Di-*t*-butylsilyl Bis(trifluoromethanesulfonate)

[85272-31-7] $C_{10}H_{18}F_6O_6S_2Si$ (MW 440.44)

InChI = 1S/C10H18F6O6S2Si/c1-7(2,3)25(8(4,5)6,21-23(17,18)9(11,12)13)22-24(19,20)10(14,15)16/h1-6H3
InChIKey = HUHKPYLEVGCJTG-UHFFFAOYSA-N

(reagent for the protection of diols)

Physical Data: bp 73–75 °C/0.35 mmHg; *d* 1.208 g cm^{-3}.
Solubility: sol most common organic solvents.
Form Supplied in: liquid.
Preparative Method: by the treatment of di-*t*-butylchlorosilane with ***Trifluoromethanesulfonic Acid***, followed by distillation (71% yield).[1]
Purification: distillation.
Handling, Storage, and Precautions: moisture sensitive; reacts with hydroxylic solvents; corrosive.

Original Commentary

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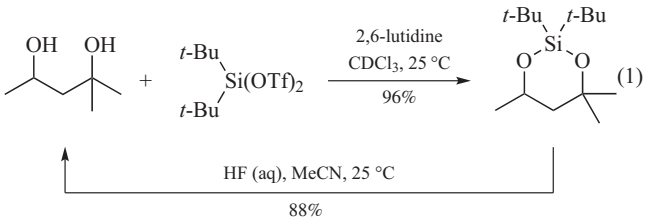
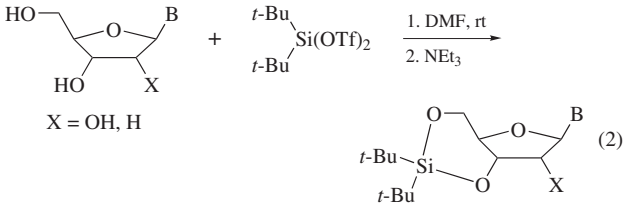
Protection of Alcohols. Di-*t*-butylsilyl bis(trifluoromethanesulfonate) is a reagent for the selective protection of polyhydroxy compounds. This reagent reacts with 1,2-, 1,3-, and 1,4-diols under mild conditions to give the corresponding dialkylsilylene derivatives in high yield (0–50 °C, 79–96%). Deprotection is conveniently achieved by using aqueous ***Hydrofluoric Acid*** in acetonitrile (eq 1).

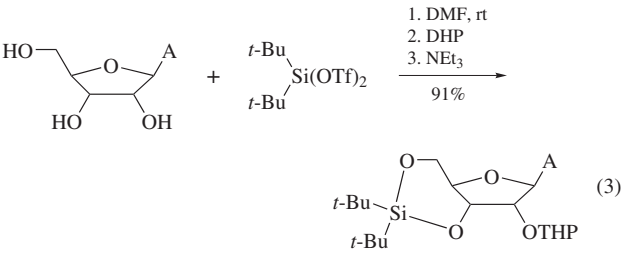


Unlike ***Di-t-butyldichlorosilane***, this reagent reacts with hindered alcohols. Even pinacol reacts to give the silylene derivative (100 °C, 24 h, 70%). Di-*t*-butylsilylene derivatives of 1,2-diols are more reactive than those of 1,3- and 1,4-diols and undergo rapid hydrolysis (5 min) in THF/H_2O at pH 10, while the 1,3- and 1,4-derivatives are unaffected at pH 4–10 (22 °C) for several hours. This protecting group is stable under the conditions of PDC oxidation of alcohols (CH_2Cl_2, 25 °C, 27 h) and tosylation of alcohols (pyridine, 25 °C, 27 h).

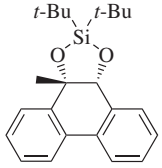
The reagent has seen limited use for the protection of alcohols but has been used to protect nucleosides (eq 2).[2–5] The procedure consists of sequential addition of the ditriflate and ***Triethylamine*** to the nucleoside in DMF. The choice of solvent is critical.



The ribonucleosides of uracil, adenine, and guanine give the protected derivative in 94–95% yield.[2] Cytidine gives a low yield of the desired product under these conditions. Subsequent studies suggested that O^2 of cytosine participates in the reaction. Addition of ***Trifluoromethanesulfonic Acid*** or ***Silver(I) Trifluoromethanesulfonate*** at 0 °C prior to addition of the silylating agent results in a 99% yield of the desired derivative.[3] The derivatives are acid sensitive, presumably due to the proximity of the 2′-hydroxy group. Acetylation, tetrahydropyranylation, methoxytetrahydropyranylation, and silylation of the 2′-hydroxy group are accomplished without affecting the dialkylsilylene protecting group. The 2′-deoxyribonucleosides, including 2′-deoxycytidine, can also be prepared by the aforementioned procedure (yields 90–99%). These cyclic silylene derivatives of nucleosides can be deprotected conveniently using tributylamine hydrofluoride in THF (5 min, 1 M, rt, 20 equiv).[4] A one-pot procedure has been reported for simultaneously protecting the 2′-, 3′-, and 5′-hydroxys of a ribonucleoside, which utilizes the acid generated upon silylating the 3′- and 5′-hydroxys for catalyzing the formation of a THP acetal at the 2′-position (eq 3).[5]



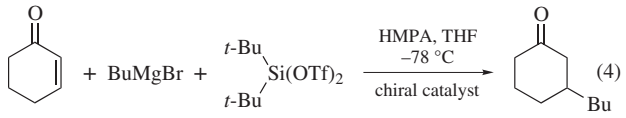
Derivatization of Alcohols. Di-*t*-butylsilyl bis(trifluoromethanesulfonate) has been used to derivatize hindered diols, to give derivatives such as (**1**), for analysis by gas chromatography–electron impact mass spectrometry.[6] The major fragmentation is that of the Si–C bonds.



(**1**)

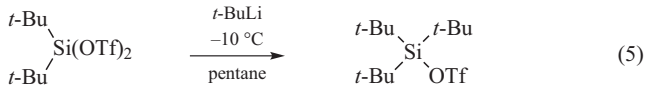
m/z 366 (M^+), 309 (M^+ – Bu), 191 (*B*)

Reagent in Enantioselective Additions. In a study of enantioselective conjugate addition to cyclohexanone it was found that the presence of HMPA and various silyl reagents markedly increases the enantioselectivity (eq 4).[7] Di-*t*-butylsilyl bis(trifluoromethanesulfonate) gives a 67% yield and 40% ee but ***t-Butyldiphenylchlorosilane*** gives a 97% yield and 78% ee.



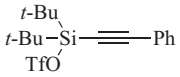
(4)

Other Substitution Reactions. An extremely hindered silyl reagent, tri-*t*-butylsilyl trifluoromethanesulfonate, was prepared from di-*t*-butylsilyl bis(trifluoromethanesulfonate) and ***t*-Butyllithium** (eq 5).[8] This reagent might find use in the protection of alcohols.

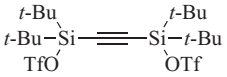


(5)

In conjunction with the study of alkyl-substituted silyl triflates, (**2**) and (**3**) have been prepared from the corresponding alkynyllithium reagents and di-*t*-butylsilyl bis(trifluoromethanesulfonate).[9]

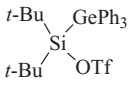


(**2**)

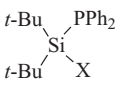


(**3**)

The preparation of other derivatives of di-*t*-butylsilyl bis(trifluoromethanesulfonate) using germanium.[10] and phosphorus[11] nucleophiles has been reported and provides bifunctional silanes such as (**4**) and (**5**).



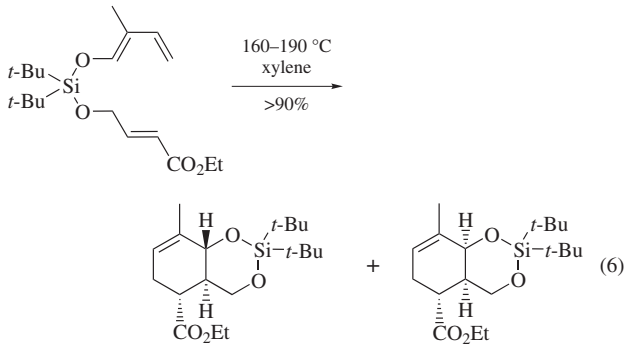
(**4**)



(**5**)

X = –C≡CPh, –$SiPh_3$, –$N(TMS)_2$, –PHPh, –O-*i*-Pr, –SPh

A compound closely related to di-*t*-butylsilyl bis(trifluoromethanesulfonate) is di-*t*-butylchlorosilyl trifluoromethanesulfonate, which has been used to tether two structurally different alcohol derivatives in order to effect an intramolecular Diels–Alder reaction (eq 6).[12]



(6)

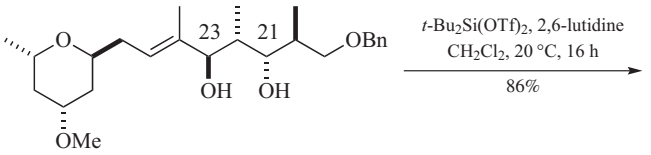
>99:<1

First Update

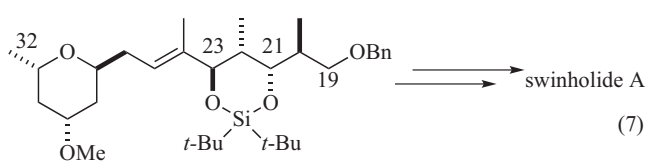
Jitendra Belani
Infinity Pharmaceuticals, Cambridge, MA, USA

In the past 10 years, there has been a dramatic increase in use of di-*tert*-butylsilyl bis(trifluoromethanesulfonate) as a protecting group for diols to provide the required orthogonality or to impart selectivity in various reactions both in synthesis of natural products and in carbohydrate and oligonucleotide syntheses.

Applications in Total Synthesis of Natural Products and Development of New Methods. Paterson et al. strategically used di-*tert*-butylsilyl bis(trifluoromethanesulfonate) to avoid differential protection of C_{21} and C_{23} hydroxyl groups in their efforts to synthesize the C_{19}–C_{32} fragment of swinholide A (eq 7).[13a] The elaboration of the fragment to the natural product was reported in the subsequent communications[13b–d] and the authors were able to remove the silylene protecting group using HF·pyridine. The authors have also reported similar application of di-*tert*-butylsilyl bis(trifluoromethanesulfonate) to protect 1,3-diols in total synthesis of concanamycin A.[14]



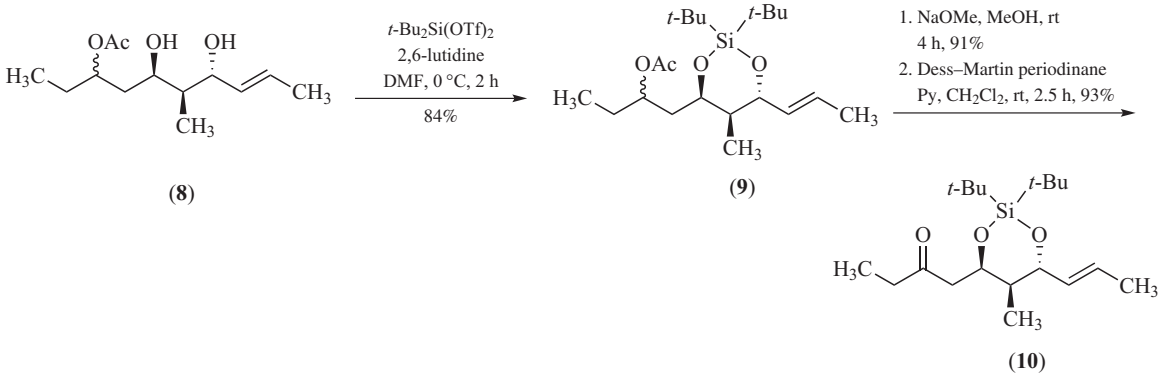
(**6**)



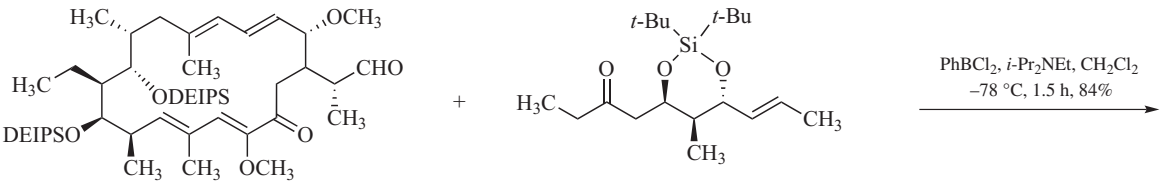
(7)

(**7**)

The first total synthesis of concanamycin F by Toshima et al. also utilized di-*tert*-butylsilyl bis(trifluoromethanesulfonate) for protection of 1,3-diols.[15] The key aldol reaction between **11** and **12** was best achieved using $PhBCl_2$ and *i*-Pr_2NEt in CH_2Cl_2 at −78 °C to provide the desired aldol **13** as the sole isomer in 84% yield. The selective deprotection of di-*tert*-butylsilylene was then achieved using HF·pyridine, which resulted in concomitant formation of the hemiacetal **15**. Removal of the diethylisopropylsilyl group using TBAF provided concanamycin F (eq 8).

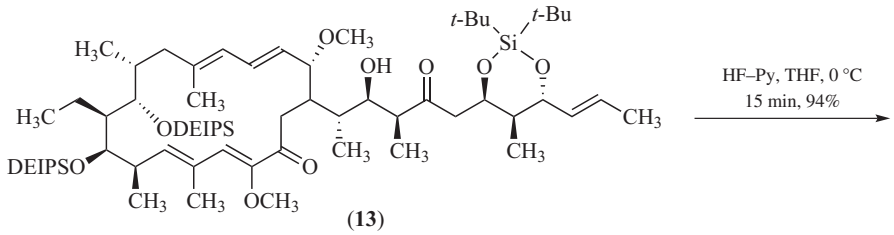


(**8**) (**9**) (**10**)

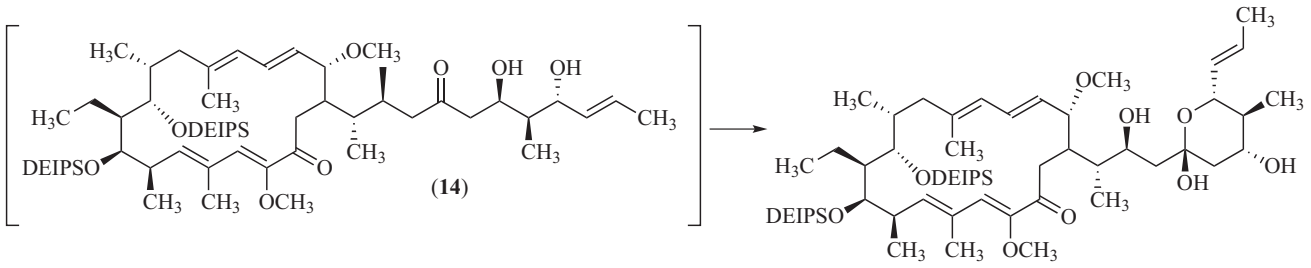


DEIPS = $SiEt_2$*i*-Pr

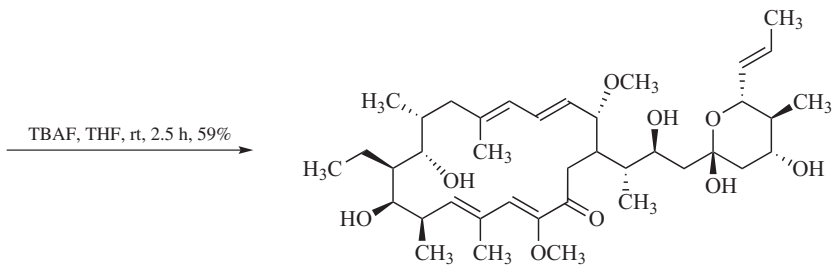
(**11**) (**12**)



(**13**)

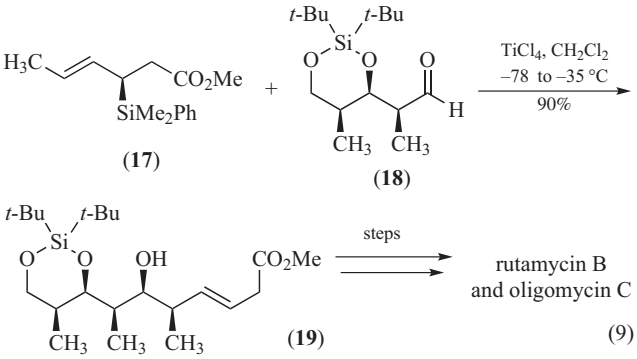


(**14**) (**15**)



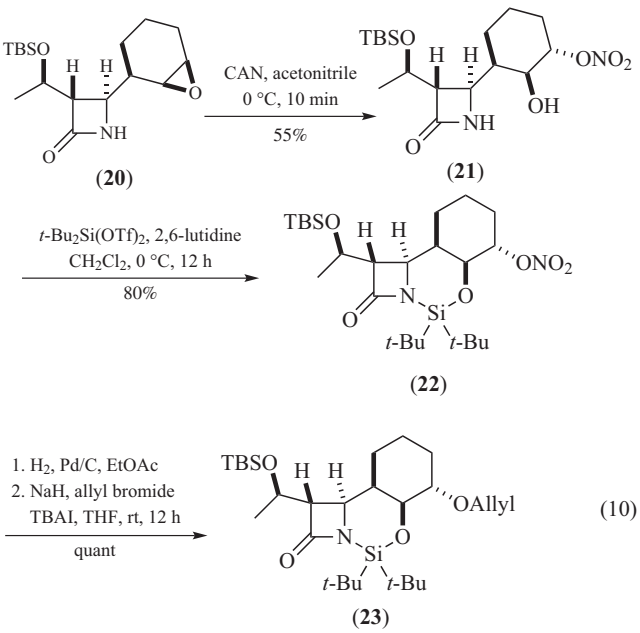
(**16**), concanamycin F (8)

In another report, Panek and Jain used chiral allylsilane methodology for construction of C_1–C_{17} polypropionate fragment of rutamycin B and oligomycin C.[16] The aldehyde partner used for the sequence consisted of a diol protected as a di-*tert*-butylsilylene **18**. The reaction proceeded in the presence of $TiCl_4$ in excellent diastereoselectivity and yield (eq 9).

