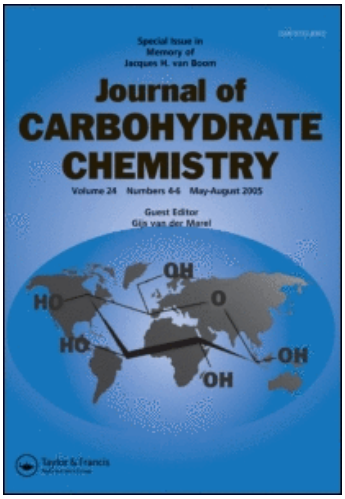


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

METAL-CATALYZED CYCLIZATION ON CARBOHYDRATE TEMPLATES. A STEREOSELECTIVE ACCESS TO ENANTIOPURE POLYCYCLIC COMPOUNDS

Denis Sinou[a]; Karim Bedjeguelal[a]
[a] Université Claude Bernard Lyon 1, Villeurbanne, Cédex, France

Online publication date: 30 June 2001

To cite this Article Sinou, Denis and Bedjeguelal, Karim(2001) 'METAL-CATALYZED CYCLIZATION ON CARBOHYDRATE TEMPLATES. A STEREOSELECTIVE ACCESS TO ENANTIOPURE POLYCYCLIC COMPOUNDS', Journal of Carbohydrate Chemistry, 20: 5, 335 — 357
To link to this Article: DOI: 10.1081/CAR-100105709
URL: http://dx.doi.org/10.1081/CAR-100105709

J. CARBOHYDRATE CHEMISTRY, 20(5), 335–357 (2001)

REVIEW

METAL-CATALYZED CYCLIZATION ON CARBOHYDRATE TEMPLATES. A STEREOSELECTIVE ACCESS TO ENANTIOPURE POLYCYCLIC COMPOUNDS

Denis Sinou* and Karim Bedjeguelal

Laboratoire de Synthèse Asymétrique, Associé au CNRS, CPE Lyon,
Université Claude Bernard Lyon 1, 43, Boulevard du 11 Novembre
1918, 69622 Villeurbanne Cédex, France

TABLE OF CONTENTS

1. INTRODUCTION

Carbohydrates constitute an abundant and inexpensive source of chiral compounds. They are recognized as versatile building blocks in synthetic organic chemistry, having a variety of functional and stereochemical features. Many of these compounds can be easily transformed into versatile synthetic intermediates,

*Corresponding author. Fax: 33 4 72448160; E-mail: sinou@univ-lyon1.fr

bearing functional groups as well as predetermined chiral centers. These intermediates can then be further elaborated for the synthesis of many naturally occurring compounds.[1]

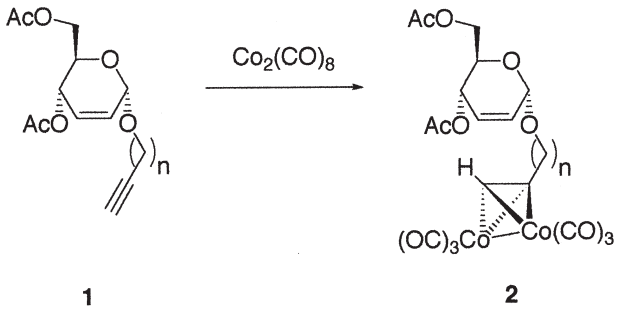
A key element in this strategy is the construction of a ring system from a carbohydrate precursor for elaboration into polycyclic chiral compounds.[2, 3] Radical cyclization has been widely used as a tool for access to these complex cyclic and heterocyclic frameworks, whereas organometallic-catalyzed cyclization reactions of carbohydrate derivatives have been less studied and only recently has this methodology attracted much attention. We describe in this short review the different organometallic-catalyzed cyclization procedures in carbohydrate chemistry affording enantiopure polycyclic systems.

2. COBALT-CATALYZED CYCLIZATION

Lindsell *et al*. Were the first workers to investigate the Pauson-Khand ring forming reaction[4,5] with carbohydrate derivatives.[6] Hex-2-enopyranosides **1** (n = 1, 2) were treated with $Co_2(CO)_8$ to give the hexacarbonyldicobalt complexes **2** (n = 1, 2) (Scheme 1); unfortunately, all attempts to promote intramolecular Pauson-Khand reaction of complexes **2** were unsuccessful.

Voelter and co-workers[7,8] obtained the hexacarbonyldicobalt complexes **5** and **6** (Z = CO_2Me) in quantitative yields by treating the acetylenic carbohydrates **3** and **4** with $Co_2(CO)_8$ in benzene at room temperature (Scheme 2). Heating of these compounds at 50°C in DMSO afforded the tricyclic compounds **7** and **8** in 75% and 77% yield, respectively.

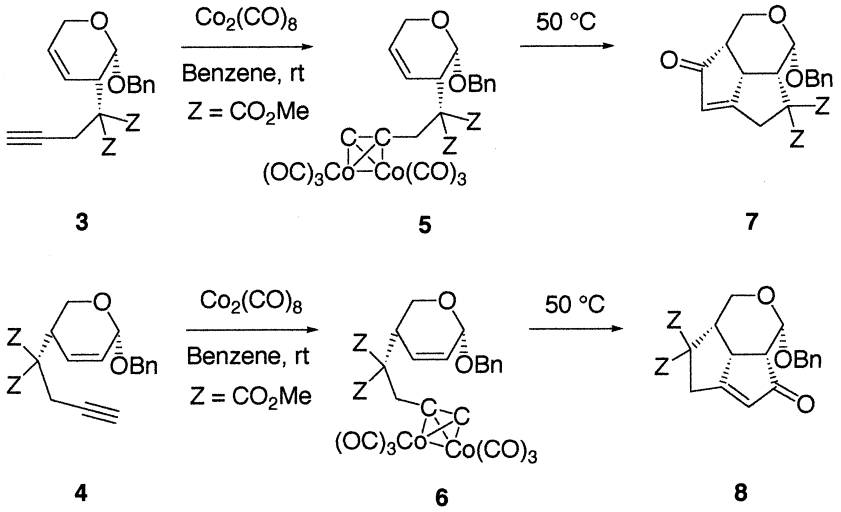
During the same period, Marco-Contelles published his results on the cobalt-mediated cycloisomerization of 1,6-enynes on carbohydrate templates.[9, 10] For example, after cobalt complex formation and *in situ* decomposition with NMO (*N*-methylmorpholine oxide), the 1,6-enynes **9**, **10** and **11** gave the cyclopentenones **12**, **13** and **14** in moderate to good yields in one synthetic operation (Scheme 3). It is to be noticed that the carbonylative insertion always takes place from the same side on which the propargyl moiety is located.



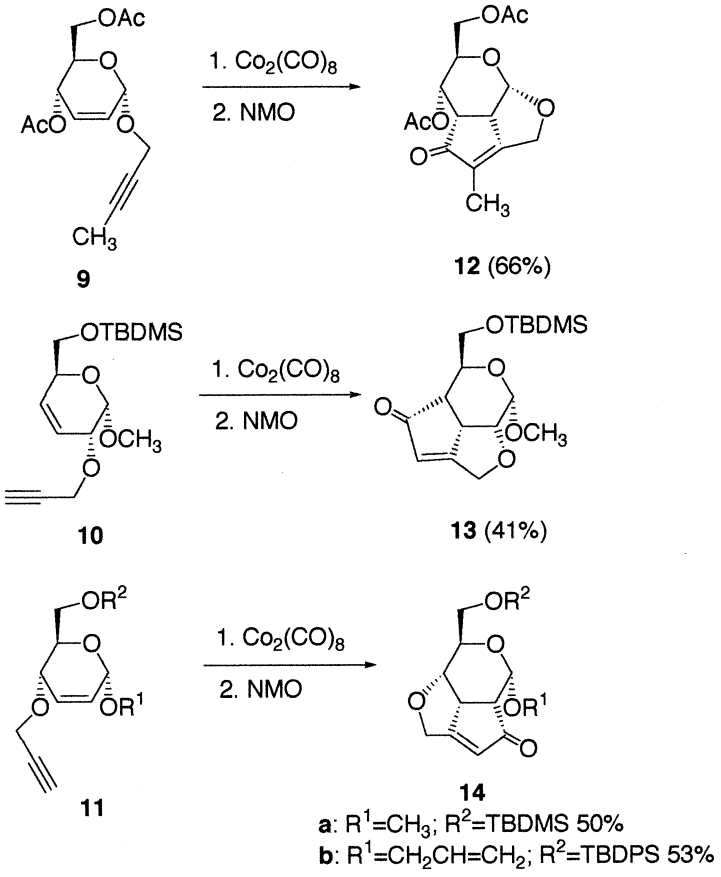
1 2

Scheme 1.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

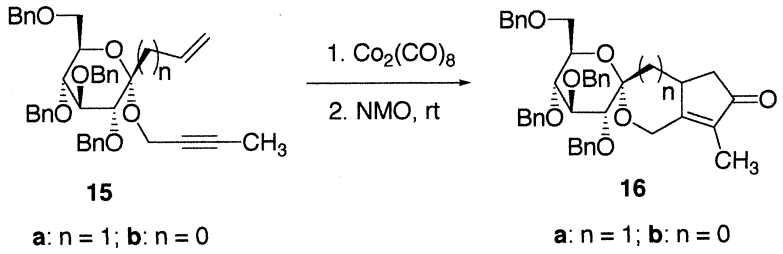


Scheme 2.



Scheme 3.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016



Scheme 4.

