An Exploratory Study of Type II [3 + 4] Cycloadditions between Vinylcarbenoids and Dienes

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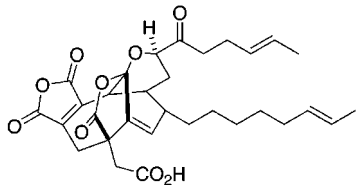
The intramolecular type II [3 + 4] cycloaddition between vinylcarbenoids and furans is a practical method for the construction of 5-oxo-10-oxatricyclo[6.2.1.$0^{4,9}$]undeca-3,8(11)-dienes, containing two anti-Bredt double bonds. These tricyclic systems are well functionalized for eventual elaboration to the natural product CP-263,114. The rhodium-stabilized vinylcarbenoids are generated by dirhodium tetracarboxylate catalyzed decomposition of vinyldiazoacetates. The [3 + 4] cycloaddition is generally considered to occur by a tandem cyclopropanation/Cope rearrangement, although evidence is presented that with these substrates the [3 + 4] cycloaddition may occur in a concerted manner.

For some time we have studied the synthetic utility of the [3 + 4] cycloaddition between rhodium-stabilized vinylcarbenoids and dienes.[1,2] Recently, CP-263,114 (**1**) has become a synthetic target of great interest on account of its novel structure and promising biological activity.[3,4] The research activity in this area has included numerous model studies[5−18] and two recent reports of total syntheses of racemic CP-263,114 by Nicolaou[19,20] and Danishefsky.[21,22] Intrigued by the possibility that the [3 + 4] cycloaddition could be a novel disconnection for the synthesis of CP-263,114, we have explored the utility of type II [3 + 4] cycloadditions between vinylcarbenoids and various dienes.[23] In this paper, we describe the scope of this chemistry, with particular emphasis on the stability and subsequent chemistry of the resulting [3 + 4] cycloaddition products which contain two anti-Bredt double bonds.



CP -263,114 (**1**)

To study the feasibility of type II intramolecular cyclopropanations, the isoprenyl-functionalized vinyldiazoacetate **2** was initially prepared. Rhodium(II) octanoate catalyzed decomposition of the vinyldiazoacetate **2** resulted in the formation of the *cis*-divinylcyclopropane **3** (eq 1). Even though *cis*-divinylcyclopropanes tend to readily rearrange to cycloheptadienes, **3** was not prone to ring expansion to **4** by a Cope rearrangement. The failure of this rearrangement is presumably due to the strain that exists in the transition-state for the Cope rearrangement[24] or in the doubly anti-Bredt product **4**.

To determine if structural variations in the divinylcyclopropane could favor the Cope rearrangement,[24] exploratory studies were extended to include the diazoacetoacetate system **5** (eq 2). $Rh_2(OAc)_4$-catalyzed decomposition of **5** resulted in the formation of the cyclopropane **6**. Silylation of **6** generated the divinylcyclopropane **7**, which

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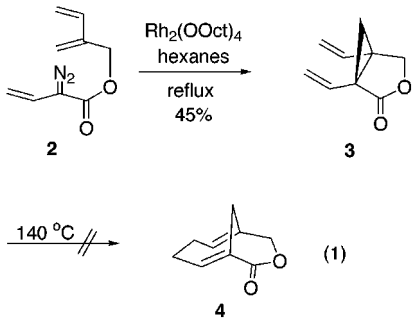
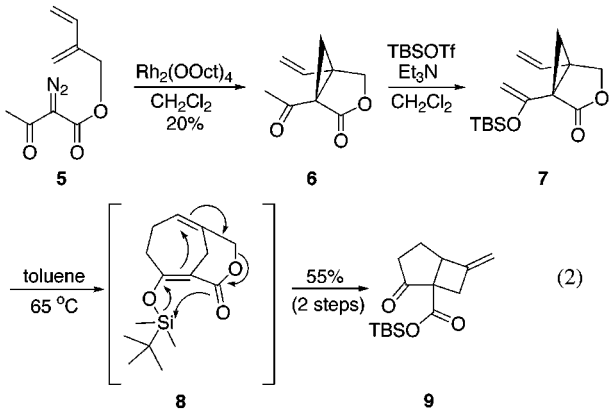
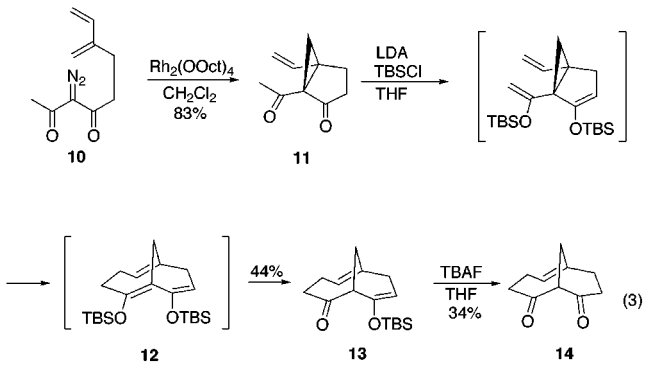


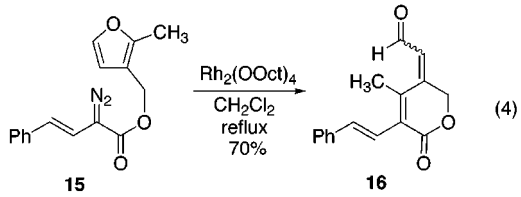
on heating to 65 °C underwent a novel rearrangement to the fused cyclobutane **9**. Most likely, this reaction proceeds via the desired product **8**, but due to the presence of the two anti-Bredt double bonds in **8**, this compound is unstable and undergoes a transannular rearrangement to form cyclobutane **9**.



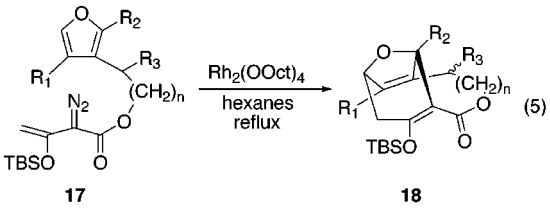
The transannular rearrangement to form fused cyclobutanes would not be possible if a ketone linkage was used instead of an ester. Consequently, the chemistry of diazodiketone **10** was explored (eq 3). The diazodiketone **10** underwent very effective intramolecular cyclopropanation to form cyclopropane **11**. Attempts to form a *cis*-divinylcyclopropane from **11** using 1 equiv of a silylating agent were unsuccessful because preferential silylation of the cyclopentanone occurred. Consequently, the reaction was carried out with two equivalents of the silylating agent and this resulted in the formation of the rather unstable monosilylated product **13**. Presumably, the desired rearrangement occurred to form **12**, but **12** was unstable and underwent desilylation of the anti-Bredt silyl enol ether to form **13**. Further verification of the structure of **13** was obtained by conversion of **13** to diketone **14**, which was sufficiently stable for complete structural characterization.



