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Enantioselective intramolecular cyclopropanation of allyl 2-diazo-3-silanyloxybut-3-enoates

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Abstract—The performance of the [Rh_2{(*S*)-ntt}$_4$]-catalyst in comparison to [Rh_2{(*S*)-pttl}$_4$] and [Rh_2{(*S*)-dosp}$_4$] has been examined with allyl 2-diazo-3-silanyloxybut-3-enoates. The best results were obtained with [Rh_2{(*S*)-pttl}$_4$], where enantioselectivity culminated at 89% ee at −78 °C. [Rh_2{(*S*)-ntt}$_4$] was slightly less selective, while [Rh_2{(*S*)-dosp}$_4$] was found less suitable for these substrates. However, even the results obtained with [Rh_2{(*S*)-pttl}$_4$] are much less satisfactory than those for the intramolecular cyclopropanation of allyl diazoacetates in the presence of [Rh_2{(*S*)-mepy}$_4$].

1. Introduction

The intramolecular cyclopropanation of allyl diazoacetate esters in the presence of chiral, non-racemic Rh(II)-carboxamidate catalysts, such as [Rh_2{(*S*)-mepy}$_4$], represents the first conclusive demonstration of the exceptional selectivity of this class of catalysts.[1] Subsequently, these catalysts were found to be efficient for a variety of other enantioselective carbene transfer reactions.[2,3] Among the various diazoacetates of interest, those stabilized by aryl or vinyl groups occupy a prominent position. Their reactions often occur with almost perfect enantioselectivities with Rh(II) prolinate-catalysts, such as [Rh_2{(*S*)-tbsp}$_4$][4] or [Rh_2{(*S*)-dosp}$_4$].[5] In contrast, the intramolecular cyclopropanation of phenyl and vinyl diazoacetates results in disappointingly low enantioselectivities. Thus Doyle reported an ee of only 25–50% for the decomposition of allyl phenyldiazoacetates in the presence of [Rh_2{(*S*)-tbsp}$_4$]. With [Rh_2{(*S*)-meaz}$_4$] as catalyst, the enantioselectivity increased significantly to 68%.[6] The enantioselectivity for allyl styryl-diazoacetates with [Rh_2{(*S*)-dosp}$_4$] varied from 2% to 87% depending on the substituents of the allylic moiety. An exceptional intramolecular cyclopropanation of a substituted allyl vinyldiazoacetate with 93% ee (at −78 °C) has already been reported by Davies, and applied to an enantioselective synthesis of 5-epitremulenolide.[7]

(Silanyloxyvinyl)diazoacetates have been used in enantioselective olefin cyclopropanations in the presence of [Rh_2{(*S*)-dosp}$_4$] with limited success.[8] However, we have recently observed, that Rh(II) carboxylate-catalysts having 1,8-naphthanoyl protected *tert*-leucin as ligand, dirhodium *tetrakis* (*S*)-*N*-1,8-naphthanoyl *tert*-leucinate, [Rh_2{(*S*)-nttl}$_4$],[9] are particularly suited for these diazo precursors. Indeed, the cyclopropanation of styrene with methyl (silanyloxyvinyl)diazoacetate in the presence of [Rh_2{(*S*)-nttl}$_4$] afforded the corresponding cyclopropane in up to 98% ee and 95% de.[10] In view of this positive result, we herein report the suitability of our [Rh_2{(*S*)-nttl}$_4$]-catalyst for enantioselective intramolecular cyclopropanations of allyl 2-diazo-3-silanyloxy-but-3-enoates **3a**–**c**.

2. Results and discussion

The diazo precursors were synthesized by straightforward methods. Commercial allylaceto-acetate **1a** was subjected to diazo transfer with *p*-acetamidobenzenesulfonyl azide in the presence of Et_3N to afford allyl 2-diazoacetoacetate **2a**,[11] which was silylated with tris-isopropylsilyl triflate (TIPSOTf) and Et_3N to give **3a** (see Experimental).[12] The same sequence was applied to **1b**[1] and **1c**, which, in turn, were accessible via acid-catalyzed ester exchange of methyl acetoacetate and cinnamyl alcohol and (*E*,*E*)-hexa-2,4-dienol, respectively. The diazo decompositions were carried out in $PhCH_3$ at 0 °C, and in a few cases, at −78 °C. The results are summarized in Table 1. With **1a**, the expected

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cyclopropane **4a** was isolated in 57–81% yield (Scheme 1 and Table 1).

Table 1. Yield and enantioselectivity for intramolecular cyclopropanation of substituted allyl 2-diazo-3-silanyloxybut-3-enoates **3a–c** in $PhCH_3$[a]

