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Stereoselectivity in Metal Carbene Addition to a Carbon-Carbon Triple Bond Tied to the Reactant Diazoacetate Through a Chiral Linker

Michael P. Doyle,[a,*] Thomas M. Weathers Jr.,[a] and Yuanhua Wang[a]

[a] Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland, 20742, USA
Fax: (+1)-301-314-2779; e-mail: mdoyle3@umd.edu

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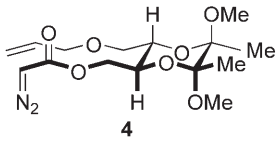
Abstract: The trajectory of a carbon-carbon triple bond onto a metal carbene for cyclopropene formation is opposite to that of a carbon-carbon double bond in the same system. Diazoacetates prepared from the butane-2,3-diacetals (BDA) of (L)- and (D)-threitol were employed to examine diastereoselectivity in cyclopropenation. The absolute configuration of the predominant isomer was opposite in intramolecular metal carbene additions to propargyl and allyl substituents. Diastereoselectivities in the dirhodium(II) carboxamidate-catalyzed diazo decomposition reactions are as high as 99:1 with match/mismatch selectivites for substrate and catalyst, dependent on catalyst configuration, and are favored in the order: $Rh_2(MEPY)_4 > Rh_2(MEOX)_4 > Rh_2(MEAZ)_4 > Rh_2(MPPIM)_4$. The reactions catalyzed by the Cu$(CH_3CN)_4PF_6$/PhBox system produce the same set of diastereoisomers in a complimentary match/mismatch selectivity that also reaches 99:1.

Keywords: addition; bis-oxazoline-ligated copper(I); cyclopropenation; diastereoselectivity; dirhodium(II) carboxamidates; macrocyclization

Introduction

Carbene addition to a carbon-carbon triple bond is a characteristic transformation in catalytic reactions of diazocarbonyl compounds,[1] and the resulting cyclopropene compounds are both stable[2] and synthetically useful.[3] Asymmetric induction has been documented in both intermolecular[4] and intramolecular[5] reactions with both chiral dirhodium(II) and chiral copper(I) catalytic systems. For example, catalytic diazo decomposition of diazoacetate **1** afforded cyclopropene **2** in high enantiomeric excess (Scheme 1), especially with $Rh_2(4S\text{-IBAZ})_4$, but copper(I)/S,S-*t*-Bu-Box was also effective. The absolute stereochemistry of **2** was established by hydrogenolysis/hydrogenation to an oxabicyclo[3.1.0]hexan-2-one whose configuration had been previously established.[6] What was missing from this and other studies was a comparative evaluation of the similarity or difference in absolute stereochemistry between addition to a carbon-carbon double bond and a carbon-carbon triple bond. Having recently reported the stereochemical preferences in intramolecular cyclopropanation reactions of the allyl diazoacetates **4** and ***ent*-4**,[7] we turned our attention to their propargyl analogues.



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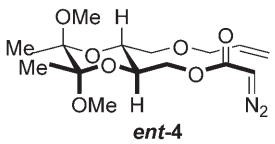
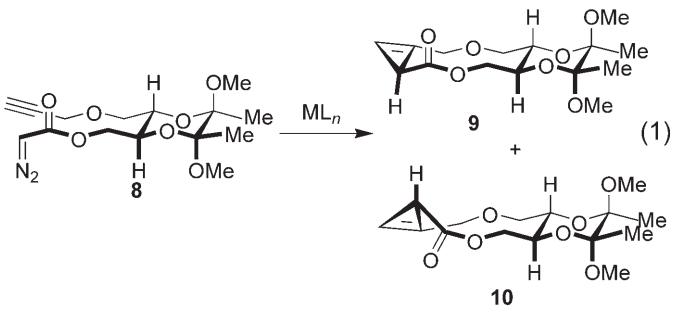


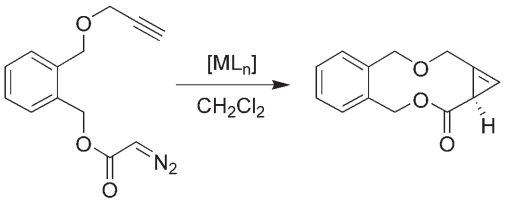
***ent*-4**

Results and Discussion

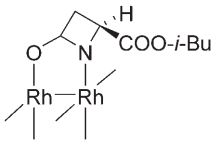
Diazoacetate **8** was prepared from the Ley alcohol **5**[8] by the sequence of steps described in Scheme 2. Catalytic diazo decomposition of **8** occurred in refluxing dichloromethane by regulated addition of the diazo compound to the catalyst solution, and product evaluation of the resultant material was accomplished using GC and ^{1}H NMR spectroscopy as well as conversion of one enantiomer of the cyclopropene to the corresponding cyclopropane compound of known configuration (*vida infra*).

