleavage of a 2° TES ether in the presence of a 3° TES ether using HOAc, H_2O, and THF to yield alcohol **123** (Scheme 53).[348]

4.3.2. Under basic/nucleophilic conditions. Recent examples of selective cleavage of a 2° silyl ether in the presence of a silyl-protected 3° alcohol using basic or nucleophilic conditions have been limited to TBAF, which has been used to deprotect a 2° TMS ether in the presence of a 3° TES ether[92] and 2° TES ethers in the



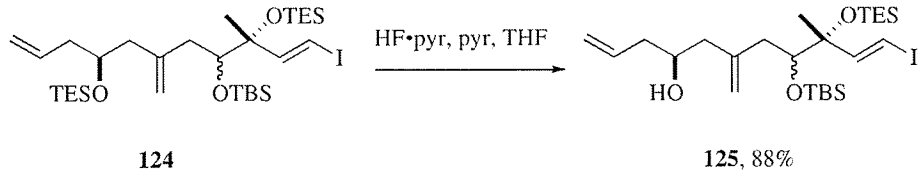
Scheme 52. Ref. 255.



Scheme 53. Ref. 348.

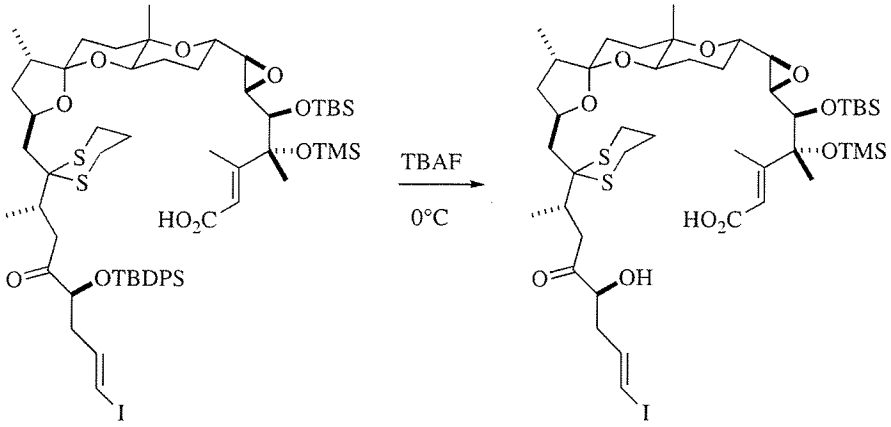
HF·pyr has also been employed in cleaving a 2° TES ether in the presence of a silyl-protected 3° alcohol.[55,185] For example, a 2° TES ether in intermediate **124** underwent selective deprotection in high yield in the presence of a 3° TES and a 2° TBS ether to yield alcohol **125** (Scheme 54).[55] Deprotection of a 2° TES ether in the presence of a 3° TES ether proved more challenging in the total synthesis of Fostriecin and required prolonged exposure to HF·pyr to achieve the desired desilylation.[185]

presence of 3° TES ethers.[92,334,350] Perhaps most interesting, though, is the report of selective desilylation of a 2° TBDPS ether in the presence of a 3° TMS ether and a 2° TBS ether in the total synthesis of Lituarines B and C.[177] Thus, differentially protected



Scheme 54. Ref. 55.

intermediate **126** underwent selective deprotection of the 2° TBDPS ether with TBAF, taking advantage of the enhanced lability of TBDPS ethers to fluoride and the severe steric crowding of the 2° and 3° silyl ethers (Scheme 55).



126 **127**, >51%

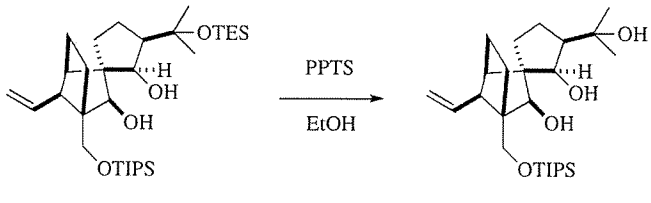
Scheme 55. Ref. 177.

5. Selective deprotection of 3° silyl ethers

Selective desilylation of a 3° silyl ether typically requires that the 3° alcohol be protected with a small, less sterically encumbered silyl group while the silyl ether that is to remain intact be protected with a larger silyl protecting group.

5.1. In the presence of 1° silyl ethers

5.1.1. Under acidic conditions. Selective deprotection of 3° silyl ethers in the presence of 1° silyl ethers is most commonly effected using acidic conditions applied to substrates in which the 3° alcohol is protected with a smaller, less hindered silyl group than the 1° alcohol. PPTS has been used to cleave a 3° TMS ether in the presence of a 1° TBDPS and a 2° TBS ether.[247] Similarly, treatment with catalytic PPTS in ethanol at ambient temperature allowed polycyclic intermediate **128** to undergo selective desilylation of the 3° TES ether without reaction at the 1° TIPS ether (Scheme 56).[351]



128 **129**, >91%

Scheme 56. Ref. 351.

TES-protected 3° alcohols have been selectively released in the presence of 1° TBDPS ethers with CSA during the formation of a cyclic ketal.[254] Thus, protected triol **130** was treated with catalytic CSA in MeOH/THF to deprotect a 2° and a 3° TES ether in the presence of a 1° TBDPS ether with cyclization to form the methyl glycoside **131** (Scheme 57).

HCl has also been used to effect the selective desilylation of a 3° TES ether in the presence of a 1° TBDPS ether.[250]

5.1.2. Under basic/nucleophilic conditions. Few examples of selective desilylation of 3° silyl ethers in the presence of 1° silyl ethers under basic conditions have been described. But, the migration of a TES group from a protected 3° alcohol to form a 2° TES ether in the presence of other silyl-protected alcohols represents an example of selective desilylation of a 3° TES ether in the presence of a 1° TBS ether. Thus, intermediate **132** was treated with $LiN(TMS)_2$ and $CeCl_3$ to yield cyclic product **133** in 82% yield (Scheme 58).[123] Selectivity is, again, achieved due to the proximity of the newly formed alkoxide to the 3° TES ether.

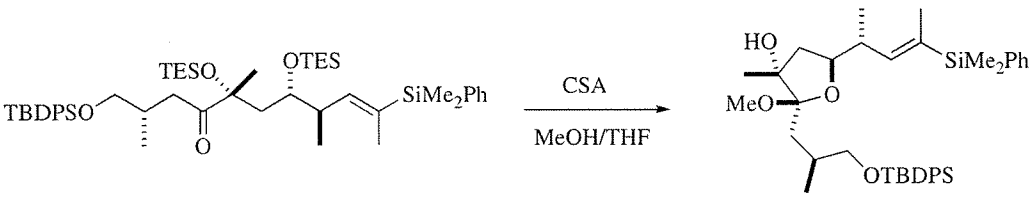
Milder conditions in the form of K_2CO_3 in methanol were used to deprotect a 3° TMS ether in the presence of a 1° TBDPS ether.[64]

5.2. In the presence of 2° and 3° silyl ethers

5.2.1. Under acidic conditions. Although relatively few in number, selective deprotections of 3° silyl ethers in the presence of 2° silyl ethers have been reported with substrates most often containing a 3° TMS and a 2° TBS ethers. Acids used to effect this selective desilylation include HOAc,[352] PPTS,[247] and HF·pyr.[352] Careful control of conditions and selection of desilylation agent can produce vastly different outcomes as demonstrated by the results achieved using silyl-protected triol **134** (Scheme 59).[352] Treatment with HOAc/THF/H_2O at room temperatures effected selective cleavage of the 3° TMS ether without removal of the TBS protecting groups on 2° alcohols to yield 3° alcohol **135**. But, the addition of a small amount of HCl and increase in temperature produced global deprotection and triol **136**. When HF·pyr was employed, the 3° TMS ether and the less hindered, allylic 2° TBS ethers underwent deprotection to yield mono TBS ether **137**. TBAF buffered with HOAc has also been reported to selectively cleave a 3° TMS ether in the presence of a 2° TMS ether.[353]

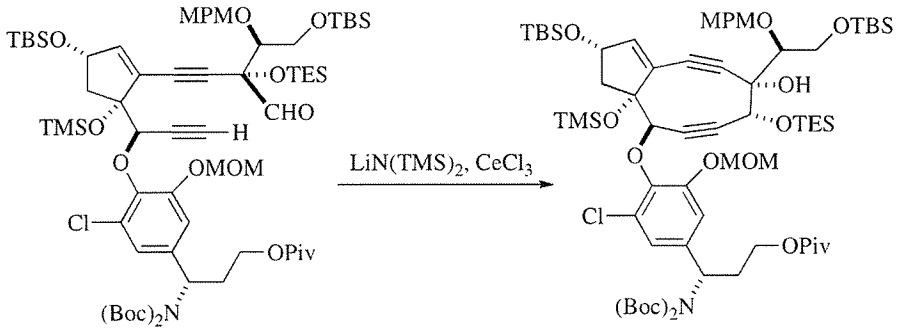
5.2.2. Under basic/nucleophilic conditions. TBAF has been used in a number of selective cleavage reactions of 3° silyl ethers in the presence of 2° or 3° silyl ethers including deprotection of a 3° TMS ether in the presence of a 2° TES,[233,306] a 2° TBS[233,306], or a 2° TBDPS ether[354] and a 3° TES ether in the presence of a 2° TBS[355] or a 3° TES ether.[350] For example, tris-silyl ether **138** underwent selective desilylation of a 3° TES ether in the presence of another 3° TES ether to yield a mixture of epoxide **139** and mesylate **140** (Scheme 60).[350] Note that the 2° TES ether is also deprotected under these conditions.

The TBAF-mediated selective deprotection of a 3° TMS ether in the presence of 2° TES and TBS ethers was the first step in



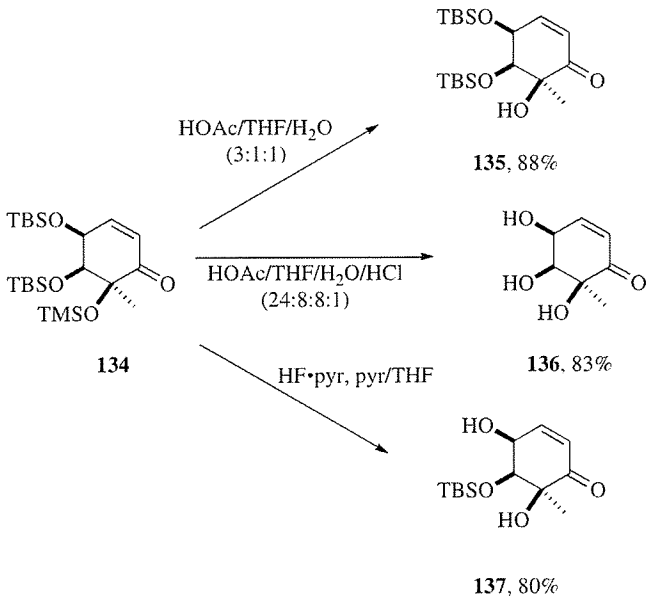
130 **131**, 86%

Scheme 57. Ref. 254.



132 **133**, 82%

Scheme 58. Ref. 123.



Scheme 59. Ref. 352.

a sequence that perhaps best exemplifies selective desilylation as a means of sequentially releasing alcohol groups (Scheme 61).[306] Triply-silyl-protected intermediate **141** was subjected to a four-step sequence consisting of selective removal of the TMS protecting group with TBAF followed by selective cleavage of the TES group with PPTS, oxidation of the newly released 2° alcohol and finally removal of the TBS group to yield diol **142**.

$LiAlH_4$ has been used to selectively desilylate a 3° TES ether in the presence of 2° TES ethers (Scheme 62).[55] Critical to this reaction's success is the neighboring acetate on intermediate **143**, which undergoes reductive cleavage with $LiAlH_4$ to form an alkoxide to which the silyl group on the vicinal alcohol migrates.

A similar neighboring group effect was exploited in the deprotection of a 3° TES ether in the presence of a number of other silyl ethers including a 2° TBS and a 3° TMS ether (see Scheme 58).[123]

6. Selective deprotection of aryl and alkyl silyl ethers

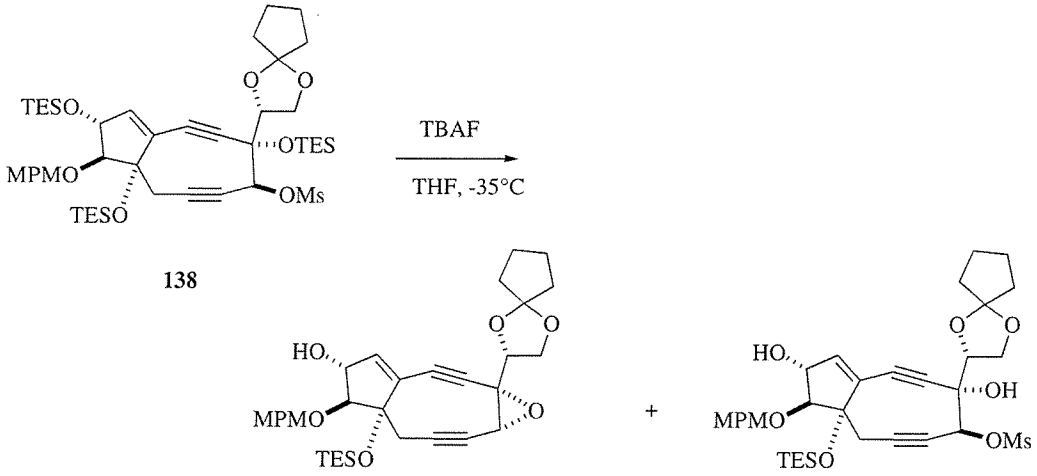
In general, selective deprotection of an alkyl silyl ether in the presence of an aryl silyl ether is favored by acidic conditions while basic conditions favor desilylation of aryl silyl ethers.[3,4]

6.1. Deprotection of alkyl silyl ethers in the presence of aryl silyl ethers

A variety of acids have been reported to effect selective cleavage of alkyl silyl ethers including the use of protic acids, Lewis acids, and in situ generation of acid. The most common example of removal of a silyl protecting group from a protected alcohol in the presence of a silyl-protected phenol is the selective desilylation of a 1° TBS ether in the presence of an aryl TBS ether. For example, formic acid was used to effect the selective desilylation of a 1° TBS ether in tris-silyl ether **145** without deprotection of two TBS-protected phenols (Scheme 63).[356] A similar example using HCO_2H was reported earlier as part of the synthesis of members of the tetrahydroisoquinoline antibiotic family.[357]

Catalytic quantities of 1-chloroethyl chloroformate[79] has been used to generate HCl in situ and TMS-Br[358] and pyridinium tribromide[359] in methanol were used to generate HBr in situ, effecting the selective deprotection of 1° TBS ethers in the presence of aryl TBS ethers. $KHSO_4$[360] and $NaHSO_4$ on silica[361] have been shown to effect the selective deprotection of 1° TBS ethers in the presence of TBS-protected phenols. $NaHSO_4$ on silica also removes TBS groups from protected 2° alcohols in the presence of aryl TBS ethers.[361]

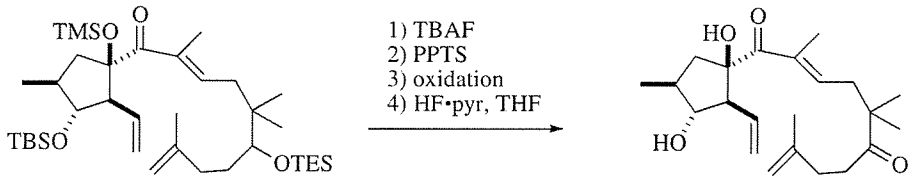
Other agents, some of which are known to generate protic acids in situ, have been used to achieve selective deprotection of alkyl silyl ethers in the presence of aryl silyl ethers. Table 4 summarizes



138

139, 58% + **140**, 15%

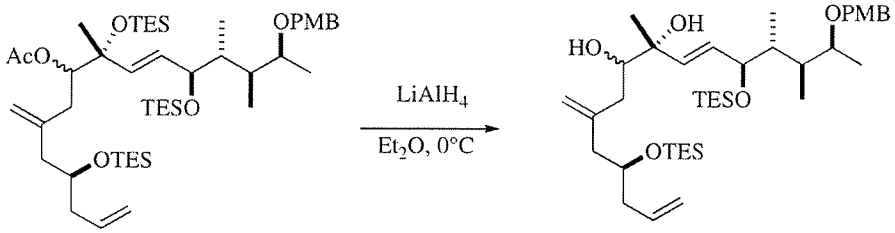
Scheme 60. Ref. 350.



