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Stereoelectronic Effects in the Fragmentation of γ-Silyloxy-β-hydroxy-α-diazocarbonyl Compounds

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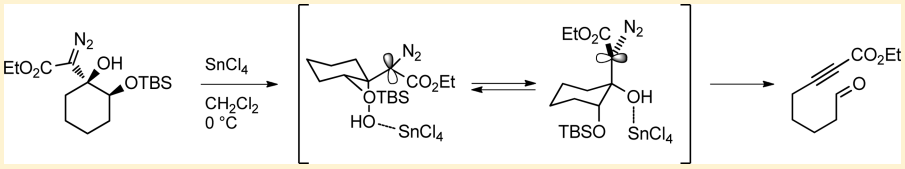
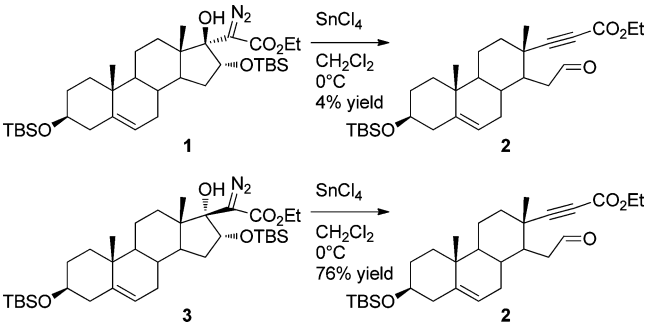
Supporting Information



ABSTRACT: A series of γ-silyloxy-β-hydroxy-α-diazocarbonyl compounds were prepared as fragmentation substrates to probe the hypothesis that steric interactions between the diazo ester and adjacent silyloxy group can play an important role in determining the success of fragmentations. Proper stereoelectronic alignment of the diazo ester and the departing hydroxyl group is necessary for productive fragmentation to occur.

Reactions that result in the cleavage of a carbon−carbon bond are important transformations because they can directly provide synthetic intermediates that are difficult to prepare by other routes and can unmask latent functional groups under chemoselective reaction conditions.[1−10] We recently reported that cyclic γ-silyloxy-β-hydroxy-α-diazocarbonyl compounds fragment in the presence of Lewis acids to provide aldehyde-tethered ynoates or ynones in high yield.[11,12] The fragmentation precursors were easily prepared for these studies by the aldol-type addition of ethyl lithiodiazoacetate to an α-silyloxy ketone.[13,14] Although high-yielding, this Aldol-type addition can result in the formation of two diastereomers, which is generally inconsequential because both stereoisomers typically fragment in similar yields. However, in the case of a more structurally complex steroid-based fragmentation substrate, a *trans*-diol diastereomer (**1**, Scheme 1) fragmented in dramatically lower yields (4%) than a *cis*-diol diastereomer (**3**, 76% yield). In this Note we describe results from a study we undertook to better understand the dependence of the fragmentation reaction on the stereochemistry of the fragmentation precursor.

Scheme 1. Unique Example of the Importance of Stereochemistry on Fragmentation Reaction Outcome



A proposed mechanism for the fragmentation of γ-silyloxy-β-hydroxy-α-diazocarbonyl compounds is shown in Scheme 2. The first step of this process is thought to be a Lewis acid assisted elimination of the β-hydroxy group to provide a vinyl diazonium intermediate (**6**),[15,16] which undergoes a Grob-type fragmentation with subsequent loss of the silyl protecting group. Alternatively, **6** may lose nitrogen to provide a vinyl cation prior to fragmentation. Loss of the β-hydroxyl group in the first step of this sequence would convert diazos **1** and **3** into a common intermediate, so the difference in reactivity observed for these compounds must arise during this initial elimination step. In order for the elimination of the β-hydroxyl to occur, the diazo and ester groups must lie in a plane that is perpendicular to the leaving group. Steric interactions that develop when the diazoester moiety is in the correct stereoelectronic orientation could account for the difference in observed reactivity for diastereomers **1** and **3**. That is, in the case of *cis*-diol isomer **3**, steric interactions involving the diazo ester should not be significant when it is oriented correctly for elimination to occur (**9**, Figure 1). Conversely, in the case of *trans*-diol diastereomer **1** significant steric interactions between the diazo ester and the adjacent silyloxy group would be expected, which may prevent the diazo ester from adopting the necessary conformation for the necessary elimination to occur (**10**, Figure 1).