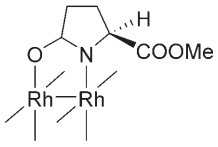
Dirhodium(II) tetraacetate-catalyzed decomposition of **8** afforded cyclopropene diastereoisomers **9** and **10** in a ratio of 83:17, respectively [Eq. (1)], and copper(I) hexafluorophosphate gave virtually identical results, with these diastereoselectivities attributed to the conformational bias of the configurationally rigid diequatorial projection in **8**. Comparative results from reactions catalyzed by representative chiral dir-

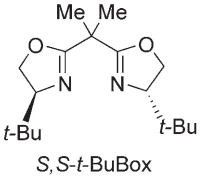




ML$_n$	
Rh$_2$(4*S*-IBAZ)$_4$	92% ee
CuPF$_6$/**3**	80% ee
Rh$_2$(5*S*-MEPY)$_4$	67% ee



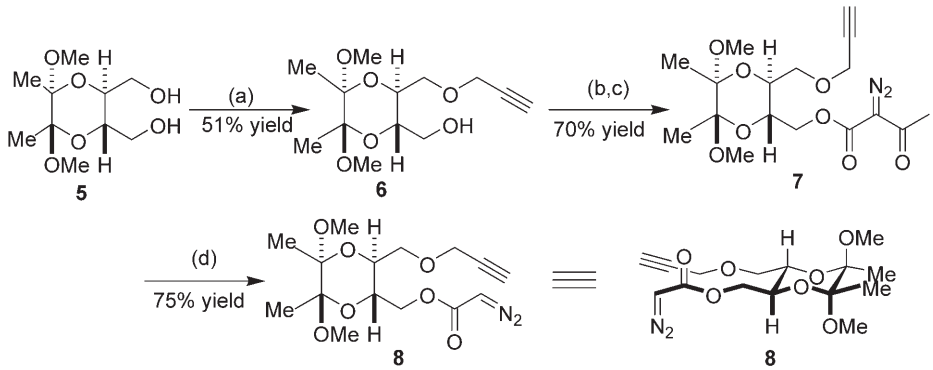




Scheme 1.

hodium(II) carboxamidate and bis-oxazoline-ligated copper(I) catalysts are reported in Table 1.

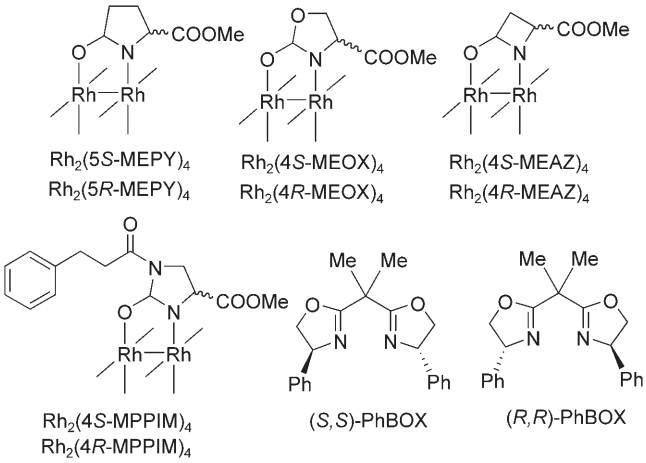
Results with achiral rhodium acetate and copper hexafluorophosphate are identical, indicating that there is no distinguishing selectivity that can be attributed solely to the metal center. Diazo decomposition of **8** catalyzed by Rh$_2$(5*S*-MEPY)$_4$ afforded an increased degree of diastereoselectivity compared to the dirhodium(II) tetraacetate-catalyzed reaction, with a 99:1 ratio (**9:10**), whereas Rh$_2$(5*R*-MEPY)$_4$ produced the cyclopropenation product with a 71:29 diastereomer ratio (**9:10**). Compared to the diastereoisomer ratio obtained for diazo decomposition of **8** by dirhodium(II) tetraacetate, Rh$_2$(5*S*-MEPY)$_4$ is the matched catalyst for **8**. The lower diastereoisomer ratio obtained from diazo decomposition of **8** by Rh$_2$(5*R*-MEPY)$_4$ compared to the diastereoisomer ratio obtained for diazo decomposition of **8** by dirhodium(II) tetraacetate makes Rh$_2$(5*R*-MEPY)$_4$ the mismatched catalyst for **8**. Similar diastereoselectivity, in which the *S* enantiomer was the matched catalyst, was seen using Rh$_2$(MEAZ)$_4$ and Rh$_2$(MEOX)$_4$. The order of catalyst diastereoselectivity is: Rh$_2$(5*S*-MEPY)$_4$ > Rh$_2$(4*S*-MEOX)$_4$ > Rh$_2$(4*S*-MEAZ)$_4$ > Rh$_2$(4*S*-MPPIM)$_4$. Catalysis by the Cu(CH$_3$CN)$_4$PF$_6$/**3** complex, afforded a 69:31 diastereoselectivity that favored **10** over **9** but, as seen for results with the PhBox ligands, this is the result for the mismatched substrate-catalyst pair. (*R,R*)-PhBox with copper(I) hexafluorophosphate gives **9** in essentially exclusive preference to **10** in a diastereomer ratio of 99:1. The formation of **9** in preference to **10** for the matched substrate-copper(I) catalyst pair is the same diastereochemical preference as that of that found for all dirhodium(II) *S*-configured carboxamidates, but the mismatched substrate-copper(I) catalyst pair drives stereochemical preference much further towards **10** relative to that for the mismatched substrate-dirhodium(II) carboxamidate catalyst pair. The evident exception to the match/mismatch considerations,