141

142, 51%

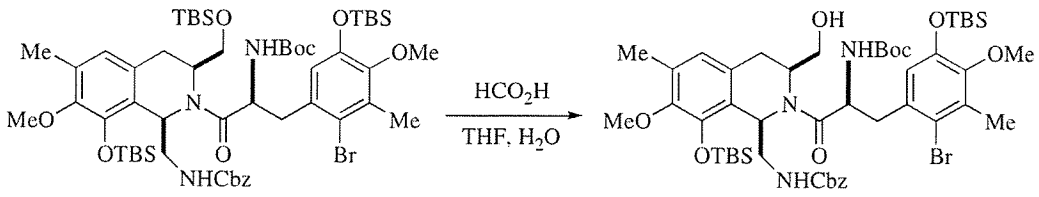
Scheme 61. Ref. 306.



143

144, 90%

Scheme 62. Ref. 55.

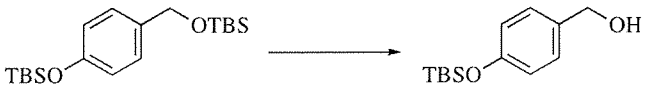


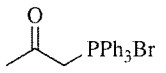
145

146, 92%

Scheme 63. Ref. 356.

Table 4
Deprotection of 1° TBS ether in the presence of an aryl TBS ether



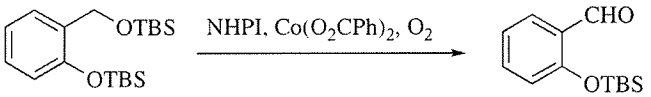
Catalyst	Conditions	Yield (%)	Ref.
Sulfated SnO_2	MeOH, rt, 15 min	96	83
$SnCl_2 \cdot 2H_2O$	EtOH/H_2O, rt, 90 min	94	87
$NiCl_2 \cdot 6H_2O$/$HSCH_2CH_2SH$	CH_2Cl_2/MeOH, rt, 20 min	80	85
NIS	MeOH, rt, 18 h	95	362
	CH_2Cl_2/MeOH, rt, 15 min	77	80

some examples of selective cleavage of 1° TBS ethers in the presence of aryl TBS ethers.

Other methods for selective deprotection of a 1° TBS ether in the presence of an aryl TBS ether include $TBPA^+ \cdot SbCl_6^-$,[100] $Fe(OTs)_3 \cdot 6H_2O$,[86] a sulfonic acid-functionalized silica,[76] $CeCl_3 \cdot 7H_2O$,[363] $Ce(OTf)_n \cdot xH_2O$[364] and I_2 in methanol.[365–367]

But, these methods are not limited to the TBS protecting group. HOAc was used to deprotect a 2° TES ether in the presence of an aryl TIPS ether.[368] TsOH was the reagent of choice to selectively cleave a 1° TBS ether in the presence of an aryl TBDPS ether.[369] 1-Chloroethyl chloroformate was effective in selectively deprotecting a 1° TES ether in the presence of an aryl TBS ether and a 1° TBDPS ether in the presence of a TBDPS-protected phenol.[79] TMS-Br was also able to cleave a 1° TIPS ether in the presence of aryl TIPS ether and a 1° TBDPS ether in the presence of an aryl TBDPS ether.[358] $FeCl_3$ has been shown to deprotect 1° TES and TBS ethers without reacting with aryl TES ethers.[89] In polar aprotic solvents, catalytic quantities of Selectfluor effect the selective deprotection of 1° TBS, TIPS, or TBDPS ethers in the presence of aryl TBS, TIPS, and TDPS ethers under microwave irradiation.[370]

Selective deprotection/oxidation sequences on 1° TBS ethers in the presence of aryl TBS ethers have been reported. For example, bis-silyl ether **147** was converted into aldehyde **148** using *N*-hydroxyphthalimide and cobalt benzoate in the presence of O_2 (Scheme 64).[371]



147 **148**, 97%

Scheme 64. Ref. 371.

$HClO_4$ on silica has been used with Ac_2O to convert 1° TBS ethers into acetate esters in the presence of aryl TBS ethers and 1° TBDPS ethers into acetate esters in the presence of aryl TBDPS ethers.[150] $FeCl_3/Ac_2O$ was reported to convert 1° TBS ethers into acetates in the presence of a TBS-protected phenol.[372] $FeCl_3$, Et_3SiH, and benzaldehyde have been used to convert 1° silyl ethers into benzyl ethers without reaction of aryl silyl ethers.[99]

6.2. Deprotection of aryl silyl ethers in the presence of alkyl silyl ethers

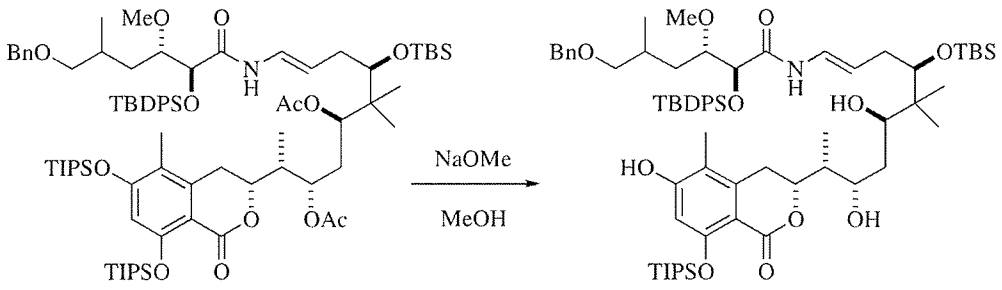
Cleavage of aryl silyl ethers is best achieved under basic conditions and it is this tendency that is exploited in selectively deprotecting aryl silyl ethers in the presence of alkyl silyl ethers. In the total synthesis of Kendomycin, Triton-B ($PhCH_2NMe_3OH$) was used to effect the selective deprotection of an aryl TBS ether in the presence of 2° TES and TBS ethers.[22,23] NaOMe was the reagent of choice in the selective desilylation of an aryl TIPS ether in intermediate **149** without cleavage of 2° TBS and TBDPS ethers (Scheme 65).[18,19] Notably, these conditions also effected the cleavage of one of the two aryl TIPS ether and removal of both acetate groups.

LiOAc in DMF has been shown to desilylate aryl TBS ethers in the presence of a variety of alkyl silyl ethers including 1° TES, TBS, and TBDPS ethers and 2° TBS ethers.[373] This method also effects cleavage of an aryl TBDPS ether in the presence of a 1° TBDPS ether. In a similar fashion, aryl TIPS ethers were selectively deprotected in the presence of 1° TBS and 2° TES ethers using KOAc in DMF/H_2O.[374]

DBU was used to selectively deprotect aryl TES, TBS, TIPS, and TBDPS ethers in the presence of 1° alcohols protected with the same silyl group.[375] High yields of desilylated product were obtained with catalytic DBU but more rapid results were achieved using 1 equiv. DBU was used to achieve selective cleavage of an aryl TBS ether in the presence of a 2° TBS ether in intermediate **151** with concomitant cyclic ether formation in the total synthesis of (±)-Lycoramine (Scheme 66).[376]

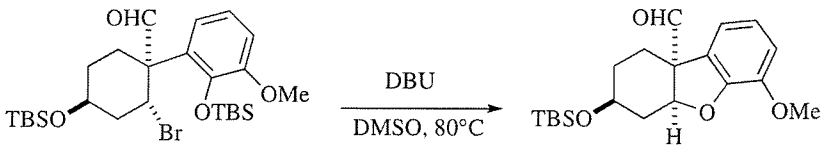
Selective deprotection of aryl TBS ethers in the presence of 2° TBS ethers has been achieved using TBAF.[24,367,377,378] For example, bis-silyl ether **153** underwent selective cleavage of the TBS-protected phenol to yield phenol **154** (Scheme 67).[377] TBAF buffered with HOAc has also been used to effect selective removal of a TBS group from a protected phenol in the presence of a 2° TBS ether.[379] Other examples of TBAF-mediated selective desilylation of aryl silyl ethers in the presence of alkyl silyl ethers include deprotection of an aryl TIPS ether in the presence of a 2° TBS ether[20] and an aryl TBS ether in the presence of a 2° TES ether.[25]

Selective deprotection of aryl TBS ethers in the presence of 1° TBS ethers using catalytic Selectfluor in methanol has been reported.[370] However, when stiochiometric Selectfluor or a polar aprotic solvent was used, the 1° TBS ether was selectively



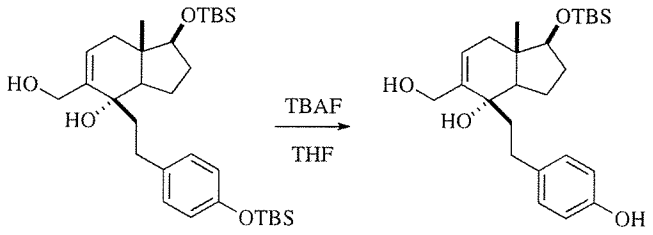
149 **150**, >95%

Scheme 65. Refs. 18,19.



151 152, 95%

Scheme 66. Ref. 376.

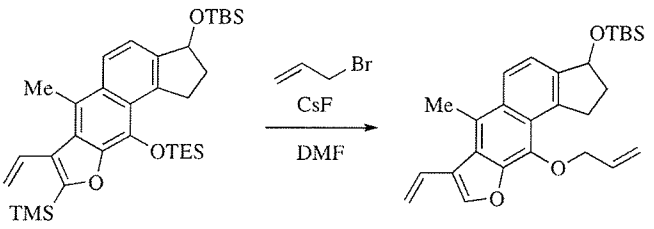


153 154, 99%

Scheme 67. Ref. 377.

cleaved.[370] KF and tetraethylene glycol have been shown to effect deprotection of aryl TBS, TIPS, and TBDPS ethers in the presence of 1° alcohols protected with the same silyl group.[246]

CsF was used in a novel one-pot selective desilylation/allylation of an aryl TES ether in the presence of a 2° TBS ether. Thus, bis-silyl ether **155** was treated with allyl bromide and CsF in DMF to yield allyl aryl ether **156** (Scheme 68).[380]



155 156, 67%

Scheme 68. Ref. 380.

6.3. Deprotection of aryl silyl ethers in the presence of another aryl silyl ether

Relatively few examples have been reported recently of deprotection of one aryl silyl ether in the presence of another. LiOAc in DMF has been reported to permit selective cleavage of TBS-protected phenols in the presence of aryl TBDPS ethers[373] and KOAc in DMF/H_2O effected selective deprotection of an aryl TIPS ether in the presence of an aryl TBDPS ether.[374]

Discrimination of one aryl TBS ether in the presence of another aryl TBS ether has been reported to occur upon treatment with in situ generated HF. Although no yield was reported, exposure of bis-silyl ether **157** to reaction conditions for 1 h resulted in deprotection of the less hindered aryl silyl ether and monosilyl ether **158**, which was isolated and characterized (Scheme 69).[381] Longer exposure resulted in desilylation of both aryl TBS ethers.

Another acidic system, $HClO_4$–SiO_2 and Ac_2O, has been demonstrated to convert aryl TBS ethers into acetate esters in the presence of aryl TBDPS ethers.[150]

7. Deprotection reactions involving silylenes

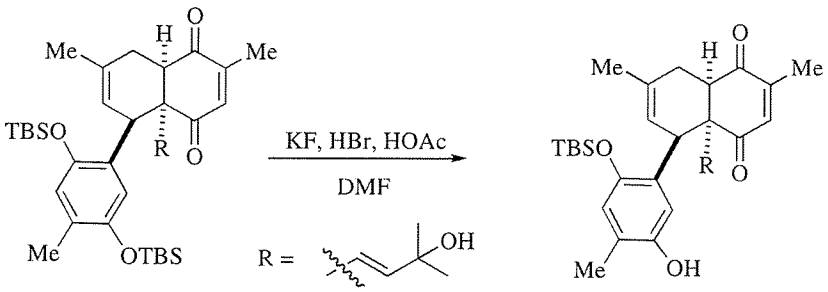
1,3-Diols can be treated with dialkyldichlorosilane to form silylenes in which one silyl moiety protects two hydroxy groups. Most often, di-*tert*-butyldichlorosilane or di-*tert*-butylsilyl triflate is used to form di-*tert*-butylsilylenes. Methods for selectively cleaving silylenes in the presence of other silyl-protected alcohols and visa versa have been compiled previously.[3,4]

7.1. Deprotection of alkyl silyl ethers in the presence of silylenes

Selective cleavage of alkyl silyl ethers in the presence of silylene-protected diols are often acid-mediated and recent examples include the use of TsOH[382–384] and PPTS[385] to selectively deprotect 2° TES ethers in the presence of di-*tert*-butylsilylene protected diols. Deprotection of a 1° TBS ether in the presence of a di-*tert*-butylsilylene protected diol in intermediate **159** was accomplished using CSA in methanol to yield alcohol **160** (Scheme 70).[386]

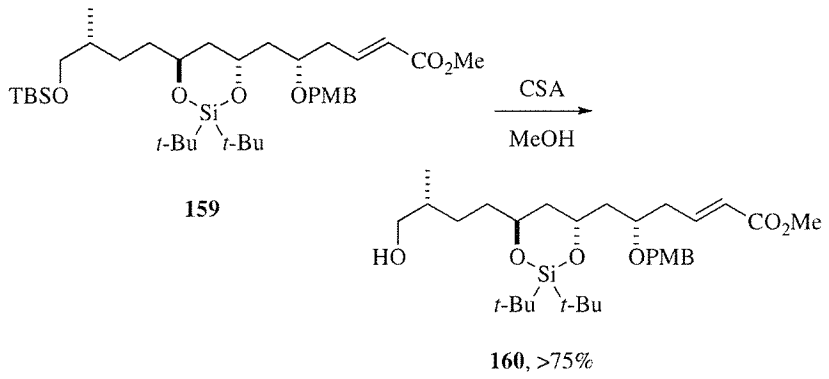
7.2. Deprotection of silylenes in the presence of alkyl silyl ethers

Dialkylsilylenes can be selectively cleaved in the presence of alkyl silyl ethers. HF·pyr was used to deprotect a di-*tert*-

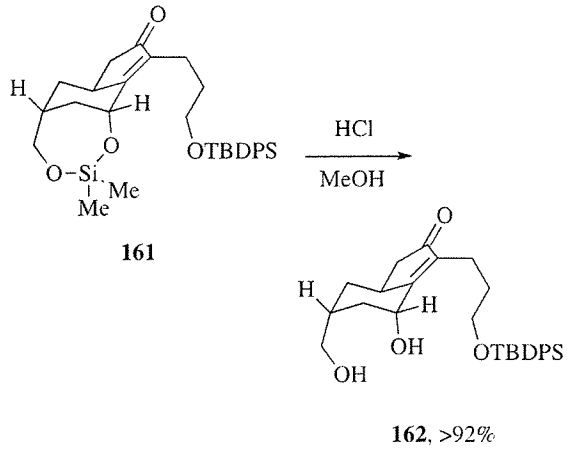


157 158

Scheme 69. Ref. 381.