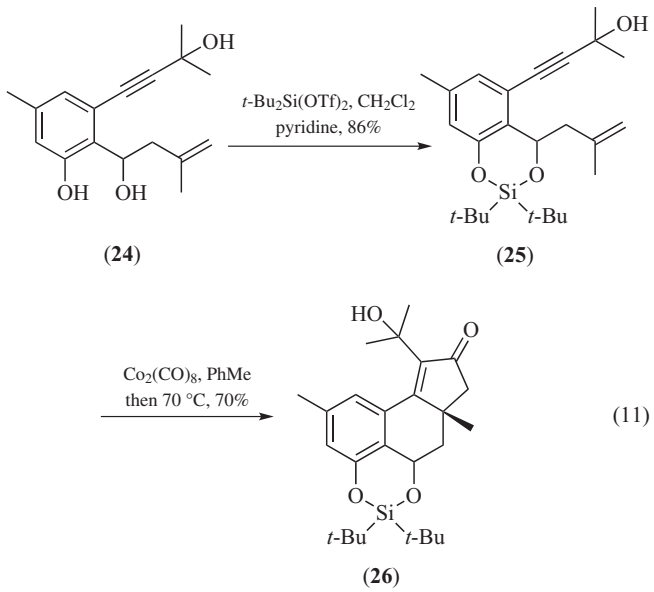


diastereoselection: >30:1 *syn*:*anti*

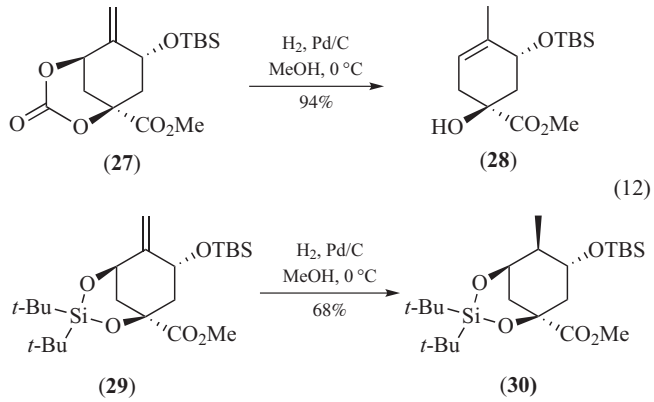
Di Fabio et al. reported synthesis of 3-alkoxy-substituted trinems from commercially available 4-acetoxy-3-[(*R*)-l-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone.[17] Epoxide **20** was treated with ceric ammonium nitrate in acetonitrile to provide the intermediate nitrate ester **21** in 55% yield. Simultaneous protection of the secondary alcohol and the amide was accomplished using di-*tert*-butylsilyl bis(trifluoromethanesulfonate) to provide the tricyclic β-lactam **22**. Removal of the nitro group by catalytic hydrogenation provided the desired secondary alcohol that was alkylated with allyl bromide to provide **23** in quantitative yield (eq 10).[17]



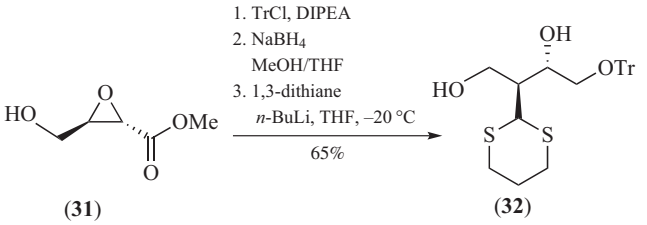
A successful approach to construction of the tricyclic core common to hamigeran terpenes was demonstrated using an intramolecular Pauson–Khand reaction.[18] For an effective cyclization, the authors report that it was necessary to tether the olefin-containing moiety to the aromatic framework to reduce its conformational mobility using the di-*tert*-butylsilylene protecting group (eq 11).



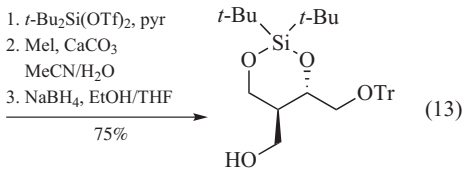
Stoltz and coworkers reported a highly selective catalytic reductive isomerization reaction using 10% Pd/C and hydrogen in MeOH. During their explorations of the total synthesis of (+)-dragmacidin F, olefin isomerization using the carbonate **27** (eq 12) was developed.[19] The authors provided evidence that the method does not proceed via a stepwise reduction/elimination sequence or a π-allylpalladium intermediate. Replacement of the carbonate by a dioxasilyl linkage (**29**), however, did not result in isomerization, only diastereoselective reduction of the *exo*-olefin was observed (eq 12).[19]



Hillaert and Van Calenbergh have reported synthesis of (*S*)-3-(hydroxymethyl)butane-1,2,4-triol, a versatile, chiral building block that can be transformed into useful compounds such as (*S*,*S*)-4-(hydroxymethyl)pyrrolidine-3-ol and oxetanocin A.[20] The authors reported a short synthesis of the protected triol **33** from the epoxide **31** in six steps. The use of di-*tert*-butylsilylene as the protecting group provided the desired differentiation of the hydroxyl groups, which was necessary for their successful investigation into the stereoselective synthesis of N-homoceramides (eq 13).[20]

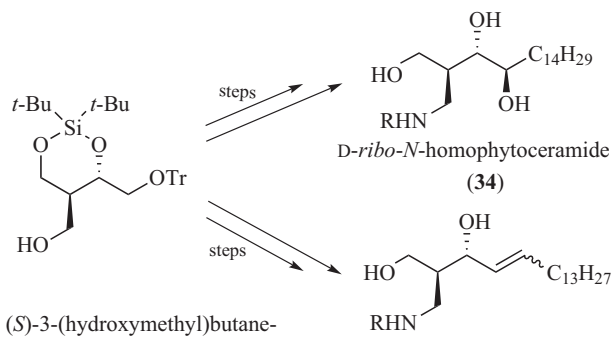


(**31**) (**32**)



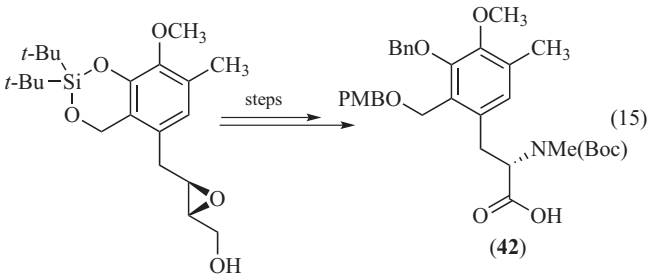
(13)

(**33**)



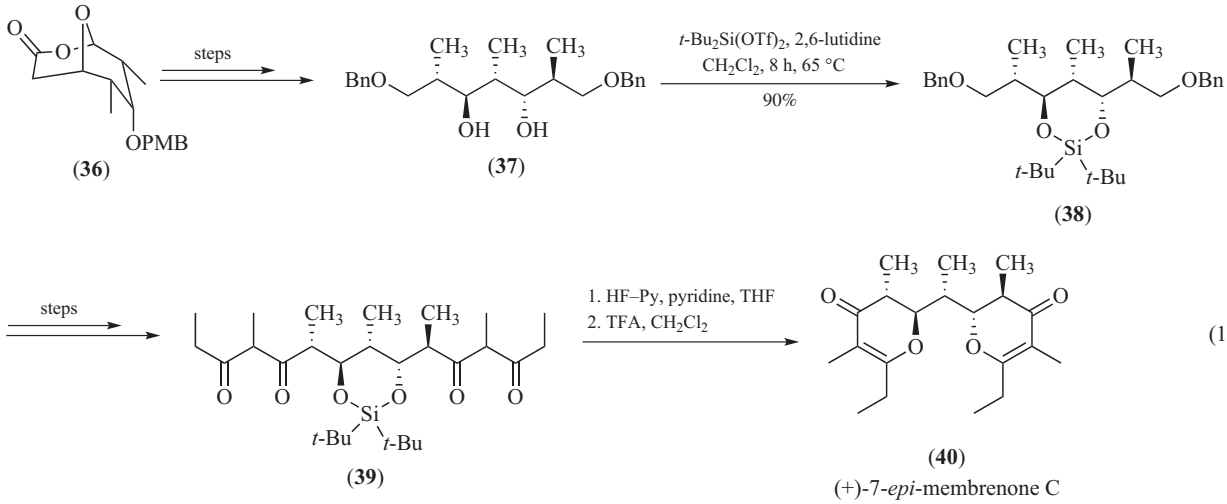
Synthesis of polypropionate marine natural product (+)-membrenone C and its 7-*epi*-isomer has been reported using a key desymmetrization technique to create five contiguous chiral centers from bicyclic precursor **36**.[21] The diol was protected using di-*tert*-butylsilyl bis(trifluoromethanesulfonate) and further elaborated into the natural product and its epimer (eq 14).[21] In a separate communication, Perkins et al. utilized di-*tert*-butylsilyl bis(trifluoromethanesulfonate) for synthesis of a model system en route to the polypropionate natural products auripyrones A and B.[22]

Danishefsky and coworkers reported studies toward the total synthesis of tetrahydroisoquinoline alkaloid, ecteinascidin.[23] The synthesis required a pentasubstituted E-ring system where they utilized the di-*tert*-butylsilylene protecting group in the sequence to prepare the amino acid **42** (eq 15). In addition to above examples, protection of 1,3-diol using di-*tert*-butylsilyl bis(trifluoromethanesulfonate) has been reported in the synthesis of brasilinolides,[24] polyol fragments of ansamycin antibiotics,[25] (±)-*epi*-stegobinone,[26] 24-demethylbafilomycin C1,[27] peloruside A,[28], bafilomycin A1,[29] premisakinolide A,[30] (+)-papulacandin D,[31] and other polyether natural products such as maitotoxin,[32] yessotoxin,[33] and gambieric acids.[34]



(15)

A mixed di-*tert*-butylsilylene has been prepared from (*S*)-5-hexen-2-ol and prochiral 1,4-pentadiene-3-ol for synthesis of (2*S*,7*S*)-dibutyroxynonane, the sex pheromone of *Sitodiplosis mosellana*. The intermediate **43** was then subjected to ring closing metathesis to provide the diene **44** in 70% yield over two steps (eq 16). Deprotection of the nine-membered silylene was achieved using TBAF under refluxing condition in the presence of molecular sieves. Reduction with H_2/PtO_2 and diacetylation yielded the desired (2*S*,7*S*)-dibutyroxynonane in 22% overall yield.[35]



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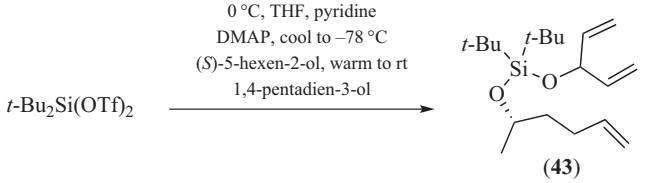
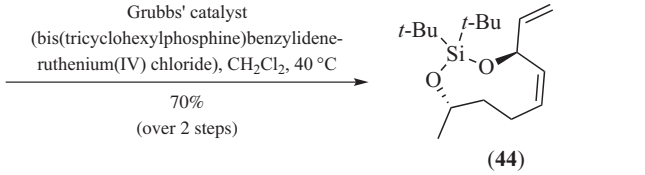
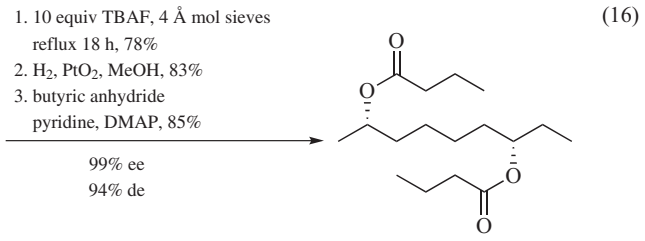


(**43**)



(**44**)

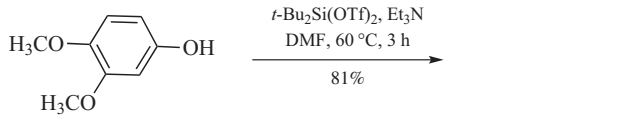


(16)

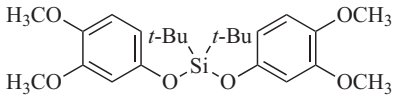
(**45**)

(2*S*,7*S*)-dibutyroxynonane

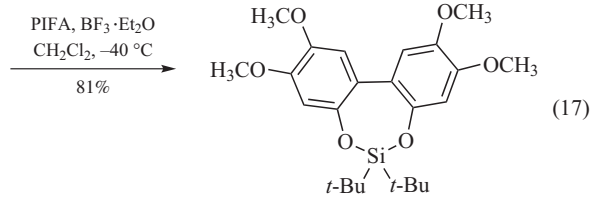
Kita and coworkers reported a novel method to prepare 2,2′-substituted biphenyl compounds using phenyliodine(III) bis(trifluoroacetate) (PIFA), a hypervalent iodine reagent.[36] The substrate for the coupling was first prepared by reacting 1 equiv of di-*tert*-butylsilyl bis(trifluoromethanesulfonate) with 2 equiv of the phenol **46**. Di-*tert*-butylsilylene **47** then underwent an intramolecular cyclization in the presence of $BF_3{\cdot}OEt_2$ to provide the desired tricyclic compound **48**. Removal of silylene ether was accomplished by TBAF in excellent yields. This sequence worked well for both 2,2′-disubstituted symmetrical and unsymmetrical biphenyls (eq 17).[36]



(**46**)

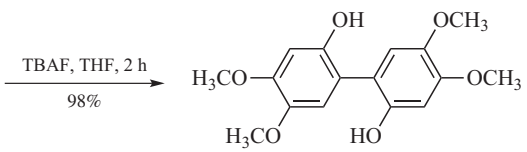


(**47**)



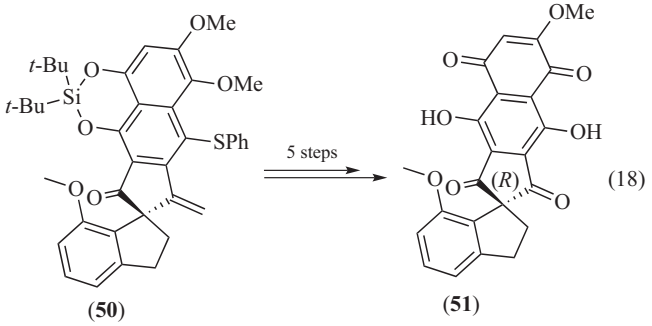
(17)

(**48**)



(**49**)

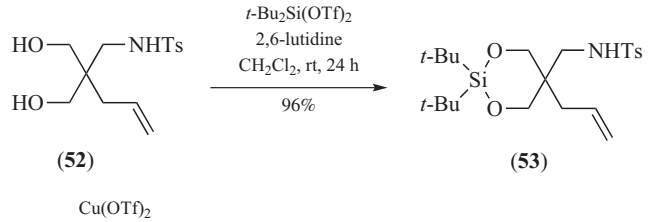
In a separate communication, Kita and coworkers also reported an enantiodivergent synthesis of an ABCDE ring analog of the antitumor antibiotic fredericamycin A via an intramolecular [4 + 2] cycloaddition. Late-stage oxidations were performed on the di-*tert*-butylsilylene for protection of phenolic hydroxyl groups. Syntheses of both (*R*)- and (*S*)-enantiomers were reported (eq 18).[37]



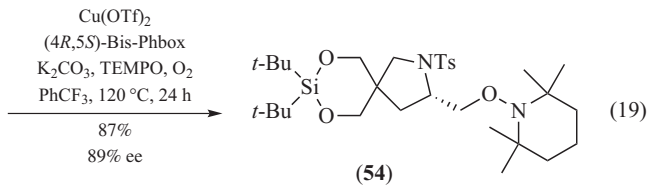
(18)

(**50**) (**51**)

In a study on copper-catalyzed enantioselective intramolecular aminooxygenation of alkenes, Chemler and coworkers showed that this reaction allows synthesis of chiral indolines and pyrrolidines.[38] Accordingly, the protected amino-diol **53** undergoes aminooxygenation in the presence of copper triflate, bisoxazoline ligands, and molecular oxygen to provide the desired spirodecane **54** in 87% yield and 89% ee (eq 19).[38]



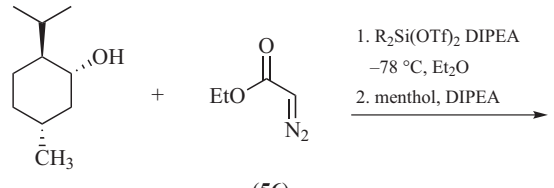
(**52**) (**53**)

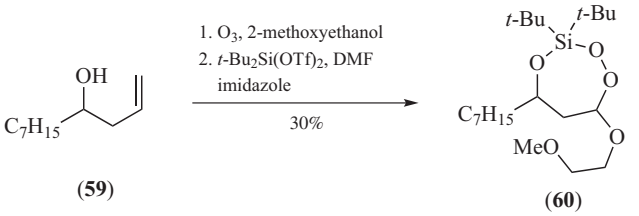


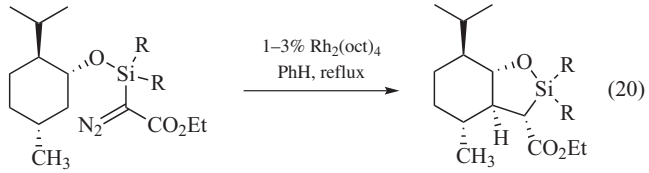
(19)

(**54**)

Craig and coworkers have reported stereocontrolled polyol synthesis via C–H insertion reactions of silicon-tethered diazoacetates.[39] Menthol was treated with di-*tert*-butylsilyl bis(trifluoromethanesulfonate) and the product was condensed with ethyl diazoacetate to provide the precursor **57a** to the C–H insertion reaction (eq 20). The rhodium(II) octanoate-catalyzed decomposition of the diazoacetate **57a**, however, did not provide the desired C–H insertion product, although the reaction was successful with diisopropylsilyl bis(trifluoromethanesulfonate) (eq 20).

