Enantioselective Syntheses of 2-Deoxyxylono-1,4-lactone and 2-Deoxyribono-1,4-lactone from 1,3-Dioxan-5-yl Diazoacetates

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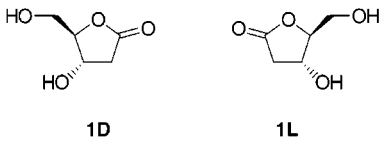
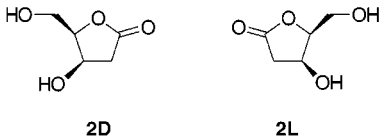
1,3-Dioxan-5-yl diazoacetates are valuable substrates for highly diastereoselective and enantioselective carbon−hydrogen insertion reactions. *trans*-2-(*tert*-Butyl)-1,3-dioxan-5-yl diazoacetate is a direct precursor to 2-deoxyribono-1,4-lactone in up to 81% ee, whereas *cis*-2-(*tert*-butyl)-1,3-dioxan-5-yl diazoacetate yields only the protected 2-deoxyxylono-1,4-lactone in up to 96% ee. However, *trans*-2-aryl-1,3-dioxan-5-yl diazoacetate (aryl = phenyl or 2-naphthyl) forms the precursor to 2-deoxyxylono-1,4-lactone in up to 95% ee but with the mirror image configuration of that produced from the *trans*-2-(*tert*-butyl) analogue. The catalysts that are most suitable for these carbon−hydrogen insertion reactions are chiral dirhodium(II) carboxamidates. 1,3-Dialkoxy-2-propyl diazoacetates give mainly 2-deoxyxylono-1,4-lactone derivatives (>90:10) with generally high enantiocontrol, but replacement of hydrogen at the 2-position of these 2-propyl diazoacetates led to a mixture of products.

2-Deoxyxylono-1,4-lactone and 2-deoxyribono-1,4-lactone are important precursors to carbohydrate- and polyhydroxy-based natural products.[1−3] However, there have been few reports of their asymmetric syntheses, and none have been general. 2-Deoxy-D-ribono-1,4-lactone (**1D**) is obtained from 2-deoxy-D-ribose and is commercially available, but its enantiomer (**1L**) and diastereoisomer, 2-deoxy-(D and L)-xylono-1,4-lactone (**2D** and **2L**), are not. We have recently reported a short synthesis

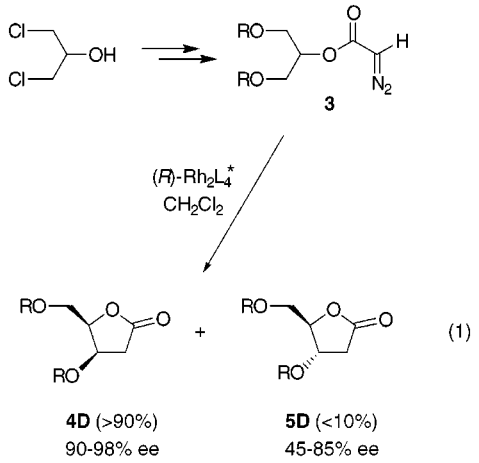


1D **1L**



2D **2L**

of **2** from 1,3-dichloro-2-propanol that produced their ether analogues (R = Me, Et, Bn) in up to 98% ee.[4] Asymmetric induction occurred by intramolecular C−H insertion from the diazoacetate **3** with diastereoisomer ratios up to 94:6 using chiral dirhodium(II) carboxamidate catalysts (eq 1). However, the preparation of **2** that



3

4D (>90%) 90-98% ee **5D** (<10%) 45-85% ee (1)

was free of its diastereomer could not be achieved, and access to 2-deoxyribonolactone **1** was restricted by inherent mechanistic limitations in the acyclic system leading to C−H insertion product(s).[5,6]

On the basis of recent successes in controlling the regio- and stereochemistry of C−H insertion from cyclohexyl diazoacetates matched with configurationally suitable chiral dirhodium(II) carboxamidate catalysts,[7] we reasoned that acetal derivatives of **3** could be utilized for highly selective syntheses of **1** and **2**. Accordingly, we anticipated virtually exclusive insertion into equatorial C−H bonds,[7] which leads to the predictions that the *trans*-disubstituted 1,3-dioxan-5-yl diazoacetate (**7**) should

(1) Dueholm, K. L.; Pederson, E. B. *Synthesis* **1992**, 1.

(2) (a) Kita, Y.; Tamura, O.; Itoh, F.; Yasuda, H.; Kishino, H.; Ke, Y. Y.; Tamura, Y. *J. Org. Chem.* **1988**, *53*, 554. (b) Hodge, R. P.; Brush, C. K.; Harris, C. M.; Harris, T. M. *J. Org. Chem.* **1991**, *56*, 1553. (c) Lee-Ruff, E.; Wan, W.-Q.; Jiang, J.-L. *J. Org. Chem.* **1994**, *59*, 2114. (d) Santiago de Alvanenga, E.; Mann, J. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2141.

(3) (a) Matsumoto, K.; Ebata, T.; Koseki, K.; Okano, K.; Kawakami, Matsushita, H. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 670. (b) Fleming, I.; Ghosh, S. K. *J. Chem. Soc., Chem. Commun.* **1992**, 1775. (c) Teng, K.; Marquez, V. E.; Milne, G. W. A.; Barchi, J. J., Jr.; Kazanietz, M. G.; Lewin, N. E.; Blumberg, P. M.; Abushanab, E. *J. Am. Chem. Soc.* **1992**, *114*, 1059. (d) Lee, J.; Marquez, V. E.; Lewin, N. E.; Kazanietz, M. G.; Bahador, A.; Blumberg, P. M. *Bio. Med. Chem. Lett.* **1993**, *3*, 1101. (e) Sharma, R.; Marquez, V. E. *Synth. Commun.* **1994**, *24*, 1937. (f) Briggs, J. C.; Dawson, A. P.; Gibson, I.; Haines, A. H.; Hook, J.; Taylor, R. J. K. *Bio. Med. Chem. Lett.* **1992**, *2*, 131.

(4) Doyle, M. P.; Dyatkin, A. B.; Tedrow, J. S. *Tetrahedron Lett.* **1994**, *35*, 3853.

(5) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley & Sons: New York, 1998.

(6) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911.

(7) Doyle, M. P.; Kalinin, A. V.; Ene, D. G. *J. Am. Chem. Soc.* **1996**, *118*, 8837.

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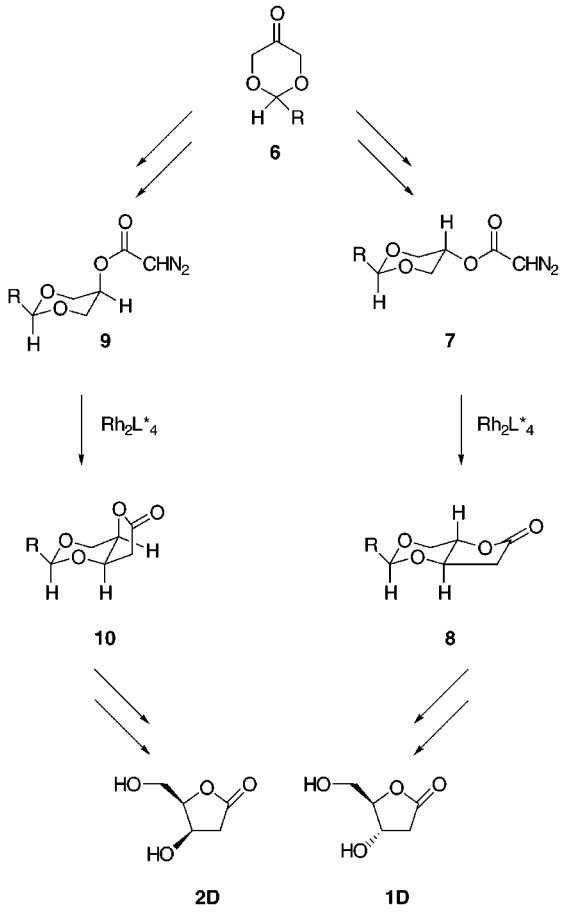
Scheme 1



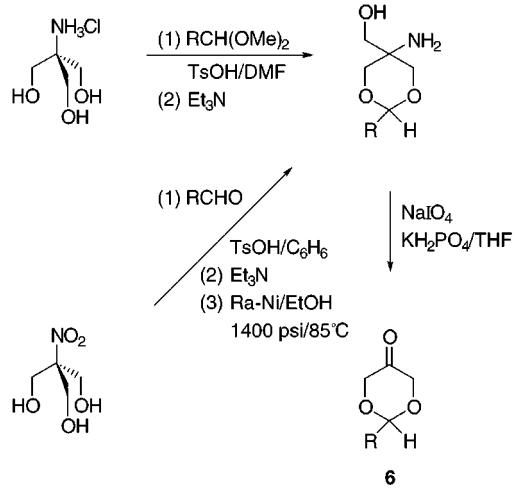
produce the insertion product **8** exclusively, whereas the *cis*-disubstituted 1,3-dioxan-5-yl diazoacetate (**9**) should form insertion product **10** exclusively (Scheme 1). Both **7** and **9** are derived from ketone **6** by stereoselective hydride reduction,[8] **8** is the acetal of 2-deoxy-D-ribono-1,4-lactone, and **10** is the acetal of 2-deoxy-D-xylono-1,4-lactone. Acetal **8** is presumably not accessible from **1D** because rearrangement and isomerization to the 3,4-acetal of the 1,5-lactone occurs under some reaction conditions.[9] We now report the synthesis of the acetals of **1** and **2** with exclusive diastereocontrol and with high enantioselectivity convertible by a single recrystallization to the enantiomerically pure products.