Application of this methodology to ketoglycosidic enynes **15a** and **15b** (treatment by dicobaltoctacarbonyl in CH_2Cl_2, then by an excess of NMO) afforded the cyclopentenone spiroacetals **16a** and **16b** in 76 and 66% yield, respectively (Scheme 4);[11] compound **16a** was isolated as a single stereoisomer, whereas **16b** was a mixture of the two diastereoisomers in a ratio 7:1.

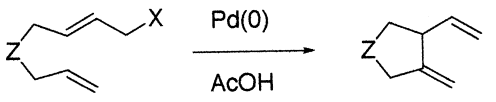
3. PALLADIUM-CATALYZED CYCLIZATION

3.1. Metallo-ene Cyclization

The "metallo-ene" type cyclization of 1-acetoxy-2,7-dienes, depicted in Scheme 5, has been extensively studied by Oppolzer for the construction of various five-membered ring compounds.[12, 13]

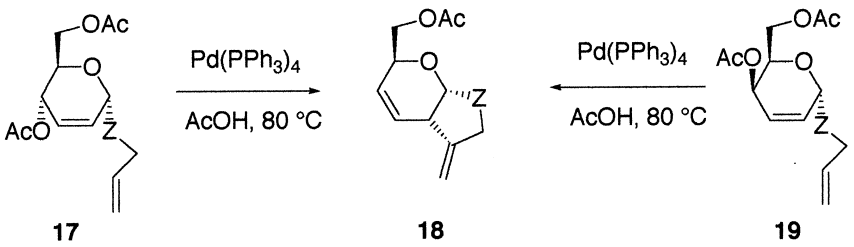
This methodology was extended by Holzapfel's group to carbohydrate molecules. Palladium(0)-catalyzed cyclization of acetoxy-1,6-diene-*C*- and *O*-glycoside **17a** and **17b** gave the *cis*-fused bicyclic compounds **18a** and **18b** in 72 and 50% yield, respectively; the reaction was carried out in acetic acid starting with **17a** and methanol starting with **17b**. The *threo* derivative **19a** gave also compound **18a** in 89% yield (Scheme 6).[14–16] The observation that both the allyl acetate derivatives **17a** and **19a** gave the same *cis* annulated cyclization product **18a** implies a relatively slow *trans-cis* isomerization of the π-allyl intermediate palladium complex, since the mechanism for the cyclization reaction proceeds in a suprafacial manner. This observation was previously made by Oppolzer who showed that cyclisation of *trans*-disposed "enophiles" occurred, although slower than *cis*-disposed "enophiles".[17]

This palladium-catalyzed cyclization was also successfully conducted on a large variety of 4-alkoxy, 4-amido, and 4-alkyl pseudoglycals (Scheme 7).[15] Sub-



$Z = CH_2$, NR, O, $C(CO_2Me)_2$; X = OAc, OH

Scheme 5.



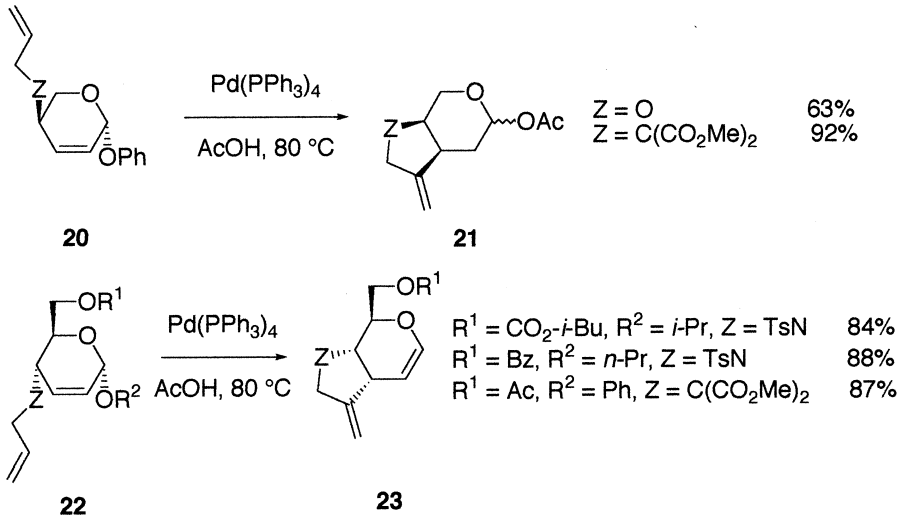
Scheme 6.

strates bearing various anomeric phenoxy-, isopropoxy-, propoxy-, or *tert*-butoxy-groups, such as **20** and **22,** readily cyclized at 80°C in acetic acid to furnish the respective bicyclic products **21** and **23** in quite good yields.

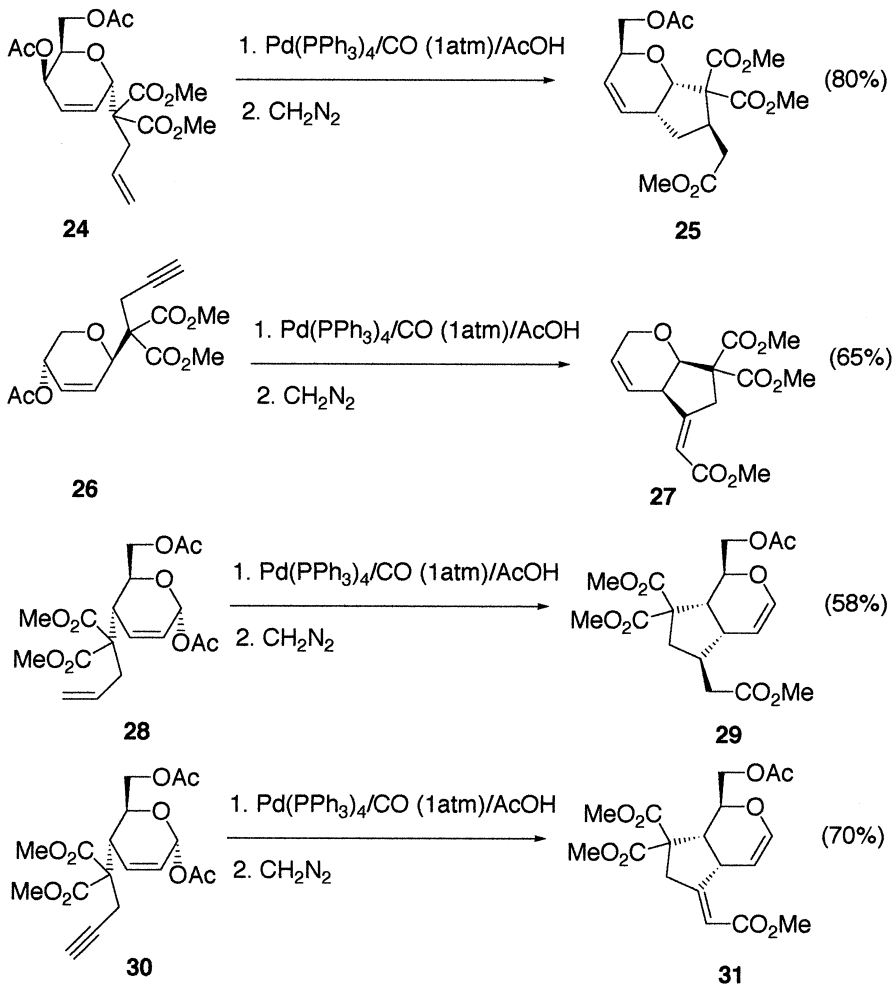
Performing the reaction under carbon monoxide, highly functionalized polycyclic compounds were obtained by trapping of the cyclized alkyl-palladium intermediate with CO *via* a cyclization/carbonylation sequence. When the cyclization was performed under 1atm of CO, 2,3-unsaturated glycosides, bearing the unsaturated allyl functionality at the anomeric center, such as **24** and **26**, or at position 4, such as **28** and **30**, gave the corresponding enantiopure bicyclic esters in quite good yields (Scheme 8).

3.2. Cycloisomerization

Another access to cyclopentadienic structures is the palladium-catalyzed cycloisomerization of enynes studied by Trost (Scheme 9).[18]



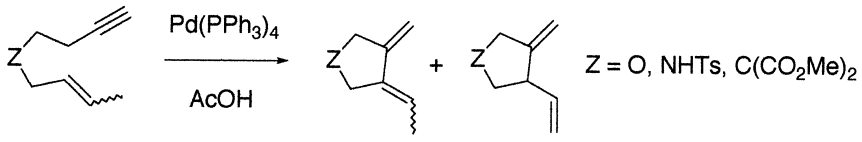
Scheme 7.



Scheme 8.

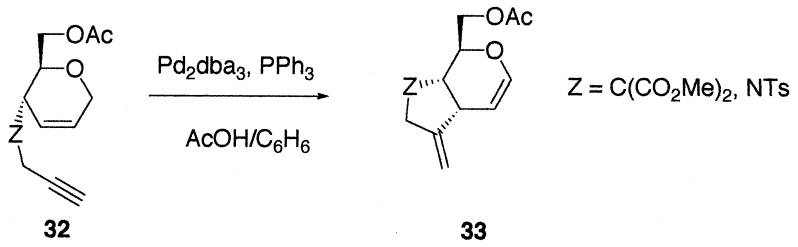
This reaction was applied by Holzapfel to carbohydrates **32** affording very nicely the corresponding bicyclic compounds **33** (Scheme 10).[14, 15]

Cycloisomerization of suitable dienyne carbohydrates **34** afforded the corresponding tricyclic products **35** in the presence of $Pd_2dba_3.CHCl_3$/tri-*o*-tolylphosphine in acetic acid/benzene at room temperature, whereas performing the reaction



Scheme 9.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016



Scheme 10.