(a) NaH, allyl bromide, NaI,THF; (b) diketene, Et$_3$N, THF; (c) MsN$_3$, Et$_3$N, THF; (d) LiOH, THF, H$_2$O

Scheme 2.

Table 1. Diastereoselectivities in intramolecular cyclopropenation reactions of **8** with dirhodium(II) and copper(I) catalysts.[a]

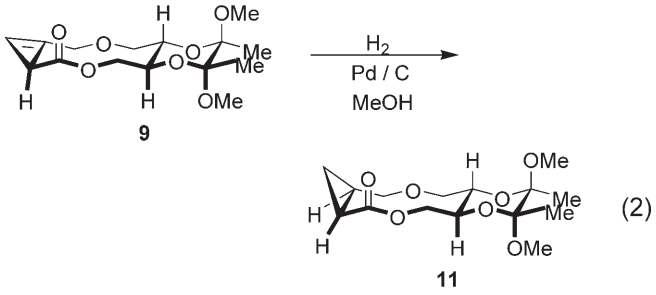


Catalyst	*dr* (**9**:**10**)[b]	Yield (**9**+**10**) [%][c]
$Rh_2(OAc)_4$	83:17	83
$Rh_2(5R\text{-MEPY})_4$	71:29	71
$Rh_2(5S\text{-MEPY})_4$	99: 1	80
$Rh_2(4R\text{-MEAZ})_4$	81:19	71
$Rh_2(4S\text{-MEAZ})_4$	91: 9	79
$Rh_2(4R\text{-MPPIM})_4$	96: 4	78
$Rh_2(4S\text{-MPPIM})_4$	89:11	75
$Rh_2(4R\text{-MEOX})_4$	82:18	35
$Rh_2(4S\text{-MEOX})_4$	98: 2	73
$Cu(CH_3CN)_4PF_6$	82:18	70
$Cu(CH_3CN)_4PF_6$/(*S*,*S*)-*t*-BuBox	39:61	72
$Cu(CH_3CN)_4PF_6$/(*S*,*S*)-PhBox	47:53	74
$Cu(CH_3CN)_4PF_6$/(*R*,*R*)-PhBox	99: 1	75

[a] Diazoacetate **1** was added over 2 h to a refluxing catalyst/DCM solution *via* a syringe pump.
[b] Product ratios were obtained by integration of the relevant signals in the ^1H NMR spectrum.
[c] Yields determined by weight of isolated product and ^1H NMR integration.

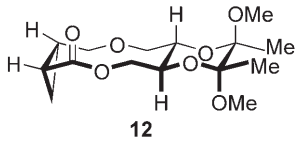
otherwise uniform, is the results obtained with $Rh_2(MPPIM)_4$ catalysts wherein the *S*-catalyst configuration gives lower product diastereoselection than the *R*-configured catalyst.

The configurations of **9** and **10** were determined by selective hydrogenation of the cyclopropene double bond of **9** with palladium on carbon [Eq. (2)] to form the corresponding cyclopropane compound, the absolute configuration of whose diastereoisomer was established by crystallographic determination.[7] That the stereochemistry of the hydrogenated material was that of **11** was determined by comparison with the ^1H NMR spectrum of the authentic material, and verified by GC analysis on an SPB-5 column to show an identical retention time to authentic **11**.