Results and Discussion

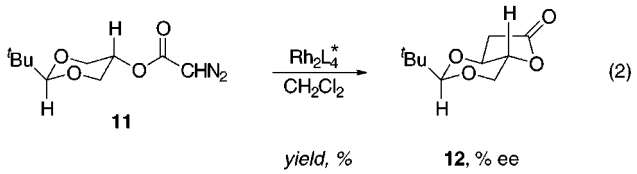
1,3-Dioxan-5-yl Diazoacetates. The preparation of **6** (R = ^{t}Bu, Ph) in high yield from either tris(hydroxymethyl)aminomethane hydrochloride or tris(hydroxymethyl)nitromethane (Scheme 2) has previously been reported.[8] The synthesis of the 2-naphthyl derivative followed the same procedure. Other pathways, especially those derived from glycerol or 1,3-dichloro-2-propanol, had been used in our attempted preparation of these compounds, but they either required more steps or produced product mixtures.

Controlled addition of *trans*-(*tert*-butyl)-acetal **11** to chiral dirhodium(II) carboxamidates in refluxing CH_2Cl_2 resulted in the enantiocontrolled production of equatorial

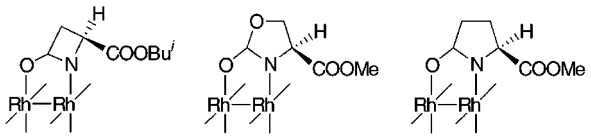
Scheme 2



C−H insertion product **12** (eq 2) in up to 81% ee. The major competing reaction was that from carbene dimer



	yield, %	**12**, % ee
Rh_2(4*S*-IBAZ)$_4$	35	81
Rh_2(4*S*-MEOX)$_4$	42	59
Rh_2(5*S*-MEPY)$_4$	49	52



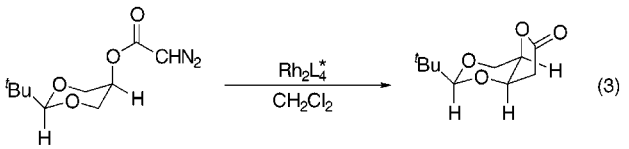
Rh_2(4*S*-IBAZ)$_4$[10] Rh_2(4*S*-MEOX)$_4$[11] Rh_2(5*S*-MEPY)$_4$[12]

formation, and isolated yields were moderate. The diastereoisomeric product from insertion into the axial C−H bond was not observed. The absolute stereochemistry of **12** formed from the *S*-series of dirhodium(II) carboxamidates was established as 4*S*,5*R* by deacetalation, according to the procedure of Rychnovsky,[13] and spectral as well as rotational comparison of **1** with literature values. This stereochemical outcome in terms of absolute configuration is identical to that of its acyclic analogues from diazo decomposition of 1,3-dialkoxy-2-propyl diazoacetates.[4]

The *cis*-(*tert*-butyl)-acetal **13** underwent C−H insertion solely into the equatorial C−H bond to give **14** in 96% ee with Rh_2(MEOX)$_4$ catalysts (eq 3). Absolute stereochemistry was established as 4*S*,5*S* from the *S*-series of carboxamidate catalysts following deacetalation by spectral and rotational comparison with literature values for **2**. Products derived from ylide formation followed by [1,2]-Stevens rearrangement, as had been observed with some

(8) Forbes, D. C.; Ene, D. G.; Doyle, M. P. *Synthesis* **1998**, 879.
(9) Han, S.-Y.; Joullie, M. M.; Petasis, N. A.; Bigorra, J.; Corbera, J.; Font, J.; Ortuño, R. M. *Tetrahedron* **1993,** *49*, 349.
(10) Doyle, M. P.; Zhou, Q.-L.; Simonsen, S. H.; Lynch, V. *Synlett* **1996**, 697.
(11) Doyle, M. P.; Dyatkin, A. B.; Protopopova, M. N.; Yang, C. I.; Miertschin, C. S.; Winchester, W. R. *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 163.
(12) Doyle, M. P.; Winchester, W. R.; Hoorn, J. A. A.; Lynch, V.; Simonsen, S. H.; Ghosh, R. *J. Am. Chem. Soc.* **1993**, *115*, 9968.
(13) Rychnovsky, S. D.; Powell, N. A. *J. Org. Chem*. **1999**, *64*, 2026.

analogous acetals and ketals,[14] were not observed in this case. The 5-*tert*-butyl group not only fixes the conformation of the reactant carbene but also apparently blocks attack by the carbene center on oxygen, thus preventing ylide formation and subsequent rearrangement.



(3)

13 **14**

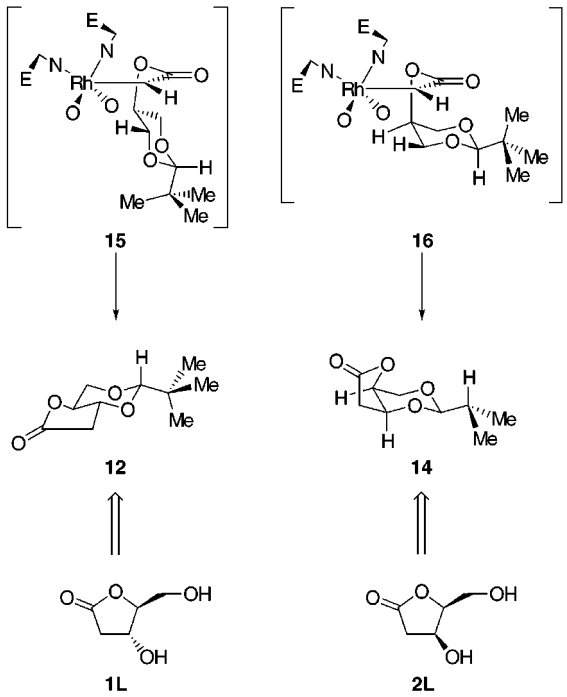
	yield, %	**14**, % ee
Rh_2(4*S*-IBAZ)$_4$	32	85
Rh_2(4*S*-MEOX)$_4$	57	96
Rh_2(4*R*-MEOX)$_4$	55	96
Rh_2(4*S*-MPPIM)$_4$	59	91

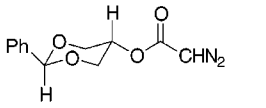
Access to both enantiomers of **12** and **14** was achieved with the use of the *R*- and *S*-forms of the catalyst. The (*R*)-$Rh_2L^*_4$ catalyst produced the D-enantiomer of the C−H insertion product, and (*S*)-$Rh_2L^*_4$ produced the L-enantiomer. The low % ee values found for diazo decomposition of **11** contrasts with those with *trans*-4-(*tert*-butyl)- and *trans*-4-methylcyclohexyl diazoacetates, where 93−96% ee was achieved,[15,16] but enantioselectivities from reactions with **11** are consistent with those obtained with the acyclic analogue **3**.[4] The difference in results between cyclohexyl and 1,3-dioxanyl systems is attributable to the ether oxygens of **11** which, as described below, are repelled by the electronegative catalyst face in the transition state for C−H insertion.

The stereoselectivity obtained for intramolecular C−H insertion with **11** and **13** is consistent with the transition state structural organization (**15** and **16**) described in Scheme 3. The depiction here is for the *S*-series of catalysts, and the probable lowest energy conformer is shown.[12] As previously reported,[7,17] C−H insertion occurs through a mechanism in which C−C and C−H bond formation occur in conjunction with carbene-C−H and C−Rh bond cleavage. Insertion into the equatorial C−H bond is favored over insertion into the axial C−H bond. Accordingly, **15** yields **12**, which can be transformed into 2-deoxy-L-ribono-1,4-lactone, and **16** yields **14**, which is directly convertible to 2-deoxy-L-xylono-1,4-lactone. Furthermore, the lower level of enantiocontrol achieved with **11** relative to *trans*-4-*tert*-butyl-1-cyclohexyl diazoacetate (95% ee with Rh_2(MEPY)$_4$ catalysts)[15,16] can be explained by a destabilizing (catalyst-oxygen)−(1,3-dioxan-oxygen) repulsion in **15**. This repulsion would be expected to be lowest with Rh_2(4*S*-IBAZ)$_4$, which has the highest volume for carbene structural organization of any of the catalysts,[10] and to be absent for **14** in **16**.

Use of the *trans*-phenyl-acetal of **7** was expected to produce **8** (R = Ph, Scheme 1), but instead, the exclusive C−H insertion product was that from formal reaction with an axial C−H bond (eq 4). Furthermore, the product formed from **17** with the *R*-series of dirhodium(II) carboxamidate catalysts yielded, after hydrogenolysis, 2-deoxy-L-xylono-1,4-lactone (**2L**), which is not the product that would have been expected from insertion into the axial C−H bond at the designated reactive site of **15**. This stereocontrol is unprecedented in metal carbene insertion reactions.[5,6,18,19] Both the diastereoisomer and enantiomer formed as **18** are opposite to that predicted in Scheme 3, and Scheme 3 is consistent with all prior results reported for enantioselective C−H insertion reactions catalyzed by chiral dirhodium(II) carboxamidates.

Scheme 3





(4)

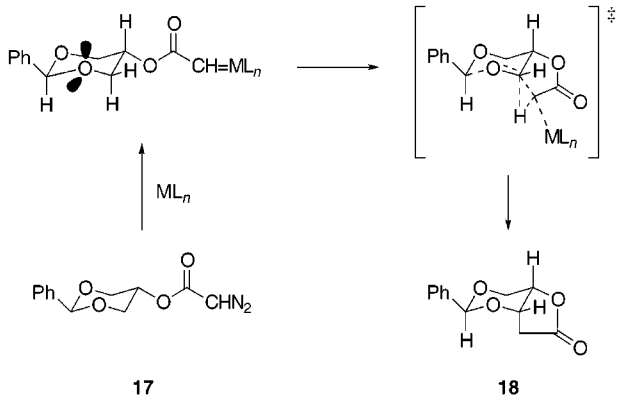
17 **18**

	yield %	**18**, % ee
Rh_2(4*S*-IBAZ)$_4$	85	88
Rh_2(4*S*-MEOX)$_4$	48	67
Rh_2(5*S*-MEPY)$_4$	71	94
Rh_2(5*R*-MEPY)$_4$	75	94

The reversal of enantiomer preference can be explained by mechanistic preference for a conformer for the metal carbene that, like **15** or **16**, is an energy minimum[12] but for which the carbene hydrogen lies between the two ligand carboxylate groups. This orientation, which has been previously evaluated in considerable detail for cyclopropanation reactions,[12,20] causes counterclockwise (rather than clockwise, as in **15** or **16**) motion of the reacting system to place the C−H bond in proximity to

(14) Doyle, M. P.; Ene, D. G.; Forbes, D. C.; Tedrow, J. S. *Tetrahedron Lett.* **1997**, *38*, 4367.
(15) Doyle, M. P.; Dyatkin, A. B.; Roos, G. H. P.; Cañas, F.; Pierson, D. A.; van Basten, A. *J. Am. Chem. Soc.* **1994**, *116*, 4507.
(16) Müller, P.; Polleux, P. *Helv. Chim. Acta* **1994**, *77*, 645.
(17) Doyle, M. P.; Westrum, L. J.; Wolthuis, W. N. E.; See, M. M.; Boone, W. P.; Bagheri, V.; Pearson, M. M. *J. Am. Chem. Soc.* **1993**, *115*, 958.
(18) Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon Press: New York, 1995; Vol. 12, Chapter 5.2.
(19) Padwa, A.; Austin, D. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1797.
(20) Doyle, M. P.; Austin, R. E.; Bailey, A. S.; Dwyer, M. P.; Dyatkin, A. B.; Kalinin, A. V.; Kwan, M. M. Y.; Liras, S.; Oalmann, C. J.; Pieters, R. J.; Protopopova, M. N.; Raab, C. E.; Roos, G. H. P.; Zhou, Q.-L.; Martin, S. F. *J. Am. Chem. Soc.* **1995**, *117*, 5763.