Scheme 70. Ref. 386.



Scheme 71. Ref. 388.

butylsilylene in the presence of a 1° TBS ethers.[387] The dimethylsilylene-protected diol in intermediate **161** was deprotected using HCl in methanol without cleavage of a 1° TBDPS ether (Scheme 71).[388]

8. Conclusion

Although protecting group-free synthetic strategies are growing in frequency and importance, the complexity of modern synthetic targets points to the continued use of silyl protecting groups for alcohols in organic synthesis. While proven methods of desilylation allow for deprotection of most substrates, newly developed methods allow flexibility when new and challenging situations are encountered. Additionally, the introduction of new methods that utilize silyl ethers to carry out, for example, enantioselective synthesis or fluorous separations also point to the need for selective desilylation methods in the future. Thus, this line of research continues to be an active area (Tables 5–15).

Table 5
Deprotection of 1° silyl ethers in the presence of another 1° silyl ether

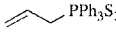
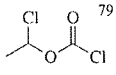
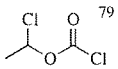
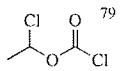
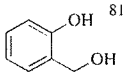
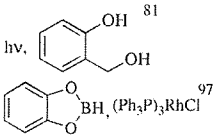
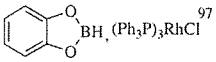
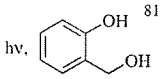
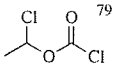
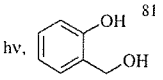
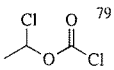
Deprotection of	In the presence of				
	1° TMS	1° TES	1° TBS	1° TIPS	1° TBDPS
1° TMS	[bmim]Cl[95] 89	Br_2/PVPP[104]	K_2CO_3[389]		K_2CO_3[279]
			Br_2/PVPP[104]		Swern[247]
			Mn^{III}–Schiff Base/H_2O_2[390]		
1° TES			CSA[11]	HOAc/μw[392]	HCl[393,394]
			HCO_2H[312]	 79	PPTS[8,9,395]
			 79	Fluorous TBAF[39]	CSA[64,396] HOAc/μw[392]
			Fluorous TBAF[39]	$FeCl_3$[89]	 79
			$FeCl_3$[89]	hν,  81	$FeCl_3$[89]
				TMS-Br/MeOH[358]	

Table 5 (*continued*)

Deprotection of	In the presence of				
	1° TMS	1° TES	1° TBS	1° TIPS	1° TBDPS
					$Fe(OTs)_3$[86]
			 [81] [97]		
			Swern[391]	 [97]	TMS-Br/MeOH[358]
				H_2/Pd–C[96]	H_2/Pd–C[96]
				$FeCl_3/Et_3SiH$/ArCHO[99]	 [81]
					Swern[248]
					$FeCl_3/Et_3SiH$/ArCHO[99]
1° TBS			PPTs[48]	HCl[14.35]	HCl[57] HOAc/μw[392]
			CrO_3/H_5IO_6[298]	AcCl/MeOH[207] HOAc/μw[392]	PPTS[16,58–65]
			TBAF[48]	 [79]	CSA[11,25,66–72]
				HF·pyr[397]	TFA/HOAc[75]
				$FeCl_3$[89]	TsOH[73,74]
				TMS-Br/MeOH[358]	PPTs/TsOH[56]
				H_2/Pd–C[96]	PMA/SiO_2[77]
				TBAF[92]	HF·pyr[175]
				Pyridinium tribromide[359]	Pyridinium tribromide[359]
				$FeCl_3/Et_3SiH$/ArCHO[99]	TMS-Cl/KF–$2H_2O$[82]
					 [81]
					Cl_3CCO_2H[145]
					BF_3-OEt_2[25,398]
					TMS-Cl[399]
					TMS-Br/MeOH[358]
					 [79]
					$(MeCN)_2PdCl_2$[400]
					$SbCl_3$[88]
					$FeCl_3$[89]
					$Fe(OTs)_3$[86]
					$NiCl_2·6H_2O/HSCH_2CH_2SH$[85]
					$CuBr_2$[84]
					LiCl/H_2O/DMF[56]
					Sulfated SnO_2[83]
					$Bi(OTf)_3$[102]
					$Sc(OTf)_3$[102]
					$SnCl_2–2H_2O$[87]
					$TBPA^+·SbCl_6^-$[100]
					CCl_4/MeOH, ultrasound[401]
					H_2/Pd–C[96] CH_3COPPh_3Br[80]
					CrO_3/H_5IO_6[298]
					$FeCl_3/Et_3SiH$/ArCHO[99]

(*continued on next page*)

Table 5 (*continued*)

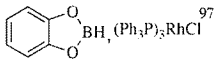
Deprotection of	In the presence of				
	1° TMS	1° TES	1° TBS	1° TIPS	1° TBDPS
1° TIPS			 [97]	Tf_2NH[78]	
1° TBDPS			TBAF/HOAc[8,9,195,402] KOH/DMPU[171] NaOH[180]	TBAF/HOAc[290,403] KOH/MeOH[91]	

Table 6
Deprotection of 1° silyl ethers in the presence of a 2° silyl ether

Deprotection of	In the presence of				
	2° TMS	2° TES	2° TBS	2° TIPS	2° TBDPS
1° TMS	HOAc/Ac_2O[151] [bmim]Cl[95] Swern[230] $NaHCO_3$[404] K_2CO_3[405]		HF·pyr[406]	K_2CO_3[282]	
1° TES		HOAc[407] PPTs[8,9,64,231,255,257,408] Swern[231–236,409,410] K_2CO_3[13] DIBAL-H[52] DDQ[411]	CSA[412] TFA[311] HCO_2H[312] $NaClO_2$ then pH 3[190] HF·pyr[190] Swern[236–238,409] DIBAL-H[52] DDQ[238]	PPTS[314] HOAc/μw[392] TMS-Br/MeOH[358]	HCl[407] PPTs[413] TBAF[263] DIBAL-H[52]
1° TBS		HOAc[147] Pyridinium tribromide[359]	HCl[57,414,415] HOAc[106–113] PPTs[48,114–126] CSA[11,24,71,72,128–143] TsOH[74,127,416–421] TFA[422] $HClO_4$–SiO_2[150] HF[423] HF·pyr[140,146,152–183] $(HF)_3$–$x$$NEt_3$[158] NH_4F[17,116,202–208] TMS-Cl/KF/MeOH[82] Pyridinium tribromide[359] CBr_4/hν[424] $ZnBr_2$[425] $SnCl_2$[425] $Bi(OTf)_3$[102] $CeCl_3·7H_2O$/NaI[144] $SbCl_3$[88] TBAF/HOAc[426] TBAF[216–220] Fluorous TBAF[39] $LiAlH_4$[427] DIBAL-H[52] $NaIO_4$[227,228] Oxone[428] I_2/MeOH[367] Al_2O_3/hexanes[218,429]	HCl[35] HOAc[226,401] HOAc/μw[392] PPTs[170] PPTs/TsOH[430] CSA[69,431–433] TsOH[434] Cl_3CCO_2H[145] HF·pyr[153,170,178,435] $(HF)_3$–$x$$NEt_3$[436] TMS-Br/$n$-$Bu_4NBr$/$Ac_2O$[437] $(CF_3CO)_2O$/MeOH[437] PCC/Celite[229]	HCl[438] HOAc[110,439] PPTs[65,440] CSA[148,149,187,323,441,442] TsOH[443,444] $BF_3·OEt_2$[445] HF·pyr[177,240,315] NBS/DMSO[446,447] TBAF[221] CrO_3/H_5IO_6[298] $TBPA^+·SbCl_6^-$[100]
1° TIPS			TBAF/HOAc[274] TBAF[222,223]	TFA[448] HF·pyr[189]	
1° TBDPS		HF·pyr[185] TBAF/HOAc[402] TMSCN/$Sc(OTf)_3$[215] DIBAL-H[52]	HF·pyr[185] TBAF/HOAc[8–11,63,70,192–201,402] TMSCN/$Sc(OTf)_3$[215] TBAF[449] NH_4F[205,209–214,450] NH_4F/HFIP[293] TAS-F[409,451] NaOH[180,224] KOH[225,452]	HF·pyr[145,186] TAS-F[172] NaOH[58,226] KOH[207,453]	HF·pyr[21,187,188] TBAF[454] NH_4F[209] Al_2O_3/hexanes[54,455]

Table 7
Deprotection of 1° silyl ethers in the presence of 3° silyl ethers

Deprotection of	In the presence of				
	3° TMS	3° TES	3° TBS	3° TIPS	3° TBDPS
1° TMS	Swern[247]				
1° TES	PPTS[255]	PPTS[8,9] KF/glycol[246] Swern[248]	PPTS[11]		
1° TBS		HF·pyr[173,241,242,435] $Sc(OTf)_3$[102] TBAF/HOAc[123]	CSA[11,69] $BF_3·OEt_2$[239] HF·pyr[240] NH_4F[243] TBAF[158] DDQ[249]		
1° TIPS		TBAF[244,245]			
1° TBDPS		HF·pyr[185]	TBAF/HOAc[8–11]		

Table 8
Deprotection of 2° silyl ethers in the presence of a 1° silyl ether

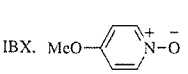
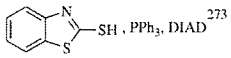
Deprotection of	In the presence of				
	1° TMS	1° TES	1° TBS	1° TIPS	1° TBDPS
2° TMS	[bmim]Cl[95]		PPTS[404]	PPTS[456]	HCl[457]
			IBX,  [294]	TBAF[92] NH_4F[270]	CSA[458] TsOH[264] TMS-OTf[459] HF·pyr[277]
2° TES			PPTS[319] HCO_2H[312] $TiCl_4$[287] MCPBA/$NaHCO_3$[124]	HOAc[315] CSA[270,271] PPTS[186,256,272–274] TsOH[275] TFA[276] $FeCl_3$[89] HF·pyr[274] TBAF[92,290] $Zn(OTf)_2$, EtSH[460]	HCl[8,9,250] HOAc[251–253] CSA[11,12,25,69,254,269] PPTS[15,16,255–257,461,462] TsOH[232,258–264] TFA[265–267] TMS-Br, MeOH[358] TMS-OTf[280,284,285,463] TES-OTf[464] $BF_3·OEt_2/Et_3SiH$[453] $Zn(OTf)_2$/EtSH[8,9,12,460] $FeCl_3$[89] HF·pyr[278–280] TBAF[290,291] DDQ[295]
2° TBS			$LiAlH_4$[53]	 [273] TMS-OTf[465]	HOAc[321] PPTS[70,466] TsOH[268,467] Amberlyst-15[172] CH_3COCl, MeOH[468] TMS-OTf[187,259,284,285] $SnCl_4$[286] $[PdCl_2(CH_3CN)_2]$[469] TBAF/HOAc[281] TBAF[292,293] CrO_3/H_5IO_6[298] $NaIO_4$[227] $TBPA^+·SbCl_6^-$[100] DDQ[296,297]
2° TIPS				TBAF/HOAc[282]	
2° TBDPS					

Table 9
Deprotection of 2° silyl ethers in the presence of another 2° silyl ether

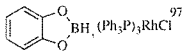
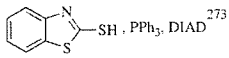
Deprotection of	In the presence of				
	2° TMS	2° TES	2° TBS	2° TIPS	2° TBDPS
2° TMS	[bmim]Cl[95] KF/chiral polyetherdiol[342]	Citric acid[470] PhCOF[341]	HOAc[435,471] TsOH[264] TFA[472,473] $SnCl_4$[474] HF·pyr[314] K_2CO_3[435,475]	HF·pyr[314]	HOAc[435] K_2CO_3[435,475]
2° TES		HOAc[299,476] CSA[141] PPTS[170] TBAF[334,335]	HOAc[113,253,299–301] CSA[11,143,302] PPTS[16,22,23,53,174,233,255–257,272–274,303–309] TsOH[260,264,275,310] TFA[311]	HOAc[313] HOAc/μw[392] CSA[69,271,302] PPTS[170,186,314]	HCl[232] HOAc[315,316] CSA[317,318] PPTS[308,319]
		 [97]	HCO_2H[312]	TMS-Br/MeOH[358]	$BF_3·OEt_2$[331]
			HF·pyr[55,185,231,310,326–330] 3HF·Et_3N[299] TES-OTf[464] TAS-F[310] TBAF[280,334–337] DDQ[345] $PdCl_2$, $CuCl_2$, O_2[347] $(NH_4)_6Mo_7O_{24}/H_2O_2$[344] $Et_2BOMe/NaBH_4$[477] EtSH, $Zn(OTf)_2$[333] Cp_2ZrHCl[306]	$(HF)_3·xNEt_3$[436] $BF_3·OEt_2/Et_3SiH$[453] $Zn(OTf)_2$/EtSH[333]	HF/CH_3CN[142,478] TBAF[263,338] K_2CO_3[479]
2° TBS			HOAc[476] CSA[322] PPTS[466,480] $SnCl_4$[286] TBAF/HOAc[426,481] HF·pyr[170,173,310,339,482] 3HF·Et_3N[299] TMS-OTf[189] $SnCl_4$[286] TAS-F[310] TBAF[20,304,307,339] NaOH[180]	HCl[483] HOAc/μw[392] CSA[484] PPTS[170,485] TsOH[434] TBAF[486,487]	HCl[320,488] HOAc[321] CSA[322–324] HF·pyr[315] TBAF/HOAc[281] TMS-OTf[187] $TiCl_4$[332] TBAF[440] $NaIO_4$[227] CrO_3/H_5IO_6[298]
			 [273] $NaIO_4$[227] Salen–Mn(III)/PhIO[343]		
2° TIPS			TBAF[50,489]	PPTS[490]	
2° TBDPS			HF·pyr[435] TBAF[177] TAS-F[491]		$NaBH_4$[54]

Table 10
Deprotection of 2° silyl ethers in the presence of 3° silyl ethers

Deprotection of	In the presence of				
	3° TMS	3° TES	3° TBS	3° TIPS	3° TBDPS
2° TMS		TBAF[92]	HOAc/HCl[492]		
2° TES		HOAc[348] PPTS[53,255,349] HF·pyr[55,185] TBAF[92,334,350]	CSA[11,12,69,271] $Zn(OTf)_2$/EtSH[8,9,12] Cp_2ZrHCl[306]		
2° TBS					
2° TIPS					
2° TBDPS	TBAF[177]				

Table 11
Deprotection of 3° silyl ethers in the presence of 1° silyl ethers

Deprotection of	In the presence of				
	1° TMS	1° TES	1° TBS	1° TIPS	1° TBDPS
3° TMS					PPTS[247] $BF_3·OEt_2$[493] K_2CO_3[64]
3° TES			$LiN(TMS)_2$, $CeCl_3$[123]	PPTS[351]	HCl[250] CSA[254]
3° TBS					
3° TIPS					
3° TBDPS					

Table 12
Deprotection of 3° silyl ethers in the presence of 2° and 3° silyl ethers