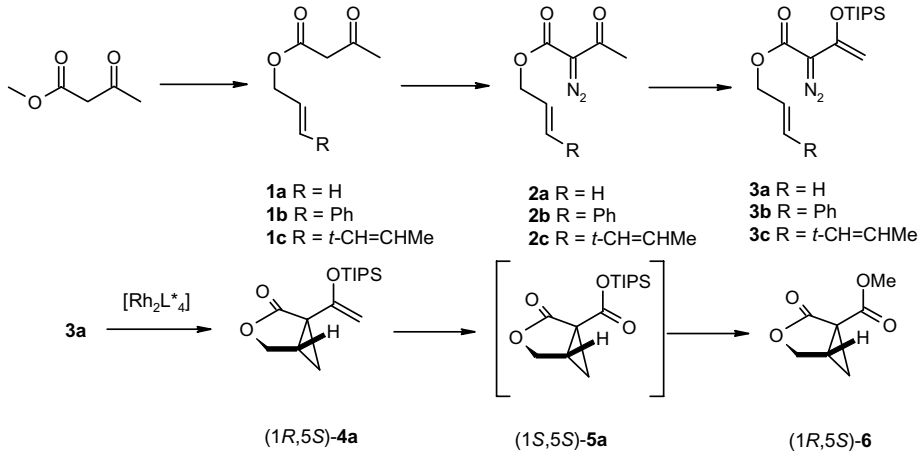
Compd	R	Ligand	Yield (%)	Ee (%)
3a	H	{(*S*)-nttl}	**4a** 81	47[c]
3a	H	{(*S*)-pttl}	**4a** 75	50[c]
3a	H	{(*S*)-pttl}[b]	**4a** 57	70[c]
3a	H	{(*S*)-dosp}	**4a** 73	05[c]
3b	Ph	{(*S*)-nttl}	**4b** 77	73[d]
3b	Ph	{(*S*)-pttl}	**4b** 93	77[d]
3b	Ph	{(*S*)-pttl}[b]	**4b** 66	89[d]
3b	Ph	{(*S*)-dosp}	**4b** 69	05[d]
3c	(*E*)-CH=CHMe	{(*S*)-nttl}	**10** 77	67[e]
3c	(*E*)-CH=CHMe	{(*S*)-pttl}	**10** 81	60[e]
3c	(*E*)-CH=CHMe	{(*S*)-pttl}[b]	**10** 71	68[e]
3c	(*E*)-CH=CHMe	{(*S*)-dosp}	**10** 65	02[e]

[a] At 0 °C.
[b] At −78 °C.
[c] (1*R*,5*S*).
[d] (1*S*,5*R*,6*S*).
[e] (3a*R*,6*R*).

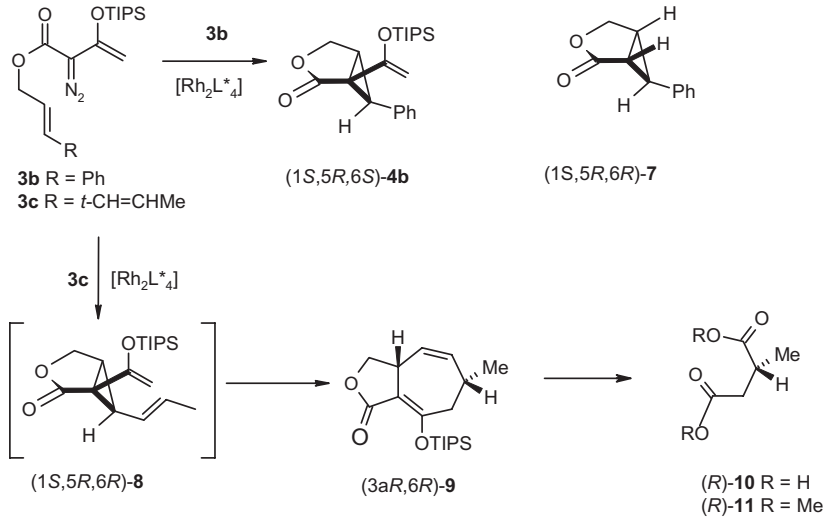
The structure of **4a** was established by its conversion to lactone **6**, which is a known compound.[13] Lactone **4a** was subjected to ozonolysis to yield **5a**, which was not characterized, but directly converted to methyl ester **6** by reaction with MeOH in the presence of *p*-toluenesulfonic acid. The enantioselectivity of the reaction of **3a** varied between 5 (with $[Rh_2\{(S)\text{-dosp}\}_4]$) and 50% ee (with $[Rh_2\{(S)\text{-pttl}\}_4]$[14]) at 0 °C, and increased to 70% ee at −78 °C. This is much lower than the enantioselectivity for the cyclopropanation of allyl diazoacetate with $[Rh_2\{(S)\text{-mepy}\}_4]$, which reaches 95%.[1] It is noteworthy, however, that $[Rh_2\{(S)\text{-mepy}\}_4]$ is generally not suitable for the decomposition of diazo esters having a second substituent at the diazo carbon.[15] The absolute configuration of (+)-**4a** was determined after its transformation to **6** as described above. A sample of **6** prepared from **3a** with $[Rh_2\{(S)\text{-nttl}\}_4]$ had $[\alpha]_D^{23} = +58.8$ for 47% ee. Comparison with the literature value of $[\alpha]_D^{25} = -163.8$ (*c* 1.32, CH_2Cl_2) for (1*S*,5*R*)-**6**[16] leads to a (1*R*,5*S*) configuration for **6** and **4a**. Lactone **6** has also been synthesized by the diazo decomposition of allyl methyl diazomalonate with $[Rh_2\{(S)\text{-meaz}\}_4]$ as catalyst in 30% yield and 57% ee,[15] and with 11% ee with a Cu-bisoxazoline catalyst.[17] The *tert*-butyl analogue of **6**, in turn, has been obtained by the intramolecular cyclopropanation of allyl *tert*-butyl malonate in up to 84% ee.[18]

The structure of the cyclization product of **3b** was assigned by comparison of the NMR data with the data of **7**, available in the literature (Scheme 2). The *exo* orientation of the phenyl substituent at C(6) in **4b** is a consequence of the well established stereoselectivity of the intramolecular cyclopropanation of allyl diazoacetates.[1,7,8] For the diazo decomposition of **3b**, $[Rh_2\{(S)\text{-pttl}\}_4]$ was again the most selective catalyst leading to an ee of 77% at 0 °C, and 89% at −78 °C. $[Rh_2\{(S)\text{-nttl}\}_4]$ was almost as efficient, however, with 74% ee at 0 °C. These results are remarkable in light of the fact that the intramolecular cyclopropanation of the parent *trans*-cinnamyl diazoacetate proceeds to **7** with $[Rh_2\{(S)\text{-mepy}\}_4]$ with only 68% ee.[1] The absolute configuration of (−)-**4b** was tentatively assigned on the grounds of comparison of its circular dichroism with that of the structurally related **8** of known absolute configuration.[10] For compounds of the same absolute configuration, the Cotton effects occur at the same wavelength and have the same sign (Fig. 1).[19]