Scheme 4

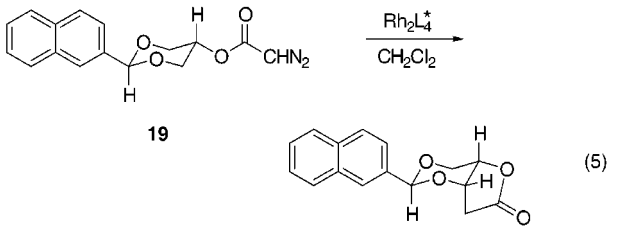


17 **18**

the carbene center for insertion. In this mechanism the (*R*)-$Rh_2L^*_4$ catalyst produces the L-enantiomer of the C−H insertion product, and (*S*)-$Rh_2L^*_4$ produces the D-enantiomer. However, the cause for this specific change is undetermined.

There are several plausible explanations for the observed diastereoselectivity, and one is that the phenyl group imparts axial C−H bond-specific electronic stabilization in the transition state for C−H insertion (Scheme 4). Another is that in the transition state for insertion the carbene substrate is in a diaxial or twist boat conformation; these would present the energetically favored equatorial C−H bond for insertion. The former explanation is supported by the observation that oxonium ylide formation/[1,2]-Stevens rearrangement, which is the principal pathway for product formation from the *cis*-phenyl-acetal of **7**,[14] is only a minor process with **17** (9% relative yield with Rh_2(4*S*-IBAZ)$_4$ and only 3% with Rh_2(MEPY)$_4$ catalysts). The latter explanation recognizes the favored axial conformation of 5-substituted 1,3-dioxanes.[21,22]

Attempts were made to further understand the cause for the unprecedented stereocontrol from C−H insertion reactions of **17**. The *p*-methoxyphenyl and *p*-nitrophenyl analogues of **17** were prepared via Scheme 2, but treatment with any of the dirhodium(II) catalysts caused catalyst destruction rather than metal carbene transformations. However, the 2-naphthyl derivative **19** underwent dirhodium(II)-catalyzed C−H insertion in high yield and with even higher enantiocontrol than for diazo decomposition of **17** (eq 5). As with **17**, the product formed



19 **20** (5)

	yield %	**20**, ee %
Rh_2(4*R*-MEOX)$_4$	68	83
Rh_2(5*S*-MEPY)$_4$	72	95

(21) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; John Wiley & Sons: New York, 1994; Chapter 11.

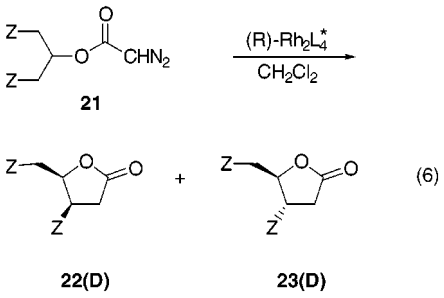
Table 1. Stereoselective Carbon−Hydrogen Insertion Reactions of 1,3-Dialkoxy-2-propyl Diazoacetates (21) Catalyzed by Chiral Dirhodium(II) Carboxamidates[a]

21, Z =	catalyst	**22**:**23**	% ee **22**	% ee **23**
OMe	Rh_2(5*R*-MEPY)$_4$	93:7	97 (3*R*,4*R*)	50 (3*S*,4*R*)
	Rh_2(5*S*-MEPY)$_4$	94:6	97 (3*S*,4*S*)	45 (3*R*,4*S*)
	Rh_2(4*S*-MEOX)$_4$	91:9	98 (3*S*,4*S*)	76 (3*R*,4*S*)
OEt	Rh_2(5*R*-MEPY)$_4$	93:7	89 (3*R*,4*R*)	50 (3*S*,4*R*)
	Rh_2(5*S*-MEPY)$_4$	94:6	90 (3*S*,4*S*)	45 (3*R*,4*S*)
	Rh_2(4*S*-MEOX)$_4$	90:10	96 (3*S*,4*S*)	85 (3*R*,4*S*)
OBn	Rh_2(5*R*-MEPY)$_4$	93:7	94 (3*R*,4*R*)	45 (3*S*,4*R*)
	Rh_2(5*S*-MEPY)$_4$	93:7	94 (3*S*,4*S*)	
	Rh_2(4*S*-MEOX)$_4$	90:10	94 (3*S*,4*S*)	

[a] Isolated yields of **22** + **23** were 65−81%.

was that from formal axial C−H insertion; hydrogenolysis of **20** yielded **2D** (from Rh_2(5*S*-MEPY)$_4$ catalysis). In contrast, the 1-naphthyl derivative gave a mixture of products upon treatment with dirhodium(II) catalysts, but C−H insertion products were not discernible. Thus the results obtained do not uniformly favor either the electronic or conformational explanation, although we would argue that electronic stabilization of the transition state for axial C−H insertion seems to be more plausible.

1,3-Dialkoxy-2-propyl Diazoacetates. A return to the results from reactions of the noncyclic diethers with chiral dirhodium(II) carboxamidates[4] is mechanistically instructive. Table 1 presents the results that were previously reported for the transformation represented in eq 6, demonstrating substantial, but not complete,



21 **22(D)** **23(D)** (6)

(a) Z = OMe, (b) Z = OEt, (c) Z = OBn

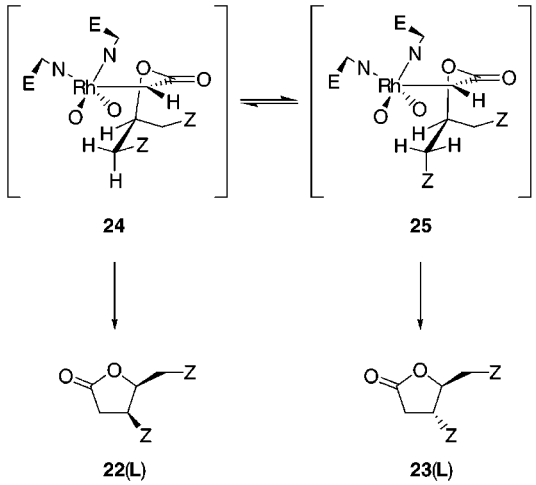
diastereocontrol. As little as 0.1 mol % of chiral catalyst was effective for these reactions. In addition, we also prepared the 2,2,2-trifluoroethyl (eq 6, Z = CF_3CH_2O) and trityl (eq 6, Z = Ph_3CO) ethers, but neither exhibited complete diastereocontrol, both giving results such as those in Table 1 (**22**:**23** between 90:10 and 94:6).

The diastereocontrol observed in these cases suggests a high preference for the transition state structural organization of **24** that is described in Scheme 5. In this acyclic system **24** and **25** can be considered to exist in equilibrium, and according to the relative amounts of **22** and **23**, **24** is dominant. In other words, repulsion of Z by the catalyst face represents a higher energy state than dipolar repulsion between Z-substituents. This is true even with Z = OCH_2CF_3 or the bulky Ph_3CO.

As might be expected from this model, replacement of hydrogen at the 2-position of **21** led to a mixture of products upon catalytic diazo decomposition (eq 7, R = Et, Ph). Diazoacetates **26** were prepared from 1,3-

(22) (a) Juaristi, E.; Diaz, F.; Cuéllar, G.; Jiménez-Vázquez, H. A. *J. Org. Chem.* **1997**, *62*, 4029. (b) Antúnez, S.; Juaristi, E. *J. Org. Chem.* **1996**, *61*, 6465.

Scheme 5



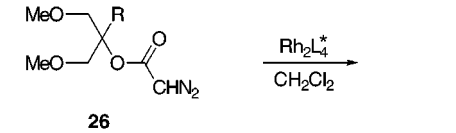
24 **25**

22(L) **23(L)**

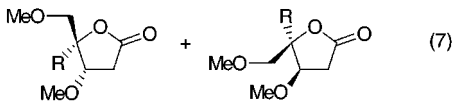
Table 2. Stereoselective Carbon−Hydrogen Insertion Reactions of 1,3-Dimethoxy-2-alkyl/aryl-2-propyl Diazoacetates (26) Catalyzed by Dirhodium(II) Compounds

	R = Et		R = Ph	
catalyst	yield, %	**27a**:**28a**	yield, %	**27b**:**28b**
$Rh_2(OAc)_4$	86	76:24	59	83:17
$Rh_2(5R\text{-MEPY})_4$	79	60:40	72	67:33
$Rh_2(4S\text{-MEOX})_4$	61	64:36	76	63:37
$Rh_2(4S\text{-MACIM})_4$	82	55:45	42	60:40
$Rh_2(cap)_4$			35	66:34

dimethoxy-2-propanone, following Grignard addition, by the same methodology used for the preparation of **21**. Using $Rh_2(5R\text{-MEPY})_4$, $Rh_2(4S\text{-MEOX})_4$, and $Rh_2(4S\text{-MACIM})_4$, in addition to achiral catalysts $Rh_2(OAc)_4$ and $Rh_2(cap)_4$, product yields and diastereoselectivities were those reported in Table 2. Reactions with **26b** (R = Ph) catalyzed by $Rh_2(OAc)_4$ and $Rh_2(cap)_4$ produced substantial amounts of aromatic cycloaddition product, but this compound was virtually absent in reactions catalyzed by the chiral dirhodium(II) carboxamidates. Enantioselectivities from these reactions were in the range of 34−72% ee, so detailed analyses were not further pursued.