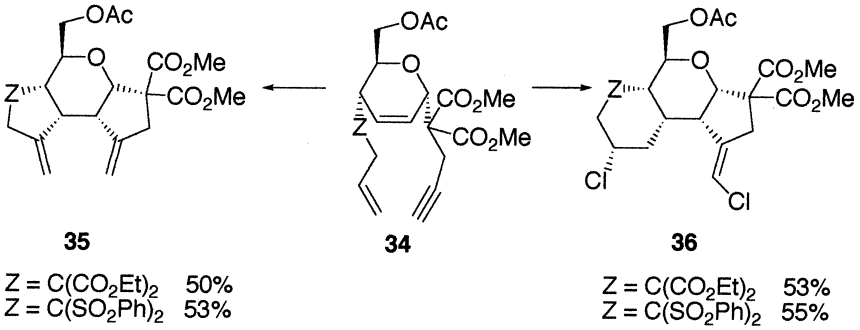
in acetic acid/acetonitrile as the solvent in the presence of $PdCl_2(CH_3CN)_2/CuCl_2$ afforded the chloro compounds **36** in quite good yields (Scheme 11).[19]

3.3. Heck-Type Cyclization

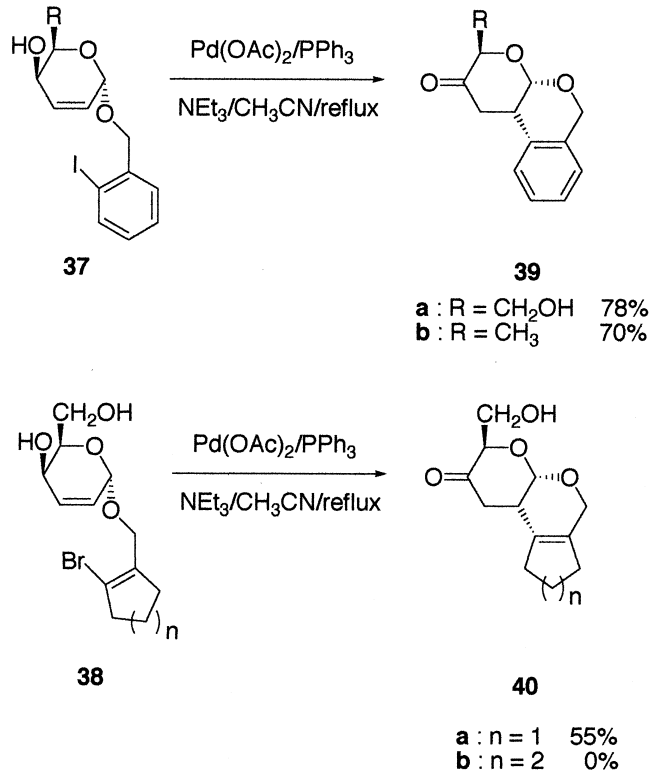
The intramolecular Heck reaction is now a well-used methodology in organic synthesis, allowing the sequential formation of several carbon-carbon bonds in a single step, even in a diastereo- and enantioselective manner.[20–24]

The application of this methodology to the alkenyl- and arylbranched chain hex-2-enopyranosides **37** and **38** afforded the *cis*-fused furo- and pyrano-[2,3*b*]pyranones **39** and **40** in good yields (Scheme 12).[25] It is noteworthy that cyclization failed for **38b** for reasons which are not clear.

An unexpected palladium-catalyzed cyclization in carbohydrate chemistry, providing bicyclic glycals and occurring *via* a dealkoxypalladation pathway, was described by Sinou and co-workers.[26,27] Reaction of unsaturated carbohydrate **41a** under the standard conditions CH_3CN-H_2O, Bu_4NHSO_4, NEt_3, $Pd(OAc)_2$, PPh_3, 80°C gave the unsaturated bicycle **42a** in 72% yield (Scheme 13). It was shown that no reaction occurred without base, and quaternary ammonium salts (bromide or hydrogensulfate) were effective in this reaction. Most importantly, the nature of the phosphine seemed crucial for the cyclization reaction: monophosphines gave chemical yields of up to 77%, whereas diphosphines gave very low yields.



Scheme 11.



37 **39**

a : R = CH_2OH 78%
b : R = CH_3 70%

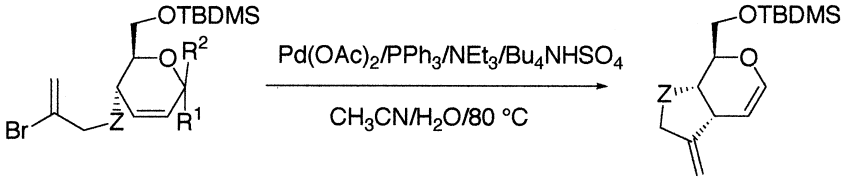
38 **40**

a : n = 1 55%
b : n = 2 0%

Scheme 12.

Under the same conditions, the unsaturated carbohydrate having no protecting group at C-6 gave the corresponding bicyclic compound in 68% yield.

This cyclization reaction was extended to the *N*-tosyl and *C*-substituted carbohydrates **41b** and **41c** to give the bicyclic aza- and *C*-compounds **42b** and **42c** in

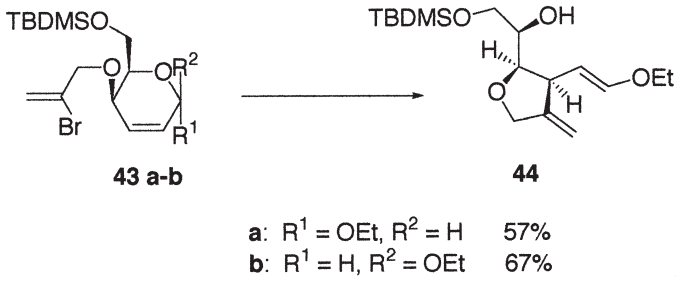


41 a-d **42 a-c**

a: $R^1 = OC_2H_5$, R^2 = H, Z = O 72%
b: $R^1 = OC_2H_5$, R^2 = H, Z = NTs 81%
c: $R^1 = OC_2H_5$, R^2 = H, Z = $C(CO_2Me)_2$ 80%
d: R^1 = H, $R^2 = OC_2H_5$, Z = O 50%

Scheme 13.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016



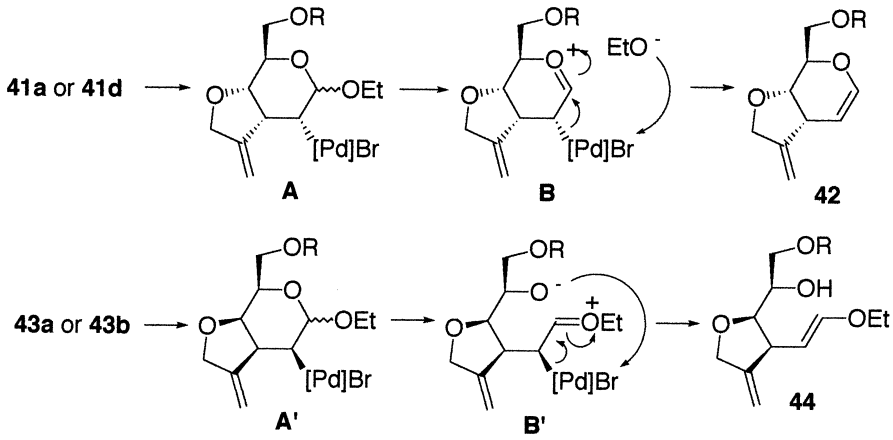
Scheme 14.

81% and 80% yield, respectively. The analogous unsaturated β-glycoside **41d** was also transformed into the bicyclic compound **42a** in 50% yield.

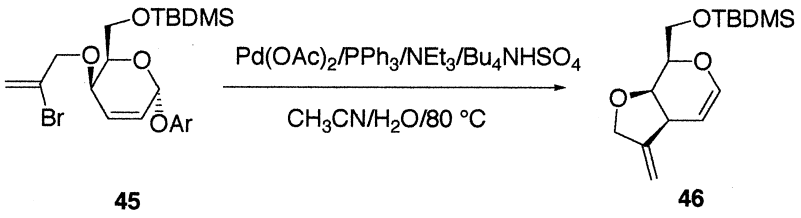
When the cyclization reaction was performed on both ethyl α- or β-4-*O*-(2′-bromoprop-2′-enyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-D-*threo*-hex-2-enopyranoside **43 a-b**, only formation of the tetrahydrofuran derivative **44** was observed in 57 and 67% yield, respectively (Scheme 14).

The formation of these different compounds was explained according to Scheme 15. The cyclization process starts with the formation of a σ-alkylpalladium intermediate **A** or **A′** by oxidative addition of compound **41a** or **41d** to the palladium(0) complex, followed by an association-insertion reaction. Cleavage of the alkoxy moiety in the case of **A**, or cleavage of the cyclic carbon-oxygen bond of **A′** afforded two intermediates **B** and **B′**, which gave the bicyclic compound **42a** or the monocyclic compound **44**, respectively. Regeneration of the palladium(0) occurs in the presence of water by ligand exchange followed by reductive elimination.