Deprotection of	In the presence of						
	2° TMS	2° TES	2° TBS	2° TIPS	2° TBDPS	3° TMS	3°TES
3° TMS	TBAF/HOAc[353] K_2CO_3[353]	TBAF[233,306]	HOAc[352] PPTS[247] HF·pyr[352] $H_2/Pd(OH)_2$–C[494] TBAF[233,306]		TBAF[354]		
3° TES		$LiAlH_4$[55]	TBAF[355] $LiN(TMS)_2$, $CeCl_3$[123]			$LiN(TMS)_2$, $CeCl_3$[123]	TBAF[350]
3° TBS 3° TIPS 3° TBDPS					TBAF[240]		

Table 13
Deprotection of alkyl silyl ethers in the presence of aryl silyl ethers

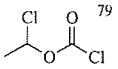
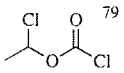
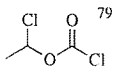
Deprotection of	In the presence of				
	ArOTMS	ArOTES	ArOTBS	ArOTIPS	ArOTBDPS
1° TMS	Br_2/PVPP[104]				
1° TES		$FeCl_3$[89]	$FeCl_3/Et_3SiH/ArCHO$[99]	HOAc[368]	
		 79			
1° TBS		$FeCl_3$[89]	HCO_2H[356,357] $HClO_4$–SiO_2[150] $KHSO_4$[360] $NaHSO_4$–SiO_2[361]		TsOH[369]
			 79		
			TMS-Br[358] Pyridinium tribromide[359] TMS-Cl, KF/MeOH[82] $FeCl_3/Et_3SiH/ArCHO$[99] $FeCl_3/Ac_2O$[372] $Fe(OTs)_3·6H_2O$/MeOH[86] $CeCl_3·7H_2O$[363] $Ce(OTf)_n·xH_2O$[364] $NiCl_2·6H_2O/HSCH_2CH_2SH$[85] sulfated SnO_2[83] $SnCl_2·2H_2O$[87] $Bi(OTf)_3$[102] NHPI/$Co(O_2CPh)_2/O_2$[371] NIS/MeOH[362] I_2/MeOH[365–367] Selectfluor/CH_3CN[370] CH_3COPPh_3Br[80] TBPA + $·SbCl_6^-$[100]		
1° TIPS				TMS-Br[358] Selectfluor/CH_3CN[370]	
1° TBDPS					$HClO_4$–SiO_2[150] TMS-Br[358]
					 79
					Selectfluor/CH_3CN[370]
2° TES				HOAc[368]	
2° TBS			$NaHSO_4$–SiO_2[361] CH_3COPPh_3Br[80] $(PhO)_2PON_3$[496]		

Table 14
Deprotection of aryl silyl ethers in the presence of alkyl silyl ethers

Deprotection of	In the presence of						
	1° TES	1° TBS	1° TIPS	1° TBDPS	2° TES	2° TBS	2° TBDPS
ArOTMS							
ArOTES	DBU[375]					CsF[380]	
ArOTBS	LiOAc[373]	KF/glycol[246] SelectFluor/MeOH[370] DBU[375,376,495] $CuBr_2$[84] LiOAc[373]		LiOAc[373]	TBAF[25] Triton-B[22,23]	TBAF[24,367,377,378] TBAF/HOAc[379] Triton-B[22,23] LiOAc[373]	
ArOTIPS		KOAc[374]	KF/glycol[246]		KOAc[374]	TBAF[20] NaOMe[18,19]	NaOMe[18,19]
ArOTBDPS				KF/glycol[246] LiOAc[373]			

Table 15
Deprotection of aryl silyl ethers in the presence of another aryl silyl ether

Deprotection of	In the presence of		
	ArOTBS	ArOTIPS	ArOTBDPS
ArOTBS	KF/HBr/HOAc/DMF[381]		$HClO_4$–SiO_2[150] LiOAc[373]
ArOTIPS		NaOMe[18,19]	KOAc[374]
ArOTBDPS			

References and notes

1. Wuts, P. G. M.; Greene, T. W. *Greene's Protective Groups in Organic Synthesis*, 4th ed.; John Wiley: Hoboken, NJ, 2007.
2. Kocienski, P. J. *Protecting Groups*, 3rd ed.; Thieme: Stuttgart, Germany, 2005.
3. Nelson, T. D.; Crouch, R. D. *Synthesis* **1996**, 1031.
4. Crouch, R. D. *Tetrahedron* **2004**, *60*, 5833.
5. Denmark, S. E.; Hammer, R. P.; Weber, E. J.; Habermas, K. L. *J. Org. Chem.* **1987**, *52*, 165.
6. Sommer, L. H. *Stereochemistry, Mechanism and Silicon*; McGraw Hill: New York, NY, 1965.
7. Ploom, A.; Panov, D.; Tuulmets, A. *Arkivoc* **2006**, *v*, 37.
8. Fuwa, H.; Ebine, M.; Sasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 9648.
9. Fuwa, H.; Ebine, M.; Bourdelais, A. J.; Baden, D. G.; Sasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 16989.
10. Takamura, H.; Kikuchi, S.; Nakamura, Y.; Yamagami, Y.; Kishi, T.; Kadota, I.; Yamamoto, Y. *Org. Lett.* **2009**, *11*, 2531.
11. Takamura, H.; Yamagami, Y.; Kishi, T.; Kikuchi, S.; Nakamura, Y.; Kadota, I.; Yamamoto, Y. *Tetrahedron* **2010**, *66*, 5329.
12. Zhang, Y.; Rohanna, J.; Zhou, J.; Iyer, K.; Rainier, J. D. *J. Am. Chem. Soc.* **2011**, *133*, 3208.
13. Garg, N. K.; Hiebert, S.; Overman, L. E. *Angew. Chem., Int. Ed.* **2006**, *45*, 2912.
14. Becker, M. H.; Chua, P.; Downham, R.; Douglas, C. J.; Garg, N. K.; Hiebert, S.; Jaroch, S.; Matsuoka, R. T.; Middelton, J. A.; Ng, F. W.; Overman, L. E. *J. Am. Chem. Soc.* **2007**, *129*, 11987.
15. Deng, L.; Ma, Z.; Zhao, G. *Synlett* **2008**, 728.
16. Fürstner, A.; Bouchez, L. C.; Funel, J.-A.; Liepins, V.; Poree, F.-H.; Gilmour, R.; Beaufils, F.; Laurich, D.; Tamiya, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 9265.
17. Ferrié, L.; Reymond, S.; Capdevielle, R.; Cossy, J. *Org. Lett.* **2007**, *9*, 2461.
18. Huang, X.; Shao, N.; Palani, A.; Aslanian, R.; Buevich, A. I. *Org. Lett.* **2007**, *9*, 2597.
19. Shao, N.; Huang, X.; Palani, A.; Aslanian, R.; Buevich, A.; Piwinski, J.; Huryk, R.; Seidel-Dugan, C. *Synthesis* **2009**, 2855.
20. Crimmins, M. T.; Stevens, J. M.; Schaaf, G. M. *Org. Lett.* **2009**, *11*, 3990.
21. Brown, L. E.; Landaverry, Y. R.; Davies, J. R.; Milinkevich, K. A.; Ast, S.; Carlson, J. S.; Oliver, A. G.; Konopelski, J. P. *J. Org. Chem.* **2009**, *74*, 5405.
22. Smith, A. B., III; Mesaros, E. F.; Meyer, E. A. *J. Am. Chem. Soc.* **2005**, *127*, 6948.
23. Smith, A. B., III; Mesaros, E. F.; Meyer, E. A. *J. Am. Chem. Soc.* **2006**, *128*, 5292.
24. Lowe, J. T.; Panek, J. S. *Org. Lett.* **2008**, *10*, 3813.
25. Tanaka, K.; Watanabe, M.; Ishibashi, K.; Matsuyama, H.; Saikawa, Y.; Nakata, M. *Org. Lett.* **2010**, *12*, 1700.
26. Roullard, E. *Angew. Chem., Int. Ed.* **2011**, *50*, 1226.
27. Young, I. S.; Baran, P. S. *Nat. Chem.* **2009**, *1*, 193.
28. Baran, P. S.; Maimone, T. J.; Richter, J. M. *Nature* **2007**, *446*, 404.
29. Hoffmann, R. W. *Synthesis* **2006**, 3531.
30. Gerfaud, T.; Xie, C.; Neuville, L.; Zhu, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 3954.
31. Harris, E. B. J.; Banwell, M. G.; Willis, A. C. *Tetrahedron Lett.* **2011**, *52*, 6887.
32. Lau, S. Y. W. *Org. Lett.* **2011**, *13*, 347.
33. Morales, C. P.; Catalán, J.; Domingo, V.; Gonzalez Delgado, J. A.; Dobado, J. A.; Herrador, M. M.; Quilez del Moral, J. F.; Barrero, A. F. *J. Org. Chem.* **2011**, *76*, 2494.
34. Hickman, V.; Alcarazo, M.; Fürstner, A. *J. Am. Chem. Soc.* **2010**, *132*, 11042.
35. Sancho, A. G.; Wang, X.; Sui, B.; Curran, D. F. *Adv. Synth. Catal.* **2009**, *351*, 1035.
36. Jung, W.-H.; Guyenne, S.; Riesco-Fagundo, C.; Mancuso, J.; Nakamura, S.; Curran, D. P. *Angew. Chem., Int. Ed.* **2008**, *47*, 1130.
37. Schaetz, A.; Zeltner, M.; Michl, T. D.; Rossier, M.; Fuhrer, R.; Stark, W. J. *Chem.—Eur. J.* **2011**, *17*, 10566.
38. Kaburagi, Y.; Kishi, Y. *Org. Lett.* **2007**, *9*, 723.
39. Fustero, S.; Sancho, A. G.; Aceña, J. L.; Sanz-Cervera, J. F. *J. Org. Chem.* **2009**, *74*, 6398.
40. Zhao, Y.; Rodrigo, J.; Hoveyda, A. H.; Snapper, M. L. *Nature* **2006**, *443*, 67.
41. Zhao, Y.; Mitra, A. W.; Hoveyda, A. H.; Snapper, M. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 8471.
42. You, Z.; Hoveyda, A. H.; Snapper, M. L. *Angew. Chem., Int. Ed.* **2009**, *48*, 547.
43. Rodrigo, J. M.; Zhao, Y.; Hoveyda, A. H.; Snapper, M. L. *Org. Lett.* **2011**, *13*, 3778.
44. Isobe, T.; Fukuda, K.; Araki, Y.; Ishikawa, T. *Chem. Commun.* **2001**, 243.
45. Sheppard, C. I.; Taylor, J. L.; Wiskur, S. L. *Org. Lett.* **2011**, *13*, 3794.
46. Shirai, N.; Moriya, K.; Kawazoe, Y. *Tetrahedron* **1986**, *42*, 2211.
47. Bastiaansen, P. M. F. M.; Orru, R. V. A.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1995**, *60*, 6154.
48. Ghosh, A. K.; Gong, G. *Org. Lett.* **2007**, *9*, 1437.
49. Paterson, I.; Steadman, V. A.; McLeod, M. D.; Trieselmann, T. *Tetrahedron* **2011**, *67*, 10119.
50. Overman, L. E.; Rhee, Y. H. *J. Am. Chem. Soc.* **2005**, *127*, 15652.
51. de Vries, E. F. J.; Brussee, J.; van der Gen, A. *J. Org. Chem.* **1994**, *59*, 7133.
52. Kuranaga, T.; Ishihara, S.; Ohtani, N.; Satake, M.; Tachibana, K. *Tetrahedron Lett.* **2010**, *51*, 6345.
53. Li, D.; Zhao, Y.; Ye, L.; Chen, C.; Zhang, J. *Synthesis* **2010**, 3325.
54. Strand, D.; Norrby, P.-O.; Rein, T. *J. Org. Chem.* **2006**, *71*, 1879.
55. Xie, J.; Ma, Y.; Horne, D. A. *Tetrahedron* **2011**, *67*, 7485.
56. Lee, H.-R.; Kang, J.-A.; Park, A.-Y.; Kim, W. H.; Chun, P.; Kim, J.; Kim, J.-A.; Lee, B.; Jeong, L. S.; Moon, H. R. *Bull. Korean Chem. Soc.* **2009**, *30*, 2043.
57. Smith, A. B., III; Xian, M.; Liu, F. *Org. Lett.* **2005**, *7*, 4613.
58. Kim, C. H.; An, H. J.; Shin, W. K.; Yu, W.; Woo, S. K.; Jung, S. K.; Lee, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 8019.
59. Sawant, K. B.; Ding, F.; Jennings, M. P. *Tetrahedron Lett.* **2006**, *47*, 939.
60. Trullinger, T. K.; Qi, J.; Roush, W. R. *J. Org. Chem.* **2006**, *71*, 6915.
61. Nagamitsu, T.; Takano, D.; Marumoto, K.; Fukuda, T.; Furuya, K.; Otoguro, K.; Takeda, K.; Kuwajima, I.; Harigaya, Y.; Omura, S. *J. Org. Chem.* **2007**, *72*, 2744.
62. Chen, Q.; Schweitzer, D.; Kane, J.; Davisson, V. J.; Helquist, P. *J. Org. Chem.* **2011**, *76*, 5157.
63. Mitchell, I. S.; Pattenden, G.; Stonehouse, J. *Org. Biomol. Chem.* **2005**, *3*, 4412.
64. Nicolaou, K. C.; Aversa, R. J.; Jin, J.; Rivas, F. *J. Am. Chem. Soc.* **2010**, *132*, 6855.
65. Tsuna, K.; Noguchi, N.; Nakada, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 9452.
66. Xie, J.; Ma, Y.; Horne, D. A. *J. Org. Chem.* **2011**, *76*, 6169.
67. Smith, A. B., III; Kim, D.-S. *Org. Lett.* **2007**, *9*, 3311.
68. Ganame, D.; Quach, T.; Poole, C.; Rizzacasa, M. A. *Tetrahedron Lett.* **2007**, *48*, 5841.
69. Johnson, H. W. B.; Majumder, U.; Rainier, J. D. *J. Am. Chem. Soc.* **2005**, *127*, 848.
70. Sanchez, C. C.; Keck, G. E. *Org. Lett.* **2005**, *7*, 3053.
71. Lee, J.; Panek, J. S. *Org. Lett.* **2009**, *11*, 4390.
72. Tsutsumi, R.; Kuranaga, T.; Wright, J. L. C.; Baden, D. G.; Ito, E.; Satake, M.; Tachibana, K. *Tetrahedron* **2010**, *66*, 6775.
73. Cohen, J. L.; Chamberlin, A. R. *J. Org. Chem.* **2007**, *72*, 9240.
74. Reddy, C. R.; Dharmapuri, G.; Rao, N. N. *Org. Lett.* **2009**, *11*, 5730.
75. Kolakowski, R. V.; Williams, L. J. *Tetrahedron Lett.* **2007**, *48*, 4761.
76. Karimi, B.; Zareyee, D. *Tetrahedron Lett.* **2005**, *46*, 4661.
77. Kumar, G. D. K.; Baskaran, S. *J. Org. Chem.* **2005**, *70*, 4520.
78. Sun, J.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 13512.
79. Yeom, C.-E.; Kim, Y. J.; Lee, S. Y.; Shin, Y. J.; Kim, B. M. *Tetrahedron* **2005**, *61*, 12227.
80. Khan, A. T.; Ghosh, S.; Choudhury, L. H. *Eur. J. Org. Chem.* **2004**, 2198.
81. Nishikubo, Y.; Kanzaki, S.; Matsumura, S.; Toshima, K. *Tetrahedron Lett.* **2006**, *47*, 8125.
82. Peng, Y.; Li, W.-D. Z. *Synlett* **2006**, 1165.
83. Bhure, M. H.; Kumar, I.; Natu, A. D.; Rode, C. V. *Synth. Commun.* **2008**, *38*, 346.
84. Bhatt, S.; Nayak, S. K. *Tetrahedron Lett.* **2006**, *47*, 8395.