26



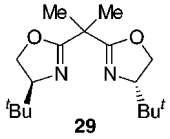
27 **28**

(7)

Finally, attempts to extend these C−H insertion reactions to Z = F, Cl, I, and N_3 in **21** were unsuccessful. The diazoacetates added dropwise to the catalyst in anhydrous CH_2Cl_2 resulted in the immediate destruction of the catalyst, presumably via oxidation. Our impression is that ylide formation in these cases was responsible for the catalyst destruction.

Conclusion. Because of the convenience of hydrogenolysis, both **18** and **20** are recommended sources for 2-deoxyxylono-1,4-lactone. Both can be crystallized conveniently to 100% ee prior to hydrogenolysis. As of now, **12** represents the best source for 2-deoxyribono-1,4-lactone formed via asymmetric catalysis; like **18** and **20**, **12** can also be recrystallized to induce further selectivity enhancement. Hydrogenolysis avoids the complexities of isomerization often obtained in acid-catalyzed processes that remove acetal/ketal protective groups.[23]

Chiral dirhodium(II) carboxamidates are the most suitable catalysts for enantiocontrol in these systems. Although we have not undertaken an exhaustive study, $CuPF_6$/bisoxazoline **29** did not show advantageous activity for C−H insertion or for ylide formation with **14** or **17**. Carbene dimer formation was the principal outcome from the use of this catalyst with these systems.



29

Experimental Section

General. ^1H NMR (300 or 400 MHz) and ^{13}C NMR (75 or 100 MHz) spectra were obtained as solutions in $CDCl_3$, unless indicated otherwise, and chemical shifts are reported in parts per million (ppm, δ) downfield from internal Me_4Si (TMS). Infrared spectra were recorded as a thin film on sodium chloride plates, and absorptions are reported in wavenumbers (cm^{-1}). Mass spectra were obtained using electron ionization at 70 eV on a quadruple instrument. Elemental analyses were performed at Texas Analytical Laboratories, Inc. or Atlantic Microlab, Inc. Methanesulfonyl azide was prepared from methanesulfonyl chloride and sodium azide[24] and used without distillation. Rhodium(II) acetate was obtained commercially and recrystallized prior to use. The preparation and characterization of the enantiomeric forms of $Rh_2(MEPY)_4$[12,25] and $Rh_2(MEOX)_4$[11] and of $Rh_2(4S\text{-IBAZ})_4$[10] have been previously reported. Dichloromethane and acetonitrile were distilled from CaH_2 prior to use. Tetrahydrofuran was distilled from sodium.

General Procedure for the Synthesis of Diazoacetates. The compounds were prepared by a two-pot modification of the three-step procedure of Doyle.[7] Diketene (24 mmol) was added via syringe over 5 min to the corresponding alcohol[8] (20 mmol) and triethylamine (2 mmol) in 50 mL of THF (HPLC grade), cooled at 0 °C. The resulting bright yellow solution was stirred for 1 h at 0 °C and then warmed to room temperature. After 24 h, triethylamine (24 mmol) and methanesulfonyl azide (24 mmol) were added via syringe, and the brown solution was stirred for 24 h at room temperature. The diazoacetoacetate was isolated, after the addition of 25 mL of water, by extraction with ether (3 × 50 mL). The organic layer was washed with water (3 × 50 mL) and brine (3 × 50 mL) and then dried over anhydrous $MgSO_4$. After filtration and removal of the solvent under reduced pressure, the crude orange diazoacetoacetate was used without further purification in the subsequent acetyl cleavage step.

Acetyl cleavage of the diazoacetoacetate was performed in THF (6 mL) to which LiOH (4 equiv, approximately 72 mmol) in 8 mL of water was added. The dark brown solution was stirred at room temperature for 20 min and then extracted with diethyl ether (3 × 15 mL). The organic phase was washed with water (3 × 15 mL) and brine (3 × 15 mL), dried over anhydrous $MgSO_4$, and filtered. The crude diazoacetate was

(23) Han, S.-Y.; Joullié, M.; Petasis, N. A.; Bigorra, J.; Corbera, J.; Font, J.; Ortuño, R. M. *Tetrahedron* **1993**, *49*, 349.

(24) Boyer, J. H.; Mack, C. H.; Goebel, W.; Morgan, L. R. *J. Org. Chem*. **1959**, *24*, 1051.

(25) Doyle, M. P.; Winchester, W. R.; Protopopova, M. N.; Kazala, A. P.; Westrum, L. J. *Org. Syn*. **1996**, *73*, 13.

obtained after evaporation of the solvent under reduced pressure. The purification of each diazoacetate is described.

***trans*-2-(*tert*-Butyl)-1,3-dioxan-5-yl diazoacetate (11)** was prepared from *trans*-2-(*tert*-butyl)-1,3-dioxan-5-ol[8] in 51% overall yield after radial chromatography (10:1 hexanes:ethyl acetate) as a yellow solid, mp 39−42 °C: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.92 (tt, J = 10.3, 5.3 Hz, 1 H), 4.73 (br s, 1 H), 4.24 (dd, J = 11.0, 5.3 Hz, 2 H), 4.02 (s, 1 H), 3.42 (dd, J = 11.0, 10.3 Hz, 2 H), 0.91 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ C=O (not detected), 107.6, 68.5, 63.3, 46.3, 34.8, 24.9; IR ($CHCl_3$) 2118 (C=N_2), 1697 (C=O) cm^{-1}. Anal. Calcd for $C_{10}H_{16}N_2O_3$: C, 52.62; H, 7.06; N, 12.27. Found: C, 52.63, H, 7.30; N, 12.32.

Catalytic Diazo Decomposition of 11. A solution of diazoacetate **11** (0.114 g, 0.570 mmol) in 5 mL of anhydrous CH_2Cl_2 was added via syringe pump at a rate of 1 mL/h to a refluxing solution of 1.0 mol % of the dirhodium(II) catalyst in CH_2Cl_2 (5 mL). Upon completion of the addition, the solution was refluxed for an additional hour, cooled at room temperature, and passed through a short silica gel plug to remove the catalyst. The plug was washed with 60 mL of CH_2Cl_2, and the solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel (2:1 hexanes:ethyl acetate) to afford **12** as a white solid, mp 32−34 °C, $[\alpha]^{28}_D$ = +13.6 (*c* 0.18, $CHCl_3$) for the product of reactions catalyzed by Rh_2(4*S*-MEOX)$_4$: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.77−4.72 (m, 1 H), 4.75 (ddd, J = 6.2, 6.0, 5.8 Hz 1 H), 4.39 (s, 1 H), 4.31 (dd, J = 12.2, 6.2 Hz, 1 H), 3.73 (dd, J = 12.2, 5.8 Hz, 1 H), 2.77 (dd, J = 18.2, 4.2 Hz, 1 H), 2.72 (dd, J = 18.2, 6.2 Hz, 1 H), 0.90 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.8, 102.0, 74.6, 68.9, 64.9, 35.8, 35.8, 24.2; IR ($CHCl_3$) 1786 (C=O) cm^{-1}; mass spectrum, *m*/*z* (relative abundance) 200(M, 0.07), 199-(M − 1, 0.7), 143(100), 115(15), 97(19), 71(12), 57(10), 43(17). Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.03; H, 7.98. Enantiomeric excesses were determined on the crude product with baseline resolution from GC analysis on a 30-m Chiraldex G-TA column operated at 100 °C (1 min) then 0.5°/min to 160 °C (10 min): retention times 73.7 min [(4*S*,5*R*)-**12**] and 75.4 min [(4*R*,5*S*)-**12**]. Deacylation of **12** according to the procedure of Rychnovaky[13] yielded 2-deoxy-1,4-ribonolactone, which was characterized by spectral means; the sign of rotation of this product established whether **12** had either the 4*S*,5*R* or 4*R*,5*S* configuration. Attempts to *trans*-acetalate **12** using benzaldehyde or its dimethyl acetal did not give satisfactory results, so *trans*-acetalation−hydrogenolysis was not further employed.

***cis*-2-(*tert*-Butyl)-1,3-dioxan-5-yl diazoacetate (13)** was prepared from *cis*-2-*tert*-butyl-1,3-dioxan-5-ol[8] in 54% overall yield after radial chromatography (10:1 hexanes:ethyl acetate) as a yellow solid, mp 88−90 °C: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.85 (br s, 1 H), 4.68 (quin, J = 1.5 Hz, 1 H), 4.15 (s, 1 H), 4.14 (dd, J = 12.9, 1.5 Hz, 2 H), 3.90 (dd, J = 12.9, 1.5 Hz, 2 H), 0.92 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ C=O (not detected), 107.4, 68.7, 68.7, 46.7, 34.9, 24.4; IR ($CHCl_3$): 2117 (C=N_2), 1687 (C=O) cm^{-1}. Anal. Calcd for $C_{10}H_{16}N_2O_4$: C, 52.62; H, 7.06; N, 12.27. Found: C, 52.79; H, 7.10; N, 12.12.