The *cis*-diol diastereomer of fragmentation precursors derived from α-silyloxy cyclohexanone (e.g., **11**, Figure 2) should have steric interactions similar to those shown for structure **10** in Figure 1, yet the cyclohexanone-based systems fragment without issue. To rationalize these observations, we hypothesize that the cyclohexyl systems undergo ring inversion

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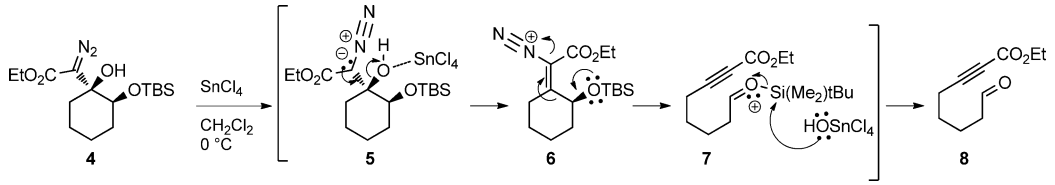
Scheme 2. Proposed Mechanism for the Fragmentation of γ-Silyloxy-β-hydroxy-α-diazocarbonyls



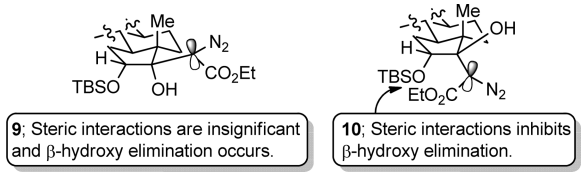


Figure 1. Steric interactions that could affect elimination of β-hydroxyl.

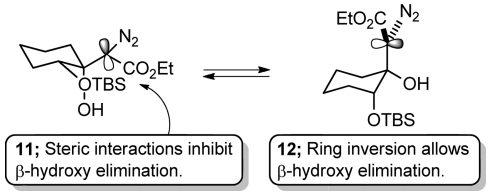


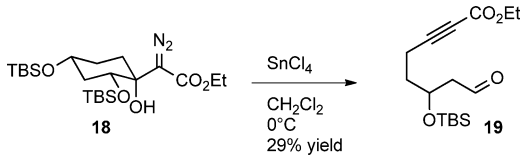
Figure 2. Ring inversion relieves steric interactions and facilitates elimination of β-hydroxyl.

to provide conformer **12** (Figure 2), in which the diazo ester adopts the stereochemical alignment necessary for elimination of the β-hydroxyl to occur. Alternatively, a twist boat conformation could also alleviate the steric interaction between the diazo ester and silyloxy group in cyclohexanone-based systems.

To test this hypothesis we have prepared several cyclohexyl-based fragmentation precursors that should be resistant to ring inversion, and we have assayed their ability to fragment. The first fragmentation precursor we prepared for these studies was γ-silyloxy-β-hydroxy-α-diazoester **13** (Scheme 3) derived from 4-*tert*-butyl cyclohexanone. In this case, the *tert*-butyl group should inhibit diazo **13** from undergoing a ring flip. In the event, treating diazo **13** under standard fragmentation conditions provided a complex mixture of products that contained only traces of the desired fragmentation product. This result supports the idea that ring inversion is necessary for fragmentation to occur since **13** should be able to adopt a twist boat conformation but did not fragment productively. In this case, a ring expansion and elimination sequence appears to be more favorable, and β-keto ester **17** was isolated in 55% yield. This ring expansion is interesting because while protic acids cause cyclic β-hydroxy-α-diazo esters to undergo ring expansion,[17,18] Lewis acids usually do so only when used in substoichiometric quantities; when used stoichiometrically, Lewis acids typically promote elimination of the hydroxy group leading to a vinyl diazonium species.[16,19] In the case of substrate **13**, a slow elimination step could result in a Lewis acid facilitated proton transfer to the diazo, which could lead to ring expansion as shown in Scheme 3. Importantly, diazo **13** was the first cyclohexyl-based fragmentation substrate we observed to not fragment productively.