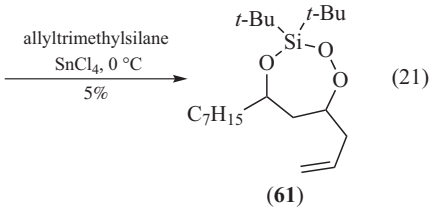






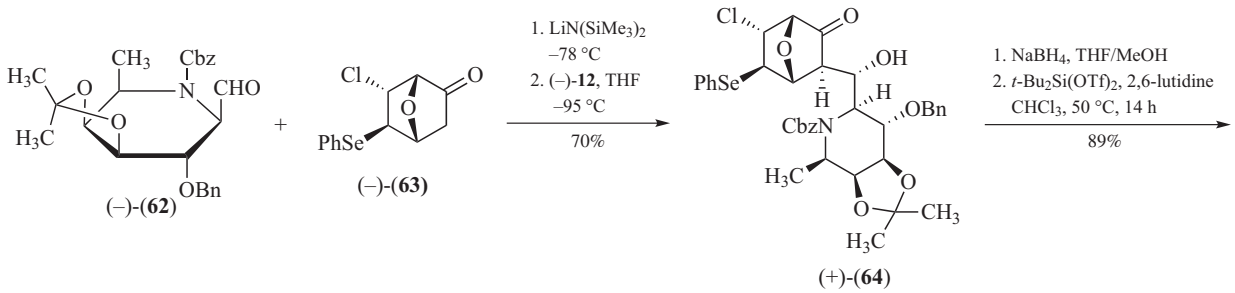
(**57a**), R = *t*-Bu; 37%
(**57b**), R = *i*-Pr; 78%

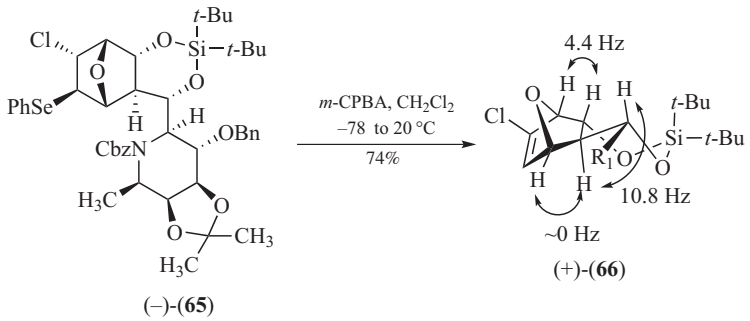
(**58a**), R = *t*-Bu; 0%
(**58b**), R = *i*-Pr; 94%

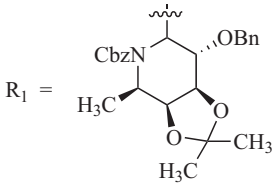


In a study about stereoselective allylation of chiral monoperoxides, Ahmed and Dussault focused on induction from 2-, 3-, and 4-substituted monoperoxyacetals.[40] It was observed that neighboring iodo-, alkoxy-, acetoxy-, and silyl, groups imparted useful levels of diastereoselection in the Lewis acid-mediated allylation of monoperoxyacetals. While investigating 1,3-stereoinduction, the homoallylic alcohol **59** was ozonized and the resultant hydroperoxy alcohol was silylated using di-*tert*-butylsilyl bis(trifluoromethanesulfonate) to provide 3-sila-1,2,4-trioxepane **60**. Unfortunately, the substrate provided only 5% of allylated silatrioxepane under $SnCl_4$-mediated allylation (eq 21).[40]

Applications in Carbohydrate and Oligonucleotide Syntheses. In efforts to synthesize aza-C-disaccharides, Baudat and Vogel used a key cross-aldolization of aldehyde **62** and (−)-(1*S*,4*R*,5*R*,6*R*)-6-chloro-5-(phenylseleno)-7-oxabicyclo-[2.2.1] heptan-2-one ((−)-**63**) to provide the product alcohol **64** stereoselectively in 70% yield.[41] The stereochemistry of the aldol product was confirmed by reduction of the ketone followed by protection of the diol using di-*tert*-butylsilyl bis(trifluoromethanesulfonate) providing a mixture of rotamers **65** resulting from benzyl carbamate. Treatment of this mixture with *m*-CPBA provided the vinyl chloride **66** that displayed typical ^{1}H NMR vicinal coupling constants, thus confirming the stereochemistry of *exo-anti* aldol (+)-**64** (eq 22). A NOE experiment further confirmed the structure of (+)-**66**.[41]

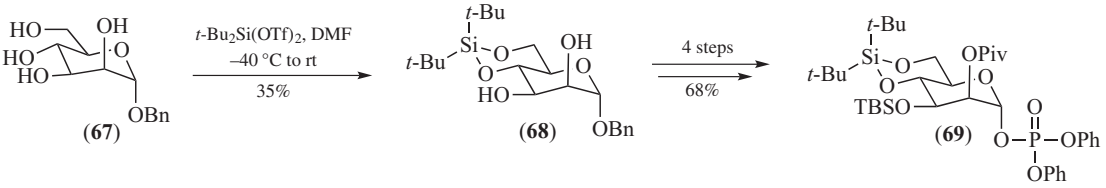




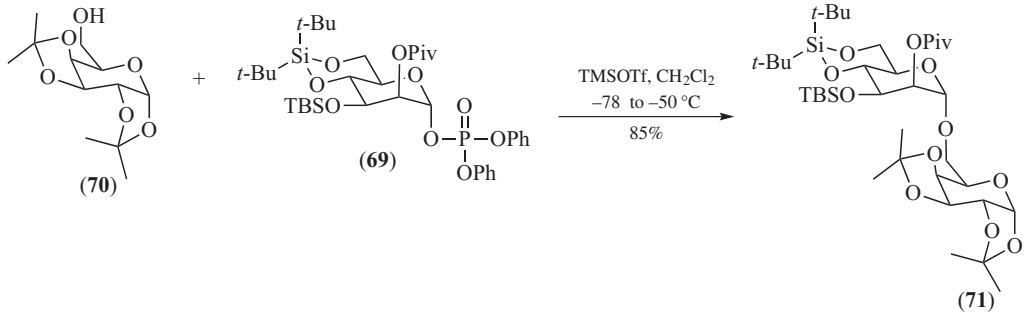


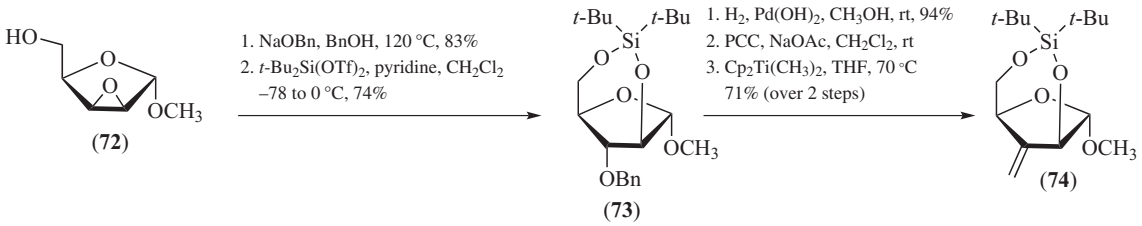
While investigating glycosyl phosphates for selective synthesis of α and β-glycosidic linkages using conformationally restrained mannosyl phosphate **69**, Seeberger and coworkers observed only the desired α-isomer **71** by virtue of the participating pivaloyl group as expected (eq 23). These reactions were high yielding, fast, and completely selective.[42]

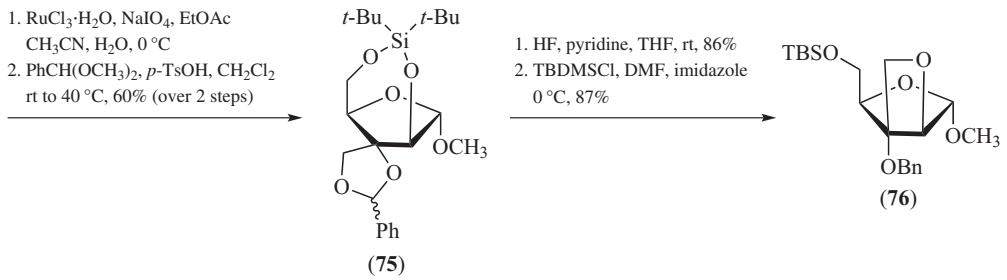
In a study of synthesis and conformational analysis of arabinofuranosyl oligosaccharide analogs in which one ring is locked into either the E_3 or °E conformation, Houseknecht and Lowary used di-*tert*-butylsilyl bis(trifluoromethanesulfonate) to protect the 1, 4-diol. The di-*tert*-butylsilylene **73** is stable under a variety of reaction conditions and can be easily removed under mild HF–pyridine conditions (eq 24).[43]

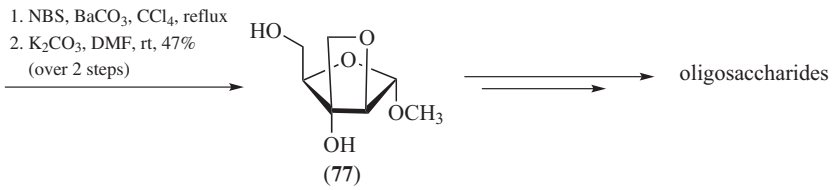


(23)



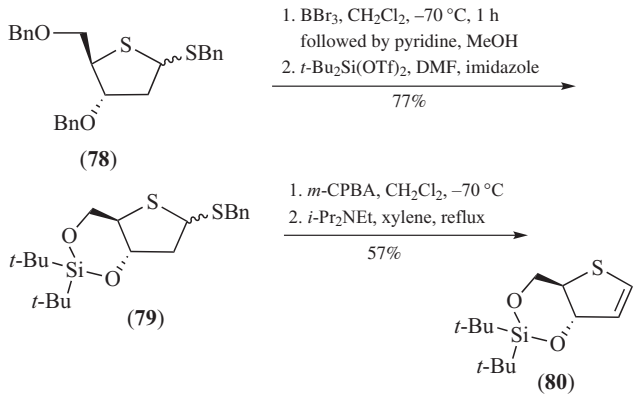






(24)

Electrophilic glycosidation of 3,5-*O*-(di-*tert* butylsilylene)-4-thioglycal **80** has been reported to exclusively provide the β-anomer of 4′-thionucleosides irrespective of the nucleobase employed. The face selectivity of the approach to 1′,2′-double bond by the incoming electrophile can be controlled by changing the protecting group of the 3′- and 5′-hydroxyl groups. Hence, approach to the α-face using NIS or PhSeCl increased in the order of 3′,5′-*O*-(di-*tert*-butylsilylene):DTBS > 3′,5′-*O*-(1,1,3,3-tetraisopropyldisilox-ane-1,3-diyl):TIPDS > 3′,5′-bis-*O*-(*tert*-butyldimethylsilyl):TBDMS (eq 25).[44]

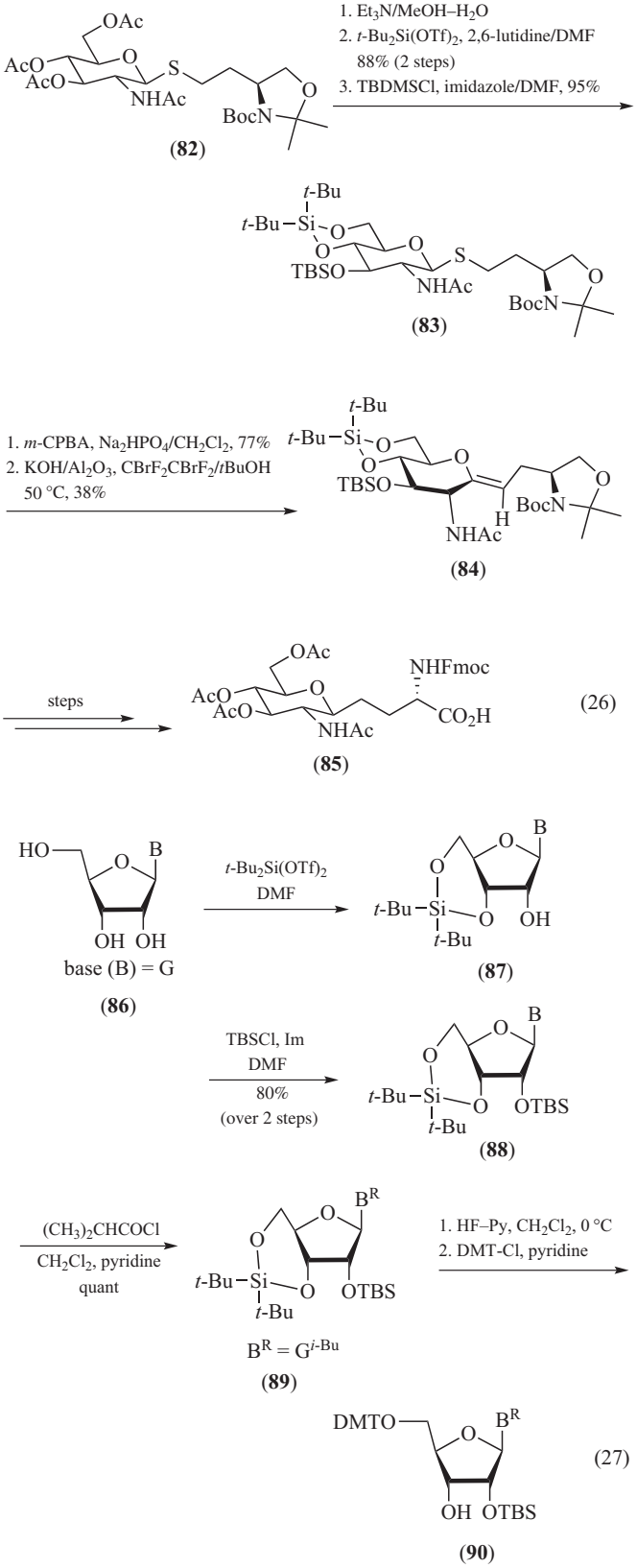


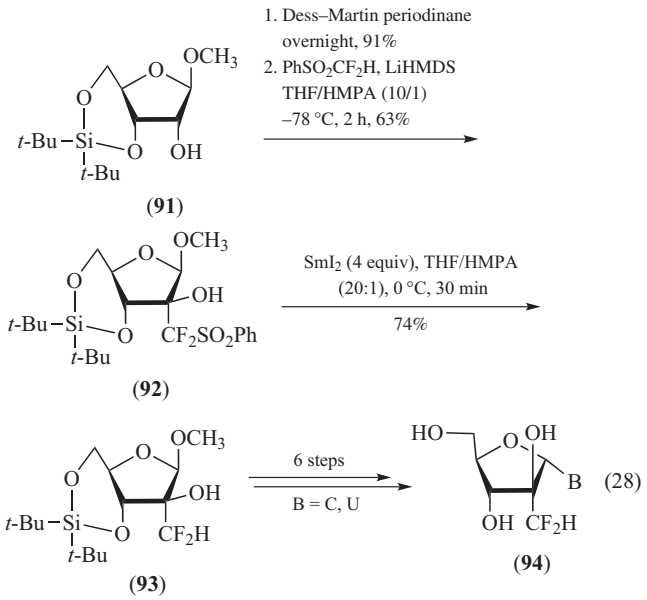
Entry	Electrophile	Base	Yield (%)
81a	PhSeCl	uracil-1-yl	88
81b	NIS	uracil-1-yl	73
81c	PhSeCl	thymin-1-yl	62
81d	PhSeCl	cytosin-1-yl	85

Ohnishiy and Ichikawa reported a stereoselective synthesis of a C-glycoside analog of *N*-Fmoc-serine β-*N*-acetylglucosaminide (**85**) using a key Ramberg–Bäcklund rearrangement.[45] The di-*tert*-butylsilylene protecting group provided the desired stability under the strongly basic conditions of the rearrangement (eq 26).

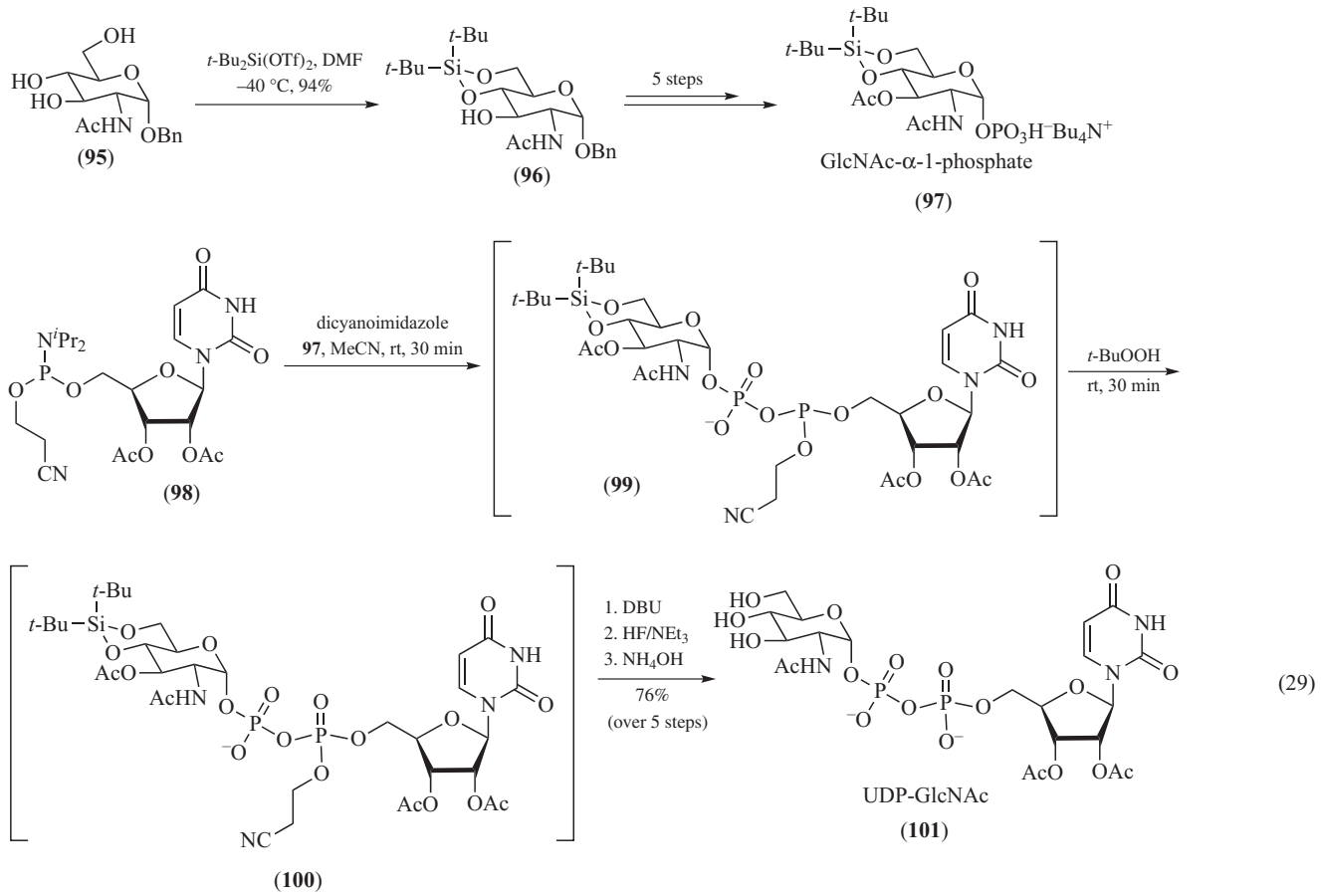
In a report on synthesis of 5′-*O*-DMT-*N*-acyl-2′-*O*-TBDMS-protected nucleoside precursors for phosphoramidite RNA synthesis, Serebryany and Beigelman used di-*tert*-butylsilyl bis(trifluoromethanesulfonate) to protect 3′- and 5′-hydroxyl functions of a nucleoside.[46] The silylated derivatives were obtained in high yields and were crystalline and easy to purify. Acylation of the N_2-position of the guanosine derivative provided crystalline compound **89** in quantitative yield. Deprotection of the silylene **89** using mild HF–pyridine followed by protection of the primary alcohol with dimethoxytrityl chloride in pyridine gave the desired compound **90** in about 60% yield over five steps (eq 27).[46]

Synthesis of 2′-*C*-difluoromethylribonucleosides has been separately reported where simultaneous protection of the 3- and 5-hydroxyl groups of the methyl D-ribose with di-*tert*-butylsilyl bis(trifluoromethanesulfonate) afforded the silylene **91**.[47] Dess–Martin periodinane oxidation of the C-2 hydroxyl group followed by nucleophilic addition of difluoromethyl phenyl sulfone in the presence of lithium hexamethyldisilazane converted **91** exclusively to sulfone **92** in 57% yield. Reduction of the sulfone using SmI_2, coupling with persilylated bases, and a sequence of deprotection steps provided the desired 2′-*C*-difluoromethylribonucleosides (eq 28).[47]



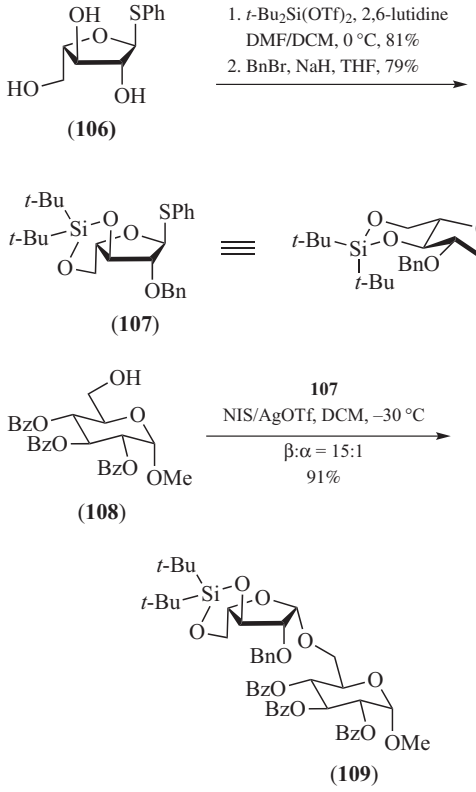


Van der Marel and coworkers reported a novel method to prepare pyrophosphates by coupling of a sugar phosphate and a nucleoside phosphoramidite.[48] Benzyl-2-acetamido-2-deoxy-α-D-glucoside **95** was first protected using di-*tert*-butylsilyl bis(trifluoromethanesulfonate) to improve solubility of GlcNAc derivative. In four additional steps, the silyl ketal was converted into the tetrabutylammonium salt of GlcNAc-α-1-phosphate **97**. Uridine phosphoramidite **98** was then coupled with GlcNAc-α-1-phosphate **97** in the presence of dicyanoimidazole. The reaction was monitored using ^{31}P NMR spectroscopy. Upon complete disappearance of amidite **99**, the mixture was treated with *t*-butylperoxide to provide diastereomeric cyanoethyl-protected pyrophosphate **100**. The cyanoethyl group was then removed by treatment with anhydrous DBU, followed by treatment with HF/Et_3N to deprotect the di-*tert*-butylsilylene group, and finally ammonium hydroxide was used to hydrolyze the acetate protecting groups to provide UDP-*N*-acetylglucosamine **101** in 76% yield (eq 29).[48]



