IMPROVED PREPARATION OF A-RING PHOSPHINE OXIDES FOR THE SYNTHESIS OF VITAMIN D ANALOGS

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ABSTRACT

A new, high yielding, two-step process for the preparation of A-ring phosphine oxides from allyl alcohols, useful for the synthesis of vitamin D analog, is described, in which triphosgene and diphenylphosphine oxide are used for chlorination and subsequent substitution reactions, respectively.

A-Ring phosphine oxides (such as 3)[1-7] are one of the most useful synthons in the synthesis of vitamin D analogs and have successfully been utilized in the synthesis of 1α,25-dihydroxyvitamin D3,[8] the hormonally active metabolite of vitamin D3, as well as many other analogs.[9-11] In order to support a clinical development program at Hoffmann-La Roche, a large quantity of A-ring phosphine oxide 3a, 1α-fluoro A-ring

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synthon, was required. During our work to create an efficient method of preparation of this compound, we improved the last two steps of the synthesis: conversion of allyl alcohol 1 to A-ring synthon 3.

The standard method[8] for the transformation of allyl alcohols to the A-ring phosphine oxides (Sch. 1), developed by the Uuskovic group, consists of three steps: (1) chlorination of allyl alcohols with NCS/Me₂S to give allyl chlorides,[12] (2) displacement of the chlorides with lithium diphenyl phosphide, and (3) oxidation of the resulting phosphines with hydrogen peroxide. Transformation of 1a into 3a has also been carried out using this protocol to give the desired A-ring phosphine oxide in 33–49% yields after chromatographic purification.[13,14]

Allyl chloride 2a obtained by this method was found to be unstable, thereby requiring a rapid chromatographic purification and an immediate subsequent reaction in order to obtain acceptable yields of 3a. Since the instability of chloride 2a seems to be increased by the presence of by-products formed from the reagents (NCS/Me₂S), several other methods were examined for this transformation. We found that the reaction of a hexane solution of allyl alcohol 1a with triphosgene[15] in the presence of an organic base (triethylamine or pyridine)[16] proceeded cleanly to give, after extractive workup, allyl chloride 2a with a suitable purity for the next reaction without chromatographic purification. More importantly, the crude allyl chloride 2a thus obtained was found to be much more stable than that obtained by the standard method[8] and could be stored at –20°C for several months without noticeable decomposition.

Additional important factors that contributed to the low yields of 3a reported by previous investigators,[13,14] are the highly sensitive nature of diphenylphosphine and its anion toward oxygen, and the reactivity of the allyl fluoride moiety toward lithium diphenyl phosphide. When excess reagent was used to compensate for the loss by oxidation, an increased amount of bis-substituted phosphine oxide 4 was produced. In addition, formation of the corresponding S₃N₂ product 5 was also a serious problem, resulting typically in less than 50% yield of the desired phosphine oxide 3a.
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In order to overcome these drawbacks, diphenylphosphine oxide was examined as an alternative. Unlike diphenylphosphine, this compound is stable in air and, although currently expensive, can be prepared by hydrolysis of inexpensive chlorodiphenylphosphine with water.\textsuperscript{[17]} To our pleasant surprise, its sodium salt (prepared by treatment of diphenylphosphine oxide with sodium hydride in DMF) reacted cleanly with chloride 2a to give 3a without formation of 4 or 5. After aqueous workup, 3a was obtained as a crystalline solid, which was recrystallized from diisopropyl ether. A second crop was obtained, after silica gel chromatography, to give 3a in a total yield of 76\% over the two steps from alcohol 1a.

The new method described herein [see general procedures in Experimental] has been successfully applied to the preparation of other A-ring phosphine oxides, such as 3b,c (Sch. 2) and the trans analogs 8a–c, in high yield from the corresponding allyl alcohols (Sch. 3).

In summary, a new protocol for the preparation of A-ring phosphine oxides 3 and the corresponding trans-isomers 8 from allyl alcohols 1 and 6, respectively, was developed. In the first step, the triphosgene method directly gave allyl chlorides of suitable purity and stability, thus eliminating the chromatographic purification required by the NCS/Me\textsubscript{3}S protocol. In the substitution reaction, the highly air-sensitive diphenylphosphine, the quality of which often varies significantly from one lot to another (a source of

\begin{align*}
1 \text{ (a: } R = -\text{OTBS)} & \quad 2 \text{ (a: } R = -\text{OTBS)} & \quad 3 \text{ (a: } R = -\text{OTBS)} \quad 76\% \text{ yield} \\
2 \text{ (b: } R = -\text{OTBS)} & \quad 3 \text{ (b: } R = -\text{OTBS)} & \quad 83\% \text{ yield} \\
2 \text{ (c: } R = -\text{OTBS)} & \quad 3 \text{ (c: } R = -\text{OTBS)} & \quad 89\% \text{ yield}
\end{align*}

\textit{Scheme 2.}
inconsistent reactions), was replaced with air-stable diphenylphosphine oxide, leading to highly reproducible yields of the A-ring phosphine oxides.