According to this mechanism, the replacement of the ethoxy group by an aryloxy group in the *threo* series, such as for compound **45**, allowed the formation of



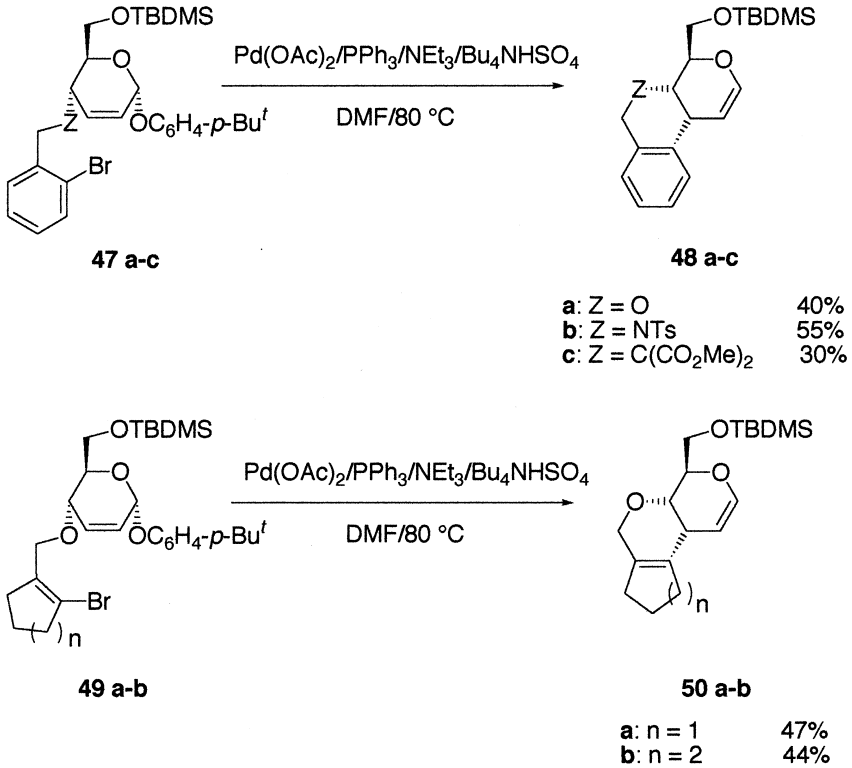
Scheme 15.



Scheme 16.

the bicyclic compound **46** (Scheme 16) .[28,29] In this case, the scission of the aglycon moiety is favored *versus* the cleavage of the carbohydrate moeity, due to the better leaving group ability of the aryloxy group *versus* an alkyloxy group.

Stereospecific access to bicyclo[4.4.0] decane systems was also possible using DMF as the solvent instead of CH_3CN-H_2O.[30,31] Cyclization of the unsaturated *p-tert*-butylphenyl hex-2-enopyranoside **47a** to the bicyclic product **48a** occurred in 40% yield in the presence of $Pd(OAc)_2$, PPh_3, Bu_4NHSO_4, and NEt_3 at 80°C in



Scheme 17.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

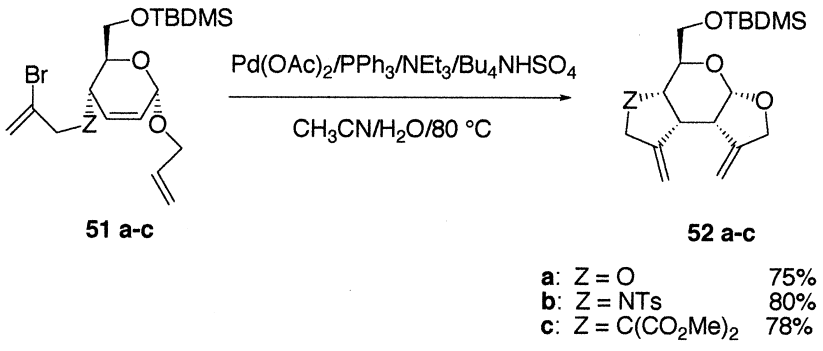
DMF as the solvent (Scheme 17). A similar reaction was performed with the *N*-tosyl and *C*-substituted unsaturated carbohydrates **47b** and **47c** to give the corresponding aza compound **48b** and carbocyclic compound **48c** in 55% and 30% yield, respectively.The cyclization process was also extended to cyclopentenyl and cyclohexenyl derivatives **49 a**-**b** to give the bicyclic compounds **50a** and **50b** in 47 and 44% yield, respectively.

Heterotricyclic systems were also accessible using this intramolecular palladium-catalyzed Heck reaction, starting from suitable unsaturated carbohydrates.[32,33] Under the above conditions [CH_3CN-H_2O, Bu_4NHSO_4, NEt_3, $Pd(OAc)_2$, PPh_3, 80°C] the unsaturated carbohydrates **51 a**-**c** afforded the tricyclic compounds **52 a**-**c**, after 24 h, in 75, 80, and 78% yield, respectively (Scheme 18).

The aglycon's structure, and particularly the degree and the position of the substitution at the double bond, has a great influence on the course of this cyclization reaction. The unsaturated carbohydrates **53a**, **53b**, and **53c** gave, respectively, the tricyclic compounds **54**, **55**, and **56** in 77, 78, and 79% yield, whereas only the bicyclic compound **42a** was obtained in 72% yield when the reaction was extended to carbohydrate **53d** (Scheme 19).This different behaviour in the last example is due to the lack of a hydrogen in the σ-alkyl intermediate for the β-H elimination leading to the tricyclic compound.

When the cyclization of compounds **41a** or **53d** was conducted under the standard conditions in the presence of sodium formate, 2-deoxy carbohydrates **57 a**-**b** were obtained in 62 and 56% yield, respectively (Scheme 20); the formation of these compounds are explained by the trapping of the intermediate σ-alkylpalladium intermediate **A** by a hydride.

Finally, a palladium-coupling reaction between ethyl or allyl 4-*O*-propargyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside **58 a-b** and C_6H_5I under the above conditions [CH_3CN-H_2O, Bu_4NHSO_4, NEt_3, $Pd(OAc)_2$, PPh_3, 80°C] led to the formation of the bicyclic and tricyclic compounds **59** and **60** in 42 and 54% yield, respectively (Scheme 21).[34]

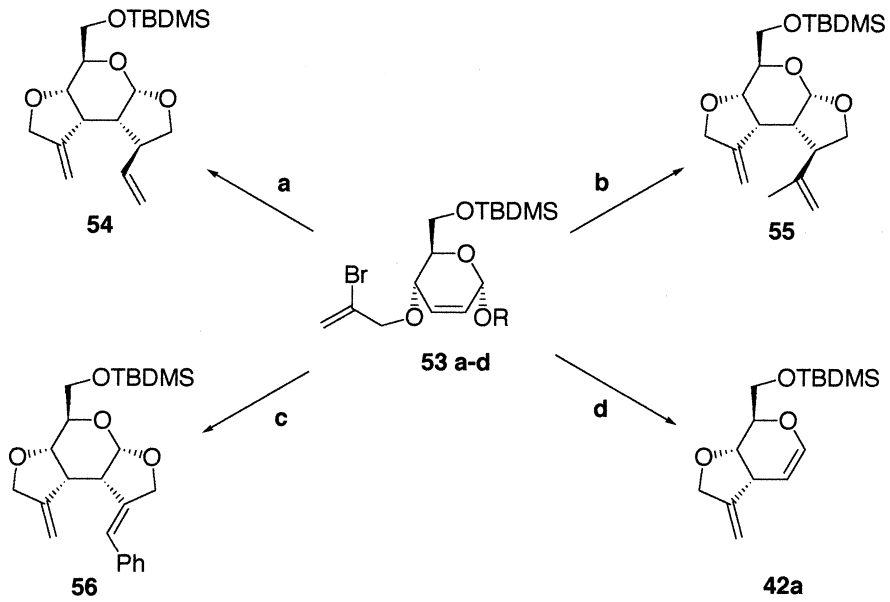


51 a-c

52 a-c

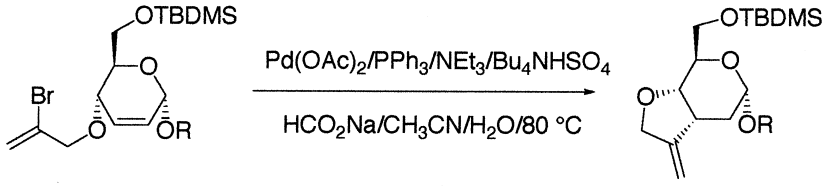
a: Z = O 75%
b: Z = NTs 80%
c: Z = $C(CO_2Me)_2$ 78%

Scheme 18.



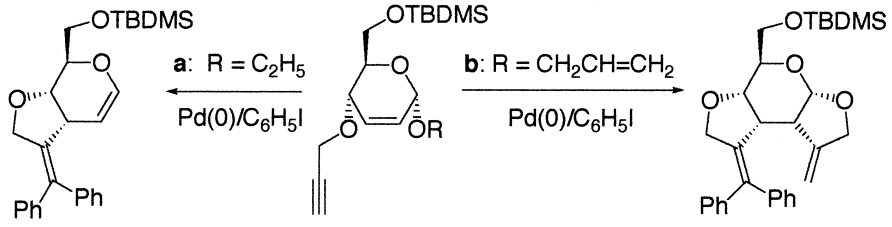
53 a: R = $CH_2CH{=}CHCH_3$; **53 b**: R = $CH_2CH{=}C(CH_3)_2$
53 c: R = $CH_2CH{=}CHPh$; **53 d**: R = $CH_2C(CH_3){=}CH_2$

Scheme 19.