Catalytic Diazo Decomposition of 13. A solution of diazoacetate **13** (0.114 g, 0.570 mmol) in 5 mL of anhydrous CH_2Cl_2 was added via syringe pump at a rate of 1 mL/h to a refluxing solution of 1.0 mol % of the dirhodium(II) catalyst in CH_2Cl_2 (5 mL). Upon completion of the addition, the solution was refluxed for an additional hour, cooled at room temperature, and passed through a short silica gel plug to remove the catalyst. The plug was washed with 60 mL of CH_2Cl_2, and the solvent was removed under reduced pressure. The residue was dissolved in refluxing hexanes, and **14** was crystallized as a white solid, mp 94−96 °C, $[\alpha]^{25}_D$ = −26.4 (*c* 0.15, EtOH) for the product obtained from the Rh_2(4*S*-MPPIM)$_4$-catalyzed reaction: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.50 (ddd, J = 3.4, 2.3, 0.8 Hz, 1 H), 4.44 (d, J = 13.6 Hz, 1 H), 4.18−4.10 (m, 1 H), 4.11 (s, 1 H), 3.93 (dd, J = 13.6, 2.3 Hz, 1 H), 2.73 (dd, J = 17.3, 4.2 Hz, 1 H), 2.62 (d, J = 17.3 Hz, 1 H), 0.89 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ C=O (not detected), 105.2, 74.2, 72.1, 65.9, 38.2, 34.9, 24.9; IR ($CHCl_3$): 1789 (C=O) cm^{-1}; mass spectrum, *m*/*z* (relative abundance) 200(M, 1), 143(100), 115-(12), 97(16), 71(18), 57(11). Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.86; H, 8.11. This stereochemistry was further confirmed by NOE experiments. Enantiomeric excesses were determined on the crude product with baseline resolution from GC analysis on a 30-m Chiraldex G-TA column operated at 150 °C: retention times 25.6 min [(4*R*,5*R*)-**14**] and 26.7 min [(4*S*,5*S*)-**14**].

***trans*-2-Phenyl-1,3-dioxan-5-yl diazoacetate (17)** was prepared from *trans*-2-phenyl-1,3-dioxan-5-ol and isolated in 62% overall yield after column chromatography on silica gel (2:1 hexanes:ethyl acetate) as a yellow solid, mp 50−52 °C: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50−7.46 (comp, 2 H), 7.41−7.35 (comp, 3 H), 5.46 (s, 1 H), 5.10 (tt, J = 10.0, 5.2 Hz, 1 H), 4.77 (br s, 1 H), 4.41 (dd, J = 11.4, 5.2 Hz, 2 H), 3.71 (dd, J = 11.4, 10.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ C=O (not detected), 137.0 (s), 129.0 (d), 128.2 (d), 126.0 (d), 101.0 (d), 68.6 (t), 63.0 (d), 46.4 (d); IR ($CHCl_3$) 2119 (C=N_2), 1696 (C=O) cm^{-1}. Anal. Calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.28. Found: C, 58.01; H, 4.92; N, 11.24.

Catalytic Diazo Decomposition of 17. A solution of diazoacetate **17** (0.124 g, 0.500 mmol) in 5 mL of anhydrous CH_2Cl_2 was added via syringe pump at a rate of 1 mL/h to a refluxing solution of 1.0 mol % of the dirhodium(II) catalyst in CH_2Cl_2 (5 mL). Upon completion of the addition, the solution was refluxed for an additional hour, cooled at room temperature, and passed through a short silica gel plug to remove the catalyst. The plug was washed with 60 mL of CH_2Cl_2, and the solvent was removed under reduced pressure. The residue was washed with ether and then dissolved in refluxing hexanes, and **18** was crystallized as a white solid, mp 141−143 °C, $[\alpha]^{25}_D$ = −3.56 (*c* 1.00, $CHCl_3$) for the product obtained from the Rh_2-(5*R*-MEPY)$_4$-catalyzed reaction: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.48−7.36 (comp, 5 H), 6.03 (s, 1 H), 4.62 (dddd, J = 4.2, 3.8, 2.2, 1.8 Hz, 1 H), 4.36 (ddddd, J = 2.4, 2.2, 2.1, 1.9, 1.8 Hz, 1 H), 4.22 (ddd, J = 12.9, 4.2, 1.9 Hz, 1 H), 4.07 (ddd, J = 12.9, 3.8, 2.1 Hz, 1 H), 2.77 (dd, J = 17.8, 1.8 Hz, 1 H), 2.72 (dd. J = 17.8, 2.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.9, 136.9, 129.4, 128.4, 126.6, 99.4, 68.1, 66.3, 66.1, 36.4; IR ($CHCl_3$) 1788 (C=O) cm^{-1}. Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.47, H, 5.48. Found: C, 65.32; H, 5.57. 3,5-*O*-Benzylidene-2-deoxy-1,4-xylonolactone (**18**) was *trans*-acetalated with acetone, catalyzed by trifluoroacetic acid, and the enantiomeric excess of the dimethyl ketal was determined by GC analysis on a 30-m Chiraldex B−PH column operated at 150 °C: retention times 37.4 min (4*S*, 5*S*) and 40.1 min (4*R*, 5*R*).

2-Deoxy-1,4-xylono lactone was obtained from the hydrogenolysis of **18** (20 mg, 0.090 mmol) dissolved in 3 mL of EtOH in the presence of 9 mg of palladium black under hydrogen atmosphere (balloon pressure). After 12 h the mixture was filtered through a Celite plug and washed with 20 mL of ethanol, and the solvent was evaporated under reduced pressure. The title compound was obtained in quantitative yield as a colorless liquid: ^{1}H NMR (1:2 $CDCl_3$:acetone-d_6, 300 MHz) δ 4.71 (ddd, J = 6.1, 4.4, 1.7 Hz, 1 H), 4.51 (ddd, J = 5.4, 5.1, 4.4 Hz, 1 H), 4.01 (dd, J = 12.2, 5.4 Hz, 1 H), 3.95 (dd, J = 12.2, 5.1 Hz, 1 H), 2.85 (dd, J = 17.6, 6.1 Hz, 1 H), 2.50 (dd, J = 17.6, 1.7 Hz, 1 H); $[\alpha]_D$ = −49.2 (*c* = 1.00, EtOH) for the product obtained from catalysis with Rh_2(5*R*-MEPY)$_4$; lit.[26] $[\alpha]^{25}_D$ = + 49.3 (*c* = 0.56, MeOH) for (4*R*,5*R*)-(+)-2-deoxyxylonolactone. Other values for specific rotation of 2-deoxy-1,4-xylonolactone have been reported,[3a,4] up to $[\alpha]^{24}_D$ = 67.3, but we believe that these values are not representative of the enantiomerically pure deoxyxylonolactone. Furthermore, the ^{1}H NMR spectrum is only consistent with the reported structure rather than the isomeric 1,5-lactone.

***trans*-5-Hydroxy-2-(2-naphthyl)-1,3-dioxane.** To a solution of tris(hydroxymethyl)aminomethane hydrochloride (5.03 g, 32 mmol) in benzene (250 mL) was added *p*-toluenesulfonic acid hydrate (6.5 g, 34 mmol) followed by 2-naphaldehyde (5.00 g, 32 mmol). The resulting solution in a one-neck flask was fitted with a Soxhlet extraction apparatus. The thimble in the

(26) Fernandez, M. V.; Durante-Lanes, P.; Lopez-Herrera, F. J. *Tetrahedron* **1990**, *46*, 7911.

Soxhlet extraction apparatus was charged with molecular sieves. Upon refluxing the color of the solution turned dark red. After 12 h, the solution was cooled to room temperature and concentrated in vacuo. Then 250 mL of dichloromethane was added, causing precipitation of a white solid which was filtered. The amino alcohol was obtained in 85% yield (9.23 g, 27.2 mmol): ^{1}H NMR (10:1 $CDCl_3$:DMSO-d_6, 300 MHz) δ 8.15 (br s, 2 H) 7.96 (s, 1 H), 7.77 (d, J = 8.5 Hz, 1 H), 7.68−7.61 (comp, 2 H), 7.46−7.38 (comp, 2 H), 7.06 (d, J = 8.0 Hz, 1 H), 5.58 (s, 1 H), 5.18 (br s, 1 H), 4.25 (d, J = 12.2 Hz, 2 H), 3.99 (d, J = 12.2 Hz, 2 H), 3.61 (s, 2 H); ^{13}C NMR (10:1 $CDCl_3$:DMSO-d_6, 75 MHz) δ 133.4, 131.4, 127.3, 127.0, 126.5, 126.4, 125.4, 125.1, 124.7, 123.0, 100.8, 68.7, 59.5, 58.9, 53.2.

To a cold (5 °C) solution containing 5-amino-5-hydroxymethyl-2-(2-naphthyl)-1,3-dioxane (9.27 g, 27.3 mmol) and KH_2PO_4 (6.80 g, 50 mmol) in 150 mL of water and 150 mL of THF was added dropwise via an addition funnel a solution of $NaIO_4$ (10.7 g, 50 mmol) in 120 mL of water. Upon completion of addition (ca. 3 h) the mixture was allowed to stir for 12 h at room temperature and then extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The ketone was obtained in 83% yield (5.20 g, 22.8 mmol) as a yellow solid, mp 80−82 °C: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.02 (s, 1 H), 7.96−7.84 (comp, 3 H), 7.62 (dd, J = 8.5, 1.5 Hz, 1 H), 7.56−7.48 (comp, 2 H), 6.07 (s, 1 H), 4.58 (dd, J = 16.6, 2.1 Hz, 2 H), 4.52 (dd, J = 16.6, 2.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 204.3, 134.0, 133.7, 132.9, 129.1, 128.4, 127.7, 126.6, 126.4, 125.6, 123.5, 98.9, 72.4, 72.3.

To a cold (0 °C) solution of 2-(2-naphthyl)-5-oxo-1,3-dioxane (3.50 g, 15.4 mmol) in anhydrous THF (250 mL) was added dropwise via syringe 1.0 M $LiAlH_4$ in THF (15 mL, 15 mmol). The resulting solution was allowed to warm to room temperature for 1 h, after which time it was diluted with Et_2O (100 mL), and 7 mL of a 1% solution of HCl was added. The organic layer was separated, dried over anhydrous $MgSO_4$, filtered,- and concentrated in vacuo to afford, after purification by chromatography (silica gel, 1:2 hexanes:ethyl acetate), *trans*-5-hydroxy-2-(2-naphthyl)-1,3-dioxane in 65% yield (2.30 g, 10.0 mmol) as a white solid, mp 120−122 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 1 H), 7.87−7.82 (comp, 3 H), 7.58 (dd, J = 8.6, 1.5 Hz, 1 H), 7.52−7.46 (comp, 2 H), 5.61 (s, 1 H), 4.38 (dd, J = 11.0, 5.0 Hz, 2 H), 4.07 (ddt, J = 11.2, 5.9, 5.0 Hz, 1 H), 3.67 (dd, J = 11.2, 11.0 Hz, 2 H), 1.69 (d, J = 5.9 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.8, 133.6, 132.9, 128.3, 128.2, 127.7, 126.4, 126.1, 125.6, 123.6, 100.9, 71.6, 61.4. Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 73.27; H, 6.05.