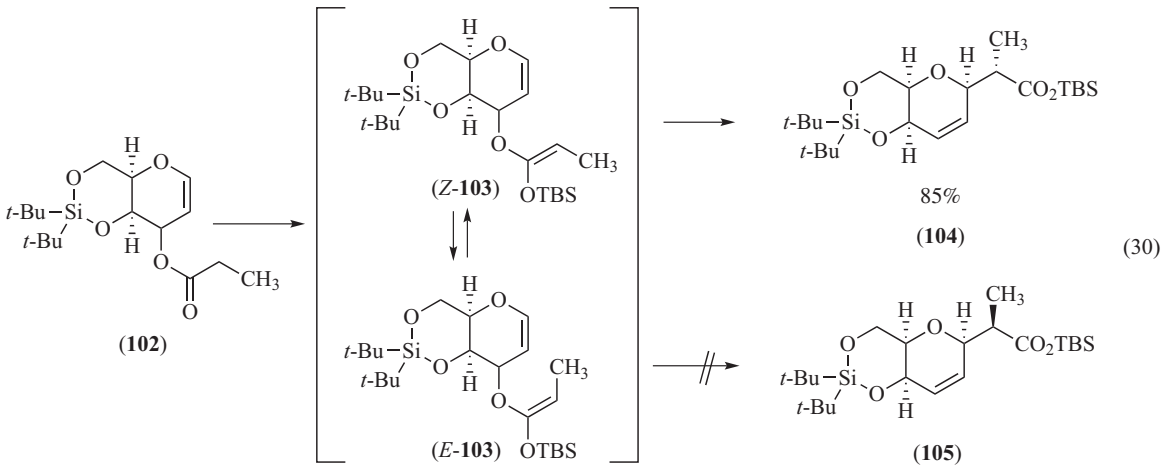
Kishi and coworkers reported a protocol to improve the overall stereoselectivity of the Ireland–Claisen rearrangement for pyranoid and furanoid glucals.[49] To prepare building blocks for marine natural product halichondrins, the authors reported synthesis of silylene **102** in two steps from D-galactal. Under the conditions reported by Ireland (LHMDS, TBSCl, HMPA, THF, −78 °C), **102** was converted to the corresponding *O*-silyl ketene acetal **103**, which was estimated as a 7.3:1 mixture of *Z*-**103** and *E*-**103** as monitored using ^{1}H NMR analysis. Upon heating at 80 °C in benzene for 1 day, this mixture furnished the carboxylate **104** as a *single diastereomer* in >85% yield, along with **102** and *E*-**103** in ca. 12% combined yield. The authors further provided experimental evidence that Claisen rearrangement took place through *Z*-**103** and that the Me stereochemistry of **104** indicated that the Claisen rearrangement proceeded exclusively via the boatlike transition state (eq 30).[49]

A practical approach for the stereoselective introduction of β-arabinofuranosides has been developed by locking an arabinosyl donor in a conformation in which nucleophilic attack from the β-face is favored.[50] This was achieved by using di-*tert*-butylsilyl bis(trifluoromethanesulfonate) to protect the C-5 and C-3 hydroxyl groups. This resulted in C-5 and O-3 in a pseudoequatorial orientation, resulting in a perfect chair conformation of the protecting group. The nucleophilic attack from the α-face is disfavored due to unfavorable steric interactions with H-2. The glycosyl donor **107** was prepared in two convenient steps from commercially available thioglycoside **106**. The coupling of the conformationally constrained glycosyl donor **107** with the glycosyl acceptor **108** in the presence of the powerful thiophilic promoter system *N*-iodosuccinimide/silver triflate (NIS/AgOTf) in DCM at −30 °C gave disaccharide **109** with excellent β-selectivity (β:α = 15:1) in 91% yield (eq 31).[50]



(31)

Another β-selective glycosylation was reported by Lowary and coworkers who intended to study ligand specificity of CS-35, a monoclonal antibody that recognizes mycobacterial lipoarabinomannan.[51] Selective glycosylation followed by two-step deprotection of the hydroxyl groups provided the desired pentasaccharide **112** in 51% overall yield (eq 32). Subsequently, Crich et al. studied the importance of the activation method for the observed selectivity in glycosylation using 3,5-*O*-(di-*tert*-butylsilylene)-2-*O*-benzylarabinothiofuranosides as glycosyl donors for the synthesis of β-arabinofuranosides.[52]



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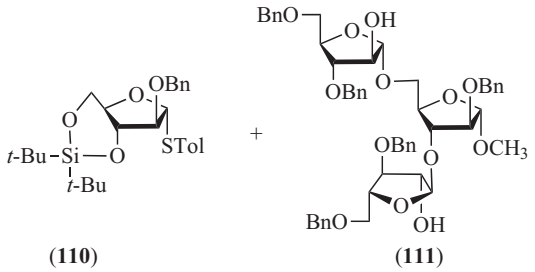
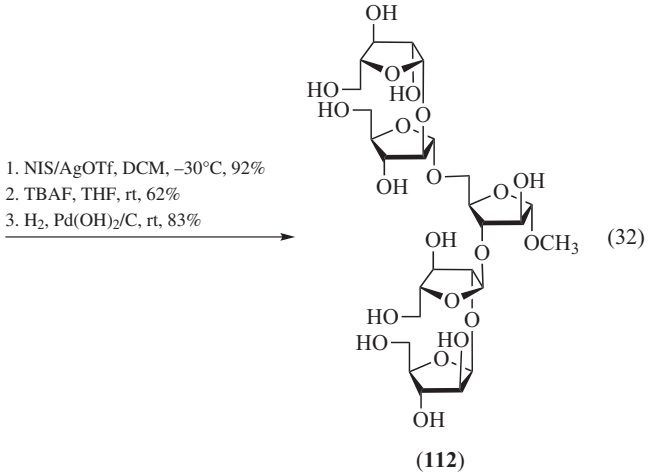


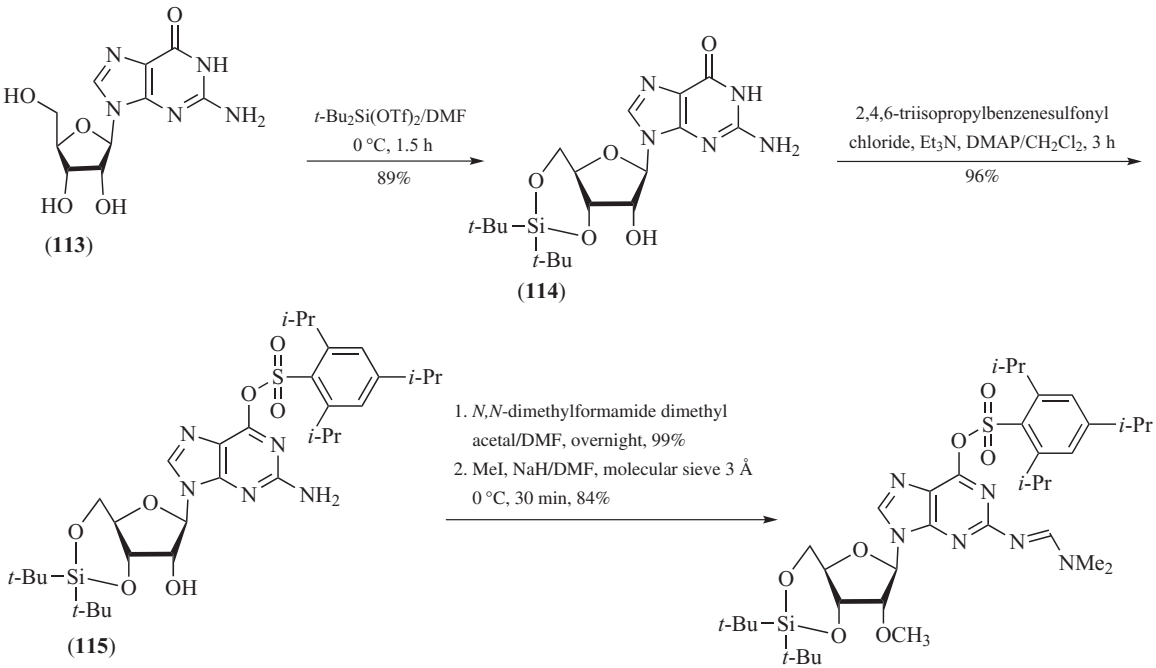
(**110**) (**111**)



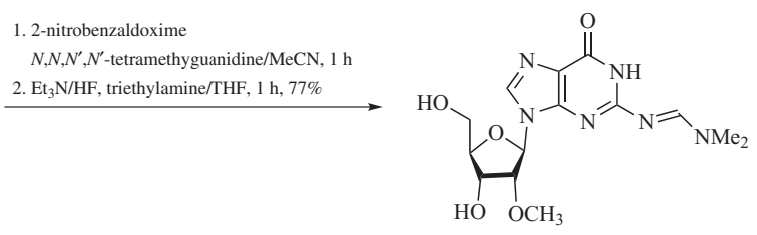
(**112**) (32)

A novel six-step synthesis of N_2-dimethylaminomethylene-2′-*O*-methylguanosine has been reported.[53] The synthesis utilizes di-*tert*-butylsilylene protection for 3′- and 5′-hydroxyl groups. The arenesulfonylation at the O_6 position of 3′-and 5′-*O*-protected guanosine without 2′-*O*-protection was found to be completely selective. Compound **117** is a useful intermediate for oligonucleotide construction (eq 33). A similar application of di-*tert*-butylsilylene protecting group was originally reported for the synthesis of N_2-isobutyryl-2′-*O*-methyl guanosine.[54]

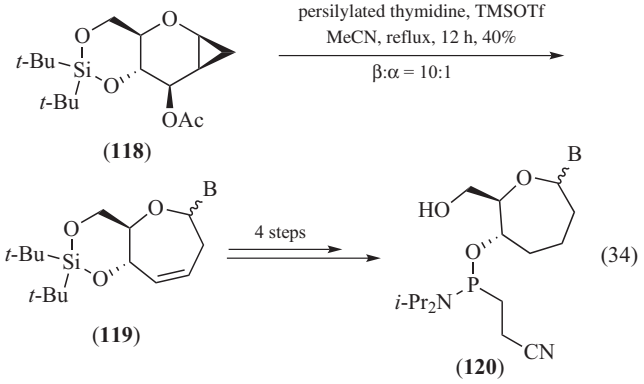
Sabatino and Damha recently reported synthesis, characterization, and properties of oxepane nucleic acids.[55] These sugar phosphate oligomers have the pentofuranose ring of DNA and RNA replaced with a seven-membered sugar ring. The oxepane nucleoside monomers were prepared from the ring expansion reaction of a cyclopropanated glycal, **118**, and their conversion into phosphoramidite derivatives. Properties of these oxepane nucleic acids were then compared to naturally occurring DNA (eq 34).



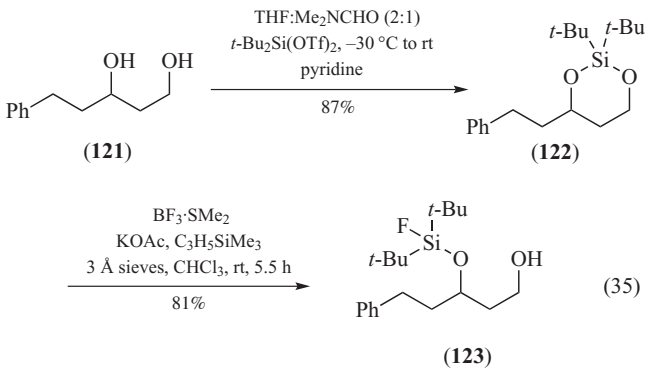
(**113**) (**114**) (**115**) (**116**)



(**117**) (33)



Regioselective Monodeprotection. The monodeprotection of di-*tert*-butylsilylene ethers prepared from substituted 1,3-pentanediols and 2,4-hexanediols has been achieved with $BF_3{\cdot}SMe_2$.[56] The reaction is highly selective and provides access to 1,3-diols silylated at the sterically more hindered position. This is consistent with coordination of boron to the sterically more accessible oxygen prior to intramolecular delivery of fluoride. The reaction conditions for deprotection are compatible with esters, allyl ethers, and TIPS ethers. The resulting secondary di-*tert*-butylfluorosilyl ethers are stable to various conditions including low pH aqueous solutions and silica gel chromatography; the di-*tert*-butylfluorosilyl ethers are readily cleaved with HF–pyridine. An example is provided below (eq 35).



Second Update

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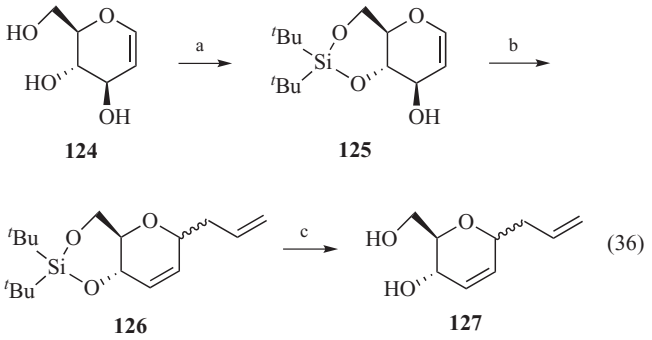
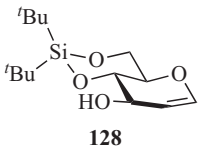
The choice of protecting groups is a very important, if not crucial, factor for glycal chemistry as particular reaction conditions for protection and deprotection may impart unsatisfactory results. For example, acid-catalyzed installation of protecting groups can produce variable quantities of rearranged products (Ferrier rearrangement) that are observed in the case of benzylidene acetal formation. Mild conditions utilized to introduce *p*-methoxybenzylidene acetal are more labile, whereas siloxanylidene acetals are often formed in low yield or with moderate regioselectivity, especially in cases using D-galactal. Based on these shortcomings, a convenient and useful protecting group has come to light—di-*tert*-butylsilyl bis(trifluoromethanesulfonate) that is generally utilized as a protecting group for diols when synthesizing natural products, oligonucleotides, and so on. Although it has been found to be useful, there are other venues where it can be exploited in reaction-based organic synthesis.

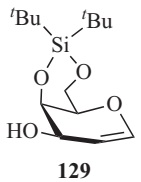
Hoberg[57] reported the protection of diols (*O*-4 and *O*-6) of D-glucal by using the di-*t*-butylsilylidene group following a similar strategy reported for the protection of ribonucleoside by Furusawa.[2] After glycosylation of D-glucal, the silylene group was removed by treatment with Bu_4NF in THF (eq 36).



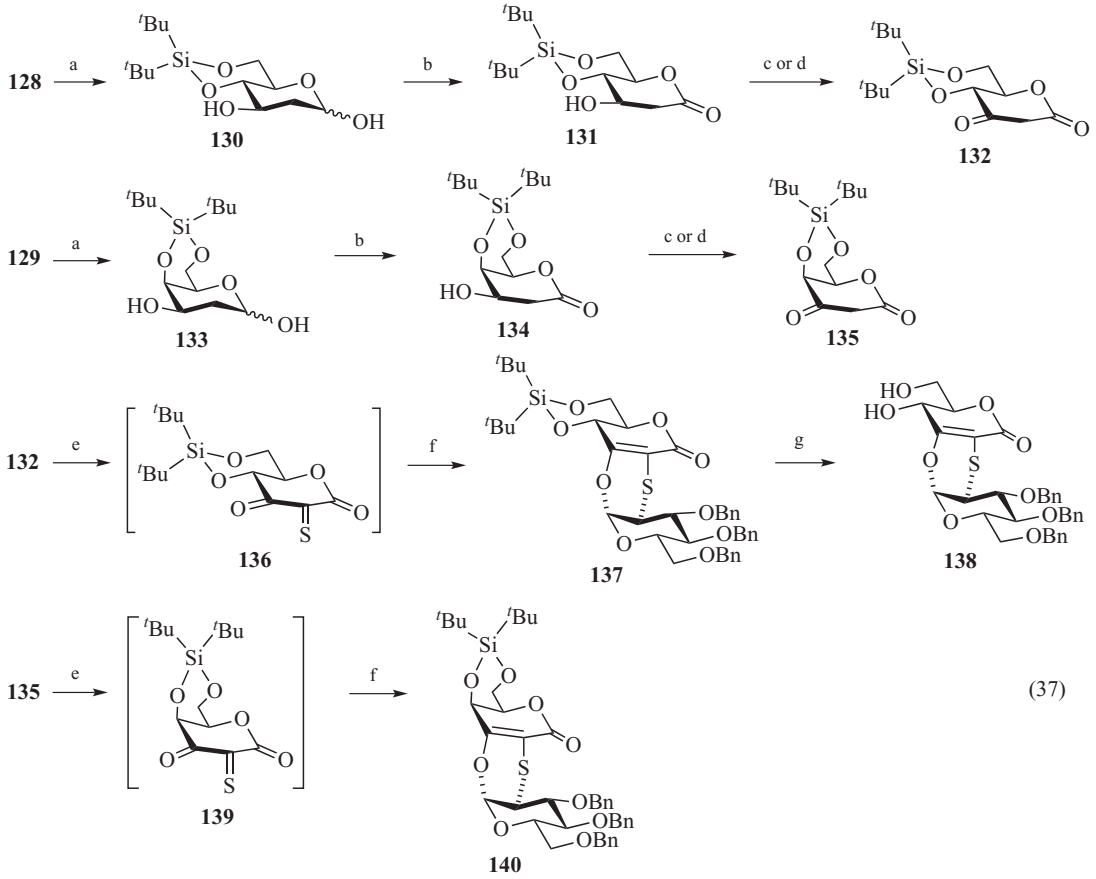
Reagents and conditions: (a) $^tBu_2Si(OTf)_2$, DMF, pyr. (b) (1) Ac_2O/Py; (2) TMS-allyl, TMSOTf; (c) Bu_4NF, THF.

In another report, Gabrielli[58] utilized the same reaction, as published by Hoberg,[57] to protect diols (*O*-4 and *O*-6) of D-glucal and D-galactal. The reaction was performed under very mild conditions (−40 °C, 30 min) using di-*t*-butylsilyl ditriflate in DMF to produce the 4,6-*O*-protected D-glucals **128** from D-glucal **124** and the 4,6-*O*-protected D-galactal **129** from **125** in 96 and 83% yield, respectively.