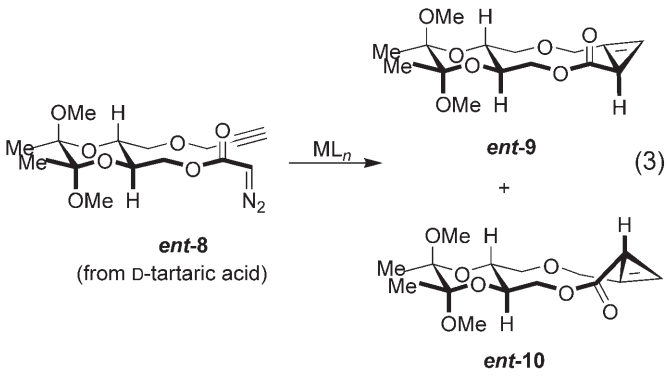


(2)

In cyclopropanation reactions of the allyl analogue of **8**, which is represented by **4**, the matched cyclopropane isomer is **12**, the diastereoisomer of **11**.



To confirm the configurational match and mismatch of conformationally biased diazoacetates with chiral dirhodium and copper catalysts, the enantiomer of **8** was prepared from D-tartaric acid; and using the method described for preparation of **8** (Scheme 2), ***ent*-8** was obtained as a yellow oil. Each intermediate in the synthesis of ***ent*-8** was compared to that from the synthesis of **8** to verify that they had equal and opposite values of optical rotation. Diazo decomposition and product evaluation were both accomplished in the same manner as that described in the decomposition of **8** [Eq. (3)]; and the results found in Table 2,



(3)

as expected, are mirror images of those reported in Table 1. Dirhodium(II) tetraacetate-catalyzed decomposition of ***ent*-8** afforded cyclopropene diastereoisomers ***ent*-9** and ***ent*-10** in a ratio of 83:17, which is consistent with the diastereoselectivity seen in dirhodium(II) tetraacetate-catalyzed decomposition of **8**.

Table 2. Diastereoselectivities in intramolecular cyclopropene reactions of ***ent*-8** catalyzed by dirhodium(II) and copper(I) catalysts.[a]

Catalyst	*dr* (***ent*-9**:***ent*-10**)[b]	Yield (***ent*-9** + ***ent*-10**) [%][c]
$Rh_2(OAc)_4$	83:17	78
$Rh_2(5R\text{-MEPY})_4$	99: 1	81
$Rh_2(5S\text{-MEPY})_4$	62:38	75
$Cu(CH_3CN)_4PF_6$	86:14	80
$Cu(CH_3CN)_4PF_6$/(*S,S*)-*t*-BuBox	97: 3	73
$Cu(CH_3CN)_4PF_6$/(*R,R*)-PhBox	46:54	75
$Cu(CH_3CN)_4PF_6$/(*S,S*)-PhBox	99: 1	77

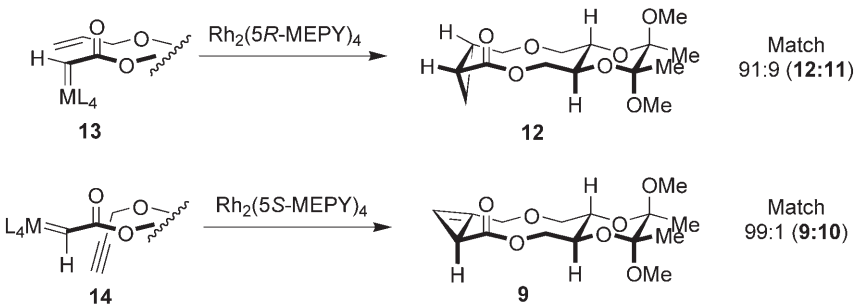
[a] Diazoacetate **2** was added over 2 h to a refluxing catalyst/DCM solution *via* syringe pump.
[b] Product ratios were obtained by integration of the relevant signals in the ^1H NMR spectrum.
[c] Yields determined by weight of isolated product and ^1H NMR integration.

The $Cu(CH_3CN)_4PF_6$/(*S,S*)-*t*-BuBox-catalyzed diazo decomposition affords a 97:3 ratio (***ent*-9**:***ent*-10**), making it a matched catalyst with ***ent*-8**; and the reduction in diastereoselectivity in diazo decomposition of ***ent*-8** by $Cu(CH_3CN)_4PF_6$/(*R,R*)-PhBox makes this a mismatched catalyst with ***ent*-8**. $Cu(CH_3CN)_4PF_6$/(*S,S*)-PhBOX exhibits higher diastereocontrol than $Cu(CH_3CN)_4PF_6$/(*S,S*)-*t*-BuBox in reactions with ***ent*-8**. As was seen in catalytic reactions of **8**, where the cyclopropene isomer configuration was opposite to that from the cyclopropane from reactions of **4**, the same outcome is found in catalytic reactions of ***ent*-8** relative to those of ***ent*-4**.

