Asymmetric Synthesis of Highly Functionalized 8-Oxabicyclo[3.2.1]octene Derivatives

Huw M. L. Davies,* Gulzar Ahmed, and Melvyn Rowen Churchill

Contribution from the Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14260-3000

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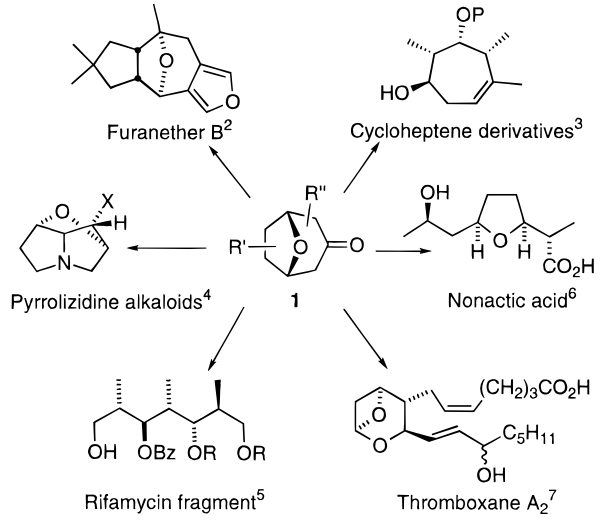
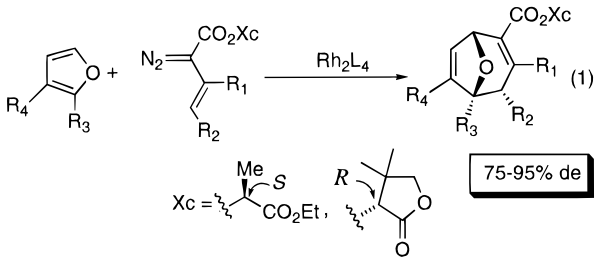
Abstract: Rhodium(II) carboxylate catalyzed decomposition of vinyldiazomethanes in the presence of furans results in a general synthesis of oxabicyclo[3.2.1]octa-2,6-diene derivatives. These oxabicyclic products are versatile intermediates in organic synthesis. The mechanism of the [3 + 4] annulation is considered to be a tandem cyclopropanation/Cope rearrangement. Such a mechanism is consistent with the excellent regio- and stereocontrol that is observed in these [3 + 4] annulations. Asymmetric synthesis of the oxabicyclic products is possible through utilization of rhodium(II) (*S*)-*N*-(*tert*-butylbenzene)sulfonylprolinate as catalyst or by using (*S*)-lactate or (*R*)-pantolactone as chiral auxiliaries on the carbenoid. The highest yields (69−95%) and asymmetric induction (82−95% de) were obtained using 3-siloxy-2-diazo-3-butenoate derivatives as the vinylcarbenoid precursors.

Stereochemically well-defined bicyclic derivatives have been extensively used as building blocks for the synthesis of natural products. A particularly useful starting unit has been the 8-oxabicyclo[3.2.1]oct-6-en-3-one system **1** as illustrated in Scheme 1.[1−7] Functionality can be introduced in a stereochemically well-defined manner at many sites in **1**, and by combining this chemistry with subsequent ring-opening reactions, a wide variety of cyclic and acyclic products containing multiple stereocenters can be obtained. Furthermore, they may be useful precursors to oxa analogs[2a] of 3-aryltropane-2-carboxylates,[8] which are of interest as potential medications for the treatment of cocaine addiction. A major drawback, however, with the utilization of 8-oxabicyclo[3.2.1]octanes in organic synthesis has been the lack of a general process for the asymmetric synthesis of these compounds. The only effective approach

Scheme 1



developed so far has been the desymmetrization of *meso*-8-oxabicyclo[3.2.1]octane derivatives.[9] This paper will describe a practical and general [3 + 4] annulation method for the asymmetric synthesis of 8-oxabicyclo[3.2.1]octanes as shown in general form in eq 1.



(1)

A number of useful methods to construct the 8-oxabicyclo-[3.2.1]octane system in racemic form have been developed over the past 25 years (Scheme 2).[1] The most widely established procedure is the [3 + 4] annulation between allyl cations and

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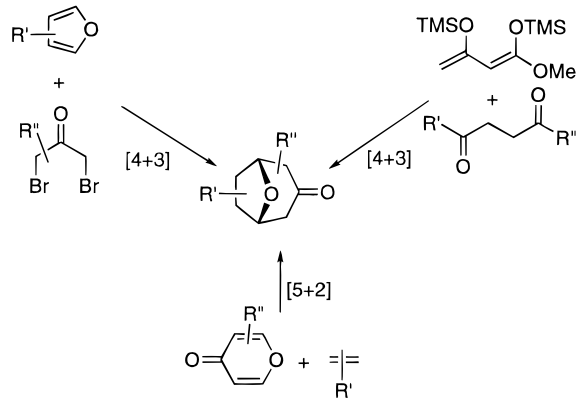
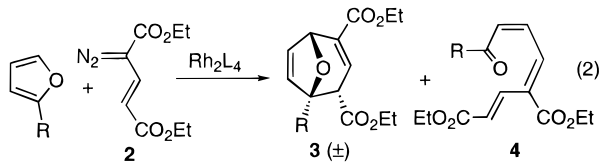
Scheme 2



furans.[1,10] The originally developed method by Hoffmann[1a] has since been optimized by Noyori[1b] through the use of iron oxyallyl complexes in place of simple allyl cations. An alternative [3 + 4] annulation strategy is the Lewis acid catalyzed annulation of 1,4-dicarbonyl compounds with 1,3-bis(trimethylsilyl)oxy dienes.[2] 8-Oxabicyclo[3.2.1]octanes can also be prepared by [5 + 2] annulations between oxidopyrylium and alkenes.[11]

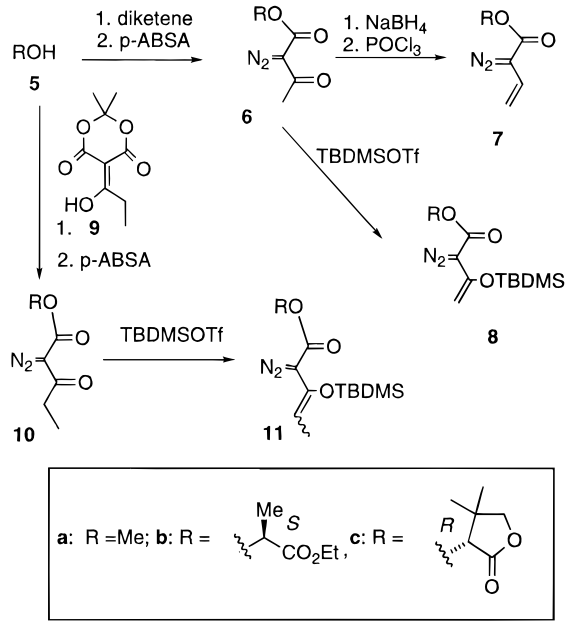
We have previously shown that the reaction of rhodium(II)-stabilized vinylcarbenoids with furans can generate 8-oxabicyclo-[3.2.1]octanes in certain cases.[12] In these earlier studies the diester **2** was used as the vinylcarbenoid precursor. The most important trends that were found are summarized in eq 2. Even



	R	**3**, %	**4**, %
a	H	62	26
b	Me	8	74
c	OMe	0	92

though 8-oxabicyclo[3.2.1]octadienes **3** could be formed, a major side product were trienes **4** which were considered to arise through the intermediacy of zwitterionic species formed by attack of the carbenoid at the α-position of the furans.[13] Consequently, electron-donating groups that favored stabilization of zwitterionic intermediates enhanced triene formation, such that in the case of 2-methoxyfuran, the triene **4c** was the exclusive product.[12] Since this work, we have extensively developed the chemistry of rhodium-stabilized vinylcarbenoids,[14] and this has included the utilization of highly efficient chiral

Scheme 3



auxiliaries on the vinylcarbenoid[15] and chiral catalysts[16] for asymmetric synthesis. In this paper we describe how we have been able to develop a practical asymmetric entry to 8-oxabicyclo-[3.2.1]octadienes by using these recent advances in the chemistry of rhodium-stabilized vinylcarbenoids.

