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Rh(I)-Catalyzed 1,4-Conjugate Addition of Alkenylboronic Acids to a Cyclopentenone Useful for the Synthesis of Prostaglandins

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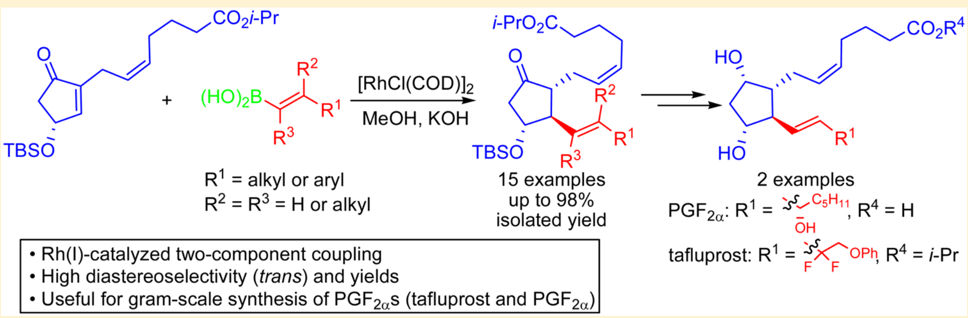
Supporting Information



ABSTRACT: An efficient and *trans*-diastereoselective Rh(I)-catalyzed 1,4-conjugate addition reaction of alkenylboronic acids and a homochiral (*R*)-4-silyloxycyclopentenone useful for the synthesis of derivatives of prostaglandins E and F is described for the first time. The reaction functions under mild conditions and is particularly rapid (≤6 h) under low power (50 W) microwave irradiation at 30 °C in MeOH in the presence of a catalytic amount of KOH. Under these conditions, 3 mol % of $[RhCl(COD)]_2$ is typically required to produce high yields. The method also functions without microwave irradiation at 3 °C in the presence of a stoichiometric amount of KOH. Under these conditions, only 1.5 mol % of $[RhCl(COD)]_2$ is needed, but the reaction is considerably slower. The method accepts a range of aryl- and alkyl-substituted alkenylboronic acids, and its utility has been demonstrated by the synthesis of $PGF_{2\alpha}$ (dinoprost) and tafluprost.

INTRODUCTION

Discovered by von Euler in the 1930s, prostaglandins[1] (PGs) are naturally occurring, monocyclic C_{20}-polyunsaturated fatty acids that regulate a host of physiological functions in animals and are employed in the clinic for the treatment of human ailments including peptic ulcers, erectile dysfunction, and pain, and to induce childbirth (e.g., **1a**) and abortion.[2] Additionally, the synthetic $PGF_{2\alpha}$ derivatives tafluprost (**1b**),[3a] travoprost (**1c**),[3b] bimatoprost (**1d**),[3c] and latanoprost (**1e**)[3d] are used for the treatment of ocular hypertension and glaucoma (Figure 1). Bimatoprost is also marketed as the beauty product Latisse. The 16,16-difluoro-PGE_1 derivative, lubiprostone (**1f**),[3e] is used orally for the treatment of constipation.

Given their therapeutic efficacy, the development of efficient and practical methods for the synthesis and manufacture of prostaglandins and their analogues has attracted great interest both in academia and in industry since the 1970s (Scheme 1).[2,4] Amidst the many synthetic approaches reported,[2,4b,5] the industrially useful Corey lactone route[6] and Sih's two-component 1,4-conjugate addition method,[7] and the elegant but less practical three-component method[8] epitomized by Noyori in the 1980s,[9] embody the more commonly used strategies.

Previously, we disclosed the use[10a,b] of the homochiral (*R*)-4-silyloxycyclopentenone isopropyl ester **2**[10c] as a pivotal starting material for the manufacture of pharmacologically useful PGE_1 and $PGF_{2\alpha}$ derivatives. Using the aforementioned two-component method, **2** was reacted with higher-order alkenyl(cyano)cuprates **3**[11] at or below −50 °C (Scheme 2). Although viable on manufacturing scales for the production of clinical-grade **1c**,[10a] **1d**,[10a] and **1f**,[10b] coupling of the electron-deficient *γ,γ-difluoro*alkenylcuprate **4** with **2**, requisite for the synthesis of tafluprost (**1b**), was unsuccessful; a more lengthy approach was required.[12a] Given this, the need for cryogenic temperatures, and wanting to avoid the use of vinyltin[11] compounds as precursors to **3**, we sought to develop an improved variant of the conventional two-component method.

Although the Hayashi−Miyaura reaction,[13] the Rh(I)-catalyzed 1,4-addition of aryl- and alkenylboron compounds to activated alkenes, has been applied to the conjugate addition

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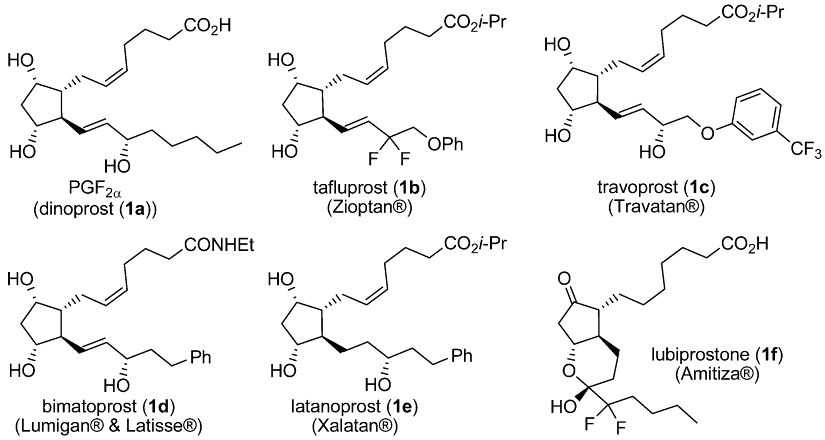
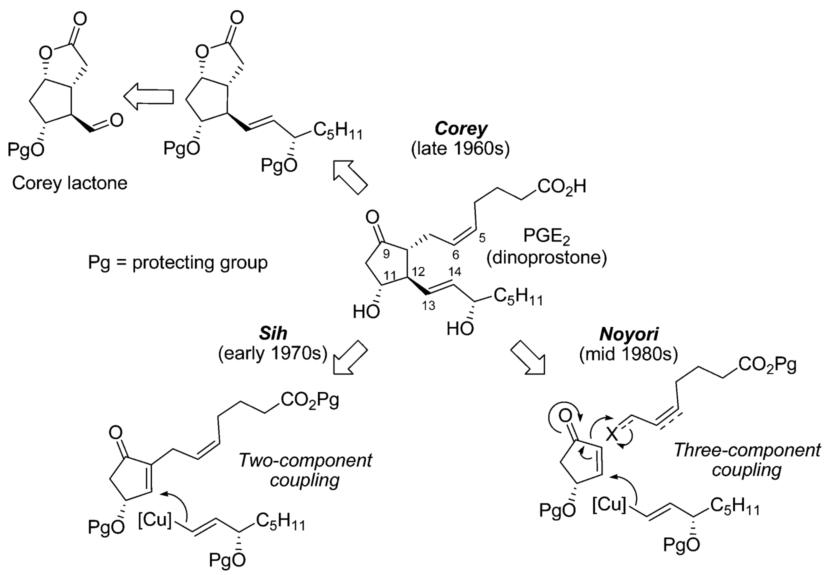
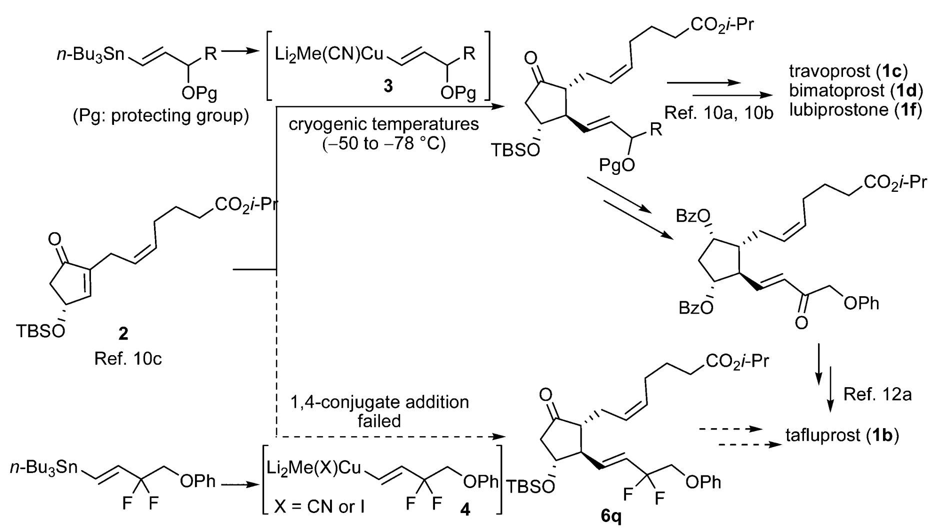


Figure 1. Clinically useful prostaglandins.

Scheme 1. Synthetic Strategies for Prostaglandins (Illustrated for Dinoprostone)



Scheme 2. Synthesis of Prostaglandin Derivatives 1b, 1c, 1d, and 1f Using Alkenyl(cyano)cuprates in the Two-Component Method[10,12a]



of alkenyl nucleophiles to cyclopentenone substrates, neither components possessed the structural complexity required to prepare prostaglandins.[14] Csákÿ et al.[14c] reported the Rh(I)-catalyzed 1,4-addition reaction of arylboronic acids and 2-aryl-

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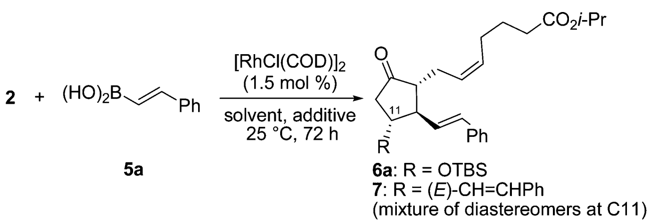
alkenylboronic acids to (*S*)-2-phenyl-4-hydroxycyclopent-2-enone, featuring an unprotected hydroxyl group. While the use of arylboronic acids provided 3,4-*trans*-substituted products, 2-aryl-alkenylboronic acids selectively gave 3,4-*cis*-substituted products, or mixtures (0.7:1−1.5:1) of the *cis*- and *trans*-substituted products, unless 3 equiv of CsF was used as an additive using aqueous dioxane as a solvent. Having experience with variants of the Hayashi−Miyaura reaction,[15] we predicted that its application to prostaglandin synthesis, if feasible,[15c] would allow for milder reaction conditions, circumvention of cryogenic temperatures, and the trading of the moisture- and air-sensitive alkenylcuprates **3** of the conventional approach for readily accessible,[16] stable, and isolable alkenylboronic acids and their derivatives. Crucially, however, to fit with the established manufacturing processes,[10a,b] it was imperative that cyclopentenone **2** could be used, that 3,4-*trans*-substituted products would be exclusively obtained, and that the reaction conditions were amenable to the use of silyl protecting groups and alkenylboronic acids substituted with alkyl substituents, including those possessing stereogenic centers, suitable for the preparation of prostaglandins such as **1a**−**1f**.

■ RESULTS AND DISCUSSION

Preliminary Results. Model studies began with the 1,4-addition of styrylboronic acid (**5a**) to enone **2** using $[RhCl(COD)]_2$ as precatalyst (Table 1). While dioxane is

Table 1. Screening of Solvents and Additives[a]



entry	solvent	additive	yield **6a** (%)[b]	yield **7** (%)[b]
1	MeOH	Et_3N	18	10
2	MeOH	piperidine	28	0
3	MeOH	*t*-$BuNH_2$	50	0
4	MeOH	KHF_2	75	0
5	EtOH	KHF_2	73	20
6	*i*-PrOH	KHF_2	74	9
7	MeOH	KOH	80	4
8	EtOH	KOH	75	9
9	*i*-PrOH	KOH	70	3
10	MeOH	K_3PO_4	60	0

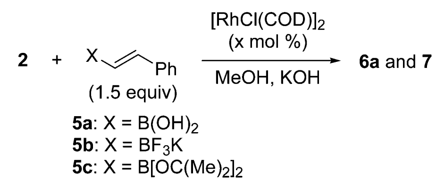
[a]Solutions of **2** (0.15 mmol), **5a** (0.225 mmol, 1.5 equiv), $[RhCl(COD)]_2$ (1.5 mol %), and amines (0.9 mmol), or aq KHF_2 (3.0 M, 0.3 mL, 0.9 mmol), aq KOH (3.1 M, 9.5 μL, 30 μmol), or aq K_3PO_4 (1.5 M, 0.6 mL, 0.9 mmol) in MeOH, or EtOH or *i*-PrOH (0.8 mL), were stirred at 25 °C for 72 h. [b]Determined by ^1H NMR analysis using 3,4,5-$(MeO)_3C_6H_2CHO$ as external standard.

commonly used in Rh(I)-catalyzed reactions,[13,14c] its toxicity[17] rendered it unattractive, and studies were therefore focused on manufacturing-applicable alcohol solvents instead. Despite prior success using the mild combination of Et_3N in MeOH for 1,2- and 1,4-additions in the presence of Rh(I) catalysts,[15a] Et_3N, piperidine, or *t*-$BuNH_2$ in MeOH promoted only low to moderate conversion of **2** to PGE_2 derivative **6a** (entries 1−3). KHF_2 in MeOH, EtOH, or *i*-PrOH (entries 4−6), on the other hand, provided considerably improved yields (73−75%), while reactions in these same solvents (entries 7−9) in the presence of KOH proved best in MeOH (80%; entry 7). K_3PO_4 in MeOH (entry 10) was inferior to KOH (entry 7) and KHF_2 (entry 4) in the same solvent.

Consistent with organocuprate additions to enone **2**,[10] the Rh(I)-catalyzed addition of **5a** occurred to the sterically more accessible *Re*-face of the C8−C12 olefin of **2** at C12, yielding **6a** as a single diastereomer.[18] Additionally, the double-addition product **7**, isolated as a ca. 8:2 mixture of **7** and 11-*epi*-**7**, was formed, presumably via elimination of the silyl ether of **6a** and subsequent Rh(I)-catalyzed addition of **5a** to the resulting α,β-unsaturated ketone. Consistent with this, subjecting **6a** to the conditions in Table 1, entry 7 at 60 °C in the presence of **5a** resulted in its conversion to **7**. This side-product initially proved persistent and troublesome, particularly at higher temperatures such as ≥60 °C and/or in the presence of a large excess of the boronic acid. In fact, in some tests, **7** dominated the product mixtures.