41a and **57a**: R = C_2H_5 ; **53d** and **57b**: R = $CH_2C(CH_3){=}CH_2$

Scheme 20.



a: R = C_2H_5 ; **b**: R = $CH_2CH{=}CH_2$

Scheme 21.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

4. METATHESIS

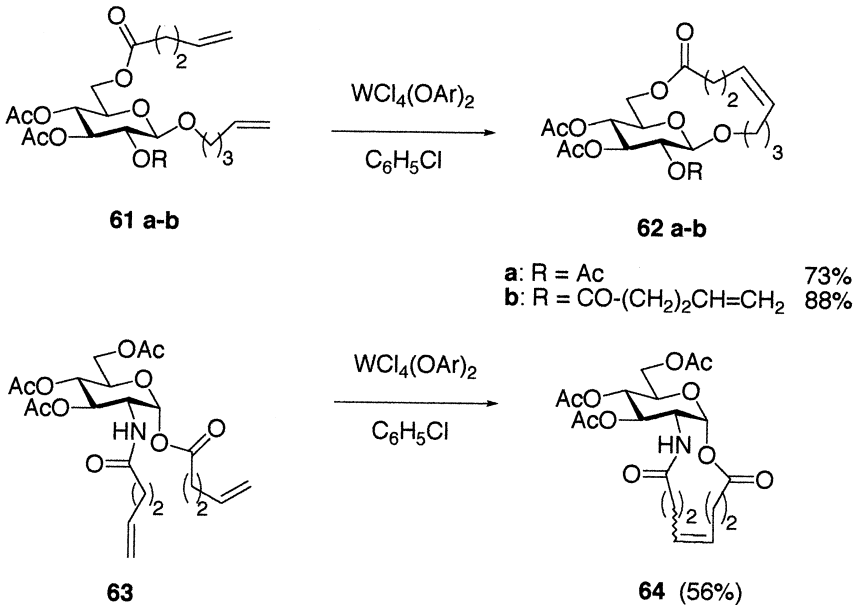
The use of olefin metathesis in organic synthesis has grown considerably during recent years. Ring-closing metathesis (RCM) reaction has found the widest application, since a variety of carbo- and heterocyclic ring systems can be obtained in quite good yields using molybdenum and ruthenium-based catalysts.[35–39]

Descotes *et al.* used a tungsten catalyst for an intramolecular carbohydrate cyclization.[40] Reactions of the unsaturated substrates **61** and **63** in chloroform at 80°C in the presence of the catalyst $WCl_4(OAr)_2$ afforded the macrocycles **62** and **64** in quite good yields (Scheme 22).

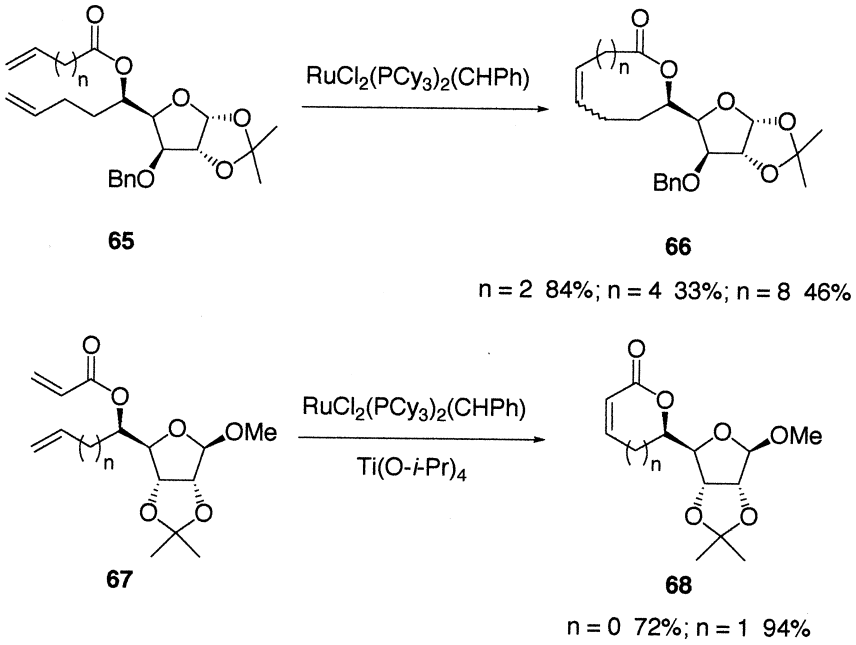
In connection with the synthesis of annonaceous acetogins and analogs, Gesson *et al.*[41] used the Grubbs' carbene catalyst $RuCl_2(PCy_3)_2(CHC_6H_5)$ for the RCM reaction of unsaturated esters **65** (Scheme 23); 9- to 15-membered lactones **66** were obtained in moderate to good yields.

A similar approach was applied to acrylates **67** derived from allylic and homoallylic alcohols by Ghosh *et al.*[42] affording enantiopure α,β-unsaturated γ- and δ-lactones **68** in quite good yields in the presence of added $Ti(O\text{-}i\text{-}Pr)_4$ (Scheme 23). The presence of this Lewis acid disrupts the possible formation of the too stable metal chelates formed between the ester carbonyl and the intermediate carbene species.

Fürstner and co-workers have used the ring-closing metathesis of alkenes for the preparation of key intermediates in the synthesis of the glycolipid tricolorin A, that exhibits significant cytotoxic properties against cultured P-388 and human breast cancer cell lines,[43,44] the glycolipid tricolorin G, the allelochemical principle

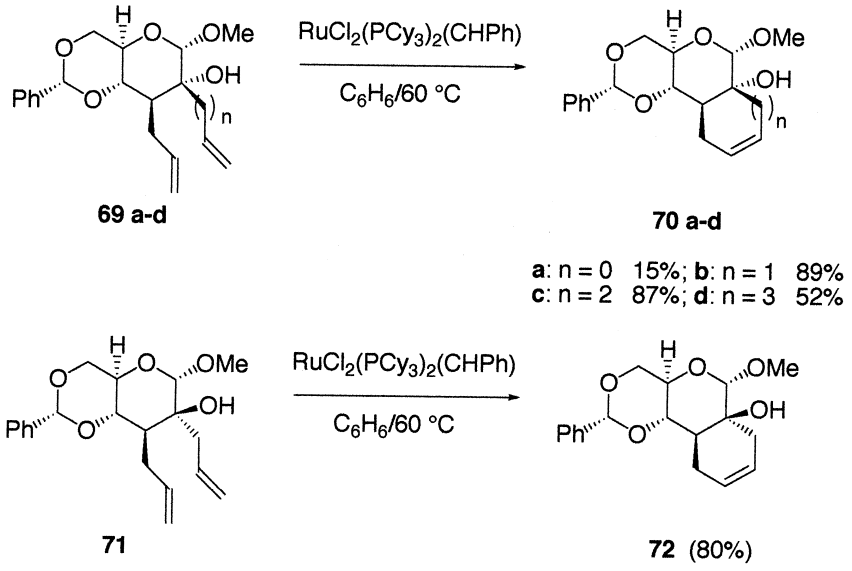


Scheme 22.



Scheme 23.

of *Ipomoea tricolor* used as a cover crop for the protection of sugar cane,[44] as well as the core segment found in the simonin, operculin, tuguajalapin, orizabin, mammoside, ouamoclin, and stoloniferin family of resin glycosides.[44] The ring-closing metathesis of alkynes was used in the total synthesis of sophorolipid lactone.[45]

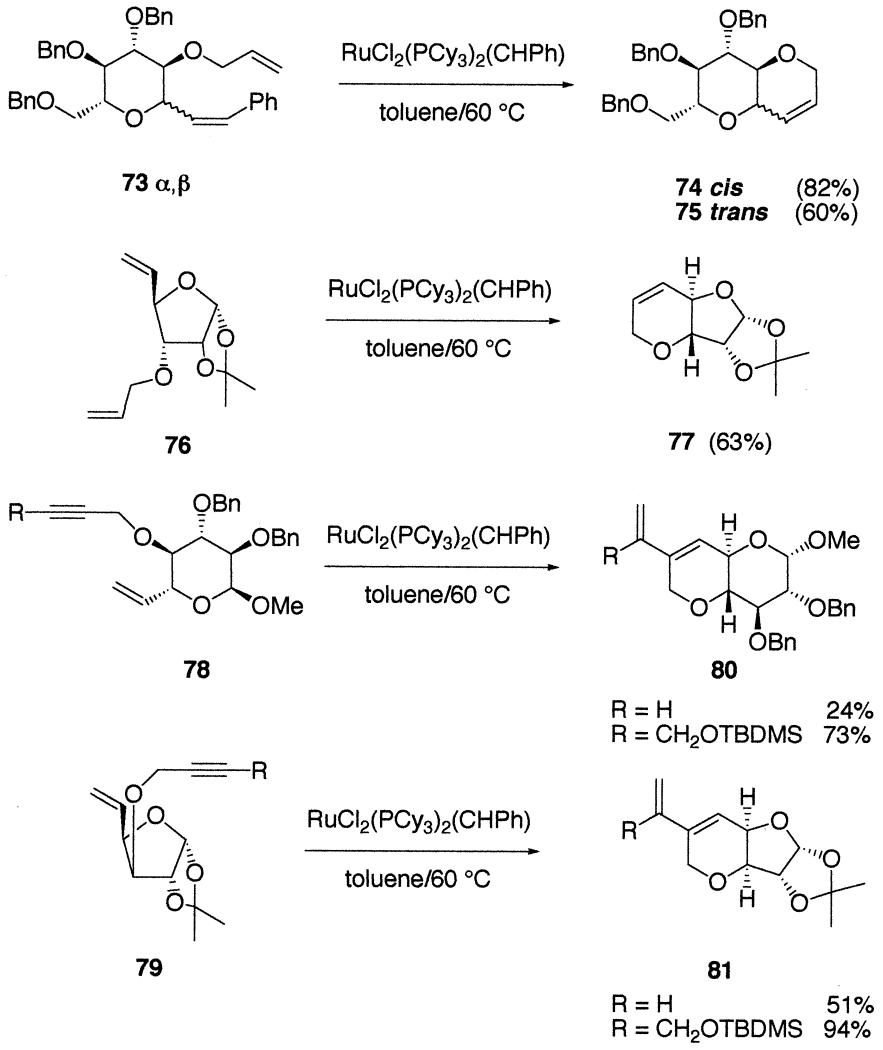


Scheme 24.