Overall, the type II [3 + 4] cycloaddition between vinylcarbenoids and dienes was not a very robust transformation, primarily due to the relative instability of the cycloaddition products. To improve the stability of the products, cycloaddition reactions were carried out with furan as the diene component. Since the diene component is constrained within a ring, transannular reactions of the [3 + 4] cycloaddition products were expected to be highly unlikely because they would lead to excessively strained products. Decomposition of phenylvinyldiazoacetate **15** failed to generate the required [3 + 4] cycloaddition product, but instead afforded the unstable triene **16** (eq 4). The unraveling of a furan ring to a triene on reaction with a metal-stabilized vinylcarbenoid is a common reaction that is usually formed from zwitterionic intermediates.[25,26]



In contrast to the phenylvinyldiazoacetate **15**, a series of siloxyvinyldiazoacetates of general structure **17** gave the desired bicyclic products **18** in moderate to good yields (eq 5). Previous results obtained for intermolecular reactions of vinyldiazoacetates with furans,[27] pyrroles,[28] and intramolecular reactions of vinyldiazoacetates with pyrroles[29] have also shown that silyloxyvinyldiazoacetates are exceptional substrates for this type of [3 + 4] cycloaddition.



	n	R_1	R_2	R_3	Yield, %
a	0	H	H	H	83
b	0	CH_2OBn	H	H	66
c	0	H	Me	H	29
d	0	H	H	Et	48
e	1	H	H	H	26

The next series of experiments were carried out on ketone derivatives instead of esters because these compounds would ultimately be required in a synthesis of CP-263,114. The general synthesis of these compounds is shown in (eq 6). Reaction of aldehyde **19** with the dianion of acetoacetone generated the aldol product **20**,

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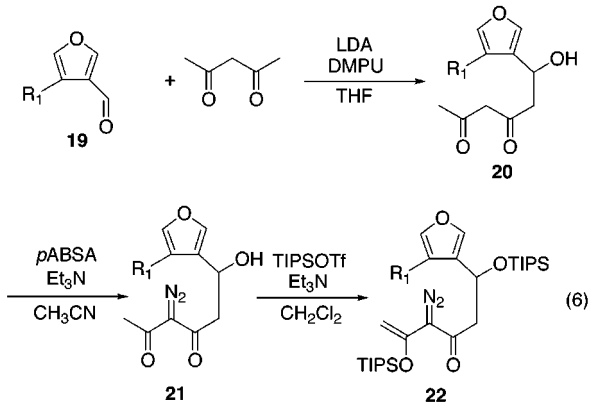
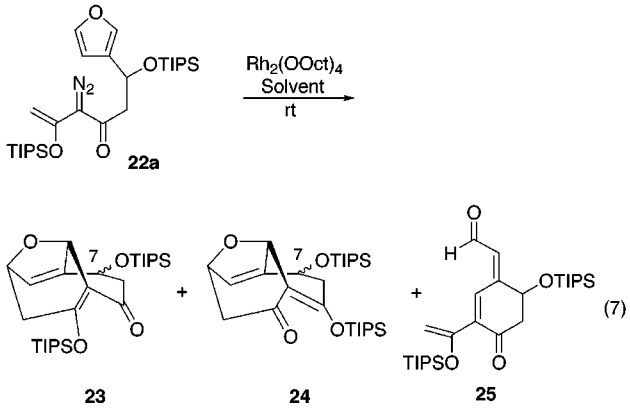
which was directly converted to diazodiketone **21** without purification. Treatment of **21** with 2 equiv of triisopropylsilyl triflate and triethylamine generated the vinyldiazoketone **22**. Gratifyingly, excellent regiocontrol was achieved in the silyl enol ether formation, where only **22** was formed.



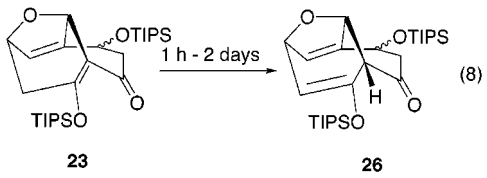
	R_1	Yield, % (**19**→**21**)
a	H	72
b	CO_2Me	71

The chemoselectivity of the rhodium(II) carbenoid mediated reaction was found to be dependent on the reaction solvent employed. When the reaction was carried out using hexane as solvent a 61:37:2 mixture of [3 + 4] cycloaddition products **23** and **24** and the triene **25** was obtained (eq 7). However, when the reaction was carried out in CH_2Cl_2 the ratio of **23** to **24** was improved to 73:17 and the amount of triene **25** increased to 10% of the product mixture. Under both sets of reaction conditions, **23** and **24** were formed as a 3:1 diastereomeric mixture.

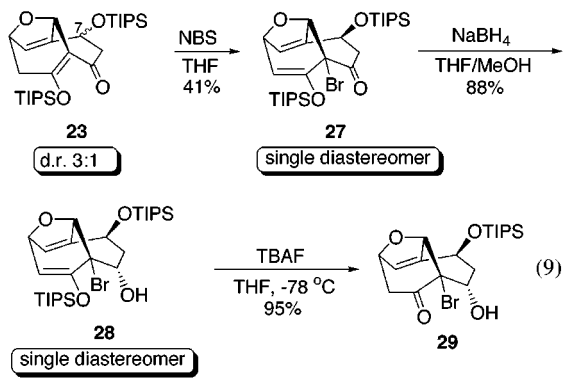


Solvent	**23: 24: 25**	Total Yield (from **21a**)	d.r. of **23**
Hexanes	61:37:2	71	3:1
CH_2Cl_2	**73:17:10**	**77**	**3:1**

Even though **23** could be isolated by chromatography in 44% yield, on standing in solution from 1 to 48 h, it rearranged to a new silyl enol ether **26** in which the alkene had migrated away from the anti-Bredt position (eq 8). This result further demonstrated the lability of these compounds, which contain two anti-Bredt double bonds.

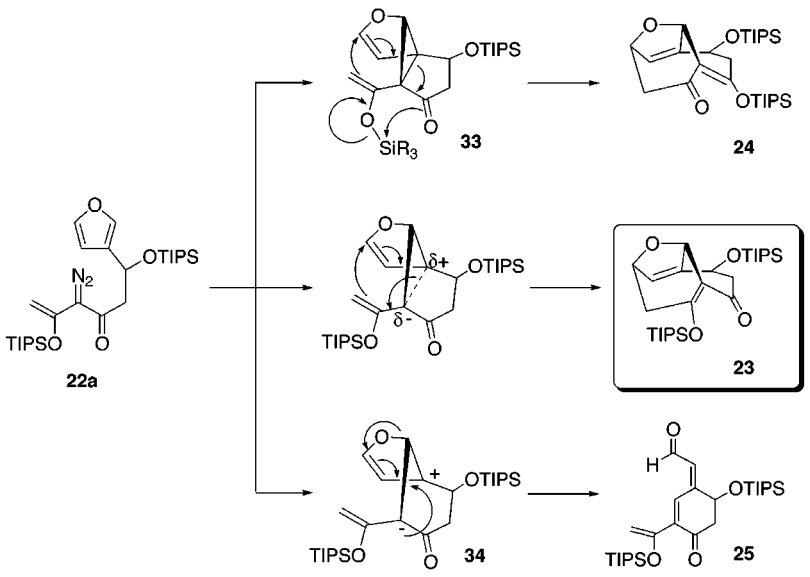


If the [3 + 4] cycloaddition methodology was to figure in a viable synthesis of CP-263,114, the initially formed doubly anti-Bredt products would have to be transformed to more stable compounds. Since the anti-Bredt silyl enol ether **23** was prone to migration away from the bridgehead position, **23** was reacted with *N*-bromosuccinimide. This resulted in bromination with enol migration to form bromide **27** (eq 9). It was envisioned that the bridgehead bromo functionality would be a useful structural motif for late stage introduction of an anti-Bredt double bond by a zinc-induced elimination of an appropriately functionalized β-bromo acetate. A remarkable feature of the bridgehead bromination was that even though **23** existed as a 3:1 mixture of diastereomers, **27** was formed as a single diastereoisomer, indicating that only the major C7 exo diastereomer of **23** was undergoing reaction. It was apparent from molecular models of **23**, that the C7 endo silyloxy group, sterically inhibited bromination. The relative stereochemistry in **27** was established using NOE difference analysis and then confirmed by X-ray crystallography (Supporting Information). Further transformations on **27** were readily achieved by reduction to the alcohol **28** and selective desilylation of the silyl enol ether in **28** to form **29**.