As Table 2 shows, the CD spectra of **4b** and **8** are superimposable at the wavelengths λ_1–λ_5. An exception occurs at λ_1, where **8** exhibits a positive Cotton effect, which is absent in **4b**. Accordingly, **4b** should have the (1*S*,5*R*,6*S*) absolute configuration. Thus the sense of asymmetric induction is inverted in going from **3a** to **3b**. Similar changes have been reported for other intramolecular cyclopropanations of substituted allylic diazoacetates.[7,20] Cyclopropane **4c** resulting from the diazo decomposition of **3c** was not isolable, but underwent a spontaneous Cope rearrangement to afford **9**.



Scheme 1.



Scheme 2.

Table 2. Cotton effect of cyclopropanes **4b** and **8**

Compd	Solvent [M] × 10^8	λ_1 (nm) $\Delta\varepsilon \times 10^{-7}$ [M^{-1} cm^{-1}]	λ_2 (nm) $\Delta\varepsilon \times 10^{-7}$ [M^{-1} cm^{-1}]	λ_3 (nm) $\Delta\varepsilon \times 10^{-7}$ [M^{-1} cm^{-1}]	λ_4 (nm) $\Delta\varepsilon \times 10^{-7}$ [M^{-1} cm^{-1}]	λ_5 (nm) $\Delta\varepsilon \times 10^{-7}$ [M^{-1} cm^{-1}]
8	C_6H_{12}	222	210	261	268	274
	6.4	+2.3	−2.2	−2.8	−4.3	−4.6
4b	C_6H_{12}	—	213	261	268	275
	6.3		−2.6	−2.0	−2.3	−2.0
8	MeCN	223	207	261	267	274
	6.1	+1.6	−4.0	−2.8	−3.2	−2.0
4b	MeCN	—	208	262	268	275
	6.6		−3.8	−1.8	−1.9	−1.6

Mechanistic considerations require that the methyl group at C(6) and the hydrogen at C(3a) are in a trans orientation,[21] and this has been experimentally confirmed.[7] The yield and enantioselectivity of the cyclopropanation/Cope rearrangement of **3c** are also included in Table 1. [Rh_2{(*S*)-nttl}$_4$] was slightly superior over [Rh_2{(*S*)-pttl}$_4$] and afforded an ee of 67% at 0 °C. The enantioselectivities reached 89% with **3c** (at −78 °C). Ozonolysis of (−)-**9** of 67% ee afforded 2-methylsuccinic acid, which was transformed to dimethyl ester **10**. Comparison of the GC retention time of **10** with that of a sample of commercial (*R*)-**10**, allowed the assignment of a (*R*)-configuration to the major component of the degradation product with 65% ee (from reaction with [Rh_2{(*S*)-nttl}$_4$]). Accordingly, the sense of induction of **3c** is identical to that (supposed) of **3b**, but opposite to that of **3a** (Fig. 1).

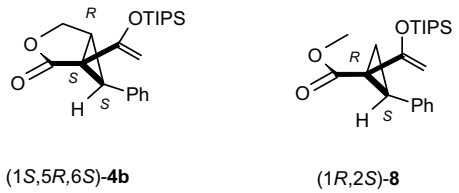


Figure 1. Configurational relationship between **4b** and **8**.

3. Conclusion

Among the catalysts examined in the present investigation, [Rh_2{(*S*)-pttl}$_4$] is best suited for the intramolecular cyclopropanation of allyl 2-diazo-3-silanyloxybut-3-

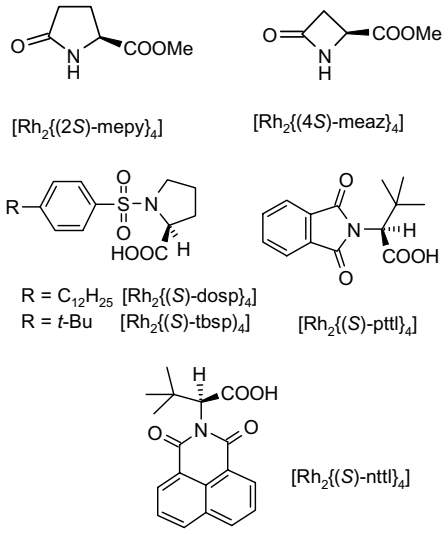


Figure 2. Ligands L*H and abbreviations of Rh(II)-catalysts.

enoates, followed by [Rh_2{(*S*)-ntt}$_4$] while [Rh_2{(*S*)-dosp}$_4$] is less suitable for these substrates. The exceptional selectivity exhibited by [Rh_2{(*S*)-nttl}$_4$] in the intermolecular cyclopropanation of styrene with alkyl 2-diazo-3-silanyloxybut-3-enoates was not observed in the intramolecular cyclopropanation. In addition, even the results obtained with [Rh_2{(*S*)-pttl}$_4$] are much less satisfactory than those for intramolecular cyclopropanation of allyl diazoacetates in the presence of [Rh_2{(*S*)-mepy}$_4$] (Fig. 2).

4. Experimental

4.1. General

See Ref. 22. The CD spectra were measured on a Jasco J-715 instrument; the wavelengths λ are indicated in nanometer, and the ellipticity in terms of [$\Delta\varepsilon$].