While using the conditions identified in Table 1, entry 7, at 50 °C (Table 2, entry 1) shortened the reaction time, more **7**

Table 2. Reaction Optimization[a]



entry	*x*	**5**	*T* (°C)	time (h)	yield **6a** (%)[b]	yield **7** (%)[b]
1[c]	1.5	**5a**	50	8	60	29
2[d]	1.5	**5a**	50	3	65	9
3[d]	1.5	**5a**	40	6	73	3
4[d]	1.5	**5a**	30	5	84	0
5[d,e]	1.5	**5a**	30	6	29	0
6[d]	3.0	**5a**	30	5	84	0
7[d,f]	1.5 + 1.5	**5a**	30	6	96[g]	0
8[d,f]	1.5 + 1.5	**5b**	30	5	48	0
9[d,f]	1.5 + 1.5	**5c**	30	5	58	0

[a]Solutions of **2** (0.15 mmol), **5a** (0.225 mmol, 1.5 equiv), $[RhCl(COD)]_2$ (1.5 mol %), and aq KOH (3.1 M, 9.5 μL, 30 μmol) in MeOH (0.8 mL) were stirred at *T* °C. [b]NMR yield using 3,4,5-$(MeO)_3C_6H_2CHO$ as external standard. [c]Conventional heating. [d]Microwave irradiation. [e]$[RhOH(COD)]_2$ was used. [f]Additional portions of $[RhCl(COD)]_2$ (1.5 mol %) and **5a** (0.5 equiv) were added after 5 h; **5b** or **5c** (0.5 equiv) was added after 3 h. [g]Isolated yield.

(29%) was produced at the expense of **6a** (60%). To our surprise, however, while conducting the reaction at 50 °C under microwave irradiation[19] further improved the reaction rate (65% yield of **6a** in 3 h), the amount of **7** (9%), rather than increasing, was significantly reduced (entry 2). Further improvements occurred under microwave irradiation when the reaction was conducted at 40 °C (73% **6a**) or 30 °C (84% **6a**), and little or no **7** was detected (entries 3 and 4). While a low yield was observed when directly employing the preactivated[20] RhOH catalyst (entry 5) and doubling the amount of $[RhCl(COD)]_2$ to 3 mol % (entry 6) garnered no improvement, adding the catalyst in two 1.5 mol %-portions along with additional **6a** after 5 h offered **6a** in an excellent 96% isolated yield (entry 7). Notably, no **7** was detected. While it was expected that the addition of extra boronic acid **5a** would

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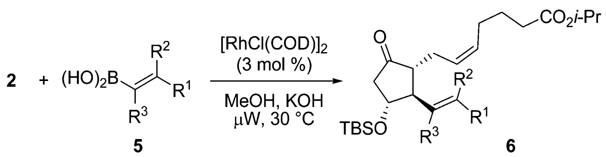
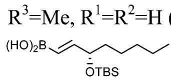
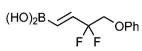
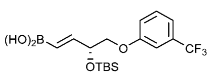
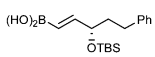
effect further conversion of **2** to **6a**, it was unexpected that an additional portion of the Rh(I) catalyst would also be beneficial. This implies that the Rh(I) catalyst was poisoned. The use of the corresponding trifluoroborate **5b** or boronic ester **5c** in place of boronic acid **5a** furnished **6a** in a 48% or 58% yield, respectively (entries 8 and 9).

Reaction Scope under Microwave. Using the same double-portion addition protocol of catalyst and boronic acid, 1,4-addition of 2-aryl-vinylboronic acids bearing electron-releasing (**5d** and **5e**) and alkyl substituents (**5f**−**5h**) to **2** led to PGE_2 derivatives **6d**−**6h** in 88−98% isolated yields (Table 3, entries 1−5). Despite their electron deficiency, both fluorine-containing boronic acids **5i** and **5j** were sufficiently reactive, giving rise to **6i** and **6j** in 80% and 92% yield (entries 6 and 7), respectively. Although nonbranching alkenylboronic acid **5k** provided **6k** in 93% yield (entry 8), less satisfactory yields were observed (38−76%) when using α-branched alkenylboronic acids **5l**, **5m**, and **5o** (entries 9, 10, and 12). Conversely, the less hindered β,β-dialkyl-substituted alkenylboronic acid **5n** afforded **6n** in 99% yield (entry 11).

Table 3. Reaction Scope under Microwave Irradiation[a]



entry	5	time (h)	yield **6** (%)[b]
1	R^1=4-MeO-Ph, R^2=R^3=H (**5d**)	6	93 (**6d**)
2[c]	R^1=3-MeO-Ph, R^2=R^3=H (**5e**)	5	93 (**6e**)
3	R^1=4-Me-Ph, R^2=R^3=H (**5f**)	6	95 (**6f**)
4	R^1=3-Me-Ph, R^2=R^3=H (**5g**)	6	98 (**6g**)
5[c]	R^1=2-Me-Ph, R^2=R^3=H (**5h**)	5	88 (**6h**)
6[c]	R^1=4-CF_3-Ph, R^2=R^3=H (**5i**)	5	80 (**6i**)
7[c]	R^1=4-F-Ph, R^2=R^3=H (**5j**)	5	92 (**6j**)
8	R^1=C_6H_{13}, R^2=R^3=H (**5k**)	6	93 (**6k**)
9[c]	R^1-R^3=$(CH_2)_4$, R^2=H (**5l**)	5	38 (**6l**)
10[c]	R^1=R^3=Me, R^2=H (**5m**)	5	37 (**6m**)
11	R^1=R^2=Me, R^3=H (**5n**)	6	99 (**6n**)
12[c]	R^3=Me, R^1=R^2=H (**5o**)	5	76 (**6o**)
13[d,e]	 (**5p**)	5	98 (**6p**)[f]
14[e,g]	 (**5q**)	6	67 (**6q**)[h]
15[c]	 (**5r**)	5	65 (**6r**)
16[c]	 (**5s**)	6	64 (**6s**)

[a]Solutions of **2** (0.15 mmol), **5** (0.225 mmol, 1.5 equiv), $[RhCl(COD)]_2$ (1.5 mol %), and aq KOH (3.1 M, 9.5 μL, 30 μmol) in MeOH (0.8 mL) were stirred under microwave irradiation at 30 °C. Additional portions of $[RhCl(COD)]_2$ (1.5 mol %) and **5** (0.5 equiv) were added after 5 h, and the reaction was irradiated for a further 1 h. [b]Chromatographically isolated yield. [c]Additional portions of $[RhCl(COD)]_2$ (1.5 mol %) and **5** (0.5 equiv) were added after 3 h instead of after 5 h, and the reaction was irradiated for a further 2 h. [d]On a 0.79 mmol scale of **2**. [e]Additional portions of $[RhCl(COD)]_2$ (1.5 mol %) and **5p** or **5q** (1.5 equiv) were added after 3 h. [f]82% isolated yield (2.65 g) on a 5.2 mmol scale of **2**. [g]Conducted at 50 °C. [h]The potassium trifluoroborate derivative of **5q** gave a 62% isolated yield of **6q** (after 13 h).

Demonstrating the Utility of the Reaction. We next explored the synthetic usefulness of the method by the syntheses of several of the pharmacologically active compounds listed in Figure 1. To this end, boronic acids **5p**, **5r**, and **5s** were synthesized from the corresponding optically active propargylic alcohols.[21] PGE_2 derivative **6p**, prepared by the reaction of **5p** with **2**, was isolated in 98% yield (entry 13), and in an unoptimized 82% yield (2.65 g) on a 5.2 mmol scale. Reduction of **6p** with L-Selectride gave protected PGF_2 **8p** in 76% yield as a single diastereomer, following chromatography (Scheme 3). Hydrolysis with NaOMe in MeOH provided carboxylic acid **9p** in 90% yield that was then desilylated in 3 *N* aq HCl in THF offering naturally occurring $PGF_{2\alpha}$, dinoprost (**1a**), in 89% yield (0.6 g).

More gratifyingly, coupling of difluoro-substituted boronic acid **5q**[21] and **2** garnered tafluprost precursor **6q** in 67% yield (entry 14), despite the conventional 1,4-addition of cuprate **4** with **2** failing to produce **6q** (Scheme 1). Reduction of **6q** with L-Selectride in THF followed by fluoride-mediated removal of the silyl ether provided tafluprost[12b] (**1b**; Scheme 4) in high yield (1.52 g, 90%). To the best of our knowledge, this is the first report of the two-component coupling approach being used for the synthesis of **1b**. Additionally, the formal syntheses of travoprost (**1c**) and bimatoprost (**1d**) were accomplished by the reaction of boronic acids **5r** or **5s** with **2** under the standard conditions giving PGE_2 derivatives **6r** or **6s** in 65% or 64% yield, respectively (entries 15 and 16). The NMR spectra of these compounds were identical to the same products previously prepared using the conventional cuprate approach.[10a]

Speculating that the presence of the *cis*-double bond in the α-side chain of cyclopentenone **2** or the PGE_2 products **6** might be responsible for the putative poisoning of the catalyst suggested above, the saturated analogue **10** of cyclopentenone **2** was synthesized for comparative purposes.[22] To our surprise, reaction of cyclopentenone **10** with styrylboronic acid (**5a**) under the conditions identified in Table 2, entry 4, furnished PGE_1 derivative **11** in only 35% (Table 4, entry 1), considerably lower than the expected >80% yield. In a competition experiment between cyclopentenones **2** and **10**, addition product **6a** was produced in 80% yield, whereas **11** was obtained in 38% yield (entry 2). Thus, contrary to that anticipated, these tests suggest that the distal double bond present in the α-side chain of **2** actually enhances the rate of the conjugate addition to the cyclopentenone, perhaps by intramolecular coordination of the Rh(I)-metal center to the two double bonds.

Reaction in the Absence of Microwave Irradiation. Despite improvements to the conventional two-component method having been realized, it was concluded that the need for microwave irradiation and the addition of extra catalyst and boronic acid was limiting, particularly if the method was to be used on manufacturing scales. With this in mind, the nonmicrowave irradiated version of the reaction was reinvestigated (Table 5). While a respectable 80% yield of **6a** had been achieved (Table 1, entry 7) in the absence of microwave irradiation at 25 °C, higher temperatures resulted in higher yields of double-addition product **7** at the expense of **6a**. It therefore followed that lowering the reaction temperature might improve the yield of **6a** further. Although **7** was no longer detected (Table 5, entry 1), conducting the conjugate

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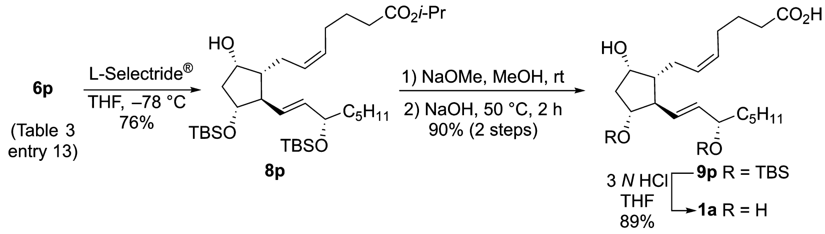
Scheme 3. Synthesis of $PGF_{2\alpha}$ (Dinoprost (1a))



Scheme 4. Synthesis of Tafluprost (1b)

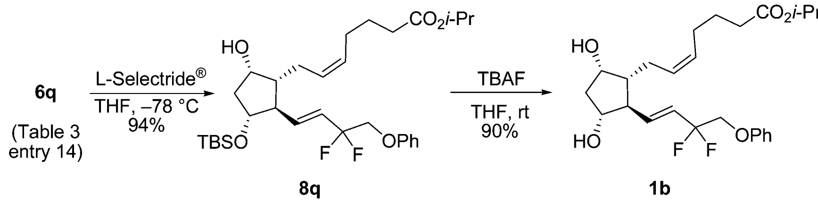
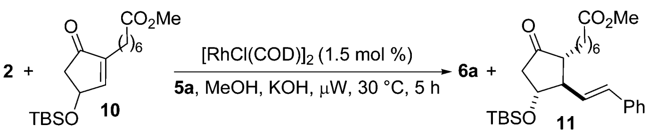


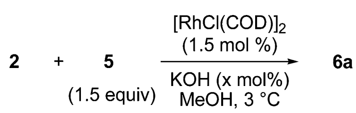
Table 4. Competition Reaction[a]



entry	2 (mmol)	10 (mmol)	6a (%)[b]	11 (%)[b]
1	0	0.15	0	35
2	0.075	0.075	80	38

[a]Solutions of **2** or **10** with indicated amount, **5a** (0.225 mmol, 1.5 equiv), $[RhCl(COD)]_2$ (1.5 mol %), and aq KOH (3.1 M, 9.5 μL, 30 μmol) in MeOH (0.8 mL) were stirred at 30 °C under microwave irradiation. [b]Isolated yield.

Table 5. Reaction Optimization without Microwave Irradation[a]



entry	x	5	time (d)	yield 6a (%)[b]	yield 7 (%)[b]
1	20	5a	3	78	0
2[c]	60	5a	3	85	0
3[d]	120	5a	3	95	0
4[d]	120	5b	3	44	0
5[d]	120	5c	3	50	0

[a]Solutions of **2** (0.15 mmol), **5** (0.225 mmol, 1.5 equiv), $[RhCl(COD)]_2$ (1.5 mol %), and aq KOH (3.1 M, 9.5 μL, 30 μmol) in MeOH (0.8 mL) were stirred at 3 °C. [b]Chromatographically isolated yield. [c]Aqueous KOH (3.1 M, 29 μL, 90 μmol) was used. [d]Aqueous KOH (6.0 M, 30 μL, 0.18 mmol) was used.

addition of **5a** and **2** at 3 °C provided no improvement (78% yield of **6a**) upon that at 25 °C. In an attempt to enhance the rate of transfer of the alkenyl group from boron to rhodium, and to reduce protodeboration, the influence of the base was examined.[23] Pleasingly, when the amount of KOH was increased from 20 to 60 mol % at 3 °C, the chemical yield of **6a** was raised to 85% (entry 2). A further improvement (95% yield; entry 3) was seen when employing 120 mol % of KOH. While the yield corresponded to that of the microwave irradiated reaction (Table 2, entry 7), the amounts of both the boronic acid **5a** and the Rh catalyst were significantly reduced. Although replacing the boronic acid with the corresponding trifluoroborate **5b** or boronic ester **5c** under the same conditions (Table 5, entries 4 and 5) was inferior to using **5a** (entry 3), the yields similarly matched those of the corresponding microwave irradiated reaction (Table 2, entries 8 and 9); again, less catalyst and alkenyl donor **5** were required.

We speculated that the enhanced boronic acid **5a** and Rh catalyst efficiency was the result of a combination of (i) improved boronic acid/boronate ($RB(OH)_2/[RB(OH)_3^-]K^+$) equilibria due to the excess base, (ii) the impediment of competitive protodeboration of the boronic acids by the use of a lower reaction temperature, and (iii) reduced over reaction of **6a** to form **7** that results from the lower reaction temperature.

Reaction Scope in the Absence of Microwave. Next, the substrate scope was reexamined (Table 6) using the same library of boronic acids already tested in the microwave irradiated version of the reaction. While the reactions were much slower at 3 °C than under microwave irradiation at 30 °C, the reaction yields were generally slightly better. The only general exception was for the conjugate addition of α-branched alkenylboronic acids **5l** and **5m** (entries 8 and 9) that provided much improved yields (90% and 98%) as compared to the microwave irradiated reaction (Table 3, entries 9 and 10). Although in some cases additional boronic acid **5** was added to the reactions to ensure good conversion of **2**, no reactions required supplemental additions of the Rh catalyst.