To further probe the hypothesis that steric interactions between the diazo ester and an adjacent group affect the course of the reaction, we prepared two fragmentation substrates based on a 2,4-dihydroxycyclohexanone scaffold. The first, diazo ester **18** (Scheme 4) derived from 2,4-bis((*tert*-butyldimethylsilyl)-

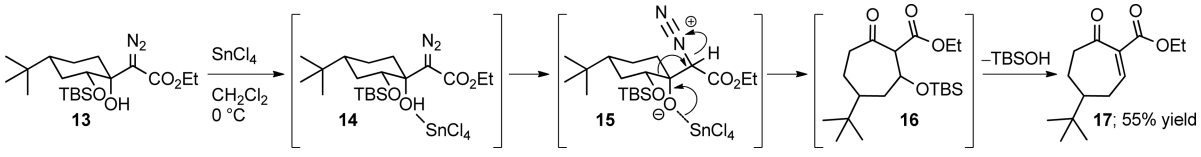
Scheme 4. Low-Yielding Ring Fragmentation



oxy)cyclohexanone,[20] should be resistant to ring inversion and should thus fragment poorly. Treating diazo ester **18** under the standard fragmentation conditions provided a complex mixture from which the desired product (**19**) was isolated in only 29% yield.[21] Although modest, this yield is higher than the yield obtained for the fragmentation of *tert*-butyl derivative **13**, which may be a reflection of the fact that OTBS has a smaller *A*-value than *tert*-butyl (1.06 vs >4.5 kcal/mol)[22,23] and thus **18** may undergo ring inversion to a greater extent than **13**. Coordination of the silyl ethers in **18** by the Lewis acid could also help facilitate ring inversion.

We prepared diazo **24** as a final substrate for these studies by the route shown in Scheme 5.[24] Diazo **24** is closely related to diazo **18** but has the alcohols tethered together by a silyl bridge. This bridge causes the diazo ester to be in an axial position on the ring, which allows it to adopt the stereoelectronic alignment needed for elimination of the β-hydroxyl without steric hindrance, and thus we expected **24** to fragment easily. When diazo **24** was treated with $SnCl_4$, copious gas evolution was noted, and when the reaction was stopped after 15 min, the NMR of the crude reaction mixture appeared to show a mixture of the expected aldehyde (**25**) and the dimeric acetal (**26**). When the fragmentation reaction was allowed to proceed for 12 h, the initially formed compounds reacted further to provide enal **27** in 83% isolated yield.

Scheme 3. First Example of a Cyclohexyl-Based Fragmentation Substrate That Failed To Fragment Productively



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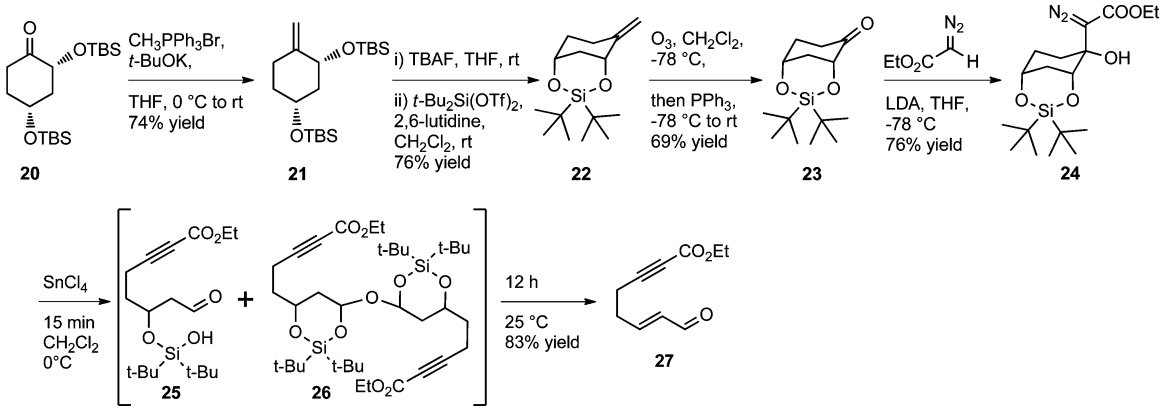
Scheme 5. Successful Ring Fragmentation



The studies presented here are consistent with our hypothesis that steric interactions involving the diazo ester play an important role in determining the success of fragmentations of γ-silyloxy-β-hydroxy-α-diazocarbonyl compounds. Proper stereoelectronic alignment of the diazo ester and the departing hydroxyl appears to be a necessary requirement for productive fragmentation, and steric interactions that inhibit this alignment from occurring are detrimental to the fragmentation process. This stereoelectronic requirement should be considered when applying this fragmentation in more complex systems.