EXPERIMENTAL

General

All reactions were performed in dried glassware under a positive pressure of nitrogen. Reaction extracts and chromatography fractions were concentrated using a Büchi rotary evaporator at approx. 10 Torr using a diaphragm pump, then at high vacuum to approx. 0.01 Torr using an oil pump. TLC analysis was performed using silica gel 60 F<sub>254</sub> precoated glass plates (EM Science), and detected by UV<sub>254</sub> or phosphomolybdic acid (PMA) stain. <sup>1</sup>H-NMR spectra were recorded on Varian spectrometers operating at 300 MHz or 400 MHz. CDCl<sub>3</sub> was treated with basic alumina prior to use. Melting points were obtained on a Thomas Hoover capillary melting point apparatus and are uncorrected. Commercial grade reagents and solvents were used without purification, except as indicated.

Representative Procedures

[1R-(1β,3Z,5α)−][3-(2-Chloroethylidene)-5-fluoro-4-methylene cyclohexyl]oxy][1,1-dimethylethyl]dimethylsilane (2a): A solution of pyridine (4.50 mL, 55.6 mmol) in hexane (20 mL) was added over 30 min to a cold solution (0°C) of allyl alcohol 1a (8.07 g, 28.2 mmol) and triphosgene (4.18 g, 14.1 mmol) in hexane (150 mL). After stirring at 0°C for 30 min and at r.t. for 30 min, the reaction mixture was washed with saturated aq. CuSO₄ solution (3 × 200 mL). The combined aqueous layers were back-extracted with
hexane (2 x 100 mL). The organic layers were combined, dried (MgSO₄), and concentrated in vacuo to give 9.0 g (overweight) of crude 2a as pale yellow oil.

- **¹H NMR (300 MHz, CDCl₃): δ 0.06 (s, 6H), 0.88 (s, 9H), 1.83-2.05 (m, 1H), 2.06-2.30 (m, 2H), 2.48 (dd, J₁ 4 Hz, J₂ 13 Hz, 1H), 4.07-2.22 (m, 3H), 5.14 (ddd, J₁ 3 Hz, J₂ 6 Hz, J₃ 50 Hz, 1H), 5.19 (s, 1H), 5.38 (s, 1H), 5.65 (t, J 7 Hz, 1H).** All other analytical and physical data were in agreement with those reported.[¹][³]

- **[3S-(1Z,3β,5β)]-[2-{3-Fluoro-5-[(1,1-dimethylethyl)dimethylsilyl]oxy}-2-methylene-1-cyclohexylideneethylidiphenylphosphine Oxide (3a):** Diphenylphosphin oxide (6.70 g, 33.1 mmol) was added portionwise, over 15 min, to a suspension of sodium hydride (1.33 g, 33.1 mmol) in DMF (50 mL) at 10°C. The resulting yellow solution was stirred at r.t. for 30 min and cooled to -60°C. Then, a solution of crude allyl chloride 2a (9.0 g, prepared above) was added dropwise over 15 min. The reaction mixture was stirred at -60°C for 2 h and then at r.t. for 1 h, diluted with ethyl ether and washed with water. The aqueous layers were extracted with ethyl ether. The organic layers were combined, dried (MgSO₄) and concentrated in vacuo to give a white solid. The crude product was recrystallized from diisopropyl ether to give 7.93 g (59.8%) of pure 3a as a white solid (m.p. 126-127°C). The mother liquor was subjected to chromatographic purification on silica gel to give 2.22 g (16.7%) of 3a. Thus, the total yield of 3a was 10.1 g (76% overall from 1a). **¹H NMR (300 MHz, CDCl₃): δ 0.08 (s, 6H), 0.82 (s, 9H), 1.70-1.97 (m, 1H), 2.05-2.27 (m, 2H), 2.42 (br d, J 13 Hz, 1H), 3.25 (m, 2H), 4.00 (m, 1H), 5.03 (dm, J 50 Hz, 1H), 5.12 (s, 1H), 5.30 (s, 1H), 5.50 (m, 1H), 7.4-7.6 and 7.7-7.8 (2m, 10H).** All other analytical and physical data were in agreement with those reported.[¹][³]