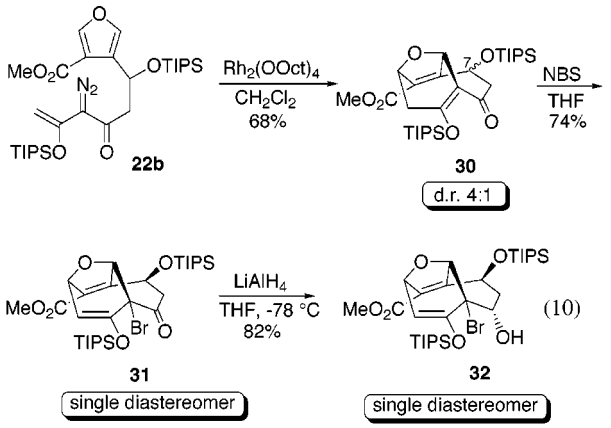


If the [3 + 4] cycloaddition strategy was actually used in a planned synthesis of CP-263,114, it would be advantageous if the chemistry could be extended to more elaborate furans. The 3-furanylester derivative **30** would be especially useful, because it could enable the introduction of the maleic anhydride moiety in CP-263,114. Rhodium(II) octanoate catalyzed decomposition of **22b** in CH_2Cl_2 resulted in the formation of **30** in 68% yield as a 4:1 diastereomeric mixture favoring the C7 exo isomer (eq 10). The reaction of **22b** was much cleaner than that of the unsubstituted derivative **22a**. Treatment of **30** with *N*-bromosuccinimide resulted in the formation of **31** in 74% yield as a single diastereomer. Once again, the minor C7 endo isomer of **30** does not appear to undergo bromination. Attempts to reduce the ketone group in **31** with a variety of reagents were initially unsuccessful.

Scheme 1



However, finally, it was discovered that reduction with lithium aluminum hydride at −78 °C resulted in the formation of the alcohol **32**. Under these conditions the ester group in **31** was left unchanged.



Discussion

The Cope rearrangement of *cis*-divinylcyclopropanes, which are formed from intramolecular type II cyclopropanations, is a demanding transformation that is only successful when a silyl enol ether is one of the vinyl components. Due to the presence of two anti-Bredt double bonds in the [3 + 4] cycloaddition products, transannular rearrangements are potentially a problem, but these can be avoided when furans are used as the diene component. Even though the initial [3 + 4] cycloaddition products are quite labile, they can be converted to stable compounds that are appropriately functionalized for further elaboration toward CP-263,114.

One of the most interesting features of this [3 + 4] cycloaddition chemistry is that three products can be formed in the reaction with furan, depending on the reaction solvent used. A reasonable explanation for this effect is shown in Scheme 1. It is well established that solvent has a major effect on vinylcarbenoid transformations.[30−32] The use of CH_2Cl_2 can lead to products derived from zwitterionic intermediates rather than cyclopropanation, but such transformations can be severely curtailed if a hydrocarbon solvent is used. The formation of trienes from the reaction of vinylcarbenoids with furans is considered to occur from fully formed zwitterionic intermediates obtained via electrophilic attack of the carbenoid at the 2-position of the furan.[25] This mechanism is consistent with the increased formation of triene **25** in the reaction of **22a** when the reaction solvent is changed from hexanes to CH_2Cl_2.

The more subtle issue in this chemistry is the effect of solvent on formation of the two [3 + 4] cycloaddition products **23** and **24**. On changing the solvent from hexane to CH_2Cl_2 the ratio of **23** to **24** changes from 61:37 to 73:17. It is plausible that the Cope rearrangement of the fully formed cyclopropane **33** is difficult to achieve and that instead an alternative ring expansion mechanism with silyl transfer occurs to form **24** (Scheme 1). The direct formation of **23** could more reasonably occur from a partially zwitterionic transition state or even the fully zwitterionic intermediate **34**.[33] Thus, even though the reaction of vinylcarbenoids with dienes has been generally considered as a cyclopropanation followed by a Cope rearrangement, in certain systems, it may be that the reaction is a stepwise or even a concerted [3 + 4] cycloaddition. It has been previously proposed that certain intramolecular reactions between vinylcarbenoids and pyrroles may be stepwise [3 + 4] cycloadditions.[29]

In summary, these studies further extend the range of transformations that are possible between vinylcarbenoids and dienes. The model studies described here demonstrate that the intramolecular type II [3 + 4] cycloadditions with furans are sufficiently robust that such an approach for the total synthesis of CP-263,114 is reasonable. Further studies to use this chemistry for the synthesis of CP-263,114 are in progress.

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(33) In Scheme 1, **34** is indicated to be formed directly from the carbene insertion, although it cannot be ruled out that **34** could have been formed by spontaneous or metal-mediated opening of **33**.

Experimental Section

General Information. ^{1}H NMR spectra were run at either 300, 400, or 500 MHz and ^{13}C NMR at either 75 or 125 MHz in $CDCl_3$. Mass spectral determinations were carried out at 70 eV. Melting points are uncorrected. IR spectra were obtained using a Nicolet Impact series 420 IR. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA.

Reactions were performed using heat-gun dried glassware under an atmosphere of argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), and hexanes were distilled from sodium benzophenone ketyl prior to use. Acetonitrile (CH_3CN), toluene, diisopropylamine, and dichloromethane (CH_2Cl_2) were distilled from calcium hydride. Column chromatography was carried out on Merck silica gel 60 (230−400 mesh). Rhodium(II) octanoate was purchased from Degussa Chemical Corporation. Commercially available reagents were used without additional purification unless otherwise stated.

1,5-Divinyl-3-oxabicyclo[3.1.0]hexan-2-one 3. A solution of diazo **2** (178 mg, 1.00 mmol) in hexanes (20 mL) was added dropwise over 2 h to a solution of rhodium(II) octanoate (8.0 mg, 10 μmol) in hexanes (40 mL) heated at reflux. The reaction mixture was heated at reflux for a further 1 h and then allowed to cool to room temperature overnight and concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 4:1) afforded cyclopropane **3** (67 mg, 45%): R_f 0.37 (petroleum ether/Et_2O, 4:1); IR (neat) 3089, 2965, 2923, 2851, 1770, 1728, 1588 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78−5.65 (m, 2 H), 5.45−5.19 (m, 4 H), 4.38 (d, 1 H, J = 9.1 Hz), 4.28 (d, 1 H, J = 9.1 Hz), 1.70 (d, 1 H, J = 4.8 Hz), 1.42 (d, 1 H, J = 4.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.1, 131.9, 128.3, 119.3, 117.9, 70.0, 37.2, 25.7, 22.5; HRMS (EI) m/z calcd for $C_9H_{10}O_2$ 150.0681, found 150.0681.

1-Acetyl-5-vinyl-3-oxabicyclo[3.1.0]hexan-2-one 6. A solution of diazo **5** (1.68 g, 8.66 mmol) in CH_2Cl_2 (40 mL) was added dropwise over 1.5 h to a solution of rhodium(II) octanoate (24 mg, 31 μmol) in CH_2Cl_2 (60 mL) at room temperature. The reaction mixture was stirred at room temperature overnight and then concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 3:2) afforded cyclopropane **6** (286 mg, 20%): R_f 0.22 (petroleum ether/Et_2O, 4:1); IR (neat) 3089, 2965, 2924, 1786, 1693, 1646, 1589, 1429, 1367, 1093 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.81 (dd, 1 H, J = 17.6, 10.9 Hz), 5.37 (d, 1 H, J = 10.9 Hz), 5.30 (d, 1 H, J = 17.6 Hz), 4.50 (d, 1 H, J = 10.3 Hz), 4.28 (d, 1 H, J = 10.3 Hz), 2.45 (s, 3 H), 2.42 (d, 1 H, J = 4.7 Hz), 1.55 (d, 1 H, J = 4.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9, 172.9, 128.9, 118.5, 68.0, 43.2, 42.6, 29.3, 24.4. Anal. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 64.89; H, 6.11.