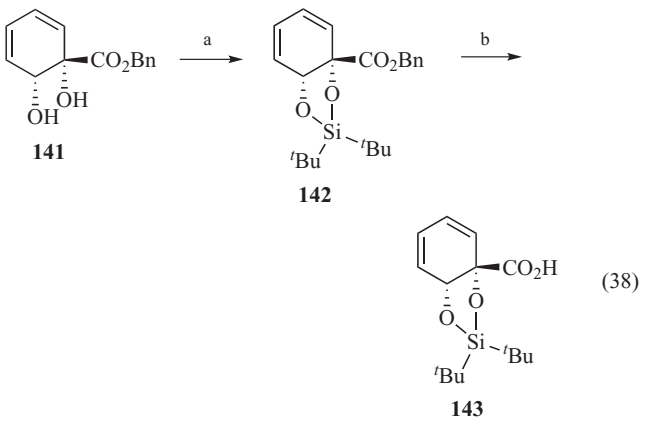
Silylidene glycals **128** and **129** are stable synthons that can subsequently undergo a series of reactions that ultimately affords the expected disaccharide **138** and **140** (eq 37).



(37)

Reagents and conditions: (a) (1) NIS, H_2O, CH_3CN, rt, 25–45 min; (2) $NaHCO_3$, $Na_2S_2O_4$, THF, rt, 3–4 h. (b) Fetizon[59] reagent, benzene, reflux, 3–20 h. (c) DMSO, trifluoroacetic anhydride, CH_2Cl_2, −60 to −30 °C, 1.5 h. (d) IBX, EtOAc, 80 °C, 2.5–3.5 h. (e) PhtNSCl, $CHCl_3$, pyr., rt, 15 min. (f) 3,4,6-Tri-*O*-benzyl-D-glucal, 60 °C, 22 h–3 days. (g) TBAF, DMF, rt, 1.5 h, 71%.

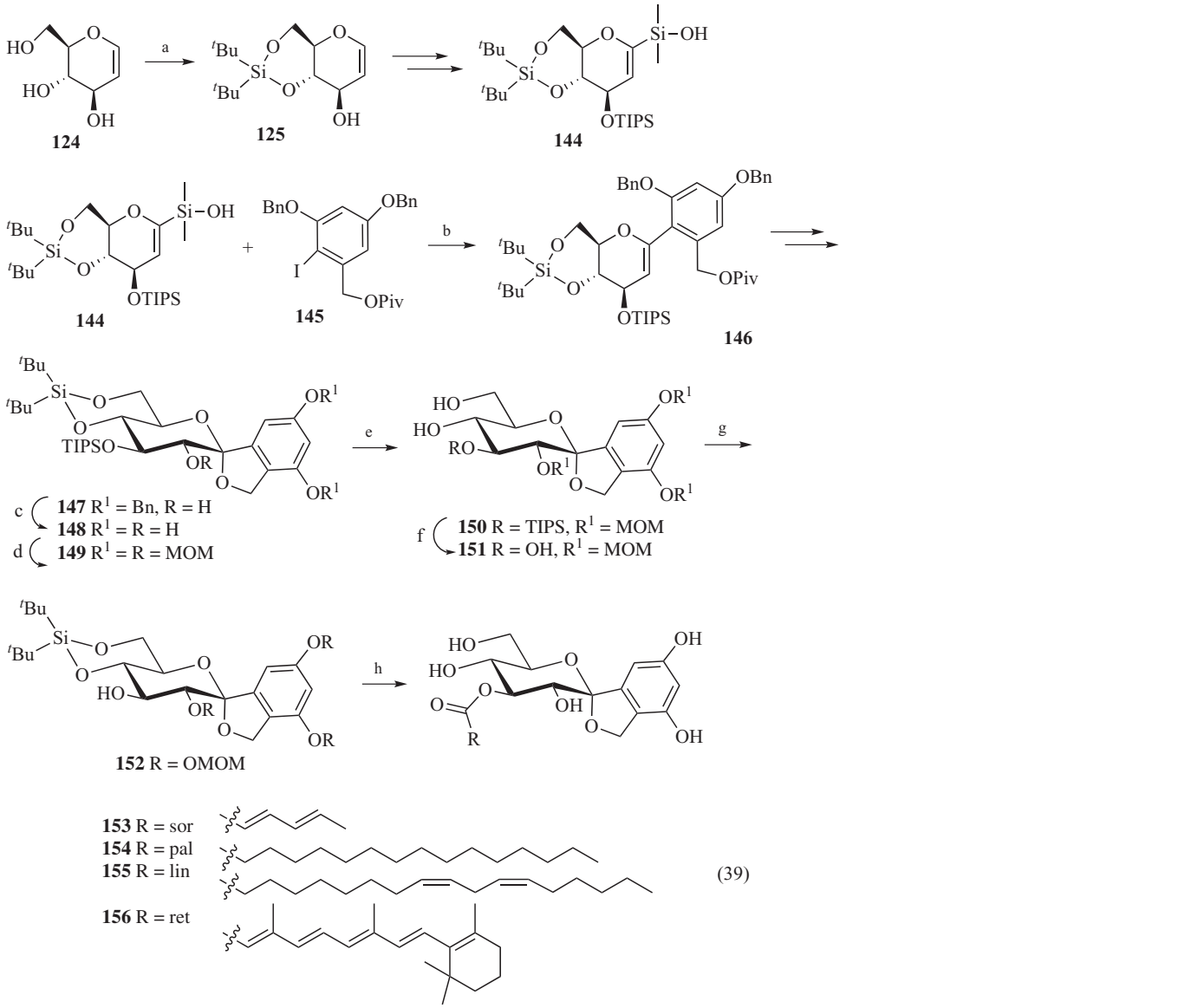
Recently, di-*t*-butylsilyl bis(trifluoromethanesulfonate) was used by Lewis and coworkers[60] for the preparation of silane derivatives by selective protection of diols in polyhydroxy compounds (eq 38).



(38)

Reagents and conditions: (a) $^tBu_2Si(OTf)_2$, NEt_3, CH_2Cl_2, rt, 9 h, 81%. (b) H_2, Pd/C MeOH, rt, 24 h, 53%.

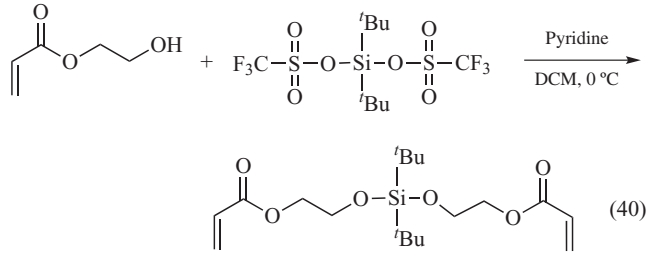
Pieters and coworkers[61] used di-*t*-butylsilyl bis(trifluoromethanesulfonate) for the protection of diols in the synthesis of derivatives for an antifungal agent named papulacandin D. Synthesis of a D-glucose moiety present in the core structure of the compound initiated with glycal **124**, which was treated with di-*t*-butylsilyl bis(trifluoromethanesulfonate) in the presence of pyridine and DMF at −40 °C to afford *O*-4- and *O*-6-protected D-glucal **125**. Following four additional steps, the synthesized silanol building block **144** and compound **145** were subjected to a palladium-catalyzed cross-coupling reaction using $Pd_2(dba)_3$ to furnish compound **146**. After several reaction transformations, compound **149** was obtained having the silane moiety intact, ultimately being treated with TBAHF in THF for removal. Deprotection of the TIPS group was achieved with TBAF and only thereafter the cyclic silyl protecting group was reinstalled to obtain compound **152**. A variety of compounds were obtained from compound **152**, all of which were treated with TBAHF in THF resulting in deprotection of the silane group to form compounds **153–156** (eq 39).



(39)

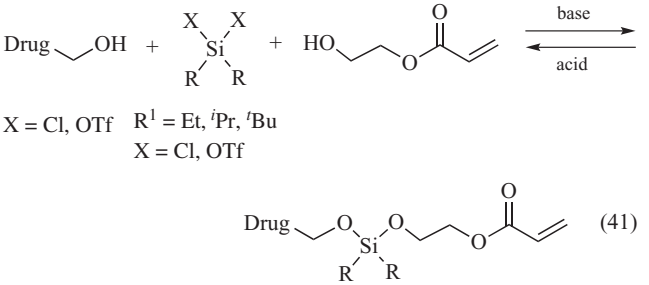
Reagents and conditions: (a) ^{t}Bu$_2$Si(OTf)$_2$, DMF, pyr. (b) $Pd_2(dba)_3{\cdot}CHCl_3$, NaO^{t}Bu, toluene, 50 °C, 6–20 h. (c) Pd/C, $NaHCO_3$, H_2, THF, rt, 1.5 h. (d) MOMCl, DIPEA, DMAP, CH_2Cl_2, rt, 4 d. (e) TBAHF, THF, rt, 2 d. (f) TBAF·3H$_2$O, THF, rt, 3 d. (g) ^{t}Bu$_2$Si(OTf)$_2$, pyr., DMF, −40 °C to rt, 2 h. (h) (1) RCOOH, NEt$_3$, 2,4,6-trichlorobenzoyl chloride, toluene, rt, 1 h, DMAP, toluene, rt, 3 h; (2) TBAHF, THF, rt, 2–3 days; (3) Dowex 50 × 8, MeOH, 50 °C, 20 h.

As a component of the synthesis of acid-sensitive biomaterials useful for drug delivery and degradable devices, Parrott et al.[62] utilized a bifunctional silyl ether linker for the construction of relevant medical devices. Di-*t*-butylsilyl ditriflate was used for the introduction of silyl ether linker in alkaline conditions (eq 40).



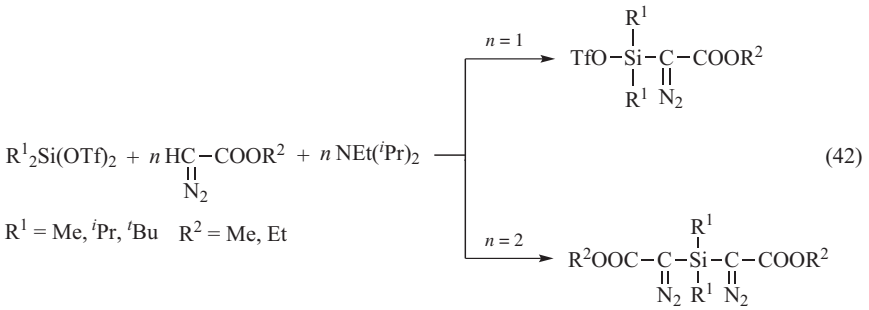
(40)

With a strategy to synthesize a safe, effective, and acid-labile prodrug, Parrott et al.[63] (eq 41) introduced bifunctional silyl ether linkers by treating di-*t*-butylsilyl ditriflate or dichlorodialkyl silane with the pendant alcohol on chemotherapeutics such as Camptothecin (CPT), Dasatinib (DAS), and Gemcitabine (GEM). The asymmetric bifunctional silyl ether prodrugs were incorporated into nanoparticles and the combination as a whole ascertained the release of therapeutics in active form under biological acidic conditions with no trace of the silyl ether modification on the drug.



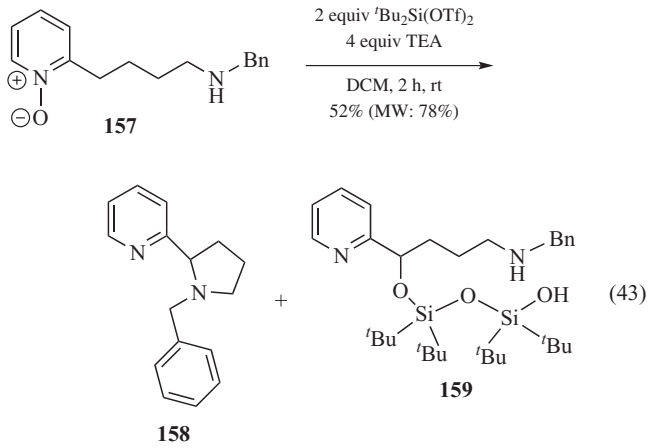
(41)

Maas and coworkers[64] reported a reaction of dialkylsilyl-bis(trifluoromethanesulfonates) with equimolar amounts of diazoacetates in the presence of a tertiary amine resulting in [(trifluoromethylsulfonyloxy)-dialkylsilyl] diazoacetates, where nucleophilic substitution of the trifloxy group could take place with alcohol to form alkyloxy- (or alkenyloxy-, alkinyloxy-)-dialkylsilylldiazoacetates. However, the same reagent when reacted with 2 equiv of diazoacetates formed dialkylsilyl-bisdiazoacetates, and with diazomethyl ketones formed the corresponding dialkylsilyl-bis(diazomethyl ketones), which was reported as being stable when the alkyl group was bulky such as the *tert*-butyl group. Therefore, the reagent di-*t*-butylsilyl-bis(trifluoromethanesulfonates) could be useful when in a 2:1 ratio (with respect to 2 equiv diazoacetates and 1 equiv di-*t*-butylsilyl-bis(trifluoromethanesulfonates)) for generating the desired product (eq 42).



(42)

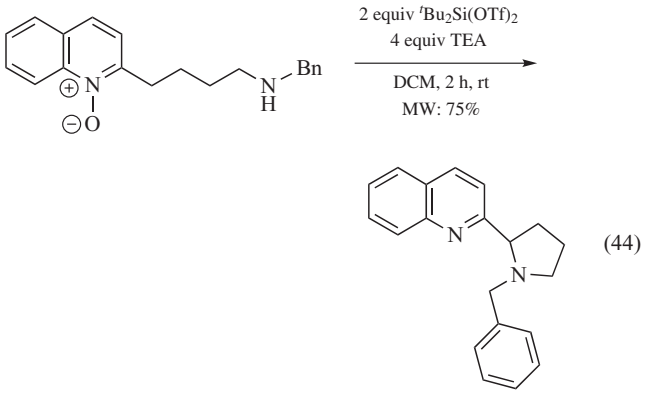
Massaro et al.[65] utilized di-*t*-butylsilyl bis(trifluoromethanesulfonate) as a promoter for a Boekelheide[66]-type reaction to synthesize pyrrolidines and piperidines from (amino-alkyl)pyridine *N*-oxides (eq 43). Generally, the Boekelheide reaction requires activation of pyridine *N*-oxides by electrophilic agents such as Ac_2O, P_2O_5, TsCl, or TFAA that make this reaction one of limited use due to the need for protection of other functional groups in the molecule that cannot tolerate the use of such reactive promoters. This reaction proceeds through the activation of the pyridine ring followed by a nucleophilic attack to form the Boekelheide intermediate. This group introduced nucleophiles bonded to the pyridine ring that undergo intramolecular cyclization to form *N*-heterocycles.



(43)

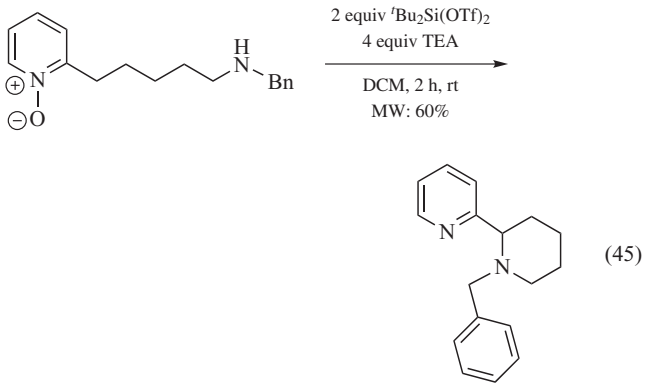
Treatment of amino pyridine *N*-oxide **157** with di-*t*-butylsilyl bis(trifluoromethanesulfonate) and triethylamine in dichloromethane resulted in intramolecular cyclization to form pyrrolidine **158** in 52% yield along with the compound **139** derived from a Boekelheide rearrangement[66] in 30% yield. Microwave irradiation (50 °C, 250 W, 20 min) increased the product yield up to 78%. The oxophilic nature of the promoter featuring a nonnucleophilic counterion was considered to be compatible in the presence of unprotected basic amines that lead to the participation of an amine in the intramolecular cyclization with activated pyridine *N*-oxide.

The analogous quinoline *N*-oxide, under the same reaction conditions, resulted in the desired cyclized product in 51% yield under normal conditions and 75% yield when microwave irradiation was used (eq 44).



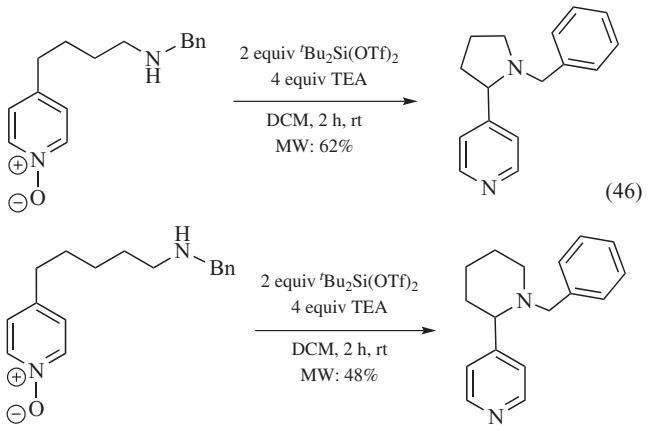
(44)

2-(*N*-Benzylpiperidine-2-yl)pyridine was synthesized in 38% yield under normal reaction conditions and in 60% yield when microwave irradiation was used from a compound having one carbon more in the alkyl chain carrying the amino group (eq 45).



(45)

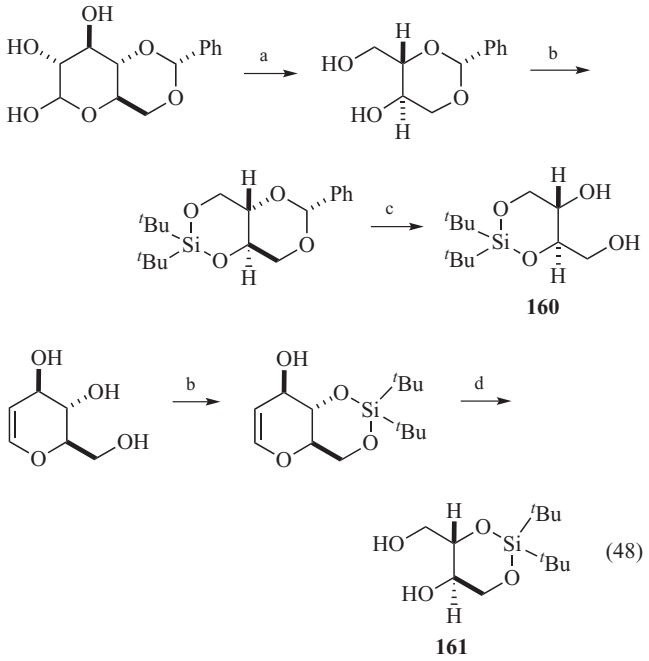
To extend the scope of this reaction, the group investigated intramolecular cyclization reactions at position 4 of the pyridine ring. When (4-aminoalkyl)pyridine *N*-oxides were subjected to the same reaction conditions, corresponding pyrrolidine and piperidine were obtained in 45 and 35% yield, respectively, under normal reaction conditions and 62 and 48%, respectively, under microwave irradiation (eq 46).