***trans*-5-Hydroxy-2-(1-naphthyl)-1,3-dioxane.** To a solution of tris(hydroxymethyl)aminomethane hydrochloride (5.03 g, 32 mmol) in benzene (250 mL) was added *p*-toluenesulfonic acid hydrate (6.5 g, 34 mmol) followed by 1-naphaldehyde (5.00 g, 32 mmol). The mixture was refluxed as described for the 2-naphthyl derivative. The resultant amino alcohol was obtained as a white solid in 82% yield (8.90 g, 26.3 mmol): ^{1}H NMR (10:1 $CDCl_3$:DMSO-d_6, 300 MHz) δ 7.90 (dd J = 16.8, 8.5 Hz, 2 H), 7.85 (d, J = 7.8 Hz, 2 H), 7.46−7.38 (comp, 3 H), 6.09 (s, 1 H), 5.41 (s, br, 3 H), 4.25 (d, J = 12.3 Hz, 2 H), 4.13 (d, J = 12.3 Hz, 2 H), 3.61 (s, 2 H); ^{13}C NMR (10:1 $CDCl_3$:DMSO-d_6, 75 MHz) δ 131.4, 130.8, 128.5, 127.8, 126.9, 124.6, 123.9, 123.1, 122.6, 121.9, 97.1, 68.0, 59.8, 58.7, 52.5.

To a cold (5 °C) suspension containing 5-amino-5-hydroxymethyl-2-(1-naphthyl)-1,3-dioxane (3.00 g, 12.0 mmol) and KH_2PO_4 (2.04 g, 15.0 mmol) in 150 mL of THF was added dropwise via an addition funnel a solution of $NaIO_4$ (3.21 g, 15.0 mmol) in 60 mL of water, and the mixture was subsequently treated in the same fashion as the 2-naphthyl derivative. The corresponding ketone was obtained in 80% yield (2.20 g, 9.6 mmol), as a yellow solid, mp 90−92 °C: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.16 (d, J = 8.0 Hz, 1 H), 7.90 (d, J = 6.0 Hz, 2 H), 7.82 (d, J = 7.0 Hz, 1 H), 7.59−7.48 (comp, 3 H), 6.48 (s, 1 H), 4.59 (dd, J = 18.8, 2.2 Hz, 4 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 204.4, 133.8, 131.7, 130.4, 130.1, 128.6, 126.5, 125.8, 124.9, 124.0, 123.6, 97.8, 72.5.

To a cold (0 °C) solution of 2-(1-naphthyl)-5-oxo-1,3-dioxane (2.50 g, 10.9 mmol) in anhydrous THF (250 mL) was added via syringe 1.0 M $LiAlH_4$ in THF (11 mL, 11 mmol) dropwise. The resulting solution was treated as described for the 2-naphthyl derivative to give, after chromatography (silica gel, 1:2 hexanes:ethyl acetate), *trans*-5-hydroxy-2-(1-naphthyl)-1,3-dioxane in 74% yield (1.85 g, 8.04 mmol) as a white solid, mp 136−138 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, J = 8.2 Hz, 1 H), 7.85 (d, J = 8.1 Hz, 2 H) 7.75 (d, J = 7.1 Hz, 1 H), 7.56−7.43 (comp, 3 H), 5.95 (s, 1 H), 4.42 (dd, J = 11.0, 5.2 Hz, 2 H), 4.27−4.10 (m, 1 H), 3.75 (dd, J = 11.0, 10.4 Hz, 1 H), 1.54 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.7, 132.5, 130.3, 129.7, 128.6, 126.2, 125.7, 124.9, 124.3, 124.0, 100.4, 71.9, 61.0. Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 73.22; H, 6.16.

***trans*-2-(2-Naphthyl)-1,3-dioxan-5-yl Diazoacetate.** *trans*-5-Hydroxy-2-(2-naphthyl)-1,3-dioxane (1.00 g, 4.35 mmol) dissolved in 25 mL of anhydrous THF was treated with triethylamine (0.044 g, 0.43 mmol) and diketene (0.548 g, 6.53 mmol) at 0 °C. The solution was allowed to come to room temperature overnight, at which point ^{1}H NMR analysis of the crude reaction mixture indicated complete conversion of the starting material to the desired acetoacetate. Triethylamine (0.659 g, 6.53 mmol) and methanesulfonyl azide (0.790 g, 6.53 mmol) were added sequentially to the solution, which was stirred for 24 h at room temperature. The solution was dissolved in 25 mL of water and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with water (3 × 50 mL) and brine (3 × 50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was dissolved in 5 mL of THF, and LiOH (0.376 g, 15.6 mmol) in 5 mL of water was added. The mixture was stirred for 2 h, at which time 30 mL of CH_2Cl_2 was added, and the mixture was extracted with water (3 × 30 mL) and brine (3 × 30 mL). The organic solution was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. Purification by column chromatography (1:1 hexanes:ethyl acetate) yielded the diazoester in 65% overall yield (0.843 g, 2.83 mmol) as a yellow solid, mp 100−102 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 1 H), 7.90−7.80 (comp, 3 H), 7.59 (dd, J = 8.6, 1.5 Hz, 1 H), 7.54−7.44 (comp, 2 H), 5.62 (s, 1 H), 5.14 (sept, J = 5.1 Hz, 1 H), 4.79 (s, br, 1 H), 4.46 (dd, J = 11.2, 5.1 Hz, 2 H), 3.77 (t, J = 11.2 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 134.5, 133.6, 132.9, 128.3, 128.2, 127.7, 126.4, 126.2, 125.6, 123.6, 101.4, 68.7, 63.0, 46.6. Anal. Calcd for $C_{16}H_{14}O_4N_2$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.27; H, 4.95; N, 9.19.

***trans*-2-(1-Naphthyl)-1,3-dioxan-5-yl Diazoacetate.** *trans*-5-Hydroxy-2-(1-naphthyl)-1,3-dioxane (1.50 g, 6.52 mmol) dissolved in 40 mL of anhydrous THF was treated with triethylamine (0.066 g, 0.65 mmol) and diketene (0.821 g, 9.78 mmol) at 0 °C. After complete reaction triethylamine (0.987 g, 9.78 mmol) and methanesulfonyl azide (1.18 g, 9.78 mmol) were added sequentially, and the resulting solution was treated as previously described for the 2-naphthyl derivative. Purification by column chromatography (1:1 hexanes:ethyl acetate), yielded the diazoester in 53% overall yield (0.103 g, 3.45 mmol) as a yellow solid, mp 108−110 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 8.5 Hz, 1 H), 7.86 (d, J = 7.8 Hz, 2 H), 7.47 (d, J = 7.1 Hz, 1 H), 7.56−7.44 (comp, 3 H), 5.98 (s, 1 H), 5.31−5.21 (m, 1 H) 4.80 (s, br, 1 H), 4.52 (dd, J = 10.0, 5.1 Hz, 2 H), 3.84 (t, J = 10.0 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 133.8, 132.3, 130.3, 129.9, 128.6, 126.3, 125.7, 124.9, 124.5, 124.1, 101.1, 69.1, 62.9, 46.5. Anal. Calcd for $C_{16}H_{14}O_4N_2$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.01; H, 4.91; N, 9.16.

3,5-*O*-(2-Naphthylidene)-2-deoxy-1,4-xylonolactone (20). *trans*-2-(2-Naphthyl)-1,3-dioxan-5-yl diazoacetate (0.298 g, 1.0 mmol) was dissolved in 10 mL of freshly distilled CH_2Cl_2 and added via syringe pump over 10 h to 1.0 mol % of the dirhodium(II) catalyst in CH_2Cl_2 (10 mL). Upon completion of the addition, the solution was refluxed for an additional hour, cooled to room temperature, and passed through a short silica gel plug to remove the catalyst. The plug was washed with 60 mL of CH_2Cl_2, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (8:1 CH_2Cl_2:EtOAc) to afford 3,5-*O*-(2-naphthylidene)-2-deoxy-1,4-xylonolactone as a white solid, mp 146−148 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 1 H), 7.92 (d, J

= 8.9 Hz, 1 H), 7.90−7.84 (comp, 2 H), 7.58−7.47 (comp, 2 H), 7.53 (d, J = 8.9 Hz, 1 H), 6.19 (s, 1 H), 4.68 (ddd, J = 4.2, 3.6, 2.2 Hz, 1 H), 4.36 (dddd, J = 4.7, 2.4, 2.1, 2.0 Hz, 1 H), 4.28 (dd, J = 12.9, 4.2 Hz, 1 H), 4.12 (dd, J = 12.9, 3.6 Hz, 1 H), 2.82 (dd, J = 17.8, 2.0 Hz, 1 H), 2.75 (dd, J = 17.8, 4.7 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.9, 133.5, 133.4, 133.2, 128.9, 128.2, 127.7, 126.7, 126.5, 126.1, 123.9, 95.8, 66.2, 60.4, 36.5, 29.7; HRMS calcd for $[C_{16}H_{14}O_4 + H]^+$ 271.2927, found 271.0970. This 2-naphthylidene-protected 2-deoxy-1,4-xylonolactone was hydrogenolyzed to 2-deoxy-1,4-xylonolactone as previously described for **18**.

1,3-Dialkoxy-2-propanol. The preparation of 1,3-diethoxy-2-propanol is representative. To a continually stirred solution of sodium ethoxide in 75 mL of ethanol, prepared by reacting freshly cut sodium (5.98 g, 0.260 mol) with absolute ethanol, at 0 °C was added 1,3-dichloro-2-propanol (12.89 g, 0.100 mol) dropwise over 30 min through an additional funnel. The reaction mixture was then heated at reflux for 90 min, after which the cooled mixture was diluted with 100 mL of ether to precipitate NaCl and then filtered. Solvents were removed under reduced pressure, and the residual yellow oil was distilled, bp 93−96.5 °C at 13 Torr, to yield 13.77 g (0.093 mol, 93% yield) of a colorless oil. 1,3-Dimethoxy-2-propanol, bp °C at Torr, was obtained in % yield; 1,3-dibenzyloxy-2-propanol, bp 175−180 °C at 0.05 Torr (lit.[27] bp 195−210 °C at 3 Torr), was obtained in 81% yield.