### Analytical Data for Synthesized Compounds

- **[3S-(1Z,3β,5β)]-[3-Fluoro-5-[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methylene-1-cyclohexylideneethylidiphenylphosphine Oxide (1a):** ¹H NMR (300 MHz, CDCl₃): δ 0.08 (s, 6H), 0.88 (s, 9H), 1.90 (m, 1H), 2.1-2.3 (m, 2H), 2.50 (brd, J 13 Hz, 1H), 4.10-4.35 (m, 3H), 4.95 (s, 1H), 5.10 (brd, J 50 Hz, 1H), 5.30 (s, 1H), 5.65 (t, J 6 Hz, 1H). All other analytical and physical data were in agreement with those reported.[¹][³]

- **[3S-(1Z,3α,5β)]-2-[3,5-Bis[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2-methylene-1-cyclohexylideneethylidiphenylphosphine Oxide (1b):** ¹H NMR (400 MHz, CDCl₃): δ 0.06 (s, 12H), 0.88 (s, 9H), 0.89 (s, 9H), 1.82 (m, 2H), 2.19 (dd, J₁ 7 Hz, J₂ 13 Hz, 1H), 2.41 (brd, J 13 Hz, 1H), 4.16 (m, 2H), 4.40 (brt, J 6 Hz, 1H), 4.77 (s, 1H), 5.17 (s, 1H), 5.54 (t, J 6 Hz, 1H). All other analytical and physical data were in agreement with those reported.[³]
[3S-(1Z,3z,55)]-2-[3S-5-Bis[(1,1-Dimethyl)dimethylsilyl]oxy]-2-methylene cyclohexyldiene]-1-chloroethane (2b): 1H NMR (300 MHz, CDCl3): δ 0.06 (s, 6H), 0.07 (s, 6H), 0.89 (s, 18H), 1.70-1.92 (m, 2H), 2.20 (dd, J1, J2 13 Hz, 1H), 2.40 (brd, J 13 Hz, 1H), 4.17 (m, 2H), 4.41 (dd, J1, J4 Hz, J2 8 Hz, 1H), 4.97 (brs, 1H), 5.24 (brs, 1H), 5.54 (t, J 8 Hz, 1H). All other analytical and physical data were in agreement with those reported.[8]

[3S-(1Z,3z,55)]-2-[3S-5-Bis[(1,1-Dimethyl)dimethylsilyl]oxy]-2-methylene cyclohexyldiene]ethyl diphenylphosphine oxide (3b): 1H NMR (300 MHz, CDCl3): δ 0.04 (4s, 12H), 0.86 (s, 9H), 0.90 (s, 9H), 1.71 (m, 1H), 1.85 (m, 1H), 2.18 (m, 1H), 2.33 (brd, J 13 Hz, 1H), 3.19 (dt, J1, J6 Hz, J3 16 Hz, 1H), 3.38 (m, 1H), 4.12 (brs, 1H), 4.36 (m, 1H), 4.75 (s, 5H), 5.16 (s, 1H), 5.34 (q, J 7 Hz, 1H), 7.4-7.55 and 7.65-7.80 (2m, 10H). All other analytical and physical data were in agreement with those reported.[8]

[3R-(1Z,3z,55)]-2-[3S-5-Bis[(1,1-Dimethyl)dimethylsilyl]oxy]-2-methylene cyclohexyldiene]ethanol (1e): Yellow oil. αD = +72.5 (c = 1.35, CH2Cl2). IR (CHCl3): 3617 cm−1. UV (MeOH): λmax = 226 nm (ε = 5650), 255 (1600). 1H NMR (300 MHz, CDCl3): δ 0.06 (s, 12H), 0.86 (s, 9H), 0.89 (s, 9H), 2.18 (m, 2H), 2.42 (m, 1H), 3.73 (m, 1H), 3.97 (m, 1H), 4.19 (dd, J1, J3 Hz, J6 Hz, J12 Hz, 1H), 4.30 (dd, J1, J6 Hz, J3 12 Hz, 1H), 4.78 (s, 1H), 5.33 (s, 1H), 5.55 (t, J 6 Hz, 1H). Anal. Calcd. for C19H24O3Si2 (398.73): C, 63.26%; H, 10.62%. Found: C, 63.12%; H, 10.58%.