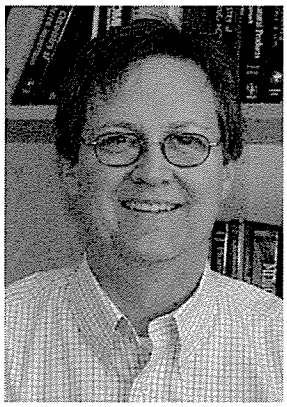
85. Khan, A. T.; Islam, S.; Choudhury, L. H.; Ghosh, S. *Tetrahedron Lett.* **2004**, *45*, 9617.
86. Bothwell, J. M.; Angeles, V. V.; Carolan, J. P.; Olson, M. E.; Mohan, R. S. *Tetrahedron Lett.* **2010**, *51*, 1056.
87. Hua, J.; Jiang, Z. Y.; Wang, Y. G. *Chin. Chem. Lett.* **2004**, *15*, 1430.
88. Wu, Q.; Wang, Y.; Chen, W.; Wang, H.; Liu, H. *Lett. Org. Chem.* **2006**, *3*, 13.
89. Yang, Y.-Q.; Cui, J.-R.; Zhu, L.-G.; Sun, Y.-P.; Wu, Y. *Synlett* **2006**, 1260.
90. Specklin, S.; Gallier, F.; Mezaache, R.; Harkat, H.; Dembelé, Y. A.; Weibel, J.-M.; Blanc, A.; Pale, P. *Tetrahedron Lett.* **2011**, *52*, 5820.
91. Corminboeuf, O.; Overman, L. E.; Pennington, L. D. *J. Org. Chem.* **2009**, *74*, 5458.
92. Sakamoto, S.; Sakazaki, H.; Hagiwara, K.; Kamada, K.; Ishii, K.; Noda, T.; Inoue, M.; Hirama, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 6505.
93. Pilcher, A. S.; Ammon, H. L.; DeShong, P. *J. Am. Chem. Soc.* **1995**, *117*, 5166.
94. DiLauro, A. M.; Seo, W.; Phillips, S. T. *J. Org. Chem.* **2011**, *76*, 7352.
95. Shaabani, A.; Rezayan, A. H.; Heidary, M.; Sarvary, A. *Monatsh. Chem.* **2008**, *139*, 1471.
96. Ikawa, T.; Hattori, K.; Sajiki, H.; Hirota, K. *Tetrahedron* **2004**, *60*, 6901.
97. Patel, P.; Chang, C.-T.; Kang, N.; Lee, G.-J.; Powell, W. S.; Rokach, J. *Tetrahedron Lett.* **2007**, *48*, 5289.
98. Behloul, C.; Guijarro, D.; Yus, M. *Tetrahedron* **2005**, *61*, 6908.
99. Iwanami, K.; Yano, K.; Oriyama, T. *Synthesis* **2005**, 2669.
100. Xu, Y.; Tang, S.; Han, J.; She, X.; Pan, X. *Tetrahedron Lett.* **2008**, *49*, 3634.
101. Muzart, J. *Synthesis* **1993**, 11.
102. Barnynch, B.; Vatèle, J.-M. *Synlett* **2011**, 2048.
103. Lambert, R. F.; Hinkle, R. J.; Ammann, S. E.; Lian, Y.; Liu, J.; Lewis, S. E.; Pike, R. D. *J. Org. Chem.* **2011**, *76*, 9269.
104. Lakouraj, M. M.; Mokhtary, M. *Lett. Org. Chem.* **2007**, *4*, 64.
105. Tajbakhsh, M.; Lakouraj, M. M.; Fadavi, A. *Synth. Commun.* **2004**, *34*, 1173.
106. Battistini, L.; Curti, C.; Zanardi, F.; Rassu, G.; Auzzas, L.; Casiraghi, G. *J. Org. Chem.* **2004**, *69*, 2611.
107. Fujiwara, K.; Goto, A.; Sato, D.; Ohtaniuchi, Y.; Tanaka, H.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2004**, *45*, 7011.
108. Sekine, M.; Aoyagi, M.; Ushioda, M.; Ohkubo, A.; Seio, K. *J. Org. Chem.* **2005**, *70*, 8400.
109. O'Neil, G. W.; Phillips, A. J. *J. Am. Chem. Soc.* **2006**, *128*, 5340.
110. Jägel, J.; Maier, M. E. *Synthesis* **2009**, 2881.
111. Li, P.; Li, J.; Arikan, F.; Ahlbrecht, W.; Dieckmann, M.; Menche, D. *J. Am. Chem. Soc.* **2009**, *131*, 11678.
112. Miles, W. H.; Connell, K. B.; Ulas, G.; Tuson, H. H.; Dethoff, E. A.; Mehta, V.; Thrall, A. J. *J. Org. Chem.* **2010**, *75*, 6820.
113. Kobayashi, K.; Fujii, Y.; Hayakawa, I.; Kigoshi, H. *Org. Lett.* **2011**, *13*, 900.
114. Nicolaou, K. C.; Bulger, P. G.; Brenzovich, W. E. *Org. Biomol. Chem.* **2006**, *4*, 2158.
115. Marshall, J. A.; Mikowski, A. M. *Org. Lett.* **2006**, *8*, 4375.
116. Crimmins, M. T.; Caussanel, F. *J. Am. Chem. Soc.* **2006**, *128*, 3128.
117. Kim, Y.; Fuchs, P. L. *Org. Lett.* **2007**, *9*, 2445.
118. Marshall, J. A.; Eidam, P. M. *Org. Lett.* **2008**, *10*, 93.
119. Dai, W.-M.; Feng, G.; Wu, J.; Sun, L. *Synlett* **2008**, 1013.
120. Custar, D. W.; Zabawa, T. P.; Hines, J.; Crews, C. M.; Scheidt, K. A. *J. Am. Chem. Soc.* **2009**, *131*, 12406.
121. Fang, L.; Yang, J.; Yang, F. *Org. Lett.* **2010**, *12*, 3124.
122. Brodmann, T.; Janssen, D.; Kalesse, M. *J. Am. Chem. Soc.* **2010**, *132*, 13610.
123. Inoue, M.; Kikuchi, T.; Hirama, M. *Tetrahedron Lett.* **2004**, *45*, 6439.
124. Ghosh, A. K.; Li, J. *Org. Lett.* **2009**, *11*, 4164.
125. D'Alfonso, A.; Pasi, M.; Porta, A.; Zanoni, G.; Vidari, G. *Org. Lett.* **2010**, *12*, 596.
126. Miyashita, K.; Tsunemi, T.; Hosokawa, T.; Ikejiri, M.; Imanishi, T. *Tetrahedron Lett.* **2007**, *48*, 3829.
127. Takahashi, K.; Matsumura, T.; Corbin, G. R. M.; Ishihara, J.; Hatakeyama, S. *J. Org. Chem.* **2006**, *71*, 4227.
128. Brittain, D. E. A.; Griffiths-Jones, C. M.; Linder, M. R.; Smith, M. D.; McCusker, C.; Barlow, J. S.; Akiyama, R.; Yasuda, K.; Ley, S. V. *Angew. Chem., Int. Ed.* **2005**, *44*, 2732.
129. Liang, N.; Datta, A. *J. Org. Chem.* **2005**, *70*, 10182.
130. Grant, S. W.; Zhu, K.; Zhang, Y.; Castle, S. L. *Org. Lett.* **2006**, *8*, 1867.
131. Kadota, I.; Nishii, H.; Ishioka, H.; Takamura, H.; Yamamoto, Y. *J. Org. Chem.* **2006**, *71*, 4183.
132. Crimmins, M. T.; DeBaillie, A. C. *J. Am. Chem. Soc.* **2006**, *128*, 4936.
133. Paterson, I.; Gardner, N. M. *Chem. Commun.* **2007**, 49.
134. Stauffer, C. S.; Bhaket, P.; Fothergill, A. W.; Rinaldi, M. G.; Datta, A. *J. Org. Chem.* **2007**, *72*, 9991.
135. Varseev, G. N.; Maier, M. E. *Org. Lett.* **2007**, *9*, 1461.
136. Inoue, M.; Saito, F.; Iwatsu, M.; Ishihara, Y.; Hirama, M. *Tetrahedron Lett.* **2007**, *48*, 2171.
137. Khalaf, J. K.; Vander Velde, D. G.; Datta, A. *J. Org. Chem.* **2008**, *73*, 5977.
138. Satoh, M.; Koshino, H.; Nakata, T. *Org. Lett.* **2008**, *10*, 1683.
139. Zeng, X.; Yin, B.; Hu, Z.; Liao, C.; Liu, J.; Li, S.; Li, Z.; Nicklaus, M. C.; Zhou, G.; Jiang, S. *Org. Lett.* **2010**, *12*, 1368.
140. Oh, H.-S.; Kang, H.-Y. *Tetrahedron* **2010**, *66*, 4307.
141. Paterson, I.; Lyothier, I. *J. Org. Chem.* **2005**, *70*, 5494.
142. Moslin, R. M.; Jamison, T. F. *J. Org. Chem.* **2007**, *72*, 9736.
143. Hong, W. P.; Noshi, M. N.; El-Awa, A.; Fuchs, P. L. *Org. Lett.* **2011**, *13*, 6342.
144. Yokokawa, F.; Inaizumi, A.; Shioiri, T. *Tetrahedron* **2005**, *61*, 1439.
145. Larivée, A.; Unger, J. B.; Thomas, M.; Wirtz, C.; Dubost, C.; Handa, S.; Fürstner, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 304.
146. Zhang, K.; Gudipati, V.; Curran, D. P. *Synlett* **2010**, 667.
147. Watanabe, K.; Iwasaki, K.; Abe, T.; Inoue, M.; Ohkubo, K.; Suzuki, T.; Katoh, T. *Org. Lett.* **2005**, *7*, 3745.
148. Trost, B. M.; Dong, G. *Nature* **2008**, *456*, 485.
149. Trost, B. M.; Dong, G. *J. Am. Chem. Soc.* **2010**, *132*, 16403.
150. Du, T.-J.; Wu, Q.-P.; Liu, H.-X.; Chen, X.; Shu, Y.-N.; Xi, X.-D.; Zhang, Q.-S.; Li, Y.-Z. *Tetrahedron* **2011**, *67*, 1096.
151. Witschi, M. A.; Gervay-Hague, J. *Org. Lett.* **2010**, *12*, 4312.
152. Haidle, A. M.; Myers, A. G. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12048.
153. Hilli, F.; White, J. M.; Rizzacasa, M. A. *Org. Lett.* **2004**, *6*, 1289.
154. Enders, D.; Lenzen, A.; Muller, M. *Synthesis* **2004**, 1486.
155. Ball, M.; Gaunt, M. J.; Hook, D. F.; Jessiman, A. S.; Kawahara, S.; Orsini, P.; Scolaro, A.; Talbot, A. C.; Tanner, H. R.; Yamanoi, S.; Ley, S. V. *Angew. Chem., Int. Ed.* **2005**, *44*, 5433.
156. Ruiz, P.; Murga, J.; Carda, M.; Marco, J. A. *J. Org. Chem.* **2005**, *70*, 713.
157. Du, Y.; Chen, Q.; Linhardt, R. J. *J. Org. Chem.* **2006**, *71*, 8446.
158. El Sous, M.; Ganame, D.; Zanatta, S.; Rizzacasa, M. A. *Arkivoc* **2006**, *vii*, 105.
159. Heapy, A. M.; Wagner, T. W.; Brimble, M. M. *Synlett* **2007**, 2359.
160. Körner, M.; Hiersemann, M. *Org. Lett.* **2007**, *9*, 4979.
161. Chrovian, C. C.; Knapp-Reed, B.; Montgomery, J. *Org. Lett.* **2008**, *10*, 811.
162. Zhan, W.; Jiang, Y.; Brodie, P. J.; Kingston, D. G. I.; Liotta, D. C.; Snyder, J. P. *Org. Lett.* **2008**, *10*, 1565.
163. Smith, A. B., III; Jurica, J. A.; Walsh, S. P. *Org. Lett.* **2008**, *10*, 5625.
164. Keck, G. E.; Giles, R. L.; Cee, V. J.; Wager, C. A.; Yu, T.; Kraft, M. B. *J. Org. Chem.* **2008**, *73*, 9675.
165. Smith, A. B., III; Dong, S.; Brenneman, J. B.; Fox, R. J. *J. Am. Chem. Soc.* **2009**, *131*, 12109.
166. Mahapatra, S.; Carter, R. G. *Org. Biomol. Chem.* **2009**, *7*, 4582.
167. Ghosh, S.; Pradhan, T. K. *J. Org. Chem.* **2010**, *75*, 2107.
168. Zanato, C.; Pignataro, L.; Ambrosi, A.; Hao, Z.; Trigili, C.; Diaz, J. F.; Barasoain, I.; Gennari, C. *Eur. J. Org. Chem.* **2011**, 2643.
169. Shashidhar, J.; Reddy, K. M.; Ghosh, S. *Tetrahedron Lett.* **2011**, *52*, 3106.
170. Blakemore, P. R.; Browder, C. C.; Hong, J.; Lincoln, C. M.; Nagornyy, P. A.; Robarge, L. A.; Wardrop, D. J.; White, J. D. *J. Org. Chem.* **2005**, *70*, 5449.
171. Smith, A. B., III; Fox, R. J.; Vanecko, J. A. *Org. Lett.* **2005**, *7*, 3099.
172. N'Zoutani, M.-A.; Lensen, N.; Pancrazi, A.; Ardisson, J. *Synlett* **2005**, 491.
173. Matsuura, F.; Peters, R.; Anada, M.; Harried, S. S.; Hao, J.; Kishi, Y. *J. Am. Chem. Soc.* **2006**, *128*, 7463.
174. Nicolaou, K. C.; Nold, A. L.; Milburn, R. R.; Schindler, C. S.; Cole, K. P.; Yamaguchi, J. *J. Am. Chem. Soc.* **2007**, *129*, 1760.
175. Chakraborty, T. K.; Goswami, R. K.; Sreekanth, M. *Tetrahedron Lett.* **2007**, *48*, 4075.
176. Shin, Y.; Fournier, J.-H.; Bruckner, A.; Madiraju, C.; Balachandran, R.; Raccor, B. S.; Edler, M. C.; Hamel, E.; Sikorski, R. P.; Vogt, A.; Day, B. W.; Curran, D. P. *Tetrahedron* **2007**, *63*, 8537.
177. Smith, A. B., III; Duffey, M. O.; Basu, K.; Walsh, S. P.; Suennemann, H. W.; Frohn, M. *J. Am. Chem. Soc.* **2008**, *130*, 422.
178. Hilli, F.; White, J. M.; Rizzacasa, M. A. *Tetrahedron* **2011**, *67*, 5054.
179. Ferrié, L.; Figadere, B. *Org. Lett.* **2010**, *12*, 4976.
180. Schuster, H.; Martinez, R.; Bruss, H.; Antonchick, A. P.; Kaiser, M.; Schürmann, M.; Waldmann, H. *Chem. Commun.* **2011**, 6545.
181. Aho, J. E.; Piisola, A.; Krishnan, K. S.; Pihko, P. M. *Eur. J. Org. Chem.* **2011**, 1682.
182. Gudipati, V.; Curran, D. P. *Tetrahedron Lett.* **2011**, *52*, 2254.
183. Yamashita, S.; Iso, K.; Kitajima, K.; Himuro, M.; Hirama, M. *J. Org. Chem.* **2011**, *76*, 2408.
184. Fukui, Y.; Bruckner, A. M.; Shin, Y.; Balachandran, R.; Day, B. W.; Curran, D. P. *Org. Lett.* **2006**, *8*, 301.
185. Gao, D.; O'Doherty, G. A. *Org. Lett.* **2010**, *12*, 3752.
186. Inoue, M.; Yamashita, S.; Tatami, A.; Miyazaki, K.; Hirama, M. *J. Org. Chem.* **2004**, *69*, 2797.
187. Pattenden, G.; Ashweek, N. J.; Baker-Glenn, C. A. G.; Kempson, J.; Walker, G. M.; Yee, J. G. K. *Org. Biomol. Chem.* **2008**, *6*, 1478.
188. Jervis, P. J.; Cox, L. R. *J. Org. Chem.* **2008**, *73*, 7616.
189. Adachi, M.; Yamada, H.; Isobe, M.; Nishikawa, T. *Org. Lett.* **2011**, *13*, 6532.
190. Zorn, N.; Lett, R. *Tetrahedron Lett.* **2006**, *47*, 4325.
191. Keaton, K. A.; Phillips, A. J. *J. Am. Chem. Soc.* **2006**, *128*, 408.
192. Paterson, I.; Bergmann, H.; Menche, D.; Berkessel, A. *Org. Lett.* **2004**, *6*, 1293.
193. Paquette, L. A.; Chang, J.; Liu, Z. *J. Org. Chem.* **2004**, *69*, 6441.
194. Fujiwara, K.; Kobayashi, M.; Yamamoto, F.; Aki, Y.-i.; Kawamura, M.; Awakura, D.; Amano, S.; Okano, A.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2005**, *46*, 5067.
195. Yoshimura, T.; Yakushiji, F.; Kondo, S.; Wu, X.; Shindo, M.; Shishido, K. *Org. Lett.* **2006**, *8*, 475.
196. Keck, G. E.; Kraft, M. B.; Truong, A. P.; Li, W.; Sanchez, C. C.; Kedei, N.; Lewin, N. E.; Blumberg, P. M. *J. Am. Chem. Soc.* **2008**, *130*, 6660.
197. Katagiri, T.; Fujiwara, K.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2008**, *49*, 3242.
198. Keck, G. E.; Li, W.; Kraft, M. B.; Kedei, N.; Lewin, N. E.; Blumberg, P. M. *Org. Lett.* **2009**, *11*, 2277.
199. Kuranaga, T.; Shirai, T.; Baden, D. G.; Wright, J. L. C.; Satake, M.; Tachibana, K. *Org. Lett.* **2009**, *11*, 217.
200. Guérinot, A.; Lepesqueux, G.; Sablé, S.; Reymond, S.; Cossy, J. *J. Org. Chem.* **2010**, *75*, 5151.
201. Elford, T. G.; Hall, D. G. *J. Am. Chem. Soc.* **2010**, *132*, 1488.
202. Schinzer, D.; Bourguet, E.; Ducki, S. *Chem.—Eur. J.* **2004**, *10*, 3217.
203. Wang, Q.; Huang, Q.; Chen, B.; Lu, J.; Wang, H.; She, X.; Pan, X. *Angew. Chem., Int. Ed.* **2006**, *45*, 3651.
204. Crimmins, M. T.; Ellis, J. M. *J. Org. Chem.* **2008**, *73*, 1649.
205. Ferrié, L.; Boulard, L.; Pradaux, F.; Bouzbouz, S.; Reymond, S.; Capdevielle, P.; Cossy, J. *J. Org. Chem.* **2008**, *73*, 1864.