1,3-Dialkoxy-2-propyl Diazoacetates (21). The preparation of 1,3-diethoxy-2-propyl diazoacetate is representative. A solution of 1,3-diethoxy-2-propanol (10.0 g, 67.5 mmol) and freshly distilled 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (9.50 g, 67.5 mmol) in xylene (67 mL) was heated with rapid stirring in a preheated oil bath at 150 °C for 30 min until acetone had evaporated.[28] Xylene was removed by distillation, and the residue was purified by bulb-to-bulb distillation (bp 100−195 °C at 0.1 Torr) to yield 12.5 g (54.0 mmol, 80% yield) of 1,3-diethoxy-2-propyl acetoacetate as a colorless oil: ^{1}H NMR δ 5.18 (quin, J = 5.1 Hz, 1 H), 3.59 (d, J = 5.1 Hz, 4 H), 3.60−3.42 (m, 4 H), 3.48 (s, 2 H), 2.28 (s, 3 H), 1.18 (t, J = 7.0 Hz, 6 H); enol form at δ 5.04 and 1.96.

Methanesulfonyl azide (6.76 g, 55.9 mmol) in 50 mL of acetonitrile was added dropwise over 45 min to a solution of 1,3-diethoxy-2-propyl acetoacetate (10.00 g, 43.0 mmol) and Et_3N (5.06 g, 51.6 mmol) in 50 mL of anhydrous acetonitrile. The resulting yellow solution was maintained at room temperature for an additional 18 h, whereupon $LiOH{\cdot}H_2O$ (5.92 g, 0.149 mol) in 57 mL of water was added, and stirring was continued for 8 h. The resulting aqueous reaction solution was diluted with 100 mL of 1:1 ether in ethyl acetate. The combined organic layer was washed with saturated aqueous NaCl (50 mL) and dried ($MgSO_4$), and the solvent was removed under reduced pressure. The resulting dark yellow oil was purified by column chromatography on silica gel eluting with 19:1 hexanes:ethyl acetate to give 1,3-diethoxy-2-propyl diazoacetate (4.35 g, 47% yield) as a yellow oil.

1,3-Dimethoxy-2-propyl Diazoacetate (21a): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.18 (quin, J = 5.0 Hz, 1 H), 4.81 (br s, 1 H), 3.52 (d, J = 5.0 Hz, 4 H), 3.34 (s, 6 H); IR (film) 2108 (C=N_2), 1696 (C=O) cm^{-1}. Anal. Calcd for $C_7H_{12}O_4N_2$: C, 44.68; H, 6.43; N, 14.87. Found: C, 44.63; H, 6.48; N, 14.92.

1,3-Diethoxy-2-propyl Diazoacetate (21b): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.17 (quin, J = 5.1 Hz, 1 H), 4.82 (br s, 1 H), 3.58 (d, J = 5.1 Hz, 4 H), 3.59−3.44 (m, 4 H), 1.18 (t, J = 7.0 Hz, 6 H); IR (film) 2112 (C=N_2), 1692 (C=O) cm^{-1}. Anal. Calcd for $C_9H_{16}O_4N_2$: C, 49.99; H, 7.46; N, 12.96. Found: C, 50.03; H, 7.53; N, 12.93.

1,3-Dibenzyloxy-2-propyl Diazoacetate (21c): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.23 (m, 10 H), 5.28 (quin, J = 5.1 Hz, 1 H), 4.79 (br s, 1 H), 4.56 (d, J = 12.0 Hz, 2 H), 4.50 (d, J = 12.0 Hz, 2 H), 3.65 (d, J = 5.1 Hz, 4 H); IR (film) 2112 (C=N_2), 1693 (C=O) cm^{-1}. Anal. Calcd for $C_{19}H_{20}O_4N_2$: C, 67.05; H, 5.92; N, 8.23. Found: C, 67.01; H, 5.98; N, 8.17.

Diazo Decomposition of 1,3-Dialkoxy-2-propyl Diazoacetates. To the dirhodium(II) catalyst (0.1 mol %) in 50 mL of refluxing dichloromethane was added by syringe pump the diazoester (1.0 mmol) in 10 mL of anhydrous dichloromethane during 10 h (1.0 mL/h). The initial color of the solution containing Rh_2(5*S*-MEPY)$_4$ or Rh_2(5*R*-MEPY)$_4$ was blue, which generally changed to an olive color by the end of the addition; with Rh_2(4*S*-MEOX)$_4$ the initial color was light red, which became light yellow at the end of the addition. After addition was complete, CH_2Cl_2 was evaporated under reduced pressure, and the lactone product(s) was isolated by column chromatography on silica (7:3 hexane:ethyl acetate). This product mixture, which was chromatographically pure, was analyzed spectroscopically, and enantiomeric excess was obtained on a Chiraldex G-TA column with baseline resolution for diethoxy derivatives.

3*O*,5*O*-Dimethyl-2-deoxy-1,4-xylonolactone: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.64 (ddd, J = 5.8, 4.8, 4.6 Hz, 1 H), 4.19 (ddd, J = 4.9, 4.8, 3.5 Hz, 1 H), 3.78 (dd, J = 11.0, 4.6 Hz, 1 H), 3.73 (dd, J = 11.0, 5.8 Hz, 1 H), 3.45 (s, 3 H), 3.38 (s, 3 H), 2.70 (dd, J = 17.6, 3.5 Hz, 1 H), 2.68 (dd, J = 17.6, 4.9 Hz, 1 H); mass spectrum, *m*/*z* (relative abundance) 160 (M, 1), 132 (1), 115 (15), 101 (93), 85 (25), 83 (35), 73 (83), 71 (92), 59 (73), 58 (100); IR (film) 1786 cm^{-1}. Anal. Calcd for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.51; H, 7.52.

3*O*,5*O*-Dimethyl-2-deoxy-1,4-ribonolactone: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.53 (ddd, J = 6.7, 4.9, 4.8 Hz, 1 H), 4.05 (ddd, J = 4.9, 2.1, 1.9 Hz, 1 H), 3.59 (dd, J = 11.0, 4.8 Hz, 1 H), 3.54 (dd, J = 11.0, 1.9 Hz, 1 H), 3.36 (s, 3 H), 3.34 (s, 3 H), 2.82 (dd, J = 18.0, 6.7 Hz, 1 H), 2.50 (dd, J = 18.0, 2.1 Hz, 1 H); mass spectrum, *m*/*z* (relative abundance) 160 (M, 1), 132 (17), 115 (11), 101 (14), 85 (10), 83 (19), 73 (41), 71 (48), 59 (40), 59 (100). Spectral data are consistent with those of 2-deoxy-1,4-lactone.[23]

3*O*,5*O*-Diethyl-2-deoxy-1,4-xylonolactone: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.60 (ddd, J = 5.9, 4.9, 4.8 Hz, 1 H), 4.22 (ddd, J = 4.8, 4.4, 3.8 Hz, 1 H), 3.78 (dd, J = 10.9, 4.9 Hz, 1 H), 3.74 (dd, J = 10.9, 5.9 Hz, 1 H), 3.66−3.37 (m, 4 H), 2.68 (dd, J = 17.4, 3.8 Hz, 1 H), 2.66 (dd, J = 17.4, 4.4 Hz, 1 H), 1.22 (t, J = 6.5 Hz, 3 H), 1.19 (t, J = 6.7 Hz, 3 H); mass spectrum, *m*/*z* (relative abundance) 188 (M, 1), 159 (18), 129 (79), 115 (16), 114 (4), 101 (62), 87 (37), 85 (52), 73 (37), 72 (86), 71 (43), 59 (100), 57 (45); IR (film) 1786 cm^{-1}. Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.38; H, 8.55.

3*O*,5*O*-Diethyl-2-deoxy-1,4-ribonolactone: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.53 (ddd, J = 4.9, 3.0, 2.1 Hz, 1 H), 4.15 (ddd, J = 6.8, 2.1, 1.9 Hz, 1 H), 3.66−3.37 (m, 6 H), 2.84 (dd, J = 18.0, 6.8 Hz, 1 H), 2.48 (dd, J = 18.0, 2.1 Hz, 1 H), 1.21 (t, J = 6.4 Hz, 3 H), 1.18 (t, J = 6.7 Hz, 3 H); mass spectrum, *m*/*z* (relative abundance) 189 (M + 1, 1), 188 (M, 6), 159 (14), 129 (11), 115 (7), 114 (25), 101 (53), 87 (29), 85 (15), 73 (26), 72 (76), 71 (11), 59 (100), 57 (23). Spectral data are consistent with those of 2-deoxy-1,4-lactone.[23]

3*O*,5*O*-Dibenzyl-2-deoxy-1,4-xylonolactone: bp 220−230 °C (0.2 Torr); $[\alpha]^{23}_D$ = −5.40 (*c* 0.537, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.22 (m, 10 H), 4.63−4.51 (m, 5 H), 4.44 (d, J = 11.9 Hz, 1 H), 3.86 (d, J = 5.3 Hz, 2 H), 2.72 (dd, J = 17.6, 3.1 Hz, 1 H), 2.62 (dd, J = 17.6, 5.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 137.8, 137.1, 128.6, 128.5, 128.1, 127.9, 127.8, 127.7, 82.0, 74.5, 73.7, 71.8, 67.7, 35.6; mass spectrum, *m*/*z* (relative abundance) 312 (M, 0.2), 222 (33), 221 (100), 115 (75), 108 (19), 107 (99), 105 (18), 97 (51), 92 (71), 91 (100), 89 (22), 79 (47), 77 (51), 71 (23), 65 (97); IR (film) 1784 cm^{-1}. Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.05; H, 6.45. Found: C, 73.14; H, 6.54.