Comparison of catalytic metal carbene addition to an allyl, the allyl group of **4** versus addition to the propargyl group of **8** shows that diastereoselectivity is greater in cyclopropenation than in cyclopropanation. However, the matched dirhodium(II) carboxamidate catalysts for decomposition of **8** were the *S* enantiomers, whereas in decomposition of **4**, the matched catalysts were the *R* enantiomers.[9] These differences suggest that the carbon-carbon double bond approach to the metal carbene intermediate and the carbon-carbon triple bond approach to the metal carbene intermediate are opposite. This difference is also seen in the diazo decompositions of **4** and **8** catalyzed by the $Cu(CH_3CN)_4PF_6$/bis-oxazoline complexes. Doyle and Hu previously described the trajectory of a carbon-carbon double bond to the carbene of dirhodium- and copper-carbene complexes.[10] However, the trajectory of an alkyne to the carbene of these metal carbenes has received limited attention,[11d–f] and the belief expressed has been that the trajectory is "end on" rather than "side on." Results from diazo decompositions of **4** and **8** show that the matched catalyst for **8** is the enantiomer of the matched catalyst for **4**, resulting in formation of the opposite stereochemistry at the carbene center of the preferred diastereoisomer (Scheme 3). This change in the stereochemistry is explained by considering the conformation of the alkene or alkyne relative to the metal carbene intermediate, as depicted in **13** and **14**. The orientation of the multiple bond with the carbene center is opposite in these two depictions: **13** is consistent with prior discussions of carbene-double bond orientation, and **14** is consistent with the results presented from this study and from the absolute stereochemistry observed in intermolecular cyclopropenation reactions.[4b] Other factors may also be operative, but this explanation is clearly consistent with the accumulated data.

Conclusions

In this investigation we report results that confirm that the trajectory of a carbon-carbon triple bond to rhodium and copper carbene complexes is opposite to that of a carbon-carbon double bond. The use of diol **5** to link propargyl and diazoacetate functionalities offers a conformationally constrained platform with which to examine catalyst influences on diastereoselectivity. Diastereomeric preferences originating from configurational matched and mismatched effects provide distinguishing selectivities on the catalysts.



13 12 14 9

Scheme 3.

Matched diastereoselectivities approach 99:1 with both rhodium and copper catalysts. With chiral dirhodium(II) carboxamidate catalysts the mismatched selectivities do not differ greatly from that found from achiral dirhodium(II) acetate catalysis; however, with chiral copper(I) bis-oxazoline catalysts mismatched selectivities are pronounced reflecting, we believe, the difference between copper's C_2-symmetric ligands in which the protruding attachments are trans and the dirhodium(II) carboxamidate's *cis*-2,2 ligand orientation.

Experimental Section

General Remarks

Preparations of copper(I) hexafluorophosphate,[11] 2,2-bis{2-[4(*S*)-*tert*-butyl-1,3-oxazolinyl]}propane [(*S*,*S*)-*t*-Bu-BOX],[12] Rh_2(*R*/*S*-MEPY)$_4$,[13] Rh_2(*R*/*S*-MPPIM)$_4$,[14] Rh_2(*R*/*S*-MEOX)$_4$,[15] and Rh_2(*R*/*S*-MEAZ)$_4$[16] have been previously reported. Other reagents were obtained commercially and used as received unless otherwise noted. All reactions were carried out under an atmosphere of nitrogen.

(2*S*,3*S*,5*R*,6*R*)-5,6-Dimethoxy-5,6-dimethyl-2-propargyloxymethyl-3-hydroxymethyl-[1,4]-dioxane (6)

To a stirred solution of (2*S*,3*S*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-2,3-di(hydroxymethyl)-[1,4]-dioxane (**5**)[8] (2.50 g, 10.7 mmol, 1.00 equiv.) in THF (125 mL) was added NaH (0.300 g, 11.6 mmol, 1.10 equivs.) as one portion. The solution instantly began to evolve gas and, over five minutes, produced a cloudy white suspension. After gas evolution had subsided, a solution of 80% (w/w) propargyl bromide in toluene (1.87 g, 12.7 mmol, 1.20 equivs.) was added as one aliquot. The cloudy solution was stirred for 12 h at room temperature, diluted with diethyl ether (125 mL) and washed with 2.5 M aqueous NH_4Cl (3×100 mL). The resultant solution was dried over anhydrous magnesium sulfate, filtered through glass wool, and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (60:40 hexane:ethyl ether) to afford alcohol **6** as a white crystalline solid; yield: 1.79 g (6.53 mmol, 51%). ^{1}H NMR (250 MHz): δ=4.18 (dd, J=16.0, 2.3 Hz, 1H), 4.08 (dd, J=16.0, 2.3 Hz, 1H), 3.87–3.71 (comp, 2H), 3.67–3.52 (comp, 4H), 3.20 (s, 6H), 2.43–2.37 (comp, 2H), 1.24 (s, 6H); ^{13}C NMR (62.5 MHz): δ=98.9, 98.8, 79.1, 70.1, 69.3, 67.8, 62.1, 58.5, 47.9, 47.8, 17.4, 17.3; $[\alpha]_D^{25}$: −76.7° (*c* 0.430, CH_2Cl_2).