(46)

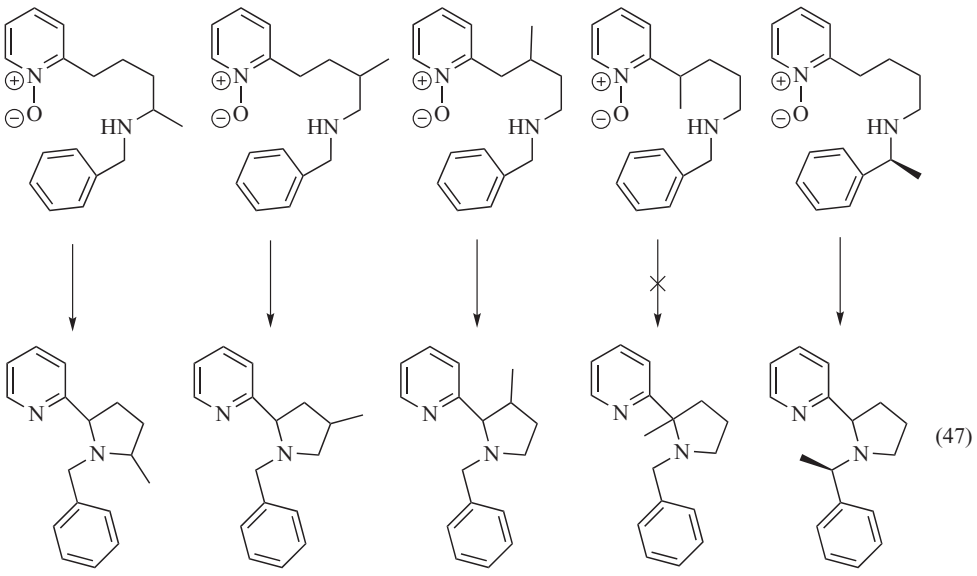
Again they investigated the effect of substituents on the lateral chain, for both the chemical and the stereochemical behavior (eq 47).

Mori and Hayashi reported[67] an enantioselective synthetic approach to 1,3-*O*-di-*tert*-butylsilylene-protected D- and L-erythritols **160** and **161** (eq 48) from D-glucose that are chiral building blocks for highly symmetrical transfused polytetrahydropyrans **162** (eq 49). Di-*t*-butylsilyl bis(trifluoromethanesulfonate) was used for the protection of the diols that was regarded as a better protecting group due to the reduced acid lability of silylene relative to an acetal.



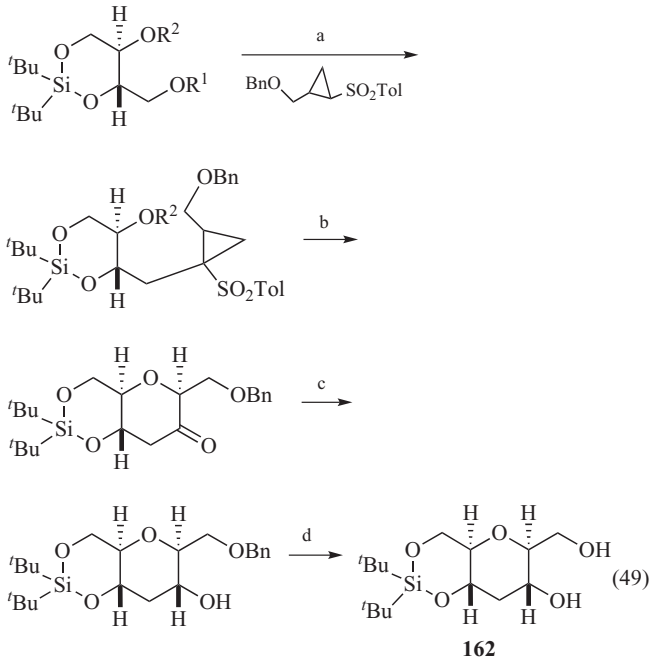
(48)

Reagents and conditions: (a) (1) $NaIO_4$, $NaHCO_3$; (2) $NaBH_4$. (b) ^{t}Bu$_2$Si(OTf)$_2$, 2,6-lutidine, DMF. (c) H_2, $Pd(OH)_2$/C, EtOAc. (d) (1) $NaIO_4$, OsO_4, MeOH, H_2O; (2) $NaBH_4$, MeOH.



50% *syn*/*anti* = 1:3 | 42% *syn*/*anti* = 3:1 | 25% ratio ca = 3:1 | 38% ratio ca = 2:1

(47)

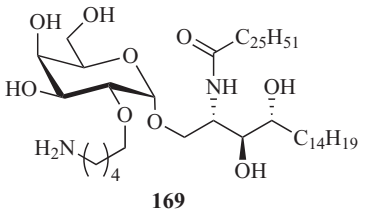


(49)

162

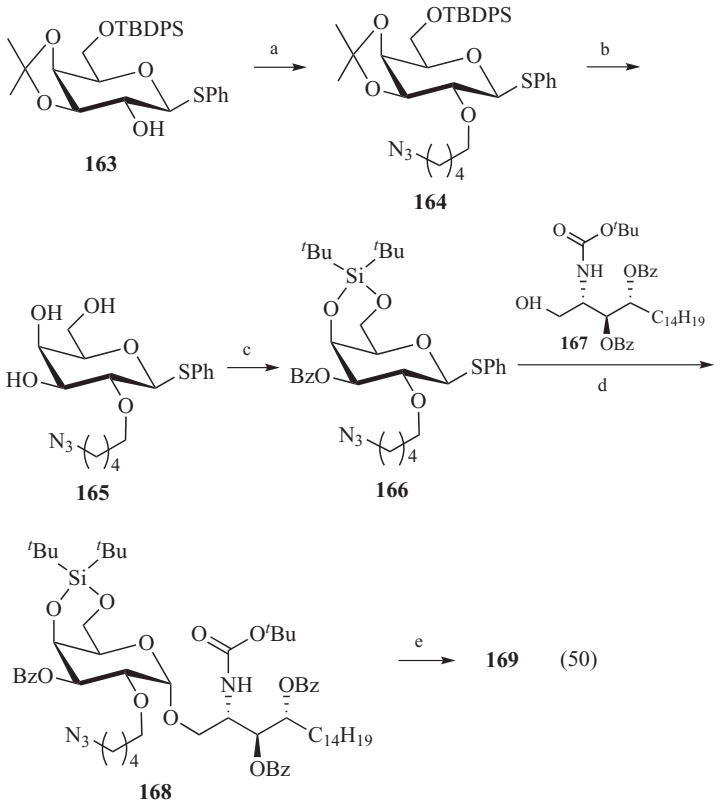
Reagents and conditions: (a) *n*-BuLi, THF, −100 °C. (b) (1) TsOH, MeOH; (2) $MgBr_2.OEt_2$; (3) DBU. (c) $NaBH_4$. (d) H_2, $Pd(OH)_2/C$.

In a report aiming to examine the mechanism of T-cell help for the production of B-cell antibodies, Besra and coworkers.[68] synthesized a novel haptenated derivative of α-D-galactosyl ceramide **169**.



169

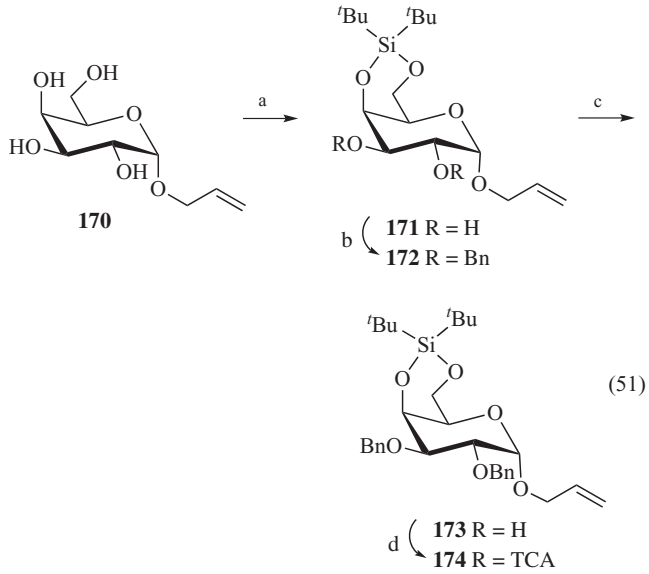
To synthesize the sugar moiety present in the hapten, di-*t*-butylsilyl-bis(trifluoromethanesulfonate) was used for the protection of *O*-4 and *O*-6 of the sugar as a cyclic silylene, which after glycosylation was deprotected by treating with TBAF in THF (eq 50).



163 **164** **165** **166** **167** **168** **169** (50)

Reagents and conditions: (a) (1) DMF, NaH, $(CH_2)_5Br_2$, quant; (2) NaN_3, DMSO, 60 °C. (b) (1) TBAF, THF, quant; (2) TFA, CH_2Cl_2, 78%. (c) (1) $^tBu_2Si(OTf)_2$, DMF, Et_3N, quant; (2) BzCl, pyr. (d) *p*-NO_2PhSCl, AgOTf, CH_2Cl_2, −78 °C, 75%. (e) (1) TBAF, THF, quant; (2) NaOMe/MeOH, 88%; (3) TFA, CH_2Cl_2, quant.; (4) $C_{25}H_{51}COCl$, THF/NaOAc (1:1), 71%; (5) H_2, Pd, MeOH, 90%.

Painter and coworkers[69] also reported the synthesis of α-D-galactosyl ceramide with the use of di-*t*-butylsilyl-bis(trifluoromethanesulfonate) (eq 51).



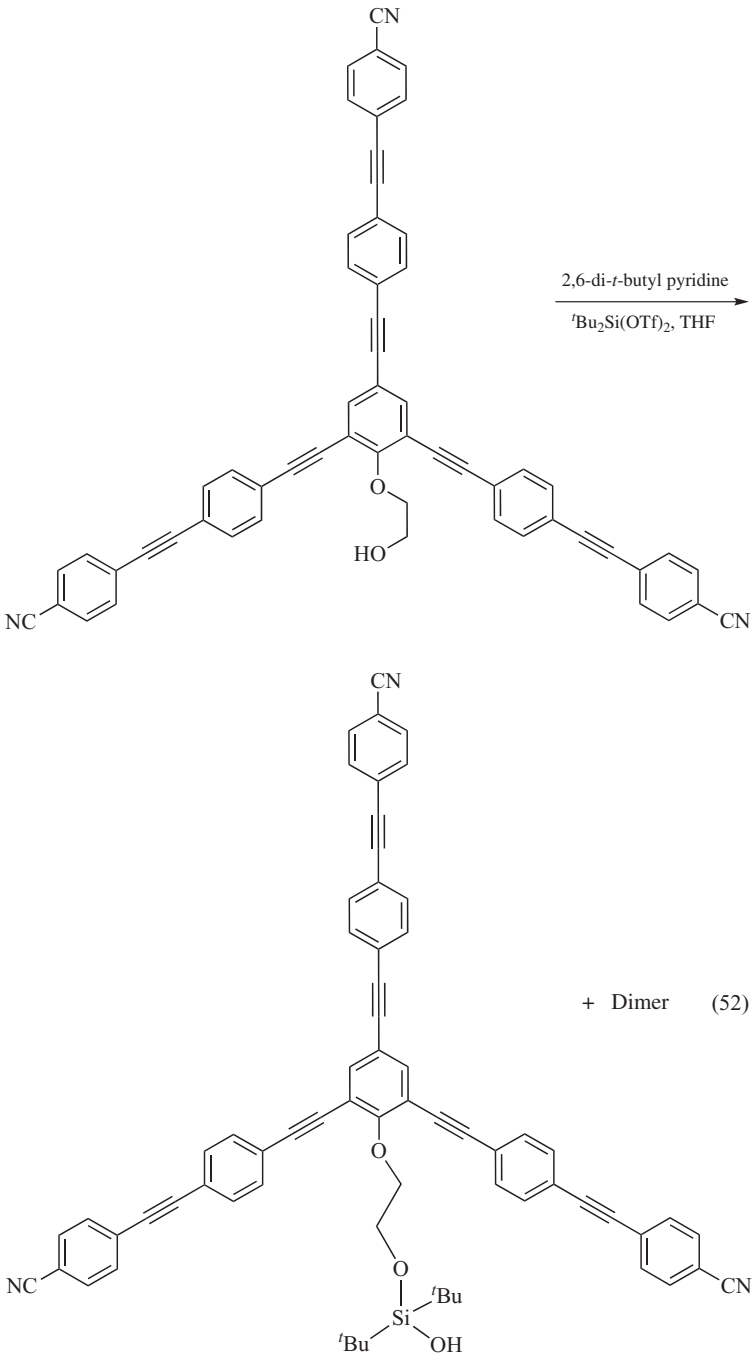
170

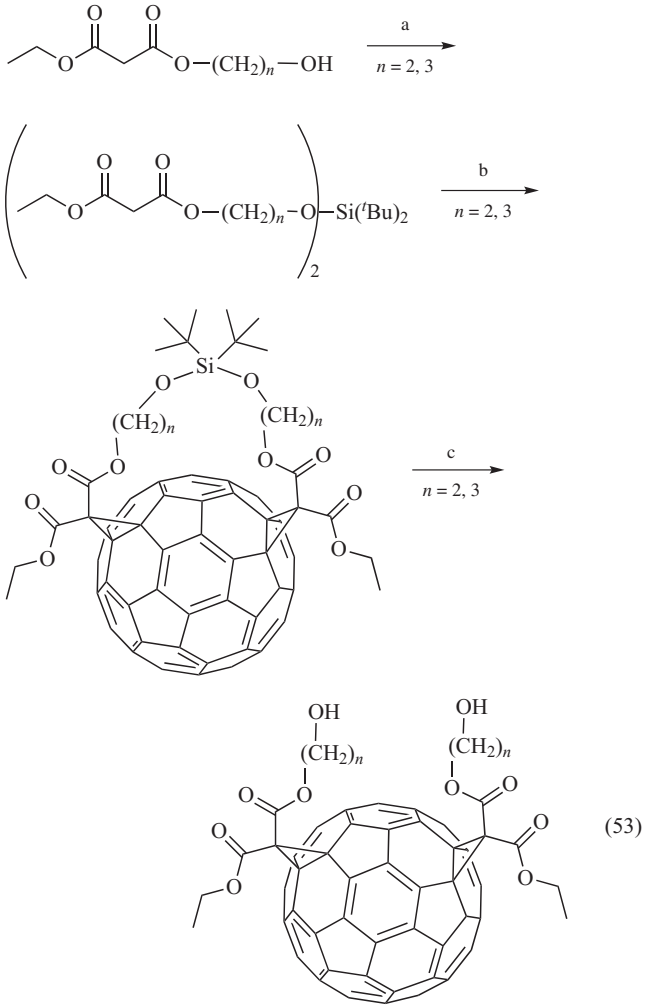
(51)

Reagents and conditions: (a) $^tBu_2Si(OTf)_2$, DMAP, pyr. (65%). (b) NaH, BnBr, DMF (66%). (c) $Ph_2P_2(COD)Ir^+PF_6^-$, THF, then AcCl, MeOH–CH_2Cl_2. (d) CCl_3CN, DBU, CH_2Cl_2 (40%).

For synthesizing microcrystalline solids in which organic molecules are bonded to each other through O–Si–O linkages, phenylacetylene nitrile molecules with an attached terminal hydroxyl group bearing an alkoxymethyl side chain was treated with di-*t*-butylsilyl-bis(trifluoromethanesulfonate) to afford covalent O–Si–O bonds between adjacent phenylacetylene molecules (eq 52).[70]

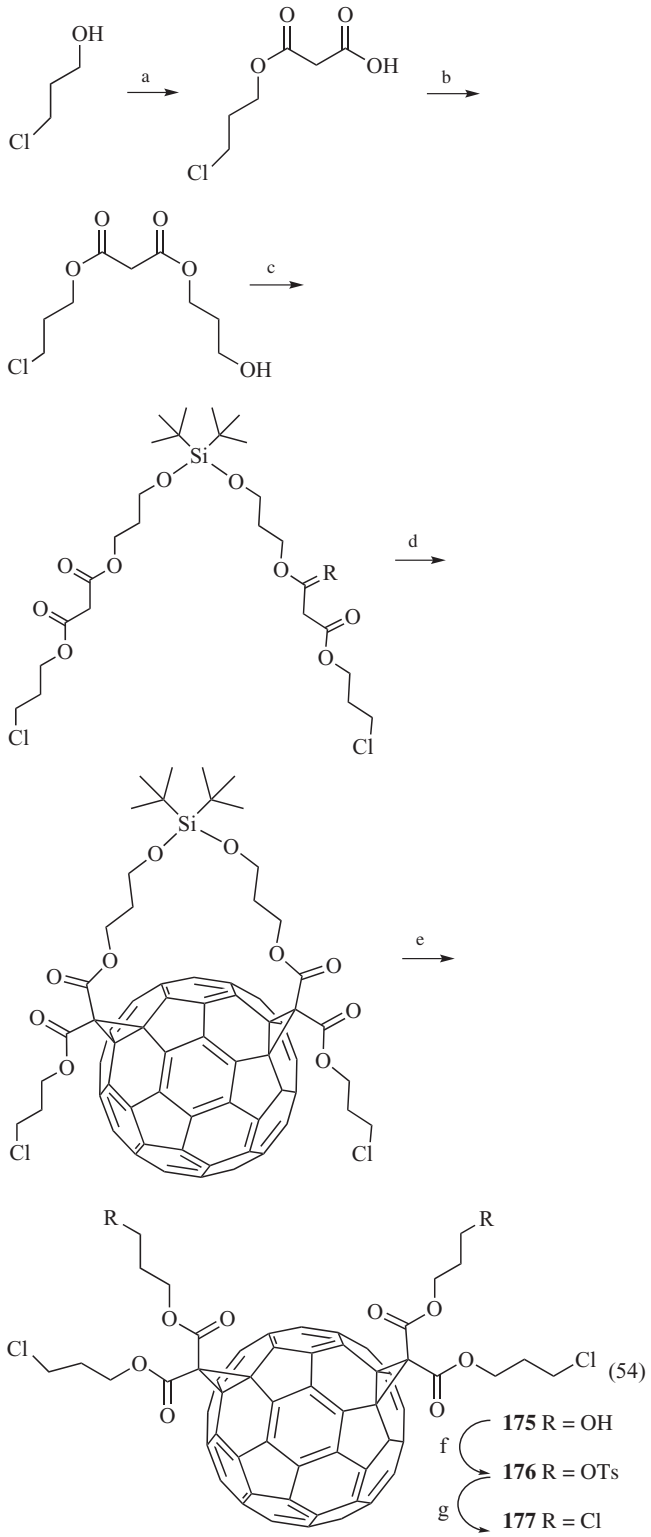
Nierengarten and coworkers[71] explored a regioselective synthesis of fullerene bis-adducts by a double or multiple Bingel[72] reaction between C_{60} and linear or macrocyclic di-*t*-butylsilylene-tethered bis-malonates. The di-*t*-butylsilylene played a role as a protecting group as well as a directing group. The deprotection of silylene was achieved by treatment with HF-pyridine in THF or 20 equiv of $BF_3{\cdot}Et_2O$ in CH_2Cl_2/CH_3CN and the product was obtained in excellent yield (eqs 53 and 54).