4.2. Synthesis of allyl 3-silanyloxy-2-diazobut-3-enoates 3a–c

4.2.1. (*E*)-(3-Phenylallyl) 3-oxo-butyrate 1b.[1] (*E*)-Cinnamyl alcohol (5.20 g, 38.8 mmol) and methyl acetoacetate (8.60 g, 74.1 mmol) was heated in the presence of Dowex 50W × 8 resin (94 mg) to 150 °C until distillation of MeOH ceased. Excess methyl acetoacetate was eliminated by evaporation under reduced pressure, and the residue distilled (0.08 Torr, T = 107–110 °C) to give **1b** as colorless oil (5.90 g, 69%). IR (film): 3028w, 1740s, 1714s, 1645w, 1578w, 1494w, 1448w, 1313m, 1259m, 1145s, 1065w, 1027w, 963s, 744s. ^{1}H NMR (500 MHz, $CDCl_3$): 2.31 (s, 3H); 3.52 (s, 2H); 4.82 (dd, J = 1.1, 6.5, 1H); 6.30 (dt, J = 6.5, 15.9, 1H); 6.70 (d, J = 15.9, 1H); 7.28–7.31 (m, 1H); 7.34–7.37 (m, 2H); 7.41–7.43 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): 30.2 (q); 50.1 (t); 65.9 (t); 122.4 (d); 126.7 (d); 128.2 (d); 128.7 (d); 134.9 (d); 136.0 (s); 166.9 (s); 200.4 (s). MS: 218 (M^+; <1), 194 (3), 119 (13), 118 (100), 104 (67), 103 (13), 102 (23), 93 (60), 82 (28), 81 (27), 69 (12), 49 (12). HR MS: 218.0943 ($C_{13}H_{14}O_3^+$; calcd 218.0943).

4.2.2. (*E*,*E*)-(Hexa-2,4-dienyl) 3-oxo-butyrate 1c.[23] Methyl acetoacetate (8.56 g, 73.8 mmol) and (*E*,*E*)-2,4-hexadien-1-ol (3.62 g, 36.9 mmol) were heated in the presence of a catalytic amount of DOWEX 50W × 8 resin (100 mg) to 150 °C, until distillation of MeOH ceased. Excess methyl acetoacetate was removed by distillation in vacuo. Compound **1c** was isolated upon distillation (p = 0.08 Torr, T = 117 °C) as colorless oil (4.01 g, 59%). IR (film): 3025w, 2934w, 1739s, 1714s, 1661w, 1444w, 1410w, 1360w, 1312m, 1266m, 1146s, 1027w, 988s, 958m, 925w. ^{1}H NMR (500 MHz, $CDCl_3$): 1.77 (d, J = 6.8, 3H); 2.27 (s, 3H); 3.46 (s, 2H); 4.63–4.65 (m, 2H); 5.54–5.66 (m, 1H); 5.73–5.81 (m, 1H); 6.03–6.08 (m, 1H); 6.23–6.30 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): 18.1 (q); 30.1 (q); 50.1 (t); 65.7 (t); 122.8 (d); 130.2 (d); 131.8 (d); 135.6 (d); 166.9 (s); 200.5 (s). MS: 182 (M^+; 11), 98 (29), 97 (99), 85 (36), 81 (100), 80 (27), 79 (52), 69 (13), 58 (11), 53 (21). HR MS: 182.0932 ($C_{10}H_{14}O_3^+$; calcd 182.0943).

4.2.3. Allyl 2-diazo-3-oxo-butyrate 2a.[1] To allyl acetoacetate (2.00 g, 14.1 mmol) and *p*-acetamidobenzenesulfonyl azide (*p*-ABSA, 3.71 g, 15.5 mmol) in acetonitrile (70 mL) was added, at 0 °C, Et_3N (2.84 g, 28.2 mmol) dropwise. After the addition, stirring was continued at rt for 3 h. The solvent was evaporated and the residue suspended in Et_2O (100 mL). *p*-Acetamidobenzenesulfonamide was separated by filtration, and then washed with Et_2O (2 × 100 mL). After evaporation of the solvent, the residue was purified by flash chromatography (SiO_2, EtOAc/pentane 20:80) to afford **2a** as a yellow liquid (2.15 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): 2.50 (s, 3H); 4.74–4.77 (m, 2H); 5.31–5.41 (m, 2H); 5.92–6.01 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 28.3 (q); 65.9 (t); 119.2 (t); 131.5 (d); 161.1 (s); 190.1 (s).

4.2.4. (*E*)-(3-Phenylallyl)-2-diazo-3-oxo-butyrate 2b.[1] To *p*-ABSA (2.41 g, 10.1 mmol) and acetoacetate **1b** (2.10 g, 9.2 mmol) in acetonitrile (45.0 mL) was added, dropwise, Et_3N (1.7 g, 16.8 mmol) at 0 °C. After stirring for 3 h at rt, the solid precipitate was eliminated by filtration and washed with Et_2O (2 × 50 mL). The solvent was evaporated, and the residue purified by flash chromatography (EtOAc/pentane 30:70) to yield a yellow oil (1.59 g, 70%). IR (film): 3030w, 2144s, 1697s, 1645s, 1492w, 1452w, 1385m, 1365m, 1315s, 1279m, 1248s, 1157s, 1028m, 973s, 744s. ^{1}H NMR (500 MHz, $CDCl_3$): 2.57 (s, 3H); 4.96 (dd, J = 1.1, 6.6, 2H); 6.37 (dt, J = 6.6, 15.9, 1H); 6.66 (d, J = 15.9, 1H); 7.33–7.37 (m, 1H); 7.39–7.43 (m, 2H); 7.47–7.48 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): 28.3 (q); 65.9 (t); 122.3 (d); 126.7 (d); 128.4 (d); 128.7 (d); 135.4 (d); 135.8 (s); 161.3 (s); 190.1 (s). MS: 244 (M^+; <1), 216 (6), 133 (46), 132 (15), 131 (13), 129 (10), 118 (13), 117 (100), 116 (14), 115 (41), 91 (24), 83 (10), 77 (12), 51 (10). HR MS: 244.0824 ($C_{13}H_{12}O_3N_2^+$; calcd 244.0848).