***tert*-Butyldimethylsilyl 6-Methylene-2-oxobicyclo[3.2.0]-heptane-1-carboxylate 9.** Triethylamine (0.15 mL, 1.1 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.22 mL, 0.94 mmol) were added to a solution of cyclopropane **6** (120 mg, 0.72 mmol) in CH_2Cl_2 (3 mL) at 0 °C. The reaction was stirred for 20 min at 0 °C and then poured into saturated aqueous $NaHCO_3$ and hexanes. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated in vacuo to afford cyclopropane **7** (210 mg), which was used in the next step without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.72 (dd, 1 H, J = 18.2, 10.9 Hz), 5.25 (d, 1 H, J = 10.9 Hz), 5.17 (d, 1 H, J = 18.2 Hz), 4.41−4.39 (m, 3 H), 4.24 (d, 1 H, J = 8.8 Hz), 1.80 (d, 1 H, J = 4.9 Hz), 1.33 (d, 1 H, J = 4.9 Hz), 0.88 (s, 9 H), 0.20 (s, 3 H), 0.17 (s, 3 H).

A solution of cyclopropane **7** (210 mg, 0.72 mmol) in toluene (10 mL) was heated at 65 °C overnight. The solvent was evaporated in vacuo, and purification by silica gel column chromatography (petroleum ether/Et_2O, 4:1) afforded silyl ester **9** (110 mg, 55% from **6**): R_f 0.77 (petroleum ether/Et_2O, 4:1); IR (neat) 2961, 2928, 2858, 2890, 1748, 1721, 1302, 1259 (cm^{-1}); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.04 (d, 1 H, J = 2.4 Hz), 5.01 (d, 1 H, J = 2.4 Hz), 3.77 (d, 1 H, J = 4.3 Hz), 3.35 (d, 1 H, J = 16.8 Hz), 2.72−2.65 (m, 2 H), 2.43 (dd, 1 H, J = 18.7, 8.3 Hz), 2.22−2.14 (m, 1H), 2.09−2.04 (m, 1 H), 0.91 (s, 9 H), 0.28 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.9, 170.4, 145.5, 109.4, 55.6, 52.1, 37.0, 36.9, 25.9, 25.3, 17.4, −5.1, −5.3; MS m/z (relative intensity) 266 (1), 265 (2), 223 (100). Due to the relative instability of this compound, no further characterization was obtained. However, full data was obtained for the free acid derived from **9** (See Supporting Information).

1-Acetyl-5-vinylbicyclo[3.1.0]hexan-2-one 11. A solution of diazo **10** (1.55 g, 8.07 mmol) in CH_2Cl_2 (40 mL) was added dropwise over 2 h to a solution of rhodium(II) octanoate (63 mg, 81 μmol) in CH_2Cl_2 (60 mL). The reaction was stirred at room temperature overnight and then concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 4:1) afforded cyclopropane **11** (1.1 g, 83%): R_f 0.43 (petroleum ether/Et_2O, 4:1); IR (neat) 3094, 3012, 2955, 2872, 1734, 1687, 1646, 1418, 1367 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.72 (dd, 1 H, J = 17.7, 10.8 Hz), 5.27 (d, 1 H, J = 17.7 Hz), 5.20 (d, 1 H, J = 10.8 Hz), 2.41 (d, 1 H, J = 5.1 Hz), 2.37−2.30 (m, 2 H), 2.34 (s, 3 H), 2.17−2.13 (m, 2 H), 1.60 (d, 1 H, J = 5.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.5, 199.5, 134.3, 115.9, 52.9, 48.2, 33.3, 29.9, 25.2, 23.6; MS m/z (relative intensity) 165 (11), 164 (100). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.03; H, 7.35.

7-(*tert*-Butyldimethylsilyloxy)bicyclo[4.3.1]deca-1,7-dien-5-one 13. *n*-BuLi (2.5 M in hexanes, 0.88 mL, 2.2 mmol) was added to a solution of diisopropylamine (0.32 mL, 2.4 mmol) in THF (4 mL) at 0 °C. After 30 min, the reaction mixture was cooled to −78 °C, and a solution of **11** (164 mg, 1.00 mmol) in THF (1 mL) was added. After 10 min, *tert*-butyldimethylsilyl chloride (0.30 g, 2.0 mmol) was added, and the reaction mixture was allowed to warm to room temperature overnight. The reaction mixture was poured into saturated aqueous $NaHCO_3$ and Et_2O, washed with water, dried (Na_2SO_4), and concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 4:1) afforded silyl enol ether **13** (123 mg, 44%): R_f 0.74 (petroleum ether/Et_2O, 4:1); IR (neat) 3048, 2955, 2934, 2887, 2856, 1703, 1646, 1486, 1191 (cm^{-1});^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70 (t, 1 H, J = 6.9 Hz), 5.08 (dd, 1 H, J = 5.1, 1.8 Hz), 3.12−3.07 (m, 1 H), 2.87 (d, 1 H, J = 15.3 Hz), 2.72 (d, 1 H, J = 12.0 Hz), 2.68−2.51 (m, 3 H), 2.29−2.14 (m, 3 H), 0.88 (s, 9 H), 0.11 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.3, 150.1, 141.9, 122.3, 109.3, 58.9, 42.5, 33.9, 28.6, 25.5, 22.6, 17.8, −4.5, −5.0; HRMS (EI) m/z calcd for $C_{12}H_{17}O_2Si$ ($-C_4H_9$, loss of *tert*-butyl group) 221.0995, found 221.0998.

Bicyclo[4.3.1]dec-1-ene-5,7-dione 14. TBAF (1 M in THF, 0.36 mL, 0.36 mmol) was added to a solution of silyl enol ether **13** (100 mg, 0.36 mmol) in THF (5 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and then poured into saturated aqueous NH_4Cl, extracted with Et_2O and EtOAc, dried (Na_2SO_4), and concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 1:1) afforded diketone **14** (20 mg, 34%): R_f 0.34 (petroleum ether/Et_2O, 1:1); IR (neat) 2950, 2918, 2815, 1718, 1687 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.74 (dd, 1 H, J = 7.2, 5.4 Hz), 3.50−3.46 (m, 1 H), 3.04 (dd, 1 H, J = 12.9, 2.7 Hz), 2.81−2.62 (m, 3 H), 2.57−2.49 (m, 2 H), 2.45−2.32 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.0, 204.9, 142.4, 122.7, 67.3, 41.8, 38.8, 31.5, 29.2, 21.5; HRMS (EI) m/z calcd for $C_{10}H_{12}O_2$ 164.0837, found 164.0840.

[4-Methyl-6-oxo-(*E*)-5-(2-phenylvinyl)-6*H*-pyran-3-ylidene]acetaldehyde 16. A solution of diazo **15** (132 mg, 0.468 mmol) in CH_2Cl_2 (20 mL) was added dropwise over 1 h to a solution of rhodium(II) octanoate (3.6 mg, 4.7 μmol) in CH_2Cl_2 (10 mL) heated at reflux. The reaction mixture was heated at reflux for a further 2 h, allowed to cool to room temperature overnight, and concentrated in vacuo. Purification by silica gel column chromatography (hexane/EtOAc, 4:1) afforded aldehyde **16** (83 mg, 70%) as a 5: 1 inseparable mixture of double bond isomers: R_f 0.55 (hexane/EtOAc, 1:1); IR (neat) 3063, 3026, 2931, 2851, 1713, 1665, 1607, 1581, 1570, 1491; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.22 (d, 1 H, J = 8.1 Hz), 7.60 (d, 1 H, J = 16.0 Hz), 7.54−7.25 (m, 5 H), 6.99 (d, 1 H, J = 16.0 Hz), 6.04 (d, 1 H, J = 8.1 Hz), 4.85 (s, 2 H), 2.50 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.4, 161.7, 146.7, 141.3, 139.2, 136.6, 129.7, 129.4, 129.1 (2C), 128.7, 127.1, 119.7, 71.0, 22.0; HRMS (EI) m/z calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0963.