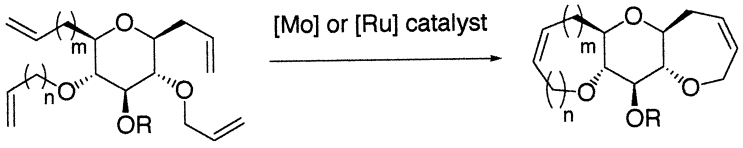
MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Five-, six-, seven-, eight-, and nine-membered carboxylic and oxygen-containing annulated ring fused carbohydrates were also prepared in good yields using the RCM reaction.[46,47] Compounds **69** and **71** afforded the *cis*-fused alcohols **70** and **72** in the presence of the Grubbs'catalyst (Scheme 24); the low yield observed for **70a** is probably due to the steric hindrance from the *trans*-fused ring system.

A complementary approach was described by van Boom *et al.*[48] on glycopyranoids and glycofuranoids. Performing the RCM reaction on the *cis*- and *trans*-1-vinyl-2-*O*-allyl systems, **73**α and **73**β afforded the corresponding *cis*- and *trans*-fused pyranopyrans **74** and **75** in good yields (Scheme 25). Even the RCM reaction of the *trans*-vinyl-*O*-allyl derivative **76** gave the *trans*-fused pyranofuran **77** in 63% yield, when the concentration of the starting material was 0.02 M, in order to



Scheme 25.



82 **83**

a: m = 1, n = 0; **b**: m = n = 1; **c**: m = 1, n = 3; **d**: m = 2, n = 1

Scheme 26.

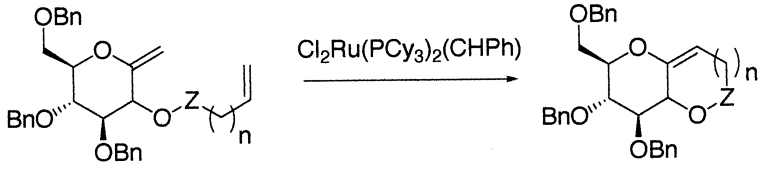
decrease the formation of dimers. One application is the construction of an intermediate in the synthesis of the functionnalized A-ring moiety of ciguatoxin.[49]

Derivatives **78** and **79**, bearing a vinyl-*O*-propargyl instead of a vinyl-*O*-allyl motif, functioned also as substrates for an enyne-ring-closing metathesis (Scheme 25); the reaction proceeded smoothly under the same conditions to give the highly functionnalized *trans*-fused pyranopyrans **80** and *cis*-fused furanopyrans **81**, respectively, in quite good yields.

Cyclization of polyunsaturated compounds **82** in the presence of the Grubbs'catalyst or the Schrock's catalyst [2,6-*i*-$Pr_2C_6H_3NMo\{OC(CF_3)_2Me\}_2$ $CHCMe_2Ph$] afforded polycyclic ethers **83 a-d** by two-directional double ring-closing metathesis (Scheme 26).[50, 51] In all cases the yields of the *trans*-fused tricyclic ethers ranged from good to excellent, higher yields being obtained with the ruthenium catalyst.

The application of the RCM cyclization to 1-exo-methylene glucose derivatives **84** (Scheme 27) in the presence of the Grubbs' catalyst allowed the preparation of bicyclic *C*-glycosylidene derivatives **85** in 20–62% yields.[52]

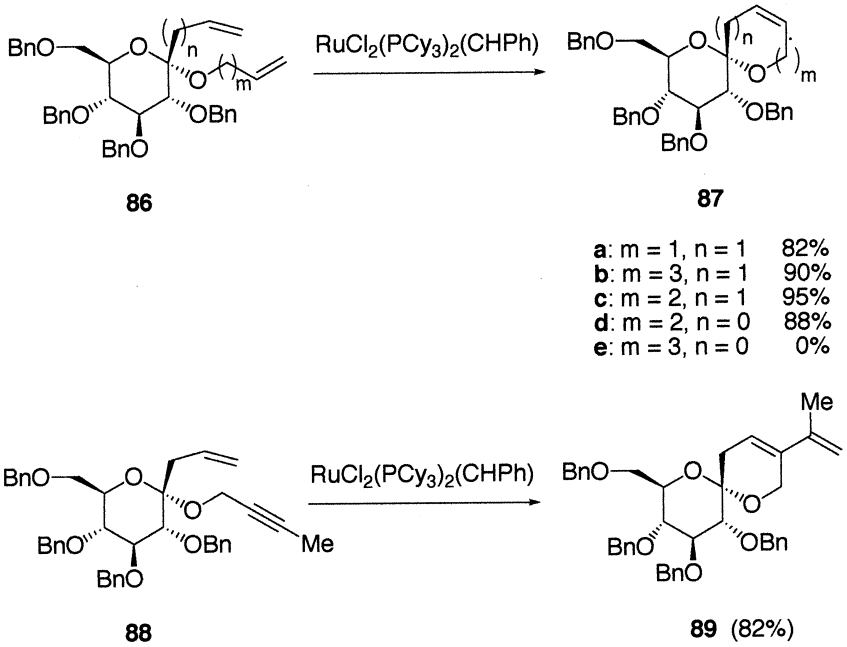
The RCM reaction has also been used as a highly stereoselective route to unsaturated spiroacetals. The cyclization of various carbohydrates **86 a-d** having a terminal alkene-*O*-alkene arrangement at the anomeric center gave the corresponding unsaturated spiroacetal derivatives **87 a-d** in excellent yields in the presence of the Grubbs' catalyst at 60°C (Scheme 28).[53] It is to be noticed that treatment of **86e** did not lead to the expected spiro compound **87e**, but to the formation of a dimeric product.



84 **85**

Z = CO, n = 1	30%
Z = CO, n = 2	51%
Z = CH_2, n = 0	20%
Z = CH_2, n = 1	62%
Z = CH_2, n = 2	54%

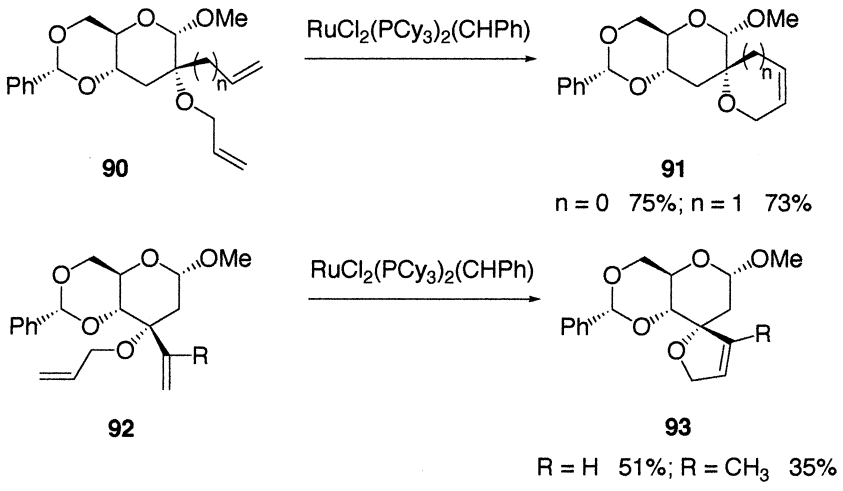
Scheme 27.



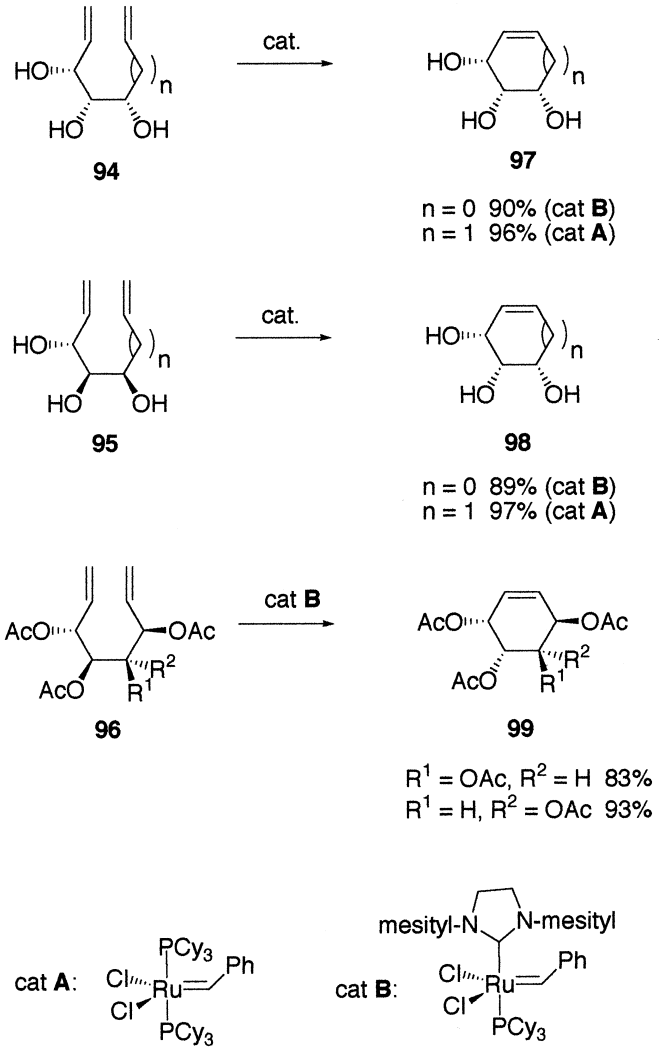
Scheme 28.