On the basis of our earlier studies,[14] vinylcarbenoid precursors containing a single electron-withdrawing group were considered to be the most promising substrates for annulation reactions with furans. The presence of at least one electron-withdrawing group is necessary for stereoselective vinylcarbenoid cyclopropanations, but having only a single electron-withdrawing group would minimize the likelihood of competing reactions occurring via zwitterionic intermediates.[17]

The synthesis of the vinylcarbenoid precursors was conveniently achieved as illustrated in Scheme 3. Treatment of ethyl (*S*)-lactate (**5b**) or (*R*)-pantolactone (**5c**) with diketene followed by *para*-acetamidobenzenesulfonyl azide (*p*-ABSA) resulted in the formation of the diazoacetoacetates **6b,c**. The methyl ester **6a** was prepared as previously reported.[18] Conversion of **6a,b** to the vinyldiazomethanes **7a,b** was readily achieved by reduction of the ketone in **6a,b** with sodium borohydride followed by dehydration of the resulting alcohol with phosphorus oxychloride in the presence of triethylamine.[19] The siloxy-substituted vinyldiazomethanes **8a**−**c** were prepared by silylation of **6a**−**c** with TBDMS triflate in the presence of triethylamine.[20] The synthesis of the methyl-substituted vinyldiazomethanes **11b** and **11c** was achieved in a related manner to the formation of **8** except that the initial reaction with the alcohol was carried out with the propionylated Meldrum's acid

(10) For recent examples of allyl cation cycloadditions with furans, see: (a) Harmata, M.; Elomari, S.; Barnes, C. L. *J. Am. Chem. Soc.* **1996**, *118*, 2860. (b) Harmata, M.; Gamlath, C. B.; Barnes, C. L.; Jones, D. E. *J. Org. Chem.* **1995**, *60*, 5077. (c) Walters, M. A.; Arcand, H. R. *J. Org. Chem.* **1996**, *61*, 1478. (d) Jin, S.; Choi, J.-R.; Oh, J.; Lee, D.; Cha, J. K. *J. Am. Chem. Soc.* **1995**, *117*, 10914.

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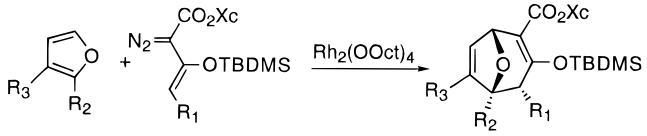
Table 1. Diastereoselective Synthesis of 3-Siloxy-8-oxabicyclo[3.2.1]octa-2,6-diene-2-carboxylates

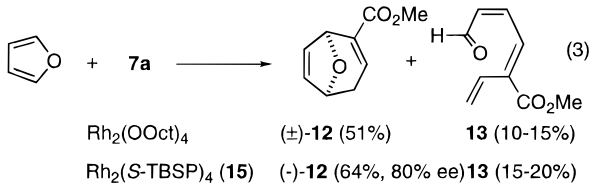


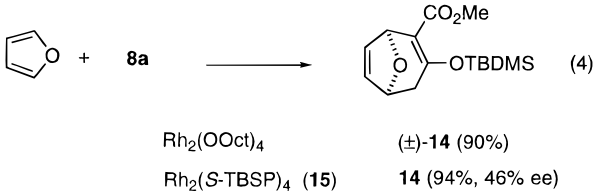
Xc	R_1	R_2	R_3	product	yield, %	de,[a] % (abs stereochem)
(*S*)-lactate	H	H	H	**17**	72	79 (1*S*)
(*R*)-pantolactone	H	H	H	**18**	82	94 (1*R*)
(*S*)-lactate	Me	H	H	**19**	62	90 (1*S*)
(*R*)-pantolactone	Me	H	H	**20**	75	95 (1*R*)
(*S*)-lactate	H	Me	H	**21**	81	75 (1*S*)
(*R*)-pantolactone	H	Me	H	**22**	91	83 (1*R*)
(*S*)-lactate	Me	Me	H	**23**	91	84 (1*S*)
(*R*)-pantolactone	Me	Me	H	**24**	69	94 (1*R*)
(*S*)-lactate	H	COMe	H	**25**	74	79 (1*S*)
(*R*)-pantolactone	H	COMe	H	**26**	65	94 (1*R*)
(*S*)-lactate	Me	COMe	H	**27**	71	80 (1*S*)
(*R*)-pantolactone	H	Me	CO_2Me	**28**	65	82 (1*R*)

[a] de determined from the ^{1}H NMR of the crude reaction mixture. All (*R*)-pantolactone derivatives can be obtained in >99% de after flash chromatography.

9 instead of diketene.[21] The *Z* configuration of **11** was shown to be the predominant form (9:1 *Z/E* for **11b**, 3.3:1 *Z/E* for **11c**) by nOe difference analysis which showed a distinctive enhancement of the vinyl methyl protons on irradiation of the silyl methyl protons.

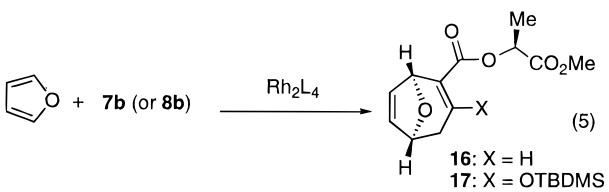
The first series of experiments were directed toward determining if conditions could be developed for high-yield formation of oxabicyclic products. As the use of nonpolar solvents had been shown to disfavor the formation of products derived from zwitterionic intermediates,[17] all reactions in the current study were carried out using hexanes as the solvent. Rhodium(II) octanoate catalyzed decomposition of **7a** in the presence of furan resulted in the formation of the oxabicycle **12** in 51% yield. The product, however, was accompanied by 10−15% yield of the unstable triene **13**. The 4:1 ratio of **12** to **13** was not very promising because on the basis of the earlier studies, the triene structure would be expected to become much more prevelant in reactions of **7a** with more electron-rich furans. A similar reaction was then carried out except that the siloxy-substituted vinyldiazomethane **8a** was used as the vinylcarbenoid precursor. In contrast to the reaction of **7a**, the reaction with **8a** as substrate was very clean, leading to the formation of the oxabicycle **14** in 90% yield.





Having found an effective vinylcarbenoid precursor that leads to a high-yield synthesis of the oxabicyclic system, some preliminary experiments were carried out to determine if these reactions could proceed with high asymmetric induction using chiral catalysis. Rhodium(II) (*S*)-*N*-(*tert*-butylbenzene)sulfonylprolinate (Rh_2(*S*-TBSP)$_4$, **15**)[16] has been shown to be a versatile catalyst in a number of asymmetric transformations involving vinylcarbenoids, but there was some concern whether this rather electron deficient rhodium(II) carboxylate would increase the occurrence of triene side products. These concerns were unfounded as the reactions with Rh_2(*S*-TBSP)$_4$ as catalyst led to similar product ratios but higher overall yields compared to the rhodium(II) octanoate catalyzed reactions. Rh_2(*S*-TBSP)$_4$ catalyzed decomposition of **7a** resulted in the formation of the oxabicycle (−)-**12** in 80% ee (64% yield) with 15−20% yield of the triene side product. On the other hand, Rh_2(*S*-TBSP)$_4$ catalyzed decomposition of **8a** in the presence of furan proceeded smoothly to form the oxabicycle **14** in excellent yield (94%) but with only moderate enantioselectivity (46% ee).

Facing the quandry that the best substrate (**8a**) for oxabicycle formation resulted in low enantioselectivity, we decided to explore if the alternative asymmetric approach for vinylcarbenoid transformations using α-hydroxy ester auxiliaries on the carbenoid[15] would lead to a more general solution for the asymmetric synthesis of oxabicycles. As these chiral auxiliaries are believed to be involved in neighboring group participation to the carbenoid, the possibility existed that these auxiliaries would also alter the chemoselectivity of these transformations. Rhodium(II) octanoate catalyzed decomposition of **7b** resulted in the formation of **16** in 63% yield but the chemoselectivity of the process compared to the methyl ester **7a** was unchanged, as about 15% of an unstable triene was also formed. The diastereoselectivity of the reaction was rather moderate, as **16** was formed in 57% de. Some improvement in the diastereoselectivity was possible through double stereodifferentiation using the lactate auxiliary in conjunction with a chiral catalyst. The reaction with Rh_2(*S*-TBSP)$_4$ resulted in an improvement of the diastereoselectivity to 68% de, while the miss-matched reaction with Rh_2(*R*-TBSP)$_4$ resulted in the formation of **16** with essentially 0% de.