[3R-(1Z,3z,55)]-2-[3S-5-Bis[(1,1-Dimethyl)dimethylsilyl]oxy]-2-methylene cyclohexyldiene]chloroethane (2e): Colorless oil. αD = +125 (c = 1.32, CH2Cl2). MS (m/e): 417 (M+H, 32%), 415 (M+H, 30), 401 (M–Me,10), 381 (12), 249 (38), 147 (65), 133 (100), 117 (62). MSHR: c for C31H30O2Si2Cl1. 1H NMR (300 MHz, CDCl3): δ 0.08 (s, 6H), 0.09 (s, 6H), 0.85 (s, 9H), 0.92 (s, 9H), 2.18 (m, 2H), 2.43 (m, 1H), 3.71 (m, 1H), 3.94 (m, 1H), 4.14 (m, 2H), 4.96 (t, J 2 Hz, 1H), 5.39 (t, J 2 Hz, 1H), 5.58 (dt, J1, J2 Hz, J3 2 Hz, 1H). Anal. Calcd. for C31H30O2Si2Cl (417.17): C, 60.46%; H, 9.91%. Found: C, 60.55%; H, 10.03%.

[3S-(1Z,3z,55)]-2-[3S-5-Bis[(1,1-Dimethyl)dimethylsilyl]oxy]-2-methylene cyclohexyldiene]diphenylphosphine oxide (3e): Colorless oil. αD = +42 (c = 1.02, CHCl3). IR (CHCl3): 1257, 836, 694 cm−1. UV (MeOH): λmax = 211 nm (ε = 23,700), 255 (2400), 272 (2100). 1H NMR (300 MHz, CDCl3): δ 0.06 (s, 6H), 0.07 (s, 6H), 0.85 (s, 9H), 0.90 (s, 9H), 2.10 (m, 2H), 2.39 (m, 1H), 3.05–3.46 (2m, 3H), 3.52 (m, 1H), 4.75 (s, 1H), 5.29 (s, 1H), 5.50 (m, 1H), 7.40–7.60 and 7.63–7.80 (2m, 10H). Anal. Calcd. for C35H30O2PSi2 (582.90): C, 68.00%; H, 8.82%. Found: C, 68.24%; H, 8.98%.

[3S-(1E,3z,55)]-3-Fluoro-5-[(1,1-Dimethyl)dimethylsilyl]oxy]-2-methylene cyclohexyldiene]ethanol (6a): Colorless oil. αD = −35.2 (c = 0.21, CHCl3). IR (CHCl3): 3609 cm−1. MS (m/e): 287 (M+H, 22%), 285 (M–H, 12), 269 (M–OH, 13), 154 (50), 137 (100). 1H NMR (300 MHz, CDCl3): δ 0.08
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(s, 6H), 0.88 (s, 9H), 1.85–2.30 (m, 3H), 2.53 (dd, J₁ 4 Hz, J₂ 9 Hz), 4.10–4.25 (m, 3H), 5.05 (s, 1H), 5.17 (ddd, J₁ 4 Hz, J₂ 7 Hz, J₃ 50 Hz, 1H), 5.19 (s, 1H), 5.86 (t, J 7 Hz, 1H). Anal. Calcld. for C₁₃H₂₇F₂O₅Si (286.46): C, 62.89%; H, 9.50%. Found: C, 62.61%; H, 9.42%.

[1R-(1β,3E,5α)][3-(2-Chloroethylidene)-5-fluoro-4-methylenecyclohexyl]oxy][1,1-dimethylthethyl]dimethyldisilane (7a): Colorless oil. MS (m/e): 305 (M+H, 14%), 303 (M–H, 18), 289 (25), 269 (M–Cl, 28), 247 (M–C₆H₄, 20), 227 (32), 211 (28), 154 (30), 137 (100). IR (CHCl₃): 837 cm⁻¹. H NMR (400 MHz, CDCl₃): δ 0.99 (s, 6H), 0.89 (s, 9H), 1.78–2.05 (m, 1H), 2.08–2.20 (m, 1H), 2.25 (dd, J₂ 7 Hz, J₃ 14 Hz, 1H), 2.56 (d, J 14 Hz, 1H), 4.11 (d, J 8 Hz, 2H), 4.18 (m, 1H), 5.10 (s, 1H), 5.18 (ddd, J₁ 4 Hz, J₂ 7 Hz, J₃ 50 Hz, 1H), 5.24 (s, 1H), 5.87 (t, J 8 Hz, 1H). Anal. Calcld. for C₁₃H₂₇ClFOSi (304.90): C, 59.09%; H, 8.60%. Found: C, 58.86%; H, 8.80%.