This cyclization was extended to the allyl-*O*-butynyl derivatives such as **88**, affording the functionalized unsaturated spiroacetal **89** in good yield (Scheme 28).[11]

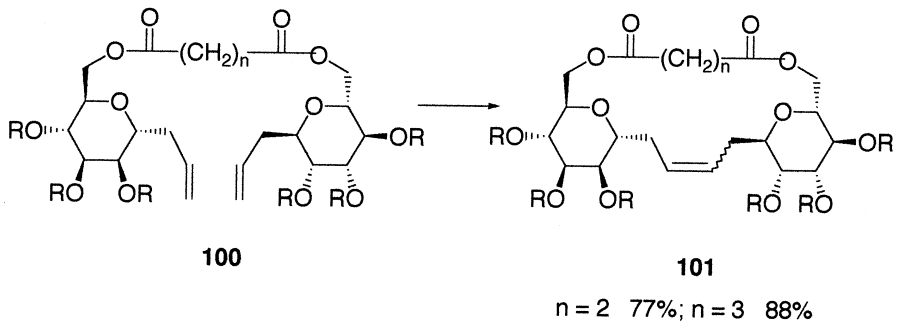
Spiroannulation of a different set of sugar derivatives using RCM was published by Jenkins et al.[46,47] The RCM reaction of compounds **90** and **92** gave the spiro dihydropyrans **91** and dihydrofurans **93** in moderate to good yields (Scheme 29).



Scheme 29.

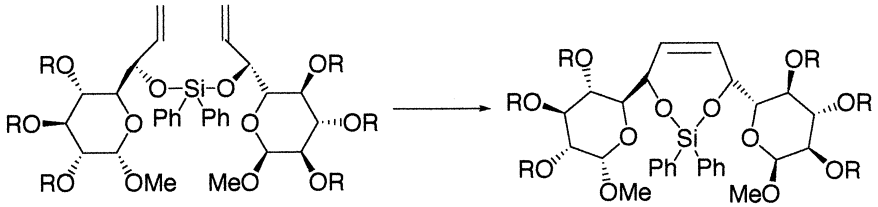


Scheme 30.



Scheme 31.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016



102 **103**

Scheme 32.

A noteworthy and general method for carbocyclization of carbohydrates used two consecutive organometallic transformations (Scheme 30).[54] In a first reaction, methyl ω-deoxy-ω-iodoglycosides undergo reductive elimination with zinc to produce a terminal double bond; the aldehyde formed is alkylated *in situ* by various organozinc reagents to give the corresponding dienes **95–96**. These dienes produce the five- and six-membered carbocycles **97–99** in quite good yields when subjected to ring-closing olefin metathesis in the presence of the commercial available Grubbs' catalyst, or in better yields using the more reactive catalyst obtained by substituting one tricyclohexylphosphine by an *N*-heterocyclic carbene ligand.

A very elegant application of the RCM reaction is the synthesis of *C*-butenyl linked homo- and hetero-disaccharides **101** using prearranged *C*-allylsaccharides **100** (Scheme 31).[55]

A similar approach was used following a silicon tethering strategy (Scheme 32).[56] RCM reaction of the C_2-symmetrical *bis*-alkoxysilane **102** in the presence of the Grubbs' catalyst afforded the seven member ring diphenylsilaketal **103** in 31% yield.

5. CONCLUSION

In conclusion, metal-catalyzed cyclization in carbohydrate chemistry, still in its infancy, provides a very valuable tool for the construction of enantiopure and highly functionalized di- and tricyclic structures in organic chemistry. This methodology, which exhibits very high selectivities and also chemiocompatibility, is a very nice complement to the radical cyclization procedure, and should find many applications in the near future for the synthesis of natural products.

6. REFERENCES

1. Hanessian, S. *Total Synthesis of Natural Products; The Chiron Approach*; Pergamon: Oxford, 1993.
2. Fraser-Reid, B. Some Progeny of 2,3-Unsaturated Sugars-They Little Resemble Grandfather Glucose : Ten Years Later. Acc. Chem. Res. **1985**, *18* (11), 347–354.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

3. Fraser-Reid, B.; Tsang, R. Carbocycles from Carbohydrates : the Annulated Sugar Approach. In *Strategies and Tactics in Organic Synthesis*; Lindberg, T. Ed.; Academic Press: New York, 1989; Vol. 2, 123–162.
4. Schore, N.E. The Pauson-Khand Cycloaddition Reaction for Synthesis of Cyclopentenone. Org. React. (N.Y.) **1991**, *40*, 1–90.
5. Schore, N.E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L.A. Eds.; Pergamon: Oxford, 1991; Vol. 5, 1037–1064.
6. Lindsell, W.E.; Preston, P.N.; Rettie, A.B. Synthesis and Characterisation of Hexacarbonyldicobalt Complexes Derived from 2-Propynyl and 3-Butynyl 4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosides. Carbohydr. Res. **1994**, *254*, 311–316.
7. Naz, N.; Al-Tel, T.H.; Al-Abedd, Y.; Voelter, W. Synthesis of Polyfunctionalized Bis-Annulated Pyranosides: Useful Intermediates for Triquinane Synthesis. Tetrahedron Lett. **1994**, *35* (46), 8581–8582.
8. Naz, N.; Al-Tel, T.H.; Al-Abed, Y.; Voelter, W.; Ficker, R.; Hiller, W. Palladium-Cobalt-Mediated Double Annulation Process: A New Strategy to Chiral and Polysubstituted Bis-Cyclopentanoids on Carbohydrate Precursors. J. Org. Chem. **1996**, *61* (10), 3250–3255.
9. Marco-Contelles, J. The Pauson-Khand Reaction on Carbohydrate Templates. I. Synthesis of Bis-Heteroannulated-Pyranosides. Tetrahedron Lett. **1994**, *35* (28), 5059–5062.
10. Marco-Contelles, J. Asymmetric Pauson-Khand Reaction. Cobalt-mediated Cycloisomerization of 1,6-Enynes in Carbohydrate Templates: Synthesis of Bis-Heteroannulated Pyranosides. J. Org. Chem. **1996**, *61* (22), 7666–7670.
11. Leeuwenburgh, M.A.; Appeldoorn, C.C.M.; van Hooft, P.A.V.; Overkleeft, H.S.; van der Marel, G.A.; van Boom, J.H. Synthesis of Highly Functionalised Carbohydrate-Derived Spiroacetals by Ring-Closing Metathesis and Pauson-Khand Reaction of Ketoglycosidic Enynes. Eur. J. Org. Chem. **2000**, (6), 873–877.
12. Oppolzer, W. In *Comprehensive Organic Synthesis*; Trost, B.M., Fleming, I., Paquette, L.A., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, 29–61.
13. Oppolzer, W. Intramolecular, Stoichiometric (Li, Mg, Zn) and Catalytic (Ni, Pd, Pt) Metallo-ene Reactions in Organic Synthesis. Angew. Chem., Int. Ed. Engl. **1989**, *28* (1), 38–52.
14. Engelbrecht, G.J.; Holzapfel, C.W. Stereoselective Palladium Catalyzed Cyclisation on Carbohydrate Templates. A Route to Chiral Cyclopentanes and Some Heterocyclic Analogs. Tetrahedron Lett. **1991**, *32* (19), 2161–2164.
15. Holzapfel, C.W.; Engelbrecht, G.J.; Marais, L.; Toerien, F. Stereocontrolled Palladium(0) Catalysed Cyclisation and Cyclisation/Carbonylation of Pseudoglycal Derivatives. Tetrahedron **1997**, *53* (11), 3957–3974.
16. Holzapfel, C.W.; Marais, L. Palladium-Catalysed Cyclisation and Cyclisation-Carbonylation of Unsaturated *C*-Glycoside Derivatives. The Importance of Relative Stereochemistry. J. Chem. Res. **1998**, (S) (2), 60–61; **1998**, (M) (2), 0411–0422.
17. Oppolzer, W.; Gaudin, J.M. Catalytic Intramolecular Palladium-Ene Reactions. Helv. Chim. Acta **1987**, *70* (6), 1477–1481.
18. Trost, B.M. Atom Economy—A Challenge for Organic Synthesis: Homogeneous Catalysis Leads the Way. Angew. Chem., Int. Ed. Engl. **1995**, *34* (3), 259–281.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