(2*R*,3*R*,5*S*,6*S*)-5,6-Dimethoxy-5,6-dimethyl-2-propargyloxymethyl-3-hydroxymethyl-[1,4]-dioxane (*ent*-6): ^{1}H NMR (250 MHz): δ=4.18 (dd, J=16.0, 2.3 Hz, 1H), 4.08 (dd, J=16.0, 2.3 Hz, 1H), 3.87–3.71 (comp, 2H), 3.67–3.52 (comp, 4H), 3.20 (s, 6H), 2.43–2.37 (comp, 2H), 1.24 (s, 6H); ^{13}C NMR (62.5 MHz): δ=98.9, 98.8, 79.1, 70.1, 69.3, 67.8, 62.1, 58.5, 47.9, 47.8, 17.4, 17.3; $[\alpha]_D^{25}$: +77.3° (*c* 0.760, CH_2Cl_2).

(2*S*,3*S*,5*R*,6*R*)-5,6-Dimethoxy-5,6-dimethyl-2-propargyloxymethyl-3-(diazoacetoacetoxy)methyl-[1,4]-dioxane (7)

To a stirred solution of (2*S*,3*S*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-2-propargyloxymethyl-3-hydroxymethyl-[1,4]-dioxane (1.4 g, 5.3 mmol, 1.0 equiv.) in THF (20 mL) cooled in an ice bath was added Et_3N (0.15 mL, 1.1 mmol, 0.20 equivs.) followed by addition of diketene (0.49 mL, 6.3 mmol, 1.2 equivs.). The resulting brown solution was stirred for 12 h, during which time the solution was allowed to warm to ambient temperature. Then Et_3N (0.88 mL, 6.3 mmol, 1.2 equivs.) was added, followed by addition of methanesulfonyl azide[17] (0.76 g, 6.3 mmol, 1.2 equivs.), and the reaction was allowed to stir for an additional 24 h. The resulting brown solution was concentrated under reduced pressure and purified by flash chromatography on silica gel (67:33 hexane:ethyl ether) to afford diazoacetoacetate **7** as a pale yellow oil; yield: 1.54 g (4.00 mmol, 74% yield). ^{1}H NMR (500 MHz): δ=4.43 (dd, J=11.7, 2.9 Hz, 1H), 4.28 (dd, J=11.7, 6.0 Hz, 1H), 4.19 (dd, J=10.7, 2.3 Hz, 2H), 4.03 (ddd, J=9.8, 6.0, 2.9 Hz, 1H), 3.85 (dt, J=9.8, 4.0 Hz, 1H), 3.68 (dd, J=10.7, 4.0 Hz, 1H), 3.61 (dd, J=10.7, 4.0 Hz, 1H), 3.25 (s, 6H), 2.49 (s, 3H), 2.45 (t, J=2.3 Hz, 1H), 1.31 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (125 MHz): δ=161.2, 98.9, 98.8, 79.1, 75.0, 69.3, 67.7, 67.6, 64.3, 47.9, 47.8, 42.8, 28.2, 17.4 (the signal consistent with a ketone carbonyl carbon was not observed but was verified by IR spectroscopy, other missing carbon signals are believed to be due to overlap of carbon signals); IR (solid deposition on KBr plate): ν=2137, 1716, 1651 cm^{-1}; $[\alpha]_D^{25}$: −57.6° (*c* 0.254, CH_2Cl_2).