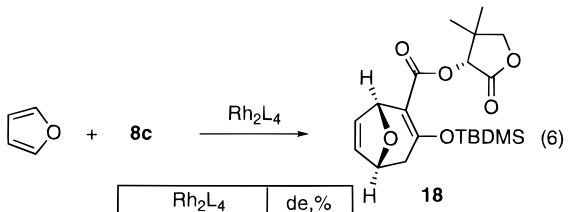


Rh_2L_4	**16**, de, %	**17**, de, %
Rh_2(OOct)$_4$	57	79
Rh_2(*S*-TBSP)$_4$	68	80
Rh_2(*R*-TBSP)$_4$	0	53

(21) Oikawa, Y.; Sugano, K.; Yonemitsu, O. *J. Org. Chem.* **1978**, *43*, 2087.

A significantly improved procedure was developed using vinyldiazomethanes that contained a 2-siloxy group and the α-hydroxy ester chiral auxiliary. Rhodium(II) octanoate catalyzed decomposition of **8b** in the presence of furan resulted in the formation of the oxabicycle **17** in good yield (72%) and diastereoselectivity (79% de). No triene side products were formed in this case. Double stereodifferentiation was observed on repeating these reactions with Rh_2(*S*-TBSP)$_4$ (80% de) and Rh_2(*R*-TBSP)$_4$ (53% de), but the overall enantioselectivity was not greatly improved compared to the achiral catalyst. One advantage, however, of using a prolinate catalyst is that the yields of these transformations were higher (97−99%) than were observed with the rhodium(II) octanoate catalyst. Similar improvement in yields by using a more electron deficient rhodium(II) catalyst has been previously observed in the reaction between carbenoids and benzene derivatives.[22]

Even higher levels of diastereoselectivity were possible by using (*R*)-pantolactone as the chiral auxiliary. Rhodium(II) octanoate catalyzed decomposition of **8c** in the presence of furan resulted in the formation of the oxabicycle **18** in 94% de and 82% yield. Double stereodifferentiation occurred using the chiral prolinate catalysts, but both catalysts resulted in lower diastereoselectivity than was obtained using the achiral rhodium(II) octanoate catalyst.



Rh_2L_4	de,%
Rh_2(OOct)$_4$	94
Rh_2(*S*-TBSP)$_4$	20
Rh_2(*R*-TBSP)$_4$	67

In order to ascertain that the tandem cyclopropanation/Cope rearrangement can be used to predictably produce a third stereogenic center into the oxabicyclic system, the next series of experiments explored the reactions of the vinyldiazomethanes **11b**. Rhodium(II) octanoate catalyzed decomposition of **11b** resulted in the formation of the *endo* product **19** in 62% yield (Table 1). The *endo* stereochemistry for **19** was readily assigned on the basis of the distinctive coupling between the C-4 and C-5 protons (J = 5 Hz for H-4 *exo*, J = 0 Hz for H-4 *endo*). No *exo* product was formed in the reaction even though the starting vinyldiazomethane consisted of a 9:1 *Z/E* mixture. The asymmetric induction in the formation of **19** was very good (90% de) and represents the highest level that we have observed in carbenoid transformations using a lactate as a chiral auxiliary. An even higher level of diastereoselectivity was observed in the reaction of furan with the pantolactone derivative **11c**, as this resulted in the exclusive formation of the *endo* product **20** in 95% de.

These reactions are applicable to a series of furans as summarized in Table 1. Both moderately electron-donating and electron-withdrawing substituents can be tolerated on the furan without appreciable change in the diastereoselectivity or overall yield for the oxabicycle formation. Only a single regioisomer of the oxabicycle is formed in each case, and this isomer is the expected product for a reaction that proceeds by a tandem cyclopropanation/Cope rearrangement where the initial cyclopropanation occurs at the sterically more accessible double bond. The pantolactone auxiliary offers a distinct advantage because all the oxabicyclic products containing this auxiliary can be conveniently obtained in greater than 99% de by column chromatography.

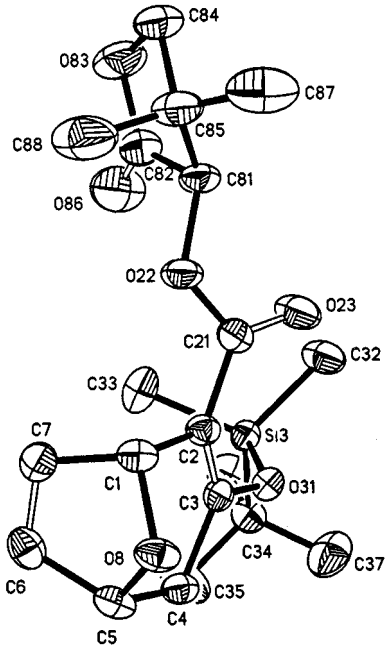


Figure 1. X-ray representation of **18**.

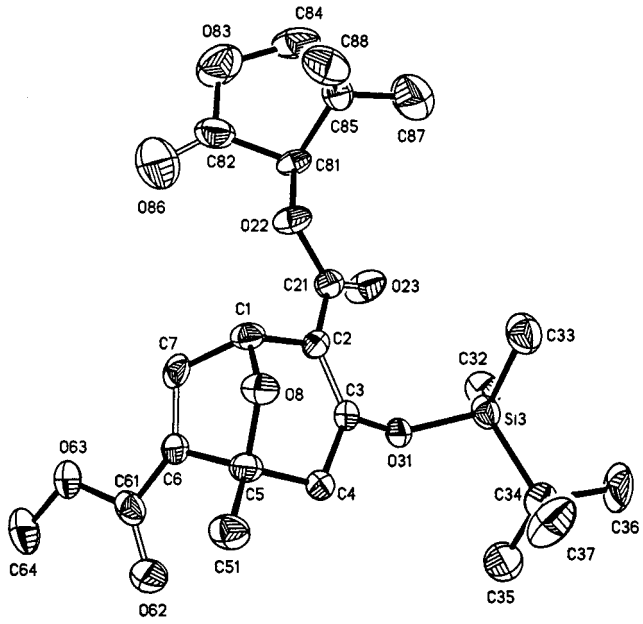


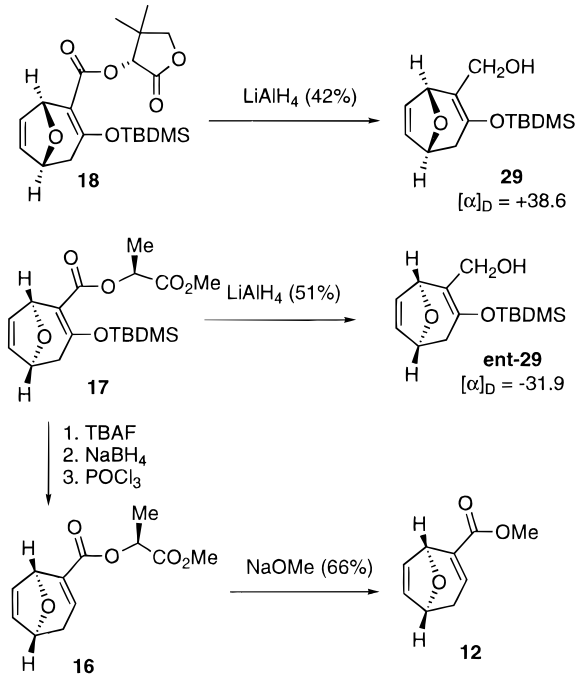
Figure 2. X-ray representation of **28**.

The absolute stereochemistry of two of the compounds in this series, **18** and **28**, was proven unequivocally by X-ray structural determination as shown in Figures 1 and 2.[23] In our earlier studies on the use of chiral auxiliaries for asymmetric cyclopropanation, it was shown that the (*S*)-lactate and (*R*)-pantolactone auxiliaries resulted in opposite asymmetric induction.[15] This was confirmed to be also the case in these reactions with furans by reduction of both **17** and **18** with lithium aluminium hydride to the resulting alcohols (**29** and **ent-29**), followed by comparison of their optical rotation (Scheme 4). The absolute stereochemistry of the products derived from the vinyldiazomethanes **7b** and **8b** was correlated by conversion of **17** to **16**. The same diastereomer of **16** was formed from **17** (derived from the reaction between furan and the siloxy substituted vinyldiazomethane **8b**) and the reaction between

(22) Kennedy, M.; McKervey, M. A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2565.

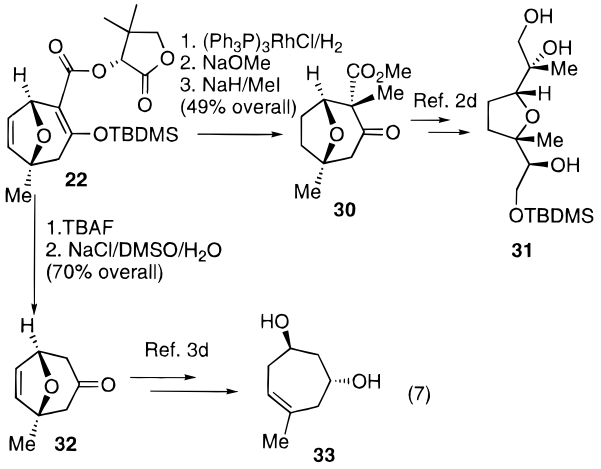
(23) Full details of the X-ray crystallographic data will be given in a separate publication.