206. Cossy, J.; Tsuchiya, T.; Reymond, S.; Kreuzer, T.; Colobert, F.; Markó, I. E. *Synlett* **2009**, 2706.
207. Liu, D.; Acharaya, H. P.; Yu, M.; Wang, J.; Yeh, V. S. C.; Kang, S.; Chiruta, C.; Jachak, S. M.; Clive, D. L. J. *J. Org. Chem.* **2009**, *74*, 7417.
208. Crimmins, M. T.; Mans, M. C.; Rodriguez, A. D. *Org. Lett.* **2010**, *12*, 5028.
209. BouzBouz, S.; Cossy, J. *Org. Lett.* **2004**, *6*, 3469.
210. Hirano, S.; Ichikawa, S.; Matsuda, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 1854.
211. Canova, S.; Bellosta, V.; Bigot, A.; Mailliet, P.; Mignani, S.; Cossy, J. *Org. Lett.* **2007**, *9*, 145.
212. Boulard, L.; BouzBouz, S.; Paris, J. M.; Cossy, J. *Synlett* **2007**, 1461.
213. Murata, T.; Sano, M.; Takamura, H.; Kadota, I.; Uemura, D. *J. Org. Chem.* **2009**, *74*, 4797.
214. Tenenbaum, J. M.; Morris, W. J.; Custar, D. W.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 5892.
215. Torikai, K.; Watanabe, K.; Minato, H.; Imaizumi, T.; Murata, M.; Oishi, T. *Synlett* **2008**, 2368.
216. Donohoe, T. J.; Harris, R. M.; Burrows, J.; Parker, J. *J. Am. Chem. Soc.* **2006**, *128*, 13704.
217. Coleman, R. S.; Berg, M. A.; Murphy, C. J. *Tetrahedron* **2007**, *63*, 3450.
218. Huckins, J. R.; de Vicente, J.; Rychnovsky, S. D. *Org. Lett.* **2007**, *9*, 4757.
219. Takamura, H.; Kadonaga, Y.; Kadota, I.; Uemura, D. *Tetrahedron* **2010**, *66*, 7569.
220. Takemura, A.; Katagiri, Y.; Fujiwara, K.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2011**, *52*, 1222.
221. Dubost, C.; Markó, I. E.; Ryckmans, T. *Org. Lett.* **2006**, *8*, 5137.
222. Evans, D. A.; Trenkle, W. C.; Zhang, J.; Burch, J. D. *Org. Lett.* **2005**, *7*, 3335.
223. Zhou, S.; Chen, H.; Liao, W.; Chen, S.-H.; Li, G.; Ando, R.; Kuwajima, I. *Tetrahedron Lett.* **2005**, *46*, 6341.
224. Cook, C.; Guinchard, X.; Liron, F.; Roulland, E. *Org. Lett.* **2010**, *12*, 744.
225. Smith, A. B., III; Razier, T. M.; Ciavarri, J. P.; Hirose, T.; Ishikawa, T. *Org. Lett.* **2005**, *7*, 4399.
226. Gowrisankar, P.; Pujari, S. A.; Kaliappan, K. P. *Chem.—Eur. J.* **2010**, *16*, 5858.
227. Li, J.; Menche, D. *Synthesis* **2009**, 1904.
228. Li, P.; Li, J.; Arikan, F.; Ahlbrecht, W.; Dieckmann, M.; Menche, D. *J. Org. Chem.* **2010**, *75*, 2429.
229. Vincent, G.; Mansfield, D. J.; Vors, J.-P.; Ciufolini, M. A. *Org. Lett.* **2006**, *8*, 2791.
230. Queron, E.; Lett, R. *Tetrahedron Lett.* **2004**, *45*, 4527.
231. Chen, J.; Forsyth, C. J. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12067.
232. Lambert, W. T.; Hanson, G. H.; Benayoud, F.; Burke, S. D. *J. Org. Chem.* **2005**, *70*, 9382.
233. Helmboldt, H.; Köhler, D.; Hiersemann, M. *Org. Lett.* **2006**, *8*, 1573.
234. Donohoe, T. J.; Cheeseman, M. D.; O'Riordan, T. J. C.; Kershaw, J. A. *Org. Biomol. Chem.* **2008**, *6*, 3896.
235. Ogawa, N.; Kobayashi, Y. *Tetrahedron Lett.* **2008**, *49*, 7124.
236. Komatsu, K.; Tanino, K.; Miyashita, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4341.
237. Zapf, C. W.; Harrison, B. A.; Drahl, C.; Sorensen, E. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 6533.
238. Yajima, A.; Toda, K.; Okada, K.; Yamane, H.; Yamamoto, M.; Hasegawa, M.; Katsuta, R.; Nukada, T. *Tetrahedron Lett.* **2011**, *52*, 3212.
239. Schwartz, B. D.; Denton, J. R.; Bernhardt, P. V.; Davies, H. M. L.; Williams, C. M. *Synthesis* **2009**, 2840.
240. Ye, Z.; Gao, T.; Zhao, G. *Tetrahedron* **2011**, *67*, 5979.
241. Muri, D.; Lohse-Frafel, N.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 4036.
242. Muri, D.; Carreira, E. M. *J. Org. Chem.* **2009**, *74*, 8695.
243. Ohyoshi, T.; Miyazawa, Y.; Aoki, K.; Ohmura, S.; Asuma, Y.; Hayakawa, I.; Kigoshi, H. *Org. Lett.* **2011**, *13*, 2160.
244. Crimmins, M. T.; Brown, B. H.; Plake, H. R. *J. Am. Chem. Soc.* **2006**, *128*, 1371.
245. Araoz, R.; Servent, D.; Molgó, J.; Iorga, B. I.; Fruchart-Gaillard, C.; Benoit, E.; Gu, Z.; Stivala, C.; Zakarian, A. *J. Am. Chem. Soc.* **2011**, *133*, 10499.
246. Yan, H.; Oh, J.-S.; Song, C. E. *Org. Biomol. Chem.* **2011**, *9*, 8119.
247. Fortner, K. C.; Kato, D.; Tanaka, Y.; Shair, M. D. *J. Am. Chem. Soc.* **2010**, *132*, 275.
248. Nonaka, H.; Maeda, N.; Kobayashi, Y. *Tetrahedron Lett.* **2007**, *48*, 5601.
249. Gopalarathnam, A.; Nelson, S. G. *Org. Lett.* **2006**, *8*, 7.
250. Taber, D. F.; Joerger, J.-M. *J. Org. Chem.* **2007**, *72*, 3454.
251. Moilanen, S. B.; Tan, D. S. *Org. Biomol. Chem.* **2005**, *3*, 798.
252. Hicks, J. D.; Flamme, E. M.; Roush, W. R. *Org. Lett.* **2005**, *7*, 5509.
253. Reymond, S.; Cossy, J. *Eur. J. Org. Chem.* **2006**, 4800.
254. Fürstner, A.; Kattnig, E.; Lepage, O. *J. Am. Chem. Soc.* **2006**, *128*, 9194.
255. Wang, Y.-G.; Takeyama, R.; Kobayashi, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 3320.
256. Allen, J. V.; Green, A. P.; Hardy, S.; Heron, N. M.; Lee, A. T. L.; Thomas, E. J. *Tetrahedron Lett.* **2008**, *49*, 6352.
257. Nicolaou, K. C.; Jiang, X.; Lindsay-Scott, P. J.; Corbu, A.; Yamashiro, S.; Bacconi, A.; Fowler, V. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 1139.
258. Geisler, L. K.; Nguyen, S.; Forsyth, C. J. *Org. Lett.* **2004**, *6*, 4159.
259. Nicolaou, K. C.; Pihko, P. M.; Bernal, F.; Frederick, M. O.; Qian, W.; Uesaka, N.; Diedrichs, N.; Hinrichs, J.; Koftis, T. V.; Loizidou, E.; Petrovic, G.; Rodriquez, M.; Sarlah, D.; Zou, N. *J. Am. Chem. Soc.* **2006**, *128*, 2244.
260. Ciblat, S.; Kim, J.; Stewart, C. A.; Wang, J.; Forgione, P.; Clyne, D.; Paquette, L. A. *Org. Lett.* **2007**, *9*, 719.
261. Trygstad, T. M.; Pang, Y.; Forsyth, C. J. *J. Org. Chem.* **2009**, *74*, 910.
262. Habrant, D.; Stewart, A. J. W.; Koskinen, A. M. P. *Tetrahedron* **2009**, *65*, 7927.
263. Wang, B.; Hansen, M.; Wang, T.; Wu, D.; Weyer, L.; Ying, L.; Engler, M. M.; Sanville, M.; Leitheiser, C.; Christmann, M.; Lu, Y.; Chen, J.; Zunker, N.; Cink, R. D.; Ahmed, F.; Lee, C.-S.; Forsyth, C. J. *J. Am. Chem. Soc.* **2011**, *133*, 1484.
264. Nicolaou, K. C.; Baker, T. M.; Nakamura, T. *J. Am. Chem. Soc.* **2011**, *133*, 220.
265. Hanessian, S.; Vakiti, R. R.; Dorich, S.; Banerjee, S.; Lecomte, F.; DelValle, J. R.; Zhang, J.; Deschênes-Simard, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 3497.
266. Sun, L.; Feng, G.; Guan, Y.; Liu, Y.; Wu, J.; Dai, W.-M. *Synlett* **2009**, 2361.
267. Chau, S. T.; Hayakawa, Y.; Sulikowski, G. A. *Org. Lett.* **2011**, *13*, 756.
268. Halim, R.; Brimble, M. A.; Merten, J. *Org. Lett.* **2005**, *7*, 2659.
269. Habrant, D.; Koskinen, A. M. P. *Org. Biomol. Chem.* **2010**, *8*, 4364.
270. Crimmins, M. T.; Shamszad, M.; Mattson, A. E. *Org. Lett.* **2010**, *12*, 2614.
271. Kadota, I.; Abe, T.; Ishitsuka, Y.; Touchy, A. S.; Nagata, R.; Yamamoto, Y. *Tetrahedron Lett.* **2007**, *48*, 219.
272. Paterson, I.; Coster, M. J.; Chen, D. Y.-K.; Oballa, R. M.; Wallace, D. J.; Norcross, R. D. *Org. Biomol. Chem.* **2005**, *3*, 2399.
273. Green, A. P.; Hardy, S.; Thomas, E. J. *Synlett* **2008**, 2103.
274. Green, A. P.; Lee, A. T. L.; Thomas, E. J. *Chem. Commun.* **2011**, 7200.
275. Jin, M.; Taylor, R. E. *Org. Lett.* **2005**, *7*, 1303.
276. Nilson, M. G.; Funk, R. L. *J. Am. Chem. Soc.* **2011**, *133*, 12451.
277. Ball, M.; Baron, A.; Bradshaw, B.; Omori, H.; MacCormick, S.; Thomas, E. J. *Tetrahedron Lett.* **2004**, *45*, 8737.
278. Nicolaou, K. C.; Vyskocil, S.; Koftis, T. V.; Yamada, Y. M. A.; Ling, T.; Chen, D. Y.-K.; Tang, W.; Petrovic, G.; Frederick, M. O.; Li, Y.; Satake, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4312.
279. Brimble, M. A.; Furkert, D. P. *Org. Biomol. Chem.* **2004**, *2*, 3573.
280. Nicolaou, K. C.; Koftis, T. V.; Vyskocil, S.; Petrovic, G.; Tang, W.; Frederick, M. O.; Chen, D. Y.-K.; Li, Y.; Ling, T.; Yamada, Y. M. A. *J. Am. Chem. Soc.* **2006**, *128*, 2859.
281. Paterson, I.; Mensche, D.; Hakansson, A. E.; Longstaff, A.; Wong, D.; Barasoain, I.; Buey, R. M.; Diaz, J. F. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2243.
282. Shimizu, Y.; Shi, S.-L.; Usuda, H.; Kanai, M.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 1103.
283. Ji, N.; O'Dowd, H.; Rosen, B. M.; Myers, A. G. *J. Am. Chem. Soc.* **2006**, *128*, 14825.
284. Nicolaou, K. C.; Koftis, T. V.; Vyskocil, S.; Petrovic, G.; Ling, T.; Yamada, Y. M. A.; Tang, W.; Frederick, M. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 4318.
285. Nicolaou, K. C.; Frederick, M. O.; Petrovic, G.; Cole, K. P.; Loizidou, E. Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 2609.
286. Canham, S. M.; Overman, L. E.; Tanis, P. S. *Tetrahedron* **2011**, *67*, 9837.
287. Angeles, A. R.; Waters, S. P.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2008**, *130*, 13765.
288. Mochirian, P.; Godin, F.; Katsoulis, I.; Fontaine, I.; Brazeau, J.-.F.; Guindon, Y. *J. Org. Chem.* **2011**, *76*, 7654.
289. Evans, P. A.; Cui, J.; Gharpure, S. J.; Hinkle, R. J. *J. Am. Chem. Soc.* **2003**, *125*, 11456.
290. Evans, D. A.; Kvoerno, L.; Mulder, J. A.; Raymer, B.; Dunn, T. B.; Beauchemin, A.; Olhava, E. J.; Juhl, M.; Kagechika, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 4693.
291. Nicolaou, K. C.; Seo, J. H.; Nakamura, T.; Aversa, R. J. *J. Am. Chem. Soc.* **2011**, *133*, 214.
292. Yang, G.; Hennig, L.; Findeisen, M.; Oehme, R.; Giesa, S.; Welzel, P. *Helv. Chim. Acta* **2004**, *87*, 1794.
293. Gille, A.; Hiersemann, M. *Org. Lett.* **2010**, *12*, 5258.
294. Nicolaou, K. C.; Li, A.; Edmonds, D. J.; Tria, G. S.; Ellery, S. P. *J. Am. Chem. Soc.* **2009**, *131*, 16905.
295. Ribes, C.; Falomir, E.; Carda, M.; Marco, J. A. *Org. Lett.* **2007**, *9*, 77.
296. Ghosh, A.; Xi, K. *Org. Lett.* **2007**, *9*, 4013.
297. Ghosh, A. K.; Xi, K. *J. Org. Chem.* **2009**, *74*, 1163.
298. Zhang, S.; Xu, L.; Trudell, M. L. *Synthesis* **2005**, 1757.
299. Durham, T. B.; Blanchard, N.; Savall, B. M.; Powell, N. A.; Roush, W. R. *J. Am. Chem. Soc.* **2004**, *126*, 9307.
300. Julian, L. D.; Newcom, J. S.; Roush, W. R. *J. Am. Chem. Soc.* **2005**, *127*, 6186.
301. Winbush, S. M.; Mergott, D. J.; Roush, W. R. *J. Org. Chem.* **2008**, *73*, 1818.
302. Florence, G. J.; Cadou, R. F. *Tetrahedron Lett.* **2010**, *51*, 5761.
303. Kadota, I.; Hu, Y.; Packard, G. K.; Rychnovsky, S. D. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 11992.
304. Paterson, I.; Findley, A. D.; Florence, G. J. *Org. Lett.* **2006**, *8*, 2131.
305. Ehrlich, G.; Hassfeld, J.; Eggert, U.; Kalesse, M. *J. Am. Chem. Soc.* **2006**, *128*, 14038.
306. Helmboldt, H.; Hiersemann, M. *J. Org. Chem.* **2009**, *74*, 1698.
307. Paterson, I.; Paquet, T. *Org. Lett.* **2010**, *12*, 2158.
308. Wender, P. A.; Schrier, A. J. *J. Am. Chem. Soc.* **2011**, *133*, 9228.
309. Kanematsu, M.; Yoshida, M.; Shishido, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 2618.
310. Lister, T.; Perkins, M. V. *Org. Lett.* **2006**, *8*, 1827.
311. Loiseleur, O.; Koch, G.; Cercus, J.; Schürch, F. *Org. Process Res. Dev.* **2005**, *9*, 259.
312. Chandra, T.; Broderick, W. E.; Broderick, J. B. *Nucleosides, Nucleotides Nucleic Acids* **2009**, *28*, 1016.
313. Jiang, Y.; Hong, J.; Burke, S. D. *Org. Lett.* **2004**, *6*, 1445.
314. Jiang, X.; Liu, B.; Lebreton, S.; De Brabander, J. K. *J. Am. Chem. Soc.* **2007**, *129*, 6386.
315. Williams, D. R.; Kiryanov, A. A.; Emde, U.; Clark, M. P.; Berliner, M. A.; Reeves, J. T. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12058.
316. Anderson, R. J.; Osborne, S. L.; Meunier, F. A.; Painter, G. F. *J. Org. Chem.* **2010**, *75*, 3541.
317. Chakraborty, T. K.; Reddy, V. R. *Tetrahedron Lett.* **2006**, *47*, 2099.
318. Chakraborty, T. K.; Reddy, V. R.; Chattopadhyay, A. K. *Tetrahedron Lett.* **2006**, *47*, 7435.
319. Wender, P. A.; DeChristopher, B. A.; Schrier, A. J. *J. Am. Chem. Soc.* **2008**, *130*, 6658.
320. Matsuo, K.; Ohtsuki, K.; Yoshikawa, T.; Shishido, K.; Yokotani-Tomita, K.; Shindo, M. *Tetrahedron* **2010**, *66*, 8407.
321. Smith, A. B., III; Smits, H.; Kim, D.-S. *Tetrahedron* **2010**, *66*, 6597.
322. Stellfeld, T.; Bhatt, U.; Kalesse, M. *Org. Lett.* **2004**, *6*, 3889.
323. Smith, A. B., III; Kim, D.-S. *Org. Lett.* **2005**, *7*, 3247.
324. Keck, G. E.; Welch, D. S.; Vivian, P. K. *Org. Lett.* **2006**, *8*, 3667.