[3S-(1E,3α,5β)][2-3-Fluoro-5-[(1,1-dimethylthethyl]dimethylsilyl]oxy]-2-methylenecyclohexyldiene]ethyl]diphenylphosphine oxide (8a): Off-white oil. χ₀ = +13.3 (ε = 0.9, CHCl₃). UV (MeOH): λ₁ = 223 (ε = 22,500, 272 (2100). IR (CHCl₃): 1255, 838, 694 cm⁻¹. MS (m/e): 493 (M+Na, 55%), 471 (M+H, 60). MSHR: for M+Na calcld 493.2098, found 493.2101. H NMR (300 MHz, CDCl₃): δ 0.00 (s, 3H), 0.01 (s, 3H), 0.84 (s, 9H), 1.68–1.92 (m, 2H), 2.04–2.16 (m, 1H), 2.31 (d, J 14 Hz, 1H), 3.08–3.26 (m, 2H), 3.93 (septet, J 4 Hz, 1H), 4.95 (s, 1H), 5.00 (s, 1H), 5.06 (dd, J₁ 3 Hz, J₃ 6 Hz, J₄ 50 Hz, 1H), 5.65 (q, J 7 Hz, 1H), 7.2–7.6 and 7.62–7.9 (2m, 10H). Anal. Calcld. for C₂₇H₄₉F₂O₂PSi (470.63): C, 68.91%; H, 7.71%. Found: C, 68.51%; H, 7.58%.

[3S-(1E,3α,5β)][2-3-5-Bis[(1,1-Dimethylthethyl]dimethylsilyl]oxy]-2-methylenecyclohexyldiene]ethanol (6b): White solid, m.p. 55–57 °C. [α]₀ = −17.9 (c = 0.78, CHCl₃). UV (MeOH): λ₁ = 222 nm (c = 6440). IR (CHCl₃): 3700, 1257 cm⁻¹. MS (m/e): 398 (M+, 10%), 380 (H₂O, 66), 367 (M–CH₂OH, 32), 341 (M–C₆H₄, 100), 323 (92). H NMR (400 MHz, CDCl₃): δ 0.06 and 0.07 (2s, 12H), 0.90 (s, 18H), 1.75 (m, 1H), 1.90 (m, 1H), 2.27 (d, J 16 Hz, 1H), 2.41 (dd, J₁ 6 Hz, J₂ 14 Hz, 1H), 4.30 (m, 3H), 4.50 (m, 1H), 4.95 (s, 1H), 4.97 (s, 1H), 5.78 (t, J 7 Hz, 1H). Anal. Calcld. for C₂₃H₃₇O₂Si₂ (398.73): C, 63.26%; H, 10.62%. Found: C, 62.99%; H, 10.69%.

[3S-(1E,3α,5β)][2-3-3,5-Bis[(1,1-Dimethylthethyl]dimethylsilyl]oxy]-2-methylenecyclohexyldiene]-1-chloroethane (7b): Yellow oil. H NMR (300 MHz, CDCl₃): δ 0.06 (s, 6H), 0.07 (s, 6H), 0.90 (s, 18H), 1.72–1.97 (m, 2H), 2.38 (m, 2H), 4.10 (m, 2H), 4.25 (s, 1H), 4.48 (m, 1H), 4.97 (s, 1H), 4.99 (s, 1H), 5.76 (t, J 6.5 Hz, 1H). Anal. Calcld. for C₂₃H₃₉ClO₂Si₂ (417.17): C, 60.46%; H, 9.91%. Found: C, 60.37%; H, 9.76%.