Scheme 4

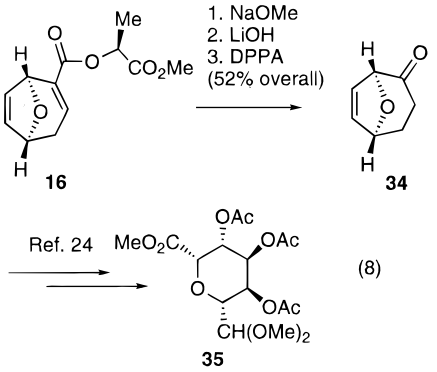


furan and the vinyldiazomethane **7b**. Finally, by conversion of **16** to **12**, it was possible to show that the lactate auxiliary and the (L)-prolinate catalyst **15** caused selection of the same face of the carbenoid (*re* face) during the cyclopropanation. The absolute stereochemistry of the other oxabicycles has been assigned on the assumption that the model for the asymmetric induction (see Discussion) is similar for all of the carbenoid transformations.

The oxabicycles are readily amenable for further conversion to a number of useful compounds that have been previously used in racemic form in synthesis. For example, the 5-methyl derivative **22**, which can be obtained in greater than 99% de by column chromatography, is readily converted to the β-ketoester **30** in 49% overall yield by catalytic hydrogenation using Wilkinson's catalyst, transesterification with sodium methoxide in methanol, followed by alkylation with methyl iodide. Racemic **30** was used by Molander in a recent synthesis of **31**, an advanced intermediate for natural product synthesis.[2d] Alternatively, **22** on treatment with tetrabutylammonium fluoride followed by sodium chloride in DMSO can be converted directly to the ketone **32** in 70% yield. The ring opening of racemic **32** was shown by Lautens to result in the stereoselective synthesis of cycloheptenediol **33**.[3d]



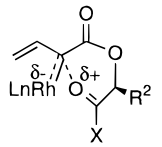
8-Oxabicyclo[3.2.1]oct-6-en-2-ones are also available from this chemistry as illustrated in eq 8. Treatment of **16** with sodium methoxide and then lithium hydroxide followed by subjecting the resulting acid to the standard Curtius rearrangement conditions resulted in the formation of 8-oxabicyclo-[3.2.1]oct-6-en-2-one (**34**) in 52% yield. Racemic **34** has been used by Vogel in a stereoselective synthesis of the β C-hexopyranoside **35**.[24]



Discussion

The tandem cyclopropanation/Cope rearrangement between vinylcarbenoids and furans is a very attractive approach for the asymmetric synthesis of oxabicyclic systems. Utilization of a 2-siloxy substituent on the the vinylcarbenoid enhances the formation of the oxabicycle, and avoids the occurrence of triene side products. The advantages associated with the use of a 2-siloxy substituted vinylcarbenoid to avoid products derived from zwitterionic intermediates has been observed in intramolecular reactions with pyrroles and has been considered to be due to either conformational effects on the carbenoid or the enhanced nucleophilicity of the vinyl group.[25] A further advantage of the 2-siloxy substituent is that it leads to the ready synthesis of the 8-oxabicyclo[3.2.1]oct-6-en-3-ones. These compounds have been typically prepared as racemates from the reaction of oxyallyl cations with furans and have been extensively used in organic synthesis. The ready access of enantiomerically pure 8-oxabicyclo[3.2.1]oct-6-en-3-ones described herein will further enhance the utility of these valuable building blocks.

The most general method to achieve asymmetric induction in these reactions was to use a chiral auxiliary on the carbenoid. (*R*)-Pantolactone was the best chiral auxiliary because it led to the highest levels of asymmetric induction (82−95% de), and furthermore, the resulting products were conveniently purified to greater than 99% de by flash chromatography. The asymmetric induction observed in these reactions can be readily rationalized by assuming that the carbonyl group of the auxiliary interacts with the carbenoid as shown in structure **36**. The



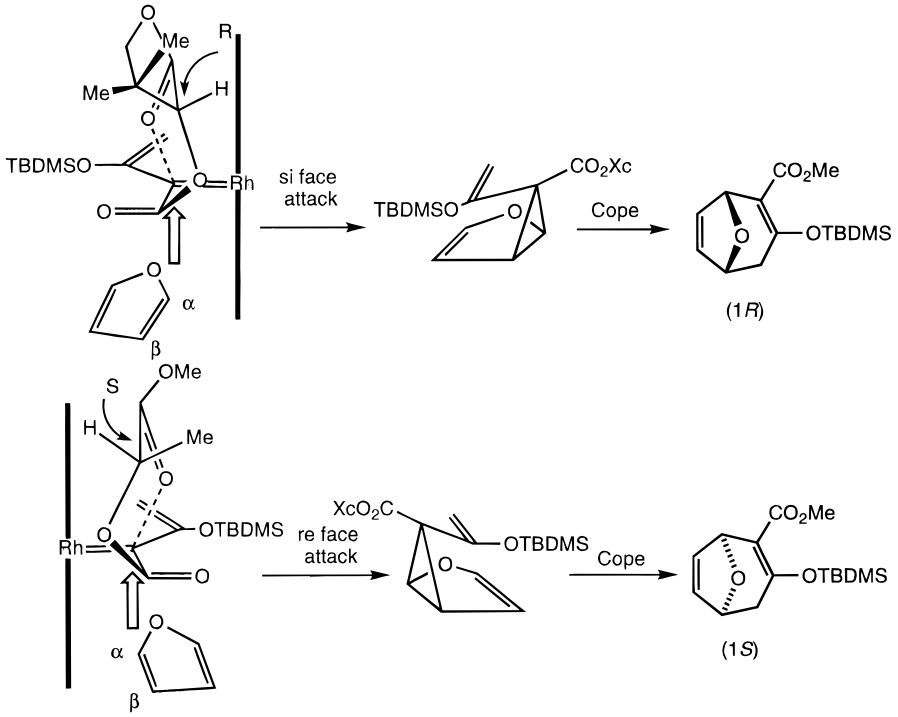
interaction allows efficient transfer of the chiral influence of the stereogenic center on the auxiliary to the carbenoid position, but the extent of the interaction is limited such that the species still has carbenoid reactivity rather than ylide reactivity.[26] In our earlier studies on asymmetric cyclopropanation using chiral

(24) (a) Fattori, D.; Vogel, P. *Tetrahedron Lett.* **1993**, *34*, 1017. (b) Fattori, D.; Henry, S.; Vogel, P. *Tetrahedron* **1993**, *49*, 1649.

(25) Davies, H. M. L.; Matasi, J. J.; Ahmed, G. *J. Org. Chem.* **1996**, *61*, 2305.

(26) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263.

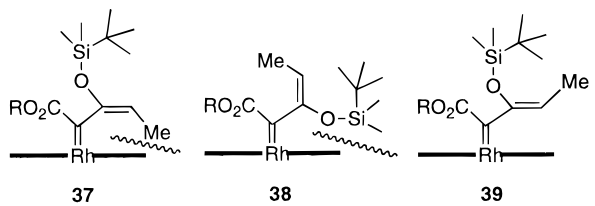
Scheme 5



auxiliaries on the vinylcarbenoid, we showed that an ester carbonyl on the auxiliary is the most suitable substituent.[15]

The favored interactions with the carbenoid for the (*S*)-lactate and (*R*)-pantolactone auxiliaries (Scheme 5) would be expected to minimize steric interactions between the auxiliary and the "wall" of the catalyst.[15] The overall effect is to block one of the two faces of the vinylcarbenoid intermediate to approach by the furan. As the (*S*)-lactate and (*R*)-pantolactone auxiliaries have opposite absolute stereochemistry they result in the formation of oxabicycles of opposite absolute stereochemistry. The observed stereochemistry is consistent with a tandem cyclopropanation/Cope rearrangement in which the first cyclopropanation occurs in a non-synchronous mode with initial interaction at the 2-position of the furan. It should be noted that if the initial interaction had occurred at the 3-position of the furan, the opposite asymmetric induction would have occurred. Indeed the opposite asymmetric induction has been observed in the reactions of vinylcarbenoids with *N*-(*tert*-butoxycarbonyl)pyrrole, where the steric influence of the *tert*-butoxycarbonyl group overides the natural tendency of the pyrrole ring for electrophilic attack at the 2-position.[15b]

One set of reactions that merit further comment is that of the methyl substituted vinyldiazomethanes, **11b** and **11c** (Table 1). Not only do these reactions proceed with very high asymmetric induction, but also, *endo* products are exclusively formed even though **11b** and **11c** consist of *E*/*Z* mixtures. The most reasonable explanation for this remarkable stereoselectivity is that only the (*Z*)-vinyldiazomethane can effectively react with furan by the rhodium-catalyzed process. As shown in structures **37** and **38**, the vinylcarbenoid derived from the (*E*)-vinyldiazomethane is unable to avoid steric hindrance with the wall of the catalyst, but this is not the case for the vinylcarbenoid **39** derived from the (*Z*)-vinyldiazomethane. The influence of steric crowding on vinylcarbenoid reactivity has been seen in many systems,[27] and the result here may represent a further example of such steric effects.