Because of decomposition of boronic acid **5p** during the attempted preparation of **6p**, as required for the synthesis of dinoprost (**1a**) (Scheme 3), the amount of KOH was reduced back to 20%. This allowed conversion to the desired product **6p** in an acceptable 72% yield on a 0.84 mmol scale without extra boronic acid being added (entry 11). While addition of **5q** to **2** (0.45 mmol) afforded **6q** in 78% yield, an additional portion of boronic acid **5q** (1.0 equiv, entry 12) was used. The method was also applicable to the syntheses of PGE derivatives **6r** (>99%) and **6s** (95%), which are precursors to travoprost (**1c**) and bimatoprost (**1d**) (entries 13 and 14), respectively.

CONCLUSION

A novel approach to the synthesis of prostaglandin derivatives and a natural prostaglandin comprising the 1,4-conjugate addition of variously substituted alkenylboronic acids to (*R*)-

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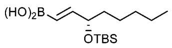
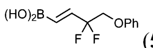
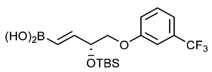
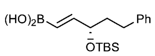
Table 6. Reaction Scope without Microwave Irradiation[a]

$$\mathbf{2} + \mathbf{5} \xrightarrow[\text{KOH, MeOH, 3 °C}]{[\text{RhCl(COD)}]_2\ (1.5\text{ mol \%})} \mathbf{6}$$

entry	5	time (d)	yield 6 (%)[b]
1	R^1=4-MeO-Ph, R^2=R^3=H (**5d**)	1.5	94 (**6d**)
2	R^1=3-MeO-Ph, R^2=R^3=H (**5e**)	2	90 (**6e**)
3	R^1=4-Me-Ph, R^2=R^3=H (**5f**)	1.5	>99 (**6f**)
4[c]	R^1=2-Me-Ph, R^2=R^3=H (**5h**)	2	90 (**6h**)
5[d]	R^1=4-CF_3-Ph, R^2=R^3=H (**5i**)	5	92 (**6i**)
6	R^1=4-F-Ph, R^2=R^3=H (**5j**)	1	93 (**6j**)
7	R^1=C_6H_{13}, R^2=R^3=H (**5k**)	3	69 (**6k**)
8[c]	R^1-R^3=$(CH_2)_4$, R^2=H (**5l**)	2	90 (**6l**)
9[e]	R^1=R^3=Me, R^2=H (**5m**)	2.5	98 (**6m**)
10[f]	R^1=R^2=Me, R^3=H (**5n**)	3	>99 (**6n**)
11[g]	 (**5p**)	1	72 (**6p**)
12[c,h]	 (**5q**)	2	78 (**6q**)
13[i]	 (**5r**)	1.2	>99 (**6r**)
14[i]	 (**5s**)	1.2	95 (**6s**)

[a]Solutions of **2** (0.15 mmol), **5** (0.225 mmol, 1.5 equiv), $[RhCl(COD)]_2$ (1.5 mol %), and aq KOH (6.0 M, 30 μL, 0.18 mmol) in MeOH (0.8 mL) were stirred at 3 °C. [b]Chromatographically isolated yield. [c]An additional portion of **5** (1.0 equiv) was added after 1 d. [d]An additional portion of **5** (1.0 equiv) was added after 3 d. [e]An additional portion of **5** (1.0 equiv) was added after 1.5 d. [f]An additional portion of **5** (1.0 equiv) was added after 2 d. [g]On a 0.84 mmol scale of **2** using 20 mol % KOH (3.1 M, 53 μL, 164 μmol). [h]On a 0.45 mmol scale of **2**. [i]An additional portion of **5** (1.0 equiv) was added after 0.7 d.

4-silyloxycyclopentenone **2** catalyzed by a simple Rh(I)-catalyst has been described. We believe this is a significant advance of the conventional two-component approach to prostaglandins that hitherto relied upon the use of organocuprates at cryogenic temperatures. The reaction is highly *trans*-diastereoselective, without the need for a fluoride additive, providing the addition products in good to excellent yields.

While the reaction is rapid (typically ≤6 h) and selective under microwave irradiation at 30 °C, a total of 3 mol % of $[RhCl(COD)]_2$ added in two 1.5 mol % portions along with an extra 0.5 equiv of boronic acid **5** were typically required to produce high yields. Although conducting the reaction at low temperature without microwave irradiation was considerably slower, the reaction often gave higher yields than the corresponding microwave irradiated reaction, when a greater than stoichiometric amount of the base was employed. Moreover, the loading of $[RhCl(COD)]_2$ was halved to 1.5 mol % and the amount of boronic acid **5** was reduced. In some instances, the nonmicrowave irradiated reaction also benefited from the addition of extra boronic acid **5**, however. The double-conjugate addition side product **7** seen in the model studies was eradicated by the use of a low reaction temperature or by employing microwave irradiation at 30 °C.

Both alkyl- and aryl-substituted boronic acids were tolerated under both microwave and nonmicrowave irradiation conditions, including those containing stereogenically disposed γ-silyloxy- (**5p**, **5r**, and **5s**) or γ,γ-difluoro substituents (**5q**). The usefulness of the method was validated by the preparation of the pharmacologically useful compounds $PGF_{2\alpha}$ (dinoprost (**1a**)) and tafluprost (**1b**) on 0.6−1.5 g scales, respectively. Moreover, precursors to access travoprost (**1c**) and bimatoprost (**1d**) were synthesized using this method.[15] Finally, as demonstrated by the successful coupling of boronic acid **5q** and **2**, this variant of the conventional approach may allow access to 1,4-addition products not accessible using organocuprates.

■ EXPERIMENTAL SECTION

Materials and Methods. All commercial chemicals and solvents were reagent grade; solvents were distilled before use. Boronic acids were either commercially available and used as supplied or were prepared using methods reported in the literature. Cyclopentenone **2** was prepared as described by Henschke et al.[10] All reactions were carried out under an atmosphere of argon or nitrogen gas. Reactions were monitored by TLC using silica gel plates; zones were detected visually under ultraviolet irradiation (254 nm) or by spraying with $KMnO_4$ solution followed by heating with a heat gun or on a hot plate. Flash column chromatography was conducted over silica gel. Reactions carried out under microwave irradiation were conducted with magnetic stirring in capped microwave vessels (anhydrous conditions were not required) using a Milestone StartSYNTH microwave reactor equipped with a variable power source (0−300 W) and an infrared temperature sensor allowing the reaction temperature to be controlled. ^{1}H NMR spectra were recorded on 400 or 600 MHz spectrometers; ^{13}C NMR spectra were recorded on 100 or 125 MHz spectrometers. Chemical shifts δ were recorded in parts per million (ppm) and were reported relative to the deuterated solvent signal (or the residual ^{1}H solvent for ^{1}H NMR spectroscopy). First-order spin multiplicities are abbreviated as follows: s (singlet), d (doublet), t (triplet), q (quadruplet), qui (quintet), and sep (septet); multiplets are abbreviated as m. High-resolution mass spectra were obtained using ESI, FAB, and APCI ionization methods, and a TOF-Q mass analyzer was used for APCI ionization. Optical rotations were measured on a polarimeter.

Preparation of Alkenylboronic Acids 5p, 5q, 5r, and 5s. *(S)-tert-Butyl-(1-ethynyl-hexyloxy)-dimethyl-silane (**S1**).*[24] To a solution of (*S*)-oct-1-yn-3-ol (11.6 mL, 76.1 mmol), imidazole (10.4 g, 153 mmol), and 4-dimethylaminopyridine (0.93 g, 7.60 mmol) in CH_2Cl_2 (100 mL) at 0−5 °C was added dropwise a solution of *tert*-butyldimethylsilyl chloride (17.2 g, 114 mmol) in CH_2Cl_2 (50 mL). The resulting white suspension was stirred at rt for 20 h. The product mixture was diluted with CH_2Cl_2 (150 mL) and mixed with saturated aqueous NH_4Cl (300 mL). The organic layer was separated, and the aqueous layer was back-extracted twice with CH_2Cl_2 (200 mL each). The combined organic layers were washed with brine (100 mL), dried over anhydrous $MgSO_4$, and concentrated. Column chromatography (eluting with 1:20 (v/v) EtOAc−*n*-heptane) afforded title alkyne **S1** as a colorless liquid (18.11 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.11 (s, 3H), 0.13 (s, 3H), 0.85−0.90 (m, 3H), 0.91 (s, 9H), 1.21−1.35 (m, 4H), 1.38−1.50 (m, 2H), 1.62−1.71 (m, 2H), 2.36 (d, *J* = 2.0 Hz, 1H), 4.33 (td, *J* = 2.1, 6.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.1 (CH_3), −4.6 (CH_3), 14.0 (CH_3), 18.2 (C), 22.6 (CH_2), 24.8 (CH_2), 25.8 (CH_3), 31.4 (CH_2), 38.6 (CH_2), 62.8 (CH), 71.8 (CH), 85.8 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3319, 2941, 2962, 1465, 1257, 1090, 837, 790, 656, 635 cm^{-1}. $[\alpha]^{25}_D$ −32.3 (*c* 1.00 in $CHCl_3$).

*(S)-2-[3-(tert-Butyl-dimethylsilanyloxy)-oct-1-enyl]-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (**S2**).*[25] A solution of alkyne **S1** (2.48 g, 10.3 mmol), 4-dimethylaminobenzoic acid (83 mg, 0.50 mmol, 5 mol %), and pinacolborane (4.5 mL, 30 mmol; as a neat oil) in *n*-heptane (10.0 mL) was heated at 100 °C for 5.5 h. After being cooled to rt, the mixture was diluted with EtOAc (30 mL) and was washed with saturated aqueous NH_4Cl solution (40 mL). Following separation of the layers, the aqueous layer was back-extracted with EtOAc (30 mL), and the combined organic layers were washed with brine (50 mL), dried over anhydrous $MgSO_4$ (2.5 g), and were filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (eluting with *n*-heptane (200 mL) then 1:50 (v/v) MTBE−*n*-heptane (750 mL)) to give the title boronic

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ester **S2** as a colorless oil (2.85 g, 7.74 mmol, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (s, 3H), 0.03 (s, 3H), 0.85−0.89 (m, 12H), 1.22−1.34 (m, 18H), 1.42−1.50 (m, 2H), 4.10−4.19 (m, 1H), 5.57 (dd, J = 1.5, 18.0 Hz, 1H), 6.56 (dd, J = 4.8, 18.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.9 (CH_3), −4.4 (CH_3), 14.0 (CH_3), 18.2 (C), 22.6 (CH_2), 24.66 (CH_2), 24.73 (CH_3), 24.8 (CH_3), 25.9 (CH_3), 31.9 (CH_2), 37.5 (CH_2), 74.2 (CH), 83.1 (C), 156.2 (CH); the C−B signal was not observed due to quadrupolar relaxation, 156.2 (CH). FTIR (KBr, neat): $\tilde{\nu}$ 3424, 2939, 2862, 1640, 1463, 1368, 1260, 1147, 1090, 998 cm^{-1}. HRMS (APCI) m/z calcd for $C_{20}H_{42}BO_4Si^-$ [M + HO$^-$] 385.2951, found 385.2970. $[\alpha]^{23}_{D}$ −1.9 (c 1.00 in $CHCl_3$).

(S,E)-{3-[(tert-Butyldimethylsilyl)oxy]oct-1-en-1-yl}boronic Acid (5p). A mixture of boronic ester **S2** (9.29 g, 25.2 mmol), $NaIO_4$ (15.0 g, 70.13 mmol), and NH_4OAc (5.15 g, 66.80 mmol) in a 2:1 (v/v) mixture of acetone and water (540 mL) was stirred at 40 °C for 20 h.[26] The acetone was evaporated under reduced pressure, and the remaining residue was extracted with EtOAc (200 mL). Following separation of the layers, the aqueous layer was back-extracted with EtOAc (200 mL), and the combined organic layers were washed with brine (200 mL), dried over anhydrous $MgSO_4$ (5.0 g), filtered, and concentrated under reduced pressure to provide the title boronic acid **5p** as a yellow clear oil (3.86 g, 13.5 mmol, 53.5%). ^{1}H NMR (400 MHz, d_6-DMSO): δ 0.00 (s, 3H), 0.03 (s, 3H), 0.86 (t, J = 7.0 Hz, 3H), 0.88 (s, 9H), 1.18−1.32 (m, 6H), 1.36−1.45 (m, 2H), 4.12 (q, J = 5.4 Hz, 1H), 5.44 (dd, J = 1.0, 17.8 Hz, 1H), 6.38 (dd, J = 5.4, 17.8 Hz, 1H), 7.57 (2H, s). ^{13}C NMR (100 MHz, d_6-DMSO): δ −4.9 (CH_3), −4.4 (CH_3), 13.8 (CH_3), 17.9 (C), 22.1 (CH_2), 24.2 (CH_2), 25.8 (CH_3), 31.2 (CH_2), 37.2 (CH_2), 74.0 (CH), 152.1 (C); the C−B signal was not observed due to quadrupolar relaxation. FTIR (KBr, neat): $\tilde{\nu}$ 3393, 2938, 2863, 1641, 1463, 1367, 1257, 1087, 1000, 833 cm^{-1}. HRMS (APCI) m/z calcd for $C_{14}H_{30}BO_3Si^-$ [M − H$^+$] 285.2063, found 285.2076. $[\alpha]^{25}_{D}$ +25.1 (c 1.00 in $CHCl_3$).

((2,2-Difluorobut-3-yn-1-yl)oxy)benzene (S3). To a round-bottom flask were sequentially added XtalFluor-E[27] (36.0 g, 157.2 mmol, 1.5 equiv), CH_2Cl_2 (36 mL), $Et_3N{\cdot}3HF$ (34.2 mL, 209.8 mmol, 2.0 equiv), and a solution of 1-phenoxybut-3-yn-2-one[28] (16.8 g, 104.9 mmol, 1.0 equiv) in CH_2Cl_2 (83 mL). The mixture was stirred until (overnight) TLC analysis indicated that the reaction was complete. The resulting mixture was extracted with a chilled (0 °C) solution of saturated aq $NaHCO_3$ until bubbling ceased. The aqueous layer was separated and back-extracted with diethyl ether (450 mL). The combined organic layers were washed with brine (60 mL), separated, dried over anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. The residue was purified by column chromatography (eluting with 1:100 (v/v) EtOAc/n-heptane) to give alkyne **S3** as a colorless oil (12.03 g, 65.9 mmol, 63% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.82 (t, J = 5.2 Hz, 1H), 4.27 (t, J = 2.4 Hz, 2H), 6.91−6.97 (m, 2H), 6.98−7.04 (m, 1H), 7.26−7.33 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 70.1 (t, J = 32 Hz; CH_2), 74.6 (t, J = 38 Hz; C), 77.1 (t, J = 7 Hz; CH), 110.8 (t, J = 235.0 Hz; C), 115.1 (CH), 122.2 (CH), 129.6 (CH), 157.8 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3723, 2938, 2857, 2353, 1700, 1498, 1303, 1250, 1167 cm^{-1}. HRMS (EI) m/z calcd for $C_{10}H_8F_2O^{+\bullet}$ [$M^{+}_{\bullet}$] 182.0543, found 182.0542.