EXPERIMENTAL SECTION

General Experimental Information. All reactions were carried out under an atmosphere of nitrogen using flame-dried glassware. Tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), and diethyl ether (Et_2O) were dried via a solvent dispensing system. $SnCl_4$ was distilled twice from P_2O_5 under inert atmosphere conditions and stored in sealed tubes under an atmosphere of nitrogen as a 1 M solution in CH_2Cl_2. Flash column chromatography was performed using silica gel (230−400 mesh), and TLC analysis was carried out using Merck 60F-254 silica on glass plates. Visualization of TLC plates was achieved using ultraviolet light, polyphosphomolybdic acid, and cerium sulfate in EtOH with H_2SO_4, ceric ammonium molybdate, or iodine. Accurate mass data was acquired in ESI mode using an orbitrap mass analyzer. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$. ^1H chemical shifts are reported in ppm (δ units) downfield from tetramethylsilane. Solvent peaks were used as internal references for all ^{13}C NMR.

Ethyl 2-(4-(*tert*-Butyl)-2-((*tert*-butyldimethylsilyl)oxy)-1-hydroxycyclohexyl)-2-diazoacetate (13). A solution of LDA (0.67 mmol) in THF (3.2 mL) was added dropwise via cannula over a period of 15 min to a −78 °C solution of *cis*-4-(*tert*-butyl)-2-((*tert*-butyldimethylsilyl)oxy)cyclohexanone[25] (160 mg, 0.56 mmol) and ethyl diazo acetate (83.5 mg, 0.73 mmol) in THF (3.2 mL). The resulting brown solution was maintained at −78 °C for 2 h at which point an aqueous saturated solution of NH_4Cl (5 mL) was added. The mixture was warmed to room temperature, additional saturated NH_4Cl (40 mL) was added, and the mixture was extracted with EtOAc (20 mL × 3). The organic layers were combined, dried over anhydrous Na_2SO_4, and evaporated to provide a yellow viscous oil that was purified by silica gel column chromatography (100:0 to 98:2 hexanes/EtOAc) to give 205 mg (89% yield) of the title compound; TLC R_f = 0.4 (96:4 hexanes/EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 4.24 − 4.00 (m, 3H), 3.09 (d, J = 2.1 Hz, 1H), 2.06−1.95 (m, 1H), 1.89 (dt, J = 14.1, 3.2 Hz, 1H), 1.72 (ddt, J = 12.1, 4.9, 2.4 Hz, 1H), 1.53−1.45 (m, 1H), 1.39−1.26 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H), 1.15−1.07 (m, 1H), 0.85 (s, 9H), 0.83 (s, 9H), 0.03 (s, 3H), −0.02 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 72.5, 70.8, 63.6, 60.0, 45.5, 33.6, 32.2, 32.1, 27.4, 25.6, 21.8, 17.7, 14.5, −4.5, −5.4; IR (thin film) 3529, 2093, 1684, 1094, 1082 cm^{-1}; HRMS (ESI) calcd for $[C_{20}H_{38}N_2O_4SiNa]^+$ 421.2493, found 421.2493.