4.2.5. (*E*,*E*)-(Hexa-2,4-dienyl)-2-diazo-3-oxo-butyrate 2c. To the ketoester **1c** (1.00 g, 5.49 mmol) and *p*-ABSA (1.45 g, 6.04 mmol) in acetonitrile (40 mL) was added dropwise, at 0 °C, Et_3N (1.00 g, 9.96 mmol) and the mixture stirred at rt for 3 h. The solvent was evaporated and the residue dissolved in Et_2O (40 mL). The solid precipitate was removed by filtration and washed with Et_2O (2 × 40 mL). After evaporation, the residue was purified by flash chromatography (SiO_2, EtOAc/pentane 20:80) to yield **1c** (1.05 g, 91%) as a yellow semi-solid. IR (film): 3025w, 2938w, 2136s, 1710s, 1655s, 1444w, 1363s, 1305s, 1245s, 1148s, 1103w, 1056s, 987s, 964m, 915w, 742s, 635s. ^{1}H NMR (500 MHz, $CDCl_3$): 1.77 (d, J = 6.8, 3H); 2.47 (s, 3H); 4.72 (d, J = 6.8, 2H); 5.60–5.66 (m, 1H); 5.76–5.82 (m, 1H); 6.03–6.09 (m, 1H), 6.28 (dd, J = 10.4, 15.3, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): 18.1 (q); 28.2 (q); 65.8 (t); 122.7 (d); 130.1 (d); 132.2 (d); 135.9 (d); 161.2 (s); 190.1 (s). MS: 208 (M^+; <1), 97 (40), 83 (12), 81 (100), 79 (21), 53 (19). HR MS: 208.0852 ($C_{10}H_{12}O_3N_2^+$; calcd 208.0848).

4.2.6. Allyl 2-diazo-3-[tri(isopropyl)silanyl-oxy]-but-3-enoate 3a. To diazoester **2a** (625 mg, 3.72 mmol) in CH_2Cl_2 (15.0 mL) was added, at 0 °C, Et_3N (414 mg, 4.1 mmol) dropwise. Triisopropylsilyl trifluorosulfonate

(TIPSSOTf, 1.141 g, 3.73 mmol) in CH_2Cl_2 was added, and the mixture stirred at 0 °C for 1 h. After dilution with hexane (40 mL), it was washed with aq 5% $NaHCO_3$ (20 mL), followed by satd NaCl (20 mL), dried over $MgSO_4$, and evaporated to give an orange oil (1.20 g, 99%). IR (film): 2946m, 2893w, 2868m, 2101s, 1710s, 1648w, 1601m, 1463m, 1371m, 1338s, 1271m, 1217w, 1160w, 1105m, 1067s, 1010s, 920w, 881m, 802m. ^{1}H NMR (300 MHz, $CDCl_3$): 1.13 (d, J = 7.0, 18H); 1.22–1.34 (m, 3H); 4.30 (d, J = 2.1, 1H); 4.74–4.75 (m, 2H); 5.03 (d, J = 2.1, 1H); 5.27–5.39 (m, 2H); 5.91–6.00 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): 12.7 (d); 18.0 (q); 65.2 (t); 89.8 (t); 118.2 (t); 132.1 (d); 140.9 (s); 164.0 (s). MS: 324 (M^+; 4), 281 (8), 253 (5), 225 (9), 170 (29), 157 (18), 129 (11), 115 (44), 113 (10), 101 (16), 99 (12), 87 (46), 85 (12), 75 (23), 73 (62), 61 (19), 59 (100). HR MS: 324.1839 ($C_{16}H_{28}O_3N_2Si^+$; calcd 324.1869).

4.2.7. (*E*)-(3-Phenylallyl)-2-diazo-3-[tri(isopropyl)silanyloxy]-but-3-enoate 3b. Same procedure with **2b**, yield 99%, orange oil. IR (film): 2945m, 2867m, 2100s, 1707s, 1637w, 1600w, 1495w, 1463m, 1383m, 1342s, 1271s, 1216w, 1062s, 1010m, 964m, 881m, 803m. ^{1}H NMR (500 MHz, $CDCl_3$): 1.11 (d, J = 7.4, 18 H); 1.22–1.32 (m, 3H); 4.29 (d, J = 2.2, 1H); 4.87 (dd, J = 1.0, 6.5, 2H); 5.02 (d, J = 2.2, 1H); 6.32 (dt, J = 6.5, 15.8, 1H); 6.67 (d, J = 15.8, 1H); 7.26–7.29 (m, 1H); 7.32–7.35 (m, 2H); 7.40–7.42 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): 12.7 (d); 17.9 (q); 65.2 (t); 98.7 (t); 123.1 (d); 126.7 (d); 128.1 (d); 128.6 (d); 134.4 (d); 136.1 (s); 140.9 (s); 164.1 (s). MS: 400 (M^+; <1), 372 (11), 330 (22), 329 (85), 281 (19), 225 (11), 157 (56), 155 (12), 131 (31), 129 (17), 128 (10), 117 (53), 116 (12), 115 (86), 103 (59), 101 (13), 91 (67), 88 (13), 87 (47), 77 (11), 75 (71), 73 (57), 61 (43), 59 (100), 45 (16). HR MS: 400.2165 ($C_{22}H_{32}N_2O_3Si^+$; calcd 400.2182).