(53)

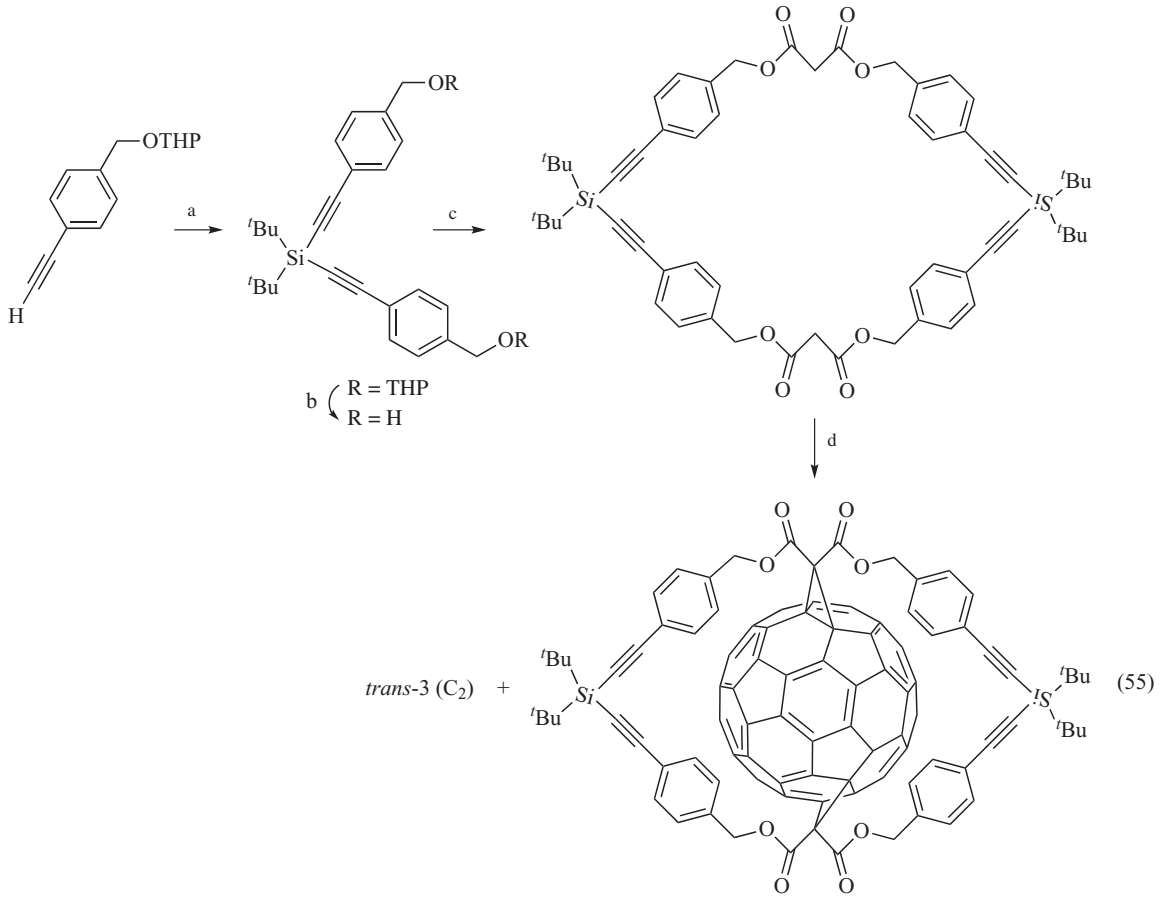
Reagents and conditions: (a) $^{t}Bu_2Si(OTf)_2$, DMF, pyr., rt, 12 h. (b) C_{60}, DBU, I_2, PhMe, −15 °C, 1 h. (c) $BF_3{\cdot}Et_2O$, CH_2Cl_2, CH_3CN, rt, 12 h.



(54)

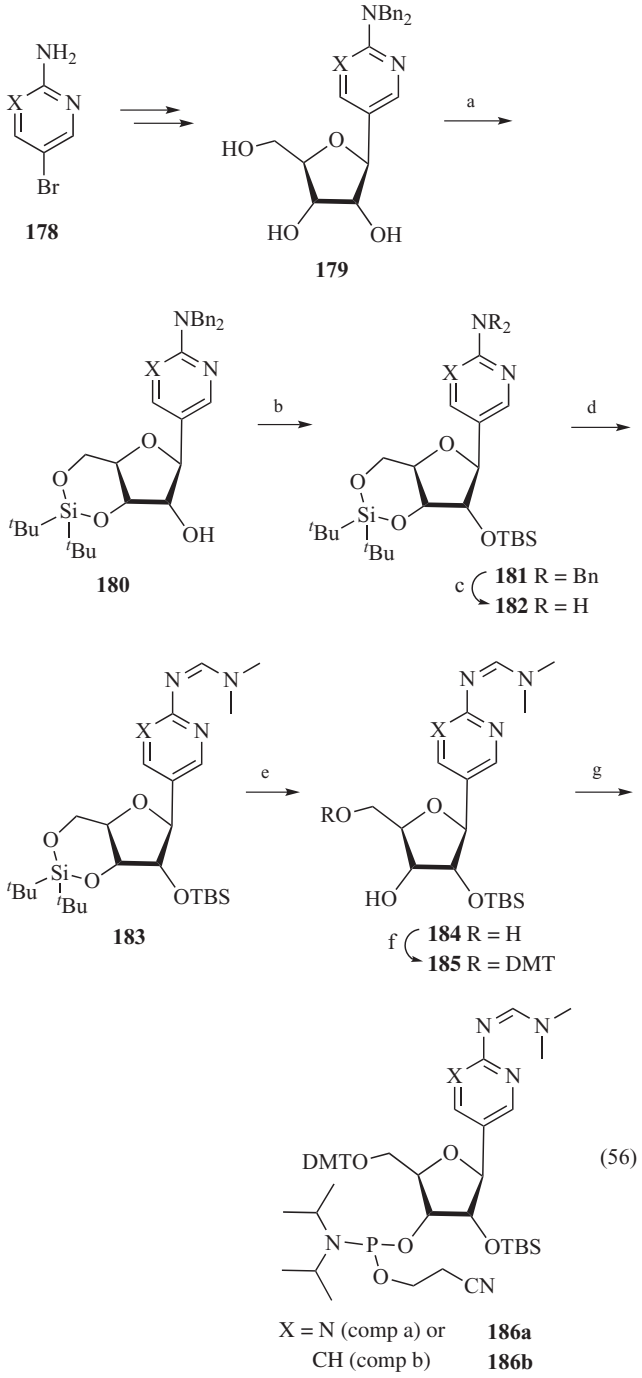
Reagents and conditions: (a) Meldrum's acid, 120 °C, 3 h. (b) 1,3-Propanediol, EDC, DPTS, CH_2Cl_2, 0 °C to rt, 12 h. (c) $^{t}Bu_2Si(OTf)_2$, DMF, pyr., rt, 4 h. (d) C_{60}, DBU, I_2, PhMe, −15 °C, 1 h. (e) $BF_3{\cdot}Et_2O$, CH_2Cl_2, CH_3CN, rt 12 h. (f) TsCl, pyr., CH_2Cl_2, 0 °C to rt, 48 h. (g) *n*-Bu_4NCl, THF, rt, 4 h.

Nierengarten and coworkers[73] also illustrated the application of di-*t*-butylsilyl bis(trifluoromethanesulfonate) in C_{60} chemistry (eq 55).



Reagents and conditions: (a) *n*-BuLi, THF, 0 °C, 1 h, then ^{t}Bu$_2$Si(OTf)$_2$, 0 °C, 1 h (81%). (b) *p*TsOH, EtOH, rt, 12 h (78%). (c) Malonyl chloride, DMAP, CH_2Cl_2, rt, 12 h (9%). (d) C_{60}, DBU, I_2, PhMe, −15 °C, 1 h (5: 8%, 6: 18%).

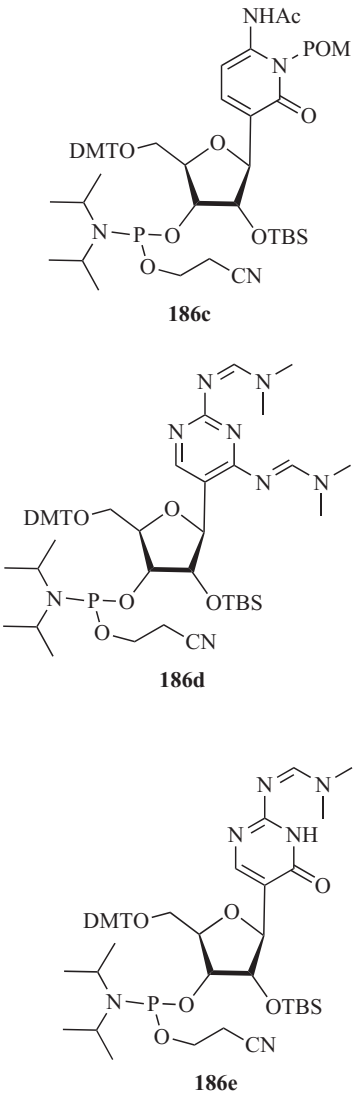
Piccirilli and coworkers[74] reported (eq 56) efficient methods for the synthesis of five C-nucleoside phosphoramidite derivatives (**186a**–**186e**). Starting from commercially available 2-amino-5-bromopyrimidine or 2-amino-5-bromopyridine **178**, they synthesized intermediate **179a** or **179b**, which reacted with ^{t}Bu$_2$Si(OTf)$_2$ in DMF to form the corresponding cyclic silylene derivatives in good yield, thus affording regioselective protection of the 2′-hydroxyl group as a 2′-*O*-TBS ether. After installing all the suitable protecting groups, silyl ether was removed with the aid of pyridinium poly-(HF) in THF.



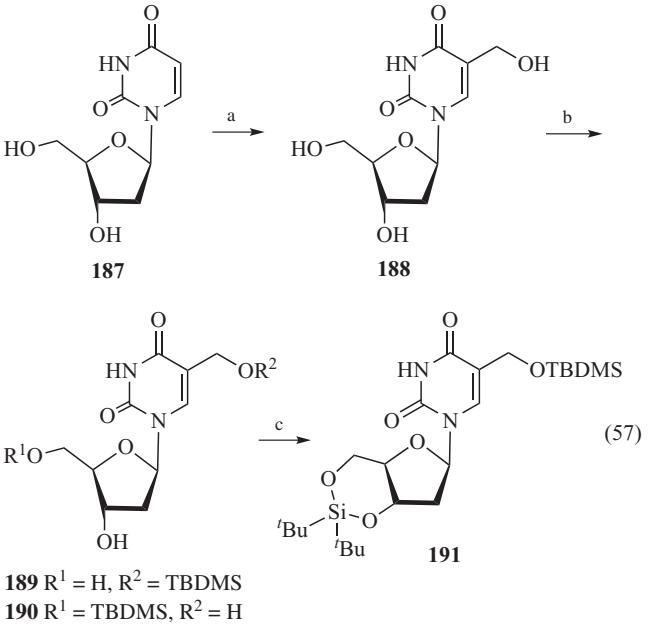
(56)

Reagents and conditions: (a) $^{t}Bu_2Si(OTf)_2$, DMF, 0 °C. (b) TBSCl, pyr., 1*H*-imidazole. (c) $(NH_4)_2Ce(NO_3)_6$, CH_3CN:H_2O (98:2), 50 °C. (d) DMF-DMA, MeOH. (e) HF-pyr., THF. (f) DMTCl, pyr. (g) *i*-$Pr_2NP(OCH_2CH_2CN)Cl$, 1-methylimidazole, *i*-Pr_2NEt, DCM.

The other synthesized nucleosides (**186c–186e**) used $^{t}Bu_2Si(OTf)_2$ to protect *O*-3′ and *O*-5′ of sugar moiety.

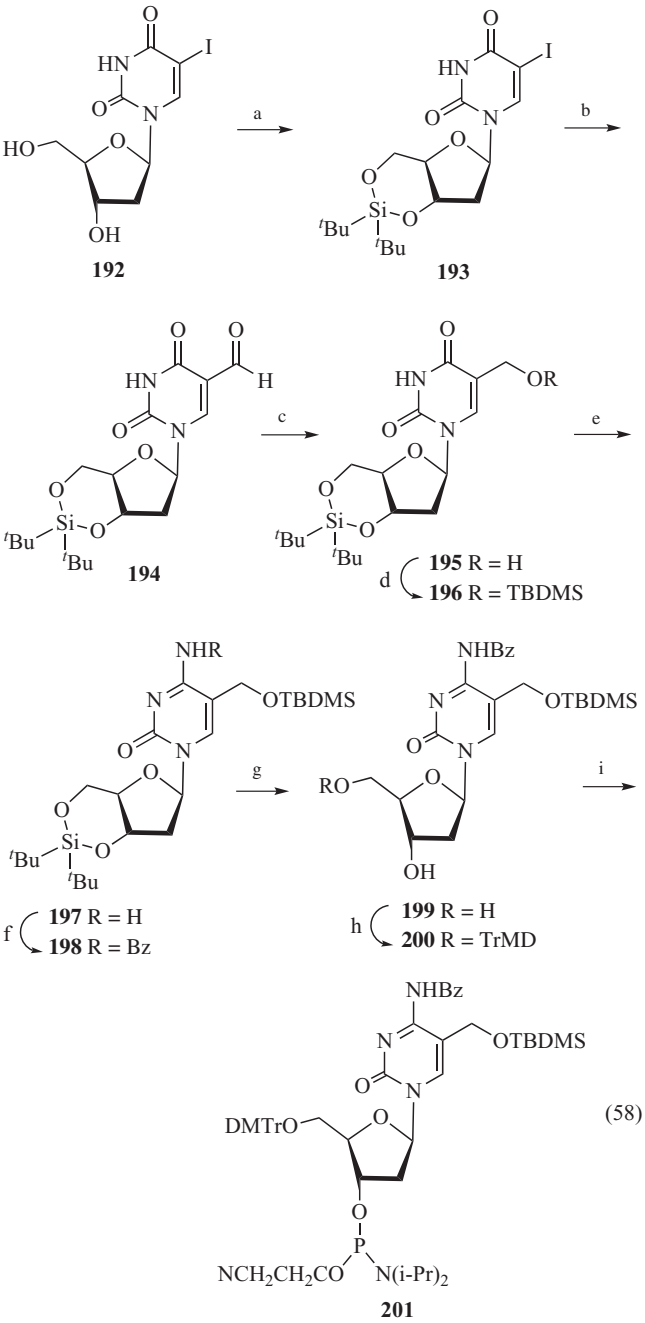


In an attempt to develop 5-hmC phosphoramidite building blocks using readily removable protecting groups, that is, TBDMS for 5-hydroxymethyl group, Dai et al.[75] utilized $^{t}Bu_2Si(OTf)_2$ group for the protection of *O*-3′ and *O*-5′. The initial strategy started with the conversion of commercially available 2′-deoxyuridine to compound **189** followed by the regioisomer **190**. Owing to the difficulty in separation of compound **189** and **190** by column chromatography, the mixture was treated with di-*t*-butylsilyl bistriflate in DMF that resulted in the protection of diol **189** to afford compound **191** leading to the separation from compound **190** (eq 57).



Reagents and conditions: (a) $(HCHO)x$, Et_3N, CH_3CN/H_2O. (b) $AgNO_3$, TBDMS-Cl, THF/pyr. (c) $^tBu_2Si(OTf)_2$, DMF.

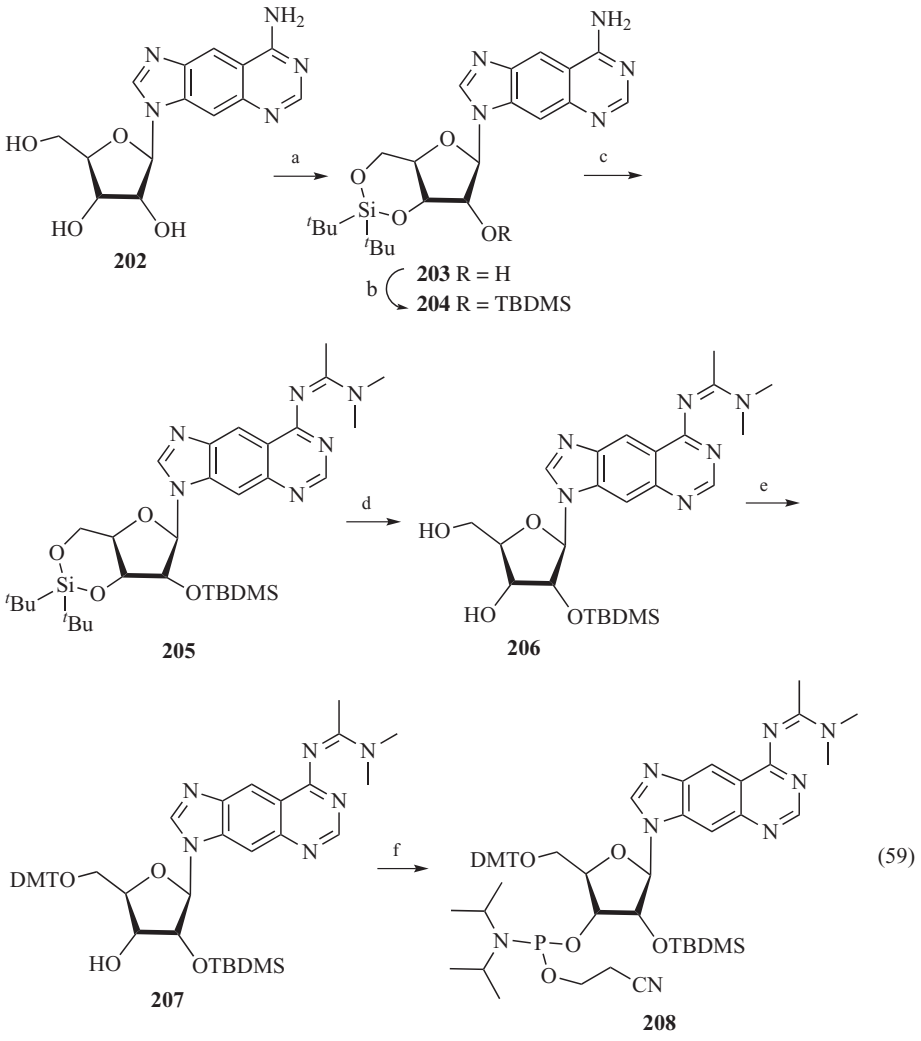
To increase the product yield, another strategy was followed by initiating the reaction with 6-iodo-3′, 5′-di-*O*-TBDMS-2′-deoxyuridine **192** and after conducting multiple steps, the desired phosphoramidite **201** was obtained. Within the synthetic strategy, the diol was protected as a silylene, the removal of which was accomplished with HF-pyridine in DMF (eq 58).



