A Practical, Convergent Route to the Key Precursor to the Tetracycline Antibiotics

David A. Kummer, Derun Li, Amelie Dion, and Andrew G. Myers*

Department of Chemistry and Chemical Biology, Harvard University, Cambridge, Massachusetts 02138

Supporting Information

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General Experimental Procedures: All reactions were performed in round-bottom flasks fitted with rubber septa under a positive pressure of argon or nitrogen, unless otherwise noted. Air- and moisture-sensitive liquids were transferred via syringe or stainless-steel cannula. Organic solutions were concentrated by rotary evaporation (house vacuum, ca. 25–40 torr) at ambient temperature, unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with silica gel (0.25 mm, 60 Å pore-size, 230–400 mesh, Merck KGA) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light, then were stained with either an aqueous sulfuric acid solution of ceric ammonium molybdate (CAM) or an aqueous sodium carbonate solution of potassium permanganate ($KMnO_4$) then briefly heated on a hot plate. Flash-column chromatography was performed as described by Still et al.,[1] employing silica gel (60 Å, 32–63 μM, standard grade, Dynamic Adsorbents, Inc.).

Materials: Dry solvents were purchased from the Aldrich Chemical Company in Sure/Seal™ glass bottles and used without purification. All reagents were purchased and used without purification with the following two exceptions: *p*-benzoquinone was recrystallized from warm (55 °C) ethanol; *tert*-butyldimethylsilyl trifluoromethanesulfonate and hexamethyldisilazane were distilled from calcium hydride under an atmosphere of argon. MP-TMT resin was purchased from Biotage and used as received. Dimethylphenylchlorosilane was purchased from Oakwood Products, Inc. and used without purification. Lithium chloride was dried in vacuo (0.1 mmHg) at 150 °C for 15 h.

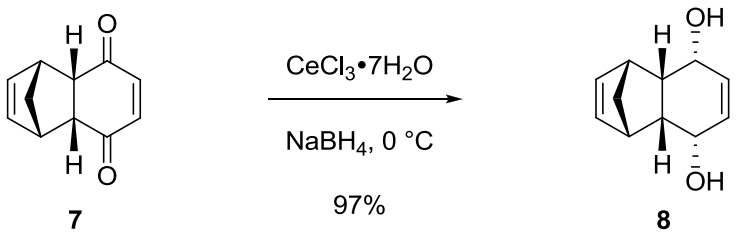
Instrumentation: Proton magnetic resonance (^{1}H NMR) spectra were recorded on Varian INOVA 500 (500 MHz) or 600 (600 MHz) NMR spectrometers at 23 °C. Proton chemical shifts

[1] Still, W. C.; Khan, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

are expressed in parts per million (ppm, δ scale) and are referenced to residual protium in the NMR solvent ($CHCl_3$, δ 7.26; C_6HD_5, δ 7.15; $CD_3S(O)CHD_2$, δ 2.54). Data are represented as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances, br = broad, app = apparent), and coupling constant (*J*) in Hertz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded on a Varian INOVA 500 (125 MHz) NMR spectrometer at 23 °C. Carbon chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$, δ 77.0; C_6D_6, δ 128.0). Infrared (IR) spectra were obtained using a Shimadzu 8400S FT-IR spectrometer and were referenced to a polystyrene standard. Data are represented as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad). High-resolution mass spectra were obtained at the Harvard University Mass Spectrometry Facility. X-ray crystallographic analysis was performed at the Harvard University X-ray Crystallographic Laboratory by Dr. Shao-Liang Zheng.

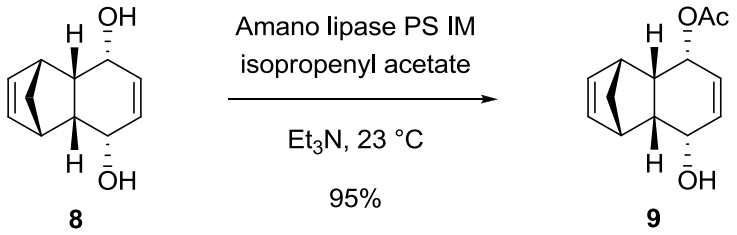
For clarity, intermediates that have not been assigned numbers in the text are numbered sequentially in the Supporting Information beginning with ***27****.*

Synthesis of cyclohexenone 2 (depicted in Scheme 4):



Meso diol 8. Sodium borohydride (13.6 g, 359 mmol, 1.23 equiv) was added in 1-g portions over 1.5 h to an ice-cooled solution of enedione[2] **7** (50.0 g, 287 mmol, 1 equiv) and cerium trichloride heptahydrate (214 g, 574 mmol, 2 equiv) in methanol (960 mL). After 30 min, saturated aqueous ammonium chloride solution (1 L) was added over the course of 30 min. The cooling bath was removed and the reaction flask was allowed to warm to 23 °C. The mixture was partitioned between half-saturated aqueous ammonium chloride solution (1 L) and ethyl acetate (1 L). The layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 1 L). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide diol **8**[3] (49.5 g, 97%) as an off-white solid. This material was used in the next transformation without purification. The characterization data obtained for diol **8** were in agreement with values previously reported.[3] ^{1}H NMR (500 MHz, *d*6-DMSO), δ: 5.65 (s, 2H), 5.10 (s, 2H), 4.67 (d, 2H, J = 3.9 Hz), 4.22–4.19 (m, 2H), 2.91–2.90 (m, 2H), 2.65–2.64 (m, 2H), 1.17 (d, 1H, J = 7.8 Hz), 1.10 (d, 1H, J = 7.8 Hz).

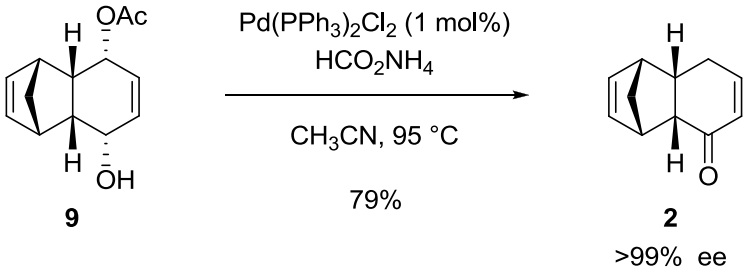
[2] Enedione **7** was prepared in >100-g batches by the procedure reported: Oda, M.; Kawase, T.; Okada, T.; Enomoto, T. *Organic Syntheses* **1996**, *73*, 253–261.
[3] (a) Marchand, A. P.; Laroe, W. D.; Sharma, G. V. M.; Suri, S. C.; Reddy, D. S. Facile *J. Org. Chem.* **1986**, *51*, 1622–1625. (b) Craze, G.-A.; Watt, I. *J. Chem. Soc., Perkin Trans. 2* **1981**, 175–184.



Mono acetate 9.[4] Immobilized lipase PS (Amano, 47.0 g) was added to a mechanically stirred solution of diol **8** (47.0 g, 264 mmol, 1 equiv) and isopropenyl acetate (87.2 mL, 792 mmol, 3 equiv) in triethylamine (754 mL). After 22 h, the slurry was filtered through a sintered-glass funnel. The filter cake was rinsed with ethyl acetate (800 mL). The filtrate was concentrated. The oily residue was partitioned between 0.2 M aqueous hydrochloric acid solution (500 mL) and ethyl acetate (800 mL). The organic layer was washed sequentially with water (500 mL) and saturated aqueous sodium chloride solution (500 mL). The washed organic layer was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide acetate **9** (55.4 g, 95%) as a yellow oil. This material was used in the next transformation without purification. The ^{1}H NMR data obtained for acetate **9** were in agreement with values previously reported.[4b] $[\alpha]^{23}_D$ +46.6 (*c* 1.09, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$), δ: 5.88 (1H, dd, *J* = 2.9, 5.9 Hz), 5.81 (1H, dd, *J* = 2.4, 5.4 Hz), 5.48–5.45 (1H, m), 5.38–5.35 (1H, m), 5.31–5.28 (1H, m), 4.49–4.45 (1H, m), 3.06 (1H, s), 3.02 (1H, dt, *J* = 3.4, 8.8 Hz), 2.85 (1H, dt, *J* = 3.4, 8.8 Hz), 2.83 (1H, s), 2.11 (3H, s), 1.55 (1H, d, *J* = 4.9 Hz), 1.36 (1H, d, *J* = 8.3 Hz), 1.30 (1H, d, *J* = 8.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 170.7, 135.5, 135.5, 132.1, 127.0, 69.8, 66.6, 49.0, 45.7, 45.0, 41.8, 38.6, 21.1. FTIR (neat), cm^{-1}: 3424 (b),

[4] (a) Takano, S.; Moriya, M.; Higashi, Y.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1993**, 177–178. (b) Takano, S.; Higashi, Y.; Kamikubo, T.; Moriya, M.; Ogasawara, K. *Synthesis* **1993**, 948–950. (c) Konno, H.; Ogasawara, K. *Synthesis* **1999**, 1135–1140.

2974 (m), 2936 (m), 1736 (s), 1371 (m), 1242 (s). HRMS (ESI): Calcd for $(C_{13}H_{16}O_3 + Na)^+$: 243.0992. Found: 243.1030.

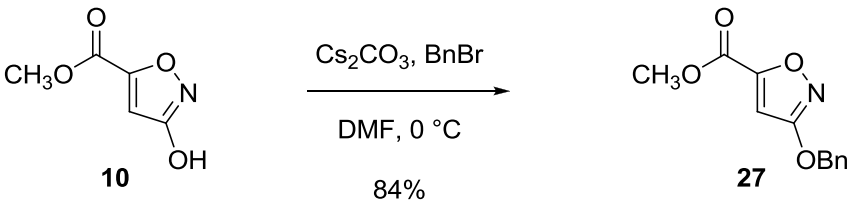


Cyclohexenone 2.[5] A solution of ammonium formate (19.9 g, 315 mmol, 1.25 equiv), acetate **9** (55.4 g, 252 mmol, 1 equiv), and bis(triphenylphosphine)palladium(II) dichloride (1.76 g, 2.52 mmol, 0.01 equiv) in acetonitrile (840 mL) was heated at reflux (bath temperature 95 °C). After 20 min, the heating bath was removed and the reaction flask was allowed to cool to 23 °C. The mixture was concentrated. The oily residue was dissolved in ethyl acetate (500 mL). The solution was filtered through a pad of silica gel, rinsing with ethyl acetate (500 mL). The filtrate was washed sequentially with half-saturated aqueous sodium bicarbonate solution (1 L) and half-saturated aqueous sodium chloride solution (1 L). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography on silica gel (7:1 hexanes–ethyl acetate initially, grading to 4:1 hexanes–ethyl acetate) to provide pure cyclohexenone **2** (31.9 g, 79%) as a yellow oil. The product was stored at –20 °C, where it formed a yellow solid. The enantiomeric excess of the purified product was determined to be >99% by chiral GC analysis (Restek Rt-βDexsm column, 30 m, 0.25 mmID, oven temperature of 40 °C for 5 min then with a uniform increase of 2 °C/min, t_R(major, cyclohexenone **2**) = 55.20 min, t_R(minor, *ent*-**2**) = 56.45 min. The ^{1}H data obtained for enone **2** were in agreement with values previously reported.[5] ^{1}H NMR (600 MHz, $CDCl_3$), δ: 6.66 (1H, ddd, J = 4.1, 4.1, 10.4 Hz), 6.14 (1H, dd, J = 2.9, 5.7 Hz), 6.09 (1H, dd, J =

[5] This procedure is adapted from that described by Ogasawara et al.: (a) Takano, S.; Higashi, Y.; Kamikubo, T.; Moriya, M.; Ogasawara, K. *Synthesis* **1993**, 948–950. (b) Takano, S.; Moriya, M.; Kamikubo, T.; Hiroya, K.; Ogasawara, K. *Tetrahedron Lett.* **1993**, *34*, 8485–8488.

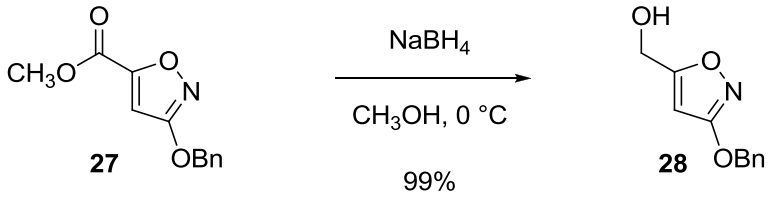
2.9, 5.7 Hz), 5.87 (1H, ddd, J = 2.5, 2.5, 10.3 Hz), 3.38 (1H, br s), 3.03 (1H, br s), 2.90 (1H, dd, J = 4.1, 10.1 Hz), 2.76 (1H, dddd, J = 3.7, 3.7, 10.3, 10.3 Hz), 2.60–2.56 (1H, m), 2.04–1.99 (1H, m), 1.42 (1H, d, J = 8.4 Hz), 1.33 (1H, d, J = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 200.4, 149.3, 137.4, 134.5, 128.9, 48.9, 48.6, 48.2, 48.1, 33.7, 27.2. FTIR (neat), cm^{-1}: 2965 (m), 2936 (m), 1657 (s), 1425 (m), 1393 (m), 1339 (m), 1248 (m). HRMS (ESI): Calcd for $(C_{11}H_{12}O + Na)^+$: 183.0780. Found: 183.0779.

Synthesis of isoxazole ester 3 (depicted in Scheme 5):



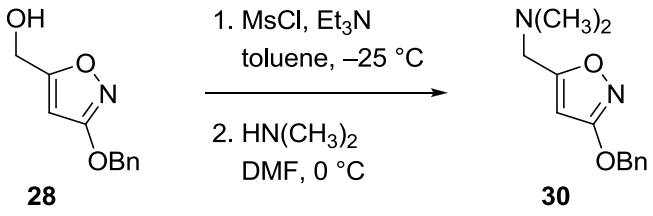
Methyl 3-(benzyloxy)isoxazole-5-carboxylate (27). Cesium carbonate (425 g, 1.30 mol, 1.3 equiv) was added in five equal portions over 25 min to a mechanically stirred solution of methyl 3-hydroxyisoxazole-5-carboxylate[6] (**10**, 143 g, 1.00 mol, 1 equiv) in dimethylformamide (2 L) at 0 °C (ice–water bath). After 30 min, the reaction flask was fitted with a 500-mL, pressure-equalizing addition funnel. Benzyl bromide (180 mL, 1.50 mol, 1.5 equiv) was added dropwise via the addition funnel over 40 min. After 4 h, 0.5 M aqueous hydrochloric acid solution (2 L) was added dropwise via the addition funnel over 30 min. After 10 min, the cooling bath was removed and the reaction flask was allowed to warm to 23 °C. The mixture was extracted with ethyl acetate (3 × 2 L). The organic layers were combined. The combined solution was washed sequentially with water (2 × 1 L) and saturated aqueous sodium chloride solution (1 L). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography on silica gel (100% hexanes initially, grading to 20% ethyl acetate–hexanes) to provide pure methyl 3-(benzyloxy)isoxazole-5-carboxylate (**27**, 195 g, 84%) as a white solid. The characterization data obtained for methyl 3-(benzyloxy)isoxazole-5-carboxylate were in agreement with values previously reported.[7]

[6] (a) Jager, V.; Frey, M. *Liebigs Ann. Chem.* **1982**, 817–820. (b) Frey, M.; Jager, V. *Synthesis* **1985**, 1100–1104.
[7] Riess, R.; Schon, M.; Laschat, S.; Jager, V. *Eur. J. Org. Chem.* **1998**, *1998*, 473–479.



3-Benzyloxy-5-(hydroxymethyl)isoxazole (28). Sodium borohydride (50.8 g, 1.34 mol, 1.2 equiv) was added in 1-g portions over 1 h to a mechanically stirred solution of methyl 3-(benzyloxy)isoxazole-5-carboxylate (**27**, 262 g, 1.12 mol, 1 equiv) in methanol (3 L) at 0 °C (ice–water bath). After 3 h, the reaction flask was fitted with a one-liter, pressure-equalizing addition funnel. 1 M Aqueous hydrochloric acid solution (2.5 L) was added dropwise via the addition funnel over 45 min. After 5 min, saturated aqueous ammonium chloride solution (1 L) was added. The cooling bath was removed and the reaction flask was allowed to warm to 23 °C. The mixture was extracted with dichloromethane (1 × 1.5 L, then 4 × 1 L). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide a white solid. The solid was dissolved in ethyl acetate (1 L). The solution was filtered through a pad of silica gel, rinsing with ethyl acetate (1 L). The filtrate was concentrated to provide pure 3-benzyloxy-5-(hydroxymethyl)isoxazole (**28**, 231 g, 99%) as a white solid. The characterization data obtained for 3-benzyloxy-5-(hydroxymethyl)isoxazole were in agreement with values previously reported.[8]

[8] Riess, R.; Schon, M.; Laschat, S.; Jager, V. *Eur. J. Org. Chem.* **1998**, *1998*, 473–479.



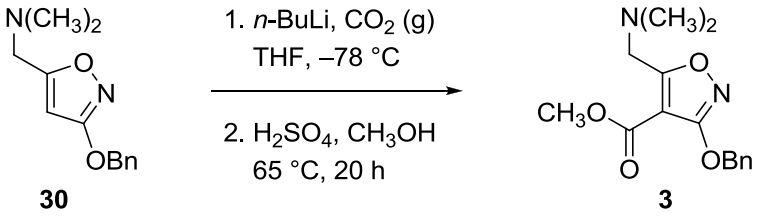
28 **30**

98 %

3-Benzyloxy-5-(dimethylaminomethyl)isoxazole: Step 1, Mesylation. Methanesulfonyl chloride (54.3 mL, 702 mmol, 1.2 equiv) was added dropwise by syringe over 30 min to a mechanically stirred solution of 3-benzyloxy-5-(hydroxymethyl)isoxazole (**28**, 120 g, 585 mmol, 1 equiv) and triethylamine (106 mL, 761 mmol, 1.3 equiv) in toluene (2.4 L) at –25 °C (using an acetone cooling bath with temperature control by periodic addition of dry ice). After 30 min, ethyl acetate (750 mL) and water (750 mL) were added sequentially. The cooling bath was removed and the reaction flask was allowed to warm to 23 °C. The layers were separated. The organic layer was washed sequentially with 0.1 M pH 5 aqueous sodium citrate buffer (1 L) and saturated aqueous sodium chloride solution (1 L). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide (3-(benzyloxy)isoxazol-5-yl)methyl methanesulfonate (**29**, not shown) as a white solid (175 g). This material was used in the next transformation without purification. Mp = 48–50 °C. ^{1}H NMR (600 MHz, $CDCl_3$), δ: 7.45–7.36 (5H, m), 6.11 (1H, s), 5.28 (2H, s), 5.18 (2H, s), 3.06 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 171.3, 165.1, 135.2, 128.5, 128.1, 97.1, 71.7, 60.5, 38.1. FTIR (neat), cm^{-1}: 1626 (s), 1506 (s), 1451 (s), 1358 (s), 1173 (s). HRMS (ESI): Calcd for $(C_{12}H_{13}NO_5S + H)^+$: 284.0587. Found 284.0475.

Step 2, Dimethylamine displacement. Liquid dimethylamine (approx. 200 mL, 2.93 mol, 5 equiv) was condensed (using a dry ice–acetone cooled cold finger) into an ice-cooled 3-L round-

bottom flask fitted with a mechanical stirrer and containing dimethylformamide (300 mL). An ice-cooled solution of the unpurified mesylate (**29**, 175 g) from step 1 above in dimethylformamide (300 mL) was added dropwise by cannula over 1 h. After 20 min, the mixture was partitioned between saturated aqueous sodium bicarbonate solution (1 L), saturated aqueous sodium chloride solution (500 mL), ethyl acetate (2 L), and hexanes (1 L). The layers were separated. The organic layer was washed sequentially with water (2 × 600 mL) and saturated aqueous sodium chloride solution (2 × 600 mL). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide pure 3-benzyloxy-5-(dimethylaminomethyl)isoxazole (**30**) as a yellow oil (134 g, 98% over two steps). TLC (50% ethyl acetate–hexanes): R_f = 0.34. ^{1}H NMR (500 MHz, $CDCl_3$), δ: 7.43–7.31 (m, 5H), 5.82 (s, 1H), 5.23 (s, 2H), 3.48 (s, 2H), 2.27 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 171.9, 171.2, 136.1, 128.8, 128.7, 128.5, 94.8, 71.7, 55.1, 45.3. FTIR (neat), cm^{-1}: 2950 (s), 1615 (s), 1494 (s), 1452 (s), 1136 (m). HRMS (ESI): Calcd for $(C_{13}H_{16}N_2O_2 + H)^+$: 232.1212. Found: 232.1220.



Methyl 3-benzyloxy-5-(dimethylaminomethyl)isoxazole-4-carboxylate (3): Step 1, Carboxylation. A titrated[9] solution of *n*-butyllithium in hexanes (2.53 M, 240 mL, 606 mmol, 1.05 equiv) was added dropwise by cannula over 45 min to a dry ice–acetone cooled, mechanically stirred solution of 3-benzyloxy-5-(dimethylaminomethyl)isoxazole (**30**, 134 g, 577 mmol, 1 equiv) in tetrahydrofuran (2 L) resulting in a heterogeneous, dark-red mixture. After 30 min, carbon dioxide gas was bubbled through the mixture using a stainless-steel needle. After 30 min, the reaction mixture became homogeneous. After 3 h, the stream of carbon dioxide gas was stopped and nitrogen gas was bubbled through the solution using a stainless-steel needle. The cooling bath was removed and the reaction flask was allowed to slowly warm to 23 °C over the course of 2 h. The flow of nitrogen gas was stopped. Hexanes (667 mL), ethyl acetate (333 mL), and 1 M aqueous sodium hydroxide solution (1 L) were added in sequence. After 20 min, the layers were separated. The organic layer was extracted sequentially with 1 M aqueous sodium hydroxide solution (500 mL) and water (500 mL). The aqueous layers were combined. The combined solution was cooled in an ice–water bath with stirring. The pH of the cold solution was adjusted to 5.5 by the dropwise addition of concentrated hydrochloric acid. The solution was removed from the cooling bath and allowed to warm to 23 °C. The solution was saturated with solid sodium chloride and then extracted with dichloromethane (2 × 1 L, then 3 × 800 mL). The organic layers were combined. The combined solution was dried over sodium

[9] Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879–1880.

sulfate. The dried solution was filtered and the filtrate was concentrated to provide 3-benzyloxy-5-(dimethylaminomethyl)isoxazole-4-carboxylic acid (**31**, not shown) as an off-white solid (131 g). This material was used in the next transformation without purification. Mp = 161–166 °C (decomp). ^{1}H NMR (600 MHz, *d*6-DMSO), δ: 15.30 (1H, br s), 7.48–7.34 (5H, m), 5.27 (2H, s), 4.06 (2H, s), 2.39 (6H, s). ^{13}C NMR (125 MHz, *d*6-DMSO), δ: 172.0, 169.1, 161.3, 135.8, 128.4, 128.3, 128.1, 104.4, 71.1, 53.0, 43.4. FTIR (neat), cm^{-1}: 1627 (m), 1504 (s) 1458 (s), 1445 (s), 1362 (s). HRMS (ESI): Calcd for $(C_{14}H_{16}N_2O_4 + H)^+$: 277.1183. Found: 277.1231.

Step 2, Esterification. Sulfuric acid (160 mL, 2.83 mol, 6 equiv) was added dropwise over 1 h to a stirring slurry of the unpurified 3-benzyloxy-5-(dimethylaminomethyl)isoxazole-4-carboxylic acid from step 1 above (**31**, 130 g, 471 mmol, 1 equiv) in methanol (1 L) at 23 °C. After all the solids dissolved, the reaction flask was equipped with a water-cooled reflux condenser and the reaction assembly was placed in an oil bath at 65 °C. After 20 h, the oil bath was removed and the reaction flask was placed in an ice–water bath. After 30 min, the pH of the reaction mixture was adjusted to 9.0 by the dropwise addition of 28% aqueous ammonium hydroxide solution. The cooling bath was removed and the reaction flask was allowed to warm to 23 °C. The reaction mixture was partitioned between water (1 L) and ethyl acetate (1 L). The layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 1 L). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The oily residue was dissolved in hexanes (1 L) at 65 °C. The solution was allowed to cool to 0 °C (ice–water bath) at which point a white solid began to precipitate. After 1 h, the solids were collected on a sintered-glass funnel, and the mother liquors were retained (for processing, see below). The solids were rinsed with ice-cooled

hexanes. The rinsed solids were dried in vacuo (0.1 mmHg) to provide the first crop of pure methyl 3-benzyloxy-5-(dimethylaminomethyl)isoxazole-4-carboxylate (**3**, 72.0 g) as a white solid.