3*O*,5*O*-Dibenzyl-2-deoxy-1,4-ribonolactone: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.24 (m, 10 H), 4.62 (ddd, J = 3.3, 3.0, 2.2 Hz, 1 H), 4.54 (d, J = 12.0 Hz, 1 H), 4.53 (d, J = 11.4 Hz, 1 H), 4.48 (d, J = 11.4 Hz, 1 H), 4.47 (d, J = 12.0 Hz, 1 H), 4.27 (dt, J = 6.9, 2.2 Hz, 1 H), 3.66 (dd, J = 10.8, 3.3 Hz, 1 H), 3.61 (dd, J = 10.8, 3.0 Hz, 1 H), 2.86 (dd, J = 18.1, 6.9 Hz, 1 H), 2.57 (dd, J = 18.1, 2.2 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.6, 137.4, 137.1, 128.7, 128.6, 128.1, 128.0, 127.8, 127.7,

(27) Olgivie, K. K.; Ngugen, N. B.; Gillan, M. F.; Radatus, B. K.; Cheriyean, V. U.; Hanna, H. R.; Smith, K. S. *Can. J. Chem*. **1984**, *62*, 24.

(28) Clemens, R. J.; Hyatt, J. A. *J. Org. Chem*. **1985**, *50*, 2431.

84.1, 76.1, 73.8, 71.3, 69.7, 35.8; mass spectrum, *m*/*z* (relative abundance) 312 (M, 1), 222 (36), 221 (100), 115 (75), 108 (21), 107 (100), 105 (22), 97 (510), 92 (71), 91 (100), 89 (21), 79 (44), 77 (43), 71 (21), 65 (97). Spectral data are consistent with those of 2-deoxy-1,4-lactone.[23]

(3*R*,4*R*)-(+)-2-Deoxy-1,4-xylonolactone. The dibenzyl ether (312 mg, 1.00 mmol) from the reaction performed with Rh_2-(5*R*-MEPY)$_4$ dissolved in 50 mL of ethyl acetate was placed in a glass vessel containing 30 mg of 20% $Pd(OH)_2$ on carbon and shaken in a Parr hydrogenator under 30 psi hydrogen for 24 h. The resulting mixture was filtered through Celite, and the solvent was evaporated under reduced pressure. Pure 2-deoxyxylonolactone (110 mg, 83% yield) was isolated by column chromatography on silica gel (9:1 ethyl acetate:methanol, R_f 0.50): $[\alpha]^{26}_D = +56.2$ (*c* 0.49, MeOH); lit.[26] $[\alpha]^{25}_D = +49.3$ (*c* 0.56, MeOH).

1,3-Dimethoxy-2-ethyl-2-propyl Diazoacetate (26a). To a magnetically stirred solution of 1,3-dimethoxy-2-ethyl-2-propyl diazoacetoacetate (2.58 g, 10.0 mmol) in acetonitrile (50 mL) was added a solution of $LiOH \cdot H_2O$ (1.26 g, 30.0 mmol) in water (25 mL). The reaction mixture was stirred at room temperature, and after 2 h, NMR analysis (sample from the reaction mixture) showed complete conversion. EtOAc (75 mL) was added, and the layers were separated. The organic layer was washed with water (1 × 100 mL) and brine (1 × 100 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvents were removed under reduced pressure, and the residual yellow oil was purified by Kugelrohr distillation (bp 55−60 °C, 0.05 Torr) to yield 1,3-dimethoxy-2-ethyl-2-propyl diazoacetate as a yellow oil (1.56 g, 7.22 mmol, 72% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.70 (bs, 1 H), 3.73 (d, J = 9.7 Hz, 2 H), 3.55 (d, J = 9.7 Hz, 2 H), 1.91 (q, J = 7.6 Hz, 2 H), 0.87 (t, J = 7.6 Hz, 3 H); ^{13}C NMR δ 165.9, 85.4, 71.7, 59.2, 46.6, 24.0, 7.0; IR ($CHCl_3$) 2114 (C=N_2), 1686 (C=O) cm^{-1}. Anal. Calcd for $C_9H_{16}O_4N_2$: C, 49.99; H, 7.46; N, 12.95. Found: C, 49.83; H, 7.40; N, 12.86.

***(E)*-5-Ethyl-4-methoxy-5-(methoxymethyl)-2(3*H*)-furanone (27a).** Enantiomer separation on a Chiraldex G-TA column operated at 120 °C for 30 min then programmed to 150 °C at 1°/min, 53.6 and 61.1 min for the two enantiomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.88 (t, J = 6.9 Hz, 1 H), 3.69 (d, J = 10.5 Hz, 1 H), 3.49 (d, J = 10.5 Hz, 1 H), 3.37 (s, 6 H), 2.74 (d, J = 6.9 Hz, 2 H), 1.71 (q, J = 7.5 Hz, 2 H), 0.97 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 88.9, 80.6, 72.2, 59.7, 58.2, 35.5, 28.1, 7.6; mass spectrum, *m*/*z* (relative abundance) 143 (97), 112 (27), 111 (100), 102 (42), 101 (45), 85 (21), 83 (59), 73 (92), 59 (100), 57 (99), 55 (57); IR ($CHCl_3$) 1771 (C=O) cm^{-1}. Anal. for the mixture of **25a** and **26a** calcd for $C_9H_{16}O_4$: C, 57.42; H, 8.57. Found: C, 57.36; H, 8.67.

***(Z)*-5-Ethyl-4-methoxy-5-(methoxymethyl)-2(3*H*)-furanone (28a).** Enantiomer separation on a Chiraldex G-TA column operated at 150 °C, 16.4 and 21.3 min for the two enantiomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.00 (dd, J = 6.9, 2.9 Hz, 1 H), 3.50 (d, J = 10.2 Hz, 1 H), 3.42 (d, J = 10.2 Hz, 1 H), 3.35 (s, 3 H), 3.31 (s, 3 H), 2.91 (dd, J = 17.9, 6.9 Hz, 1 H), 2.50 (dd, J = 17.9, 2.9 Hz), 1.89−1.68 (comp, 2 H), 0.97 (t, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.3, 90.2, 79.2, 75.5, 59.5, 57.4, 36.1, 24.0, 8.0; mass spectrum, *m*/*z* (relative abundance) 143 (92), 112 (13), 111 (100), 102 (32), 101 (27), 83 (30), 73 (46), 58 (99), 57 (84), 55 (27); IR ($CHCl_3$) 1770 (C=O) cm^{-1}. Anal. for **28a**: see **27a**.

1,3-Dimethoxy-2-phenyl-2-propyl Diazoacetate (26b). To a magnetically stirred solution of 1,3-dimethoxy-2-phenyl-2-propyl diazoacetoacetate (2.0 g, 6.54 mmol) in acetonitrile (40 mL) was added a solution of $LiOH \cdot H_2O$ (0.82 g, 19.6 mmol) in water (17 mL). The reaction mixture was stirred at room temperature, and after 1.5 h NMR analysis (sample from the reaction mixture) showed complete conversion. EtOAc (50 mL) was added, and the layers were separated. The organic layer was washed with water (1 × 100 mL) and brine (1 × 100 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvents were removed under reduced pressure, and the residual yellow oil was purified by column chromatography (silica gel, 1:9 EtOAc:hexane) to yield 1,3-dimethoxy-2-phenyl-2-propyl diazoacetate as a yellow oil (1.13 g, 4.28 mmol, 65% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.26 (comp, 5 H), 4.83 (br s, 1 H), 4.02 (d, J = 9.7 Hz, 2 H), 3.96 (d, J = 9.7 Hz, 2 H), 3.38 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 139.9, 128.2, 127.7, 125.1, 84.3, 74.1, 59.5, 47.0; IR ($CHCl_3$) 2115 (C=N_2), 1695 (C=O) cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_4N_2$: C, 59.08; H, 6.10; N, 10.60. Found: C, 59.17; H, 6.16; N, 10.51.

***(Z)*-4-Methoxy-5-(methoxymethyl)-5-phenyl-2(3*H*)-furanone (27b).** Enantiomer separation on a Chiraldex G-TA column operated at 150 °C, 68.6 and 78.9 min for the two enantiomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47−7.43 (comp, 2 H), 7.40−7.29 (comp, 3 H), 4.18 (dd, J = 7.6, 7.2 Hz, 1 H), 3.98 (d, J = 10.8 Hz, 1 H), 3.56 (d, J = 10.8 Hz, 1 H), 3.47 (s, 3 H), 3.36 (s, 3 H), 2.87 (dd, J = 17.0, 7.2 Hz, 1 H), 2.71 (dd, J = 17.0, 7.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 139.8, 128.6, 128.1, 124.4, 88.9, 83.0, 75.5, 59.8, 58.3, 35.1; mass spectrum, *m*/*z* (relative abundance), 204 (11), 191 (99), 160 (100), 159 (100), 131 (62), 121 (71), 115 (13), 105 (98), 103 (20), 91 (35), 77 (93), 58 (47), 51 (30); IR ($CHCl_3$) 1779 (C=O) cm^{-1}. Anal. for the mixture of **25b** and **26b** calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.09; H, 6.87.

***(E)*-4-Methoxy-5-(methoxymethyl)-5-phenyl-2(3H)-furanone (28b).** Enantiomer separation on a Chiraldex G-TA column operated at 150 °C, 75.9 and 90.2 min for the two enantiomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.27 (comp, 5 H), 4.31 (dd, J = 6.3 Hz, 1.9 Hz, 1 H), 3.81 (d, J = 10.7 Hz, 1 H), 3.48 (d, J = 10.7 Hz, 1 H), 3.35 (s, 3 H), 3.14 (s, 3 H), 3.07 (dd, J = 17.8, 6.3 Hz, 1 H), 2.56 (dd, J = 17.8, 1.9 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2, 135.8, 128.0, 127.9, 125.9, 91.4, 80.1, 78.7, 59.7, 56.9, 36.2; mass spectrum, *m*/*z* (relative abundance) 236 (M, 2), 206 (24), 191 (90), 160 (92), 159 (100), 131 (64), 121 (79), 105 (100), 103 (28), 91 (63), 77 (99), 58 (89), 51 (41); IR ($CHCl_3$) 1782 (C=O) cm^{-1}. Anal. for **26b**: see **26a**.

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