Potassium (*E*)-(3,3-Difluoro-4-phenoxybut-1-en-1-yl)-trifluoroborate (S4). A mixture of 2,5-dimethylhexa-2,4-diene (27 mL, 189.4 mmol) in THF (15 mL) and a 1 M solution of $BH_3{\cdot}THF$ in THF (86 mL, 86.0 mmol) was stirred for 3 h at 0 °C.[29] To this was then added a solution of alkyne **S3** (6.3 g, 34.5 mmol) in THF (37 mL) while maintaining the temperature at 0 °C. The reaction mixture was stirred at rt for 3 h before being cooled in an ice bath and carefully quenched with water (13 mL). After being stirred at rt for an additional 1.5 h, a 37% aqueous solution of formaldehyde (31 mL) was added. The mixture was stirred overnight, quenched with brine (30 mL), and the resulting mixture was extracted three times with EtOAc (50 mL each). The organic layers were combined, dried over anhydrous $MgSO_4$, filtered, and evaporated to give crude (*E*)-(3,3-difluoro-4-phenoxybut-1-en-1-yl)boronic acid (**5q**).

To a solution of the above prepared boronic acid **5q** in MeCN (143 mL) was added a solution of KF (7.27 g, 125.3 mmol) in water (11 mL). The mixture was stirred until no solid could be seen,[30] and then a solution of L-(+)-tartaric acid (9.7 g, 64.6 mmol) in THF (50 mL) was added over a period of 20 min. The mixture was stirred for 30 min, and was then filtered. The filter cake was washed with MeCN (114 mL), the combined organic layers were concentrated, and the resulting residue was slurried in diethyl ether (30 mL) for 1 h. The solids were filtered off, and the filtered cake was dried under reduced pressure to provide trifluoroborate **S4** as a white solid (7.6 g, 26.2 mmol, 76% yield). ^{1}H NMR (400 MHz, d_6-DMSO): δ 4.28 (t, J = 13.2 Hz, 2H), 5.79 (dt, J = 10.9, 18.3 Hz, 1H), 6.60 (dq, J = 3.1, 18.3 Hz, 1H), 6.98−7.07 (m, 3H), 7.30−7.38 (m, 2H). ^{13}C NMR (100 MHz, d_6-DMSO): δ 69.1 (t, J = 31.0 Hz; CH_2), 115.2 (CH), 120.2 (t, J = 236.0 Hz; C), 121.7 (CH), 126.5 (tq, J = 4.0, 24.0 Hz; CH), 130.0 (CH), 158.4 (C); the C−B signal was not observed due to quadrupolar relaxation. FTIR (KBr, neat): $\tilde{\nu}$ 2927, 1640, 1494, 1445, 1294, 1267, 1169, 1134, 1090, 1033 cm^{-1}. HRMS (ESI) m/z calcd for $C_{10}H_9OF_5B^-$ [M − K$^+$] 251.0667, found 251.0669; mp > 260 °C.

(E)-(3,3-Difluoro-4-phenoxybut-1-en-1-yl)boronic Acid (5q). A mixture of a solution of trifluoroborate **S4** (1.5 g, 5.2 mmol) in water (5 mL) and silica gel (0.31 g, 5.2 mmol) was stirred at 30 °C overnight. The mixture was filtered and evaporated providing the title boronic acid **5q** as a white solid (1.0 g, 4.4 mmol, 85% yield). ^{1}H NMR (400 MHz, d_6-DMSO): δ 4.40 (t, J = 12.9 Hz, 2H), 6.12 (dt, J = 2.4, 18.4 Hz, 1H), 6.60 (dt, J = 11.1, 18.4 Hz, 1H), 6.95−7.10 (m, 3H), 7.30−7.40 (m, 2H), 8.2 (s, 2H). ^{13}C NMR (100 MHz, d_6-DMSO): δ 68.7 (t, J = 31.5 Hz; CH_2), 115.3 (CH), 119.3 (t, J = 238.5 Hz; C), 122.0 (CH), 130.0 (CH), 131.6 (CH), 138.7 (t, J = 25.0 Hz; CH), 158.1 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3398, 3296, 2936, 1594, 1494, 1372, 1294, 1250, 1164, 1088 cm^{-1}. HRMS (EI) m/z calcd for $C_{10}H_{11}BF_2O_3^{+\bullet}$ [$M^{+}_{\bullet}$] 228.0769, found 228.0768; mp decomposed at >150 °C.

(S)-tert-Butyldimethyl((1-(3-(trifluoromethyl)phenoxy)but-3-yn-2-yl)oxy)silane (S5). Following the method preparing **S1**, the parent alcohol (0.7 g, 3.04 mmol) was used, and **S5** was isolated as a colorless oil (1.1 g, > 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.13 (s, 3H), 0.17 (s, 3H), 0.91 (s, 9H), 2.47 (d, J = 2.1 Hz, 1H), 4.10 (d, J = 6.0 Hz, 2H), 4.74 (dt, J = 2.1, 6.0 Hz, 1H), 7.09 (dd, J = 2.2, 8.3 Hz, 1H), 7.14 (s, 1H), 7.21 (d, J = 7.8 Hz, 1H), 7.38 (dd, J = 8.0, 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.0 (CH_3), −4.8 (CH_3), 18.2 (C), 25.7 (CH_3), 62.1 (CH), 72.3 (CH_2), 73.7 (CH), 82.0 (C), 111.6 (q, J = 4.0 Hz, CH), 117.8 (q, J = 4.0 Hz, CH), 118.3 (CH), 123.9 (q, J = 271.0 Hz, C), 130.0 (CH), 131.9 (q, J = 32.0 Hz, C), 158.7 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3309, 2942, 2863, 1603, 1455, 1331, 1251, 1170, 1128, 1056, 970 cm^{-1}. HRMS (FAB) m/z calcd for $C_{17}H_{22}F_3O_2Si^-$ [M − H$^+$] 343.1347, found 343.1339. $[\alpha]^{30}_{D}$ −26.5 (c 1.00, $CHCl_3$).

(S,E)-tert-Butyldimethyl((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(3-(trifluoromethyl)phenoxy)but-3-en-2-yl)oxy)silane (S6). To a solution of catechol (70.0 mg, 0.58 mmol) in THF (1.3 mL) at 0 °C was added BH_3 (1.0 M in THF, 0.58 mL, 0.58 mmol) slowly, and the reaction mixture was stirred for 1 h at 0 °C and at rt for an additional 1 h. To the stirred solution were added **S5** (0.2 g, 0.58 mmol) and dicyclohexylborane (0.1 M, 0.3 mL, 0.03 mmol) in THF at 0 °C. The reaction mixture was warmed to rt, and after being stirred for another 6 h at rt, pinacol (0.1 g, 0.85 mmol) was added to the resultant mixture at 0 °C, and the mixture was allowed to warm to rt and was stirred for 48 h. Bubbling air into the solution for 2 h was carried out at rt. The resulting mixture was diluted with hexane, washed with water, and the organic layer was separated and dried over Na_2SO_4, filtered, and evaporated to give a yellow oil, which was purified by column chromatography (eluting with n-hexane/EtOAc = 40/1) to give boronic ester **S6** as a colorless oil (0.23 g, 0.5 mmol, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.08 (s, 3H), 0.09 (s, 3H), 0.91 (s, 9H), 1.28 (s, 12H), 3.86 (dd, J = 7.5, 9.4 Hz, 1H), 3.95 (J = 4.1, 9.4 Hz, 1H), 4.55−4.65 (m, 1H), 5.86 (dd, J = 1.7, 17.9 Hz, 1H), 6.66 (dd, J = 4.1, 17.9 Hz, 1H), 7.05 (d, J = 8.3 Hz, 1H), 7.09 (s, 1H), 7.19 (d, J = 7.6 Hz, 1H), 7.37 (dd, J = 8.0, 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.8 (CH_3), −4.7 (CH_3), 18.3 (C), 24.7 (CH_3), 24.8 (CH_3), 25.8 (CH_3), 72.1 (CH_2), 72.5 (CH), 83.3 (C), 111.2 (q, J = 4.0 Hz, CH), 117.4 (q, J = 4.0 Hz, CH), 118.1 (CH), 123.9 (q, J = 271.0 Hz, C), 129.9 (CH), 131.8 (q, J = 32.0 Hz, C), 151.0 (CH),

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158.7 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2941, 2863, 1641, 1604, 1455, 1332, 1249, 1136, 1044, 982, 889 cm^{-1}. HRMS (FAB) m/z calcd for $C_{23}H_{35}BF_3O_4Si^-$ [M − H$^+$] 471.2355, found 471.2342. $[\alpha]^{29}_D$ −1.5 (c 1.00, $CHCl_3$).

*(R,E)-(3-((tert-Butyldimethylsilyl)oxy)-5-phenylpent-1-en-1-yl)-boronic Acid (**5r**).* To a solution of boronic ester **S6** (0.23 g, 0.5 mmol, 1 equiv) in acetone and water (5 mL, 2:1) were added sodium metaperiodate (0.33 g, 1.5 mmol, 3.1 equiv) and ammonium acetate (0.11 g, 1.5 mmol, 3.0 equiv). The reaction mixture was warmed to rt, and after being stirred for 48 h, the volatile was removed under reduced pressure. The residue was diluted with EtOAc, and the organic phase was separated. The aqueous layer was extracted with EtOAc, and the combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to provide boronic acid **5r** as a colorless oil (0.18 g, 0.46 mmol, 95% yield). ^{1}H NMR (400 MHz, d_6-DMSO): δ 0.08 (s, 3H), 0.10 (s, 3H), 0.90 (s, 9H), 3.91 (J = 7.7, 10.1 Hz, 1H), 4.11 (J = 3.5, 10.1 Hz, 1H), 4.54−4.66 (m, 1H), 5.75 (dd, J = 1.3, 17.9 Hz, 1H), 6.54 (dd, J = 4.5, 18.0 Hz, 1H), 7.20−7.35 (m, 3H), 7.55 (dd, J = 8.0 Hz, 1H), 7.71 (s, 2H). ^{13}C NMR (100 MHz, d_6-DMSO): δ −3.9 (CH_3), −3.8 (CH_3), 18.9 (C), 26.6 (CH_3), 72.9 (CH_2), 73.6 (CH), 111.8 (q, J = 4.0 Hz, CH), 118.1 (q, J = 4.0 Hz, CH), 119.8 (CH), 124.9 (q, J = 271.0 Hz, C), 129.9 (CH), 131.1 (q, J = 32 Hz, C), 131.6 (CH), 148.3 (CH), 159.7 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3387, 2941, 2864, 1640, 1453, 1332, 1249, 1166, 1130, 1056, 991 cm^{-1}. HRMS (FAB) m/z calcd for $C_{17}H_{25}BF_3O_4Si^-$ [M − H$^+$] 389.1567, found 389.1563. $[\alpha]^{29}_D$ +19.9 (c 1.00, $CHCl_3$).

*(R)-tert-Butyldimethyl((5-phenylpent-1-yn-3-yl)oxy)silane (**S7**).* Following the method preparing **S1**, the parent alcohol (1.2 g, 7.49 mmol) was used, and **S7** was isolated as a colorless oil (1.8 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.11 (s, 3H), 0.13 (s, 3H), 0.91 (s, 9H), 1.95−2.05 (m, 2H), 2.42 (d, J = 2.0 Hz, 1H), 2.69−2.84 (m, 2H), 4.37 (dt, J = 1.7, 6.4 Hz, 1H), 7.15−7.23 (m, 3H), 7.25−7.32 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.1 (CH_3), −4.5 (CH_3), 18.2 (C), 25.8 (CH_3), 31.3 (CH_2), 40.2 (CH_2), 62.1 (CH), 72.4 (CH), 85.3 (C), 125.9 (CH), 128.36 (CH), 128.43 (CH), 141.6 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3303, 3031, 2942, 2861, 1597, 1463, 1254, 1097, 973, 841, 778 cm^{-1}. HRMS (FAB) m/z calcd for $C_{17}H_{25}OSi^-$ [M − H$^+$] 273.1680, found 273.1679. $[\alpha]^{31}_D$ −11.2 (c 1.00, $CHCl_3$).

*(S,E)-tert-Butyldimethyl((5-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-3-yl)oxy)silane (**S8**).* Following the method preparing **S6**, the parent alkyne (0.2 g, 0.72 mmol) was used, and **S8** was isolated as a colorless oil (0.22 g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.02 (s, 3H), 0.04 (s, 3H), 0.91 (s, 9H), 1.27 (s, 12H), 1.78−1.88 (m, 2H), 2.59−2.72 (m, 2H), 4.20−4.28 (m, 1H), 5.63 (dd, J = 1.4, 18.0 Hz, 1H), 6.61 (dd, J = 4.8, 18.0 Hz, 1H), 7.13−7.22 (m, 3H), 7.23−7.31 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.9 (CH_3), −4.4 (CH_3), 18.2 (C), 24.7 (CH_3), 24.8 (CH_3), 25.9 (CH_3), 31.1 (CH_2), 39.1 (CH_2), 73.6 (CH), 83.1 (C), 125.6 (CH), 128.3 (CH), 128.4 (CH), 142.4 (C), 155.6 (CH). FTIR (KBr, neat): $\tilde{\nu}$ 2941, 2861, 1643, 1463, 1351, 1258, 1148, 1105, 973, 840, 777.4 cm^{-1}. HRMS (FAB) m/z calcd for $C_{23}H_{38}BO_3Si^-$ [M − H$^+$] 401.2689, found 401.2683. $[\alpha]^{30}_D$ +13.6 (c 1.00, $CHCl_3$).

*(R,E)-(3-((tert-Butyldimethylsilyl)oxy)-5-phenylpent-1-en-1-yl)-boronic Acid (**5s**).* Following the method preparing **5r**, the parent boronic ester (0.22 g, 0.55 mmol) was used, and **5s** was isolated as a colorless oil (0.18 g, 98%). ^{1}H NMR (400 MHz, d_6-DMSO): δ 0.04 (s, 3H), 0.07 (s, 3H), 0.92 (s, 9H), 1.70−1.84 (m, 2H), 2.62 (t, J = 8.0 Hz, 2H), 4.22 (ddd, J = 5.7, 5.7, 5.7 Hz, 1H), 5.52 (d, J = 18.0 Hz, 1H), 6.48 (dd, J = 5.7, 18.0 Hz, 1H), 7.17−7.24 (m, 3H), 7.26−7.35 (m, 2H), 7.64 (s, 2H). ^{13}C NMR (100 MHz, d_6-DMSO): δ −3.9 (CH_3), −3.5 (CH_3), 18.9 (C), 26.7 (CH_3), 31.6 (CH_2), 40.1 (CH_2), 74.5 (CH), 126.6 (CH), 129.1 (CH), 129.2 (CH), 142.9 (C), 152.4 (CH); the C−B signal was not observed due to quadrupolar relaxation. FTIR (KBr, neat): $\tilde{\nu}$ 3028, 2942, 2859, 1637, 1359, 1257, 1093, 998, 834, 777, 701 cm^{-1}. HRMS (FAB) m/z calcd for $C_{17}H_{28}BO_3Si^-$ [M − H$^+$] 319.1900, found 319.1896. $[\alpha]^{30}_D$ +19.4 (c 1.00, $CHCl_3$).