4.2.8. (*E*,*E*)-(Hexa-2,4-dienyl)-2-diazo-3-[tri-(isopropyl)-silanyloxy]-but-3-enoate 3c. Same procedure with **2c**. Yield 96%, orange oil. IR (film): 2945w, 2868w, 2100s, 1708s, 1663w, 1637w, 1600w, 1463w, 1383m, 1342s, 1270w, 1217w, 1155w, 1102m, 1062s, 1009m, 986s, 919w, 881m, 802m, 683s. ^{1}H NMR (400 MHz, $CDCl_3$): 1.01 (d, J = 7.1, 18H); 1.13–1.21 (m, 3H); 1.70 (d, J = 6.0, 3H); 4.18 (d, J = 2.2, 1H); 4.62 (d, J = 6.6, 1H); 4.92 (d, J = 2.1, 1H); 5.53–5.61 (m, 1H); 5.65–5.76 (m, 1H); 5.95–6.02 (m, 1H); 6.15–6.25 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 12.7 (d); 18.0 (q); 65.1 (t); 89.7 (t); 123.7 (d); 130.4 (d); 131.5 (d); 135.1 (d); 140.9 (s); 164.2 (s). MS: 364 (M^+; <1), 157 (21), 155 (36), 87 (28), 81 (100), 73 (34), 59 (39). HR MS: 364.2154 ($C_{19}H_{32}O_3N_2Si^+$; calcd 364.2182).

4.3. Diazo decomposition of allyl 3-silanyloxy-2-diazobut-3-enoates 3a–c

4.3.1. Sample run. [Rh_2{(*S*)-nttl}$_4$] (13.9 mg, 0.01 mmol) was activated by heating in vacuo, dissolved in toluene and cooled to 0 °C. Diazoacetate **3a** (152.4 mg, 0.47 mmol) in toluene (1.0 mL) was added dropwise. After 1 h of stirring, the solvent was evaporated and the residue purified by flash chromatography (SiO_2, Et_2O/pentane 15:85) to afford a colorless oil.

4.3.2. (1*R*,5*S*)-1-[1-Tri(isopropyl)silanyloxy-vinyl]-3-oxa-bicyclo[3.1.0]hexan-2-one 4a. Yield 113.1 mg (81%); $[\alpha]_D^{20} = +49$ (*c* 1.17, $CHCl_3$, for 47% ee). IR (film): 2945m, 2867m, 1770s, 1626m, 1464m, 1370m, 1319s, 1257m, 1190s, 1111w, 1079s, 1031s, 1017s, 992s, 919w, 881s, 823m. ^{1}H NMR (400 MHz, $CDCl_3$): 1.10 (d, J = 7.1, 18H); 1.20–1.29 (m, 3H); 1.82 (dd, J = 4.5, 7.8, 1H); 2.48 (dt, J = 4.8, 7.8, 1H); 4.19 (d, J = 9.1, 1H); 4.33 (dd, J = 4.8, 9.4, 1H); 4.41 (d, J = 1.8, 1H); 4.95 (d, J = 1.8, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): 12.6 (d); 17.6 (t); 18.1 (q); 24.1 (d); 30.9 (s); 67.5 (t); 91.3 (t); 149.8 (s); 174.3 (s). MS: 296 (M^+; <1); 255 (6), 254 (20), 253 (100), 209 (12), 167 (14), 139 (31), 125 (10), 103 (38), 85 (10), 79 (14), 77 (21), 75 (75), 61 (47), 59 (25). HR SM: 296.1843 ($C_{16}H_{28}O_3Si^+$; calcd 296.1808). Enantiomer separation by GC (TAKEO-methyl, isothermal at 130 °C): τ_1 = 15.7 min [(1*S*,5*R*)-**3a**] minor; τ_2 = 17.1 min [(1*R*,5*S*)-**3a**] major.

4.3.3. (1*S*,5*R*,6*S*)-6-Phenyl-1-[1-tri(isopropyl)-silanyloxyviny]-3-oxa-bicyclo[3.1.0]hexan-2-one 4b. Colorless oil. For yield and ee: see Table 1. $[\alpha]_D^{20} = -17$ (*c* 0.58, $CHCl_3$, for 61% ee); $[\alpha]_D^{20} = -26$ (*c* 0.67, $CHCl_3$, for 89% ee). IR (film): 2944w, 2866w, 1770s, 1627w, 1463w, 1370m, 1311w, 1262m, 1240w, 1181m, 1094m, 1054s, 1013s, 955s, 956w, 881m. ^{1}H NMR (500 MHz, $CDCl_3$): 0.96 (d, J = 7.4, 9H); 0.97 (d, J = 7.3, 9H); 1.06–1.15 (m, 3H); 2.53 (d, J = 4.9, 1H); 2.92 (t, J = 4.8, 1H); 4.29 (d, J = 1.8, 1H); 4.34 (d, J = 9.1, 1H); 4.39 (d, J = 1.8, 1H); 4.45 (dd, J = 4.8, 9.2, 1H); 7.16–7.28 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): 12.4 (d); 18.9 (q); 27.1 (d); 34.9 (d); 39.9 (s); 67.9 (t); 95.7 (t); 127.2 (d); 128.0 (d); 128.2 (d); 133.9 (s); 147.6 (s); 174.0 (s). MS: 329 (M^+; 94), 155 (12), 115 (15), 103 (25), 91 (100), 75 (45), 61 (27), 59 (21). HR MS: 329.1590 ($C_{19}H_{25}O_3Si^+$; calcd 329.1573). Enantiomer separation by HPLC (OD-H, *i*-PrOH/hexane 1:9, 0.5 mL/min): τ_1 = 15.5 min [(1*S*,5*R*,6*R*)-**4b**] major; τ_2 = 17.3 min [(1*R*,5*S*,6*S*)-**4b**] minor; or SFC (OD-H, 2% MeOH): τ_1 = 9.9 min (major); τ_2 = 11.0 min (minor).