(ε = 23,170), 265 (2900), 272 (200). IR (CHCl₃): 1255, 1074 cm⁻¹. MS (m/e): 605 (M + Na, 85%), 583 (M + H, 55). HRMS: for M+Na calemd. 605.3006, found 605.3009. ¹H NMR (300 MHz, CDCl₃): δ 0.06 (s, 6H), 0.07 (s, 6H), 0.90 (s, 18H), 1.76 (m, 1H), 2.04 (m, 1H), 3.04–3.22 (m, 2H), 4.10 (m, 1H), 4.40 (m, 1H), 4.76 (s, 1H), 4.80 (s, 1H), 5.55 (dd, J₁ 7 Hz, J₂ 14 Hz, 1H), 7.4–7.6 and 7.7–7.85 (2m, 10H). Anal. Calcd. for C₃₁H₅₁O₃PS₂ (582.90): C, 68.08%; H, 8.82%. Found: C, 68.02%; H, 8.94%.

[3R-(1E,3s,5s)]-2-[3,5-Bis[(1,1-Dimethylethyl)dimethylsilyloxy]-2-methylenecyclohexylidenemethyl]ethanol (6e): White solid, m.p. 52–55°C. [α]D²⁵ = +69.7 (ε = 1.1, CHCl₃). UV (MeOH): λmax = 213 nm (ε = 6400). IR (KBr): 3290, 1255, 834 cm⁻¹. MS (m/e): 421 (M + Na, 100%), 399 (M + H, 30), 381 (M–OH, 22), 378 (10), 201 (55). MSHR: for M + Na calemd. 421.2564, found 421.2566. ¹H NMR (300 MHz, CDCl₃): δ 0.06 (s, 12H), 0.87 (s, 9H), 0.92 (s, 9H), 1.90 (m, 1H), 2.20 (m, 1H), 2.78 (dd, J₁, J₂ 3 Hz), J₃ 11 Hz, 1H), 3.70 (m, 1H), 4.05 (m, 1H), 4.22 (m, 2H), 5.02 (s, 1H), 5.05 (s, 1H), 5.76 (dt, J₁ 2 Hz, J₂ 6 Hz, 1H). Anal. Calcd. for C₂₂H₄₂O₂Si₂ (398.73): C, 63.26%; H, 10.62%. Found: C, 63.26%; H, 10.56%.

[3R-(1E,3s,5s)]-2-[3,5-Bis[(1,1-Dimethylethyl)dimethylsilyloxy]-2-methylenecyclohexylidenemethyl]-1-chloroethane (7c): Pale yellow oil. [α]D²⁵ = +101.7 (ε = 1.43, CHCl₃). UV (MeOH): λmax = 225 nm (ε = 9440). IR (KBr): 1647, 1258, 836 cm⁻¹. MS (m/e): 417 (M + H), 415 (M + Cl), 410 (M – CH₃), 381 (M–Cl), 359 (M–C₁H₃), 285 (M–OTBS). ¹H NMR (300 MHz, CDCl₃): δ 0.08 (s, 6H), 0.10 (s, 6H), 0.90 (s, 9H), 0.91 (s, 9H), 1.58 (m, 2H), 1.93 (m, 1H), 2.19 (m, 1H), 2.80 (ddd, J₁ 4 Hz, J₂ 6 Hz, J₃ 11 Hz, 1H), 4.03–4.18 (m, 3H), 5.02 (t, J 2 Hz, 1H), 5.09 (t, J 2 Hz, 1H), 5.82 (dt, J₁ 2 Hz, J₂ 7 Hz, 1H). Anal. Calcd. for C₂₂H₄₂ClO₂Si₂ (417.17): C, 60.46%; H, 9.91%. Found: C, 60.62%; H, 9.84%.

[3R-(1E,3s,5s)]-2-[3,5-Bis[(1,1-Dimethyl)dimethylsilyloxy]-2-methylenecyclohexylidenemethyl]diphenylphosphine oxide (8c): IR (CHCl₃): 836, 695 cm⁻¹. MS (m/e): 583 (M + H), 525 (M-C₆H₅), 451 (M–OTBS), 393 (100%), 319 (451-HOTBS), 201 (P(OH)₃). ¹H NMR (300 MHz, CDCl₃): δ 0.0 (s, 12H), 0.85 (s, 9H), 0.88 (s, 9H), 1.49 (m, 2H), 2.15 (m, 1H), 2.49 (m, 1H), 3.09 (m, 2H), 3.27 (m, 1H), 3.86 (m, 1H), 4.80 (s, 1H), 5.40 (q, J 7 Hz, 1H), 7.3–7.5 and 7.6–7.8 (2m, 10H). Anal. Calcd. for C₃₃H₃₅O₃PS₂ (582.90): C, 68.00%; H, 8.82%. Found: C, 67.63%; H, 8.67%.

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