General Procedures for the Synthesis of PGE_2 Derivatives 6a−6h. All of the NMR spectra presented in the Supporting Information were obtained from samples produced using method A described below.

*Method A: Using Microwave Irradiation (50 W) at 30 °C (Exemplified for **6a**).* A solution of isopropyl (Z)-7-[(3R)-3-($tert$-butyl-dimethyl-silanyloxy)-5-oxo-cyclopent-1-enyl]-hept-5-enoate (**2**) (57 mg, 0.15 mmol), (E)-styreneboronic acid (**5a**) (0.22 mmol), $[RhCl(COD)]_2$ (1.1 mg, 2.2 μmol), and aqueous KOH (9.5 μL, 3.1 M, 30 μmol) in MeOH (1.0 mL) was stirred under microwave irradiation at 30 °C (50 W). After 5 h, additional (E)-styreneboronic acid (**5a**) (74 μmol) and $[RhCl(COD)]_2$ (1.1 mg, 2.2 μmol) were added, and the reaction mixture was stirred for another hour under microwave irradiation (30 °C; 50 W). The product mixture was concentrated under reduced pressure, and the resulting residue was purified by column chromatography (eluting with 1:80 (v/v) acetone−hexanes) affording cyclopentanone **6a** as a colorless oil (70 mg, 96%).

*Method B: Without Microwave Irradiation at 3 °C (Exemplified for **6a**).* A solution of isopropyl (Z)-7-[(3R)-3-($tert$-butyl-dimethyl-silanyloxy)-5-oxo-cyclopent-1-enyl]-hept-5-enoate (**2**) (57 mg, 0.15 mmol), (E)-styreneboronic acid (**5a**) (0.22 mmol), $[RhCl(COD)]_2$ (1.1 mg, 2.2 μmol), and aqueous KOH (30 μL, 6.0 M, 0.18 mmol) in MeOH (1.0 mL) was stirred at 3 °C. After being stirred for 3 days, the product mixture was concentrated under reduced pressure, and the resulting residue was purified by column chromatography (eluting with 1:80 (v/v) acetone−hexanes) affording cyclopentanone **6a** (69 mg, 95%).

*(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-5-oxo-2-((E)-styryl)cyclopentyl)hept-5-enoate (**6a**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (s, 3H), 0.03 (s, 3H), 0.86 (s, 9H), 1.20 (d, J = 6.2 Hz, 6H), 1.65 (qui, J = 7.5 Hz, 2H), 2.05 (ddd, J = 7.0, 7.0, 7.0 Hz, 2H), 2.12−2.29 (m, 4H), 2.33−2.45 (m, 2H), 2.57−2.74 (m, 2H), 4.13 (ddd, J = 8.1, 8.1, 8.1 Hz, 1H), 4.97 (sep, J = 6.2 Hz, 1H), 5.30−5.47 (m, 2H), 6.05 (dd, J = 8.6, 15.8 Hz, 1H), 6.50 (d, J = 15.8 Hz, 1H), 7.20−7.26 (m, 1H), 7.27−7.38 (m, 4H) (the relative stereochemistry of C8 and C13 was determined from a 2D-NOESY spectrum of **7a**; see the Supporting Information). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.7 (CH_3), −4.6 (CH_3), 18.1 (C), 21.8 (CH_3), 24.8 (CH_2), 25.1 (CH_2), 25.7 (CH), 26.7 (CH_2), 34.1 (CH_2), 47.6 (CH_2), 54.1 (CH), 54.4 (CH), 67.4 (CH), 73.1 (CH), 126.1 (CH), 126.5 (CH), 127.4 (CH), 128.6 (CH), 129.8 (CH), 131.0 (CH), 132.9 (CH), 137.1 (C), 173.1 (C), 214.7 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2935, 2861, 1736, 1593, 1459, 1372, 1250, 1107, 838, 745 cm^{-1}. HRMS (ESI) m/z calcd for $C_{29}H_{45}O_4Si$ [M + H$^+$] 485.3081, found 485.3064. $[\alpha]^{27}_D$ −57.4 (c 1.00, $CHCl_3$).

*(Z)-Isopropyl 7-((1R,2S,3RS)-5-Oxo-2,3-di((E)-styryl)cyclopentyl)-hept-5-enoate (**7** and 11-epi-**7**).* In some reactions (see Tables 1 and 2), an inseparable 83:17 diastereomeric mixture of **7** and 11-*epi*-**7** was produced along with **6a**; the **7** and 11-*epi*-**7** mixture was isolated by column chromatography of the crude **6a**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (d, J = 6.2 Hz, 6H), 1.65 (qui, J = 7.6 Hz, 2H), 1.96−2.12 (m, 2H), 2.13−2.35 (m, 4H), 2.36−2.58 (m, 3H), 2.62−2.85 (m, 2H), 4.97 (sep, J = 6.4 Hz, 1H), 5.31−5.50 (m, 2H), 6.06−6.22 (m, 2H), 6.41 (d, J = 11.5 Hz, 1H), 6.45 (d, J = 11.5 Hz, 1H), 7.16−7.38 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8 (CH_3), 24.8 (CH_2), 25.0 (CH_2), 26.7 (CH_2), 30.9 (CH_2), 34.1 (CH_2), 44.4 (CH), 51.7 (CH), 55.5 (CH), 67.4 (CH), 77.2 (CH), 126.18 (CH), 126.22 (CH), 126.5 (CH), 127.4 (CH), 127.5 (CH), 128.5 (CH), 128.6 (CH), 130.3 (CH), 131.0 (CH), 131.2 (CH), 132.5 (CH), 137.0 (C), 173.1 (C), 216.7 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3446, 2975, 1730, 1640, 1443, 1375, 1217, 1164, 1102, 963 cm^{-1}. HRMS (ESI) m/z calcd for $C_{31}H_{37}O_3^+$ [M + H$^+$] 457.2743, found 457.2738. $[\alpha]^{24}_D$ −149.5 (c 0.46, $CHCl_3$).

*(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-((E)-4-methoxystyryl)-5-oxocyclopentyl)hept-5-enoate (**6d**).* Following method A, the title compound was isolated as a colorless oil (72 mg, 93%). Following method B, the reaction was stirred for 1.5 d (73 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 3H), 0.02 (s, 3H), 0.85 (s, 9H), 1.20 (d, J = 6.3 Hz, 6H), 1.64 (qui, J = 7.5 Hz, 2H), 2.05 (ddd, J = 7.0, 7.0, 7.0 Hz, 2H), 2.11−2.26 (m, 4H), 2.35−2.43 (m, 2H), 2.55−2.72 (m, 2H), 3.81 (s, 3H), 4.10 (ddd, J = 8.1, 8.1, 8.1 Hz, 1H), 4.97 (sep, J = 6.3 Hz, 1H), 5.27−5.46 (m, 2H), 5.89 (dd, J = 8.6,

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15.7 Hz, 1H), 6.44 (d, J = 15.7 Hz, 1H), 6.85 (d, J = 8.7 Hz, 2H), 7.28 (d, J = 8.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.8 (CH_3), −4.7 (CH_3), 18.0 (C), 21.8 (CH_3), 24.8 (CH_2), 25.1 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 34.1 (CH_2), 47.6 (CH_2), 54.1 (CH), 54.4 (CH), 55.2 (CH_3), 67.4 (CH), 73.1 (CH), 114.0 (CH), 126.5 (CH), 127.2 (CH), 127.5 (CH), 129.9 (C), 130.9 (CH), 132.3 (CH), 159.0 (C), 173.1 (C), 214.9 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2939, 2863, 1737, 1604, 1512, 1463, 1371, 1246, 1166, 1109 cm^{-1}. HRMS (ESI) m/z calcd for $C_{30}H_{47}O_5Si$ [M + H$^+$] 515.3187, found 515.3182. $[\alpha]^{22}_D$ −50.6 (c 1.00, $CHCl_3$).

(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-((E)-3-methoxystyryl)-5-oxocyclopentyl)hept-5-enoate (6e). Following method A, the additional portions of $[RhCl(COD)]_2$ and **5e** were added after 3 h (instead of after 5 h), and the reaction was irradiated for a further 2 h; the title compound was isolated as a colorless oil (72 mg, 93%). Following method B, the reaction was stirred for 2 d (70 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (s, 3H), 0.02 (s, 3H), 0.85 (s, 9H), 1.20 (d, J = 6.2 Hz, 6H), 1.64 (qui, J = 7.5 Hz, 2H), 2.05 (ddd, J = 7.1, 7.1, 7.1 Hz, 2H), 2.13−2.27 (m, 4H), 2.32−2.45 (m, 2H), 2.57−2.73 (m, 2H), 3.81 (s, 3H), 4.12 (ddd, J = 8.1, 8.1, 8.1 Hz, 1H), 4.97 (sep, J = 6.2 Hz, 1H), 5.29−5.46 (m, 2H), 6.04 (dd, J = 8.6, 15.7 Hz, 1H), 6.47 (d, J = 15.7 Hz, 1H), 6.79 (dd, J = 2.0, 8.0 Hz, 1H), 6.89 (dd, J = 2.0, 3.8 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 7.18−7.25 (m, 1H). ^{13}C NMR (100 MHz): δ −4.8 (CH_3), −4.7 (CH_3), 18.0 (C), 21.8 (CH_3), 24.8 (CH_2), 25.1 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 34.0 (CH_2), 47.5 (CH_2), 54.0 (CH), 54.3 (CH), 55.1 (CH_3), 67.3 (CH), 73.0 (CH), 111.6 (CH), 112.8 (CH), 118.8 (CH), 126.4 (CH), 129.5 (CH), 130.1 (CH), 131.0 (CH), 132.7 (CH), 138.5 (C), 159.8 (C), 173.0 (C), 214.6 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2945, 2862, 1737, 1666, 1590, 1463, 1375, 1257, 1156, 1108 cm^{-1}. HRMS (ESI) m/z calcd for $C_{30}H_{47}O_5Si^+$ [M + H$^+$] 515.3187, found 515.3172. $[\alpha]^{25}_D$ −65.1 (c 1.00, $CHCl_3$).

(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-((E)-4-methylstyryl)-5-oxocyclopentyl)hept-5-enoate (6f). Following method A, the title compound was isolated as a colorless oil (71 mg, 95%). Following method B, the reaction was stirred for 1.5 d (74 mg, >99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 3H), 0.02 (s, 3H), 0.85 (s, 9H), 1.20 (d, J = 6.2 Hz, 6H), 1.64 (qui, J = 7.5 Hz, 2H), 2.04 (ddd, J = 7.1, 7.1, 7.1 Hz, 2H), 2.12−2.28 (m, 4H), 2.34 (s, 3H), 2.35−2.42 (m, 2H), 2.56−2.74 (m, 2H), 4.11 (ddd, J = 8.1, 8.1, 8.1 Hz, 1H), 4.97 (sep, J = 6.2 Hz, 1H), 5.29−5.45 (m, 2H), 5.98 (dd, J = 8.7, 15.7 Hz, 1H), 6.46 (d, J = 15.7 Hz, 1H), 7.13 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.8 (CH_3), −4.7 (CH_3), 18.0 (C), 21.1 (CH_3), 21.8 (CH_3), 24.8 (CH_2), 25.0 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 34.1 (CH_2), 47.6 (CH_2), 54.1 (CH), 54.4 (CH), 67.3 (CH), 73.0 (CH), 126.0 (CH), 126.5 (CH), 128.7 (CH), 129.3 (C), 130.9 (CH), 132.7 (CH), 134.3 (C), 137.1 (C), 173.1 (C), 214.8 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2938, 2863, 1737, 1509, 1463, 1372, 1250, 1110, 964, 841 cm^{-1}. HRMS (ESI) m/z calcd for $C_{30}H_{47}O_4Si$ [M + H$^+$] 499.3238, found 499.3244. $[\alpha]^{23}_D$ −40.2 (c 1.00, $CHCl_3$).

(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-((E)-3-methylstyryl)-5-oxocyclopentyl)hept-5-enoate (6g). Following method A, the title compound was isolated as a colorless oil (73 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (s, 3H), 0.03 (s, 3H), 0.86 (s, 9H), 1.20 (d, J = 6.4 Hz, 6H), 1.65 (qui, J = 7.6 Hz, 2H), 2.05 (ddd, J = 7.1, 7.1, 7.1 Hz, 2H), 2.12−2.27 (m, 4H), 2.30−2.41 (m, 2H), 2.35 (s, 3H), 2.57−2.73 (m, 2H), 4.12 (ddd, J = 8.1, 8.1, 8.1 Hz, 1H), 4.97 (sep, J = 6.4 Hz, 1H), 5.28−5.46 (m, 2H), 6.03 (dd, J = 8.6, 15.8 Hz, 1H), 6.47 (d, J = 15.8, 1H), 7.06 (d, J = 7.2 Hz, 1H), 7.13−7.23 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.8 (CH_3), −4.6 (CH_3), 18.0 (C), 21.4 (CH_3), 21.8 (CH_3), 24.8 (CH_2), 25.1 (CH_2), 25.7 (CH_3), 26.7 (CH_2), 34.1 (CH_2), 47.6 (CH_2), 54.1 (CH), 54.3 (CH), 67.4 (CH), 73.1 (CH), 123.2 (CH), 126.5 (CH), 126.9 (CH), 128.2 (CH), 128.5 (CH), 129.5 (CH), 131.0 (CH), 133.0 (CH), 137.0 (C), 138.1 (C), 173.1 (C), 214.8 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2939, 2863, 1737, 1600, 1463, 1375, 1253, 1112, 971, 884 cm^{-1}. HRMS (ESI) m/z calcd for $C_{30}H_{47}O_4Si^+$ [M + H$^+$] 499.3238, found 499.3242. $[\alpha]^{23}_D$ −51.1 (c 1.00, $CHCl_3$).