Ethyl 4-(*tert*-Butyl)-7-oxocyclohept-1-enecarboxylate (17). A 1 M solution of $SnCl_4$ (414 μL, 0.41 mmol) was added as a single stream to a 0 °C solution of diazoester **13** (165 mg, 0.41 mmol) in CH_2Cl_2 (8.5 mL). The reaction mixture was maintained at 0 °C until gas evolution ceased (∼10 to 15 min). The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ (1.5 mL), stirred for 5 min at 0 °C, and transferred into a separatory funnel containing additional saturated aqueous $NaHCO_3$ (30 mL). The aqueous layer was extracted with pentane (10 mL × 3), the organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure, and the resulting residue was purified by silica gel column chromatography (98:2 hexanes/EtOAc) to provide 54 mg (55% yield) of **17** as a colorless oil; TLC R_f = 0.9 (80:20 hexanes/EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 6.97 (d, J = 4.6 Hz, 1H), 4.31 (q, J = 7.1 Hz, 2H), 2.53 (d, J = 16.0 Hz, 1H), 2.37 (d, J = 19.4 Hz, 1H), 2.11−1.98 (m, 2H), 1.93 (d, J = 12.7 Hz, 1H), 1.34 (t, J = 7.1 Hz, 3H), 1.31−1.24 (m, 1H), 1.10 (ddd, J = 24.9, 12.4, 5.0 Hz, 1H), 0.87 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.0, 164.7, 149.8, 135.9, 61.8, 43.2, 32.1, 28.4, 27.0, 23.4, 22.8, 14.0; IR (thin film) 2871, 1736, 1671, 1638, 1185, 1157, 1022 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{23}O_3]^+$ 239.1642, found 239.1643.

Ethyl 2-(2,4-Bis((*tert*-butyldimethylsilyl)oxy)-1-hydroxycyclohexyl)-2-diazoacetate (18). Diazo ester **18** was prepared from 2,4-bis((*tert*-butyldimethylsilyl)oxy)cyclohexanone (**20**)[20] (1.45 g, 4.05 mmol) using the procedure described for the synthesis of diazo ester **13**. The product was purified by silica gel column chromatography (100:0 to 92:8 hexanes/EtOAc) to give 1.26 g (66% yield) of **18** as a yellow solid. A 100 mg sample of this material was crystallized from MeOH (3 mL) to provide 65 mg of analytically pure product (mp = 113−114 °C). TLC R_f = 0.5 (96:4 hexanes/EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 4.26−4.06 (m, 3H), 3.69−3.07 (m, 1H), 3.07 (d, J = 2.3 Hz, 1H), 2.03 (tdd, J = 13.5, 4.8, 2.4 Hz, 1H), 1.94−1.82 (m, 2H), 1.74−1.60 (m, 3H), 1.26 (t, J = 7.1 Hz, 3H), 0.881 (s, 9H), 0.876 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.002 (s, 3H), 0.001 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 70.2, 70.0, 68.4, 63.4, 60.2, 40.6, 30.3, 30.2, 25.8, 25.6, 18.1, 17.7, 14.5, −4.6, −4.67, −4.72, −5.4; IR (thin film) 3486, 2095, 1676, 1098, 1070 cm^{-1}; HRMS (ESI) calcd for $[C_{22}H_{44}N_2O_5Si_2Na]^+$ 495.2681, found 495.2675.

Ethyl 6-((*tert*-Butyldimethylsilyl)oxy)-8-oxooct-2-ynoate (19). Aldehyde **19** was obtained from diazo ester **18** (400 mg, 0.85 mmol) by the procedure described for the synthesis of **17**. The crude product was purified by silica gel column chromatography (98:2 to 75:25 hexanes/EtOAc) to provide 78 mg (29% yield) of **19** as a viscous oil. TLC R_f = 0.3 (92:8 hexanes/EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 9.80 (t, J = 2.2 Hz, 1H), 4.34−4.27 (app. p, J = 5.7 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 2.57 (dd, J = 5.6, 2.2 Hz, 2H), 2.42 (t, J = 7.3 Hz, 2H), 1.82 (t, J = 6.8 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H), 0.87 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.1, 153.6, 88.1, 73.6, 66.4, 61.8, 50.6, 35.1, 25.7, 17.9, 14.6, 14.0,

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−4.7; IR (thin film) 2858, 2237, 1712, 1254 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{29}O_4Si]^+$ 313.1830, found 313.1831.