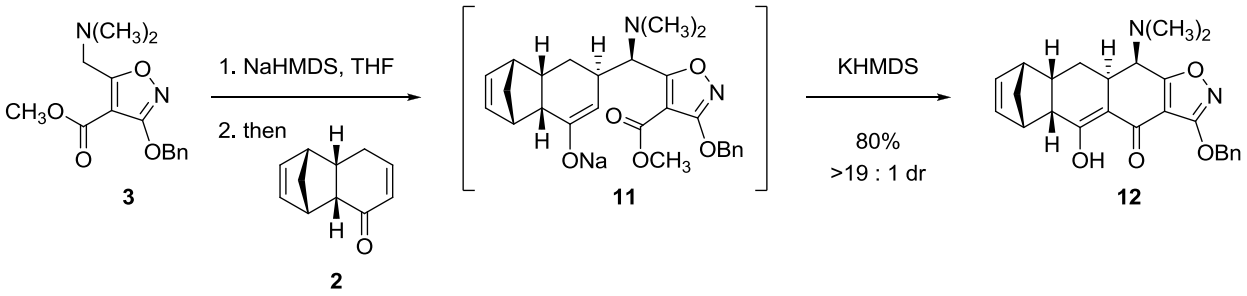
The mother liquors were concentrated. The oily residue was dissolved in hexanes (800 mL) at 65 °C. The solution was allowed to cool to 0 °C (ice–water bath) at which point a white solid began to precipitate. After 1 h, the solids were collected on a sintered-glass funnel, and the mother liquors were retained (for processing, see below). The solids were rinsed with ice-cooled hexanes. The rinsed solids were dried in vacuo (0.1 mmHg) to provide the second crop of pure methyl 3-benzyloxy-5-(dimethylaminomethyl)isoxazole-4-carboxylate (**3**, 16.0 g) as a white solid.

The mother liquors were concentrated. The oily residue was dissolved in hexanes (500 mL) at 65 °C. The solution was allowed to cool to 0 °C (ice–water bath) at which point a white solid began to precipitate. After 1 h, the solids were collected on a sintered-glass funnel, and the mother liquors were retained (for processing, see below). The solids were rinsed with ice-cooled hexanes. The rinsed solids were dried in vacuo (0.1 mmHg) to provide the third crop of pure methyl 3-benzyloxy-5-(dimethylaminomethyl)isoxazole-4-carboxylate (**3**, 17.0 g) as a white solid. The total weight of methyl 3-benzyloxy-5-(dimethylaminomethyl)isoxazole-4-carboxylate (**3**)[10] obtained was 105 g (63%, two steps). Mp = 37–39 °C. TLC (50% acetone–hexanes): R_f = 0.55 (UV, CAM). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 7.49–7.48 (m, 2H), 7.41–7.34 (m, 3H), 5.36 (s, 2H), 3.90 (s, 2H), 3.85 (s, 3H), 2.36 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 176.2, 168.9, 161.5, 135.6, 128.5, 128.3, 127.8, 102.1, 71.7, 53.6, 51.8, 45.2. FTIR (neat), cm^{-1}: 2951 (m),

[10] Stork, G.; Hagedorn, A. A. *J. Am. Chem. Soc.* **1978**, *100*, 3609–3611.

2826 (m), 2778 (m), 1719 (s), 1614 (s), 1508 (s), 1451 (s), 1360 (s), 1308 (s), 1109 (s). HRMS (ESI): Calcd for $(C_{15}H_{18}N_2O_4 + H)^+$: 291.1339. Found: 291.1227.

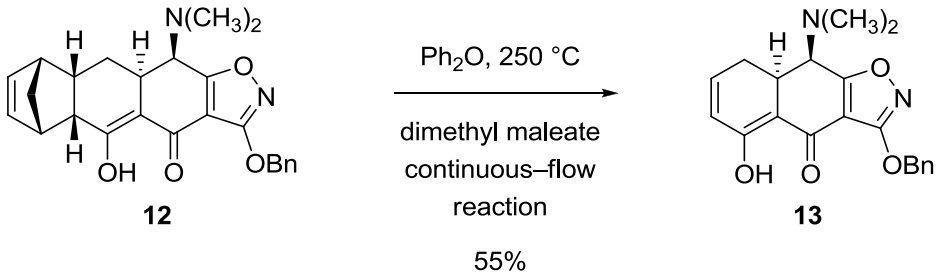
Michael–Claisen cyclization reaction (depicted in Scheme 6):



Michael–Claisen cyclization product 12. A 1.0 M solution of sodium bis(trimethylsilyl)amide in tetrahydrofuran (Aldrich, 447 mL, 447 mmol, 1.05 equiv) was added dropwise by cannula over 30 min to a mechanically stirred solution of methyl 3-benzyloxy-5-(dimethylaminomethyl)isoxazole-4-carboxylate (**3**, 130 g, 447 mmol, 1.05 equiv) in tetrahydrofuran (3 L) at –78 °C (dry ice–acetone bath). After 10 min, the cooling bath was removed and the reaction flask was allowed to warm to –20 °C over the course of 30 min. After 30 min, the reaction flask was placed in a dry ice–acetone cooling bath at –78 °C. After 30 min, a solution of enone **2** (68.0 g, 424 mmol, 1 equiv) in tetrahydrofuran (120 mL) was added dropwise by cannula over the course of 45 min. After 30 min, a 0.50 M solution of potassium bis(trimethylsilyl)amide in toluene (Aldrich, 894 mL, 447 mmol, 1.05 equiv) was added dropwise by cannula over the course of 70 minutes. After 2 h, the cooling bath was removed and the reaction flask was allowed to warm to –20 °C over 1 h. The reaction flask was placed into a –20°C dry ice–acetone cooling bath (temperature control by periodic addition of dry ice). After 6 h, saturated aqueous ammonium chloride solution (1.5 L) and saturated aqueous sodium chloride solution (400 mL) were added sequentially. The cooling bath was removed and the reaction flask was allowed to warm to 23 °C. The biphasic mixture was extracted with ethyl acetate (2 × 1 L, 1 × 600 mL). The organic layers were combined. The combined solution was

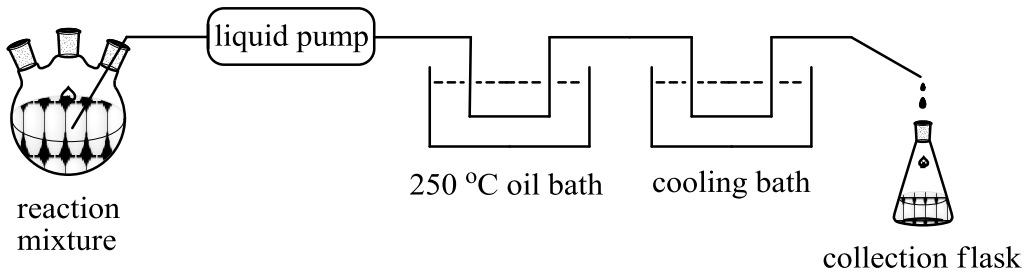
dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography on silica gel (10% ethyl acetate–hexanes initially, then grading to 25% ethyl acetate–hexanes) to provide pure Michael–Claisen cyclization product **12** as a pale yellow foam (143 g, 80%). TLC (33% ethyl acetate–hexanes): R_f = 0.38 (UV, CAM). $[\alpha]^{23}_D$ –7.28 (*c* 0.70, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 15.16 (s, 1H), 7.50–7.49 (m, 2H), 7.38–7.32 (m, 3H), 6.04–6.00 (m, 2H), 5.39–5.34 (m, 2H), 3.61 (d, *J* = 6.5 Hz, 1H), 3.20 (s, 1H), 2.91 (s, 1H), 2.87 (dd, 1H, *J* = 4.0, 9.0 Hz), 2.75–2.71 (m, 2H), 2.17–2.10 (m, 1H), 2.13 (s, 6H), 1.80 (dd, 1H, *J* = 5.0, 15.0 Hz), 1.46 (d, 1H, *J* = 8.5 Hz), 1.42 (d, 1H, *J* = 8.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 183.8, 180.9, 176.6, 167.6, 135.6, 135.4, 135.1, 128.4, 128.3, 128.2, 107.9, 105.4, 72.2, 58.2, 50.9, 49.5, 46.8, 42.7, 41.9, 37.5, 34.1, 26.0. FTIR (neat), cm^{-1}: 2964 (s), 2937 (s), 1627 (s), 1610 (s), 1573 (s), 1506 (s), 1330 (s). HRMS (ESI): Calcd for $(C_{25}H_{26}N_2O_4 + Na)^+$: 441.1785. Found: 441.1793.

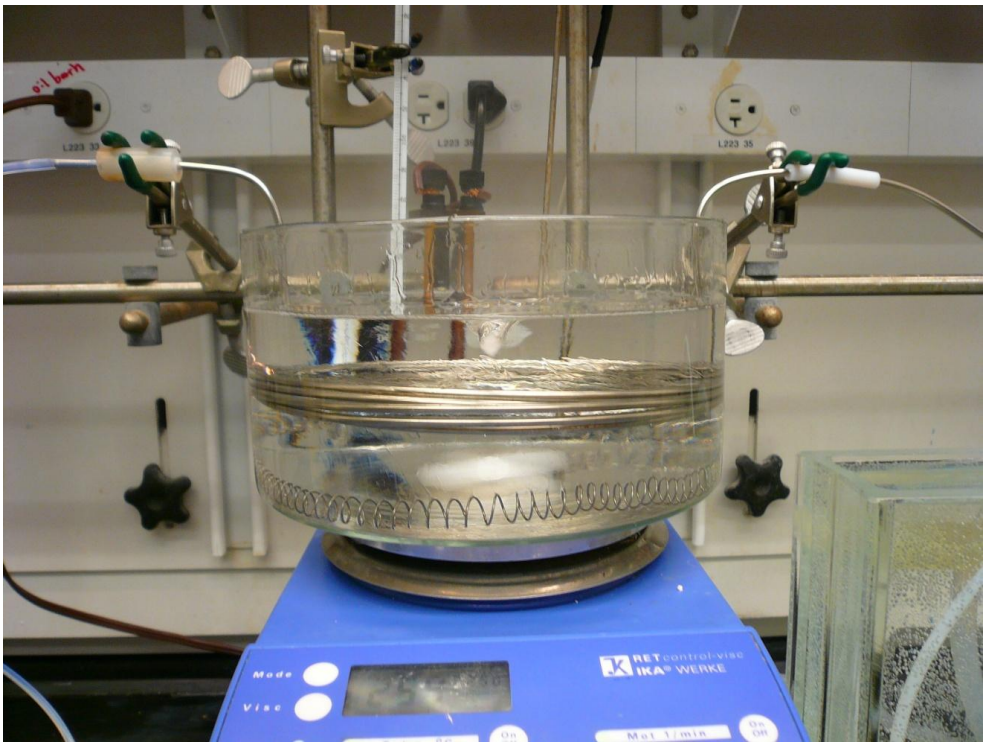
Synthesis of AB enone 1 (depicted in Scheme 7):

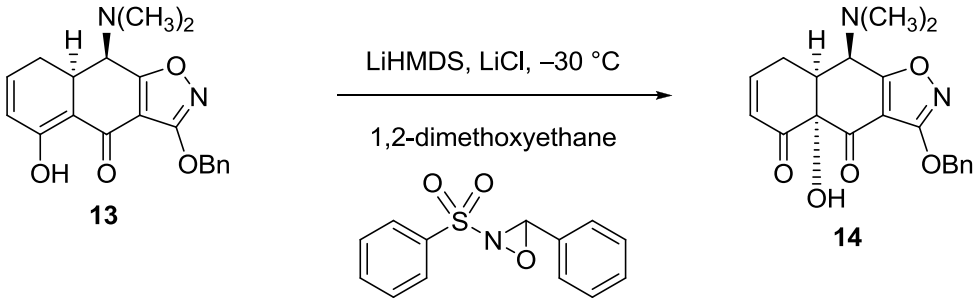


Retro-Diels–Alder product 13. A special reaction assembly was constructed for this transformation (see illustration and photographs that follow for details). A solution of Michael–Claisen cyclization product **12** (143 g, 341 mmol, 1 equiv) and dimethyl maleate (213 mL, 1.71 mol, 5 equiv) in diphenyl ether (14 L) was deoxygenated by bubbling argon gas through the solution with a stainless-steel needle for 1 h. The deoxygenated solution was pumped continuously (FMI Q pump, CERAMPUMP®) through a stainless-steel tube (304 grade stainless-steel, 3.18 mm outer diameter, 2.16 mm inner diameter, 3 m length, VWR) preheated to 250 °C followed by a Teflon tube (3-m length) in a water bath (23 °C) at a rate of 12 mL/min. The product was collected and placed into a 23 °C water bath. Hexanes (18 L) was added and the resulting mixture was mechanically stirred. A solution of hydrogen chloride in ether (2.0 M, 290 mL, 580 mmol, 1.7 equiv) was added dropwise over 30 min causing a solid to precipitate. After 1.5 h, the slurry was filtered through a pad of Celite, rinsing sequentially with hexanes (3 L) and hexanes–ethyl acetate (10:1, 2.4 L). The washed filter cake–Celite mixture was suspended in ethyl acetate (1.1 L) with stirring. 1 M Aqueous dipotassium hydrogen phosphate solution (600 mL) was added. After 20 min, the slurry was filtered through a sintered-glass funnel. The filtrate was collected. The layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 400 mL). The combined organic layers were dried over sodium sulfate.

The dried solution was filtered and the filtrate was concentrated. The residue was dissolved in a mixture of ethyl acetate (60 mL) and hexanes (90 mL) at 60 °C with stirring. After all the solids dissolved, the heating bath was removed and the flask was allowed to cool to 23 °C. The flask was then cooled to –20 °C. After 30 min, a precipitate began to form. After 6 h, the solids were collected on a sintered-glass funnel. The solids were washed with a mixture of hexanes and ethyl acetate (10:1, 15 mL) to provide the retro-Diels–Alder product **13** as a pale-yellow solid (31.0 g, mp = 103–105 °C). The filtrate was concentrated. The residue was purified by flash-column chromatography on silica gel (10% ethyl acetate–hexanes initially, then grading to 50% ethyl acetate–hexanes) to provide the retro-Diels–Alder product **13** as a pale yellow solid (36.0 g, mp = 103–105 °C). The total weight of pure retro-Diels–Alder product **13** obtained was 67.0 g (55%). TLC (33% ethyl acetate–hexanes): R_f = 0.24 (UV, CAM). $[\alpha]^{23}_{D}$ +373 (*c* 0.65, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 15.06 (s, 1H), 7.52–7.51 (m, 2H), 7.40–7.33 (m, 3H), 6.60 (ddd, 1H, *J* = 2.4, 6.0, 9.0 Hz), 6.04 (dd, 1H, *J* = 3.0, 9.0 Hz), 5.40 (s, 2H), 3.84 (d, 1H, *J* = 7.2 Hz), 3.40 (dt, 1H, *J* = 7.2, 15.6 Hz), 2.96–2.89 (m, 1H), 2.37–2.32 (m, 1H), 2.27 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 181.2, 175.6, 172.6, 167.6, 142.3, 135.2, 128.5, 128.4, 128.3, 124.2, 107.7, 102.1, 73.3, 57.6, 41.9, 34.9, 25.6. FTIR (neat), cm^{-1}: 2978 (s), 2939 (s), 2831 (s), 2360 (s), 1627(s), 1566 (s), 1504 (s). HRMS (ESI): Calcd for $(C_{20}H_{20}N_2O_4 + H)^+$: 353.1496. Found: 353.1508.



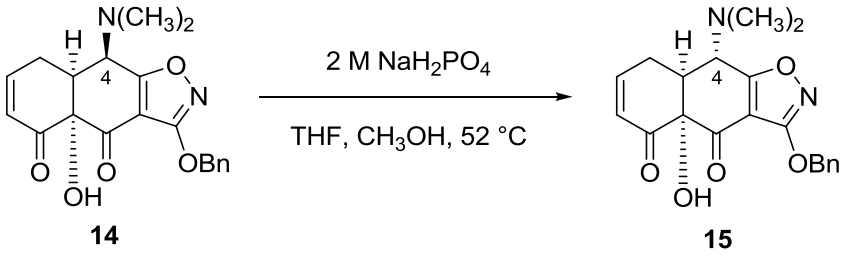




Alcohol 14 (initial scale-up procedure). An ice-cooled solution of lithium bis(trimethylsilyl)amide in 1,2-dimethoxyethane [obtained by adding a titrated[11] solution of *n*-butyllithium in hexanes (2.50 M, 83.6 mL, 209 mmol, 1.1 equiv) dropwise to a dry ice–acetone cooled solution of hexamethyldisilazane (45.7 mL, 219 mmol, 1.15 equiv) in 1,2-dimethoxyethane (225 mL), followed by stirring in an ice–water cooling bath for 30 min] was added dropwise by cannula over 45 min to a mechanically stirred slurry of retro-Diels–Alder product **13** (67.0 g, 190 mmol, 1 equiv) and lithium chloride (8.70 g, 209 mmol, 1.1 equiv) in 1,2-dimethoxyethane (500 mL) at –30 °C (cooled using an acetone bath with temperature control by periodic addition of dry ice). After 10 min, a slurry of *trans*-2-(phenylsulfonyl)-3-phenyloxaziridine[12] (60.5 g, 219 mmol, 1.15 equiv) in 1,2-dimethoxyethane (355 mL) was added dropwise by syringe over the course of 1 h. After 15 h, an additional portion of *trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (5.26 g, 0.1 equiv) was added. After 1 h, an additional portion of *trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (3.40 g, 0.07 equiv) was added. After 1 h, 1 M aqueous hydrochloric acid solution (700 mL), water (700 mL), hexanes (470 mL), and ethyl acetate (240 mL) were added. The cooling bath was removed and the reaction flask was allowed to warm to 23 °C. The layers were separated. The organic layer was extracted with

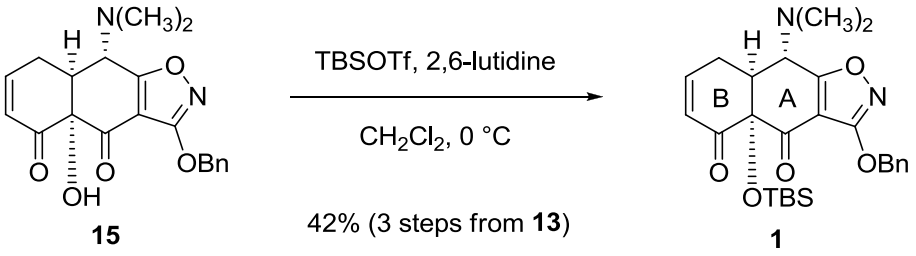
[11] Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879–1880.
[12] Vishwakarma, L.C.; Stringer, O. D.; Davis, F. A. (±)-*trans*-2-(phenylsulfonyl)-3-Phenyloxaziridine. *Organic Syntheses* **1988**, *66*, 203–207.

0.5 M aqueous hydrochloric acid solution (3 × 150 mL). The aqueous layers were combined. The combined solution was partitioned between saturated aqueous sodium chloride solution (200 mL), hexanes (350 mL), and ethyl acetate (50 mL). The layers were separated. The aqueous layer was washed with a mixture of hexanes and ethyl acetate (1:1, 6 × 700 mL). The washed aqueous layer was mechanically stirred, then water (2 L) and dichloromethane (1.5 L) were added. The pH of the biphasic mixture was adjusted to 7.5 by the addition of dipotassium hydrogen phosphate trihydrate (350 g). After 20 min, the layers were separated. The aqueous layer was extracted with dichloromethane (2 × 1 L). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide alcohol **14** (48.0 g, 68% crude yield, an accurate yield is reported after the subsequent steps, C4-epimerization and hydroxyl protection, see below) as a purple foam. This material was used in the next transformation without purification. A small sample was purified by radial chromatography (1:1 hexanes–ethyl acetate initially, then grading to 1:1 hexanes–acetone) to provide pure alcohol **14** as a white foam. TLC (50% acetone–hexanes): R_f = 0.42 (UV, CAM). $[\alpha]^{23}_D$ +373 (*c* 0.65, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$), δ: 7.49–7.47 (m, 2H), 7.40–7.34 (m, 3H), 7.00–6.97 (m, 1H), 6.24 (dd, 1H, *J* = 2.5, 10.5 Hz), 5.36 (s, 2H), 4.65 (br s, 1H), 4.48 (d, 1H, *J* = 5.0 Hz), 3.10 (dt, 1H, *J* = 5.0, 10.5 Hz), 2.80 (dt, 1H, *J* = 5.5, 20.0 Hz), 2.62 (s, 6H), 2.49–2.41 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 195.0, 185.7, 180.4, 167.9, 149.8, 134.9, 128.6, 128.5, 128.2, 126.9, 106.1, 80.4, 72.4, 59.9, 47.1, 44.5, 26.5. FTIR (neat), cm^{-1}: 3435 (s), 2926 (m), 1703 (s), 1683 (s), 1595(s), 1473 (s), 1369 (s). HRMS (ESI): Calcd for $(C_{20}H_{20}N_2O_5 + Na)^+$: 391.1264. Found: 391.1266.



14 **15**

Alcohol 15 (initial scale-up procedure). A biphasic mixture of the unpurified alcohol **14** from the experiment above (48.0 g, 130 mmol) in tetrahydrofuran (370 mL), methanol (370 mL), and 2 M aqueous sodium dihydrogen phosphate solution (550 mL) was deoxygenated by bubbling argon gas through the solution with a stainless-steel needle for 30 min. The reaction flask was equipped with a water-cooled reflux condenser, and the assembly was placed in a heating bath at 52 °C. After 15 h, the heating bath was removed and the reaction flask was allowed to cool to 23 °C. Water (1.2 L), ethyl acetate (800 mL), hexanes (200 mL), and dipotassium hydrogen phosphate (380 g) were added in sequence. After 30 min, the layers were separated. The aqueous layer was extracted in sequence with ethyl acetate–hexanes (2:1, 1 × 800 mL) and dichloromethane (2 × 800 mL). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide the alcohol **15** (43.0 g, a 11.1:1 mixture of **15** and its C4-epimer, the starting material **14**) as a dark brown foam. This material was used in the next transformation without purification.

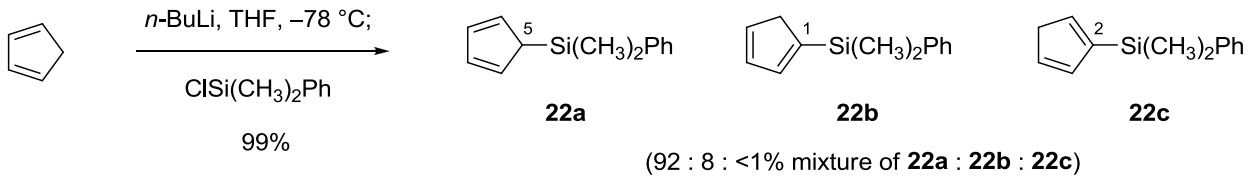


AB Enone 1 (initial scale-up procedure). *tert*-Butyldimethylsilyl trifluoromethanesulfonate (37.0 mL, 164 mmol, 1.4 equiv) was added dropwise by syringe to an ice-cooled solution of the unpurified alcohol **15** from the experiment above (43.0 g, 117 mmol, 1 equiv) and 2,6-lutidine (24.0 mL, 210 mmol, 1.8 equiv) in dichloromethane (800 mL). After 15 min, the cooling bath was removed and the reaction flask was allowed to warm to 23 °C. After 20 min, pH 7 phosphate buffer solution (600 mL), water (500 mL), and saturated aqueous sodium chloride solution (100 mL) were added in sequence. After 20 min, the layers were separated. The aqueous layer was extracted with dichloromethane (1 × 1 L, then 1 × 800 mL). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was dissolved in a mixture of dichloromethane–ethyl acetate (98:2, 100 mL). The solution was filtered through a pad of silica gel, rinsing with dichloromethane–ethyl acetate (98:2, 3 L). The filtrate was concentrated. The residue was dissolved in a mixture of ethyl acetate (100 mL) and hexanes (200 mL) at 55 °C. The solution was allowed to cool to 23 °C causing a white precipitate to form. After 12 h, the solids were collected on a sintered-glass funnel. The solids were rinsed with hexanes–ethyl acetate (7:1, 16 mL), and the mother liquors were retained (for processing, see below). The washed solids were dried in vacuo (0.1 mmHg) to provide pure AB enone **1** as a white solid (10.5 g, mp = 148–150 °C).

The mother liquors were concentrated. The oily residue was purified by flash-column chromatography on silica gel (100% hexanes initially, then grading to 10% ethyl acetate–hexanes) to provide pure AB enone **1** (28.6 g) as a light-yellow foam. The total weight of AB enone **1** obtained was 39.1 g (42% yield, three steps, from **13**). TLC (20% ethyl acetate–hexanes): R_f = 0.34 (UV, CAM). $[\alpha]^{23}_D$ +150 (*c* 1.00, $CHCl_3$). Literature $[\alpha]^{23}_D$ +138 (*c* 0.52, $CHCl_3$).[13] ^{1}H NMR (600 MHz, $CDCl_3$), δ: 7.51 (d, 2H, *J* = 1.5 Hz), 7.50–7.34 (m, 3H), 6.94 (m, 1H), 6.10 (ddd, 1H, *J* = 10.3, 1.5, 1.5 Hz), 5.36 (m, 2H), 3.79 (d, 1H, *J* = 10.7 Hz), 2.83 (m, 2H), 2.78 (m, 1H), 2.46 (s, 6H), 0.84 (s, 9H), 0.27 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 193.1, 187.6, 181.3, 167.4, 149.2, 135.0, 128.5, 128.4(5), 128.4(2), 128.3, 108.3, 83.2, 72.5, 59.5, 47.8, 41.9, 26.0, 25.5, 19.0, –2.5, –4.1. FTIR (neat), cm^{-1}: 2942 (s), 1719 (s), 1678 (s), 1602 (m), 1510 (s), 1053 (s), 733 (s). HRMS (ESI): Calcd for $(C_{26}H_{34}N_2O_5 + H)^+$: 483.2315. Found: 483.2310.