(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-((E)-2-methylstyryl)-5-oxocyclopentyl)hept-5-enoate (6h). Following method A, the additional portions of $[RhCl(COD)]_2$ and **5h** were added after 3 h (instead of after 5 h) and the reaction was irradiated for a further 2 h; the title compound was isolated as a colorless oil (66 mg, 88%). Following method B, boronic acid **5h** (1.0 equiv) was added after 1 d, and the reaction was stirred for another 1 d (67 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.03 (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 1.20 (d, J = 6.2 Hz, 6H), 1.65 (qui, J = 7.4 Hz, 2H), 2.07 (ddd, J = 6.9, 6.9, 6.9 Hz, 2H), 2.13−2.28 (m, 4H), 2.34 (s, 3H), 2.37−2.45 (m, 2H), 2.60−2.76 (m, 2H), 4.15 (ddd, J = 8.1, 8.1, 8.1 Hz, 1H), 4.97 (sep, J = 6.2 Hz, 1H), 5.32−5.47 (m, 2H), 5.93 (dd, J = 8.6, 15.6 Hz, 1H), 6.72 (d, J = 15.6 Hz, 1H), 7.11−7.20 (m, 3H), 7.38−7.44 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.72 (CH_3), −4.65 (CH_3), 18.0 (C), 19.7 (CH_3), 21.8 (CH_3), 24.8 (CH_2), 25.1 (CH_2), 25.7 (CH_3), 26.7 (CH_2), 34.0 (CH_2), 47.6 (CH_2), 54.4 (CH), 54.5 (CH), 67.3 (CH), 73.0 (CH), 125.5 (CH), 126.1 (CH), 126.6 (CH), 127.3 (CH), 130.2 (CH), 130.7 (CH), 130.9 (CH), 131.2 (CH), 135.1 (C), 136.2 (C), 173.0 (C), 214.7 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3454, 2948, 1737, 1647, 1462, 1375, 1253, 1107, 969, 880 cm^{-1}. HRMS (ESI) m/z calcd for $C_{30}H_{47}O_4Si$ [M + H$^+$] 499.3238, found 499.3234. $[\alpha]^{25}_D$ −53.4 (c 1.00, $CHCl_3$).

(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-5-oxo-2-((E)-4-(trifluoromethyl)styryl)cyclopentyl)hept-5-enoate (6i). Following method A, the additional portions of $[RhCl(COD)]_2$ and **5i** were added after 3 h (instead of after 5 h), and the reaction was irradiated for a further 2 h; the title compound was isolated as a colorless oil (66 mg, 80%). Following method B, boronic acid **5i** (1.0 equiv) was added after 3 d, and the reaction was stirred for another 2 d (77 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ −0.01 (s, 3H), 0.02 (s, 3H), 0.85 (s, 9H), 1.18 (d, J = 6.2 Hz, 6H), 1.64 (qui, J = 7.5 Hz, 2H), 2.04 (ddd, J = 7.2, 7.2, 7.2 Hz, 2H), 2.14−2.29 (m, 4H), 2.35−2.44 (m, 2H), 2.59−2.75 (m, 2H), 4.13 (ddd, J = 8.2, 8.2, 8.2 Hz, 1H), 4.96 (sep, J = 6.2 Hz, 1H), 5.27−5.48 (m, 2H), 6.16 (dd, J = 8.6, 15.8 Hz, 1H), 6.54 (d, J = 15.8 Hz, 1H), 7.44 (d, J = 8.2 Hz, 2H), 7.57 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.7 (CH_3), 18.0 (C), 21.8 (CH_3), 24.8 (CH_2), 25.1 (CH_2), 25.6 (CH_3), 26.6 (CH_2), 34.0 (CH_2), 47.5 (CH_2), 54.2 (CH), 54.3 (CH), 67.4 (CH), 72.8 (CH), 124.2 (q, J = 270.2 Hz; C), 125.6 (q, J = 4.0 Hz; CH), 126.2 (CH), 126.4 (CH), 129.2 (q, J = 33.0 Hz; C), 131.1 (CH), 131.7 (CH), 132.6 (CH), 140.4 (C), 173.0 (C), 214.1 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2941, 2866, 1739, 1617, 1464, 1373, 1252, 1163, 1118, 840, 777 cm^{-1}. HRMS (ESI) m/z calcd for $C_{30}H_{44}F_3O_4Si^+$ [M + H$^+$] 553.2955, found 553.2936. $[\alpha]^{29}_D$ −40.4 (c 1.00, $CHCl_3$).

(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-((E)-4-fluorostyryl)-5-oxocyclopentyl)hept-5-enoate (6j). Following method A, the additional portions of $[RhCl(COD)]_2$ and **5j** were added after 3 h (instead of after 5 h), and the reaction was irradiated for a further 2 h; the title compound was isolated as a colorless oil (69 mg, 92%). Following method B, the reaction was stirred for another 1 d (70 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ −0.01 (s, 3H), 0.01 (s, 3H), 0.85 (s, 9H), 1.19 (d, J = 6.2 Hz, 6H), 1.64 (qui, J = 7.5 Hz, 2H), 2.04 (ddd, J = 7.1, 7.1, 7.1 Hz, 2H), 2.11−2.27 (m, 4H), 2.32−2.45 (m, 2H), 2.54−2.74 (m, 2H), 4.11 (ddd, J = 8.6, 8.6, 8.6 Hz, 1H), 4.96 (sep, J = 6.2 Hz, 1H), 5.27−5.47 (m, 2H), 5.95 (dd, J = 8.6, 15.7 Hz, 1H), 6.46 (d, J = 15.7 Hz, 1H), 7.00 (dd, J = 8.6, 8.7 Hz, 2H), 7.27−7.35 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.8 (CH_3), −4.7 (CH_3), 18.0 (C), 21.8 (CH_3), 24.8 (CH_2), 25.1 (CH_2), 25.6 (CH_3), 26.6 (CH_2), 34.1 (CH_2), 47.5 (CH_2), 54.1 (CH), 54.3 (CH), 67.4 (CH), 72.9 (CH), 115.5 (d, J = 21.0 Hz; CH), 126.5 (CH), 127.5 (d, J = 8.0 Hz; CH), 129.5 (CH), 131.0 (CH), 131.7 (CH), 133.2 (d, J = 3.0 Hz; C), 162.2 (d, J = 245.0 Hz; C), 173.0 (C), 214.5 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2939, 1737, 1603, 1463, 1373, 1232, 1154, 1111, 845, 777 cm^{-1}. HRMS (ESI) m/z calcd for $C_{29}H_{44}FO_4Si$ [M + H$^+$] 503.2987, found 503.2970. $[\alpha]^{30}_D$ −44.7 (c 1.00, $CHCl_3$).

(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-((E)-oct-1-en-1-yl)-5-oxocyclopentyl)hept-5-enoate (6k). Following method A, the title compound was isolated as a colorless oil (69 mg, 93%). Following method B, the reaction mixture was stirred for 3 d (51 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.02 (s, 3H), 0.03 (s,

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3H), 0.86 (s, 9H), 1.21 (d, J = 6.4 Hz, 6H), 1.23−1.42 (m, 10H), 1.58−1.71 (m, 3H), 1.95−2.07 (m, 5H), 2.08−2.18 (m, 1H), 2.20−2.26 (m, 2H), 2.26−2.44 (m, 3H), 2.61 (ddd, J = 1.2, 7.1, 18.3 Hz, 1H), 3.98 (ddd, J = 8.5, 8.5, 8.5 Hz, 1H), 5.00 (sep, J = 6.4 Hz, 1H), 5.26 (dd, J = 8.4, 15.2 Hz, 1H), 5.30−5.44 (m, 2H), 5.49−5.59 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.7 (CH_3), 14.1 (CH_3), 18.1 (C), 21.8 (CH_3), 22.6 (CH_2), 24.8 (CH_2), 24.9 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 28.9 (CH_2), 29.3 (CH_2), 31.7 (CH_2), 32.6 (CH_2), 34.1 (CH_2), 47.6 (CH_2), 53.5 (CH), 54.2 (CH), 67.3 (CH), 73.1 (CH), 126.8 (CH), 129.6 (CH), 130.6 (CH), 134.0 (CH), 173.1 (C), 215.3 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2930, 2860, 1739, 1462, 1371, 1250, 1111, 968, 839, 775 cm^{-1}. HRMS (ESI) m/z calcd for $C_{29}H_{53}O_4Si^+$ [M + H$^+$] 493.3708, found 493.3702. $[\alpha]^{23}_D$ −54.5 (c 1.00, $CHCl_3$).

*(Z)-Isopropyl 7-((1R,2S,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-(cyclohex-1-en-1-yl)-5-oxocyclopentyl)hept-5-enoate (**6l**).* Following method A, the additional portions of $[RhCl(COD)]_2$ and **5l** were added after 3 h (instead of after 5 h), and the reaction was irradiated for a further 2 h; the title compound was isolated as a colorless oil (26 mg, 38%). Following method B, boronic acid **5l** (1.0 equiv) was added after 1 d, and the reaction was stirred for another 1 d (63 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (s, 3H), 0.02 (s, 3H), 0.86 (s, 9H), 1.22 (d, J = 6.3 Hz, 6H), 1.56−1.68 (m, 6H), 1.82−1.98 (m, 2H), 1.99−2.08 (m, 4H), 2.09−2.16 (m, 1H), 2.17−2.31 (m, 5H), 2.37 (dd, J = 8.5, 12.3 Hz, 1H), 2.63 (dd, J = 7.3, 18.5 Hz, 1H), 4.11 (ddd, J = 8.1, 8.1, 8.1 Hz, 1H), 4.99 (sep, J = 6.3 Hz, 1H), 5.28−5.43 (m, 2H), 5.54−5.60 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.9 (CH_3), −4.8 (CH_3), 18.0 (C), 21.8 (CH_3), 22.6 (CH_2), 22.9 (CH_2), 24.9 (CH_2), 25.2 (CH_2), 25.3 (CH_2), 25.4 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 34.2 (CH_2), 47.7 (CH_2), 51.7 (CH), 58.4 (CH), 67.4 (CH), 70.9 (CH), 125.9 (CH), 126.8 (CH), 130.5 (CH), 134.1 (C), 173.1 (C), 215.7 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3450, 2935, 2862, 1738, 1634, 1463, 1375, 1249, 1111, 884 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{47}O_4Si^+$ [M + H$^+$] 463.3238, found 463.3240. $[\alpha]^{29}_D$ −53.5 (c 1.00, $CHCl_3$).

*(Z)-Isopropyl 7-((1R,2S,3R)-2-((E)-But-2-en-2-yl)-3-((tert-butyldimethylsilyl)oxy)-5-oxocyclopentyl)hept-5-enoate (**6m**).* Following method A, the additional portions of $[RhCl(COD)]_2$ and **5m** were added after 3 h (instead of after 5 h), and the reaction was irradiated for a further 2 h; the title compound was isolated as a colorless oil (24 mg, 37%). Following method B, boronic acid **5m** (1.0 equiv) was added after 1.5 d, and the reaction was stirred for another 1 d (64 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ −0.01 (s, 3H), 0.01 (s, 3H), 0.85 (s, 9H), 1.22 (d, J = 6.3 Hz, 6H), 1.54−1.69 (m, 8H), 1.95−2.08 (m, 2H), 2.10−2.32 (m, 6H), 2.58−2.72 (m, 1H), 3.04 (dd, J = 9.0, 12.2 Hz, 1H), 4.16 (ddd, J = 8.8 Hz, 1H), 4.99 (sep, J = 6.0 Hz, 1H), 5.28−5.44 (m, 2H), 5.46−5.55 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.0 (CH_3), −4.9 (CH_3), 13.4 (CH_3), 17.9 (C), 18.7 (CH_3), 21.8 (CH_3), 24.8 (CH_2), 24.9 (CH_2), 25.7 (CH_3), 26.4 (CH_2), 34.1 (CH_2), 47.7 (CH_2), 50.7 (CH), 51.7 (CH), 67.4 (CH), 70.0 (CH), 125.0 (CH), 126.6 (CH), 130.6 (CH), 131.4 (C), 173.1 (C), 215.4 (C); FTIR (KBr, neat) $\tilde{\nu}$ 3452, 2938, 1736, 1667, 1461, 1373, 1250, 1108, 972, 838 cm^{-1}. HRMS (ESI) m/z calcd for $C_{25}H_{45}O_4Si$ [M + H$^+$] 437.3081, found 437.3087. $[\alpha]^{25}_D$ −43.6 (c 1.00, $CHCl_3$).

*(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-(2-methylprop-1-en-1-yl)-5-oxocyclopentyl)hept-5-enoate (**6n**).* Following method A, the title compound was isolated as a colorless oil (65 mg, 99%). Following method B, boronic acid **5n** (1.0 equiv) was added after 2 d, and the reaction was stirred for another 1 d (66 mg, >99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 3H), 0.02 (s, 3H), 0.86 (s, 9H), 1.22 (d, J = 6.4 Hz, 6H), 1.60−1.70 (m, 2H), 1.66 (s, 3H), 1.74 (s, 3H), 1.92−1.99 (m, 1H), 2.01−2.08 (m, 2H), 2.12−2.34 (m, 5H), 2.58−2.66 (m, 1H), 2.67−2.77 (m, 1H), 3.95 (ddd, J = 8.1, 8.1, 8.1 Hz, 1H), 4.92 (d, J = 9.6 Hz, 1H), 5.00 (sep, J = 6.4 Hz, 1H), 5.27−5.44 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.0 (CH_3), 18.0 (C), 18.7 (CH_3), 21.8 (CH_3), 24.8 (CH_2), 25.0 (CH_2), 25.6 (CH_3), 25.8 (CH_3), 26.5 (CH_2), 34.1 (CH_2), 47.6 (CH_2), 49.4 (CH), 55.2 (CH), 67.4 (CH), 73.6 (CH), 125.4 (CH), 127.0 (CH), 130.4 (CH), 135.4 (C), 173.1 (C), 215.6 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2937, 2855, 1738, 1463, 1373, 1248, 1150, 1108, 880, 834 cm^{-1}. HRMS (ESI) m/z calcd for $C_{25}H_{45}O_4Si^+$ [M + H$^+$] 437.3082, found 437.3096. $[\alpha]^{23}_D$ −68.2 (c 1.00, $CHCl_3$).

*(Z)-Isopropyl 7-((1R,2S,3R)-3-((tert-Butyldimethylsilyl)oxy)-5-oxo-2-(prop-1-en-2-yl)cyclopentyl)hept-5-enoate (**6o**).* Following method A, the additional portions of $[RhCl(COD)]_2$ and **5o** were added after 3 h (instead of after 5 h), and the reaction was irradiated for a further 2 h; the title compound was isolated as a colorless oil (48 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.016 (s, 3H), 0.024 (s, 3H), 0.86 (s, 9H), 1.22 (d, J = 6.2 Hz, 6H), 1.58−1.69 (m, 3H), 1.73 (s, 3H), 2.04 (ddd, J = 6.9, 6.9, 6.9 Hz, 2H), 2.10−2.35 (m, 5H), 2.50 (dd, J = 8.3, 12.0 Hz, 1H), 2.66 (dd, J = 7.1, 18.4 Hz, 1H), 4.13 (ddd, J = 8.2, 8.2, 8.2 Hz, 1H), 4.85 (s, 1H), 4.93 (s, 1H), 4.99 (sep, J = 6.2 Hz, 1H), 5.28−5.45 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.9 (CH_3), −4.8 (CH_3), 18.0 (C), 19.6 (CH_3), 21.8 (CH_3), 24.8 (CH_2), 25.3 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 34.1 (CH_2), 47.7 (CH_2), 52.2 (CH), 57.7 (CH), 67.4 (CH), 71.3 (CH), 114.2 (CH_2), 126.5 (CH), 130.8 (CH), 142.4 (C), 173.1 (C), 215.2 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3421, 2950, 2862, 1738, 1636, 1376, 1253, 1107, 888, 837, 786 cm^{-1}. HRMS (ESI) m/z calcd for $C_{24}H_{43}O_4Si$ [M + H$^+$] 423.2925, found 423.2927. $[\alpha]^{25}_D$ −85.4 (c 1.00, $CHCl_3$).