37 **38** **39**

In summary, this study has resulted in a very practical approach for the asymmetric synthesis of oxabicyclic systems. These oxabicyclic compounds represent valuable building blocks in organic synthesis. Furthermore, the study illustrates the complimentarity of the chiral auxiliary and chiral catalyst approaches for asymmetric transformations using vinylcarbenoid intermediates.

Experimental Section

General Methods: Diethyl ether, hexane and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl. Dichloromethane and acetonitrile were distilled from calcium hydride. Toluene and benzene were dried over molecular sieves (4 Å). ^{1}H and ^{13}C NMR spectra were recorded on 300 MHz, 400 MHz or 500 MHz NMR spectrometers. Column chromatography was carried out on silica gel 60 (230−400 mesh). Thin layer chromatography (TLC) was performed on Whatman (TLC) paper. Furans, diketene and Meldrum's acid were purchased from Aldrich chemical company. 5-Propionyl-Meldrum's acid,[20] rhodium(II) prolinate catalyst **15**,[16] **6a**−**c**,[15b] **7a,b**,[15b] and *p*-acetamidobenzenesulfonyl azide[19] were prepared by the literature methods.

Methyl 2-Diazo-3-[(1,1-dimethylethyl)dimethylsiloxy]-3-butenoate (8a). Triethylamine (2 mL, 14.3 mmol) was added to a stirring solution of **6a** (3.1 g, 10.1 mmol) in dichloromethane (26 mL) at 0 °C under argon. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (2.8 mL, 12.2 mmol) was added over 5 min and the mixture was further stirred for 30 min at 0 °C. The reaction mixture was diluted with hexanes (100 mL), and the organic phase was washed with dilute aqueous sodium bicarbonate (100 mL) and brine (100 mL). The organic layer was dried ($MgSO_4$), and the solvent was removed under reduced pressure to yield **8a** as a yellow oil (essentially quantitative yield) which was used without further purification: IR (neat) 2950, 2893, 2857, 2107, 1714, 1669, 1610, 1466, 1440, 1352 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.98 (d, J = 1.8 Hz, 1 H), 4.23 (d, J = 1.8 Hz, 1 H), 3.78 (s, 3 H),

(27) (a) Davies, H. M. L.; Houser, J. H.; Thornley C. *J. Org. Chem.* **1995**, *60*, 7529. (b) Davies, H. M. L.; Hu, B.; Saikali, E.; Bruzinski, P. R. *J. Org. Chem.* **1994**, *59*, 4535.

0.90 (s, 9 H), 0.21 (s, 6 H). Due to lack of stability, elemental analysis was not attempted on **8a**.

(*S*)-2-Ethoxy-1-methyl-2-oxoethyl 2-Diazo-3-[(1,1-dimethylethyl)-dimethylsiloxy]-3-butenoate (8b) was prepared from **6b** (1.0 g, 4.38 mmol) in essentially quantitative yield by treatment with *tert*-butyldimethylsilyl trifluoromethanesulfonate and triethylamine according to the procedure described for the synthesis of **8a**: IR (neat) 2960, 2939, 2887, 2862, 2106, 1760, 1718, 1667, 1615 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.17 (q, $J = 7.6$ Hz, 1 H), 4.97 (d, $J = 2.0$ Hz, 1 H), 4.24 (d, $J = 2.0$ Hz, 1 H), 4.21 (q, $J = 6.8$ Hz, 2 H), 1.50 (d, $J = 7.6$ Hz, 3 H), 1.27 (t, $J = 6.8$ Hz, 3 H), 0.91 (s, 9 H), 0.22 (s, 6 H). Due to lack of stability, elemental analysis was not attempted on **8b**.

(*R*)-Tetrahydro-4,4-dimethyl-2-oxo-3-furanyl 2-Diazo-3-[(1,1-dimethylethyl)dimethylsiloxy]-3-butenoate (8c) was prepared from **6c** (1.7 g, 7.08 mmol) in essentially quantitative yield by treatment with *tert*-butyldimethylsilyl trifluoromethanesulfonate and triethylamine according to the procedure described for the synthesis of **8a**: IR (neat) 2960, 2934, 2898, 2862, 2112, 1796, 1724, 1615 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.43 (s, 1 H), 4.95 (d, $J = 2.0$ Hz, 1 H), 4.25 (d, $J = 2.0$ Hz, 1 H), 4.05 (d, $J = 9.8$ Hz, 1 H), 4.02 (d, $J = 9.8$ Hz, 1 H), 1.21 (s, 3 H), 1.07 (s, 3 H), 0.89 (s, 9 H), 0.21 (s, 6 H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 172.4, 163.0, 140.3, 90.7, 76.1, 75.1, 39.9, 25.3, 22.7, 19.5, 17.8, −5.0, −5.1 (*C* = N_2 not observed). Due to lack of stability, elemental analysis was not attempted on **8c**.

(*S*)-2-Ethoxy-1-methyl-2-oxoethyl 2-Diazo-3-oxopentanoate (10b). A solution of ethyl (*S*)-(-)-lactate (2.39 g, 20.28 mmol), 5-propionyl Meldrum's acid (4.0 g, 19.98 mmol) and pyridine (1.7 mL, 21.01 mmol) in benzene (50 mL) was heated at 60−65 °C for 16 h under argon. The mixture was then cooled to room temperature, diluted with Et_2O (50 mL), and the resulting mixture was washed with sat. aq. NH_4Cl (100 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel with 1:3 Et_2O:hexanes as solvents to yield (*S*)-2-ethoxy-1-methyl-2-oxoethyl 3-oxopentanoate as an oil (2.65 g, 62% yield): $R_f = 0.64$ in 1:1 Et_2O:hexanes: IR (neat) 2989, 2943, 2904, 1757, 1717, 1632 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.11 (q, $J = 6.8$ Hz, 1 H), 4.20 (q, $J = 6.8$ Hz, 2 H), 3.51 (s, 2 H), 2.61 (q, $J = 6.8$ Hz, 2 H), 1.50 (d, $J = 6.8$ Hz, 3 H), 1.27 (t, $J = 6.8$ Hz, 3 H), 1.08 (t, $J = 6.8$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.9, 170.4, 166.7, 69.1, 61.2, 48.3, 35.7, 16.3, 13.6, 7.0. Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.33; H, 7.46. Found: C, 55.70; H, 7.51.

Triethylamine (1.6 mL, 11.47 mmol) was added to a stirred solution of *p*-acetamidobenzenesulfonyl azide (2.75 g, 11.45 mmol) and (*S*)-2-ethoxy-1-methyl-2-oxoethyl 3-oxopentanoate (2.45 g, 11.34 mmol) in acetonitrile (20 mL) at 0−5 °C under argon. The reaction mixture was stirred overnight at room temperature and then diluted with 1:1 Et_2O:hexane (150 mL). The resulting precipitate was filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel with 1:3 Et_2O:hexanes as solvent to yield **10b** as an oil (2.2 g, 80% yield), $R_f = 0.32$ in Et_2O:hexane: IR (neat) 2983, 2943, 2881, 2137, 1762, 1723, 1666 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.12 (q, $J = 6.6$ Hz, 1 H), 4.16 (q, $J = 7.1$ Hz, 2 H), 2.78 (q, $J = 7.1$ Hz, 2 H), 1.47 (d, $J = 6.6$ Hz, 3 H), 1.22 (t, $J = 7.1$ Hz, 3 H), 1.05 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.8, 170.9, 161.4, 69.6, 61.9, 33.9, 17.0, 14.2, 8.3 (*C* = N_2 not observed). Anal. Calcd for $C_{10}H_{14}N_2O_5$: C, 49.58; H, 5.83; N, 11.56. Found: C, 49.66; H, 5.88; N, 11.59.