(2*R*,3*R*,5*S*,6*S*)-5,6-Dimethoxy-5,6-dimethyl-2-propargyloxymethyl-3-(diazoacetoacetoxy)methyl-[1,4]-dioxane (*ent*-7): ^{1}H NMR (500 MHz): δ=4.43 (dd, J=11.7, 2.9 Hz, 1H), 4.28 (dd, J=11.7, 6.0 Hz, 1H), 4.19 (dd, J=10.7, 2.3 Hz, 2H), 4.03 (ddd, J=9.8, 6.0, 2.9 Hz, 1H), 3.85 (dt, J=9.8, 4.0 Hz, 1H), 3.68 (dd, J=10.7, 4.0 Hz, 1H), 3.61 (dd, J=10.7, 4.0 Hz, 1H), 3.25 (s, 6H), 2.49 (s, 3H), 2.45 (t, J=2.3 Hz, 1H), 1.31 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (125 MHz): δ=161.2, 98.9, 98.8, 79.1, 75.0, 69.3, 67.7, 67.6, 64.3, 47.9, 47.8, 42.8, 28.2, 17.4 (the signal consistent with one carbonyl carbon was not observed but was verified by IR spectroscopy, other missing carbon signals are believed to be due to overlap of carbon signals); IR (solid deposition on KBr plate): ν=2137, 1716, 1651 cm^{-1}; $[\alpha]_D^{25}$: +58.5° (*c* 0.470, CH_2Cl_2).

(2*S*,3*S*,5*R*,6*R*)-5,6-Dimethoxy-5,6-dimethyl-2-propargyloxymethyl-3-(diazoacetoxy)methyl-[1,4]-dioxane (8)

To a stirred solution of (2*S*,3*S*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-2-propargyloxymethyl-3-(diazoacetoacetoxy)methyl-[1,4]-dioxane (1.48 g, 3.86 mmol, 1.00 equivs.) in THF (25 mL) was added $LiOH\cdot H_2O$ (0.541 g, 19.3 mmol, 5.00 equivs.) dissolved in deionized water (25 mL). The resultant yellow solution was allowed to stir fast enough to disrupt the liquid/liquid interface for 40 min and was monitored by ^{1}H NMR until disappearance of the peak at 2.49 ppm was achieved. The solution was then washed with 2.5 M aqueous NH_4Cl (3×40 mL), dried over anhydrous magnesium sulfate, filtered through glass wool, and concentrated under re-

duced pressure. The resulting yellow oil was subjected to flash chromatography on silica gel (67:33 hexane:ethyl ether) to afford diazoacetate **8** as a yellow oil; yield: 0.885 g (2.59 mmol, 67% yield). ^{1}H NMR (250 MHz): $\delta = 4.82$ (s, broad, 1H), 4.34–4.24 (comp, 2H), 4.19 (dd, $J = 9.0$, 2.4 Hz, 2H), 3.99 (ddd, $J = 9.8$, 5.8, 3.3 Hz, 1H), 3.83 (dt, $J = 9.8$, 4.0 Hz, 1H), 3.67 (dd, $J = 10.7$, 4.0 Hz, 1H), 3.61 (dd, $J = 10.7$, 4.0 Hz, 1H), 3.26 (s, 3H), 3.25 (s, 3H), 2.46 (t, $J = 2.4$ Hz, 1H), 1.31 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (62.5 MHz): $\delta = 98.9$, 98.7, 79.2, 74.9, 69.1, 68.0, 67.8, 63.8, 58.5, 47.9, 47.7, 46.2, 17.5, 17.4 (the signal consistent with a carbonyl carbon was not observed but was verified by IR spectroscopy); IR (solid deposition on KBr plate): $\nu = 2111$, 1698 cm^{-1}; HR-MS (FAB+): calcd. for $C_{15}H_{22}O_7N_2$: 343.1505; found: 343.1495; $[\alpha]_D^{25}$: −60.9° (*c* 0.860, CH_2Cl_2).

(2*R*,3*R*,5*S*,6*S*)-5,6-Dimethoxy-5,6-dimethyl-2-propargyloxymethyl-3-(diazoacetoxy)methyl-[1,4]-dioxane (*ent*-8): ^{1}H NMR (250 MHz): $\delta = 4.82$ (s, broad, 1H), 4.34–4.24 (comp, 2H), 4.19 (dd, $J = 9.0$, 2.4 Hz, 2H), 3.99 (ddd, $J = 9.8$, 5.8, 3.3 Hz, 1H), 3.83 (dt, $J = 9.8$, 4.0 Hz, 1H), 3.67 (dd, $J = 10.7$, 4.0 Hz, 1H), 3.61 (dd, $J = 10.7$, 4.0 Hz, 1H), 3.26 (s, 3H), 3.25 (s, 3H), 2.46 (t, $J = 2.4$ Hz, 1H), 1.31 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (62.5 MHz): $\delta = 98.9$, 98.7, 79.2, 74.9, 69.1, 68.0, 67.8, 63.8, 58.5, 47.9, 47.7, 46.2, 17.5, 17.4; IR (solid deposition on KBr plate): $\nu = 2111$, 1698 cm^{-1}; $[\alpha]_D^{25}$: +60.8° (*c* 1.04, CH_2Cl_2).