4.3.4. (3a*R*,6*R*)-6-Methyl-8-[tri(isopropyl)-silanyloxy]-3,3a,6,7-tetrahydrocyclohepta[*c*]-furan-1-one 9. Colorless oil. For yield and ee: see Table 1. $[\alpha]_D^{20} = -40$ (*c* 1.04, $CHCl_3$, for 67% ee). IR (film): 2944w, 2891w, 2866w, 1750s, 1632s, 1462w, 1368w, 1353w, 1310w, 1250w, 1174s, 1152s, 1122w, 1069w, 1031m, 986m, 918w, 880m, 800m. ^{1}H NMR (400 MHz, $CDCl_3$): 1.11 (d, J = 7.1, 18H); 1.23–1.35 (m, 3H); 2.10 (ddd, J = 16.7, 10.3, 2.5, 1H); 2.52 (dt, J = 16.7, 3.3, 1H); 2.63–2.71 (m, 1H); 3.77 (dd, J = 9.1, 8.3, 1H); 3.92–3.98 (m, 1H); 4.38 (dd, J = 9.8, 8.3, 1H); 5.46 (ddd, J = 10.2, 2.8, 1.8, 1H); 5.56 (ddd, J = 10.2, 5.6, 2.8, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 13.6 (d); 18.0 (q); 18.1 (q); 20.8 (q); 29.6 (d); 36.2 (d); 42.3 (t); 69.7 (t); 106.1 (s); 129.8 (d); 137.2 (d); 163.6 (s); 168.6 (s). MS: 294 (23), 293 ($M-43^+$; 100), 103 (19), 75 (29), 61 (16), 59 (15). HR MS: 293.1589 ($C_{16}H_{25}O_3Si^+$; calcd 293.1573). Enantiomer separation by HPLC (OD-H,

i-PrOH/hexane 1:9, 0.25 mL/min): τ_1 = 18.9 min [(3a*S*, 6*S*)-**9**] minor; τ_2 = 19.8 min [(3a*R*,6*R*)] major.

4.4. Ozonolysis of 4a; methyl (1*R*,5*S*)-2-oxo-3-oxabicyclo[3.1.0]hexanecarboxylate 6

Lactone **4a** (375 mg, 1.27 mmol) was ozonized in CH_2Cl_2 (30 mL) at −78 °C for 10 min, until the blue color persisted. The mixture was purged with oxygen, then treated with Me_2S (470 μL, 6 mmol) and allowed to reach room temperature within 24 h. It was washed with satd $NaHCO_3$ (2 × 20 mL), then H_2O (2 × 20 mL), dried, and evaporated to afford crude **5a** (306 mg, 81%), which was transesterified by refluxing with *p*-toluenesulfonic acid (30.5 mg) in MeOH (16 mL) overnight. After the addition of solid $NaHCO_3$, the mixture was concentrated and extracted with Et_2O (20 mL). Work-up afforded 99.6 mg (61%) of **6**. Mp 69–72 °C, lit.[24] 68–72 °C; lit.[16] 46–47 °C, $[\alpha]_D$ = +58.8 (*c* 1.23, CH_2Cl_2) for 48% ee. Lit.[16] $[\alpha]_D^{25}$ = −163.9 (*c* 1.32, $CHCl_3$) for (1*S*,5*R*)-**6**. Enantiomer separation by GC (Lipodex E), 10 min at 100 °C, then 1 °C/min to 150 °C, 10 min at 150 °C. τ_1 = 27.6 min (1*R*,5*S*), major; τ_2 = 29.8 min (1*S*,5*R*), minor.

4.5. Ozonolysis of 9; dimethyl (*R*)-methylsuccinate (*R*)-11

Lactone **9** (90 mg, 0.27 mmol) with 68% ee was ozonized in MeOH (12 mL) at −78 °C, and then treated at room temperature with formic acid (1.5 mL) and H_2O_2 (30%, 0.8 mL). After 30 min of stirring at room temperature, the mixture was heated to reflux for 30 min, cooled, treated with formic acid (1.0 mL), and heated again to reflux for 30 min. When all peroxides were decomposed, H_2O (4.0 mL) was added, and the mixture extracted with AcOEt (3 × 10 mL). After the evaporation of the solvent, the residue was recrystallized from AcOEt/pentane, and gave 10 mg (28%) of (*R*)-2-methylsuccinic acid (*R*)-**10**, which was converted in 42% yield to the dimethyl ester (R)-**11** by treatment with MeOH and *p*-toluenesulfonic acid. Enantiomer separation by GC: (FS-Hydrodex β-6-TBDMS): τ_1 = 40.4 min (*R*)-**11**, major; τ_2 = 41.5 min (*S*)-**11**, minor, by comparison with commercial sample; ee 65%.