((4-Methylenecyclohexane-1,3-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (21). A mixture of $Ph_3P^+CH_3Br^-$ (13.6 g, 38.1 mmol) and THF (142 mL) was cooled to 0 °C, and potassium *tert*-butoxide (4.3 g, 38.1 mmol) was added in a single portion. The resulting yellow mixture of ylide was maintained at 0 °C for 20 min. A solution of 2,4-bis((*tert*-butyldimethylsilyl)oxy)cyclohexanone (**20**)[20] (5.06 g, 14.1 mmol) in THF (51 mL) was added to the ylide solution. The reaction mixture was maintained at 0 °C for 10 min and then at room temperature for 3 h at which point water (300 mL) was added, and the aqueous layer was extracted with Et_2O (50 mL × 3). The organic layers were combined, dried over anhydrous Na_2SO_4, and evaporated to a residue that was purified by column chromatography (98:2 hexanes/EtOAc) to give 3.74 g (74% yield) of **21** as a viscous oil; TLC R_f = 0.6 (98:2 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.00 (s, 1H), 4.74 (s, 1H), 3.97 (d, J = 7.1 Hz, 1H), 3.78−3.66 (m, 1H), 2.33 (dd, J = 14.7, 4.2 Hz, 1H), 2.18−2.07 (m, 1H), 1.95−1.82 (m, 2H), 1.40 (dd, J = 23.0, 11.5 Hz, 1H), 1.34−1.22 (m, 1H), 0.92 (s, 9H), 0.89 (s, 9H), 0.07 (s, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.4, 105.6, 70.5, 69.7, 46.8, 36.6, 30.2, 25.9, 18.4, 18.2, −4.6, −4.9, −5.0; IR (thin film) 1662, 1470, 1077, 835 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{41}O_2Si_2]^+$ 357.2640, found 357.2639.

3,3-Di-*tert*-butyl-6-methylene-2,4-dioxa-3-silabicyclo[3.3.1]nonane (22). A 1 M solution of tetrabutyl ammonium fluoride (23.3 mL, 23.3 mmol) was added to a solution of **21** (3.7 g, 10.4 mmol) in THF (93 mL), and the mixture was maintained at room temperature for 1 h. After the starting material was fully consumed as judged by TLC analysis, silica gel was added, and the reaction mixture was evaporated to dryness to give the crude product mixture on silica gel. This solid was loaded onto a prepacked column of silica gel, and the product was eluted with hexanes/EtOAc (gradient elution 50:50 to 0:100; TLC 100% EtOAc, R_f = 0.1) to obtain 1.34 g of impure diol as a viscous oil that was used without further purification. A mixture of the diol (610 mg, 4.76 mmol), CH_2Cl_2 (98 mL), and distilled 2,6-lutidine (2.2 mL, 19.0 mmol) was maintained under a nitrogen atmosphere, and t-$Bu_2Si(OTf)_2$ (1.7 mL, 5.23 mmol) was added dropwise within 2 min. The reaction mixture was maintained at room temperature for 24 h at which point saturated aqueous NH_4Cl (100 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4, and evaporated to provide a residue that was purified by column chromatography (100:0 to 96:4 hexanes/EtOAc) to give 975 mg (76% yield) of **22** as a viscous oil. *Note:* Best results were obtained when the silica gel column was packed with 100% hexanes containing 0.5% Et_3N prior to loading the crude product; the mobile phase used for elution did not contain Et_3N; TLC R_f = 0.9 (96:4 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.86 (s, 1H), 4.75 (s, 1H), 4.51 (s, 1H), 4.36 (s, 1H), 3.13−3.04 (m, 1H), 2.67 (ddd, J = 14.7, 6.8, 3.7 Hz, 1H), 2.13 (dd, J = 15.3, 6.3 Hz, 1H), 2.09−2.02 (m, 1H), 1.64−1.51 (m, J = 6.9 Hz, 2H), 1.07 (s, 9H), 1.05 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.4, 110.3, 73.6, 67.8, 37.1, 33.4, 29.1, 28.4, 24.8, 21.6, 21.4; IR (thin film) 1652, 1480, 1106 cm^{-1}; HRMS (ESI) calcd for $[C_{15}H_{29}O_2Si]^+$ 269.1931, found 269.1928.