(*R*)-Tetrahydro-4,4-dimethyl-2-oxo-3-furanyl 2-Diazo-3-oxopentanoate (10c). A solution of (*R*)-(-)-pantolactone (2.8 g, 21.51 mmol), 5-propionyl Meldrum's acid (4.3 g, 21.48 mmol) and pyridine (1.8 mL, 22.25 mmol) in benzene (50 mL) was heated at 65−70 °C for 40 h under argon. The mixture was then cooled to room temperature, diluted with Et_2O (50 mL), and the resulting mixture was washed with sat. aq. NH_4Cl (100 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel with 1:1 Et_2O:hexanes as solvent to yield (*R*)-tetrahydro-4,4-dimethyl-2-oxo-3-furanyl 3-oxopentanoate as an oil (4.11 g, 84% yield): $R_f = 0.14$ in 1:1 Et_2O:hexanes: IR (neat) 2975, 2938, 1789, 1755, 1716 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.38 (s, 1 H), 4.01 (s, 2 H), 3.63 (d, $J = 15.9$ Hz, 1 H), 3.53 (d, $J = 15.9$ Hz, 1 H), 2.56 (q, $J = 7.2$ Hz, 2 H), 1.21 (s, 3 H), 1.09 (s, 3 H), 1.06 (t, $J = 7.2$ Hz, 3 H).

Triethylamine (2 mL, 14.34 mmol) was added to a stirred solution of *p*-acetamidobenzenesulfonyl azide (3.35 g, 13.47 mmol) and (*R*)-tetrahydro-4,4-dimethyl-2-oxo-3-furanyl 3-oxopentanoate (3.18 g, 13.47 mmol) in acetonitrile (40 mL) at rt under argon. The reaction mixture was stirred overnight at rt and then diluted with 1:1 Et_2O:pentane (150 mL). The resulting precipitate was filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel with 1:1 Et_2O:pentane as solvent to yield **10c** as an oil (3.52 g, 99% yield), $R_f = 0.26$ in Et_2O:hexane: IR (neat) 2980, 2939, 2135, 1792, 1733, 1664 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.44 (s, 1 H), 4.07 (d, $J = 9.4$ Hz, 1 H), 4.05 (d, $J = 9.4$ Hz, 1 H), 2.83 (q, $J = 7.3$ Hz, 2 H), 1.23 (s, 3 H), 1.10 (t, $J = 7.3$ Hz, 3 H), 1.10 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.7, 171.9, 160.3, 76.0, 75.5, 39.9, 33.5, 22.5, 19.5, 7.7 (*C* = N_2 not observed). Anal. Calcd for $C_{11}H_{14}N_2O_5$: C, 51.97; H, 5.55; N, 11.02. Found: C, 51.85; H, 5.53; N, 10.95.

(*S*)-2-Ethoxy-1-methyl-2-oxoethyl (*Z*)-2-Diazo-3-[(1,1-dimethylethyl)dimethylsiloxy]pentanoate (11b) was prepared from **10b** (1.7 g, 7.02 mmol) in essentially quantitative yield by treatment with *tert*-butyldimethylsilyl trifluoromethanesulfonate and triethylamine according to the procedure described for the synthesis of **8a**: IR (neat) 2965, 2934, 2867, 2096, 1765, 1713, 1662 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.22 (q, $J = 7.0$ Hz, 1 H), 5.12 (q, $J = 7.0$ Hz, 1 H), 4.17 (q, $J = 7.1$ Hz, 2 H), 1.63 (d, $J = 7.0$ Hz, 3 H), 1.47 (d, $J = 7.0$ Hz, 3 H), 1.24 (t, $J = 7.1$ Hz, 3 H), 0.92 (s, 9 H), 0.14 (s, 3 H), 0.12 (s, 3 H). Due to lack of stability, elemental analysis was not attempted on **11b**.

(*R*)-Tetrahydro-4,4-dimethyl-2-oxo-3-furanyl (*Z*)-2-Diazo-3-[(1,1-dimethylethyl)dimethylsiloxy]pentanoate (11c) was prepared from **10c** (0.60 g, 2.36 mmol) in essentially quantitative yield by treatment with *tert*-butyldimethylsilyl trifluoromethanesulfonate and triethylamine according to the procedure described for the synthesis of **8a**: IR (neat) 2959, 2930, 2858, 2094, 1791, 1717, 1654 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.43 (s, 1 H), 5.25 (q, $J = 7.0$ Hz, 0.77 H for *Z* isomer), 5.08 (q, $J = 7.0$ Hz, 0.23 H for *E* isomer), 4.06 (d, $J = 9.1$ Hz, 1 H), 4.02 (d, $J = 9.1$ Hz, 1 H), 1.67 (d, $J = 7.0$ Hz, 2.3 H for *Z* isomer), 1.58 (d, $J = 7.0$ Hz, 0.69 H for *E* isomer), 1.22 (s, 3 H), 1.08 (s, 3 H), 0.95 (s, 9 H), 0.16 (s, 3 H), 0.09 (s, 3 H). Due to lack of stability, elemental analysis was not attempted on **11c**.

Methyl 8-Oxabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (12). A solution of **7a** (0.45 g, 3.57 mmol) in hexane (100 mL) was added dropwise over 1h to a refluxing solution of rhodium (II) octanoate (0.027 g, 0.034 mmol) and furan (2.43 g, 35.78 mmol) in hexane (100 mL) under argon. The resulting solution was refluxed for a further 15 min, the solvent was removed and the residue was purified by column chromatography on silica gel using Et_2O/pentane (1:4) as solvent to give **12** as colorless oil (0.31 g, 51% yield): IR (neat) 2960, 2893, 2851, 2800, 1713, 1641, 1589 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.56 (brt, $J = 3.5$ Hz, 1 H), 6.53 (dd, $J = 5.8$, 1.5 Hz, 1 H), 5.97 (dd, $J = 5.8$, 1.5 Hz, 1 H), 5.17 (br s, 1 H), 4.90 (d, $J = 5.8$ Hz, 1 H), 3.72 (s, 3 H), 2.74 (dddd, $J = 19.8$, 5.8, 3.0, 1.2 Hz, 1 H) 1.87 (dd, $J = 19.8$, 4.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 137.6, 135.9, 135.3, 127.6, 76.8, 75.3, 51.5, 26.8. Anal. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 64.93; H, 6.09. Reaction with Rhodium-(II) (*S*)-prolinate (**15**) gave **12** in 64% yield and 80% ee (1*S*,5*S* isomer); $[\alpha]^{25}_D = -43.3°$ (*c* 1.0, $CHCl_3$). Enantiomeric excess (% ee) was determined by ^1H NMR at 300 MHz using tris[3-(heptafluoropropyl-hydroxymethylene)-(-)-camphorate] praseodymium(III) derivative (0.07 equiv.) and the integration of the split signals due to the methoxy group.

Methyl 3-[(1,1-Dimethylethyl)dimethylsiloxy]-8-oxabicyclo[3.2.1]-octa-2,6-diene-2-carboxylate (14) was prepared from **8a** (10.0 g, 39.0 mmol) in 90% yield by treatment with rhodium(II) octanoate and furan in hexane according to the procedure described for the synthesis of **12**: IR (neat) 2955, 2924, 2900, 2858, 1722, 1692, 1608 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.53 (d, $J = 5.8$ Hz, 1 H), 5.92 (d, $J = 5.8$ Hz, 1 H), 5.30 (brs, 1 H), 4.90 (d, $J = 6.1$ Hz, 1 H), 3.68 (s, 3 H), 2.68 (dd, $J = 17.7$, 6.1 Hz, 1 H), 1.77 (d, $J = 17.7$ Hz, 1 H), 0.91 (s, 9 H), 0.17 (s, 3 H), 0.15 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 157.0, 138.0, 126.8, 113.9, 76.6, 75.7, 50.7, 33.5, 25.5, 18.2, −3.7, −3.8. Anal. Calcd for $C_{15}H_{24}O_4Si$: C, 60.78; H, 8.16. Found: C, 60.72; H, 8.15. Reaction with **15** gave a 94% yield and 46% ee (1*S*,5*S* isomer) of **14**. Enantiomeric excess (% ee) was determined by HPLC using a Diacel Chiralcel OD analytical column with 1% isopropanol

in hexane with a flow rate of 0.85 mL/min. UV 254 nm, $T_R = 11$ min (1*S*, 5*R*), 13 min (1*R*, 5*S*),