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References

1. (a) Doyle, M. P.; Pieters, R. J.; Martin, S. F.; Austin, R. E.; Oalman, C. J.; Müller, P. *J. Am. Chem. Soc.* **1991**, *113*, 1423–1424; (b) Doyle, M. P.; Austin, R. E.; Bailey, A. S.; Dwyer, M. P.; Dyatkin, A. B.; Kalinin, A. V.; Kwan, M. M.; Liraqs, S.; Oalman, C. J.; Pieters, R. J.; Protopopova, M. N.; Raab, C. E.; Roos, G. H. P.; Zjou, Q.; Martin, S. F. *J. Am. Chem. Soc.* **1995**, *117*, 5763–5775.
2. (a) Müller, P.; Polleux, P. *Helv. Chim. Acta* **1994**, *77*, 645–654; (b) Doyle, M. P.; Dyatkin, A. B.; Roos, G. H. P.; Cañas, F.; Pierson, D. A.; van Basten, A.; Müller, P.; Polleux, P. *J. Am. Chem. Soc.* **1994**, *116*, 4507–4508.
3. (a) Doyle, M. P. *Aldrichim. Acta* **1996**, *29*, 3–11; Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*; Wiley-Interscience: New York, 1998, pp 112–162; (b) Doyle, M. P. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed., 2nd ed.; Wiley: New York, 2000, Chapter 5.
4. Kennedy, M.; Mc Kervey, M. A.; Maguire, A. R.; Roos, G. H. P. *J. Chem. Soc., Chem. Commun.* **1990**, 361–362.
5. (a) Davies, H. M. L. *Aldrichim. Acta* **1997**, *30*, 107–114; (b) Davies, H. L. M. *Eur. J. Org. Chem.* **1999**, 2459; (c) Davies, H. M. L.; Antoulinakis, E. G. *Org. React.* **2001**, *57*, 1–326; (d) Davies, H. L. M.; Hutcheson, D. K. *Tetrahedron Lett.* **1993**, *34*, 7243–7247; (e) Davies, H. L. M.; Bruzinski, P. R.; Lake, D. H.; Kone, N.; Fall, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6897–6907.
6. Doyle, M. P.; Hu, W.; Weathers, T. M., Jr. *Chirality* **2003**, *15*, 369–373.
7. (a) Davies, H. M. L.; Doan, B. D. *J. Org. Chem.* **1999**, *64*, 8501–8508; (b) Davies, H. M. L.; Doan, B. D. *Tetrahedron Lett.* **1996**, *37*, 3967–3970.
8. Davies, H. M. L.; Ahmed, G.; Calvo, R. L.; Churchill, M. R.; Churchill, D. G. *J. Org. Chem.* **1998**, *63*, 2641.
9. Mueller, P.; Allenbach, Y.; Robert, E. *Tetrahedron: Asymmetry* **2003**, *14*, 779–785.
10. Müller, P.; Bernardinelli, G.; Allenbach, Y. F.; Ferri, M.; Flack, H. D. *Org. Lett.* **2004**, *6*, 1725–1728.
11. Julia, S.; Cannic, G.; Linstrumelle, G. *C.R. Acad. Sci., Ser. C: Sci. Chim.* **1967**, *264*, 1890–1892.
12. Ueda, Y.; Roberge, G.; Vinet, V. *Can. J. Chem.* **1984**, *62*, 2936–2940.
13. (a) Kitaori, K.; Mikami, M.; Furukawa, Y.; Yoshimoto, H.; Otera, J. *Synlett* **1998**, 499; (b) Inoue, T.; Kitagama, O.; Ochiai, O.; Taguchi, T. *Tetrahedron: Asymmetry* **1995**, *6*, 691–692; (c) Fliche, C.; Braun, J.; Le Goffic, F. *Synth. Commun.* **1991**, *21*, 1429–1432.
14. (a) Hashimoto, S. I.; Watanabe, N.; Ikegami, S. *Tetrahedron Lett.* **1990**, *31*, 5173–5174; (b) Hashimoto, S. I.; Watanabe, N.; Sato, T.; Shiro, M.; Ikegami, S. *Tetrahedron Lett.* **1993**, *34*, 5109–5112; (c) Hashimoto, S. I.; Watanabe, N.; Ikegami, S. *Synlett* **1994**, 353–355; (d) Watanabe, N.; Anada, M.; Hashimoto, S.; Ikegami, S. *Synlett* **1994**, 1031–1033.
15. (a) Doyle, M. P.; Davies, S. B.; Hu, W. *Org. Lett.* **2000**, *2*, 1145–1147; (b) Doyle, M. P.; Hu, W. *ARKIVOC* **2003**, *VII*, 15–22.
16. Pirrung, M. C.; Dunlap, S. E.; Trinks, U. P. *Helv. Chim. Acta* **1989**, *72*, 1301–1310.
17. Koskinen, A. M. P.; Muñoz, L. *J. Org. Chem.* **1993**, *58*, 879–886.
18. (a) Müller, P.; Boléa, C. *Helv. Chim. Acta* **2001**, *84*, 1093–1111; (b) Müller, P.; Boléa, C. *Helv. Chim. Acta* **2002**, *85*, 483–494; (c) Müller, P.; Bolea, C. *Synlett* **2000**, 826–828; (d) Boléa, C. Ph.D. Thesis, Thesis No. 3251, University of Geneva, 2001.
19. (a) Nakanishi, K.; Berova, N.; Woody, R. W. *Circular Dichroism, Principles and Applications*; VCH: Weinheim, 1994; (b) Mislow, K. *Introduction to Stereochemistry*; W.A. Bemjamin: New York, 1965.

20. Fox, M. E.; Li, C.; Marino, J. P.; Overman, L. E. *J. Am. Chem. Soc.* **1999**, *121*, 5467–5480.
21. Piers, E. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 8, pp 971–998.
22. Müller, P.; Nury, P. *Helv. Chim. Acta* **2001**, *84*, 662–677.
23. (a) Takekawa, Y.; Shishido, K. *J. Org. Chem.* **2001**, *66*, 8490–8503; (b) Hudlicky, T.; Reddy, R. D.; Bhaskar, D.; Govindan, S. V.; Kulp, T.; Still, B.; Sheth, J. P. *J. Org. Chem.* **1983**, *48*, 3422–3428.
24. Koskinen, A. M. P.; Hassella, H. *J. Org. Chem.* **1993**, *58*, 4479–4480.