325. Smith, A. B., III; Adams, C. M.; Lodise Barbosa, S. A.; Degnan, A. P. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12042.
326. Paterson, I.; Gottschling, D.; Menche, D. *Chem. Commun.* **2005**, 3568.
327. Fürstner, A.; Bindl, M.; Jean, L. *Angew. Chem., Int. Ed.* **2007**, *46*, 9275.
328. Crimmins, M. T.; Slade, D. J. *Org. Lett.* **2006**, *8*, 2191.
329. Li, F.; Tartakoff, S. S.; Castle, S. L. *J. Org. Chem.* **2009**, *74*, 9082.
330. Takizawa, A.; Fujiwara, K.; Doi, E.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2006**, *47*, 747.
331. Nakamura, A.; Kaji, Y.; Saida, K.; Ito, M.; Nagatoshi, Y.; Hara, N.; Fujimoto, Y. *Tetrahedron Lett.* **2005**, *46*, 6373.
332. Iida, A.; Okazaki, H.; Misaki, T.; Sunagawa, M.; Sasaki, A.; Tanabe, Y. *J. Org. Chem.* **2006**, *71*, 5380.
333. Tsukano, C.; Ebine, M.; Sasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 4326.
334. Smith, A. B., III; Tomioka, T.; Risatti, C. A.; Sperry, J. B.; Sfouggatakis, C. *Org. Lett.* **2008**, *10*, 4359.
335. Smith, A. B. I.; Risatti, C. A.; Atasoylu, O.; Bennett, C. S.; TenDyke, K.; Xu, Q. *Org. Lett.* **2010**, *12*, 1792.
336. Cachoux, F.; Isarno, T.; Wartmann, M.; Altmann, K.-H. *Angew. Chem., Int. Ed.* **2005**, *44*, 7469.
337. White, J. D.; Smits, H.; Hamel, E. *Org. Lett.* **2006**, *8*, 3947.
338. Wang, B.; Forsyth, C. J. *Org. Lett.* **2006**, *8*, 5223.
339. Chen, Q.-H.; Ganesh, T.; Brodie, P.; Slebodnick, C.; Jiang, Y.; Banerjee, A.; Bane, S.; Snyder, J. P.; Kingston, D. G. I. *Org. Biomol. Chem.* **2008**, *6*, 4542.
340. Milgram, B. C.; Liau, B. B.; Shair, M. D. *Org. Lett.* **2011**, *13*, 6436.
341. Poisson, T.; Dalla, V.; Papamicael, C.; Dupas, G.; Marsais, F.; Levacher, V. *Synlett* **2007**, 381.
342. Yan, H.; Jang, H. B.; Lee, J.-W.; Kim, H. K.; Lee, S. W.; Yang, J. W.; Song, C. E. *Angew. Chem., Int. Ed.* **2010**, *49*, 8915.
343. Murahashi, S.-I.; Noji, S.; Hirabayashi, T.; Komiya, N. *Synlett* **2004**, 1739.
344. Chin, Y.-J.; Wang, S.-Y.; Loh, T.-P. *Org. Lett.* **2009**, *11*, 3674.
345. Ghosh, A. K.; Xu, X.; Kim, J. H.-.; Xu, C.-X. *Org. Lett.* **2008**, *10*, 1001.
346. Müller, S.; Mayer, T.; Sasse, F.; Maier, M. E. *Org. Lett.* **2011**, *13*, 3940.
347. Park, P. K.; O'Malley, S. J.; Schmidt, D. R.; Leighton, J. L. *J. Am. Chem. Soc.* **2006**, *128*, 2796.
348. Shibahara, S.; Fujino, M.; Tashiro, Y.; Takahashi, K.; Ishihara, J.; Hatakeyama, S. *Org. Lett.* **2008**, *10*, 2139.
349. Jung, M. E.; Yoo, D. *Org. Lett.* **2011**, *13*, 2698.
350. Kobayashi, S.; Hori, M.; Wang, G. X.; Hirama, M. *J. Org. Chem.* **2006**, *71*, 636.
351. Nicolaou, K. C.; Ortiz, A.; Zhang, H.; Guella, G. *J. Am. Chem. Soc.* **2010**, *132*, 7153.
352. Stevenson, N. G.; De Savi, C.; Harrity, J. P. A. *Synlett* **2006**, 2272.
353. Glossop, P. A.; Hoogenraad, M.; Peakman, T. M.; Roberts, D. F. *Steroids* **2008**, *73*, 574.
354. Kotoku, N.; Sumii, Y.; Kobayashi, M. *Org. Lett.* **2011**, *13*, 3514.
355. Fernández, C.; Gómez, G.; Lago, C.; Moman, E.; Fall, Y. *Synlett* **2005**, 2163.
356. Dong, W.; Liu, W.; Liao, X.; Guan, B.; Chen, S.; Liu, Z. *J. Org. Chem.* **2011**, *76*, 5363.
357. Lane, J. W.; Chen, Y.; Williams, R. M. *J. Am. Chem. Soc.* **2005**, *127*, 12684.
358. Shah, S. T. A.; Guiry, P. J. *Org. Biomol. Chem.* **2008**, *6*, 2168.
359. Martinez-Solorio, D.; Jennings, M. P. *Tetrahedron Lett.* **2008**, *49*, 5175.
360. Arumugam, P.; Karthikeyan, G.; Perumal, P. T. *Chem. Lett.* **2004**, *33*, 1146.
361. Das, B.; Reddy, K. R.; Thirupathi, P. *Tetrahedron Lett.* **2006**, *47*, 5855.
362. Karimi, B.; Zamani, A.; Zareyee, D. *Tetrahedron Lett.* **2004**, *45*, 9139.
363. Jin, C.; Burgess, J. P.; Gopinathan, M. B.; Brine, G. A. *Tetrahedron Lett.* **2006**, *47*, 943.
364. Wu, X.; Zhou, J.; Snider, B. B. *J. Org. Chem.* **2009**, *74*, 6245.
365. Smith, A. B., III; Sperry, J. B.; Han, Q. *J. Org. Chem.* **2007**, *72*, 6891.
366. Dai, M.; Danshefsky, S. J. *Tetrahedron Lett.* **2008**, *49*, 6610.
367. Wang, Z.; Dai, M.; Park, P. K.; Danishefsky, S. J. *Tetrahedron* **2011**, *67*, 10249.
368. Sun, H.; Abbott, J. R.; Roush, W. R. *Org. Lett.* **2011**, *13*, 2734.
369. Zhang, J.; Wang, X.; Wang, W.; Quan, W.; She, X.; Pan, X. *Tetrahedron* **2007**, *63*, 6990.
370. Shah, S. T. A.; Singh, S.; Guiry, P. J. *J. Org. Chem.* **2009**, *74*, 2179.
371. Karimi, B.; Rajabi, J. *Org. Lett.* **2004**, *6*, 2841.
372. Kumar, D.; Rokita, S. E. *Tetrahedron Lett.* **2004**, *45*, 2887.
373. Wang, B.; Sun, H.-X.; Sun, Z.-H. *J. Org. Chem.* **2009**, *74*, 1781.
374. Wang, B.; Sun, H.-X.; Chen, B.; Sun, Z.-H. *Green. Chem.* **2009**, *11*, 1112.
375. Yeom, C.-E.; Kim, H. W.; Lee, S. Y.; Kim, B. M. *Synlett* **2007**, 146.
376. Fan, C.-A.; Tu, Y.-Q.; Song, Z.-L.; Zhang, E.; Shi, L.; Wang, M.; Wang, B.; Zhang, S.-Y. *Org. Lett.* **2004**, *6*, 4691.
377. Frie, J. L.; Jeffrey, C. S.; Sorensen, E. J. *Org. Lett.* **2009**, *11*, 5394.
378. Morales, C. A.; Layton, M. E.; Shair, M. D. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12036.
379. Roush, W. R.; Neitz, R. J. *J. Org. Chem.* **2004**, *69*, 4906.
380. Anderson, E. A.; Alexanian, E. J.; Sorensen, E. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 1998.
381. Arkoudis, E.; Lykakis, I. N.; Gryparis, C.; Stratakis, M. *Org. Lett.* **2009**, *11*, 2988.
382. Furuta, H.; Hase, M.; Noyori, R.; Mori, Y. *Org. Lett.* **2005**, *7*, 4061.
383. Perkins, M. V.; Sampson, R. A.; Joannou, J.; Taylor, M. R. *Tetrahedron Lett.* **2006**, *47*, 3791.
384. Tsubone, K.; Hashizume, K.; Fuwa, H.; Sasaki, M. *Tetrahedron Lett.* **2011**, *52*, 548.
385. Denmark, S. E.; Regens, C. S.; Kobayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, 2774.
386. Paterson, I.; Mühlthau, F. A.; Cordier, C. J.; Housden, M. P.; Burton, P. M.; Loiseleur, O. *Org. Lett.* **2009**, *11*, 353.
387. Dai, Q.; Song, C.-X.; Pan, T.; He, C. *J. Org. Chem.* **2011**, *76*, 4182.
388. Nakayama, A.; Kogure, N.; Kitajima, M.; Takayama, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 8025.
389. Pollex, A.; Hiersemann, M. *Org. Lett.* **2005**, *7*, 5705.
390. Tajbakhsh, M.; Hosseinzadeh, R.; Golchoubian, H.; Razavian, R. *Lett. Org. Chem.* **2008**, *5*, 308.
391. Nakahata, T.; Satoh, Y.; Kuwahara, S. *Tetrahedron Lett.* **2008**, *49*, 2438.
392. Crouch, R. D.; Williams, A. B. *Synth. Commun.* **2006**, *36*, 959.
393. Nicolaou, K. C.; Lizos, D. E.; Kim, D. W.; Schlawe, D.; de Noronha, R. G.; Longbottom, D. A.; Rodriquez, M.; Bucci, M.; Cirino, G. *J. Am. Chem. Soc.* **2006**, *128*, 4460.
394. Nicolaou, K. C.; Kim, D. W.; Schlawe, D.; Lizos, D. E.; de Noronha, R. G.; Longbottom, D. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 4925.
395. Hara, A.; Morimoto, R.; Ishikawa, Y.; Nishiyama, S. *Org. Lett.* **2011**, *13*, 4036.
396. Wittenberg, R.; Beier, C.; Dräger, G.; Jas, G.; Jasper, C.; Monenschein, H.; Kirschning, A. *Tetrahedron Lett.* **2004**, *45*, 4457.
397. Mulzer, J.; Sieg, A.; Brucher, C.; Müller, D.; Martin, H. J. *Synlett* **2005**, 685.
398. McLeod, M. C.; Wilson, Z. E.; Brimble, M. A. *Org. Lett.* **2011**, *13*, 5382.
399. Murakami, Y.; Shindo, M.; Shishido, K. *Synlett* **2005**, 664.
400. Wilson, M. S.; Woo, J. C. S.; Dake, G. R. *J. Org. Chem.* **2006**, *71*, 4237.
401. McGowan, G.; Thomas, E. J. *Org. Biomol. Chem.* **2009**, *7*, 2576.
402. Wong, C.-M.; Loh, T.-P. *Tetrahedron Lett.* **2006**, *47*, 4485.
403. Ebine, M.; Fuwa, H.; Sasaki, M. *Org. Lett.* **2008**, *10*, 2275.
404. Hoye, T. R.; Danielson, M. E.; May, A. E.; Zhao, H. *J. Org. Chem.* **2010**, *75*, 7052.
405. Sarpe, V. A.; Kulkarni, S. S. *J. Org. Chem.* **2011**, *76*, 6866.
406. Brennan, N. K.; Guo, X.; Paquette, L. A. *J. Org. Chem.* **2005**, *70*, 732.
407. Lucas, B. S.; Gopalsamuthiram, V.; Burke, S. D. *Angew. Chem., Int. Ed.* **2007**, *46*, 769.
408. Mehta, G.; Lakshminath, S. *Tetrahedron Lett.* **2006**, *47*, 327.
409. Hicks, J. D.; Roush, W. R. *Org. Lett.* **2008**, *10*, 681.
410. Nonaka, H.; Ogawa, N.; Maeda, N.; Wang, Y.-G.; Kobayashi, Y. *Org. Biomol. Chem.* **2010**, *8*, 5212.
411. Trost, B. M.; Waser, J.; Meyer, A. *J. Am. Chem. Soc.* **2007**, *129*, 14556.
412. Domon, D.; Fujiwara, K.; Ohtaniuchi, Y.; Takezawa, A.; Takeda, S.; Kawasaki, H.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2005**, *46*, 8279.
413. Chandrasekhar, S.; Sudhakar, A. *Org. Lett.* **2010**, *12*, 236.
414. Beshore, D. C.; Smith, A. B., III. *J. Am. Chem. Soc.* **2007**, *129*, 4148.
415. Harried, S. S.; Croghan, M. D.; Kaller, M. R.; Lopez, P.; Zhong, W.; Hungate, R.; Reider, P. J. *J. Org. Chem.* **2009**, *74*, 5975.
416. Ramachandran, P. V.; Srivastava, A.; Hazra, D. *Org. Lett.* **2007**, *9*, 157.
417. Chandrasekhar, S.; Rambabu, C.; Reddy, A. S. *Org. Lett.* **2008**, *10*, 4355.
418. Miyashita, K.; Tsunemi, T.; Hosokawa, T.; Ikejiri, M.; Imanishi, T. *J. Org. Chem.* **2008**, *73*, 5360.
419. Yadav, J. S.; Rao, K. S.; Reddy, B. V. S. *Lett. Org. Chem.* **2009**, *6*, 4.
420. Yaragoria, S.; Muthyala, R. *Tetrahedron Lett.* **2010**, *51*, 467.
421. Ma, J.-Y.; Huang, W.; Wei, B.-G. *Tetrahedron Lett.* **2011**, *52*, 4598.
422. Gu, W.; Silverman, R. B. *J. Org. Chem.* **2011**, *76*, 8287.
423. Reiff, E. A.; Nair, S. K.; Henri, J. T.; Greiner, J. F.; Reddy, B. S.; Chakrasali, R.; David, S. A.; Chiu, T.-L.; Amin, E. A.; Himes, R. H.; Vander Velde, D. G.; Georg, G. I. *J. Org. Chem.* **2010**, *75*, 86.
424. Chen, M.-Y.; Patkar, L. N.; Lu, K.-C.; Lee, A. S.-Y.; Lin, C.-C. *Tetrahedron* **2004**, *60*, 11465.
425. ElMarrouni, A.; Fukuda, A.; Heras, M.; Arseniyadis, S.; Cossy, J. *J. Org. Chem.* **2010**, *75*, 8478.
426. Pérez, M.; del Pozo, C.; Reyes, F.; Rodriguez, A.; Francesch, A.; Echavarren, A. M.; Cuevas, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 1724.
427. Elliott, M. C.; Paine, J. S. *Org. Biomol. Chem.* **2009**, *7*, 3455.
428. Mandel, A. L.; Bellosta, V.; Curran, D. P.; Cossy, J. *Org. Lett.* **2009**, *11*, 3282.
429. Kramp, G. J.; Kim, M.; Gais, H.-J.; Vermeeren, C. *J. Am. Chem. Soc.* **2005**, *127*, 17910.
430. Malik, H. A.; Chaulagain, M. R.; Montgomery, J. *Org. Lett.* **2009**, *11*, 5734.
431. Suzuki, M.; Kambe, M.; Tokuyama, H.; Fukuyama, T. *J. Org. Chem.* **2004**, *69*, 2831.
432. Das, S.; Abraham, S.; Sinha, S. C. *Org. Lett.* **2007**, *9*, 2273.
433. Sabitha, G.; Srinivas, R.; Yadav, J. S. *Synthesis* **2011**, 3343.
434. Lambert, W. T.; Roush, W. R. *Org. Lett.* **2005**, *7*, 5501.
435. Kirsch, S. F.; Bach, T. *Chem.—Eur. J.* **2005**, *11*, 7007.
436. König, C. M.; Gebhardt, B.; Schleth, C.; Dauber, M.; Koert, U. *Org. Lett.* **2009**, *11*, 2728.
437. Stamatov, S. D.; Stawinski, J. *Org. Biomol. Chem.* **2010**, *8*, 463.
438. Dineen, T. A.; Roush, W. R. *Org. Lett.* **2005**, *7*, 1355.
439. Álvarez, C.; Pérez, M.; Zúñiga, A.; Gómez, G.; Fall, Y. *Synthesis* **2010**, 3883.
440. Andreou, T.; Costa, A. M.; Esteban, L.; Gonzàlez, L.; Mas, G.; Vilarussa, J. *Org. Lett.* **2005**, *7*, 4083.
441. Prasad, B. R. V.; Meshram, H. M. *Tetrahedron: Asymmetry* **2010**, *21*, 1837.
442. Wu, J.; Panek, J. S. *J. Org. Chem.* **2011**, *76*, 9900.
443. Paquette, L. A.; Efremov, I.; Liu, Z. *J. Org. Chem.* **2005**, *70*, 505.
444. Mohapatra, D. K.; Das, P. P.; Pattanayak, M. R.; Gayatri, G.; Sastry, G. N.; Yadav, J. S. *Eur. J. Org. Chem.* **2010**, 4775.
445. Hande, S. M.; Uenishi, J. *Tetrahedron Lett.* **2009**, *50*, 189.
446. Chang, S.-K.; Paquette, L. A. *Synlett* **2005**, 2915.
447. Paquette, L. A.; Chang, S.-K. *Org. Lett.* **2005**, *7*, 3111.
448. Crimmins, M. T.; Zuccarello, J. L.; Cleary, P. A.; Parrish, J. D. *Org. Lett.* **2006**, *8*, 159.
449. Matsuo, G.; Kawamura, K.; Hori, N.; Matsukura, H.; Nakata, T. *J. Am. Chem. Soc.* **2004**, *126*, 14374.
450. Yadav, J. S.; Bezawada, P.; Chenna, V. *Tetrahedron Lett.* **2009**, *50*, 3772.