General Procedure for Diazo Decomposition by Dirhodium(II) Catalysts

The procedure for diazo decomposition of **8** with Rh_2(4*S*-MEAZ)$_4$ is representative. To a refluxing solution of Rh_2(4*S*-MEAZ)$_4$ (3.4 mg, 0.0044 mmol, 0.010 equiv.) in DCM (5.0 mL) was added a solution of **8** (0.12 g, 0.44 mmol, 1.0 equiv.) dissolved in DCM (5 mL) *via* syringe pump at a rate of 5 mL h.$^{-1}$ The resulting solution was heated at reflux for an additional 1 h before filtration through a silica gel plug, which was rinsed with ethyl ether (20 mL). The resulting crude solution was concentrated under reduced pressure to afford a mixture of products. A small aliquot was then removed for NMR analysis to determine the ratio of the products. Isolation of products was accomplished by flash chromatography on silica gel (67:33 hexane:ethyl ether).

General Procedure for Diazo Decomposition by Copper(I) Catalysts

The procedure for diazo decomposition of **8** catalyzed by $Cu(CH_3CN)_4PF_6$/(S,S-*t*-BuBOX) is representative. A round-bottom flask charged with copper(I) hexafluorophosphate (27.1 mg, 0.0730 mmol, 0.100 equiv.) and bis-oxazoline **3** (25.6 mg, 0.0860 mmol, 0.120 equivs.) in DCM (5.0 mL) was heated at reflux for 30 min (heating at reflux for 30 min was omitted if the bis-oxazoline ligand was not employed in the reaction). After 30 min, a solution of diazo compound (0.250 g, 0.730 mmol, 1.00 equiv.) in DCM (5 mL) was added *via* syringe pump at a rate of 5 mL h.$^{-1}$ The resulting solution was then heated at reflux for an additional 1 h before filtration through a silica gel plug, which was rinsed with ethyl ether (20 mL). Concentration under reduced pressure afforded a mixture of products. A small aliquot was then removed for NMR analysis to determine the ratio of the products.

(1*S*,5*S*,11*S*,13*R*,14*R*)-13,14-Dimethoxy-13,14-dimethyl-3,9,12,15-tetraoxatricyclo[9.4.0.0^{5,7}]pentadec-6-en-4-one (9): ^{1}H NMR (500 MHz): $\delta = 6.67$ (s, 1H), 4.80 (dd, $J = 11.0$, 3.4 Hz, 1H), 4.54 (d, $J = 13.9$ Hz, 1H), 4.34 (d, $J = 13.9$ Hz, 1H), 4.02 (dt, $J = 3.4$, 10.0 Hz, 1H), 3.79 (dd, $J = 10.4$, 2.0 Hz, 1H), 3.69 (d, $J = 10.4$ Hz, 1H), 3.61 (d, $J = 10.0$ Hz, 1H), 3.54 (t, $J = 11.0$ Hz, 1H), 3.26 (s, 3H), 3.24 (s, 3H), 2.23 (s, 1H), 1.33 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 179.3$, 112.9, 99.5, 99.2, 98.7, 71.8, 68.6, 63.4, 62.7, 61.9, 48.0, 47.9, 20.2, 17.5, 17.4; HR-MS (FAB+): calcd. for $C_{15}H_{22}O_7Li$: 321.1526; found: 321.1552.

(1*S*,5*R*,11*S*,13*R*,14*R*)-13,14-Dimethoxy-13,14-dimethyl-3,9,12,15-tetraoxatricyclo[9.4.0.0^{5,7}]pentadec-6-en-4-one (10): ^{1}H NMR (400 MHz): $\delta = 6.74$ (t, $J = 1.4$ Hz, 1H), 4.50 (d, $J = 13.7$ Hz, 1H), 4.36 (t, $J = 10.8$ Hz, 1H), 4.32 (dt, $J = 13.7$, 1.4 Hz, 1H), 3.99 (ddd, $J = 10.8$, 9.6, 3.8 Hz, 1H), 3.89 (dd, $J = 10.8$, 3.8 Hz, 1H), 3.75 (dd, $J = 9.9$, 4.9 Hz, 1H), 3.65 (dd, $J = 9.9$, 1.3 Hz, 1H), 3.60 (ddd, $J = 9.6$, 4.9, 1.3 Hz, 1H), 3.28 (s, 3H), 3.27 (s, 3H), 2.25 (d, $J = 1.4$ Hz, 1H), 1.31 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.4$, 112.6, 99.1, 98.9, 98.5, 71.8, 71.3, 67.2, 64.1, 61.5, 48.06, 48.03, 20.1, 17.5, 17.3; HR-MS (FAB+): calcd. for $C_{15}H_{22}O_7Li$: 321.1526; found: 321.1530.

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