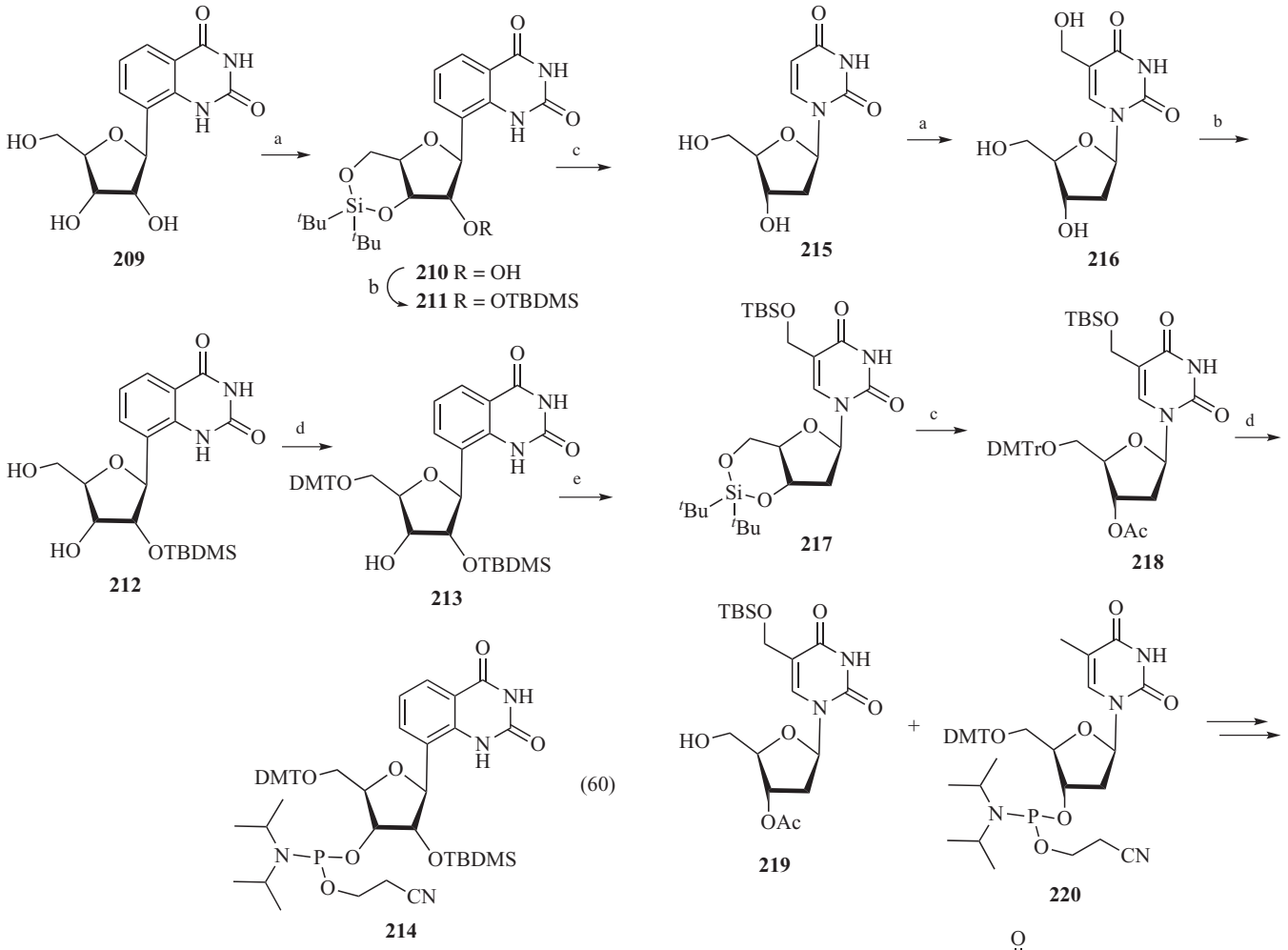
Reagents and conditions: (a) $^tBu_2Si(OTf)_2$, DMF, 0 °C. (b) $Pd_2(dba)_3$, $CHCl_3/Ph_3P$, CO, toluene. (c) $NaBH_4$, $CeCl_3$, MeOH. (d) TBDMS-Cl/imidazole, DMF. (e) 1,2,4-triazole, $POCl_3$, NH_4OH/dioxane. (f) BzCl/pyr. (g) HF-pyr., THF. (h) DMTr-Cl, pyr. (i) $(i\text{-Pr})_2NP(Cl)OCH_2CH_2CN$, $i\text{-Pr}_2NEt$, DCM.

In an effort to synthesize two xRNA (size-expanded RNA) monomer phosphoramidite derivatives (compounds **208** and **214**) for their successful incorporation into synthetic oligoribonucleotides to examine their use as probes of positional steric sensitivity in RNAi, Kool and coworkers[76] exploited di-*t*-butylsilyl bistriflate for the protection of diol of rxA (size-expanded versions of adenosine) triol **202** as well as rxU (size-expanded versions of uridine) triol **209**.[77] The silylene protection ascertained the required regiospecific protection of xRNA monomer for automated oligonucleotide synthesis (eqs 59 and 60).

Reagents and conditions: (a) $^{t}Bu_2Si(OTf)_2$, DMF, 0 °C to rt, 1 h, 85%. (b) TBDMSCI, imidazole, pyr., rt, overnight, 88%. (c) *N*,*N*-Dimethylacetamide dimethyl acetal, MeOH, rt, 90%. (d) HF-pyr., THF, 0 °C to rt, 15 min, 87%. (e) DMTCI, DMAP, pyr., 12 h, 86%. (f) 2-Cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite, 1-methylimidazole, *i*-Pr_2NEt, CH_2Cl_2, rt, 6 h, 87%.



(59)

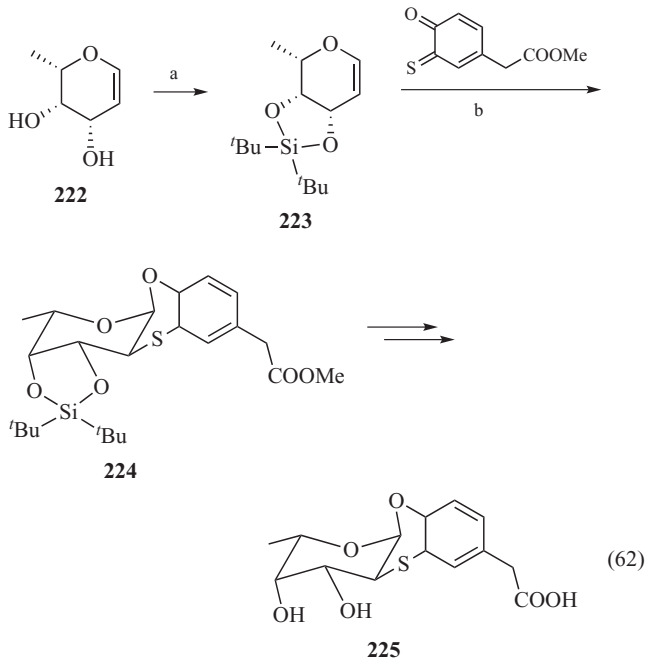


Reagents and conditions: (a) $^{t}Bu_2Si(OTf)_2$, DMF, 0 °C to rt, 1 h, 71%. (b) TBDMSCI, imidazole, pyr., rt, overnight, 89%. (c) HF-pyr., THF, 0 °C to rt, 15 min, 86%. (d) DMTCI, $AgNO_3$, 2,6-di-*t*-butylpyridine, CH_3CN, rt, 20 min, 82%. (e) 2-Cyanoethyl *N,N,N′,N′*-tetraisopropylphosphordiamidite, pyridinium trifluoroacetate, CH_3CN, rt, 18 h, 92%.

In the mechanistic studies of spore photoproduct lyase, via single cysteine mutation, Li's research group[78] synthesized TpTOH **221** from thymine residue **215**. After installation of the hydroxyl group on the methyl moiety of the thymine, the diol **216** was protected using di-*t*-butylsilyl bistriflate (eq 61).

Reagents and conditions: (a) (HCHO)*x*, Et_3N, H_2O. (b) (1) $^{t}Bu_2Si(OTf)_2$, DMF; (2) $AgNO_3$, TBSCI, THF/pyr. (c) (1) HF-pyr., THF; (2) DMTrCI, pyr.; (3) Ac_2O/pyr. (d) *p*-TsOH, MeOH.

Richichi et al.[79] reported the use of di-*t*-butylsilyl bis(trifluoromethanesulfonate) for the synthesis of α-*O*-fucosyl derivative **225** (eq 62).



(62)

Reagents and conditions: (a) $^t Bu_2Si(OTf)_2$, pyr., 0 °C, 1 h, 62%. (b) $CHCl_3$, 0 °C, 48 h, 76%.

1. Corey, E. J.; Hopkins, P. B., *Tetrahedron Lett.* **1982**, *23*, 4871.
2. Furusawa, K.; Ueno, K.; Katsura, T., *Chem. Lett.* **1990**, 97.
3. Furusawa, K., *Chem. Express* **1991**, *6*, 763.
4. Furusawa, K., *Chem. Lett.* **1989**, 509.
5. Furusawa, K.; Sakai, T., *Jpn. Kokai Tokkyo Koho* **1989**, 629.
6. Brooks, C. J. W.; Cole, W. J., *Analyst (London)* **1985**, *110*, 587.
7. Ahn, K.-H.; Klassen, R. B.; Lippard, S. J., *Organometallics* **1990**, *9*, 3178.
8. Uhlig, W., *Chem. Ber.* **1992**, *125*, 47.
9. Uhlig, W., *Z. Anorg. Allg. Chem.* **1991**, *603*, 109.
10. Uhlig, W., *J. Organomet. Chem.* **1991**, *421*, 189.
11. Uhlig, W., *Z. Anorg. Allg. Chem.* **1991**, *601*, 125.
12. Gillard, J. W.; Fortin, R.; Grimm, E. L.; Maillard, M.; Tjepkema, M.; Bernstein, M. A.; Glaser, R., *Tetrahedron Lett.* **1991**, *32*, 1145.
13. (a) Paterson, I.; Cumming, J. G.; Ward, R. A.; Lamboley, S., *Tetrahedron* **1995**, *51*, 9393. (b) Paterson, I.; Smith, J.; Ward, R. A., *Tetrahedron* **1995**, *51*, 9413. (c) Paterson, I.; Ward, R. A.; Smith, J. D.; Cumming, J. G.; Yeung, K., *Tetrahedron* **1995**, *51*, 9437. (d) Paterson, I.; Yeung, K.; Ward, R. A.; Smith, J. A.; Cumming, J. G.; Lamholey, S., *Tetrahedron* **1995**, *51*, 9467.
14. Paterson, I.; McLeodl, M. D., *Tetrahedron Lett.* **1997**, *38*, 4183.
15. Toshima, K.; Jyojima, K.; Miyamoto, N.; Katohno, M.; Nakata, M.; Matsumura, S., *J. Org. Chem.* **2001**, *66*, 1708.
16. Panek, J. S.; Jain, N. F., *J. Org. Chem.* **2001**, *66*, 2747.
17. Di Fabio, R.; Rossi, T.; Thomas, R. J., *Tetrahedron Lett.* **1997**, *38*, 3587.
18. Madu, C. E.; Lovely, C. J., *Org. Lett.* **2007**, *9*, 4697.
19. Caspi, D. D.; Garg, N. K.; Stoltz, B. M., *Org. Lett.* **2005**, *7*, 2513.
20. Hillaert, U.; Van Calenbergh, S., *Org. Lett.* **2005**, *7*, 5769.
21. Yadav, J. S.; Srinivas, R.; Sathaiah, K., *Tetrahedron Lett.* **2006**, *47*, 1603.
22. Perkins, M. V.; Sampson, R. A.; Joannou, J.; Taylor, M. R., *Tetrahedron Lett.* **2006**, *47*, 3791.
23. Chan, C.; Zheng, S.; Zhou, B.; Guo, J.; Heid, R. H.; Wright, B. J. D.; Danishefsky, S. J., *Angew. Chem., Int. Ed.* **2006**, *45*, 1749.
24. Paterson, I.; Mühlthau, F. A.; Cordier, C. J.; Housden, M. P.; Burton, P. M.; Loiseleur, O., *Org. Lett.*, **2009**, *11*, 353.
25. Obringer, M.; Barbarotto, M.; Choppin, S.; Colobert, F., *Org. Lett.* **2009**, *11*, 3542.
26. Calad, S. A.; Cirakovic, J.; Woerpel, K. A., *J. Org. Chem.* **2007**, *72*, 1027.
27. Guan, Y.; Wu, J.; Sun, L.; Dai, W., *J. Org. Chem.* **2007**, *72*, 4953.
28. Engers, D. W.; Bassindale, M. J.; Pagenkopf, B. L., *Org. Lett.* **2004**, *6*, 663.
29. Quéron, E.; Lett, R., *Tetrahedron Lett.* **2004**, *45*, 4533.
30. Nakamura, R.; Tanino, K.; Miyashita, M., *Org. Lett.* **2005**, *7*, 2929.
31. Denmark, S. E.; Kobayashi, T.; Regens, C. S., *Tetrahedron* **2010**, *66*, 4745.
32. Nicolaou, K. C.; Gelin, C. F.; Seo, J. H.; Huang, Z.; Umezawa, T., *J. Am. Chem. Soc.* **2010**, *132*, 9900.
33. Watanabe, K.; Suzuki, M.; Murata, M.; Oishi, T., *Tetrahedron Lett.* **2005**, *46* 3991.
34. Clark, J. S.; Kimber, M. C.; Robertson, J.; McErlean, C. S.; Wilson, C., *Angew. Chem., Int. Ed.* **2005**, *44*, 6157.
35. Hooper, A. M.; Dufour, S.; Willaert, S.; Pouvreau, S.; Pickett, J. A., *Tetrahedron Lett.* **2007**, *48*, 5991.
36. Takada, T.; Arisawa, M.; Gyoten, M.; Hamada, R.; Tohma, H.; Kita, Y., *J. Org. Chem.* **1998**, *63*, 7698.
37. Akai, S.; Tsujino, T.; Fukuda, N.; Iio, K.; Takeda, Y.; Kawaguchi, K.; Naka, T.; Higuchi, K.; Kita, Y., *Org. Lett.* **2001**, *3*, 4015.
38. Fuller, P. H.; Kim, J.; Chemler, S. R., *J. Am. Chem. Soc.* **2008**, *130*, 17638.
39. Kablean, S. N.; Marsden, S. P.; Craig, A. M., *Tetrahedron Lett.* **1998**, *39*, 5109.
40. Ahmed, A.; Dussault, P. H., *Tetrahedron* **2005**, *61*, 4657.
41. Baudat, A.; Vogel, P., *J. Org. Chem.* **1997**, *62*, 6252.
42. Plante, O. J.; Palmacci, E. R.; Seeberger, P. H., *Org. Lett.* **2000**, *2*, 3841.
43. Houseknecht, J. B.; Lowary, T. L., *J. Org. Chem.* **2002**, *67*, 4150.
44. Haraguchi, K.; Takahashi, H.; Shiina, N.; Horii, C.; Yoshimura, Y.; Nishikawa, A.; Sasakura, E.; Nakamura, K. T.; Tanaka, H., *J. Org. Chem.* **2002**, *67*, 5919.
45. Ohnishiy, Y.; Ichikawa, Y., *Bioorg. Med. Chem. Lett.* **2002**, *12*, 997.
46. Serebryany, V.; Beigelman, L., *Tetrahedron Lett.* **2002**, *43*, 1983.
47. Ye, J.; Liao, X.; Piccirilli, J. A., *J. Org. Chem.* **2005**, *70*, 7902.
48. Gold, H.; Van Delft, P.; Meeuwenoord, N.; Codée, J. D.; Filippov, D. V.; Eggink, G.; Overkleeft, H. S.; Van der Marel, G. A., *J. Org. Chem.* **2008**, *73*, 9458.
49. Chen, C.; Namba, K.; Kishi, Y., *Org. Lett.* **2009**, *11*, 409.
50. Zhu, X.; Kawatkar, S.; Rao, Y.; Boons, G., *J. Am. Chem. Soc.* **2006**, *128*, 11948.
51. Rademacher, C.; Shoemaker, G. K.; Kim, H.;, Zheng, R. B.; Taha, H.; Liu, C.; Nacario, R. C.; Schriemer, D. C.; Klassen, J. S.; Peters, T.; Lowary, T. L., *J. Am. Chem. Soc.* **2007**, *129*, 10489.
52. Crich, D.; Pedersen, C. M.; Bowers, A. A.; Wink, D. J., *J. Org. Chem.* **2007**, *72*, 1553.
53. Mukobata, T.; Ochi, Y.; Ito, Y.; Wada, S.; Urata, H., *Bioorg. Med. Chem. Lett.* **2010**, *20*, 129.
54. Zlatev, I.; Vasseur, J.; Morvan, F., *Tetrahedron* **2007**, *63*, 11174.
55. Sabatino, D.; Damha, M. J., *J. Am. Chem. Soc.* **2007**, *129*, 8259.
56. Yu, M.; Pagenkopf, B. L., *J. Org. Chem.* **2002**, *67*, 4553.
57. Hoberg, J. O., *Carbohydr. Res*. **1997**, *300*, 365.
58. Gabrielli, G.; Melani, F.; Bernasconi, S.; Lunghi, C.; Richichi, B.; Rollin, P.; Venturi, C.; Nativi, C., *J. Carbohydr. Chem*. **2009**, *28*, 124.
59. Fetizon, M.; Golfier, M.; Mourgues, P., *Tetrahedron Lett.* **1972**, *43*, 4445.
60. Griffen, J. A.; Kenwright, S. J.; Shehada, S. A.; Wharry, S.; Moody, T. S.; Lewis, S. E., *Org. Chem. Front.* **2014**, *1*, 79.

61. van der Kaaden, M.; Breukink, E.; Pieters, R. J., *Beilstein J. Org. Chem.* **2012**, *8*, 732.
62. Parrott, M. C.; Luft, J. C.; Byrne, J. D.; Fain, J. H.; Napier, M. E.; DeSimone, J. M., *J. Am. Chem. Soc.* **2010**, *132*, 17928.
63. Parrott, M. C.; Finniss, M.; Luft, J. C.; Pandya, A.; Gullapalli, A.; Napier, M. E.; DeSimone, J. M., *J. Am. Chem. Soc.* **2012**, *134*, 7978.
64. Fronda, A.; Krebs, F.; Daucher, B.; Werle, T.; Mass, G., *J. Organomet. Chem.* **1992**, *424*, 253.
65. Massaro, A.; Mordini, A.; Mingardi, A.; Klein, J.; Andreotti, D., *Eur. J. Org. Chem.* **2011**, 271.
66. Boekelheide, V.; Linn, W. J., *J. Am. Chem. Soc.* **1954**, *76*, 1286.
67. Mori, Y.; Hayashi, H., *J. Org. Chem*. **2001**, *66*, 8666.
68. Veerapen, N.; Leadbetter, E. A.; Brenner, M. B.; Cox, L. R.; Besra, G. S., *Bioconjug. Chem*. **2010**, *21*, 741.
69. Lee, A.; Farrand, K. J.; Dickgreber, N.; Hayman, C. M.; Jurs, S.; Hermnas, I. F.; Painter, G. F., *Carb. Res.* **2006**, *341*, 2785.
70. Kiang, Y. H.; Gardner, G. B.; Lee, S.; Xu, Z., *J. Am. Chem. Soc.* **2000**, *122*, 6871.
71. Guerra, S.; Trinh T. M. N.; Schillinger, F.; Muhlberger, L.; Sigwalt, D.; Holler, M.; Nierengarten, J. F., *Tetrahedron Lett*. **2013**, *54*, 6251.
72. Bingel, C., *Chem. Ber.* **1993**, *126*, 1957.
73. Sigwalt, D.; Holler, M.; Nierengarten, J. F., *Tetrahedron Lett*. **2013**, *54*, 3160.
74. Lu, J.; Li, N. S.; Koo, S. C.; Piccirilli, J. A., *J. Org. Chem*. **2009**, *74*, 8021.
75. Dai, Q.; Song, C. X.; Pan, T.; He, C., *J. Org. Chem*. **2011**, *76*, 4182.
76. Hernández, A. R.; Peterson, L. W.; Kool, E. T., *ACS Chem. Biol*. **2012**, *7*, 1454.
77. Hernández, A. R.; Kool, E. T., *Org. Lett*. **2011**, *13*, 676.
78. Yang, L.; Lin, G.; Nelson, R. S.; Jian, T.; Li, L., *Biochemistry* **2012**, *51*, 7173.
79. Richichi, B.; Imberty, A.; Gillon, E.; Bosco, R.; Sutkeviciute, I.; Fieschi, F.; Nativi, C., *Org. Biomol. Chem.* **2013**, *11*, 4086.