[13] The optical rotation for AB enone **1** of 93% ee reported by Brubaker and Myers (*Org. Lett.* **2007**, *9*, 3523–3525) was $[\alpha]^{23}_D$ –138 (*c* 0.52, $CHCl_3$), which is in error. The correct rotation for AB enone **1** of 93% ee is $[\alpha]^{23}_D$ +138 (*c* 0.52, $CHCl_3$).

Introduction of the dimethylphenylsilyl group (depicted in Scheme 10):



22a **22b** **22c**

(92 : 8 : <1% mixture of **22a** : **22b** : **22c**)

5-Dimethylphenylsilylcyclopentadiene (22a). The following experimental procedure is a modification of the protocol reported by Landais and Parra-Rapado.[14] The primary modification here is the use of water and hexanes during the workup. A newly titrated[15] solution of *n*-butyllithium in hexanes (2.50 M, 351 mL, 879 mmol, 1 equiv) was added dropwise by cannula over 25 min to a cold (–78 °C, dry ice–acetone bath) solution of freshly cracked cyclopentadiene (58.1 g, 879 mmol, 1 equiv) in tetrahydrofuran (880 mL). After 20 min, a white precipitate began to form. After 30 min, dropwise addition of a solution of dimethylphenylchlorosilane (150 g, 879 mmol, 1 equiv) in tetrahydrofuran (800 mL) by cannula was initiated and completed within 45 min. After 1 h, water (100 mL) was added. The cooling bath was replaced with a water bath at ambient temperature (23 °C). After 20 min, the product mixture was partitioned between water (1 L) and hexanes (1 L). The layers were separated. The aqueous layer was extracted with hexanes (1 × 500 mL). The organic layers were combined. The combined solution was washed with half-saturated aqueous sodium chloride solution (500 mL). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated in vacuo (first at 40 mmHg, then at 0.1 mmHg) at 23 °C for 2 h to provide 5-dimethylphenylsilylcyclopentadiene as a pale-yellow liquid (175 g, 99 %, a 92:8:<1 mixture of

[14] Landais, Y.; Parra-Rapado, L. *Eur. J. Org. Chem.* **2000**, 401–418.
[15] Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879–1880.

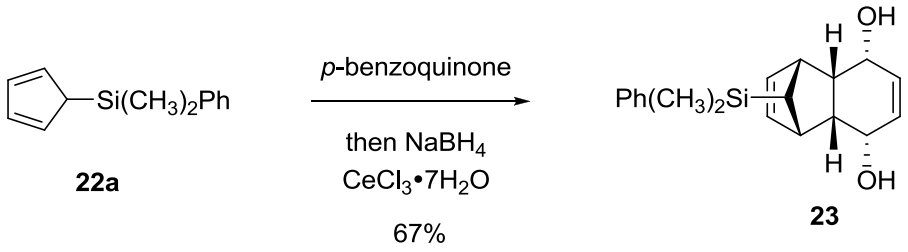
22a:**22b**:**22c**). The product was stored at −80 °C where it formed an off-white solid. This material was used in the next transformation without purification. The ^{1}H NMR data obtained for 5-dimethylphenylsilylcyclopentadiene were in agreement with values previously reported.[14] A small sample of the product was purified by flash-column chromatography on silica gel (2.5% dichloromethane–pentanes initially, then grading to 5% dichloromethane–pentanes) to provide 5-dimethylphenylsilylcyclopentadiene (**22a**) as a clear, colorless liquid [>95:5 mixture of 5-dimethylphenylsilylcyclopentadiene (**22a**) and its two positional isomers] and 1-dimethylphenylsilylcyclopentadiene (**22b**) as a clear, colorless liquid [89:11 mixture of 1-dimethylphenylsilylcyclopentadiene (**22b**) and its positional isomer 2-dimethylphenylsilylcyclopentadiene (**22c**)]. These products were retained (for study, see below) and stored at −80 °C.

Alternatively, the crude product mixture was purified by dissolving a 500-mg sample in hexanes (2 mL). The solution was placed into a dry ice–acetone bath which led to precipitation of a white solid. After 5 min, hexanes (1 mL) were added. After 20 min, the liquid supernatant was removed by syringe, then hexanes (2 mL) were added to the solids that remained. After 5 min, the liquid supernatant was removed by syringe, then hexanes (1 mL) were added to the solids that remained. The liquid supernatant was removed by syringe. The solids that remained were dried in vacuo (0.1 mmHg) at −78 °C. The flask was then warmed in an ice–water bath, causing the solids to melt. 5-Dimethylphenylsilylcyclopentadiene was thus obtained as a clear, colorless liquid (>95:5 mixture of 5-dimethylphenylsilylcyclopentadiene (**22a**) and its two positional isomers) and was stored at −80 °C.

^{1}H NMR (600 MHz, *d*6-benzene, >95:5 mixture of 5-dimethylphenylsilylcyclopentadiene and its two positional isomers, asterisk denotes minor silicon isomers), δ: 7.44–7.42 (2H, m),

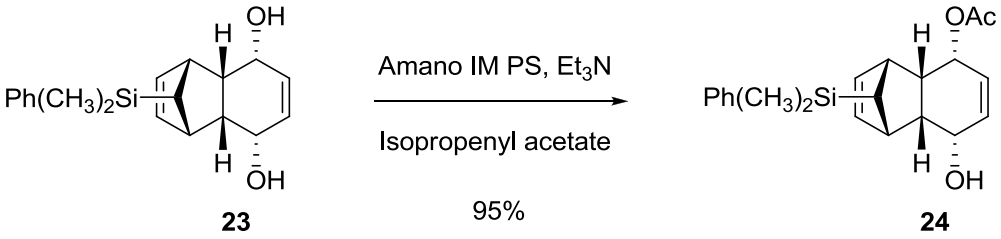
7.20–7.18 (3H, m), 6.86* (1H, app t, *J* = 1.3 Hz), 6.61 (2H, br s), 6.54* (2H, app d, *J* = 1.3 Hz), 6.46 (2H, br s), 3.48 (1H, br s), 2.86* (2H, app d, *J* = 1.5 Hz), 2.78* (2H, app q, *J* = 1.3 Hz), 0.38* (6H, s), 0.37* (6H, s), 0.06 (6H, s).

^{1}H NMR (600 MHz, *d*6-benzene, 89:11 mixture of 1-dimethylphenylsilylcyclopentadiene and 2-dimethylphenylsilylcyclopentadiene, asterisk denotes minor silicon isomers), δ: 7.49–7.47 (2H, m), 7.21–7.17 (3H, m), 6.86 (1H, app t, *J* = 1.3 Hz), 6.69–6.67* (1H, m), 6.54 (2H, app d, *J* = 1.3 Hz), 6.37–6.34* (1H, m), 2.86 (2H, app d, *J* = 1.5 Hz), 2.78* (2H, app q, *J* = 1.3 Hz), 0.38* (6H, s), 0.37 (6H, s), 0.07* (6H, s).



Meso diol 23. An ice-cooled solution of the mixture of dimethylphenylsilyl-substituted cyclopentadienes (124 g, 92% **22a**, 569 mmol **22a**, 1 equiv **22a**) in a mixture of methanol (133 mL) and dichloromethane (66 mL) was added dropwise by cannula over 30 min to an ice-cooled solution of *p*-benzoquinone (63.3 g, 586 mmol, 1.03 equiv) in a mixture of methanol (800 mL) and dichloromethane (400 mL). After 12 h, cerium trichloride heptahydrate (109 g, 293 mmol, 0.51 equiv) was added in four equal portions over 10 min. After 15 min, sodium borohydride (22.2 g, 586 mmol, 1.03 equiv) was added in 1-g portions over 45 min so as to maintain an internal reaction temperature between 5–10 °C. After 10 min, the product mixture was concentrated to half its original volume. Ethyl acetate (500 mL) was added and the mixture was filtered through a pad of silica gel, rinsing with ethyl acetate (1 L). The filtrate was mechanically stirred while 1 M aqueous citric acid solution (250 mL) was added dropwise. After 15 min, the resulting biphasic mixture was partitioned between 1 M aqueous citric acid solution (750 mL) and ethyl acetate (1 L). The layers were separated. The organic layer was washed sequentially with water (2 × 500 mL), 1 M aqueous sodium carbonate solution containing 10 % by volume 1 M aqueous sodium sulfite solution (3 × 500 mL), and saturated aqueous sodium chloride solution (500 mL). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide a light-yellow solid. The solid (158 g) was dissolved in boiling dichloromethane (350 mL) and hot (60 °C) hexanes (900 mL)

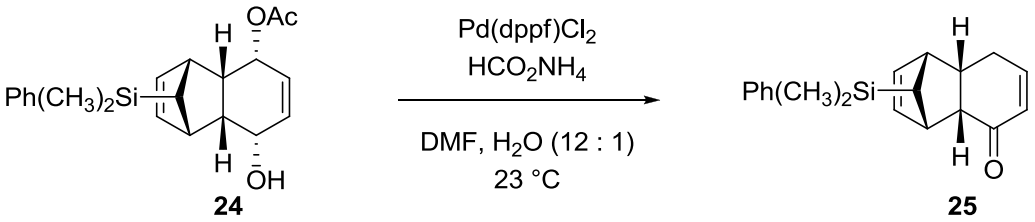
was then added slowly over 10 min. The resulting solution was allowed to cool slowly to 23 °C during which time a white crystalline solid formed. The mixture was cooled in an ice–water bath. After 1 h, the solids were collected on a sintered-glass funnel. The solids were washed with ice-cooled hexanes. The washed solids were dried in vacuo (0.1 mmHg) at 23 °C providing the pure meso diol **23** (129 g, 67% yield from the total mass of 124 g, 73% yield based on the amount of **22a** present) as a white crystalline solid. Mp = 98–100 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.45–7.43 (m, 2H), 7.33–7.31 (m, 3H), 5.82 (s, 2H), 5.55 (s, 2H), 4.41–4.39 (m, 2H), 3.11 (s, 2H), 2.79–2.78 (m, 2H), 1.63 (d, 2H, J = 5.6 Hz), 1.23 (s, 1H), 0.21 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 140.2, 135.0, 133.5, 131.9, 128.5, 127.6, 66.7, 51.7, 47.8, 45.2, –1.3; FTIR (neat), cm^{-1}: 3383 (br), 2967 (w), 2911 (w). HRMS (ESI): Calcd for $(C_{19}H_{24}O_2 + Na)^+$: 335.1438. Found: 335.1465.



23 **24**

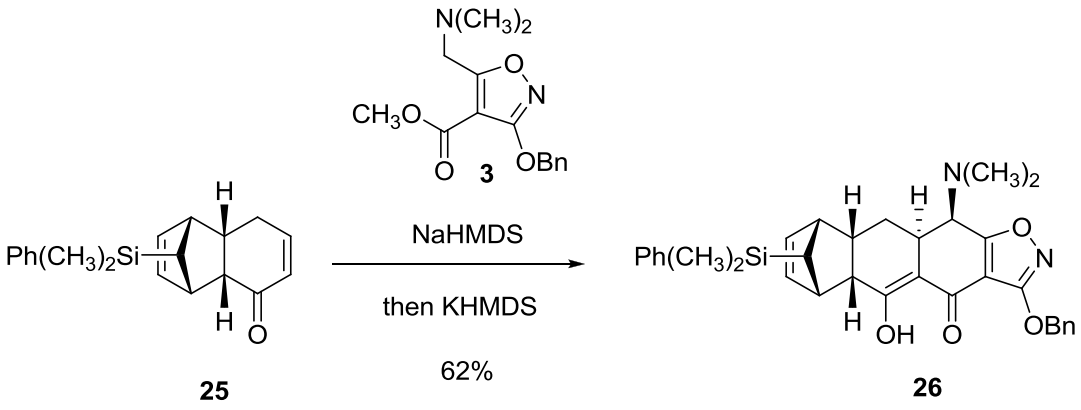
Monoacetate 24. Immobilized lipase PS (Amano, 150 g) was added to a mechanically stirred solution of meso diol **23** (150 g, 480 mmol, 1 equiv) and isopropenyl acetate (168 g, 1.68 mmol, 3.5 equiv) in triethylamine (1.6 L). After 20 h, the slurry was filtered through a sintered-glass funnel. The filter cake was rinsed with ethyl acetate (1 L). The filtrate was concentrated. The oily residue was partitioned between saturated aqueous ammonium chloride solution (800 mL) and ethyl acetate (1.5 L). The layers were separated. The organic layer was washed sequentially with saturated aqueous sodium bicarbonate solution (800 mL) and saturated aqueous sodium chloride solution (800 mL). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide an off-white solid. The solid (161 g) was dissolved in ethyl acetate (1.2 L) and charcoal (32.0 g, Darco G-60) was added to the solution. The resulting slurry was stirred at 50 °C for 60 min, then was cooled to 23 °C. The cooled slurry was filtered through a pad of Celite, rinsing with ethyl acetate (1 L). The filtrate was concentrated in vacuo (0.1 mmHg) to provide the pure monoacetate **24** (159 g, 94%) as a white solid. Mp = 68–72 °C. $[\alpha]^{23}_{D}$ +46.6 (*c* 1.00, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.44–7.42 (m, 2H), 7.33–7.31 (m, 3H), 5.76 (dd, 1H, *J* = 2.8, 5.4 Hz), 5.69 (dd, 1H, *J* = 2.8, 5.4 Hz), 5.43–5.40 (m, 1H), 5.38–5.35 (m, 1H), 5.27–5.24 (m, 1H), 4.78–4.44 (m, 1H), 3.14 (s, 1H), 3.03–2.99 (m, 1H), 2.91 (s, 1H), 2.87–2.84 (m, 1H), 2.11 (s, 3H), 1.52 (d, 1H, *J* = 6.1 Hz), 1.17 (s, 1H), 0.19 (s, 3H), 0.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.7, 140.1,

135.3, 135.1, 133.5, 131.8, 128.5, 127.6, 126.7, 70.1, 66.7, 50.4, 48.5, 47.8, 44.0, 40.8, 21.1, −1.3, −1.4; FTIR (neat), cm^{-1}: 3455 (br), 3067 (w), 2967 (w), 1738 (s), 1371 (s), 1246 (s); HRMS (ESI): Calcd for $(C_{21}H_{26}O_3Si + Na)^+$ 377.1543, found 377.1544.



Cyclohexenone 25. A solution of ammonium formate (48.0 g, 0.760 mmol, 1.5 equiv) and monoacetate **24** (180 g, 0.510 mmol, 1 equiv) in dimethylformamide (1.3 L) and water (100 mL) was deoxygenated by bubbling argon gas through the solution with a stainless-steel needle for 40 min. [1,1′-Bis(diphenylphosphino)ferrocene]dichloropalladium(II)•CH_2Cl_2 (16.9 g, 0.020 mmol, 0.04 equiv) was added in one portion. After 16 h, the reaction flask was placed in a −10 °C cooling bath (acetone bath with temperature control by periodic addition of dry ice). Methyl *tert*-butyl ether (500 mL), water (250 mL), and charcoal (36.0 g, Darco® G-60) were added in sequence. After 1 h, the product mixture was filtered through a pad of Celite, rinsing with methyl *tert*-butyl ether (500 mL). Water (500 mL) was added to the filtrate. The layers were separated. The organic layer was washed sequentially with saturated aqueous sodium chloride solution (4 × 300 mL), saturated aqueous sodium bicarbonate solution (2 × 300 mL), and water (1 × 300 mL). The washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated to provide a brown solid. The solid (135 g) was dissolved in methyl *tert*-butyl ether (1 L), then MP-TMT resin (Biotage, 73.0 g) was added. The resulting slurry was stirred at 23 °C. After 16 h, the mixture was filtered through a sintered-glass funnel, rinsing with methyl *tert*-butyl ether (200 mL). The filtrate was concentrated in vacuo (0.1 mmHg) at 23 °C to provide cyclohexenone **25** (124 g, 82%) as an orange solid. This material was used in the next transformation without purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.44–7.42 (m, 2H), 7.34–7.32 (m, 3H), 6.63 (ddd, 1H, *J* = 4.1, 4.1, 10.3

Hz), 6.03 (dd, 1H, *J* = 2.8, 5.6 Hz), 5.98 (dd, 1H, *J* = 2.9, 5.7 Hz), 5.84 (ddd, 1H, *J* = 2.3, 2.3, 10.3 Hz), 3.50–3.48 (m, 1H), 3.09–3.07 (m, 1H), 2.92 (dd, 1H, *J* = 4.0, 9.8 Hz), 2.74 (dddd, 1H, *J* = 3.5, 3.5, 10.3, 10.3), 2.55 (m, 1H), 2.01–1.96 (m, 1H), 1.21 (s, 1H), 0.21 (s, 3H), 0.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 200.8, 149.6, 139.9, 137.5, 134.5, 133.8, 129.4, 129.0, 128.0, 52.3, 51.9, 51.4, 50.8, 36.5, 27.7, –1.22, –1.23.



Michael–Claisen cyclization product 26. A solution of sodium hexamethyldisilazide [obtained by dissolving solid sodium hexamethyldisilazide (93.2 g, 483 mmol, 1.15 equiv) in tetrahydrofuran (500 mL)] was added dropwise by cannula over 30 min to a mechanically stirred solution of methyl 3-benzyloxy-5-(dimethylaminomethyl)isoxazole-4-carboxylate (**3**, 134 g, 462 mmol, 1.1 equiv) in tetrahydrofuran (1.2 L) at −50 °C (using an acetone cooling bath with temperature control by periodic addition of dry ice). After 1 h, a fine off-white suspension formed, at which point a solution of cyclohexenone **25** (124 g, 421 mmol, 1 equiv) in tetrahydrofuran (200 mL) was added dropwise by cannula over 40 min. After 1 h, a solution of potassium hexamethyldisilazide [obtained by dissolving solid potassium hexamethyldisilazide (88.0 g, 421 mmol, 1 equiv) in tetrahydrofuran (420 mL)] was added dropwise by cannula over 30 min. The reaction mixture was allowed to warm to −20 °C over the course of 1 h. After 2 h, the reaction mixture was allowed to warm to −10 °C over 20 min. After 2 h, water (300 mL) was added. The cooling bath was removed and the reaction flask was allowed to warm to 23 °C. The reaction mixture was concentrated. The oily residue was partitioned between water (500 mL) and ethyl acetate (1 L). The layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 500 mL). The organic layers were combined. The combined solution was washed

with saturated aqueous sodium chloride solution (500 mL). The washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated. The oily residue was dissolved in methyl *tert*-butyl ether (1.2 L) and the resulting solution was mechanically stirred with cooling in an ice–water bath. A solution of hydrochloric acid in ether (2 M, 260 mL, 520 mmol, 1.24 equiv) was added dropwise by syringe over 30 min, during which time a white precipitate began to form. After 1 h, the suspension was filtered through a sintered-glass funnel. The filter cake was washed sequentially with methyl *tert*-butyl ether (2 × 500 mL) and ether (500 mL). The filter cake was dried in vacuo (0.1 mmHg) at 23 °C. The dried filter cake (250 g) was dissolved in a mixture of dichloromethane (1.4 L) and ethyl acetate (800 mL). After 30 min, an off-white solid began to precipitate. After 1 h, the slurry was concentrated to a volume of approximately 1.6 L. The concentrated slurry was filtered through a sintered-glass funnel. The filter cake was rinsed with ethyl acetate (2 × 400 mL) and the mother liquors were retained (for processing, see below). The filter cake was dried in vacuo (0.1 mmHg) at 23 °C to afford the Michael–Claisen cyclization product **26** as its hydrochloride salt, an off-white solid (155 g).

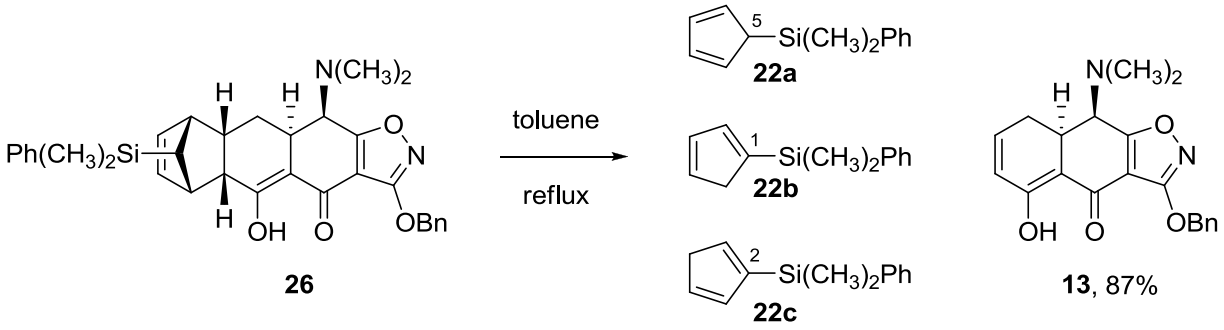
The mother liquors were concentrated. The residue was partitioned between 1 M aqueous dipotassium hydrogen phosphate solution (400 mL) and dichloromethane (800 mL). The layers were separated. The organic layer was washed with saturated aqueous sodium chloride solution (400 mL). The washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was dissolved in dichloromethane (75 mL) and the resulting solution was filtered through a pad of neutral alumina, rinsing with 20% ethyl acetate–hexanes. The filtrate was concentrated. The residue was dissolved in ether (226 mL) and the resulting solution was cooled in an ice–water bath.

A solution of hydrochloric acid in ether (2 M, 23 mL) was added over 20 min, during which time a white precipitate began to form. After 1 h, the slurry was filtered through a sintered-glass funnel. The filter cake was rinsed with ether (50 mL). The filter cake was dried in vacuo (0.1 mmHg) at 23 °C to afford an off-white solid. The solid was dissolved in a mixture of dichloromethane (200 mL) and ethyl acetate (150 mL). The resulting solution was concentrated to a volume of approximately 150 mL, at which point precipitation of an off-white solid began to occur. The resulting slurry was cooled in an ice–water bath. After 30 min, the slurry was filtered through a sintered-glass funnel. The filter cake was rinsed with ethyl acetate (50 mL) then dried in vacuo (0.1 mmHg) at 23 °C to provide a second crop of the Michael–Claisen cyclization product **26** as its hydrochloride salt, an off-white solid (10.0 g). The total weight of the hydrochloride salt isolated was 165 g. Mp = 158–160 °C (decomp). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 15.05 (s, 1H), 12.86 (br s, 1H), 7.52–7.50 (m, 2H), 7.43–7.31 (m, 8H), 5.94–5.91 (m, 2H, 5.40 (s, 2H), 4.35 (d, *J* = 5.6 Hz, 1H), 3.33 (br s, 1H), 3.12–3.09 (m, 2H), 2.98–2.96 (m, 2H), 2.85 (br s, 3H), 2.54–2.46 (m, 4H), 2.35–2.32 (m, 1H), 1.39 (s, 1H), 0.20 (s, 3H), 0.19 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.5, 182.0, 168.3, 168.2, 139.3, 135.8, 135.7, 134.6, 133.7, 129.3, 129.2, 129.0, 128.9, 128.0, 111.8, 103.3, 73.3, 58.1, 54.5, 52.5, 50.6, 45.5 (br), 45.4, 39.7, 38.3 (br), 35.0, 28.0, 27.2, –1.29, –1.31. FTIR (neat), cm^{-1}: 3053 (m), 2959 (m), 1644 (br), 1609 (br), 1512 (s). HRMS (ESI): Calcd for $(C_{33}H_{38}N_2O_4Si + H)^+$ 554.2595. Found 554.2504.

The hydrochloride salt (165 g) was dissolved in a mixture of dichloromethane (1 L) and ethyl acetate (500 mL). The resulting solution was concentrated to a volume of approximately 500 mL, at which point precipitation of an off-white solid began to occur. The resulting slurry was cooled in an ice–water bath. After 30 min, the slurry was filtered through a sintered-glass

funnel. The filter cake was rinsed sequentially with ethyl acetate (400 mL) and ether (400 mL). The washed filter cake was partitioned between 1 M aqueous dipotassium hydrogen phosphate solution (400 mL) and dichloromethane (800 mL). The layers were separated. The organic layer was washed sequentially with 1 M aqueous dipotassium hydrogen phosphate solution (400 mL) and saturated aqueous sodium chloride solution (400 mL). The washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated to provide the Michael–Claisen cyclization product **26** (146 g, 62%) as a white foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 15.1 (s, 1H), 7.52–7.50 (m, 2H), 7.47–7.28 (m, 8H), 5.92 (t, 2H, *J* = 1.4 Hz), 5.37 (s, 2H), 3.59 (d, 1H, *J* = 6.8 Hz), 3.32 (s, 1H), 2.98 (s, 1H), 2.91-2.88 (m, 1H), 2.76–2.69 (m, 2H), 2.17–2.08 (m, 1H), 2.13 (s, 6H), 1.78 (dd, 1H, *J* = 4.8, 15.1 Hz), 1.35 (s, 1H), 0.20 (s, 3H), 0.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 184.2, 181.0, 177.0, 168.0, 139.9, 135.6, 135.5, 135.4, 133.8, 129.0, 128.9, 128.8, 128.7, 127.9, 108.3, 105.8, 72.6, 58.6, 53.9, 52.9, 50.1, 45.4, 45.4, 42.3, 40.5, 34.6, 26.7, –1.20. FTIR (neat), cm^{-1}: 2953 (m), 1738 (s), 1630 (s), 1611 (s), 1508 (s), 1244 (s). HRMS (ESI): Calcd for $(C_{33}H_{36}N_2O_4Si + H)^+$ 553.2517. Found 553.2211.