*(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-((S,E)-3-((tert-butyldimethylsilyl)oxy)oct-1-en-1-yl)-5-oxocyclopentyl)hept-5-enoate (**6p**).* Following method A, a solution of **2** (0.30 g, 0.79 mmol), boronic acid **5p** (1.2 mmol), $[RhCl(COD)]_2$ (5.8 mg, 11.6 μmol), and aqueous KOH (50 μL, 3.1 M, 155 μmol) in MeOH (5.3 mL) was stirred under microwave irradiation at 30 °C (50 W). After 3 h, additional boronic acid **5p** (1.2 mmol) and $[RhCl(COD)]_2$ (5.8 mg, 11.6 μmol) were added, and the reaction mixture was stirred for 2 h under microwave irradiation (30 °C; 50 W). The mixture was concentrated under reduced pressure, and the resulting residue was purified by column chromatography (eluting with 1:80 (v/v) acetone−hexanes), affording cyclopentanone **6p** as a colorless oil (0.48 g, 98%). On an unoptimized 5.2 mmol scale of **2**, this reaction provided compound **6p** in 82% yield (2.65 g). Using method B, a mixture of **2** (0.32 g, 0.84 mmol), boronic acid **5p** (1.26 mmol), $[RhCl(COD)]_2$ (6.2 mg, 12.5 μmol), and aqueous KOH (53 μL, 3.1 M, 164 μmol) in MeOH (5.6 mL) was stirred at 3 °C. After stirring for 1 d, the product mixture was concentrated under reduced pressure, and the resulting residue was purified by column chromatography (eluting with 1:80 (v/v) acetone−hexanes) affording cyclopentanone **6p** (0.38 g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.02 (s, 3H), 0.04 (s, 3H), 0.049 (s, 3H), 0.052 (s, 3H), 0.83−0.90 (m, 3H), 0.87 (s, 9H), 0.89 (s, 9H), 1.22 (d, J = 6.4 Hz, 6H), 1.23−1.38 (m, 6H), 1.38−1.48 (m, 2H), 1.64 (qui, J = 7.5 Hz, 2H), 1.98−2.10 (m, 3H), 2.15 (dd, J = 8.4, 18.2 Hz, 1H), 2.21−2.33 (m, 3H), 2.34−2.52 (m, 2H), 2.63 (ddd, J = 1.1, 7.0, 18.2 Hz, 1H), 3.98−4.13 (m, 2H), 4.99 (sep, J = 6.4 Hz, 1H), 5.27−5.44 (m, 2H), 5.45−5.63 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.72 (CH_3), −4.66 (CH_3), −4.61 (CH_3), −4.3 (CH_3), 14.0 (CH_3), 18.0 (C), 18.2 (C), 21.8 (CH_3), 22.6 (CH_2), 24.8 (CH_2), 25.1 (CH_2), 25.2 (CH_2), 25.8 (CH_3), 25.9 (CH_3), 26.7 (CH_2), 31.9 (CH_2), 34.1 (CH_2), 38.6 (CH_2), 47.7 (CH_2), 52.7 (CH), 53.9 (CH), 67.4 (CH), 72.6 (CH), 73.3 (CH), 126.6 (CH), 128.6 (CH), 130.8 (CH), 136.5 (CH), 173.1 (C), 215.4 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2937, 2861, 1738, 1577, 1467, 1371, 1250, 1107, 835, 774 cm^{-1}. HRMS (ESI) m/z calcd for $C_{35}H_{70}O_5NSi_2^+$ [M + NH_4^+] 640.4787, found 640.4775. $[\alpha]^{26}_D$ −29.6 (c 1.00, $CHCl_3$).

*(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-((E)-3,3-difluoro-4-phenoxybut-1-en-1-yl)-5-oxocyclopentyl)hept-5-enoate (**6q**).* Following method A, a solution of **2** (57 mg, 0.15 mmol), boronic acid **5q** (0.22 mmol), $[RhCl(COD)]_2$ (1.1 mg, 2.2 μmol), and aqueous KOH (9.5 μL, 3.1 M, 30 μmol) in MeOH (1.0 mL) was stirred under microwave irradiation at 30 °C (50 W). After 3 h, additional boronic acid **5q** (74 μmol) and $[RhCl(COD)]_2$ (1.1 mg, 2.2 μmol) were added, and the reaction mixture was stirred for another 2 h under microwave irradiation (30 °C; 50 W). The mixture was concentrated under reduced pressure, and the resulting residue was purified by column chromatography (eluting with 1:80 (v/v) acetone−hexanes) affording cyclopentanone **6q** as a colorless oil (57 mg, 67%). Under the same reaction conditions, replacing boronic acid **5q** with its corresponding potassium trifluoroborate derivative provided **6q** in

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62% (53 mg). Using method B, a mixture of **2** (0.17 g, 0.45 mmol), boronic acid **5q** (0.66 mmol), [RhCl(COD)]$_2$ (3.3 mg, 6.6 μmol), and aqueous KOH (90 μL, 6.0 M, 0.54 mmol) in MeOH (3.0 mL) was stirred at 3 °C. After the mixture was stirred for 1 d, boronic acid **5q** (0.45 mmol) was added. After the mixture was stirred for an additional 1 d, the product mixture was concentrated under reduced pressure, and the resulting residue was purified by column chromatography (eluting with 1:80 (v/v) acetone−hexanes) affording cyclopentanone **6q** (0.2 g, 78%). ^{1}H NMR (600 MHz, CDCl$_3$): δ 0.040 (s, 3H), 0.044 (s, 3H), 0.86 (s, 9H), 1.21 (d, J = 6.3 Hz, 6H), 1.55−1.64 (m, 2H), 2.01 (ddd, J = 7.2, 7.2, 7.2 Hz, 2H), 2.11−2.22 (m, 4H), 2.31−2.42 (m, 2H), 2.57 (dd, J = 8.7, 20.2 Hz, 1H), 2.66 (ddd, J = 1.0, 7.2, 18.4 Hz, 1H), 4.09 (ddd, J = 8.7, 8.7, 8.7 Hz, 1H), 4.14−4.25 (m, 2H), 4.98 (sep, J = 6.3 Hz, 1H), 5.26−5.32 (m, 1H), 5.36−5.43 (m, 1H), 5.83−5.92 (m, 1H), 6.09−6.18 (m, 1H), 6.91 (d, J = 8.0 Hz, 2H), 7.00 (dd, J = 7.4, 7.4 Hz, 1H), 7.30 (dd, J = 7.4, 8.0 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$): δ −4.8 (CH$_3$), −4.7 (CH$_3$), 18.0 (C), 21.8 (CH$_3$), 24.7 (CH$_2$), 25.0 (CH$_2$), 25.7 (CH$_3$), 26.6 (CH$_2$), 34.0 (CH$_2$), 47.4 (CH$_2$), 53.0 (CH), 53.8 (CH), 67.4 (CH), 69.4 (t, J = 35.0 Hz; CH$_2$), 72.3 (CH), 114.7 (CH), 117.9 (t, J = 238.5 Hz; C), 121.8 (CH), 125.5 (t, J = 24.8 Hz; CH), 126.0 (CH), 129.6 (CH), 131.4 (CH), 136.9 (t, J = 9.0 Hz; CH), 157.9 (C), 173.0 (C), 213.6 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2939, 2863, 1737, 1592, 1490, 1463, 1375, 1307, 1250, 1158 cm^{-1}. HRMS (ESI) m/z calcd for $C_{31}H_{50}F_2NO_5Si$ [M + NH$_4^+$] 582.3421, found 582.3406. $[\alpha]^{24}_D$ −45.0 (c 1.00, CHCl$_3$).

*(Z)-Isopropyl 7-((1R,2R,3R)-3-((tert-Butyldimethylsilyl)oxy)-2-((S,E)-3-((tert-butyldimethylsilyl)oxy)-4-(3-(trifluoromethyl)-phenoxy)but-1-en-1-yl)-5-oxocyclopentyl)hept-5-enoate **(6r)**.* Following method A, the additional portions of [RhCl(COD)]$_2$ and **5r** were added after 3 h (instead of after 5 h), and the reaction was irradiated for a further 2 h; the title compound was isolated as a colorless oil (71 mg, 65%). Following method B, boronic acid **5r** (1.0 equiv) was added after 0.7 d, and the reaction was stirred for another 0.5 d (108.0 mg, >99%). ^{1}H NMR (400 MHz): δ 0.046 (s, 3H), 0.05 (s, 3H), 0.10 (s, 3H), 0.11 (s, 3H), 0.87 (s, 9H), 0.91 (s, 9H), 1.21 (d, J = 6.0 Hz, 6H), 1.58−1.72 (m, 3H), 1.98−2.11 (m, 2H), 2.12−2.45 (m, 5H), 2.52 (dt, J = 7.6, 11.6 Hz, 1H), 2.59−2.70 (m, 1H), 3.80−3.92 (m, 2H), 4.07 (ddd, J = 8.2, 8.2, 8.2 Hz, 1H), 4.51−4.60 (m, 1H), 4.99 (sep, J = 6.0 Hz, 1H), 5.25−5.48 (m, 2H), 5.64−5.81 (m, 2H), 7.03 (dd, J = 2.0, 8.0 Hz, 1H), 7.08 (s, 1H), 7.20 (d, J = 7.6 Hz, 1H), 7.38 (dd, J = 8.0, 8.0 Hz, 1H). ^{13}C NMR (100 MHz): δ −4.7 (CH$_3$), −4.65 (CH$_3$), −4.5 (CH$_3$), 18.0 (C), 18.3 (C), 21.8 (CH$_3$), 24.8 (CH$_2$), 25.1 (CH$_2$), 25.7 (CH$_3$), 25.8 (CH$_3$), 26.7 (CH$_2$), 34.1 (CH$_2$), 47.6 (CH$_2$), 53.1 (CH), 54.1 (CH), 67.4 (CH), 70.9 (CH), 72.6 (CH$_2$), 72.9 (CH), 111.0 (q, J = 4.0 Hz, CH), 117.5 (q, J = 4.0 Hz, CH), 118.06 (CH), 123.9 (q, J = 271.0 Hz, C), 126.5 (CH), 130.0 (CH), 130.9 (CH), 131.5 (CH), 131.9 (q, J = 32.0 Hz, C), 132.3 (CH), 158.9 (C), 173.0 (C), 214.7 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2945, 2862, 1737, 1602, 1457, 1330, 1249, 1167, 1123, 839 cm^{-1}. HRMS (ESI) m/z calcd for [$C_{38}H_{61}F_3O_6Si_2$ + NH$_4^+$] 744.4297, found 744.4291. $[\alpha]^{29}_D$ −35.6 (c 1.00, CHCl$_3$).

*(Z)-Isopropyl 7-((1R,2S,3R)-3-((tert-Butyldimethylsilyl)oxy)-2((S,E)-3((tert-butyldimethylsilyl)-oxo)-5-phenylpentyl-1-en-1-yl)hept-5-enoate **(6s)**.* Following method A, the additional portions of [RhCl(COD)]$_2$ and **5s** were added after 3 h (instead of after 5 h), and the reaction was irradiated for a further 2 h; the title compound was isolated as a colorless oil (63 mg, 64%). Following method B, boronic acid **5s** (1.0 equiv) was added after 0.7 d, and the reaction was stirred for another 0.5 d (93.6 mg, 95%). ^{1}H NMR (400 MHz): δ 0.03 (s, 3H), 0.05 (s, 3H), 0.06 (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 0.92 (s, 9H), 1.22 (d, J = 6.4 Hz, 6H), 1.57−1.72 (m, 3H), 1.74−1.89 (m, 2H), 1.92−2.11 (m, 3H), 2.11−2.43 (m, 4H), 2.52 (dt, J = 7.6, 10.8 Hz, 1H), 2.56−2.74 (m, 3H), 4.08 (ddd, J = 7.6, 7.6, 7.6 Hz, 1H), 4.20 (q, J = 5.5 Hz, 1H), 4.99 (sep, J = 6.4 Hz, 1H), 5.28−5.47 (m, 2H), 5.50−5.68 (m, 2H), 7.12−7.22 (m, 3H), 7.23−7.32 (m, 2H). ^{13}C NMR (100 MHz): δ −4.7 (CH$_3$), −4.63 (CH$_3$), −4.59 (CH$_3$), −4.2 (CH$_3$), 18.0 (C), 18.2 (C), 21.8 (CH$_3$), 24.8 (CH$_2$), 25.3 (CH$_2$), 25.8 (CH$_3$), 25.9 (CH$_3$), 26.7 (CH$_2$), 31.6 (CH$_2$), 34.1 (CH$_2$), 40.2 (CH$_2$), 47.7 (CH$_2$), 52.7 (CH), 53.9 (CH), 67.4 (CH), 72.1 (CH), 73.3 (CH), 125.7 (CH), 126.6 (CH), 128.27 (CH), 128.33 (CH), 129.2 (CH), 130.9 (CH), 135.9 (CH), 142.3 (C), 173.1 (C), 215.3 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3465, 2950, 2859, 1736, 1630, 1462, 1376, 1252, 1103, 1020, 834 cm^{-1}. HRMS (ESI) m/z calcd for [$C_{38}H_{64}O_5Si_2$ + NH$_4^+$] 674.4631, found 674.4611. $[\alpha]^{29}_D$ −35.9 (c 1.00, CHCl$_3$).