3,3-Di-*tert*-butyl-2,4-dioxa-3-silabicyclo[3.3.1]nonan-6-one (23). In a two-necked RBF, a solution of **22** (950 mg, 3.54 mmol) in CH_2Cl_2 (50 mL) was cooled to −78 °C, and ozone gas was bubbled through the solution in an efficient fume hood until the solution became blue (~5−10 min) at which point the solution was purged with N_2 until it became colorless. Triphenylphosphine (4.60 g, 17.7 mmol) was added, and the reaction mixture was warmed to room temperature. After maintaining the reaction mixture at room temperature for 3 h, the solvent was evaporated, and the crude product was purified by column chromatography (100:0 to 90:10 hexanes/EtOAc) to provide 662 mg (69% yield) of **23** as a white waxy solid. *Note:* Best results were obtained when the silica gel column was packed with 100% hexanes containing 0.5% Et_3N prior to loading the crude product; the mobile phase used for elution did not contain Et_3N. TLC R_f = 0.5 (92:8 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.44 (d, J = 1.1 Hz, 1H), 4.21 (d, J = 3.8 Hz, 1H), 3.27 (ddd, J = 16.8, 10.5, 8.8 Hz, 1H), 2.88 (ddd, J = 15.5, 7.8, 3.9 Hz, 1H), 2.34 (dd, J = 15.2, 7.7 Hz, 2H), 2.03−1.92 (m, 1H), 1.79 (d, J = 15.6 Hz, 1H), 1.09 (s, 9H), 1.05 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.9, 74.6, 66.5, 35.6, 33.0, 32.9, 28.7, 27.8, 21.3, 21.2; IR (thin film) 1720, 1121 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{27}O_3Si]^+$ 271.1724, found 271.1721.

Ethyl 2-(3,3-Di-*tert*-butyl-6-hydroxy-2,4-dioxa-3-silabicyclo-[3.3.1]nonan-6-yl)-2-diazoacetate (24). Diazo ester **24** was prepared from **23** (618 g, 2.28 mmol) using the procedure described for the synthesis of diazo ester **13**. The reaction mixture was purified by silica gel column chromatography (96:4 to 85:15 hexanes/EtOAc) to give 665 mg (76% yield) of diazo ester **24** as a yellow amorphous solid. *Note:* Best results were obtained when the silica gel column was packed with 96:4 hexanes/EtOAc containing 0.5% Et_3N prior to loading the crude product; the mobile phase used for elution did not contain Et_3N. TLC R_f = 0.5 (88:12 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.74 (d, J = 4.3 Hz, 1H), 4.27 (s, 1H), 4.26−4.18 (m, 2H), 3.38 (s, 1H), 2.72−2.58 (m, 2H), 1.99 (d, J = 11.8 Hz, 1H), 1.81 (dd, J = 15.1, 4.9 Hz, 1H), 1.71 (d, J = 15.4 Hz, 1H), 1.51 (tdd, J = 14.4, 5.1, 3.0 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H), 1.12 (s, 9H), 1.11 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.4, 73.4, 71.4, 66.4, 61.2, 60.7, 32.4, 30.5, 29.1, 28.6, 27.2, 21.6, 21.5, 14.4; IR (thin film) 3520, 2089, 1700, 1128, 1015 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{32}N_2O_5SiNa]^+$ 407.1973, found 407.1970.

(*E*)-Ethyl 8-Oxooct-6-en-2-ynoate (27). Aldehyde **27** was synthesized from diazo ester **24** (100 mg, 0.26 mmol) using the procedure described for the synthesis of **17** except the reaction was allowed to warm to room temperature and was then maintained at room temperature for 12 h. The crude reaction mixture was purified by silica gel column chromatography (100% CH_2Cl_2) to provide 39 mg (83% yield) of aldehyde **27** as a viscous oil. TLC R_f = 0.1 (92:8 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.49 (d, J = 7.7 Hz, 1H), 6.81 (dt, J = 15.7, 6.4 Hz, 1H), 6.13 (ddt, J = 15.6, 7.7, 1.4 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 2.61−2.55 (m, 2H), 2.55−2.45 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.3, 154.0, 153.3, 133.8, 86.2, 74.1, 61.8, 30.2, 17.2, 13.8; IR (thin film) 2826, 2749, 2238, 1706, 1691, 1640, 1253, 1126, 1070 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_{13}O_3]^+$ 181.0859, found 181.0859.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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