(1*S*)-2-Ethoxy-1-methyl-2-oxoethyl (1*S*,5*S*)-8-Oxabicyclo[3.2.1]-octa-2,6-diene-2-carboxylate (16) was prepared from **7b** (2.0 g, 9.5 mmol) in 63% yield by treatment with rhodium(II) octanoate and furan in hexane according to the procedure described for the synthesis of **12**; diastereomeric excess (57% *de*) was determined from the ratio of the signals for the 6-vinyl proton of the two isomers in the ^{1}H NMR of the crude reaction mixture: IR (neat) 2986, 2944, 1755, 1718, 1636 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.68 (brs, 1 H), 6.57 (dd, J = 5.8, 1.5 Hz, 1 H), 6.53 (dd, J = 5.8, 1.5 Hz, minor isomer), 5.98 (dd, J = 5.8, 1.5 Hz, 1 H), 5.20 (brs, 1 H), 5.13 (q, J = 7.0 Hz, 1 H), 4.93 (d, J = 5.8 Hz, 1 H), 4.20 (q, J = 7.0 Hz, 2 H), 2.78 (ddd, J = 19.8, 6.1, 3.0 Hz, 1 H) 1.90 (dd, J = 19.8, 3.9 Hz, 1 H), 1.52 (d, J = 7.0 Hz, 3 H), 1.27 (t, J = 7.0 Hz, 3 H). Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.93; H, 6.42. Reaction with **15** and **ent-15** gave **16** in 51% and 44% yields, and 68% and 0% *de* respectively.

(1*S*)-2-Ethoxy-1-methyl-2-oxoethyl (1*S*,5*S*)-3-[(1,1-Dimethylethyl)dimethylsiloxy]-8-oxabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (17) was prepared from **8b** (0.64 g, 1.87 mmol) in 72% yield by treatment with rhodium(II) octanoate and furan in hexane according to the procedure described for the synthesis of **12**; diastereomeric excess (79% *de*) was determined from the ratio of the signals for the 6-vinyl proton of the two isomers in ^{1}H NMR of the crude reaction mixture: IR (neat) 2960, 2934, 2903, 2862, 1755, 1724, 1687, 1610 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.59 (dd, J = 5.8, 1.5 Hz, 1 H), 6.54 (dd, J = 5.8, 1.5 Hz, minor isomer), 5.93 (dd, J = 5.8, 1.5 Hz, 1 H), 5.35 (s, 1 H), 5.12 (q, J = 7.0 Hz, 1 H), 4.92 (dd, J = 6.1, 1.5 Hz, 1 H), 4.16 (q, J = 7.1 Hz, 2 H), 2.70 (dd, J = 17.8, 6.1 Hz, 1 H) 1.80 (d, J = 17.8 Hz, 1 H), 1.48 (d, J = 7.0 Hz, 3 H), 1.24 (t, J = 7.1 Hz, 3 H), 0.90 (s, 9 H), 0.19 (s, 3 H), 0.17 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 163.2, 158.6, 138.3, 126.8, 113.3, 76.6, 75.7, 67.7, 60.8, 33.5, 25.4, 18.0, 16.7, 13.7, −3.9. Anal. Calcd for $C_{19}H_{30}O_6Si$: C, 59.66; H, 7.90. Found: C, 59.55; H, 7.89. Reaction with **15** and **ent-15** gave **17** in 97% and 99% yields, and 80% and 53% *de* respectively.

(3*R*)-Tetrahydro-4,4-dimethyl-2-oxo-3-furanyl (1*R*,5*R*)-3-[(1,1-Dimethylethyl)dimethylsiloxy]-8-oxabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (18) was prepared from **8c** (1.1 g, 3.1 mmol) in 82% yield by treatment with rhodium(II) octanoate and furan in hexane according to the procedure described for the synthesis of **12**; diastereomeric excess (94% *de*) was determined from the ratio of the signals for the 6-vinyl proton of the two isomers in ^{1}H NMR of the crude reaction mixture: mp 101−102 °C (ether); $[\alpha]^{25}_D = +30.0°$ (*c* 1.03, $CHCl_3$); IR (neat) 2961, 2928, 2863, 1786, 1726, 1607 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.64 (dd, J = 6.1, 1.8 Hz, 1 H), 6.54 (dd, J = 6.1, 1.8 Hz, minor isomer), 5.97 (dd, J = 6.1, 1.8 Hz, 1 H), 5.45 (s, 1 H), 5.33 (s, 1 H), 4.95 (dd, J = 6.1, 1.8 Hz, 1 H), 4.06 (d, J = 8.5 Hz, 1 H), 4.02 (d, J = 8.5 Hz, 1 H), 2.75 (dd, J = 17.7, 6.1 Hz, 1 H), 1.86 (d, J = 17.7 Hz, 1 H), 1.22 (s, 3 H), 1.14 (s, 3 H), 0.94 (s, 9 H), 0.22 (s, 3 H), 0.21 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 161.5, 160.7, 138.4, 127.0, 112.7, 76.6, 76.1, 75.6, 73.7, 40.0, 25.4, 22.7, 19.8, 18.0, −3.9. Anal. Calcd for $C_{20}H_{30}O_6Si$: C, 60.80; H, 7.66. Found: C, 60.74; H, 7.61. Reaction with **15** and **ent-15** gave **18** in 83% and 67% yields, and 20% and 70% *de* respectively.

(3*R*)-Tetrahydro-4,4-dimethyl-2-oxo-3-furanyl (1*R*,5*R*)-3-[(1,1-Dimethylethyl)dimethylsiloxy]-5-methyl-8-oxabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (22) was prepared from **8c** (5.15 g, 14.54 mmol) in 91% yield by treatment with rhodium(II) octanoate and 2-methylfuran in hexane according to the procedure described for the synthesis of **12**; diastereomeric excess (83% *de*) was determined from the ratio of the signals for the 6-vinyl proton of the two isomers in ^{1}H NMR of the crude reaction mixture: $[\alpha]^{25}_D = +31.8°$ (*c* 1.15, $CHCl_3$); IR (neat) 2975, 2933, 2896, 2865, 1793, 1730, 1687, 1608 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.54 (dd, J = 5.5, 1.2 Hz, 1 H), 6.44 (dd, J = 5.5, 1.2 Hz, minor isomer), 5.75 (d, J = 5.5 Hz, 1 H), 5.45 (s, 1 H), 5.36 (d, J = 1.2 Hz, 1 H), 4.05 (d, J = 9.1 Hz, 1 H), 4.01 (d, J = 9.1 Hz, 1 H), 2.43 (d, J = 17.7 Hz, 1 H), 1.96 (d, J = 17.7 Hz, 1 H), 1.47 (s, 3 H), 1.21 (s, 3 H), 1.12 (s, 3 H), 0.94 (s, 9 H), 0.22 (s, 3 H), 0.20 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6, 161.7, 138.0, 130.9, 112.3, 82.5, 77.1, 76.7, 76.2, 73.7, 40.7, 40.1, 25.4, 23.5, 22.8, 19.8, 18.1, −3.8. Anal. Calcd for $C_{21}H_{32}O_6Si$: C, 61.74; H, 7.89. Found: C, 61.71; H, 7.91.

(1*R*,5*R*)-3-[(1,1-Dimethylethyl)dimethylsiloxy]-2-hydroxymethyl-8-oxabicyclo[3.2.1]octa-2,6-diene (29). To a stirring mixture of $LiAlH_4$ (0.20 g, 5.0 mmol) in THF (30 mL) at 0 °C under argon was added **17** (or **18**) (0.48 g, 1.25 mmol) in THF (25 mL) dropwise. The mixture was warmed to 10−15 °C and stirred for 2 h. The mixture was then quenched with sat. aq. NH_4Cl (1 mL) and filtered through celite. The solution was concentrated and the residue was purifed by silica gel chromatography with 1:1 Et_2O:pentane as solvent to yield an oil (**29**) 0.17 g (51% yield (42% yield from **18**), $R_f = 0.60$ in Et_2O: $[\alpha]^{25}_D = +38.8°$ (*c* 1.02, $CHCl_3$) for **29** from **18**; $[\alpha]^{25}_D = -32.06°$ (*c* 1.16, $CHCl_3$) for **ent-29** from **17**; IR (neat) 3425, 2960, 2934, 2962, 1672 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (dd, J = 6.1, 1.5 Hz, 1 H), 5.92 (dd, J = 6.1, 1.5 Hz, 1 H), 4.92 (dd, J = 6.1, 1.5 Hz, 1 H), 4.89 (s, 1 H), 4.26 (dd, J = 11.9, 5.7 Hz, 1 H), 4.13 (dd, J = 11.9, 5.7 Hz, 1 H), 2.60 (dd, J = 17.0, 6.1 Hz, 1 H), 1.65 (d, J = 17.0 Hz, 1 H), 1.29 (t, J = 5.7 Hz, 1 H), 0.89 (s, 9 H), 0.11 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.5, 138.2, 126.4, 121.1, 77.2, 77.1, 57.7, 31.7, 25.5, 18.0, −3.6, −4.0; HRMS calcd for $C_{10}H_{15}O_3Si$ (M − *t*-butyl) 211.0790, found 211.0788. Anal. Calcd for $C_{14}H_{24}O_3Si$: C, 62.64; H, 9.01. Found: C, 62.72; H, 9.09.