Retro-Diels–Alder reaction with dimethylphenylsilyl substitution (depicted in Scheme 10):

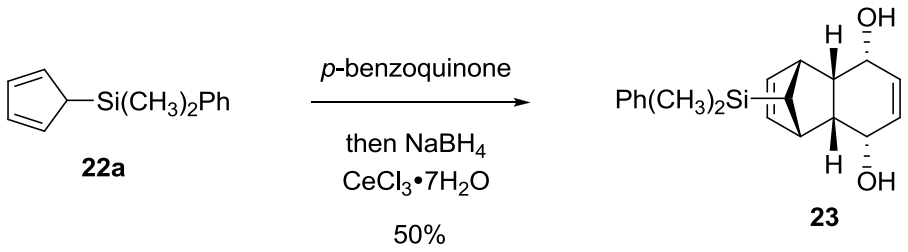


Retro-Diels–Alder product 13 (protocol used on scale). A solution of the Michael–Claisen cyclization product **26** (85.0 g, 154 mmol) in toluene (769 mL) was deoxygenated by bubbling argon gas through the solution with a stainless-steel needle for 30 min. The reaction flask was fitted with a water-cooled reflux condenser and the assembly was placed in an oil bath. The reaction flask was heated at reflux (oil bath temperature of 120 °C). After 10 h, the heating bath was removed and the reaction flask was allowed to cool to 23 °C. The reaction mixture was concentrated. The oily residue was dissolved in a mixture of ethyl acetate (60 mL) and hexane (370 mL) at 60 °C. The resulting solution was allowed to cool to 23 °C. After 40 min, a solid began to precipitate and the flask was placed in an ice–water bath. After 10 min, the solids were collected on a sintered-glass funnel. The solids were rinsed with hexanes (50 mL) and the mother liquors were retained (for processing, see below). The rinsed solids were dried in vacuo (0.1 mmHg) at 23 °C to provide the first crop of the retro-Diels–Alder product **13** as yellow prisms (38.0 g, mp 103–105 °C).

The mother liquors were concentrated. The oily residue was filtered through a pad of silica gel, rinsing with hexanes (1.5 L). The filtrate was concentrated by rotary evaporation,

affording a mixture of dimethylphenylsilyl cyclopentadienes enriched in the **22a** isomer (28.5 g, 142 mmol, isomeric distribution: 75% **22a** : 18% **22b** : 7% **22c**) as a light-yellow liquid in 93% yield. The silica-gel pad was then rinsed with 30% ethyl acetate–hexanes (3 L). The eluent was concentrated. The residue was dissolved in a mixture of ethyl acetate (16 mL) and hexanes (65 mL) at 60 °C. The solution was allowed to cool to 23 °C, and seeds of the yellow, crystalline solid from the first crop were added. Within 10 min crystallization began to occur. After 40 min, the suspension was cooled in an ice–water bath. After 2 h, the crystals were collected on a sintered-glass funnel. The crystals were rinsed with hexanes (50 mL). The rinsed crystals were dried in vacuo (0.1 mmHg) at 23 °C to provide a second crop of the retro-Diels–Alder product **13** as a yellow, crystalline solid (9.40 g, mp 103–105 °C). The total weight of the retro-Diels–Alder product obtained was 47.4 g (135 mmol, 87%). Characterization data for this compound were identical to those reported above.

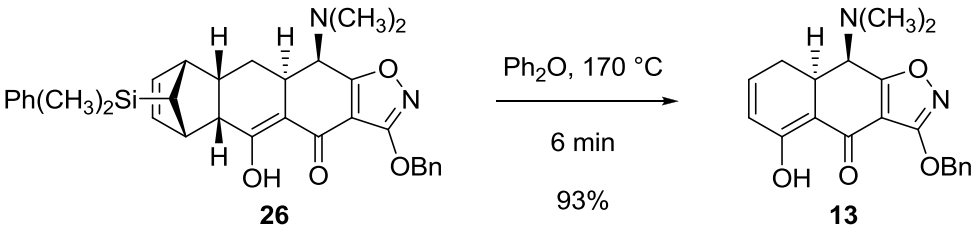
Recycling of 5-dimethylphenylsilylcyclopentadiene (depicted in Scheme 10):



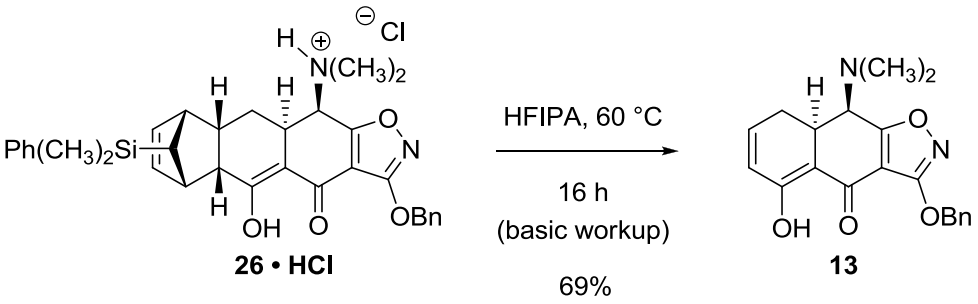
Meso diol 23 (5-dimethylphenylsilylcyclopentadiene recycling procedure). An ice-cooled solution of the dimethylphenylsilylcyclopentadiene isomers recovered from the retro-Diels–Alder reaction above (28.5 g, 75% **22a**, 107 mmol **22a**, 1 equiv **22a**) in a mixture of methanol (52 mL) and dichloromethane (28 mL) was added dropwise by cannula over 30 min to an ice-cooled solution of *p*-benzoquinone (14.6 g, 135 mmol, 1.26 equiv) in a mixture of methanol (180 mL) and dichloromethane (77 mL). After 16 h, cerium trichloride heptahydrate (50.5 g, 135 mmol, 1.26 equiv) was added in four equal portions over 10 min. After 15 min, sodium borohydride (2.56 g, 67.7 mmol, 0.63 equiv) was added in 200-mg portions over 30 min. After 30 min, the product mixture was concentrated to half its original volume. Ethyl acetate (200 mL) was added and the mixture was filtered through a pad of silica gel, rinsing with ethyl acetate (300 mL). The filtrate was stirred while 1 M aqueous citric acid solution (150 mL) was added dropwise. After 15 min, the resulting biphasic mixture was partitioned between 1 M aqueous citric acid solution (250 mL) and ethyl acetate (300 mL). The layers were separated. The organic layer was washed sequentially with water (2 × 300 mL), 1 M aqueous sodium carbonate solution containing 10 % by volume 1 M aqueous sodium sulfite solution (3 × 200 mL), and saturated aqueous sodium chloride solution (200 mL). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide a light-yellow solid. The solid was dissolved in boiling dichloromethane (100 mL) and hot (60

°C) hexanes (225 mL) was then added slowly over 10 min. The resulting solution was allowed to cool slowly to 23 °C during which time a white crystalline solid formed. The mixture was cooled in an ice–water bath. After 1 h, the solids were collected on a sintered-glass funnel. The solids were washed with ice-cooled hexanes. The washed solids were dried in vacuo (0.1 mmHg) at 23 °C providing the pure meso diol **23** (22.4 g, 50% yield from the total diene mass of 28.5 g, 67% yield from the amount of **22a** present, mp 98–100 °C) as a white crystalline solid. Characterization data for this compound were identical to those reported above.

Alternative retro-Diels–Alder reaction conditions (depicted in Scheme 11):

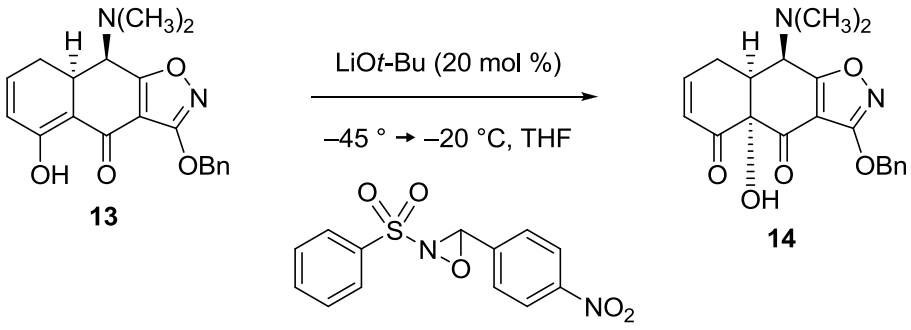


Retro-Diels–Alder product 13 (alternative reaction conditions). A solution of Michael–Claisen cyclization product **26** (3.31 g, 5.99 mmol, 1 equiv) in diphenyl ether (17.1 mL) was deoxygenated by bubbling argon gas through the solution using a stainless-steel needle for 30 min. The reaction flask was placed into a 170 °C oil bath. After 6 min, the hot oil bath was removed and the reaction flask was placed in a 23 °C water bath. After 10 min, hexanes (10 mL) were added. The solution was loaded onto a column of silica gel (150 mL, deactivated with triethylamine). The column was flushed sequentially with hexanes (~200 mL) and 5% ether–hexanes (~200 mL) to remove diphenyl ether. The filtrate was disposed. The column was flushed with a final 700-mL volume of 100% ether. The filtrate was concentrated to provide the retro-Diels–Alder product **13** as a yellow solid (2.06 g, 93%). Characterization data for this compound were identical to those reported above.



Retro-Diels–Alder product 13 (alternative reaction conditions). A solution of the hydrochloride salt of Michael–Claisen cyclization product **26** (**26•HCl**, 250 mg, 0.424 mmol, 1 equiv) in hexafluoroisopropanol (2.2 mL) was heated at reflux. After 12 h, the heating bath was removed and the reaction flask was allowed to cool to 23 °C. The reaction mixture was partitioned between 1 M aqueous dipotassium hydrogen phosphate solution (50 mL) and dichloromethane (50 mL). The layers were separated. The organic layer was washed with saturated aqueous sodium chloride solution (50 mL). The washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (100% hexanes initially, grading to 30% ethyl acetate–hexanes) to provide pure retro-Diels–Alder product **13** as a yellow solid (104 mg, 69%). Characterization data for this compound were identical to those reported above.

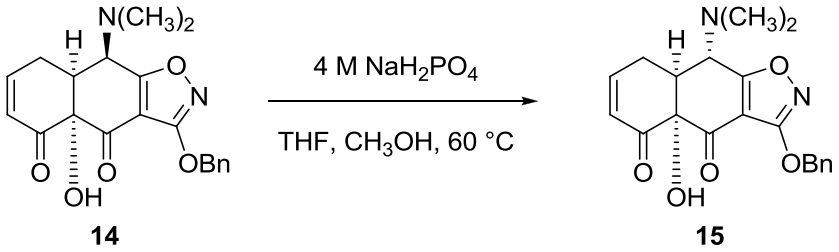
Synthesis of AB enone 1 (later reactions, optimized, depicted in Scheme 12):



Alcohol 16 (optimized scale-up procedure). A solution of lithium *tert*-butoxide [obtained by dissolving solid lithium *tert*-butoxide (2.15 g, 26.9 mmol, 0.2 equiv) in tetrahydrofuran (53 mL)] was added dropwise by cannula over 10 min to a mechanically stirred slurry of 3-(4-nitrophenyl)-2-(phenylsulfonyl)-oxaziridine[16] (49.4 g, 161 mmol, 1.2 equiv) and retro-Diels–Alder product **13** (47.4 g, 135 mmol, 1 equiv) in tetrahydrofuran (384 mL) at –40 °C (cooled using an acetone bath with temperature control by periodic addition of dry ice). The slurry was allowed to warm to –20 °C over 60 min. After 30 min, ethyl acetate (522 mL) was added and the reaction flask was fitted with a one-liter, pressure-equalizing addition funnel. 1 M Aqueous hydrochloric acid solution (522 mL) was added dropwise via the addition funnel over 20 min. After 10 min, the cooling bath was removed and the reaction flask was allowed to warm to 23 °C. After 1.5 h, all solids had dissolved, forming a biphasic mixture with two well defined homogeneous layers. The layers were separated. The organic layer was extracted with 1 M aqueous hydrochloric acid solution (300 mL). The aqueous layers were combined. The combined solution was washed with ethyl acetate (2 × 300 mL). The washed solution was mechanically stirred with cooling in an ice–water bath, and the pH was adjusted to 9 by the slow addition of 23% aqueous ammonium hydroxide solution. Ethyl acetate (1.5 L) was added. After

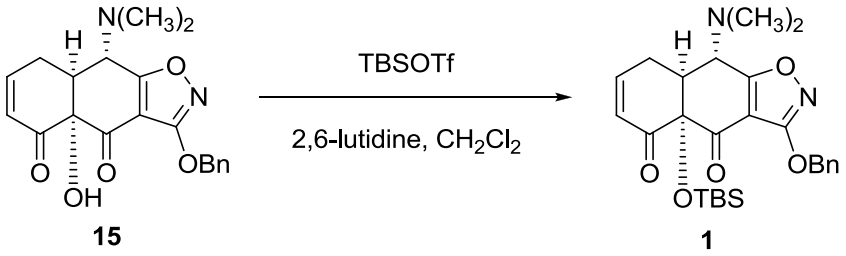
[16] Vishwakarma, L. C.; Stringer, O. D.; Davis, F. A. *Organic Syntheses* **1993**, *Coll. Vol. 8*, 546.

30 min, the layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 300 mL). The organic layers were combined. The combined solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated to provide the alcohol **14** (42.5 g, 115 mmol) as a light purple solid. This material was used in the next transformation without purification. Characterization data for this compound were identical to those reported above.



14 **15**

Alcohol 15 (optimized scale-up procedure). A biphasic mixture of the unpurified alcohol **14** from the experiment above (42.5 g, 115 mmol), methanol (192 mL), tetrahydrofuran (385 mL), and 4 M aqueous sodium dihydrogen phosphate solution (433 mL) was deoxygenated by bubbling argon gas through the solution with a stainless-steel needle for 45 min. The reaction flask was fitted with a water-cooled reflux condensor, and the assembly was placed in a heating bath at 60 °C. After 20 h, the heating bath was removed and the reaction flask was allowed to cool to 23 °C. The reaction mixture was partitioned between water (500 mL) and ethyl acetate (1 L). The layers were separated. The organic layer was washed with water (4 × 300 mL). The aqueous layers were combined and the combined solution was extracted with ethyl acetate (2 × 300 mL). The organic layers were combined. The combined solution was washed with saturated aqueous sodium chloride solution (500 mL). The washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated to provide alcohol **15** (41.2 g, 112 mmol, a 12.8:1 mixture of **15** and its C4-epimer, the starting material **14**) as a light-brown foam. This material was used in the next transformation without purification. Characterization data for this compound were identical to those reported above.



15 **1**

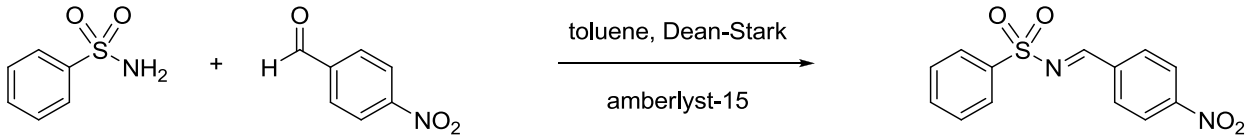
AB enone 1 (optimized scale-up procedure). *tert*-Butyldimethylsilyl trifluoromethanesulfonate (32.1 mL, 140 mmol, 1.25 equiv) was added dropwise by syringe to an ice-cooled solution of the unpurified alcohol **15** from the experiment above (41.2 g, 112 mmol, 1 equiv) and 2,6-lutidine (19.5 mL, 168 mmol, 1.5 equiv) in dichloromethane (560 mL). After 10 min, the cooling bath was removed and the reaction flask was allowed to warm to 23 °C. After 30 min, methanol (9.00 mL, 224 mmol, 2 equiv) was added. After 20 min, ethyl acetate (300 mL) was added. The reaction mixture was concentrated to half its original volume. The concentrated solution was partitioned between water (300 mL) and ethyl acetate (200 mL). The layers were separated. The aqueous layer was extracted with ethyl acetate (300 mL). The organic layers were combined. The combined solution was washed sequentially with 0.1 M pH 5 aqueous sodium citrate buffer solution (2 × 250 mL) and saturated aqueous sodium chloride solution (250 mL). The washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated to afford an orange solid. The orange solid was dissolved in ethyl acetate (250 mL) and charcoal (8.00 g, Darco-60) was added to the solution. The resulting slurry was warmed with stirring in a 50 °C heating bath. After 30 min, the heating bath was removed and the flask was allowed to cool to 23 °C. The slurry was filtered through a pad of Celite, rinsing with ethyl acetate. The filtrate was concentrated to half its original volume, during which time a white precipitate began to form. The solids were collected on a sintered-glass funnel and the mother liquors were retained (for processing, see below). The

solids were rinsed with ice-cooled hexanes (100 mL). The rinsed solids were dried in vacuo (0.1 mmHg) at 23 °C to provide the first crop of pure AB enone **1** as a white solid (31.6 g, mp 148–150°C).

The mother liquors were concentrated to afford an orange solid. The solid was dissolved in dichloromethane (50 mL) and the resulting solution was filtered through a pad of silica gel, eluting with 20% ethyl acetate–hexanes. The filtrate was concentrated to afford an orange solid. The solid was dissolved in a mixture of ethyl acetate (20 mL) and heptanes (80 mL) at 55 °C. The resulting solution was slowly cooled to 0 °C, at which point a white precipitate began to form. The solids were collected on a sintered-glass funnel and the mother liquors were retained (for processing, see below). The solids were rinsed with ice-cooled hexanes (50 mL). The rinsed solids were dried in vacuo (0.1 mmHg) at 23 °C to provide the second crop of pure AB enone **1** as a white solid (6.00 g, mp 148–150 °C).

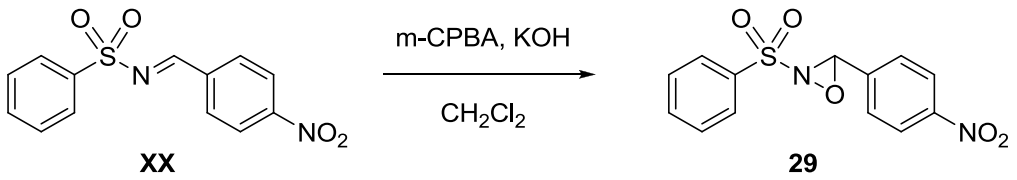
The mother liquors were concentrated to afford an orange solid. The solid was dissolved in a mixture of ethyl acetate (15 mL) and heptanes (60 mL) at 55°C. The resulting solution was slowly cooled to 0 °C, at which point a white precipitate began to form. The solids were collected on a sintered-glass funnel. The solids were rinsed with ice-cooled hexanes (50 mL). The rinsed solids were dried in vacuo (0.1 mmHg) at 23 °C to provide the third crop of pure AB enone **12** as a white solid (4.00 g, mp 149–151 °C). The total weight of pure AB enone **1** obtained was 41.6 g (86 mmol, 64%, 3 steps). $[\alpha]^{24}_{D}$ +148 (*c* 1.13, $CHCl_3$). Characterization data for this compound were identical to those reported above.

Synthesis of 3-(4-Nitrophenyl)-2-(phenylsulfonyl)-oxaziridine:



***N*-(4-Nitrobenzylidene)benzenesulfonamide.**[17] A two-liter, single-necked, round-bottomed flask equipped with a magnetic stir bar was charged with benzenesulfonamide (40.0 g, 254 mmol, 1 equiv), 4-nitrobenzaldehyde (38.5 g, 254 mmol, 1 equiv), amberlyst 15 ion-exchange resin (2.00 g), and toluene (850 mL). The flask was equipped with a water-cooled reflux condenser and a Dean-Stark trap. The reaction assembly was placed in an oil bath heated to 123 °C. After 30 min, all the solids had dissolved (except the amberlyst 15 resin). After 20 h, heating was discontinued and the flask was allowed to cool to 23 °C, at which point a solid began to precipitate. The solids were dissolved in a mixture of ethyl acetate (2 L) and acetone (1 L). The solution was filtered through a sintered-glass funnel. The filtrate was concentrated to provide a yellow solid. The yellow solid was dissolved in boiling ethyl acetate (1 L). The solution was allowed to cool to 23 °C at which point a yellow crystalline solid formed. The solids were collected on a sintered-glass funnel. The solids were rinsed with ice-cooled ethyl acetate. The washed solids were dried in vacuo (0.1 mmHg) at 23 °C providing pure *N*-(4-nitrobenzylidene)benzenesulfonamide (33 g, 45%) as a yellow crystalline solid. ^{1}H NMR (500 MHz, $CDCl_3$), δ: 9.14 (1H, s), 8.34 (2H, d, J = 9.0 Hz), 8.12 (2H, d, J = 9.0 Hz), 8.05–8.03 (2H, m), 7.70–7.67 (1H, m), 7.62–7.58 (2H, m).

[17] This procedure is adapted from that of Davis et al.: *Organic Syntheses* **1993**, *Coll. Vol. 8*, 546.

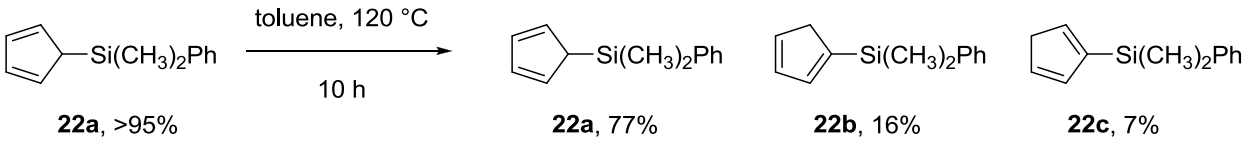


XX **29**

3-(4-Nitrophenyl)-2-(phenylsulfonyl)-oxaziridine.[18] Powdered potassium hydroxide (11.7 g, 209 mmol, 1.35 equiv) was added in 1-g portions over 5 min to an ice-cooled, mechanically stirred solution of *meta*-chloroperoxybenzoic acid (77% w/w, 46.9 g, 209 mmol, 1.35 equiv) in dichloromethane (1 L), forming a white slurry. After 25 min, *N*-(4-nitrobenzylidene)benzenesulfonamide (45.0 g, 155 mmol, 1 equiv) was added in 5-g portions over 10 min. After 30 min, the slurry was filtered through a pad of Celite, rinsing with dichloromethane (1 L). The filtrate was washed sequentially with saturated aqueous sodium sulfite solution (800 mL) and 1 M aqueous potassium carbonate solution (2 × 500 mL). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide 3-(4-nitrophenyl)-2-(phenylsulfonyl)-oxaziridine as an off-white solid (46.7 g, 98%). ^{1}H NMR (500 MHz, $CDCl_3$), δ: 8.27 (2H, d, J = 8.5 Hz), 8.06 (2H, d, J = 8.5 Hz), 7.82–7.78 (1H, m), 7.69–7.63 (4H, m), 5.60 (1H, s).

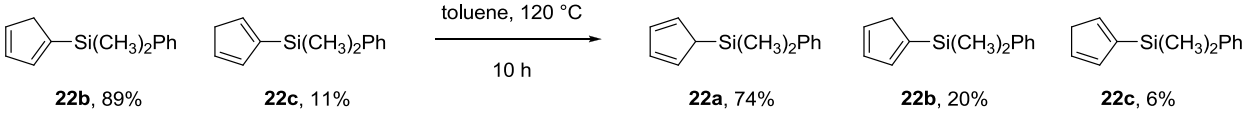
[18] This procedure is adapted from that of Ruano et al.: Ruano, J. L. G.; Aleman, J.; Fajardo, C.; Parra, A. *Org. Lett.* **2005**, *7*, 5493–5496.

Thermodynamics of dimethylphenylsilylcyclopentadiene:



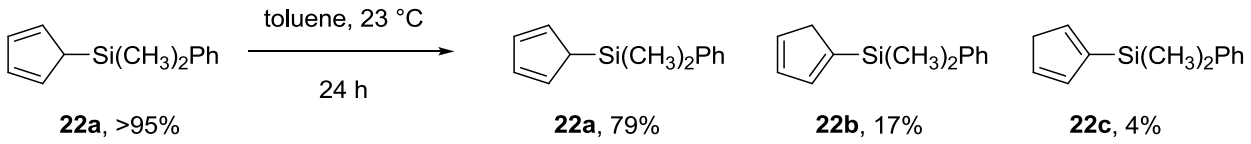
22a, >95% **22a**, 77% **22b**, 16% **22c**, 7%

Dimethylphenylsilylcyclopentadiene equilibration. A solution of 5-dimethylphenylsilylcyclopentadiene (**22a**, >95%, 56.0 mg, 0.280 mmol, 1 equiv) in toluene (1.4 mL) was heated at 120 °C. After 10 h, the solution was allowed to cool to 23 °C. The solution was concentrated and the oily residue was analyzed by ^{1}H NMR (600 MHz, *d*6-benzene, 23 °C). The isomeric distribution was found to be 77% **22a**, 16% **22b**, and 7% **22c**.