19. Holzapfel, C.W.; Marais, L. Palladium-Catalysed Cascade Reactions of Unsaturated Carbohydrate Derivatives. Synthesis of Enantiopure Tricyclic Compounds. Tetrahedron Lett. **1997**, *38* (49), 8585–8586.
20. Trost, B.M. Cyclizations via Palladium-Catalyzed Allylic Alkylations. Angew. Chem., Int. Ed. Engl. **1989**, *23* (9), 1173–1192.
21. Grigg, R. Heterocycle Synthesis by Palladium Catalyzed Cyclisation-Anion Capture Processes. A Powerful New Strategy. J. Heterocycl. Chem. **1994**, *31* (3), 631–639.
22. De Meijere, A.; Meyer, F.E. Fine Feathers Make Fine Birds: the Heck Reaction in Modern Garb. Angew. Chem., Int. Ed. Engl. **1994**, *33* (23–24), 2379–2411.
23. Heumann, A.; Regnier, M. The Stereochemistry of Palladium-Catalyzed Cyclization Reactions: Addition to π-Allyl Intermediates. Tetrahedron **1995**, *51* (4), 975–1015.
24. Negishi, E.; Coperet, C.; Ma, S.; Liou, S.Y.; Liu, F. Cyclic Carbopalladation. A Versatile Synthetic Methodology for the Construction of Cyclic Organic Compounds. Chem. Rev. **1996**, *96* (1), 365–393.
25. Tenaglia, A.; Karl, F. Intramolecular Heck Reaction of Hex-2-enopyranosides: an Easy Entry to *cis*-Fused Furo- or Pyrano[2,3*b*]pyranones. Synlett **1996**, (4), 327–329.
26. Nguefack, J.F.; Bolitt, V.; Sinou, D. An Unexpected Palladium-Catalyzed Cyclization on Carbohydrate Templates. J. Chem. Soc., Chem. Commun. **1995**, (18), 1893–1894.
27. Nguefack, J.F.; Bolitt, V.; Sinou, D. Palladium-Mediated Cyclization on Carbohydrate Templates. 1. Synthesis of Enantiopure Bicyclic Compounds. J. Org. Chem. **1997**, *62* (5), 1341–1347.
28. Bedjeguelal, K.; Joseph, L.; Bolitt, V.; Sinou, D. Aglycon Directed Palladium β-Alkoxyelimination on Carbohydrate Templates. Tetrahedron Lett. **1999**, *40* (1), 87–90.
29. Bedjeguelal, K.; Joseph, L.; Bolitt, V.; Sinou, D. Palladium-Mediated Cyclization on Carbohydrate Templates. 3. Extension of the Cyclization to the *Threo* Series. J. Carbohydr. Chem. **2000**, *19* (2), 221–232.
30. Bedjeguelal, K.; Bolitt, V.; Sinou, D. Intramolecular Heck Cyclization-β-Alkoxy Elimination in Carbohydrate Chemistry. A Simple Route to Enantiopure Annelated Dioxatricyclic Compounds. Synlett **1999**, (6), 762–764.
31. Sinou, D.; Bedjeguelal, K. Palladium-Mediated Cyclization on Carbohydrate Templates. Synthesis of Enantiopure Annelated Tricyclic Compounds. Eur. J. Org. Chem. **2000**, (24), 4071–4077.
32. Nguefack, J.F.; Bolitt, V.; Sinou, D. Palladium-mediated Cyclization on Carbohydrate Templates. A New Route to Bis-Annulated Pyranosides. Tetrahedron Lett. **1996**, *37* (1), 59–62.
33. Nguefack, J.F.; Bolitt, V.; Sinou, D. Palladium-Mediated Cyclization on Carbohydrate Templates. 2. Synthesis of Enantiopure Tricyclic Compounds. J. Org. Chem. **1997**, *62* (20), 6827–6832.
34. Nguefack, J.F.; Bolitt, V.; Sinou, D. Tandem Sonogashira Reaction-Heck Cyclization in Carbohydrate Chemistry. An Easy Access to Substituted Bi- and Tricyclic Enantiopure Compounds. Carbohydr. Lett. **1997**, *2* (6), 395–402.
35. Fürstner, A. Recent Advancements in Ring Closing Olefin Metathesis. Top. Catal. **1997**, *4* (3, 4), 285–299.
36. Schuster, M.; Blechert, S. Olefin Metathesis in Organic Chemistry. Angew. Chem., Int. Ed. Engl. **1997**, *36* (19), 2036–2056.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

37. Grubbs, R.H.; Chang, S. Recent Advances in Olefin Metathesis and Its Application in Organic Synthesis. Tetrahedron **1998**, *54* (18), 4413–4450.
38. Armstrong, S.K. Ring Closing Diene Metathesis in Organic Synthesis. J. Chem. Soc., Perkin Trans. 1 **1998**, (2), 371–388.
39. Fürstner, A. Alkene Metathesis in Organic Synthesis; Springer-Verlag, Berlin, 1998.
40. Descotes, G; Ramza, J.; Basset, J.-M.; Pagano, S.; Gentil, E.; Banoub, J. Synthesis and Structural Characterization of Macrocyclic Carbohydrate Derivatives Obtained from Catalytic Metathesis Reactions with Chloro-Aryloxide Complexes of Tungsten. Tetrahedron **1996**, *52* (33), 10903–10920.
41. El Sukkari, H.; Gesson, J.-P; Renoux, B. Ring-Closing Metathesis and Cross Metathesis of Carbohydrate Derivatives. Tetrahedron Lett. **1998**, *39* (23), 4043–4046.
42. Ghosh, A.K.; Cappiello, J.; Shin, D. Ring-Closing Metathesis Strategy to Unsaturated γ- and δ-Lactones: Synthesis of Hydroxyethylene Isostere for Protease Inhibitors. Tetrahedron Lett. **1998**, *39* (26), 4651–4654.
43. Fürstner, A.; Müller, T. Metathesis Route to Resin Glycosides: Formal Total Synthesis of Tricolorin A. J. Org. Chem. **1998**, *63* (3), 424–425.
44. Fürstner, A.; Müller, T. Efficient Total Synthesis of Resin Glycosides and Analogues by Ring-Closing Olefin Metathesis. J. Am. Chem. Soc. **1999**, *121* (34), 7814–7821.
45. Fürstner, A.; Radkowski, K.; Grabowski, J.; Wirtz, C.; Mynott, R. Ring-Closing Alkyne Metathesis. Application to the Total Synthesis of Sophorolipid Lactone. J. Org. Chem. **2000**, *65* (25), 8758–8762.
46. Holt, D.J.; Barker, W.D.; Jenkins, P.R.; Davies L.D.; Garratt, S.; Fawcett, J.; Russell, D.R.; Ghosh, S. Ring-Closing Metathesis in Carbohydrate Annulation. Angew. Chem., Int. Ed. Engl. **1998**, *37* (23), 3298–3300.
47. Holt, D.J.; Barker, W.D.; Jenkins, P.R.; Panda, J.; Ghosh, S. Stereoselective Preparation of Enantiomerically Pure Annulated Carbohydrates Using Ring-Closing Metathesis. J. Org. Chem. **2000**, *65* (2), 482–493.
48. Leeuwenburgh, M.A.; Kulker, C.; Duynstee, H.I.; Overkleeft, H.S.; van der Marel, G.A.; van Boom, J.H. A Convenient Route to *cis*- and *trans*-Fused Bicyclic Ethers by Ruthenium Mediated Ring-Closing Metathesis of Diene and Enyne Carbohydrate Derivatives. Tetrahedron, **1999**, *55* (27), 8253–8262.
49. Oguri, H.; Tanaka, S.I; Oishi, T.; Hirama, M. A Very Short Route to the Functionalized A-Ring Moiety of Ciguatoxin. Tetrahedron Lett. **2000**, *41* (6), 975–978.
50. Leeuwenburgh, M.A.; Kulker, C. ; Overkleeft, H.S.; van der Marel, A.; van Boom, J.H. Synthesis of a *trans*-fused Tricyclic Ether Using a Novel Differentially Protected Glucal. Synlett **1999**, (12), 1942–1944.
51. Clark, J.S.; Hamelin, O. Synthesis of Polycyclic Ethers by Two-Directional Double Ring-Closing Metathesis. Angew. Chem., Int. Ed. Engl. **2000**, *39* (2), 372–373.
52. Dirat, O.; Vidal, T.; Langlois, Y. A New Route to *C*-Glycosylidene Compounds Mediated by Olefin Metathesis. Tetrahedron Lett. **1999**, *40* (?), 4801–4802.
53. van Hooft, P.A.V.; Leeuwenburgh, M.A.; Overkleeft, H.S.; van der Marel, G.A.; van Boeckel, C.A.A.; van Boom, J.H. A Novel and Flexible Synthesis of Pyranose Spiroacetal Derivatives. Tetrahedron Lett. **1998**, *39* (33), 6061–6064.
54. Hyldtoft, L.; Madsen, R. Carbohydrate Carbocyclization by a Novel Zinc-Mediated Domino Reaction and Ring-Closing Olefin Metathesis. J. Am. Chem. Soc. **2000**, *122* (35), 8444–8452.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

55. Fan, G.-T.; Hus, T.-S.; Lin, C.-C.; Lin, C.-C. Ring-Closing Olefin Metathesis of Prearranged *C*-Allyl Saccharides for the Synthesis of *C*-Butenyl Linked Homo- and Hetero-Disaccharides. Tetrahedron Lett. **2000**, *41* (34), 6593–6597.
56. Lobbel, M.; Köll, P. Ring-Closing Metathesis as a New Strategy for the *C*-*C* Coupling of Monosaccharides Derivatives via Silicon Tethering. Tetrahedron: Asymmetry **2000**, *11* (2), 393–396.

Received January 4, 2001
Accepted March 22, 2001

Request Permission or Order Reprints Instantly!