451. Lira, R.; Roush, W. R. *Org. Lett.* **2007**, *9*, 533.
452. Giufreddi, G.; Bobbio, C.; Gouverneur, V. *J. Org. Chem.* **2006**, *71*, 5361.
453. Fuwa, H.; Sasaki, M. *Org. Lett.* **2010**, *12*, 584.
454. Kosaki, Y.; Ogawa, N.; Kobayashi, Y. *Tetrahedron Lett.* **2010**, *51*, 1856.
455. Strand, D.; Rein, T. *Org. Lett.* **2005**, *7*, 2779.
456. Crimmins, M. T.; Vanier, G. S. *Org. Lett.* **2006**, *8*, 2887.
457. Zhang, Z.; Chen, J.; Yang, Z.; Tang, Y. *Org. Lett.* **2010**, *12*, 5554.
458. Kagawa, N.; Ihara, M.; Toyota, M. *Org. Lett.* **2006**, *8*, 875.
459. Heidebrecht, R. W., Jr.; Gulledge, B.; Martin, S. F. *Org. Lett.* **2010**, *12*, 2492.
460. Kuranaga, T.; Ohtani, N.; Tsutsumi, R.; Baden, D. G.; Wright, J. L. C.; Satake, M.; Tachibana, K. *Org. Lett.* **2011**, *13*, 696.
461. Evans, D. A.; Scheerer, J. R. *Angew. Chem., Int. Ed.* **2005**, *44*, 6038.
462. Shimizu, T.; Satoh, T.; Murakoshi, K.; Sodeoka, M. *Org. Lett.* **2005**, *7*, 5573.
463. Wang, C.; Forsyth, C. J. *Org. Lett.* **2006**, *8*, 2997.
464. Liu, L. L.; Chiu, P. *Chem. Commun.* **2011**, 3416.
465. Lebel, H.; Parmentier, M. *Org. Lett.* **2007**, *9*, 3563.
466. Smith, A. B., III; Foley, M. A.; Dong, S.; Orbin, A. *J. Org. Chem.* **2009**, *74*, 5987.
467. Toma, T.; Kita, Y.; Fukuyama, T. *J. Am. Chem. Soc.* **2010**, *132*, 10233.
468. Dong, C.-G.; Henderson, J. A.; Kaburagi, Y.; Sasaki, T.; Kim, D.-S.; Kim, J. T.; Urabe, D.; Guo, H.; Kishi, Y. *J. Am. Chem. Soc.* **2009**, *131*, 15642.
469. Yang, G.; Mansourova, M.; Hennig, L.; Findeisen, M.; Oehme, R.; Giesa, S.; Welzel, P. *Helv. Chim. Acta* **2004**, *87*, 1807.
470. Jung, M. E.; Yoo, D. *Org. Lett.* **2007**, *9*, 3543.
471. Rafferty, R. J.; Williams, R. M. *Tetrahedron Lett.* **2011**, *52*, 2037.
472. Ren, G.-B.; Wu, Y. *Org. Lett.* **2009**, *11*, 5638.
473. Ren, G.-B.; Huang, Y.-X.; Sun, Y.-P.; Li, Z.-H.; Wu, Y. *J. Org. Chem.* **2010**, *75*, 5048.
474. Bhat, V.; Allan, K. M.; Rawal, V. H. *J. Am. Chem. Soc.* **2011**, *133*, 5798.
475. Kirsch, S. F.; Bach, T. *Synthesis* **2005**, 2657.
476. Hua, Z.; Carcache, D. A.; Tian, Y.; Li, Y.-M.; Danishefsky, S. J. *J. Org. Chem.* **2005**, *70*, 9849.
477. Wang, X.; Wang, W.; Zheng, H.; Su, Y.; Jiang, T.; He, Y.; She, X. *Org. Lett.* **2009**, *11*, 3136.
478. Moslin, R. M.; Jamison, T. F. *J. Am. Chem. Soc.* **2006**, *128*, 15106.
479. Ley, S. V.; Antonello, A.; Balskus, E. P.; Booth, D. T.; Christensen, S. B.; Cleator, E.; Gold, H.; Hogenauer, K.; Hünger, U.; Myers, R. M.; Oliver, S. F.; Simic, O.; Smith, M. D.; Søhoel, H.; Woolford, A. J. A. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12073.
480. Yakambram, P.; Puranik, V. G.; Gurjar, M. K. *Tetrahedron Lett.* **2006**, *47*, 3781.
481. Lu, Y.; Krische, M. J. *Org. Lett.* **2009**, *11*, 3108.
482. Shiina, I.; Takasuna, Y.; Suzuki, R.; Oshiumi, H.; Komiyama, Y.; Hitomi, S.; Fukui, H. *Org. Lett.* **2006**, *8*, 5279.
483. Barry, C. S.; Elsworth, J. D.; Seden, P. T.; Bushby, N.; Harding, J. R.; Alder, R. W.; Willis, C. L. *Org. Lett.* **2006**, *8*, 3319.
484. Mandal, A. K.; Schneekloth, J. S., Jr.; Kuramochi, K.; Crews, C. M. *Org. Lett.* **2006**, *8*, 427.
485. Hoye, T. R.; Eklov, B. M.; Jeon, J.; Khoroosi, M. *Org. Lett.* **2006**, *8*, 3383.
486. Hamajima, A.; Isobe, M. *Org. Lett.* **2006**, *8*, 1205.
487. Hamajima, A.; Isobe, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2941.
488. Burke, C. P.; Swingle, M. R.; Honkanen, R. E.; Boger, D. L. *J. Org. Chem.* **2010**, *75*, 7505.
489. Oh, C. H.; Rhim, C. Y.; Kim, M.; Park, D. I.; Gupta, A. K. *Synlett* **2005**, 2694.
490. Robertson, J.; Chovatia, P. T.; Fowler, T. G.; Withey, J. M.; Woollaston, D. J. *Org. Biomol. Chem.* **2010**, *8*, 226.
491. Tortosa, M.; Yakelis, N. A.; Roush, W. R. *J. Org. Chem.* **2008**, *73*, 9657.
492. Lambert, T. H.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2006**, *128*, 426.
493. Furuta, H.; Hasegawa, Y.; Mori, Y. *Org. Lett.* **2009**, *11*, 4382.
494. Fuwa, H.; Goto, T.; Sasaki, M. *Org. Lett.* **2008**, *10*, 2211.
495. Zhu, J. R.; Xue, J. J.; Li, W. Z.; Chen, X. S.; Li, Y. *Chin. Chem. Lett.* **2010**, *21*, 273.
496. Bugaut, X.; Guinchard, X.; Roulland, E. *J. Org. Chem.* **2010**, *75*, 8190.

Biographical sketch



R. David Crouch graduated from Duke University in 1978 with a B.A. degree in chemistry. After six years of teaching in the secondary school science in Maryland, he returned to graduate studies, completing an M.S. degree in chemistry at Shippensburg University in 1985. He then moved to The Johns Hopkins University and joined Professor Gary Posner's research group, earning an M.A. degree in 1988 and a Ph.D. in 1991. Following a three-year appointment as an assistant professor at Coker College in South Carolina, he joined the chemistry department at Dickinson College in 1994 as an assistant professor, was promoted to associate professor in 2000 and professor in 2010.