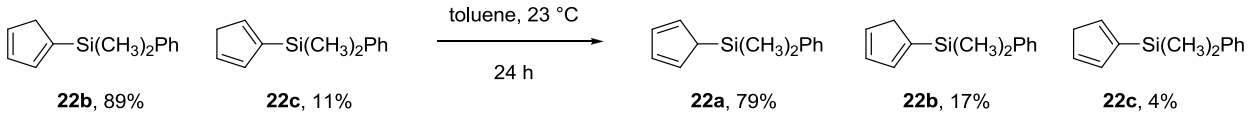
22b, 89% **22c**, 11% **22a**, 74% **22b**, 20% **22c**, 6%

Dimethylphenylsilylcyclopentadiene equilibration. A solution of 1-dimethylphenylsilylcyclopentadiene (**22b**) and 2-dimethylphenylsilylcyclopentadiene (**22c**) (89:11, 56.0 mg, 0.280 mmol, 1 equiv) in toluene (1.4 mL) was heated at 120 °C. After 10 h, the solution was allowed to cool to 23 °C. The solution was concentrated and the oily residue was analyzed by ^{1}H NMR (600 MHz, *d*6-benzene, 23 °C). The isomeric distribution was found to be 74% **22a**, 20% **22b**, and 6% **22c**.



22a, >95% **22a**, 79% **22b**, 17% **22c**, 4%

Dimethylphenylsilylcyclopentadiene equilibration. A solution of 5-dimethylphenylsilylcyclopentadiene (**22a**, >95%, 56.0 mg, 0.280 mmol, 1 equiv) in toluene (1.4 mL) was stirred at 23 °C. After 24 h, the solution was concentrated and the oily residue was analyzed by ^{1}H NMR (600 MHz, *d*6-benzene, 23 °C). The isomeric distribution was found to be 79% **22a**, 17% **22b**, and 4% **22c**.



22b, 89% **22c**, 11% **22a**, 79% **22b**, 17% **22c**, 4%

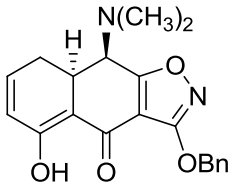
Dimethylphenylsilylcyclopentadiene equilibration. A solution of 1-dimethylphenylsilylcyclopentadiene (**22b**) and 2-dimethylphenylsilylcyclopentadiene (**22c**) (89:11, 30.0 mg, 0.150 mmol, 1 equiv) in toluene (1.4 mL) was stirred at 23 °C. After 24 h, the solution was concentrated and the oily residue was analyzed by ^{1}H NMR (600 MHz, *d*6-benzene, 23 °C). The isomeric distribution was found to be 79% **22a**, 17% **22b**, and 4% **22c**.

X-ray Crystallographic Laboratory

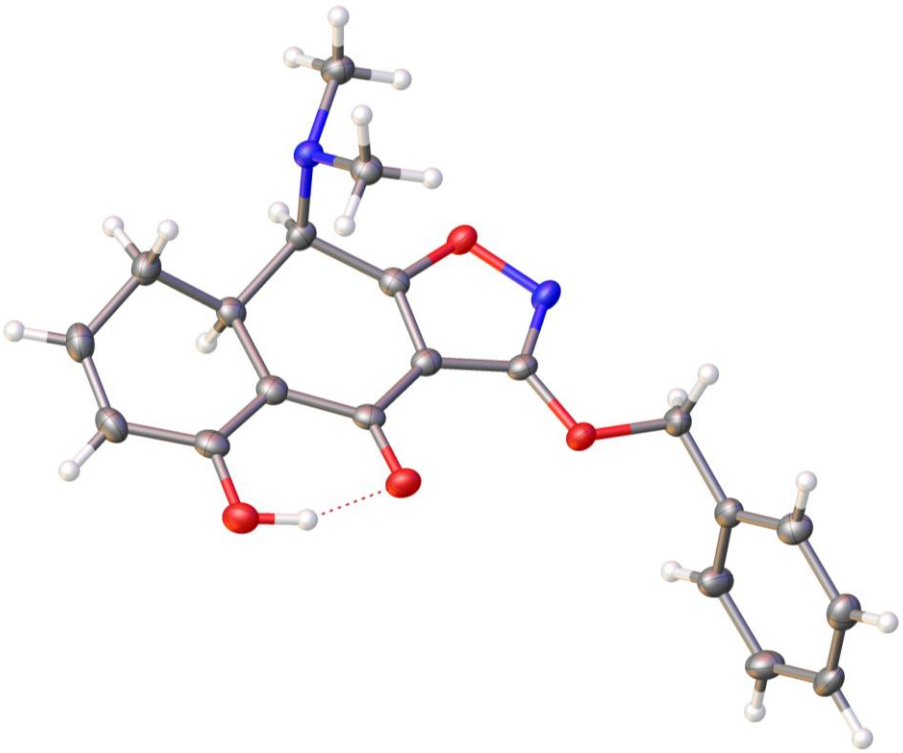
Harvard University

Structure Report

for



13



X-Ray Crystallography: Data were collected from a crystal mounted on a Bruker APEX II DUO CCD diffractometer equipped with an Oxford Cryosystems nitrogen flow apparatus using $Cu_{K\alpha}$ radiation (λ=1.54178 Å) at 100 K. The collection method involved 1.0° scans in ω at 30°, 55°, 80° and 105° in 2θ. Data integration to 0.84-Å resolution was carried out using SAINT V7.46 A with reflection spot size optimization.[19] Absorption corrections were made with the program SADABS.[20] The structure was solved by the direct methods procedure and refined by least-squares methods against F^2 using SHELXS-97 and SHELXL-97.[20] Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were allowed to ride on the respective atoms. Crystal data as well as details of data collection and refinement are summarized in Table S1, geometric parameters are listed in Table S2, and hydrogen-bond parameters are listed in Table S3. The graphic depicted on page S55 was generated using the Olex2 program,[21] the ORTEP plot of Figure S1 was generated with the SHELXL-97 program,[20] and the graphic depicted in Figure S2 was generated with Accelrys DS Visualizer 2.0.[22]

Table S1. Experimental details.

	RDP
Crystal data	
Chemical formula	$C_{20}H_{20}N_2O_4$
M_r	352.38
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	100
a, b, c (Å)	6.4713 (2), 12.2439 (3), 21.5133 (6)
V (Å^3)	1704.58 (8)
Z	4

[19] Bruker AXS (2009). SMART and SAINTPLUS. Bruker AXS, Madison, Wisconsin.
[20] Sheldrick, G. M *Acta Crys.* **2008**, *A64*, 112–122.
[21] Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H *J. Appl. Cryst.* **2009**, *42*, 339–341.
[22] Accelrys DS Visualizer v2.0.1.7347, 2007, Accelrys Software Inc.

Radiation type	Cu *K*α
μ (mm^{-1})	0.79
Crystal size (mm)	0.28 × 0.22 × 0.18
Data collection	
Diffractometer	CCD area detector diffractometer
Absorption correction	Multi-scan *SADABS*
T_{min}, T_{max}	0.809, 0.871
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	42649, 2922, 2902
R_{int}	0.040
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.026, 0.070, 1.08
No. of reflections	2922
No. of parameters	242
No. of restraints	0
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$)	0.15, -0.16
Absolute structure	Flack H D (1983), Acta Cryst. A39, 876-881
Flack parameter	0.05 (15)

Computer programs: *APEX2* v2009.3.0, *SAINT* 7.46A, *SHELXS97*, *SHELXL97*, Bruker *SHELXTL*.[19,20]

Table S2. Selected geometric parameters (Å, °)

O1—C1	1.3409 (16)	C7—C8	1.3762 (18)
O1—N1	1.4424 (13)	C8—C9	1.4339 (18)
O2—C7	1.3372 (17)	C9—C10	1.4586 (18)
O2—H2	0.96 (2)	C10—C11	1.4345 (18)

O3—C9	1.2629 (16)	C12—C13	1.4982 (19)
O4—C11	1.3339 (15)	C12—H12A	0.9900
O4—C12	1.4593 (15)	C12—H12B	0.9900
N1—C11	1.3097 (17)	C13—C14	1.3821 (19)
N2—C20	1.4587 (16)	C13—C18	1.3913 (19)
N2—C19	1.4619 (16)	C14—C15	1.383 (2)
N2—C2	1.4695 (16)	C14—H14	0.9500
C1—C10	1.3547 (19)	C15—C16	1.386 (2)
C1—C2	1.5006 (18)	C15—H15	0.9500
C2—C3	1.5583 (17)	C16—C17	1.383 (2)
C2—H2A	1.0000	C16—H16	0.9500
C3—C8	1.5231 (18)	C17—C18	1.385 (2)
C3—C4	1.5298 (18)	C17—H17	0.9500
C3—H3	1.0000	C18—H18	0.9500
C4—C5	1.5049 (19)	C19—H19A	0.9800
C4—H4A	0.9900	C19—H19B	0.9800
C4—H4B	0.9900	C19—H19C	0.9800
C5—C6	1.332 (2)	C20—H20A	0.9800
C5—H5	0.9500	C20—H20B	0.9800
C6—C7	1.452 (2)	C20—H20C	0.9800
C6—H6	0.9500		
C1—O1—N1	108.37 (9)	C1—C10—C11	103.81 (11)
C7—O2—H2	103.7 (12)	C1—C10—C9	121.62 (12)
C11—O4—C12	114.70 (10)	C11—C10—C9	134.34 (13)
C11—N1—O1	104.62 (10)	N1—C11—O4	122.92 (12)
C20—N2—C19	111.11 (10)	N1—C11—C10	112.32 (12)
C20—N2—C2	112.03 (10)	O4—C11—C10	124.75 (12)
C19—N2—C2	114.30 (10)	O4—C12—C13	108.68 (10)
O1—C1—C10	110.87 (11)	O4—C12—H12A	110.0
O1—C1—C2	120.96 (11)	C13—C12—H12A	110.0
C10—C1—C2	127.70 (12)	O4—C12—H12B	110.0
N2—C2—C1	112.26 (10)	C13—C12—H12B	110.0

N2—C2—C3	114.41 (10)	H12A—C12—H12B	108.3
C1—C2—C3	107.62 (10)	C14—C13—C18	118.54 (13)
N2—C2—H2A	107.4	C14—C13—C12	121.11 (12)
C1—C2—H2A	107.4	C18—C13—C12	120.26 (12)
C3—C2—H2A	107.4	C13—C14—C15	120.83 (13)
C8—C3—C4	110.29 (11)	C13—C14—H14	119.6
C8—C3—C2	116.03 (10)	C15—C14—H14	119.6
C4—C3—C2	111.23 (10)	C14—C15—C16	120.27 (13)
C8—C3—H3	106.2	C14—C15—H15	119.9
C4—C3—H3	106.2	C16—C15—H15	119.9
C2—C3—H3	106.2	C17—C16—C15	119.45 (13)
C5—C4—C3	110.88 (12)	C17—C16—H16	120.3
C5—C4—H4A	109.5	C15—C16—H16	120.3
C3—C4—H4A	109.5	C16—C17—C18	119.99 (13)
C5—C4—H4B	109.5	C16—C17—H17	120.0
C3—C4—H4B	109.5	C18—C17—H17	120.0
H4A—C4—H4B	108.1	C17—C18—C13	120.90 (13)
C6—C5—C4	120.96 (13)	C17—C18—H18	119.6
C6—C5—H5	119.5	C13—C18—H18	119.6
C4—C5—H5	119.5	N2—C19—H19A	109.5
C5—C6—C7	119.67 (13)	N2—C19—H19B	109.5
C5—C6—H6	120.2	H19A—C19—H19B	109.5
C7—C6—H6	120.2	N2—C19—H19C	109.5
O2—C7—C8	122.22 (13)	H19A—C19—H19C	109.5
O2—C7—C6	116.40 (12)	H19B—C19—H19C	109.5
C8—C7—C6	121.36 (13)	N2—C20—H20A	109.5
C7—C8—C9	118.95 (12)	N2—C20—H20B	109.5
C7—C8—C3	118.09 (12)	H20A—C20—H20B	109.5
C9—C8—C3	122.42 (11)	N2—C20—H20C	109.5
O3—C9—C8	122.99 (12)	H20A—C20—	109.5

		H20C	
O3—C9—C10	121.43 (12)	H20B—C20—H20C	109.5
C8—C9—C10	115.58 (11)		
C1—O1—N1—C11	0.48 (12)	C3—C8—C9—O3	-178.19 (11)
N1—O1—C1—C10	0.23 (13)	C7—C8—C9—C10	173.80 (11)
N1—O1—C1—C2	172.96 (10)	C3—C8—C9—C10	2.36 (16)
C20—N2—C2—C1	83.13 (13)	O1—C1—C10—C11	-0.79 (13)
C19—N2—C2—C1	-44.39 (14)	C2—C1—C10—C11	-172.90 (12)
C20—N2—C2—C3	-153.85 (10)	O1—C1—C10—C9	174.47 (10)
C19—N2—C2—C3	78.64 (13)	C2—C1—C10—C9	2.36 (19)
O1—C1—C2—N2	-69.01 (14)	O3—C9—C10—C1	-169.16 (11)
C10—C1—C2—N2	102.38 (15)	C8—C9—C10—C1	10.30 (17)
O1—C1—C2—C3	164.22 (10)	O3—C9—C10—C11	4.4 (2)
C10—C1—C2—C3	-24.39 (17)	C8—C9—C10—C11	-176.14 (13)
N2—C2—C3—C8	-92.03 (13)	O1—N1—C11—O4	178.50 (11)
C1—C2—C3—C8	33.47 (14)	O1—N1—C11—C10	-0.99 (13)
N2—C2—C3—C4	35.12 (14)	C12—O4—C11—N1	6.22 (17)
C1—C2—C3—C4	160.61 (10)	C12—O4—C11—C10	-174.34 (11)
C8—C3—C4—C5	-48.59 (14)	C1—C10—C11—N1	1.14 (14)
C2—C3—C4—C5	-178.80 (11)	C9—C10—C11—N1	-173.21 (12)
C3—C4—C5—C6	34.30 (18)	C1—C10—C11—O4	-178.34 (11)

C4—C5—C6—C7	-1.7 (2)	C9—C10—C11—O4	7.3 (2)
C5—C6—C7—O2	165.97 (13)	C11—O4—C12—C13	-165.96 (11)
C5—C6—C7—C8	-15.6 (2)	O4—C12—C13—C14	-106.43 (14)
O2—C7—C8—C9	3.58 (18)	O4—C12—C13—C18	77.16 (15)
C6—C7—C8—C9	-174.80 (12)	C18—C13—C14—C15	-2.1 (2)
O2—C7—C8—C3	175.39 (11)	C12—C13—C14—C15	-178.57 (13)
C6—C7—C8—C3	-3.00 (17)	C13—C14—C15—C16	1.3 (2)
C4—C3—C8—C7	35.04 (14)	C14—C15—C16—C17	0.2 (2)
C2—C3—C8—C7	162.65 (11)	C15—C16—C17—C18	-0.9 (2)
C4—C3—C8—C9	-153.45 (12)	C16—C17—C18—C13	0.0 (2)
C2—C3—C8—C9	-25.85 (16)	C14—C13—C18—C17	1.5 (2)
C7—C8—C9—O3	-6.75 (18)	C12—C13—C18—C17	177.98 (13)

Table S3. Hydrogen-bond parameters

D—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (°)
O2—H2···O3	0.96 (2)	1.62 (2)	2.5205 (13)	153.7 (18)

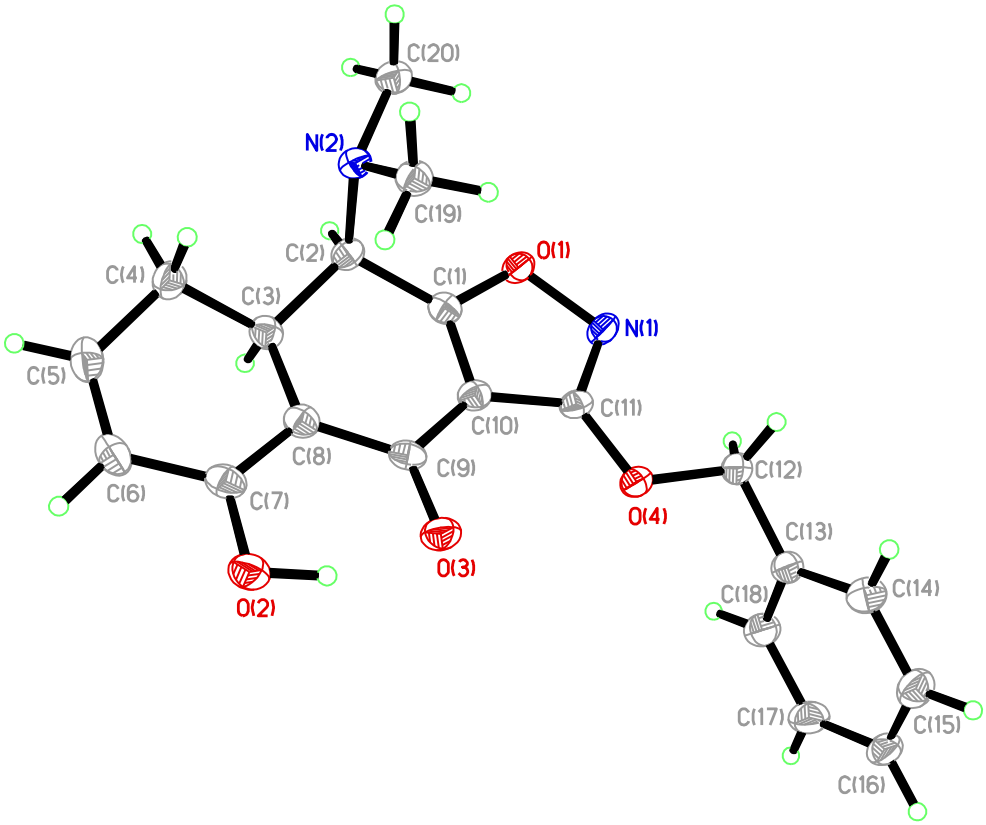


Figure S1. Perspective views showing 50% probability displacement.

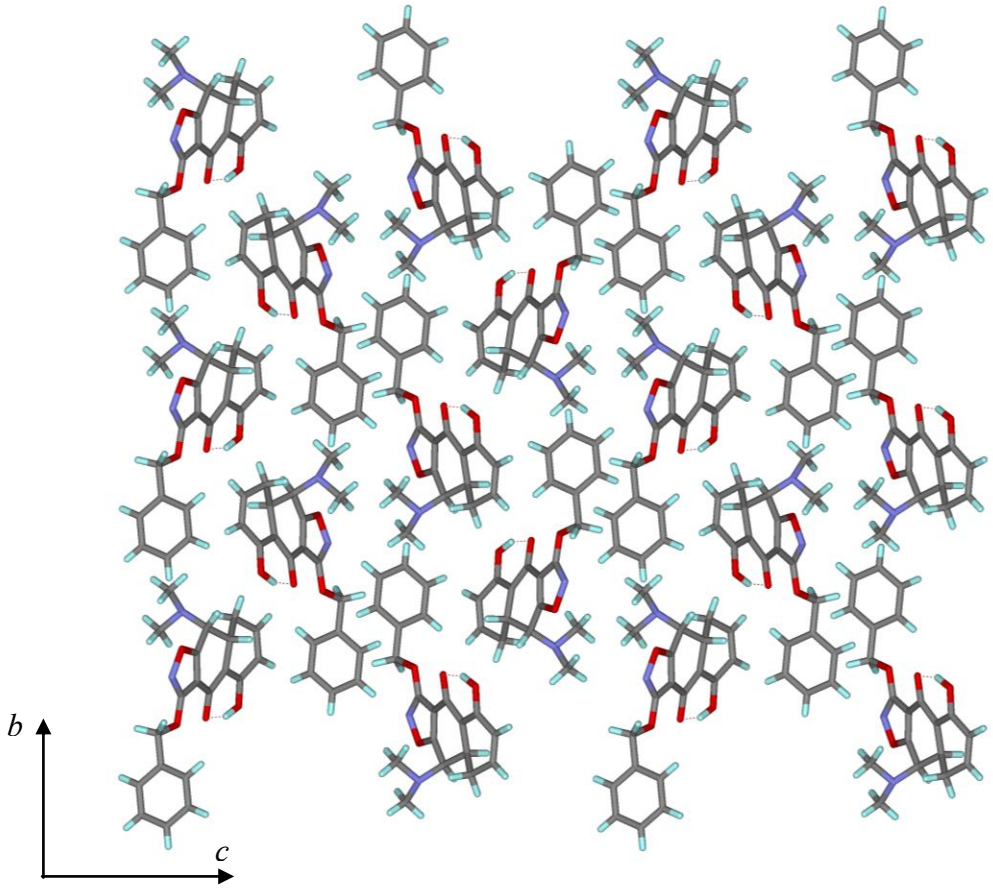


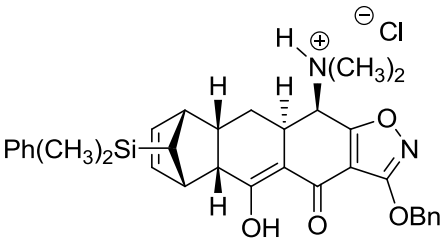
Figure S2. Three-dimensional supramolecular architecture viewed along the *a*-axis direction.

X-ray Crystallographic Laboratory

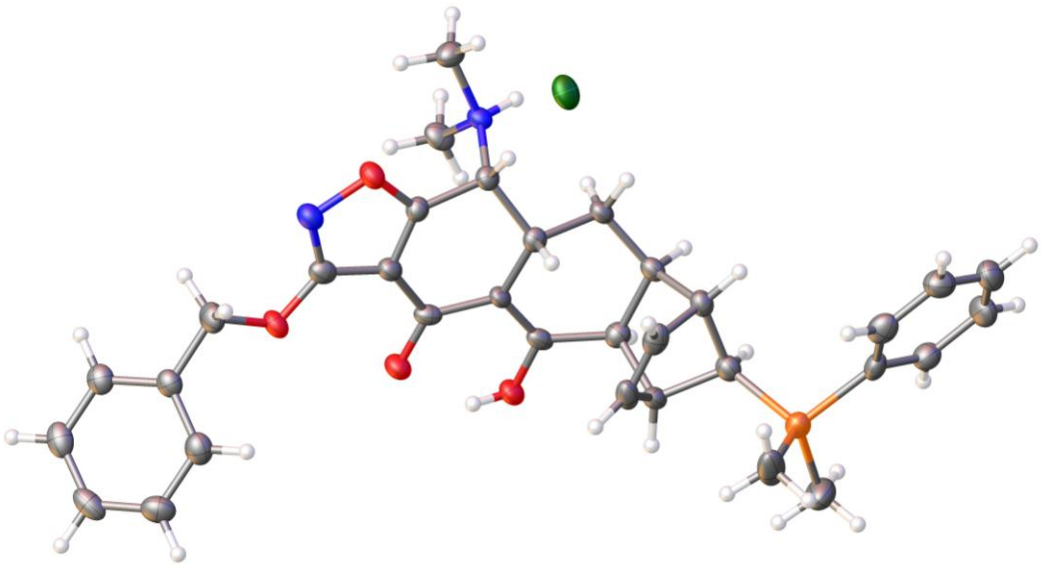
Harvard University

Structure Report

for



26 • HCl



X-Ray Crystallography: Data were collected from a crystal mounted on a Bruker APEX II DUO CCD diffractometer equipped with an Oxford Cryosystems nitrogen flow apparatus using $Mo_{K\alpha}$ radiation (λ=0.71073 Å) at 100 K. The collection method involved 0.5° scans in ω at 28° in 2θ. Data integration to 0.82-Å resolution was carried out using SAINT V7.46 A with reflection spot size optimization.[19] Absorption corrections were made with the program SADABS.[20] The structure was solved by the direct methods procedure and refined by least-squares methods against F^2 using SHELXS-97 and SHELXL-97.[20] Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were allowed to ride on the respective atoms. Crystal data as well as details of data collection and refinement are summarized in Table S4, geometric parameters are listed in Table S5, and hydrogen-bond parameters are listed in Table S6. The graphic depicted on page S64 was generated using the Olex2 program,[21] the ORTEP plot of Figure S3 was generated with the SHELXL-97 program,[20] and the graphic depicted in Figure S4 was generated with Accelrys DS Visualizer 2.0.[22]

Table S4. Experimental details.