Typical Procedure for the Preparation of Dioxatricycles 18a−e. 3-(*tert*-Butyldimethylsilyloxy)-6,10-dioxatricyclo[6.2.1.0^{4,9}]undeca-3,8(11)-dien-5-one 18a. Triethylamine (0.50 mL, 3.6 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.60 mL, 2.6 mmol) were added to a solution of 3-furanylmethyl 2-diazo-3-oxobutanoate (0.44 g, 2.1 mmol) in CH_2Cl_2 (35 mL) at 0 °C. The reaction mixture was stirred for 20 min at 0 °C and then poured into dilute aqueous $NaHCO_3$ and hexanes. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated in vacuo to afford diazo **17a** (0.68 g). The material was used in the subsequent reaction without purification: IR (neat) 2957, 2931, 2886, 2858, 2102, 1710, 1607 (cm^{-1}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.40 (s, 1H), 6.44 (s, 1H), 5.11 (s, 2H), 4.99 (s, 1H), 4.99 (d, 1H, J = 1.9 Hz), 4.24 (d, 1H, J = 1.9 Hz), 0.91 (s, 9H), 0.22 (s, 6H).

A solution of diazo **17a** (680 mg, 2.1 mmol) in hexanes (50 mL) was added dropwise over 25 min to a solution of rhodium(II) octanoate (17 mg, 22 μmol) in hexanes heated at reflux. The reaction mixture was heated at reflux for a further 1 h, then concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 1:1) afforded **18a** (520 mg, 83% from 3-furanylmethyl 2-diazo-3-oxobutanoate): IR (neat) 2954, 2929, 2858, 1732, 1600; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.20 (s, 3 H), 0.23 (s, 3 H), 0.90 (s, 9 H), 1.75 (d, 1 H, J = 17.6 Hz), 2.81 (dd, 1 H, J = 5.4, 17.6 Hz), 4.95 (d, 1 H, J = 12.6 Hz), 4.97 (s, 1 H), 5.04 (d, 1 H, J = 12.6 Hz), 5.28 (d, 1 H, J = 5.4 Hz), 5.36 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 150.6, 146.3, 117.2, 115.2, 79.0, 76.9, 65.2, 34.1, 25.5, 18.2, −4.1, −4.9. Anal. Calcd for $C_{15}H_{22}O_4Si$: C, 61.19; H, 7.53. Found: C, 61.06; H, 7.50.

3-(*tert*-Butyldimethylsilyloxy)-11-benzyloxymethyl-6,10-dioxatricyclo[6.2.1.0^{4,9}]undeca-3,8(11)-dien-5-one 18b. Purification by silica gel column chromatography (petroleum ether/Et_2O, 1:1) afforded **18b** in 66% yield from 4-benzyloxymethyl-3-furanylmethyl 2-diazo-3-oxobutanoate: R_f 0.48 (petroleum ether/Et_2O, 1:1); IR (neat) 3058, 3022, 2965, 2929, 2856, 2882, 2360, 2334, 1744, 1600, 1346, 1263, 1155 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.28 (m, 5 H), 5.31 (d, 1 H, J = 6.4 Hz), 4.96 (s, 2 H), 4.90 (s, 1 H), 4.48 (d, 1 H, J = 11.7 Hz), 4.44 (d, 1 H, J = 11.7 Hz), 4.14 (d, 1 H, J = 12.7 Hz), 4.07 (d, 1 H, J = 12.7 Hz), 2.78 (dd, 1 H, J = 17.2, 6.4 Hz), 1.98 (d, 1 H, J = 17.2 Hz), 0.92 (s, 9 H), 0.25 (s, 3 H), 0.20 (s,3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 150.6, 141.4, 137.3, 127.9, 127.4, 127.3, 127.0, 114.6, 79.5, 77.0, 71.9, 63.2, 63.0, 33.6, 24.8, 17.5, −4.8, −5.9; MS m/z (relative intensity) 251 (19), 208 (6); HRMS (EI) m/z calcd for $C_{11}H_{11}O_5Si$ 251.0376, found 251.0750.

3-(*tert*-Butyldimethylsilyloxy)-9-methyl-6,10-dioxatricyclo[6.2.1.0^{4,9}]undeca-3,8(11)-dien-5-one 18c. Purification by silica gel column chromatography (petroleum ether/Et_2O, 4:1) afforded **18c** in 29% yield from 2-methyl-3-furanylmethyl 2-diazo-3-oxobutanoate as a white solid: R_f 0.33 (petroleum ether/Et_2O, 4:1); mp 124−126 °C; IR (neat) 2960, 2934, 2828, 2856, 1739, 1594, 1150, 1000 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.35 (s, 1 H), 5.23 (d, 1 H, J = 5.7 Hz), 4.95 (s, 2 H), 2.81 (dd, 1 H, J = 17.2, 5.7 Hz), 1.76 (d, 1 H, J = 17.2 Hz), 1.55 (s, 3 H), 0.91 (s, 9 H), 0.24 (s, 3 H), 0.21(s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8, 149.9, 147.5, 119.2, 118.1, 81.3, 77.3, 64.2, 33.9, 25.2, 18.2, 17.0, −4.5, −5.2. Anal. Calcd for $C_{16}H_{24}O_4Si$: C, 62.30; H, 7.84. Found: C, 62.19; H, 7.63.

3-(*tert*-Butyldimethylsilyloxy)-7-ethyl-6,10-dioxatricyclo[6.2.1.0^{4,9}]undeca-3,8(11)-dien-5-one 18d. Purification by silica gel column chromatography (petroleum ether/Et_2O, 4:1) afforded **18d** in 48% yield from 1-(3-furanyl)propyl 2-diazo-3-oxobutanoate as a 2:1 mixture of separable diastereomers. **18d** (major exo diastereomer): R_f 0.50 (petroleum ether/Et_2O, 4:1); IR (neat) 2961, 2934, 2858, 1737, 1601, 1471, 1346, 1259 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.30 (s, 1 H), 5.27 (d, 1 H, J = 4.6 Hz), 4.96 (t, 1 H, J = 6.1 Hz), 4.93 (s, 1 H), 2.79 (dd, 1 H, J = 17.7, 4.6 Hz), 2.01−1.94 (m, 1 H), 1.83−1.78 (m, 1 H), 1.73 (d, 1 H, J = 17.7 Hz), 1.00 (t, 3 H, J = 7.5 Hz), 0.91 (s, 9 H), 0.24 (s, 3 H), 0.21 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 150.5, 149.7, 116.8, 115.8, 78.9, 78.2, 75.7, 33.5, 27.1, 25.3, 18.0, 8.9, −4.4, −5.2; HRMS (EI) m/z calcd for $C_{17}H_{26}O_4Si$ 322.1600, found 322.1518. **18d** (minor endo diastereomer): R_f 0.40 (petroleum ether/Et_2O, 4:1); IR (neat) 2955, 2928, 2858, 1743, 1607, 1465, 1346, 1259 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.28 (s, 1 H), 5.27 (d, 1 H, J = 6.3 Hz), 5.12 (t, 1 H, J = 5.7 Hz), 4.91 (s, 1 H), 2.79 (dd, 1 H, J = 17.6, 6.3 Hz), 2.00−1.93 (m, 1 H), 1.81−1.72 (m, 1 H), 1.68 (d, 1 H, J = 17.6 Hz), 0.98 (t, 3 H, J = 7.5 Hz), 0.90 (s, 9 H), 0.23 (s, 3 H), 0.19 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 149.8, 149.6, 114.4, 114.2, 78.4, 76.9, 76.5, 33.4, 27.5, 24.8, 17.6, 8.2, −4.7, −5.3; HRMS (EI) m/z calcd for $C_{17}H_{26}O_4Si$ 322.1600, found 322.1598.