*(Z)-Isopropyl 7-((1R,2R,3R,5S)-3-[(tert-Butyldimethylsilyl)oxy]-2-{(S,E)-3-[(tert-butyldimethylsilyl)oxy]oct-1-en-1-yl}-5-hydroxycyclopentyl)hept-5-enoate **(8p)**.* To a solution of cyclopentanone **8p** (80 mg, 0.13 mmol) in THF (6.4 mL) at −78 °C was added a 1.0 M THF solution of L-Selectride (0.15 mL, 0.15 mmol). The mixture was stirred at −78 °C for 20 min, and was then warmed to ambient temperature and was concentrated under reduced pressure. The residue was purified by column chromatography (eluting with 1:8 (v/v) EtOAc−hexanes) affording the title PGF$_{2\alpha}$ derivative **8p** (61 mg, 76%) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.01 (s, 3H), 0.04 (s, 3H), 0.046 (s, 3H), 0.049 (s, 3H), 0.87 (s, 9H), 0.88 (s, 9H), 0.83−0.90 (m, 3H), 1.22 (d, J = 6.2 Hz, 6H), 1.23−1.52 (m, 9H), 1.67 (qui, J = 7.5 Hz, 2H), 1.77−1.92 (m, 2H), 2.04−2.21 (m, 3H), 2.22−2.39 (m, 4H), 2.68 (d, J = 9.3 Hz, 1H), 3.98−4.15 (m, 3H), 4.99 (sep, J = 6.2 Hz, 1H), 5.28−5.39 (m, 2H), 5.41−5.52 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$): δ −4.9 (CH$_3$), −4.8 (CH$_3$), −4.6 (CH$_3$), −4.3 (CH$_3$), 14.0 (CH$_3$), 17.8 (C), 18.2 (C), 21.8 (CH$_3$), 22.6 (CH$_2$), 25.0 (CH$_2$), 25.8 (CH$_3$), 25.9 (CH$_3$), 26.6 (CH$_2$), 26.7 (CH$_2$), 31.8 (CH$_2$), 34.2 (CH$_2$), 38.6 (CH$_2$), 42.9 (CH$_2$), 51.8 (CH), 56.4 (CH), 67.3 (CH), 73.2 (CH), 74.7 (CH), 80.0 (CH), 129.2 (CH), 129.5 (CH), 130.8 (CH), 134.4 (CH), 173.2 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3433, 2936, 1722, 1636, 1457, 1250, 1088, 832, 659, 503 cm^{-1}. HRMS (ESI) m/z calcd for $C_{35}H_{69}O_5Si_2^+$ [M + H$^+$] 625.4678, found 625.4676. $[\alpha]^{23}_D$ −6.3 (c 1.00, CHCl$_3$).

*(Z)-7-((1R,2R,3R,5S)-3-[(tert-Butyldimethylsilyl)oxy]-2-{(S,E)-3-[(tert-butyldimethylsilyl)oxy]oct-1-en-1-yl}-5-hydroxycyclopentyl)-hept-5-enoic Acid **(9p)**.* A mixture of PGF$_{2\alpha}$ derivative **8p** (1.70 g, 2.7 mmol) in MeOH (20 mL) and 25% NaOMe in MeOH (9.3 mL, 41 mmol) was stirred at rt until no more **8p** was detected by TLC (eluting with 1:4 EtOAc−n-heptane). 10% Aqueous NaOH (10 mL) was added, and the mixture was stirred at 50 °C for 2 h. The solution was cooled to rt and was extracted with 10% aqueous citric acid (60 mL). The layers were separated, and the aqueous layer was back-extracted three times with EtOAc (60 mL each). The organic layers were combined, washed with brine (150 mL), dried over anhydrous MgSO$_4$ (4.0 g), filtered, and concentrated under reduced pressure. The resulting residue was purified by column purification over silica gel (eluting with 1:2 (v/v) EtOAc−n-heptane (800 mL)) to give the title PGF$_{2\alpha}$ derivative **9p** (1.42 g, 2.44 mmol, 90% yield) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.02 (s, 3H), 0.04 (s, 3H), 0.048 (s, 3H), 0.051 (s, 3H), 0.82−0.90 (m, 3H), 0.87 (s, 9H), 0.88 (s, 9H), 1.21−1.34 (m, 7H), 1.35−1.55 (m, 3H), 1.69 (qui, J = 7.4 Hz, 2H), 1.79−1.92 (m, 2H), 2.02−2.21 (m, 3H), 2.21−2.39 (m, 4H), 3.99−4.07 (m, 2H), 4.09−4.14 (m, 1H), 5.29−5.39 (m, 2H), 5.41−5.50 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$): δ −4.9 (CH$_3$), −4.7 (CH$_3$), −4.6 (CH$_3$), −4.3 (CH$_3$), 14.0 (CH$_3$), 17.9 (C), 18.3 (C), 22.6 (CH$_2$), 24.7 (CH$_2$), 25.0 (CH$_2$), 25.8 (CH$_3$), 25.9 (CH$_3$), 26.5 (CH$_2$), 26.7 (CH$_2$), 31.8 (CH$_2$), 33.4 (CH$_2$), 38.5 (CH$_2$), 42.9 (CH$_2$), 51.9 (CH), 56.5 (CH), 73.3 (CH), 74.7 (CH), 80.0 (CH), 129.0 (CH), 129.7 (CH), 130.8 (CH), 134.4 (CH), 179.0 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3446, 2937, 2863, 2356, 1714, 1252, 1081, 965, 837 cm^{-1}. HRMS (ESI) m/z calcd for $C_{32}H_{62}O_5Si_2Na$ [M + Na$^+$] 605.4028, found 605.4018. $[\alpha]^{25}_D$ +15.5 (c 1.00, CHCl$_3$).

*(Z)-7-((1R,2R,3R,5S)-3-Hydroxy-2-{(S,E)-3-hydroxy-oct-1-en-1-yl}-5-hydroxycyclopentyl)hept-5-enoic Acid (PGF$_{2\alpha}$; Dinoprost **(1a)**).* A mixture of PGF$_{2\alpha}$ derivative **9p** (1.1 g, 1.9 mmol) in THF (19 mL) and 3 N aqueous HCl (6.3 mL, 19 mmol) was stirred at rt for 6 h. The reaction mixture was neutralized with saturated aqueous NaHCO$_3$ (30 mL) and extracted twice with EtOAc (40 mL each). The organic layers were combined, washed with brine (50 mL), dried over anhydrous MgSO$_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (33 g; eluting with 1:20 (v/v) MeOH−CH$_2$Cl$_2$ (300 mL) then 1:5 (v/v) MeOH−CH$_2$Cl$_2$ (500 mL)) to give dinoprost (**1a**) as a colorless oil (595 mg, 89%). ^{1}H NMR (400 MHz, d_4-MeOH): δ 0.91 (t, J = 6.8 Hz, 3H), 1.29−1.38 (m, 6H), 1.43−1.52 (m, 2H), 1.58−1.69 (m, 4H),

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2.07−2.14 (m, 3H), 2.15−2.23 (m, 1H), 2.23−2.31 (m, 3H), 2.35 (ddd, J = 4.8, 6.8, 10.4 Hz, 1H), 3.80−3.87 (m, 1H), 4.01 (q, J = 5.2 Hz, 1H), 4.10 (td, J = 1.8, 4.5 Hz, 1H), 5.31−5.39 (m, 1H), 5.43−5.55 (m, 3H). ^{13}C NMR (100 MHz, d_4-MeOH): δ 14.6 (CH_3), 23.8 (CH_2), 26.32 (CH_2), 26.35 (CH_2), 26.5 (CH_2), 27.8 (CH_2), 33.1 (CH_2), 35.0 (CH_2), 38.5 (CH_2), 44.4 (CH_2), 50.9 (CH), 56.2 (CH), 72.3 (CH_2), 74.1 (CH_2), 77.9 (CH), 130.4 (CH), 130.5 (CH), 134.3 (CH), 136.6 (CH), 178.5 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3346, 3006, 2954, 2930, 2858, 1708, 1550, 1456, 1409, 1237, 1081, 1053, 1025, 969 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{34}O_5Na^+$ [M + Na$^+$] 377.2298, found 377.2298. $[\alpha]^{20}_{D}$ +23.7 (c 0.50, THF).

*(Z)-Isopropyl 7-{(1R,2R,3R,5S)-3-[(tert-Butyldimethylsilyl)oxy]-2-((E)-3,3- difluoro-4-phenoxybut-1-en-1-yl)-5-hydroxycyclopentyl}-hept-5-enoate (**8q**).* A mixture of a THF (15 mL) solution of protected PGE derivative **6q** (1.42 g, 2.51 mmol) and a 1.0 M THF solution of L-Selectride (3.45 mL, 3.45 mmol) was stirred at −78 °C for 40 min. The mixture was warmed to ambient temperature and was washed with saturated aqueous NH_4Cl (5 mL). The layers were separated, and the aqueous layer was back-extracted three times with EtOAc (15 mL each). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and evaporated to afford the crude product as an oil. This was purified by column chromatography over silica gel (eluting with 1:8 (v/v) EtOAc−hexanes) to afford the title protected PGF$_{2\alpha}$ derivative **8q** (1.34 g, 94%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.027 (s, 3H), 0.034 (s, 3H), 0.86 (s, 9H), 1.21 (d, J = 6.2 Hz, 6H), 1.52−1.61 (m, 1H), 1.65 (m, 2H), 1.73−1.83 (m, 1H), 2.01−2.15 (m, 4H), 2.20−2.27 (m, 2H), 2.27−2.47 (m, 3H), 4.05−3.93 (m, 1H), 4.08−4.23 (m, 3H), 4.99 (sep, J = 6.2 Hz, 1H), 5.28−5.49 (m, 2H), 5.76 (dt, J = 11.1, 15.8 Hz, 1H), 6.14 (ddt, J = 2.2, 9.3, 15.8 Hz, 1H), 6.87−6.94 (m, 2H), 6.96−7.03 (m, 1H), 7.25−7.33 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.9 (CH_3), −4.7 (CH_3), 17.9 (C), 21.8 (CH_3), 24.9 (CH_2), 25.7 (CH_3), 26.1 (CH_2), 26.6 (CH_2), 34.1 (CH_2), 43.4 (CH_2), 50.4 (CH), 55.7 (CH), 67.4 (CH), 69.5 (t, J = 35.0 Hz; CH_2), 73.5 (CH), 78.5 (CH), 114.7 (CH), 118.1 (t, J = 239.0 Hz; C), 121.7 (CH), 123.6 (t, J = 25.0 Hz; CH), 128.8 (CH), 129.5 (CH), 129.8 (CH), 138.6 (t, J = 9.0 Hz; CH), 158.0 (C), 173.2 (C). FTIR (KBr, neat): $\tilde{\nu}$ 3451, 2954, 2879, 1724, 1595, 1498, 1463, 1375, 1301, 1246, 1101 cm^{-1}. HRMS (ESI) m/z calcd for $C_{31}H_{49}F_2O_5Si$ [M + H$^+$] 567.3312, found 567.3316. $[\alpha]^{26}_{D}$ −9.4 (c 0.11, $CHCl_3$).

*(Z)-Isopropyl 7-[(1R,2R,3R,5S)-2-((E)-3,3-Difluoro-4-phenoxybut-1-en-1-yl)-3,5- dihydroxycyclopentyl]hept-5-enoate (Tafluprost (**1b**)).* To a THF (7 mL) solution of protected PGF$_{2\alpha}$ derivative **8q** (2.11 g, 3.73 mmol) at 0 °C was added a 1.0 M THF solution of TBAF (4.5 mL, 4.5 mmol). The mixture was allowed to warm to room temperature over a 30 min period and was then stirred for another 3 h. The product mixture was washed with saturated aqueous NH_4Cl (2.5 mL), and the layers were separated. The aqueous phase was back-extracted three times with EtOAc (20 mL each), and the organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and evaporated to afford the crude product. This was purified by column chromatography (eluting with 1:5 (v/v) EtOAc−hexanes) to afford tafluprost[12] (**1b**) as a colorless oil (1.52 g, 90%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.22 (d, J = 6.3 Hz, 6H), 1.58−1.71 (m, 3H), 1.85 (dt, J = 1.3, 14.6 Hz, 1H), 2.01−2.14 (m, 4H), 2.26 (td, J = 3.0, 7.4 Hz, 2H), 2.29−2.38 (m, 1H), 2.47 (td, J = 4.2, 9.6 Hz, 1H), 4.00−4.05 (m, 1H), 4.16−4.24 (m, 3H), 5.00 (sep, J = 6.3 Hz, 1H), 5.34−5.43 (m, 2H), 5.80 (dt, J = 11.1, 15.7 Hz, 1H), 6.10 (ddt, J = 2.4, 9.1, 15.7 Hz, 1H), 6.89−6.94 (m, 2H), 6.97−7.02 (m, 1H), 7.27−7.32 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.80 (CH_3), 21.82 (CH_3), 24.8 (CH_2), 25.7 (CH_2), 26.6 (CH_2), 34.0 (CH_2), 43.0 (CH_2), 50.5 (CH), 55.8 (CH), 67.7 (CH), 69.5 (t, J = 34.5 Hz; CH_2), 73.3 (CH), 78.0 (CH), 114.8 (CH), 118.2 (t, J = 240.0 Hz; C), 121.8 (CH), 123.6 (t, J = 24.8 Hz; CH), 128.6 (CH), 129.6 (CH), 130.1 (CH), 138.6 (t, J = 8.3 Hz; CH), 158.0 (C), 173.4 (C). ^{19}F NMR (564 MHz): δ −103.4 (d, J = 255.2 Hz), −104.1 (d, J = 255.5 Hz). FTIR (KBr, neat): $\tilde{\nu}$ 3410, 2929, 1720, 1593, 1494, 1376, 1247, 1156, 1103, 1052 cm^{-1}. HRMS (ESI) m/z calcd for $C_{25}H_{35}F_2O_5^+$ [M + H$^+$] 453.2447, found 453.2449. $[\alpha]^{23}_{D}$ +21.6 (c 1.00, $CHCl_3$).

(Z)-Methyl-7-((1R,2R*,3R*)-3-((tert-butyldimethylsilyl)oxy)-5-oxo-2-((E)-styryl)cyclopentyl)hept-5-enoate (**11**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (s, 3H), 0.02 (s, 3H), 0.86 (s, 9H), 1.21−1.35 (m, 6H), 1.36−1.47 (m, 1H), 1.51−1.68 (m, 3H), 2.03−2.12 (m, 1H), 2.19−2.30 (m, 3H), 2.59 (dt, J = 8.4, 11.6 Hz, 1H), 2.67 (ddd, J = 1.0, 7.0, 18.2 Hz, 1H), 3.64 (s, 3H), 4.11 (ddd, J = 8.1, 8.1, 8.1 Hz, 1H), 6.05 (dd, J = 8.6, 16.0 Hz, 1H), 6.52 (d, J = 16.0 Hz, 1H), 7.21−7.27 (m, 1H), 7.29−7.39 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.8 (CH_3), −4.7 (CH_3), 18.1 (C), 24.9 (CH_2), 25.7 (CH_3), 26.6 (CH_2), 27.9 (CH_2), 28.9 (CH_2), 29.3 (CH_2), 34.0 (CH_2), 47.5 (CH_2), 51.4 (CH_3), 54.2 (CH), 54.9 (CH), 73.0 (CH), 126.1 (CH), 127.4 (CH), 128.6 (CH), 130.1 (CH), 132.7 (CH), 137.1 (C), 174.2 (C), 215.6 (C). FTIR (KBr, neat): $\tilde{\nu}$ 2931, 1743, 1638, 1463, 1250, 1116, 965, 838, 777 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{42}O_4NaSi$ [M + Na$^+$] 481.2750, found 481.2751.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01913.

^{1}H and ^{13}C NMR spectra of compounds **S1**, **S2**, **5p**, **S3**, **S4**, **5q**, **S5**, **S6**, **5r**, **S7**, **S8**, **5s**, and **7**/11-*epi*-**7**; PGE$_2$ derivatives **6a**−**6s** and **11**; PGF$_{2\alpha}$ derivatives **8p**, **9p**, **1a**, **8q**, and **1b**; and the 2D NOESY spectrum of **6a** (PDF)

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Notes

The authors declare no competing financial interest.

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