(1*R*,2*S*,5*S*)-2,5-Dimethyl-2-(methoxycarbonyl)-8-oxabicyclo[3.2.1]-octan-3-one (30). Tris(triphenylphosphine)rhodium(I) chloride (0.07 g, 0.0756 mmol) and **22** (1.58 g, 3.87 mmol, >99% *de*) in EtOH (100 mL) was hydrogenated under 45 psi of H_2 in Parr hydrogenation instrument for 20 h. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography with 1:3 ether:pentane as solvent to yield a colorless oil 1.59 g (100%): $[\alpha]^{25}_D = +0.89°$ (*c* 1.016, $CHCl_3$); IR (neat) 2962, 2929, 2857, 1792, 1728, 1617 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.45 (s, 1 H), 4.99 (dd, J = 5.8, 1.2 Hz, 1 H), 4.04 (d, J = 8.8 Hz, 1 H), 4.01 (d, J = 8.8 Hz, 1 H), 2.52 (dd, J = 17.4, 1.2 Hz, 1 H), 2.14 (m, 2 H), 2.05 (d, J = 17.4 Hz, 1 H), 1.85 (m, 1 H), 1.73 (m, 1 H), 1.42 (s, 3 H), 1.20 (s, 3 H), 1.10 (s, 3 H), 0.95 (s, 9 H), 0.23 (s, 3 H), 0.20 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 161.8, 161.7, 111.6, 79.1, 76.1, 74.1, 73.5, 47.4, 40.1, 36.2, 35.5, 26.5, 25.6, 22.9, 20.0, 18.3, −3.6, −3.7. Anal. Calcd for $C_{21}H_{34}O_6Si$: C, 61.43; H, 8.35. Found: C, 61.26; H, 8.27.

Sodium (0.80 g, 34.7 mmol) was added to MeOH (50 mL) at rt. The mixture was then cooled to 0 °C, the colorless oil from above (1.59 g, 3.87 mmol) in MeOH (30 mL) was added, and the resulting mixture was warmed to rt over 20 h. The mixture was quenched with sat. aq. NH_4Cl (20 mL), diluted with H_2O (100 mL), and extracted with CH_2Cl_2 (2 × 30 mL). The organic layer was dried ($MgSO_4$) and then concentrated under reduced pressure. Silica gel chromatography with 1:3 Et_2O:pentane yielded 0.5 g (66%) of an oil. The spectral data was consistent with the previously reported data.[2d]

To a stirring mixture of NaH (0.080 g, 2.0 mmol, 60% in oil) in THF (10 mL) at rt was added the oil from above (0.2 g, 1.01 mmol) in THF (10 mL) under argon. The mixture was stirred for 1 h at rt, then cooled to 0 °C, and MeI (0.25 mL, 4.01 mmol) was added. The resulting mixture was warmed to rt over 3 h. The solvent was removed under reduced pressure, ether (100 mL) was added, and the mixture was filtered through celite and concentrated. Silica gel chromatography with 1:3 ether:pentane yielded **30** as a colorless solid 0.17 g (77%): $[\alpha]^{25}_D = -89.53°$ (*c* 1.3, $CHCl_3$). The spectral data was consistent with the previously reported data.[2d]

(1*R*,5*S*)-1-Methyl-8-oxabicyclo[3.2.1]oct-6-ene-3-one (32). To a stirred solution of **22** (0.67 g, 1.64 mmol, +99% *de*) at 0 °C under argon was added TBAF (1.7 mL, 1.7 mmol, 1 M in THF), and the mixture was warmed to rt over 30 min. The mixture was quenched with sat. aq. NH_4Cl (25 mL) and H_2O (50 mL), and extracted with CH_2Cl_2 (2 × 50 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was purified by silica gel chromatography with 1:1 ether:hexanes as solvent to yield an oil 0.42 g (86%). Sodium chloride (0.5 g, 8.55 mmol), the oil from above (0.26 g, 0.88 mmol), H_2O (0.1 mL, 11.1 mmol) in DMSO (4 mL) were heated at 160−70 °C in an oil bath under argon for 1 h. During the heating, additional H_2O (0.1 mL) was added. The mixture was then cooled to rt, and the resulting mixture was poured onto a silica gel column and chromatographed with ether:pentane (1:3 to 1:1) as solvent gradient. Concentration of the fractions under reduced pressure with a bath temperature below 5 °C yielded **31** as an oil 0.10 g (82%): $R_f = 0.15$ in Et_2O: hexane (1:1); $[\alpha]^{25}_D = +32.2°$ (*c* 0.85, $CHCl_3$); IR (neat) 2975, 2933, 2896, 1719 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.17 (dd, J = 5.9,

1.8 Hz, 1 H), 6.02 (d, J = 5.9 Hz, 1 H), 5.04 (d, J = 5.0 Hz, 1 H), 2.67 (dd, J = 16.1, 5.0 Hz, 1 H), 2.52 (d, J = 16.1 Hz, 1 H), 2.38 (t, J = 16.1 Hz, 1 H), 2.27 (d, J = 16.1 Hz, 1 H), 1.48 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.1, 136.3, 133.1, 83.4, 77.5, 52.5, 45.1, 22.9. HRMS calcd for $C_8H_{10}O_2$ 138.0680, found 138.0685. The spectral data was consistent with the previously reported data.[3d]

(1*S*,5*S*)-8-Oxabicyclo[3.2.1]oct-6-en-2-one (34). To a stirred solution of **16** (1.25 g, 5.0 mmol) in MeOH (30 mL) at 0 °C under argon was added NaOMe (2.27 g, 40 mmol). The mixture was stirred for 3 h, and then diluted with water (50 mL) and sat. aq. NH_4Cl (50 mL), and extracted with CH_2Cl_2 (2 × 50 mL). The organic layer was dried ($MgSO_4$) and concentrated to give **12**: 0.66 g (80%), $[\alpha]^{25}_D = -30.7°$ (*c* 0.80, $CHCl_3$). To a stirred solution of **12** (2.1 g, 12.65 mmol) in MeOH (20 mL) and water (10 mL) at rt in water bath under argon was added LiOH (0.7 g, 16.68 mmoL). The mixture was stirred for 14 h, diluted with water (150 mL) and brine (100 mL), and then extracted with ether (100 mL). The aqueous layer was acidifed to pH 1 with 3 M H_2SO_4, and then extracted with CH_2Cl_2 (5 × 50 mL). The organic layer was dried ($MgSO_4$) and the solvent was removed under reduced pressure to yield the acid 1.68 g (88%) which was used directly without further purification. Diphenylphosphoryl azide (DPPA) (2.4 mL, 11.13 mmol) was added dropwise to a stirring solution of the acid (1.68 g, 11.05 mmol) and triethylamine (2.3 mL, 16.5 mmol) in toluene (20 mL) and MeCN (5mL) at 0 °C under argon. The mixture was stirred for 90 min at 0 °C, H_2O (1 mL) was added, the mixture was heated to reflux for a further 3 h, and then cooled to rt. Purification by chromatography on silica gel using 1:3 ether:hexanes as solvent and concentration of the fractions under reduced pressure with a bath temperature below 5 °C yielded **34** as an oil 1.01 g (73%): R_f = 0.23 in Et_2O:hexane (1:1); $[\alpha]^{25}_D = -693.1°$ (*c* 1.6, $CHCl_3$) from **12** (chiral catalyst); $[\alpha]^{25}_D = -716.0°$ (*c* 1.2, $CHCl_3$) from **16**. The spectral data was consistent with the previously reported data.[24b]

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Supporting Information Available: Details of the synthesis and characterization for compounds **19**−**21** and **23**−**28** (5 pages). See any current masthead page for ordering and Internet access instructions.

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