3-(*tert*-Butyldimethylsilyloxy)-6,11-dioxatricyclo-[7.2.1.0^{4,10}]dodeca-3,9(12)-dien-5-one 18e. Purification by silica gel column chromatography (petroleum ether/Et_2O, 1:1) afforded **18e** in 26% yield from 2-(3-furanyl)ethyl 2-diazo-3-oxobutanoate: R_f 0.33 (petroleum ether/Et_2O, 1:1); IR (neat) 2955, 2934, 2898, 2867, 1739, 1646, 1263, 1191 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.46 (dd, 1 H, J = 1.5, 1.5 Hz), 5.03 (ddd, 1 H, J = 5.3, 1.5, 1.5 Hz), 4.73 (s, 1 H), 4.38 (ddd, 1 H, J = 12.1, 2.9, 3.9 Hz), 3.85 (ddd, 1 H, J = 12.1, 12.0, 1.8 Hz), 2.77 (ddddd, 1 H, J = 16.8, 3.9, 1.8, 1.5, 1.5 Hz), 2.76 (dd, 1 H, J = 17.3, 5.3 Hz), 2.60 (ddd, 1 H, J = 16.8, 12.0, 2.9 Hz), 1.80 (d, 1 H, J = 17.3 Hz), 0.89 (s, 9 H), 0.21 (s, 3 H), 0.18 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 151.4, 148.6, 117.6, 114.2, 78.2, 77.7, 71.4, 34.2, 29.0, 25.4, 17.9, −4.2, −4.3. Anal. Calcd for $C_{16}H_{24}O_4Si$: C, 62.30; H, 7.84. Found: C, 62.15; H, 7.89.

Typical Procedure for the Preparation of Diazos 21a,b. 3-Diazo-6-hydroxy-6-(3-furanyl)-2,4-hexanedione 21a. 2,4-Pentanedione (3.29 mL, 32.0 mmol, distilled) and DMPU (5.80 mL, 48.0 mmol) were added to a solution of LDA [(diisopropylamine (10.8 mL, 76.8 mmol) and *n*-BuLi (2.56 M in hexanes, 27.5 mL, 70 mmol)] in THF (120 mL) at −78 °C. The reaction mixture was stirred at −78 °C for 30 min, 3-furaldehyde **19a** (2.77 mL, 32.0 mmol, distilled) was then added, and the reaction mixture was allowed to warm to 0 °C over 2 h. Saturated aqueous NH_4Cl and water were added, and the reaction mixture was extracted with Et_2O. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated in vacuo to afford diketo alcohol **20a** (exists as mixture of diketone and enol tautomer, 9.30 g). The material was used in the subsequent reaction without purification: IR (neat) 3416, 3145, 2959, 2873, 1712, 1611, 1500 (cm^{-1}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.35 (s), 7.43−7.38 (m, 2 H), 6.41−6.39 (s, 1 H), 5.53 (s), 5.29−5.24 and 5.15−5.10 (dd, 1 H), 2.97−2.54 (m, 2 H), 2.04 and 2.01 (s, 3 H); MS m/z (relative intensity) 196 (21), 138 (23), 110 (17).

p-Acetamidobenzenesulfonyl azide (*p*-ABSA) (7.68 g, 32.0 mmol) was added to a solution of diketo alcohol **20a** (9.3 g, 32 mmol) in CH_3CN (160 mL) and stirred for 15 min. Triethylamine (9.12 mL, 64.0 mmol) was added, and the reaction mixture was stirred at room temperature for a further 4 h. The reaction mixture was concentrated in vacuo, and the residue was slurried in Et_2O, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (hexanes/EtOAc, 3:1) afforded diazo **21a** (5.14 g, 72% from **19a**): R_f 0.49 (hexanes/EtOAc, 1:2); IR (neat): 3451, 3141, 2981, 2924, 2132, 1656, 1506, 1367 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, 1 H, J = 1.7 Hz), 7.38 (d, 1 H, J = 1.7 Hz), 6.39 (s, 1 H), 5.19 (dt, 1 H, J = 8.8, 8.1 Hz), 3.24 (d, 1 H, J = 8.1 Hz), 3.17 (d, 2 H, J = 8.8 Hz), 2.41 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.4, 188.0, 143.4, 139.0, 127.5, 108.4, 70.3, 47.9, 29.3, 28.3; MS m/z (relative intensity) 194 (37), 176 (1). Anal. Calcd for $C_{10}H_{10}O_4N_2$: C, 54.05; H, 4.54. Found: C, 53.80; H, 4.47.

Methyl 4-(4-Diazo-1-hydroxy-3,5-dioxohexyl)-3-furancarboxylate 21b. Purification by silica gel column chromatography (petroleum ether/Et_2O, 1:1) afforded **21b** in 71% yield from **19b**: R_f 0.70 (Et_2O); IR (neat) 3462, 3146, 3001, 2960, 2929, 2856, 2132, 1729, 1677, 1656, 1553 (cm^{-1}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1 H), 7.44 (s, 1 H), 5.35 (ddd, 1 H, J = 11.7, 7.1, 6.6 Hz), 4.32 (d, 1 H, J = 6.6 Hz), 3.84 (s, 3 H), 3.24−3.14 (m, 2 H), 2.44 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.5, 190.4, 164.8, 149.7, 141.0, 127.3, 116.8, 63.1, 52.0, 47.3, 29.7, 28.7; HRMS (EI) m/z calcd for $C_{12}H_{12}O_6$ ($M^+ - N_2$) 252.0643, found 252.0634.

3,7-Di(triisopropylsilyloxy)-10-oxatricyclo[6.2.1.0^{4,9}]-undeca-3,8(11)-dien-5-one 23 and 5,7-di(triisopropylsilyloxy)-10-oxatricyclo[6.2.1.0^{4,9}]undeca-4,8(11)-dien-3-one 24. Triisopropylsilyl trifluoromethanesulfonate (0.93 mL, 3.5 mmol) was added dropwise over 10 min to a solution of diazo **21a** (350 mg, 1.6 mmol) and triethylamine (0.57 mL, 4.1 mmol) in CH_2Cl_2 (15 mL) at 0 °C. The reaction mixture was stirred for 3 h at 0 °C, diluted with hexanes, washed successively with water and brine, dried (Na_2SO_4), and concentrated in vacuo to afford diazo **22a** (1.0 g). The material was used in the subsequent reaction without purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (s, 2 H), 6.39 (s, 1 H), 5.35 (t, 1 H, J = 6.5 Hz), 5.15 (s, 1 H), 4.35 (d, 1 H, J = 2.1 Hz), 3.02 (dd, 1 H, J = 14.3, 6.8 Hz), 2.71 (dd, 1 H, J = 14.3, 6.8 Hz), 1.20 (m, 6 H), 1.08 (t, 18 H, J = 7.2 Hz), 1.00 (d, 18 H, J = 7.2 Hz).

A solution of diazo **22a** (1.07 g, 2.00 mmol) in hexanes (15 mL) was added dropwise over 30 min to a solution of rhodium(II) octanoate (16 mg, 20 μmol) in hexanes (20 mL). The reaction mixture was stirred at room temperature for 1 h and then concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 9:1) afforded two regioisomeric oxatricycles **23** (397 mg, 39% from **21a**, 3:1 inseparable mixture of diastereomers) and **24** (320 mg, 32% from **21a**, 3:1 inseparable mixture of diastereomers). A trace amount of aldehyde **25** was also formed according to the ^{1}H NMR spectrum of the crude reaction mixture. The ratio of **23**:**24**:**25** in the crude reaction mixture was found to be 61:37:2 according to the ^{1}H NMR spectrum.

23: R_f 0.23 (petroleum ether/Et_2O, 9:1); IR (neat) 2943, 2892, 2866, 1719, 1693, 1567 (cm^{-1}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.30 (s, 1 H), 5.21 (s, 1 H), 5.18 (d, 1 H, J = 6.2 Hz), 4.92 (t, 1 H, J = 6.2 Hz), 2.89−2.50 (m, 3 H), 1.69 (d, 1 H, J = 17.2 Hz), 1.27−1.16 (m, 6 H), 1.11−0.99 (m, 36 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.7, 154.2, 146.1, 126.2, 115.6, 78.1, 46.8, 62.8, 53.8, 33.4, 17.8, 17.7, 12.8, 11.9; HRMS (EI) m/z calcd for $C_{28}H_{50}O_4Si_2$ 506.3248, found 506.3250.

24: R_f 0.15 (petroleum ether/Et_2O, 9:1); IR (neat) 2945, 2887, 2865, 1688, 1560, 1465, 1390, 1353, 879, 676 (cm^{-1}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.42 (s, 1 H), 5.17 (d, 2 H, J = 6.2 Hz), 4.88 (s, 1 H), 2.95 (dd, 1 H, J = 16.7, 6.2 Hz), 2.80 (dd, 1 H, J = 17.4, 6.2 Hz), 2.51 (d, 1 H, J = 16.7 Hz), 1.77. ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.8, 156.9, 148.5, 130.8, 114.9, 78.5, 77.8, 65.1, 34.7, 22.6, 17.9, 17.7, 12.4, 12.2; HRMS (EI) m/z calcd for $C_{28}H_{50}O_4Si_2$ 506.3248, found 506.3217.

[6-(Triisopropylsilyloxy)-3-(1-(triisopropylsilyloxy)vinyl)-4-oxocyclohex-2-enylidene]acetaldehyde 25. A solution of diazo **22a** (1.0 g, 1.6 mmol) in CH_2Cl_2 (30 mL) was added dropwise over 1 h to a solution of rhodium(II) octanoate (13 mg, 17 μmol) in CH_2Cl_2 (15 mL) at room temperature. The reaction mixture was stirred at room temperature for a further 30 min and then concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 19:1) afforded **23** (355 mg, 44% from **21a**, 3:1 inseparable mixture of diastereomers), **24** (200 mg, 25% from **21a**, 3:1 inseparable mixture of diastereomers), and **25** (65 mg, 8% from **21a**). The ratio of **23**:**24**:**25** in the crude reaction mixture was found to be 73:17:10 according to the ^{1}H NMR spectrum.

25: R_f 0.35 (petroleum ether/Et_2O, 9:1); IR (neat) 2946, 2866, 2722, 1726, 1678, 1598, 1550, 1460, 885 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.28 (d, 1 H, J = 7.7 Hz), 8.44 (s, 1 H), 6.42 (d, 1 H, J = 7.7 Hz), 5.66 (s, 1 H), 4.83 (dd, 1 H, J = 10.6, 5.0 Hz), 4.80 (s, 1 H), 2.99 (dd, 1 H, J = 15.2, 5.0 Hz), 2.82 (dd, 1 H, J = 15.2, 10.6 Hz), 1.31−1.23 (m, 6 H), 1.12−0.98 (m, 36 H). ^{13}C NMR (75 MHz, $CDCl_3$) 216.6, 189.6, 149.0, 134.5, 132.5, 130.9, 128.8, 101.2, 68.1, 30.3, 17.9, 17.8, 12.9, 12.7; HRMS (EI) m/z calcd for $C_{28}H_{50}O_4Si_2$ 506.3248, found 506.3285.

3,7-Di(triisopropylsilyloxy)-10-oxatricyclo[6.2.1.0^{4,9}]-undeca2,8(11)-dien-5-one 26. Upon standing, **23** rearranged to **26**, which was purified by silica gel column chromatography (petroleum ether/Et_2O, 4:1): R_f 0.54 (petroleum ether/Et_2O, 9:1); IR (neat) 2955, 2893, 2867, 1734, 1631, 1470 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.22 (s, 1 H), 5.35 (d, 1 H, J = 5.6 Hz), 5.29 (d, 1 H, J = 4.8 Hz), 5.06 (t, 1 H, J = 3.5 Hz), 5.01 (d, 1 H, J = 4.8 Hz), 3.49 (d, 1 H, J = 5.6 Hz), 2.77 (dd, 1 H, J = 13.9, 3.5 Hz), 2.55 (d, 1 H, J = 13.9 Hz), 1.18−1.05 (m, 6 H), 1.03−1.01 (m, 36 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.7 (s), 147.8 (s), 139.4 (s), 131.3 (d), 105.5 (d), 78.8 (d), 77.8 (d), 67.4 (d), 58.4 (d), 52.2 (t), 17.9 (q), 17.8 (q), 12.5 (d), 11.9 (d); MS m/z (relative intensity) 506 (1), 463 (40), 435 (19), 349 (2); HRMS (EI) m/z calcd for $C_{28}H_{50}O_4Si_2$ (−C_3H_7, loss of isopropyl group) 463.2700, found 463.2699.

4-Bromo-3,7-di(triisopropylsilyloxy)-10-oxatricyclo-[6.2.1.0^{4,9}]undeca-2,8(11)-dien-5-one 27. *N*-Bromosuccinimide (1.8 g, 9.9 mmol) was added to a solution of oxatricycle **23** (5.0 g, 9.9 mmol) in THF (150 mL) in a flask covered with aluminum foil. The reaction mixture was stirred at 0 °C for 2 h, diluted with Et_2O, washed successively with saturated aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 19:1) afforded bromoketone **27** (2.4 g, 41%): R_f 0.47 (petroleum ether/Et_2O, 4:1); mp 108−110 °C (MeOH); IR (neat) 2950, 2893, 2867, 1744, 1625, 1470 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.41 (s, 1 H), 5.40 (s, 1 H), 5.29 (d, 1 H, J = 4.4 Hz), 5.11−5.10 (m, 2 H), 2.84 (dd, 1 H, J = 13.9, 2.6 Hz), 2.67 (dd, 1 H, J = 13.9, 3.3 Hz), 1.20−1.00 (m, 42 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.3 (s), 147.5 (s), 138.3 (s), 134.2 (d), 105.9 (d), 87.3 (d), 78.2 (d), 72.3 (s), 67.0 (d), 50.1 (t), 17.9 (q), 17.8 (q), 12.6 (d), 11.8 (d); HRMS (EI) m/z calcd for $C_{25}H_{42}O_4Si_2Br$ (−C_3H_7, loss of an isopropyl group) 541.1833, found 541.1805.

4-Bromo-3,7-di(triisopropylsilyloxy)-10-oxatricyclo-[6.2.1.0^{4,9}]undeca-2,8(11)-dien-5-ol 28. Sodium borohydride (93 mg, 2.5 mmol) was added to a solution of bromoketone **27** (481 mg, 0.822 mmol) in methanol (1.5 mL) and THF (4.5 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature overnight, quenched with water, and extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 19:1) afforded alcohol **28** (426 mg, 88%): R_f 0.51 (petroleum ether/Et_2O, 1:1); IR (neat) 3542, 2950, 2871, 1630, 1475 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.19 (s, 1 H), 5.30 (d, 1 H, J = 4.6 Hz), 5.28 (s, 1 H), 4.95 (d, 1 H, J = 4.6 Hz), 4.87 (t, 1 H, J = 2.6 Hz), 4.30 (ddd, 1 H, J = 8.2, 4.0, 4.0 Hz), 3.51 (d, 1 H, J = 8.2 Hz), 2.36 (ddd, 1 H, J = 13.0, 4.0, 4.0 Hz), 1.54 (dd, 1 H, J = 13.0, 2.6 Hz), 1.27−1.18 (m, 3 H), 1.17−1.07 (m, 18 H), 1.07−1.02 (m, 18 H), 0.89−0.83 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.8, 139.4, 12.8, 108.9, 85.9, 77.6, 72.2, 66.9, 66.3, 43.9, 18.0, 17.9, 12.7, 11.9; HRMS (EI) m/z calcd for $C_{25}H_{44}O_4Si_2Br$ (−C_3H_7, loss of an isopropyl group) 543.1962, found 543.1901.

4-Bromo-5-hydroxy-7-(triisopropylsilyloxy)-10-oxatricyclo[6.2.1.0^{4,9}]undec-8(11)-en-3-one 29. TBAF (0.24 mL, 0.24 mmol, 1 M in THF) was added to a solution of alcohol **28** (140 mg, 0.24 mmol) in THF (10 mL) at −78 °C. The reaction mixture was stirred at −78 °C for 15 min and then poured into ice−water and extracted with CH_2Cl_2. The organic phase was dried (Na_2SO_4) and concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 3:1) afforded bromoketone **29** (100 mg, 95%): R_f 0.34 (petroleum ether/Et_2O, 1:1); IR (neat) 2956, 2897, 2871, 1710, 1470 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (s, 1 H), 5.12 (d, 1 H, J = 4.2 Hz), 5.03 (s, 1 H), 4.87 (s, 1 H), 4.18 (m, 1 H), 3.74 (d, 1 H, J = 11.3 Hz), 3.14 (dd, 1 H, J = 16.3, 4.2 Hz), 2.46 (dd, 1 H, J = 13.9, 3.1 Hz), 2.19 (d, 1 H, J = 16.3 Hz), 2.84 (dt, 1 H, J = 13.9, 3.1 Hz), 1.13−0.84 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.9, 146.5, 123.7, 83.2, 79.0, 71.9, 65.6, 45.5, 42.4, 29.6, 17.8, 11.8; HRMS (EI) m/z calcd for $C_{16}H_{24}O_4SiBr$ (−C_3H_7, loss of an isopropyl group) 387.0627, found 387.0662.

Methyl3,7-Di(triisopropylsilyloxy)-5-oxo-10-oxatricyclo-[6.2.1.0^{4,9}]undeca-3,8(11)-diene-11-carboxylate 30. Triethylamine (0.36 mL, 0.26 mmol) and then triisopropylsilyl trifluoromethanesulfonate (0.59 mL, 0.22 mmol) were added to a solution of diazo **21b** (55 mg, 0.21 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, and then additional triethylamine (0.36 mL, 0.26 mmol) and triisopropylsilyl trifluoromethanesulfonate (0.59 mL, 0.22 mmol) were added and the mixture stirred at 0 °C for a further 1 h. The reaction mixture was then diluted with hexanes and poured into saturated aqueous $NaHCO_3$ and hexanes. The

organic phase was washed with brine, dried (Na_2SO_4), and concentrated in vacuo to afford diazo **22b** (128 mg). The material was used in the subsequent reaction without purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1 H), 7.45 (s, 1 H), 5.72 (dd, 1 H, J = 7.5, 3.9 Hz), 5.18 (s, 1 H), 4.33 (d, 1 H, J = 2.2 Hz), 3.81 (s, 3 H), 3.00 (dd, 1 H, J = 13.9, 7.5 Hz), 2.86 (dd, 1 H, J = 13.9, 3.9 Hz), 1.26−1.18 (m, 6 H), 1.07−0.97 (m, 36 H).

A solution of diazo **22b** (1.95 g, 3.29 mmol) in hexanes (60 mL) was added dropwise over 30 min to a solution of rhodium(II) octanoate (26 mg, 33 μmol) in CH_2Cl_2 (100 mL). The reaction mixture was stirred for a further 10 min and then concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 19:1) afforded oxatricycle **30** (1.27 g, 68%) as a 4:1 inseparable mixture of diastereomers. **30**: R_f 0.68 (petroleum ether/Et_2O, 4:1); IR (neat): 2943, 2868, 1720, 1571, 1462 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.51 (dd, 1 H, J = 5.7, 4.1 Hz), 5.45 (d, 1 H, J = 5.7 Hz), 5.35 (s, 1 H), 3.75 (s, 3 H), 2.85−2.78 (m, 3 H), 1.97 (d, 1 H, J = 17.4 Hz), 1.24−1.09 (m, 6 H), 1.06−1.03 (m, 36 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.7 (s), 164.4 (s), 163.4 (s), 146.8 (s), 124.0 (s), 118.0 (s), 79.0 (d), 78.5 (d), 62.4 (d), 54.6 (t), 51.3 (q), 33.0 (t), 17.8 (q), 17.6 (q), 12.7 (d), 11.9 (d); HRMS (EI) m/z calcd for $C_{30}H_{52}O_6Si_2$ 564.3348, found 564.3302.

Methyl 4-Bromo-3,7-di(triisopropylsilyloxy)-5-oxo-10-oxatricyclo[6.2.1.0^{4,9}]undeca-2,8(11)-diene-11-carboxylate 31. *N*-Bromosuccinimide (47.6 mg, 0.277 mmol) was added to a solution of oxatricycle **30** (151 mg, 0.267 mmol) in THF (6 mL) at 0 °C, in a flask covered with aluminum foil. The reaction mixture was stirred at 0 °C for 2 h, diluted with Et_2O, and washed successively with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. Purification by silica gel column chromatography (petroleum ether/Et_2O, 19:1) afforded bromoketone **31** (127 mg, 74%): R_f 0.29 (petroleum ether/Et_2O, 19:1); IR (neat) 2956, 2897, 2876, 1726, 1630 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67 (dd, 1 H, J = 3.3, 2.9 Hz), 5.54 (s, 1 H), 5.44 (*d*, 1 H, J = 4.8 Hz), 5.23 (d, 1 H, J = *4*.8 Hz), 3.75 (s, 3 ^{H}), 2.82 (d_d, 1 H, J = 14.3, 3.3 Hz), 2.59 (dd, 1 H, J = 14.3, 2.9 Hz), 1.14−0.94 (m, 42 H); ^{13}C NMR (125 MHz, CDCl3) δ 193.3, 162.6, 149.5, 147.2, 138.1, 105.8, 88.8, 78.6, 70.8, 65.9, 51.9, 49.0, 17.7, 17.6, 12.5, 11.8; HRMS (EI) m/z calcd for $C_{27}H_{44}O_6Si_2Br$ ($-C_3H_7$, loss of an isopropyl group) 599.1860, found 599.1889.

Methyl 4-Bromo-5-hydroxy-3,7-(triisopropylsilyloxy)-10-oxatricyclo[6.2.1.0^{4,9}]undeca-2,8(11)-diene-11-carboxylate 32. A solution of lithium aluminum hydride (823 μL, 0.823 mmol, 1 M in THF) was added dropwise over 5 min to a solution of bromoketone **31** (530 mg, 0.823 mmol) in THF (15 mL) at −78 °C. The reaction mixture was stirred at −78 °C for 1 h, acetone (1.0 mL) was added, and stirring was continued for a further 10 min. The reaction mixture was poured into saturated aqueous NH_4Cl solution and extracted with Et_2O. The organic phase was washed successively with water and brine, dried (Na_2SO_4), and concentrated in vacuo. Purification by silica gel chromatography (pentane/Et_2O, 20:1) afforded alcohol **32** (437 mg, 82%): R_f 0.36 (pentane/Et_2O, 20:1); IR (neat) 3542, 2951, 2871, 1737, 1657, 1625, 1476, 1438, 1337, 1247, 1225 (cm^{-1}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.45 (s, 1H), 5.44 (d, 1H, J = 4.8 Hz), 5.38 (s, 1H), 5.06 (d, 1H, J = 4.8 Hz), 4.29 (ddd, 1H, J = 12.1, 8.8, 4.4 Hz), 3.71 (s, 3H), 3.46 (d, 1H, J = 8.8 Hz), 2.32 (dt, 1H, J = 13.6, 4.1 Hz), 1.46 (dt, 1H, J = 12.8, 2.2 Hz), 0.84−1.26 (br m, 42H); ^{13}C NMR (75 MHz, $CDCl_3$) 162.7, 150.7, 148.5, 137.0, 108.8, 87.5, 78.0, 71.8, 65.3, 65.0, 51.6, 42.8, 17.8, 17.7, 12.5, 11.7. Anal. Calcd for $C_{30}H_{53}O_6Si_2Br$: C, 55.79; H, 8.27. Found: C, 55.93; H, 8.25.

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Supporting Information Available: Experimental data for **2**, **5**, **10**, **15**, **19**, and precursors to **17**, ^{1}H NMR spectral data for **2**, **3**, **5**, **10**, **13**−**16**, **18b**, **18d** (endo), **18d** (exo), **21b**, and **23**−**31**, and X-ray crystallographic data for **27**. This material is available free of charge via the Internet at http://pubs.acs.org.

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