	AD-2-5
Crystal data	
Chemical formula	$C_{33.25}H_{37.25}Cl_{1.50}N_2O_4Si$
M_r	610.17
Crystal system, space group	Orthorhombic, $P2_12_12$
Temperature (K)	100
a, b, c (Å)	8.3338 (7), 25.680 (2), 15.2004 (12)
V (Å^3)	3253.0 (5)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.23
Crystal size (mm)	0.32 × 0.26 × 0.10

Data collection	
Diffractometer	CCD area detector diffractometer
Absorption correction	Multi-scan *SADABS* (Sheldrick, 2009)
T_{min}, T_{max}	0.929, 0.977
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	18394, 6403, 4579
R_{int}	0.071
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.061, 0.167, 1.06
No. of reflections	6403
No. of parameters	388
No. of restraints	0
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	1.22, -0.35
Absolute structure	Flack H D (1983), Acta Cryst. A39, 876-881
Flack parameter	-0.08 (10)

Computer programs: *APEX2* v2009.3.0, *SAINT* 7.46A, *SHELXS97*, *SHELXL97*, Bruker *SHELXTL*.[19,20]

Table S5. Selected geometric parameters (Å, °)

Si1—C25	1.836 (5)	C14—C15	1.490 (5)
Si1—C24	1.856 (5)	C14—H14A	1.0000
Si1—C26	1.865 (4)	C16—C17	1.494 (6)
Si1—C23	1.881 (4)	C16—H16A	0.9900
O1—C15	1.350 (5)	C16—H16B	0.9900
O1—N1	1.417 (4)	C17—C18	1.379 (6)
O2—C1	1.339 (5)	C17—C22	1.389 (6)
O2—C16	1.458 (5)	C18—C19	1.379 (6)

O3—C3	1.258 (4)	C18—H18A	0.9500
O4—C5	1.329 (5)	C19—C20	1.373 (7)
O4—H4O	0.8400	C19—H19A	0.9500
N1—C1	1.308 (5)	C20—C21	1.367 (7)
N2—C33	1.484 (5)	C20—H20A	0.9500
N2—C32	1.486 (5)	C21—C22	1.386 (6)
N2—C14	1.509 (5)	C21—H21A	0.9500
N2—H2N	0.8811	C22—H22A	0.9500
C1—C2	1.412 (6)	C23—H23A	1.0000
C2—C15	1.324 (5)	C24—H24A	0.9800
C2—C3	1.459 (5)	C24—H24B	0.9800
C3—C4	1.428 (5)	C24—H24C	0.9800
C4—C5	1.360 (6)	C25—H25A	0.9800
C4—C13	1.507 (5)	C25—H25B	0.9800
C5—C6	1.481 (6)	C25—H25C	0.9800
C6—C11	1.545 (6)	C26—C27	1.392 (6)
C6—C7	1.577 (5)	C26—C31	1.402 (6)
C6—H6A	1.0000	C27—C28	1.381 (6)
C7—C8	1.511 (6)	C27—H27A	0.9500
C7—C23	1.515 (6)	C28—C29	1.374 (7)
C7—H7A	1.0000	C28—H28A	0.9500
C8—C9	1.304 (6)	C29—C30	1.384 (7)
C8—H8A	0.9500	C29—H29A	0.9500
C9—C10	1.503 (6)	C30—C31	1.384 (6)
C9—H9A	0.9500	C30—H30A	0.9500
C10—C23	1.538 (6)	C31—H31A	0.9500
C10—C11	1.563 (5)	C32—H32A	0.9800
C10—H10A	1.0000	C32—H32B	0.9800
C11—C12	1.518 (5)	C32—H32C	0.9800
C11—H11A	1.0000	C33—H33A	0.9800
C12—C13	1.533 (5)	C33—H33B	0.9800
C12—H12A	0.9900	C33—H33C	0.9800
C12—H12B	0.9900	C1S—Cl2	1.710 (9)

C13—C14	1.540 (5)	C1S—Cl2^{i}	1.710 (9)
C13—H13A	1.0000	C1S—H1SA	0.9644
C25—Si1—C24	109.2 (3)	C2—C15—O1	111.1 (3)
C25—Si1—C26	110.7 (2)	C2—C15—C14	128.1 (4)
C24—Si1—C26	109.2 (2)	O1—C15—C14	120.9 (3)
C25—Si1—C23	106.7 (2)	O2—C16—C17	108.1 (3)
C24—Si1—C23	114.8 (2)	O2—C16—H16A	110.1
C26—Si1—C23	106.23 (18)	C17—C16—H16A	110.1
C15—O1—N1	107.9 (3)	O2—C16—H16B	110.1
C1—O2—C16	115.0 (3)	C17—C16—H16B	110.1
C5—O4—H4O	109.5	H16A—C16—H16B	108.4
C1—N1—O1	104.3 (3)	C18—C17—C22	119.7 (4)
C33—N2—C32	111.0 (3)	C18—C17—C16	120.3 (4)
C33—N2—C14	111.3 (3)	C22—C17—C16	119.9 (4)
C32—N2—C14	114.5 (3)	C17—C18—C19	119.8 (4)
C33—N2—H2N	99.8	C17—C18—H18A	120.1
C32—N2—H2N	95.2	C19—C18—H18A	120.1
C14—N2—H2N	123.4	C20—C19—C18	120.0 (4)
N1—C1—O2	122.3 (4)	C20—C19—H19A	120.0
N1—C1—C2	112.7 (3)	C18—C19—H19A	120.0
O2—C1—C2	125.0 (4)	C21—C20—C19	121.1 (4)
C15—C2—C1	104.0 (3)	C21—C20—H20A	119.4
C15—C2—C3	121.4 (4)	C19—C20—H20A	119.4
C1—C2—C3	134.6 (4)	C20—C21—C22	119.2 (5)
O3—C3—C4	123.2 (4)	C20—C21—H21A	120.4
O3—C3—C2	120.7 (4)	C22—C21—H21A	120.4
C4—C3—C2	116.1 (3)	C21—C22—C17	120.1 (4)
C5—C4—C3	119.4 (3)	C21—C22—H22A	119.9
C5—C4—C13	120.0 (3)	C17—C22—H22A	119.9
C3—C4—C13	119.9 (3)	C7—C23—C10	93.2 (3)
O4—C5—C4	121.8 (4)	C7—C23—Si1	118.8 (3)

O4—C5—C6	112.6 (4)	C10—C23—Si1	118.1 (3)
C4—C5—C6	125.5 (4)	C7—C23—H23A	108.6
C5—C6—C11	115.4 (3)	C10—C23—H23A	108.6
C5—C6—C7	110.6 (3)	Si1—C23—H23A	108.6
C11—C6—C7	102.8 (3)	Si1—C24—H24A	109.5
C5—C6—H6A	109.3	Si1—C24—H24B	109.5
C11—C6—H6A	109.3	H24A—C24—H24B	109.5
C7—C6—H6A	109.3	Si1—C24—H24C	109.5
C8—C7—C23	101.0 (3)	H24A—C24—H24C	109.5
C8—C7—C6	105.3 (3)	H24B—C24—H24C	109.5
C23—C7—C6	100.6 (3)	Si1—C25—H25A	109.5
C8—C7—H7A	115.9	Si1—C25—H25B	109.5
C23—C7—H7A	115.9	H25A—C25—H25B	109.5
C6—C7—H7A	115.9	Si1—C25—H25C	109.5
C9—C8—C7	107.1 (4)	H25A—C25—H25C	109.5
C9—C8—H8A	126.5	H25B—C25—H25C	109.5
C7—C8—H8A	126.5	C27—C26—C31	117.1 (4)
C8—C9—C10	108.2 (4)	C27—C26—Si1	121.0 (3)
C8—C9—H9A	125.9	C31—C26—Si1	121.8 (3)
C10—C9—H9A	125.9	C28—C27—C26	121.2 (4)
C9—C10—C23	100.0 (3)	C28—C27—H27A	119.4
C9—C10—C11	108.0 (3)	C26—C27—H27A	119.4
C23—C10—C11	99.9 (3)	C29—C28—C27	120.8 (4)
C9—C10—H10A	115.6	C29—C28—H28A	119.6
C23—C10—H10A	115.6	C27—C28—H28A	119.6
C11—C10—H10A	115.6	C28—C29—C30	119.5 (4)
C12—C11—C6	114.7 (3)	C28—C29—H29A	120.3
C12—C11—C10	117.9 (3)	C30—C29—H29A	120.3
C6—C11—C10	101.9 (3)	C29—C30—C31	119.8 (5)
C12—C11—H11A	107.2	C29—C30—H30A	120.1

C6—C11—H11A	107.2	C31—C30—H30A	120.1
C10—C11—H11A	107.2	C30—C31—C26	121.6 (4)
C11—C12—C13	114.8 (3)	C30—C31—H31A	119.2
C11—C12—H12A	108.6	C26—C31—H31A	119.2
C13—C12—H12A	108.6	N2—C32—H32A	109.5
C11—C12—H12B	108.6	N2—C32—H32B	109.5
C13—C12—H12B	108.6	H32A—C32—H32B	109.5
H12A—C12—H12B	107.5	N2—C32—H32C	109.5
C4—C13—C12	111.2 (3)	H32A—C32—H32C	109.5
C4—C13—C14	116.8 (3)	H32B—C32—H32C	109.5
C12—C13—C14	111.1 (3)	N2—C33—H33A	109.5
C4—C13—H13A	105.6	N2—C33—H33B	109.5
C12—C13—H13A	105.6	H33A—C33—H33B	109.5
C14—C13—H13A	105.6	N2—C33—H33C	109.5
C15—C14—N2	110.8 (3)	H33A—C33—H33C	109.5
C15—C14—C13	106.7 (3)	H33B—C33—H33C	109.5
N2—C14—C13	115.6 (3)	Cl2—C1S—Cl2^{i}	112.2 (9)
C15—C14—H14A	107.8	Cl2—C1S—H1SA	109.0
N2—C14—H14A	107.8	Cl2^{i}—C1S—H1SA	109.3
C13—C14—H14A	107.8		
C15—O1—N1—C1	0.2 (4)	C4—C13—C14—C15	36.9 (4)
O1—N1—C1—O2	179.6 (3)	C12—C13—C14—C15	165.8 (3)
O1—N1—C1—C2	0.0 (4)	C4—C13—C14—N2	-86.8 (4)
C16—O2—C1—N1	-4.2 (5)	C12—C13—C14—N2	42.1 (4)
C16—O2—C1—C2	175.3 (4)	C1—C2—C15—O1	0.3 (5)

N1—C1—C2—C15	-0.2 (5)	C3—C2—C15—O1	178.2 (4)
O2—C1—C2—C15	-179.8 (4)	C1—C2—C15—C14	-179.1 (4)
N1—C1—C2—C3	-177.7 (4)	C3—C2—C15—C14	-1.1 (7)
O2—C1—C2—C3	2.7 (7)	N1—O1—C15—C2	-0.3 (5)
C15—C2—C3—O3	-170.7 (4)	N1—O1—C15—C14	179.1 (3)
C1—C2—C3—O3	6.5 (7)	N2—C14—C15—C2	104.0 (5)
C15—C2—C3—C4	10.8 (6)	C13—C14—C15—C2	-22.6 (6)
C1—C2—C3—C4	-172.1 (4)	N2—C14—C15—O1	-75.3 (5)
O3—C3—C4—C5	-1.7 (6)	C13—C14—C15—O1	158.1 (3)
C2—C3—C4—C5	176.8 (4)	C1—O2—C16—C17	-174.2 (3)
O3—C3—C4—C13	-172.2 (4)	O2—C16—C17—C18	-123.9 (4)
C2—C3—C4—C13	6.3 (5)	O2—C16—C17—C22	57.9 (5)
C3—C4—C5—O4	6.4 (6)	C22—C17—C18—C19	2.4 (6)
C13—C4—C5—O4	176.9 (3)	C16—C17—C18—C19	-175.7 (4)
C3—C4—C5—C6	-169.1 (4)	C17—C18—C19—C20	-1.4 (6)
C13—C4—C5—C6	1.3 (6)	C18—C19—C20—C21	-0.3 (6)
O4—C5—C6—C11	173.2 (3)	C19—C20—C21—C22	1.0 (7)
C4—C5—C6—C11	-10.9 (6)	C20—C21—C22—C17	0.1 (7)
O4—C5—C6—C7	-70.7 (4)	C18—C17—C22—C21	-1.8 (6)
C4—C5—C6—C7	105.2 (5)	C16—C17—C22—C21	176.4 (4)

C5—C6—C7—C8	-54.1 (4)	C8—C7—C23—C10	-49.8 (3)
C11—C6—C7—C8	69.6 (4)	C6—C7—C23—C10	58.3 (3)
C5—C6—C7—C23	-158.7 (3)	C8—C7—C23—Si1	74.9 (4)
C11—C6—C7—C23	-35.0 (4)	C6—C7—C23—Si1	-177.1 (3)
C23—C7—C8—C9	33.2 (4)	C9—C10—C23—C7	49.9 (3)
C6—C7—C8—C9	-71.1 (4)	C11—C10—C23—C7	-60.6 (3)
C7—C8—C9—C10	0.7 (4)	C9—C10—C23—Si1	-75.3 (4)
C8—C9—C10—C23	-33.7 (4)	C11—C10—C23—Si1	174.2 (3)
C8—C9—C10—C11	70.2 (4)	C25—Si1—C23—C7	71.5 (4)
C5—C6—C11—C12	-11.2 (5)	C24—Si1—C23—C7	-49.6 (4)
C7—C6—C11—C12	-131.6 (4)	C26—Si1—C23—C7	-170.4 (3)
C5—C6—C11—C10	117.3 (4)	C25—Si1—C23—C10	-177.1 (3)
C7—C6—C11—C10	-3.1 (4)	C24—Si1—C23—C10	61.8 (4)
C9—C10—C11—C12	62.0 (5)	C26—Si1—C23—C10	-59.0 (4)
C23—C10—C11—C12	166.0 (3)	C25—Si1—C26—C27	27.2 (4)
C9—C10—C11—C6	-64.5 (4)	C24—Si1—C26—C27	147.5 (4)
C23—C10—C11—C6	39.6 (4)	C23—Si1—C26—C27	-88.2 (4)
C6—C11—C12—C13	41.4 (5)	C25—Si1—C26—C31	-155.3 (4)
C10—C11—C12—C13	-78.6 (4)	C24—Si1—C26—C31	-35.0 (4)
C5—C4—C13—	28.7 (5)	C23—Si1—C26—	89.3 (4)

C12		C31	
C3—C4—C13—C12	-160.9 (3)	C31—C26—C27—C28	0.5 (6)
C5—C4—C13—C14	157.6 (4)	Si1—C26—C27—C28	178.1 (3)
C3—C4—C13—C14	-32.0 (5)	C26—C27—C28—C29	0.6 (7)
C11—C12—C13—C4	-49.8 (4)	C27—C28—C29—C30	-1.4 (7)
C11—C12—C13—C14	178.3 (3)	C28—C29—C30—C31	0.9 (7)
C33—N2—C14—C15	73.9 (4)	C29—C30—C31—C26	0.2 (7)
C32—N2—C14—C15	-53.0 (4)	C27—C26—C31—C30	-0.9 (6)
C33—N2—C14—C13	-164.6 (3)	Si1—C26—C31—C30	-178.5 (3)
C32—N2—C14—C13	68.5 (4)		

Symmetry code(s): (i) -*x*+1, -*y*+1, *z*.

Table S6. Hydrogen-bond parameters

D—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (°)
AD-2-5				
O4—H4O···O3	0.84	1.80	2.510 (4)	141.8
N2—H2N···Cl1^{i}	0.88	2.12	2.993 (3)	173.3

Symmetry code(s): (i) *x*+1/2, -*y*+1/2, -*z*+1.

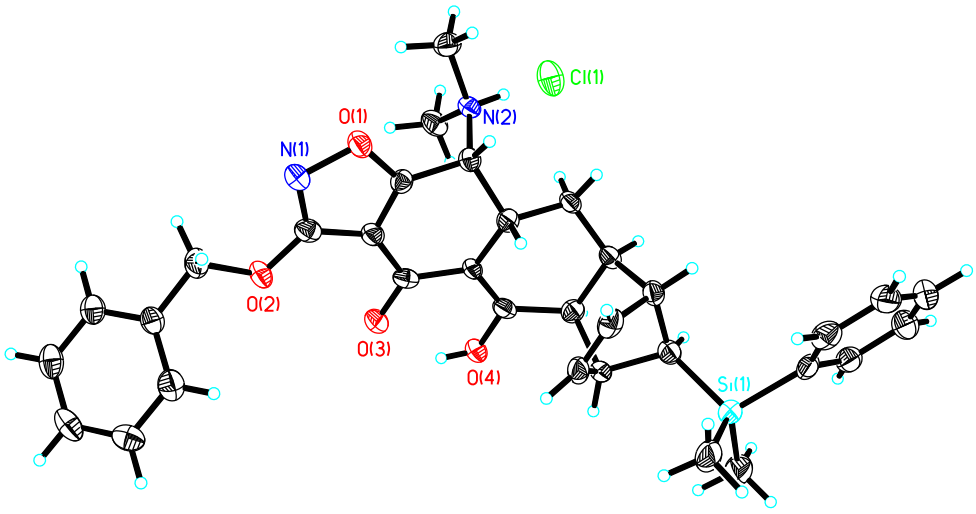


Figure S3. Perspective views showing 50% probability displacement ellipsoids (the disorder CH_2Cl_2 has been omitted).

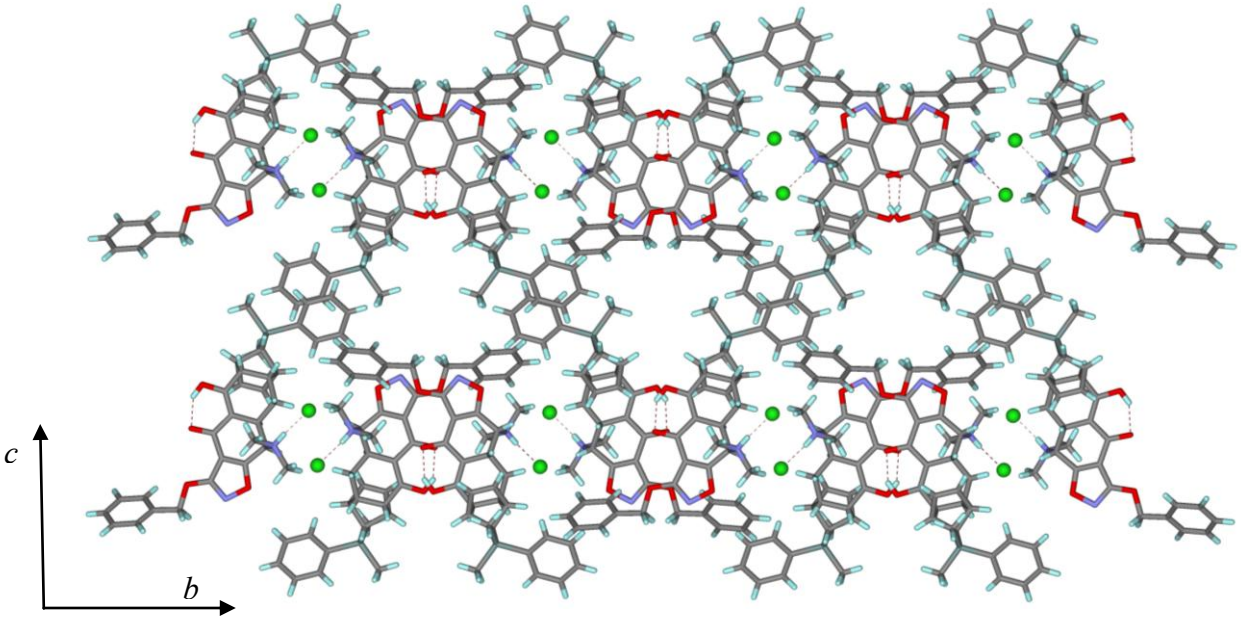
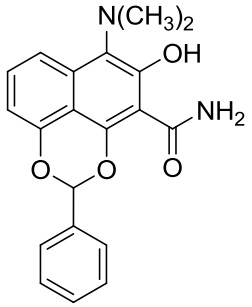


Figure S4. Three-dimensional supramolecular architecture viewed along the *a*-axis direction (the disorder CH_2Cl_2 has been omitted).

Characterization data and X-ray crystal structure data of the by-product depicted in ref 19:



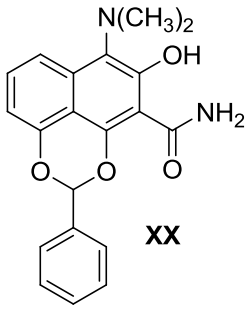
^{1}H NMR (500 MHz, $CDCl_3$), δ: 7.92 (d, 1H, J = 8.8 Hz), 7.82 (br s, 1H), 7.72–7.70 (m, 2H), 7.55–7.53 (m, 3H), 7.46 (t, 1H, J = 7.8 Hz), 6.80 (d, 1H, J = 7.3 Hz), 6.31 (s, 1H), 5.80 (br s, 2H), 2.92 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 171.9, 157.3, 151.3, 149.5, 136.7, 135.1, 130.9, 130.1, 129.3, 128.5, 127.1, 117.7, 108.1, 106.8, 101.1, 100.5, 43.3. FTIR (neat), cm^{-1}: 3439 (s), 2926 (m), 1782 (s), 1664 (s), 1630 (s), 1593 (br), 1422 (s), 1373 (s). HRMS (ESI): Calcd for $(C_{20}H_{18}N_2O_4 + H)^+$: 351.1345. Found: 351.1389.

X-ray Crystallographic Laboratory

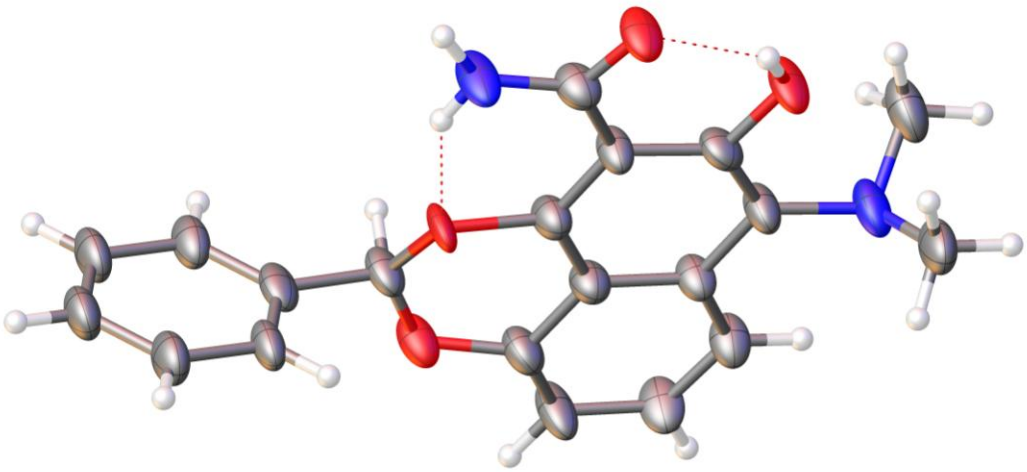
Harvard University

Structure Report

for



XX



X-Ray Crystallography: Data were collected from a crystal mounted on a Bruker APEX II DUO CCD diffractometer equipped with an Oxford Cryosystems nitrogen flow apparatus using $Mo_{K\alpha}$ radiation (λ=0.71073 Å) at 100 K. The collection method involved 0.5° scans in ω at 26° in 2θ. Data integration to 0.82-Å resolution was carried out using SAINT V7.46 A with reflection spot size optimization.[23] Absorption corrections were made with the program SADABS.[24] The structure was solved by the direct methods procedure and refined by least-squares methods against F^2 using SHELXS-97 and SHELXL-97.[20] Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were allowed to ride on the respective atoms. Crystal data as well as details of data collection and refinement are summarized in Table S7, geometric parameters are listed in Table S8, and hydrogen-bond parameters are listed in Table S9. The graphic depicted on page S76 was generated using the Olex2 program,[25] the ORTEP plots of Figure S5 were generated with the SHELXL-97 program,[20] and the graphic depicted in Figure S6 was generated with Accelrys DS Visualizer 2.0.[26]

Table S7. Experimental details.

Crystal data	
Chemical formula	$C_{20}H_{18}N_2O_4$
M_r	350.36
Crystal system, space group	Triclinic, *P*-1
Temperature (K)	100
a, *b*, *c* (Å)	8.4645 (18), 9.265 (2), 13.880 (3)
α, β, γ (º)	101.300 (15), 98.534 (14), 106.220 (14)
V (Å^3)	1000.8 (4)

[23] Bruker AXS (2009). SMART and SAINTPLUS. Bruker AXS, Madison, Wisconsin.
[24] Sheldrick, G. M *Acta Crys.* **2008**, *A64*, 112–122.
[25] Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H *J. Appl. Cryst.* **2009**, *42*, 339–341.
[26] Accelrys DS Visualizer v2.0.1.7347, 2007, Accelrys Software Inc.

Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.08
Crystal size (mm)	0.16 × 0.08 × 0.03
Data collection	
Diffractometer	CCD area detector diffractometer
Absorption correction	MULTI-SCAN *SADABS* (Bruker, 2005)
T_{min}, T_{max}	0.987, 0.998
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	11619, 3833, 1391
R_{int}	0.079
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.090, 0.187, 1.00
No. of reflections	3833
No. of parameters	287
No. of restraints	289
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$)	0.24, -0.32

Computer programs: *APEX2* v2009.3.0, *SAINT* 7.46A, *SHELXS97*, *SHELXL97*, Bruker *SHELXTL*.[19,20]

Table S8. Selected geometric parameters (Å, °)

O1—C11	1.254 (5)	C13—H13B	0.9800
O2—C2	1.359 (5)	C13—H13C	0.9800
O2—H2O	0.9802	O3—C14	1.253 (14)
N1—C11	1.316 (6)	O4—C14	1.458 (18)
N1—H1NA	0.8961	C14—C15	1.470 (12)

N1—H1NB	0.8350	C14—H14A	1.0000
N2—C12	1.439 (6)	C15—C16	1.3900
N2—C13	1.445 (6)	C15—C20	1.3900
N2—C3	1.455 (6)	C16—C17	1.3900
C1—C10	1.385 (6)	C16—H16A	0.9500
C1—C2	1.410 (6)	C17—C18	1.3900
C1—C11	1.438 (6)	C17—H17A	0.9500
C2—C3	1.336 (6)	C18—C19	1.3900
C3—C4	1.432 (6)	C18—H18A	0.9500
C4—C5	1.385 (6)	C19—C20	1.3900
C4—C9	1.408 (6)	C19—H19A	0.9500
C5—C6	1.363 (6)	C20—H20A	0.9500
C5—H5A	0.9500	O3'—C14'	1.278 (9)
C6—C7	1.390 (6)	O4'—C14'	1.451 (15)
C6—H6A	0.9500	C14'—C15'	1.486 (7)
C7—C8	1.338 (6)	C14'—H14B	1.0000
C7—H7A	0.9500	C15'—C16'	1.3900
C8—O3	1.37 (3)	C15'—C20'	1.3900
C8—O3'	1.394 (16)	C16'—C17'	1.3900
C8—C9	1.410 (6)	C16'—H16B	0.9500
C9—C10	1.382 (6)	C17'—C18'	1.3900
C10—O4'	1.33 (3)	C17'—H17B	0.9500
C10—O4	1.48 (5)	C18'—C19'	1.3900
C12—H12A	0.9800	C18'—H18B	0.9500
C12—H12B	0.9800	C19'—C20'	1.3900
C12—H12C	0.9800	C19'—H19B	0.9500
C13—H13A	0.9800	C20'—H20B	0.9500
C2—O2—H2O	118.6	H13A—C13—H13C	109.5
C11—N1—H1NA	132.8	H13B—C13—H13C	109.5
C11—N1—H1NB	111.9	C14—O3—C8	119 (2)
H1NA—N1—H1NB	115.3	C14—O4—C10	106 (2)
C12—N2—C13	113.5 (4)	O3—C14—O4	127 (3)

C12—N2—C3	113.0 (4)	O3—C14—C15	115.9 (18)
C13—N2—C3	112.1 (4)	O4—C14—C15	104 (2)
C10—C1—C2	115.3 (4)	O3—C14—H14A	102.2
C10—C1—C11	123.5 (4)	O4—C14—H14A	102.2
C2—C1—C11	121.2 (4)	C15—C14—H14A	102.2
C3—C2—O2	116.6 (4)	C16—C15—C20	120.0
C3—C2—C1	124.6 (4)	C16—C15—C14	123.2 (11)
O2—C2—C1	118.8 (4)	C20—C15—C14	116.7 (11)
C2—C3—C4	119.8 (4)	C15—C16—C17	120.0
C2—C3—N2	123.8 (4)	C15—C16—H16A	120.0
C4—C3—N2	116.3 (4)	C17—C16—H16A	120.0
C5—C4—C9	118.8 (4)	C18—C17—C16	120.0
C5—C4—C3	124.3 (4)	C18—C17—H17A	120.0
C9—C4—C3	116.9 (4)	C16—C17—H17A	120.0
C6—C5—C4	120.5 (4)	C17—C18—C19	120.0
C6—C5—H5A	119.8	C17—C18—H18A	120.0
C4—C5—H5A	119.8	C19—C18—H18A	120.0
C5—C6—C7	121.8 (5)	C18—C19—C20	120.0
C5—C6—H6A	119.1	C18—C19—H19A	120.0
C7—C6—H6A	119.1	C20—C19—H19A	120.0
C8—C7—C6	118.1 (5)	C19—C20—C15	120.0
C8—C7—H7A	120.9	C19—C20—H20A	120.0
C6—C7—H7A	120.9	C15—C20—H20A	120.0
C7—C8—O3	118.9 (9)	C14'—O3'—C8	119.3 (11)
C7—C8—O3'	121.5 (6)	C10—O4'—C14'	116 (2)
C7—C8—C9	122.7 (4)	O3'—C14'—O4'	113.0 (11)
O3—C8—C9	117.3 (9)	O3'—C14'—C15'	112.4 (9)
O3'—C8—C9	115.6 (6)	O4'—C14'—C15'	107.7 (14)
C10—C9—C4	120.8 (4)	O3'—C14'—H14B	107.9
C10—C9—C8	121.1 (4)	O4'—C14'—H14B	107.9
C4—C9—C8	118.1 (4)	C15'—C14'—H14B	107.9
O4'—C10—C9	116.1 (7)	C16'—C15'—C20'	120.0
O4'—C10—C1	121.3 (7)	C16'—C15'—C14'	122.5 (6)

C9—C10—C1	122.5 (4)	C20'—C15'—C14'	117.5 (6)
C9—C10—O4	120.0 (11)	C15'—C16'—C17'	120.0
C1—C10—O4	117.1 (10)	C15'—C16'—H16B	120.0
O1—C11—N1	117.1 (4)	C17'—C16'—H16B	120.0
O1—C11—C1	120.1 (4)	C18'—C17'—C16'	120.0
N1—C11—C1	122.8 (5)	C18'—C17'—H17B	120.0
N2—C12—H12A	109.5	C16'—C17'—H17B	120.0
N2—C12—H12B	109.5	C17'—C18'—C19'	120.0
H12A—C12—H12B	109.5	C17'—C18'—H18B	120.0
N2—C12—H12C	109.5	C19'—C18'—H18B	120.0
H12A—C12—H12C	109.5	C20'—C19'—C18'	120.0
H12B—C12—H12C	109.5	C20'—C19'—H19B	120.0
N2—C13—H13A	109.5	C18'—C19'—H19B	120.0
N2—C13—H13B	109.5	C19'—C20'—C15'	120.0
H13A—C13—H13B	109.5	C19'—C20'—H20B	120.0
N2—C13—H13C	109.5	C15'—C20'—H20B	120.0
C10—C1—C2—C3	-0.4 (8)	C10—C1—C11—O1	173.3 (5)
C11—C1—C2—C3	177.8 (5)	C2—C1—C11—O1	-4.8 (8)
C10—C1—C2—O2	-179.7 (5)	C10—C1—C11—N1	-7.7 (8)
C11—C1—C2—O2	-1.5 (7)	C2—C1—C11—N1	174.2 (5)
O2—C2—C3—C4	-179.9 (5)	C7—C8—O3—C14	-168.3 (15)
C1—C2—C3—C4	0.8 (8)	C9—C8—O3—C14	0(2)
O2—C2—C3—N2	0.7 (8)	C9—C10—O4—C14	-25 (4)
C1—C2—C3—N2	-178.6 (5)	C1—C10—O4—C14	161.2 (18)
C12—N2—C3—C2	-65.3 (7)	C8—O3—C14—O4	-27 (3)
C13—N2—C3—C2	64.5 (7)	C8—O3—C14—C15	-160.5 (14)
C12—N2—C3—C4	115.3 (5)	C10—O4—C14—O3	38 (4)
C13—N2—C3—C4	-114.9 (5)	C10—O4—C14—C15	176 (2)
C2—C3—C4—C5	178.8 (5)	O3—C14—C15—C16	-94 (2)
N2—C3—C4—C5	-1.8 (8)	O4—C14—C15—C16	122 (2)
C2—C3—C4—C9	-2.3 (7)	O3—C14—C15—C20	89.1 (19)
N2—C3—C4—C9	177.1 (5)	O4—C14—C15—C20	-55 (2)

C9—C4—C5—C6	0.5 (7)	C20—C15—C16—C17	0.0
C3—C4—C5—C6	179.4 (5)	C14—C15—C16—C17	-176.6 (16)
C4—C5—C6—C7	-0.1 (8)	C15—C16—C17—C18	0.0
C5—C6—C7—C8	-0.5 (8)	C16—C17—C18—C19	0.0
C6—C7—C8—O3	168.5 (11)	C17—C18—C19—C20	0.0
C6—C7—C8—O3'	-173.4 (7)	C18—C19—C20—C15	0.0
C6—C7—C8—C9	0.7 (8)	C16—C15—C20—C19	0.0
C5—C4—C9—C10	-177.4 (5)	C14—C15—C20—C19	176.9 (15)
C3—C4—C9—C10	3.6 (7)	C7—C8—O3'—C14'	160.0 (8)
C5—C4—C9—C8	-0.3 (7)	C9—C8—O3'—C14'	-14.5 (12)
C3—C4—C9—C8	-179.3 (5)	C9—C10—O4'—C14'	29.5 (19)
C7—C8—C9—C10	176.7 (5)	C1—C10—O4'—C14'	-150.4 (10)
O3—C8—C9—C10	8.8 (12)	C8—O3'—C14'—O4'	43.2 (17)
O3'—C8—C9—C10	-8.8 (8)	C8—O3'—C14'—C15'	165.3 (8)
C7—C8—C9—C4	-0.4 (8)	C10—O4'—C14'—O3'	-52 (2)
O3—C8—C9—C4	-168.3 (10)	C10—O4'—C14'—C15'	-176.8 (12)
O3'—C8—C9—C4	174.1 (7)	O3'—C14'—C15'—C16'	-49.9 (11)
C4—C9—C10—O4'	176.6 (13)	O4'—C14'—C15'—C16'	75.2 (12)
C8—C9—C10—O4'	-0.5 (14)	O3'—C14'—C15'—C20'	131.1 (9)
C4—C9—C10—C1	-3.5 (8)	O4'—C14'—C15'—C20'	-103.9 (11)
C8—C9—C10—C1	179.5 (5)	C20'—C15'—C16'—C17'	0.0
C4—C9—C10—O4	-177 (2)	C14'—C15'—C16'—C17'	-179.0 (9)
C8—C9—C10—O4	6(2)	C15'—C16'—C17'—C18'	0.0
C2—C1—C10—O4'	-178.3 (13)	C16'—C17'—C18'—C19'	0.0
C11—C1—C10—O4'	3.5 (15)	C17'—C18'—C19'—C20'	0.0
C2—C1—C10—C9	1.8 (7)	C18'—C19'—C20'—C15'	0.0

C11—C1—C10—C9	-176.4 (5)	C16'—C15'—C20'—C19'	0.0
C2—C1—C10—O4	175 (2)	C14'—C15'—C20'—C19'	179.1 (8)
C11—C1—C10—O4	-3(2)		

Table S9. Hydrogen-bond parameters

D—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (º)
O2—H2O···O1	0.98	1.76	2.488 (4)	128.5
N1—H1NA···O1^{i}	0.90	2.04	2.868 (5)	154.0
N1—H1NB···O4	0.83	1.85	2.58 (2)	145.4
N1—H1NB···O4'	0.83	1.96	2.669 (14)	142.1

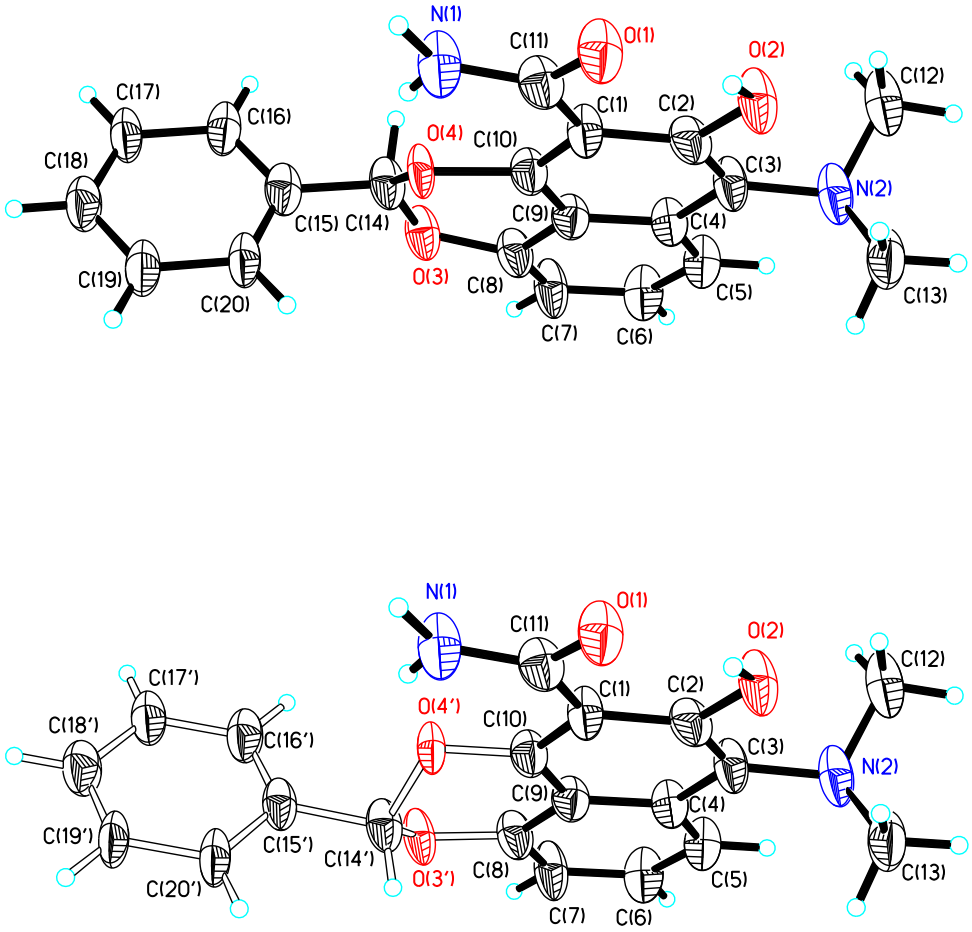


Figure S5. Perspective views showing 50% probability displacement.

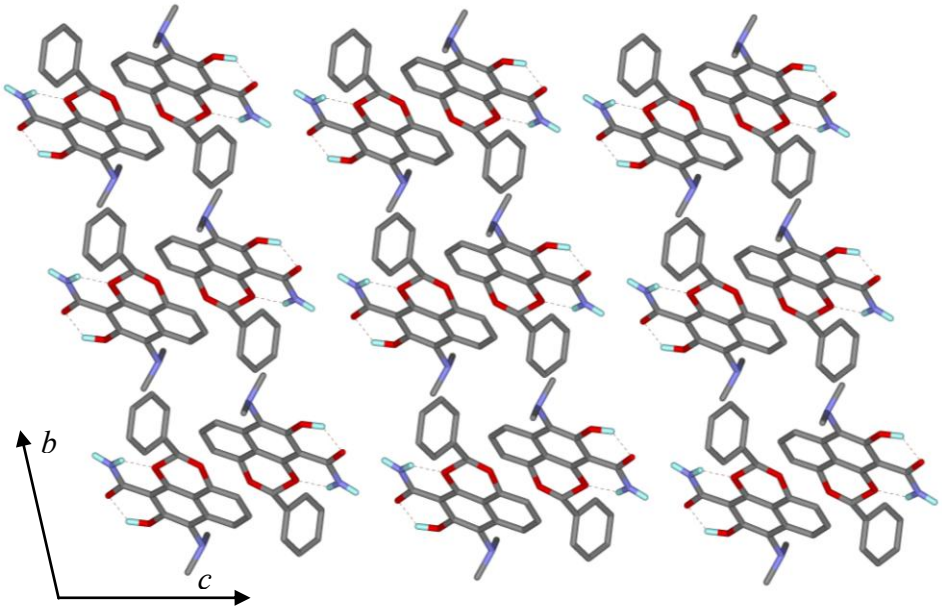
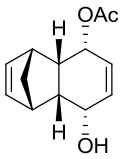
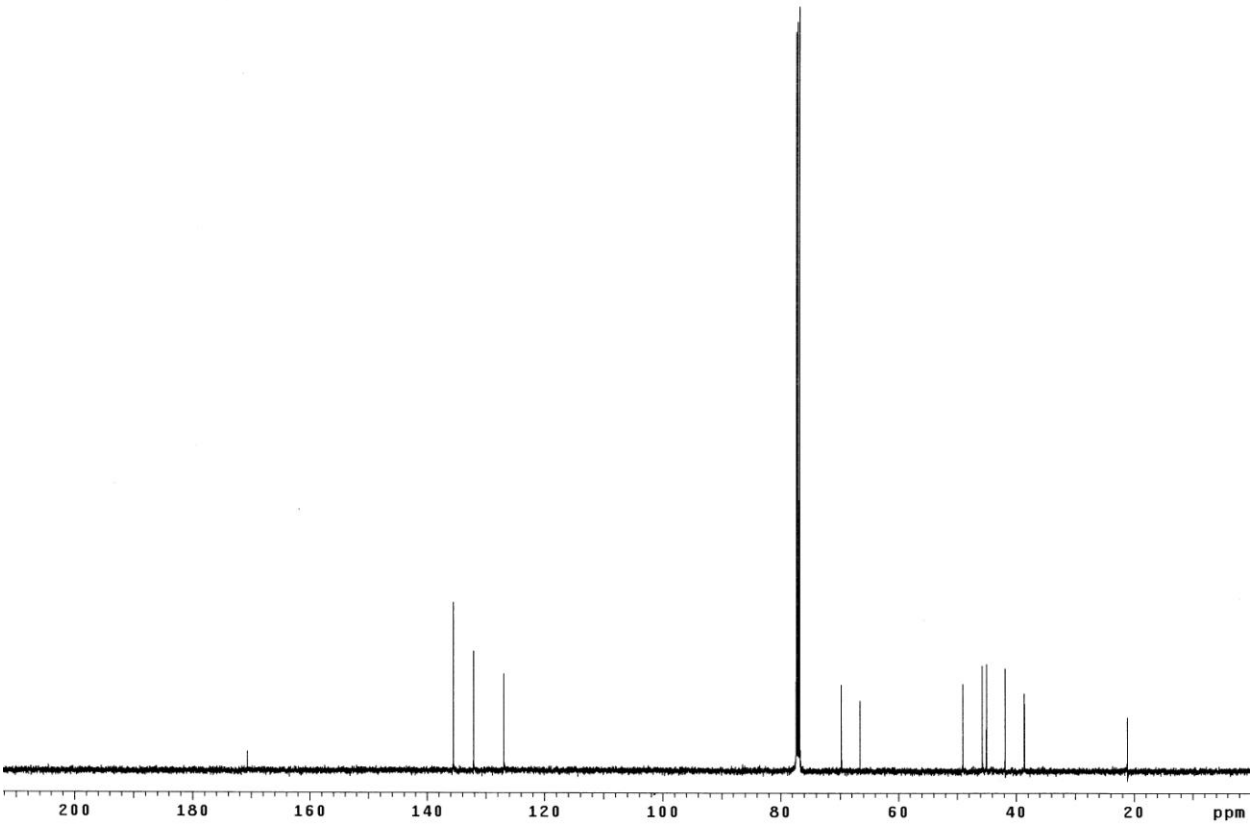


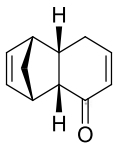
Figure S6. Three-dimensional supramolecular architecture viewed along the *a*-axis direction.

Copies of ^{1}H NMR and ^{13}C NMR Spectra:

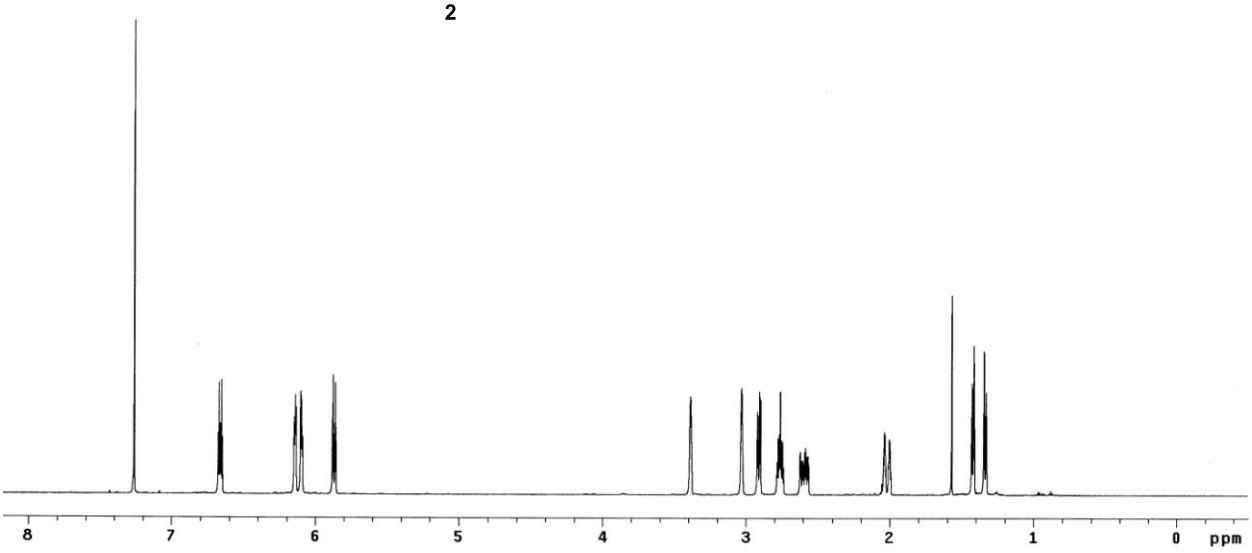


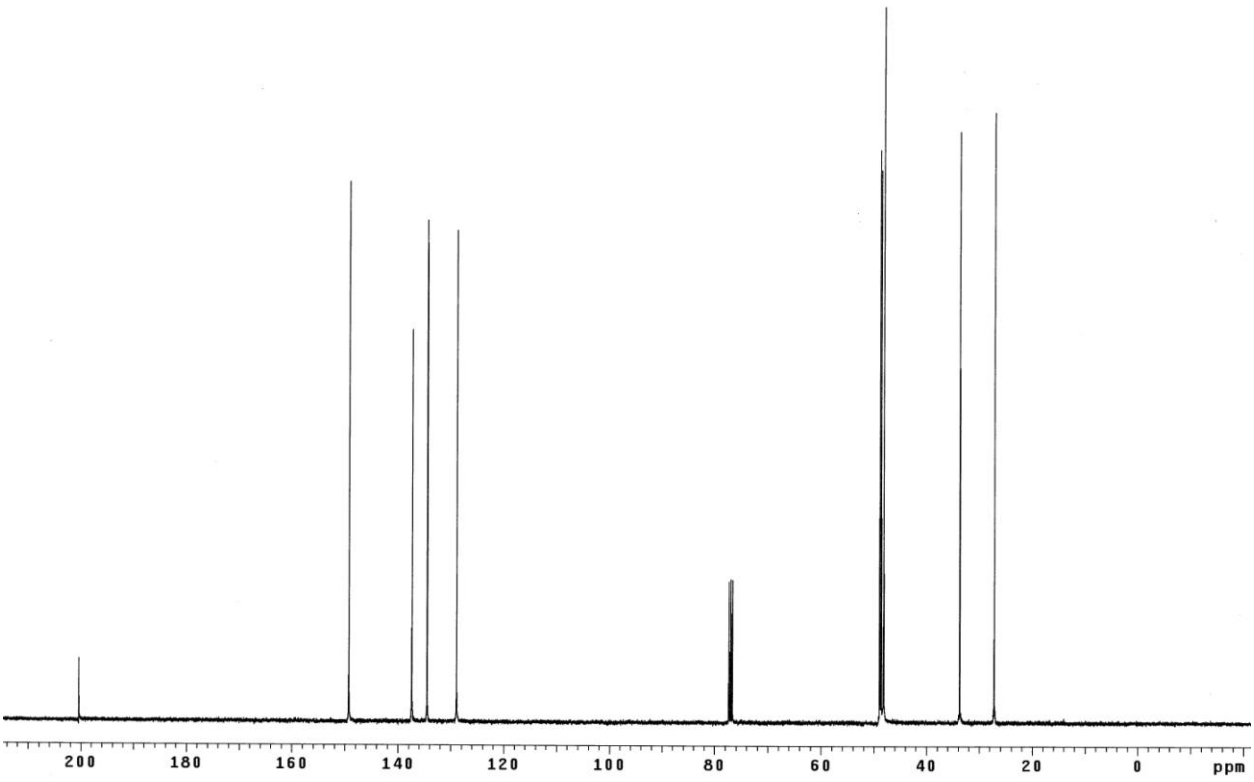
9

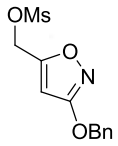




2

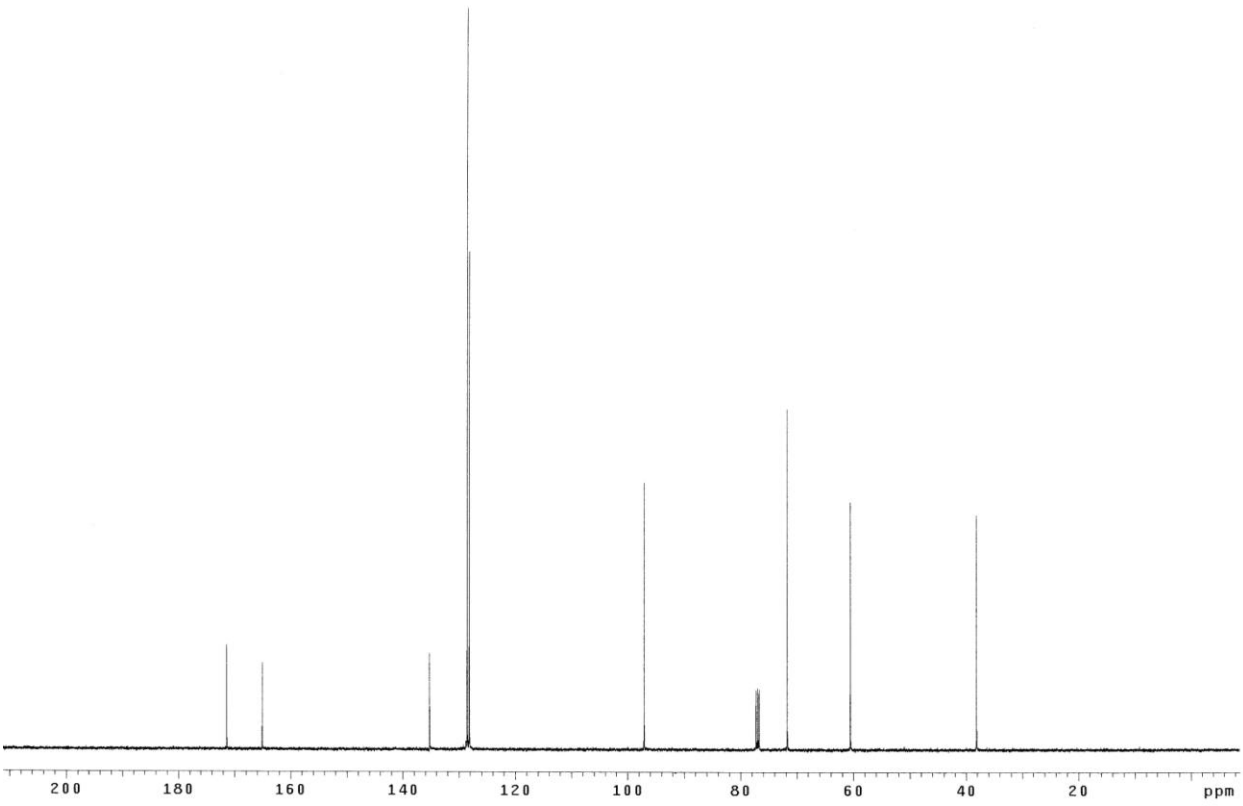


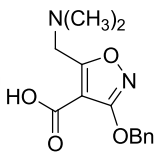




29

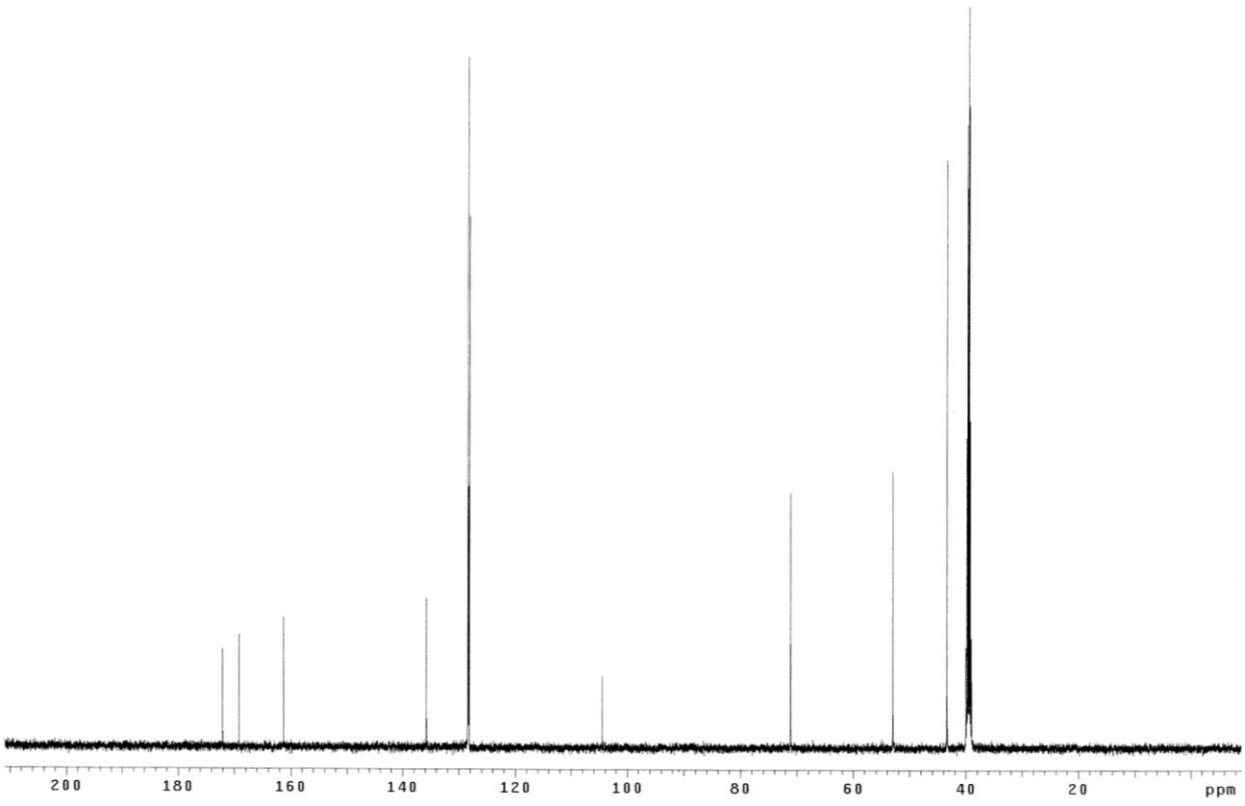
(not subject to purification)

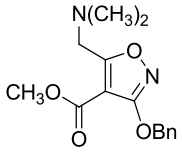




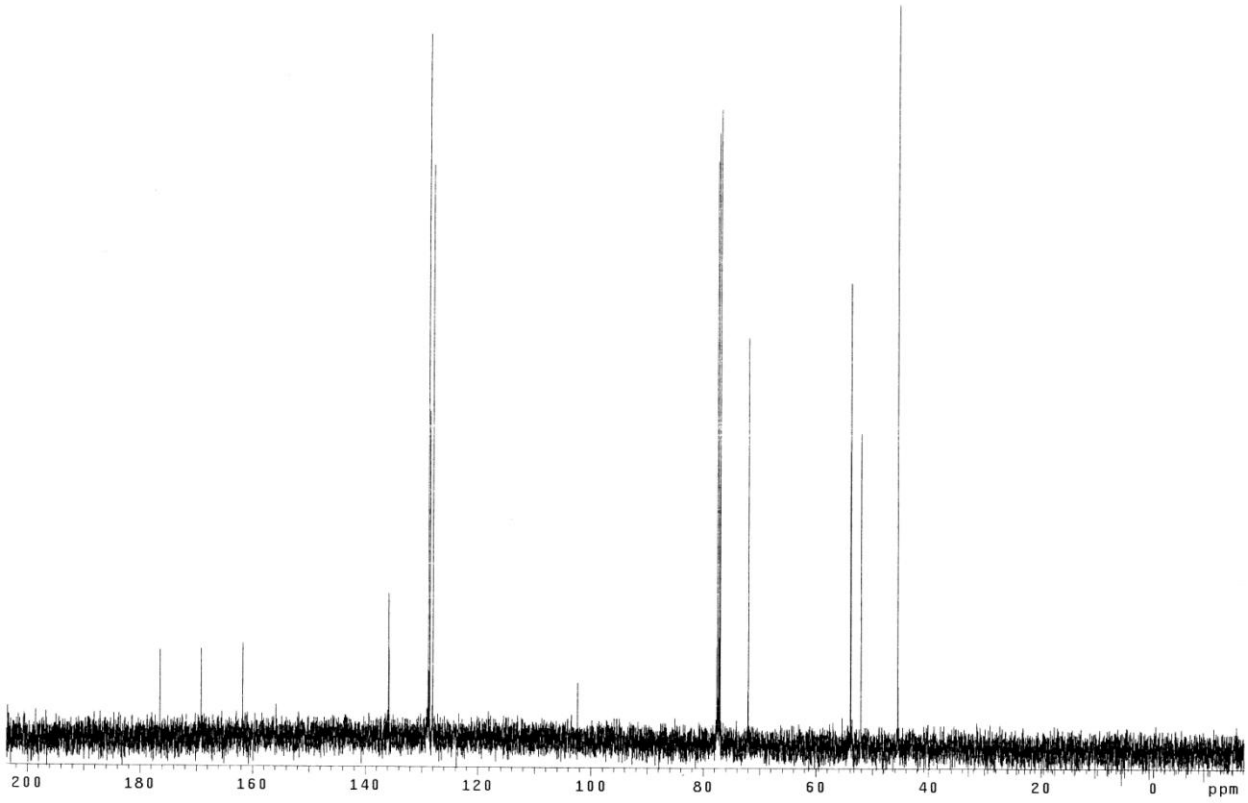
31

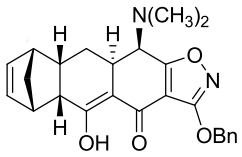
(not subject to purification)



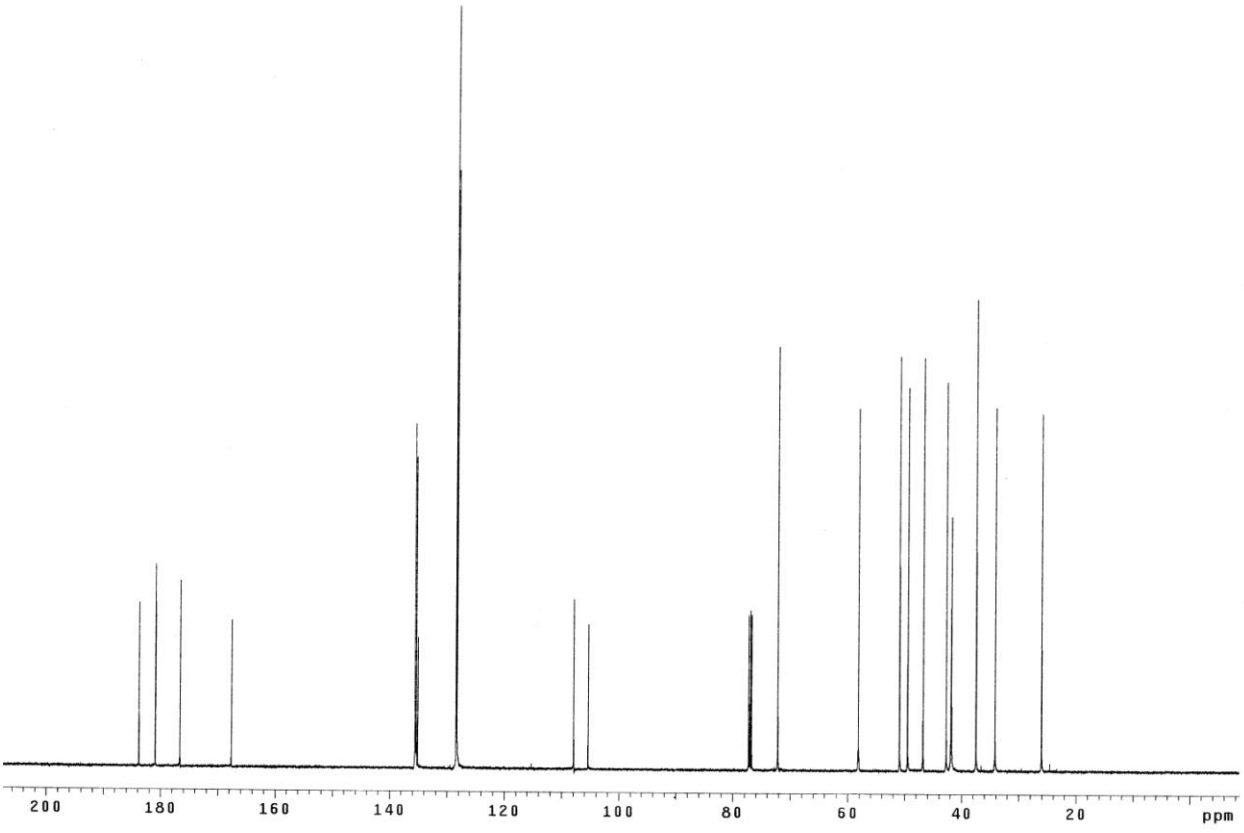


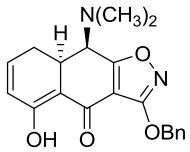
3



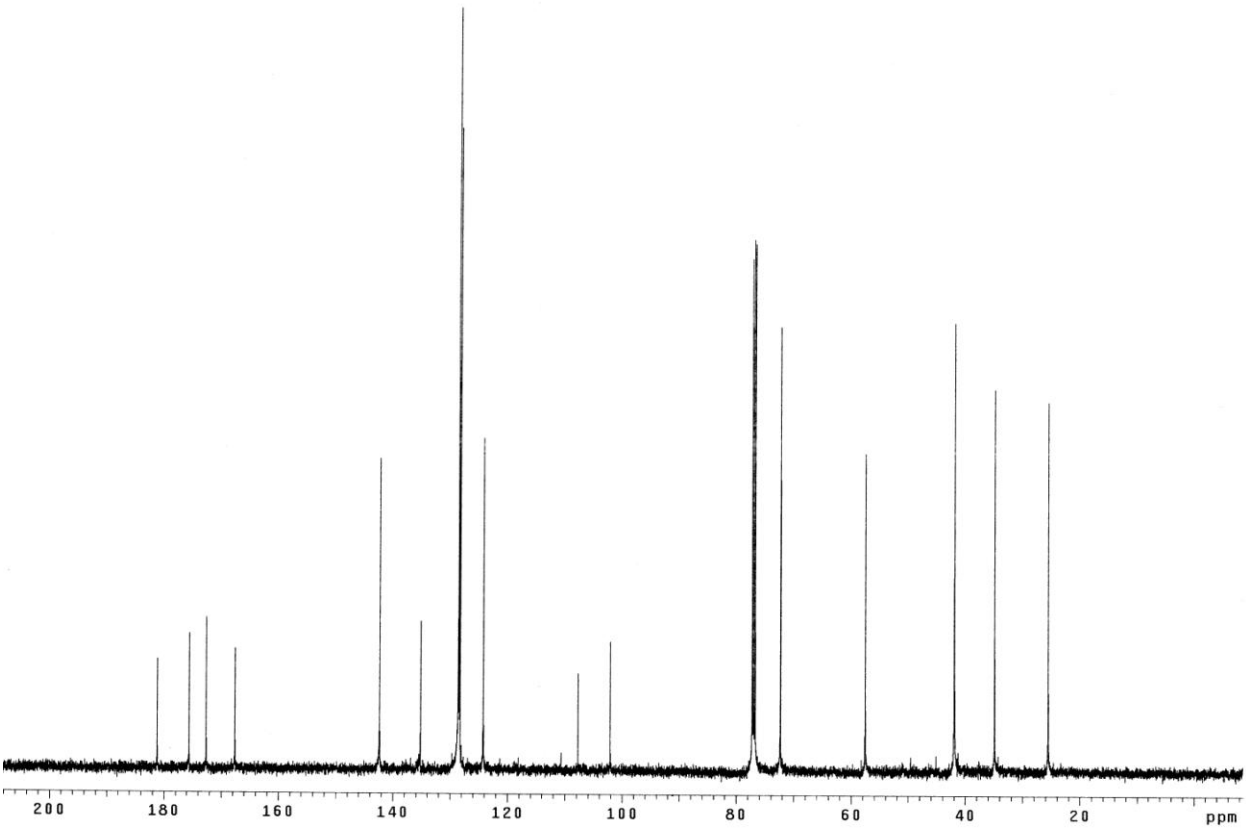


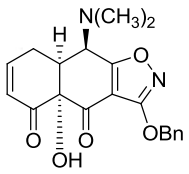
12



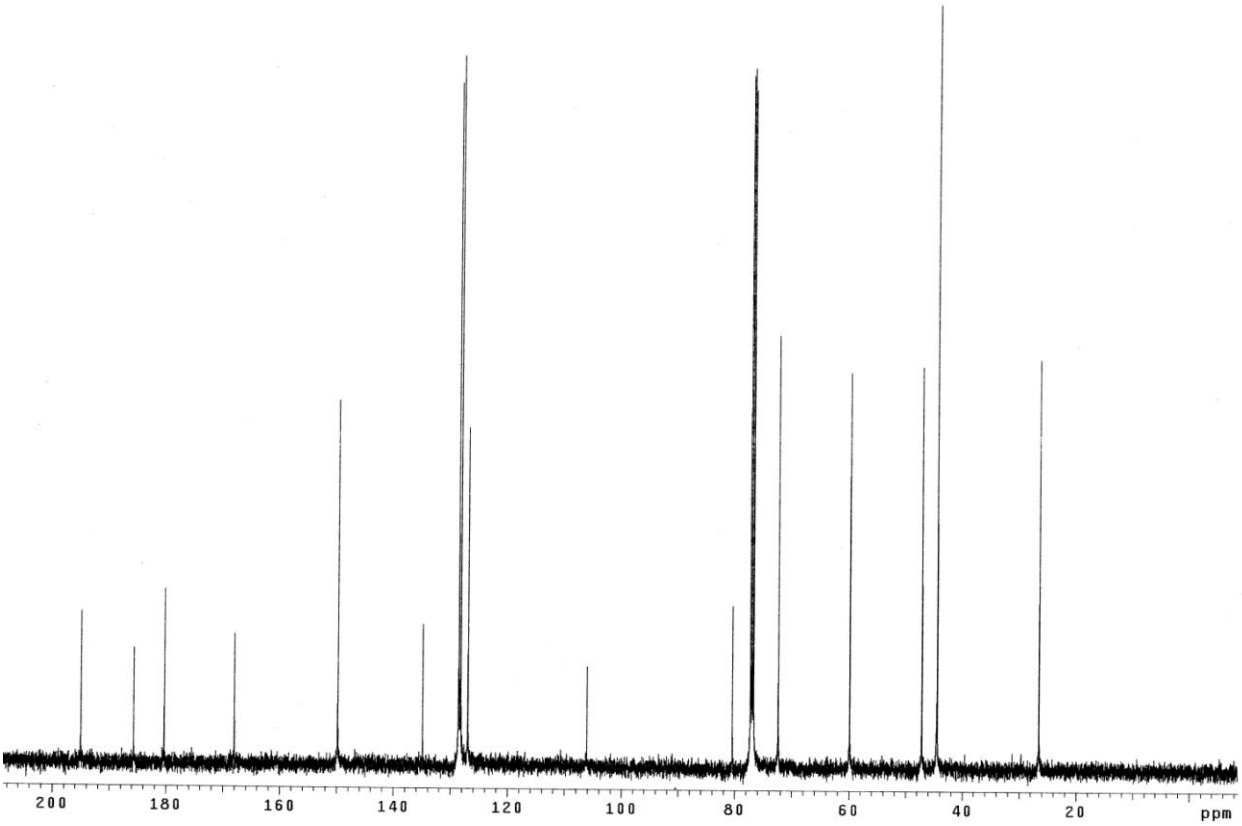


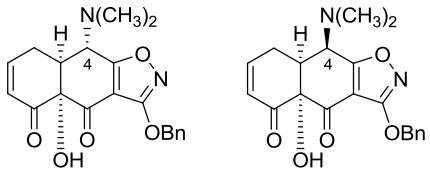
13





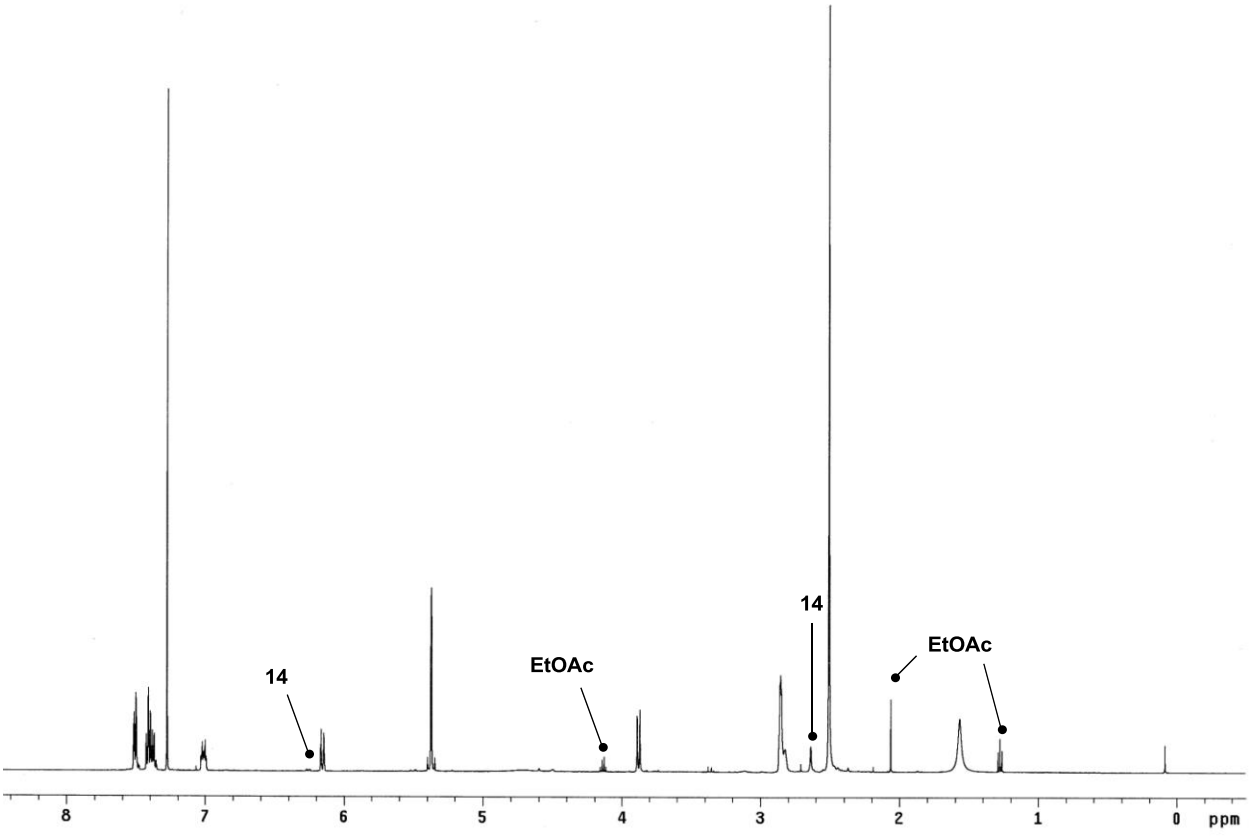
14

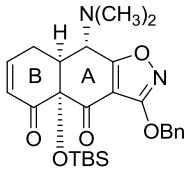




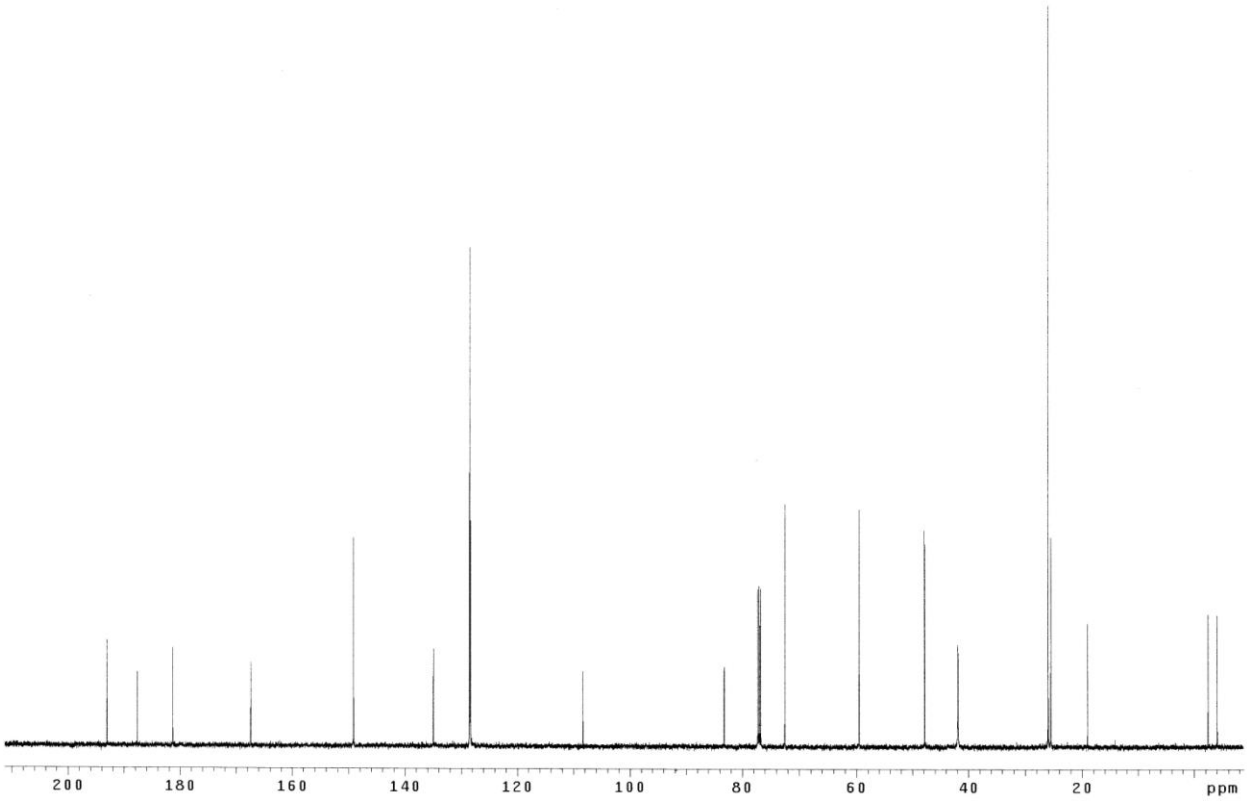
15 **14**

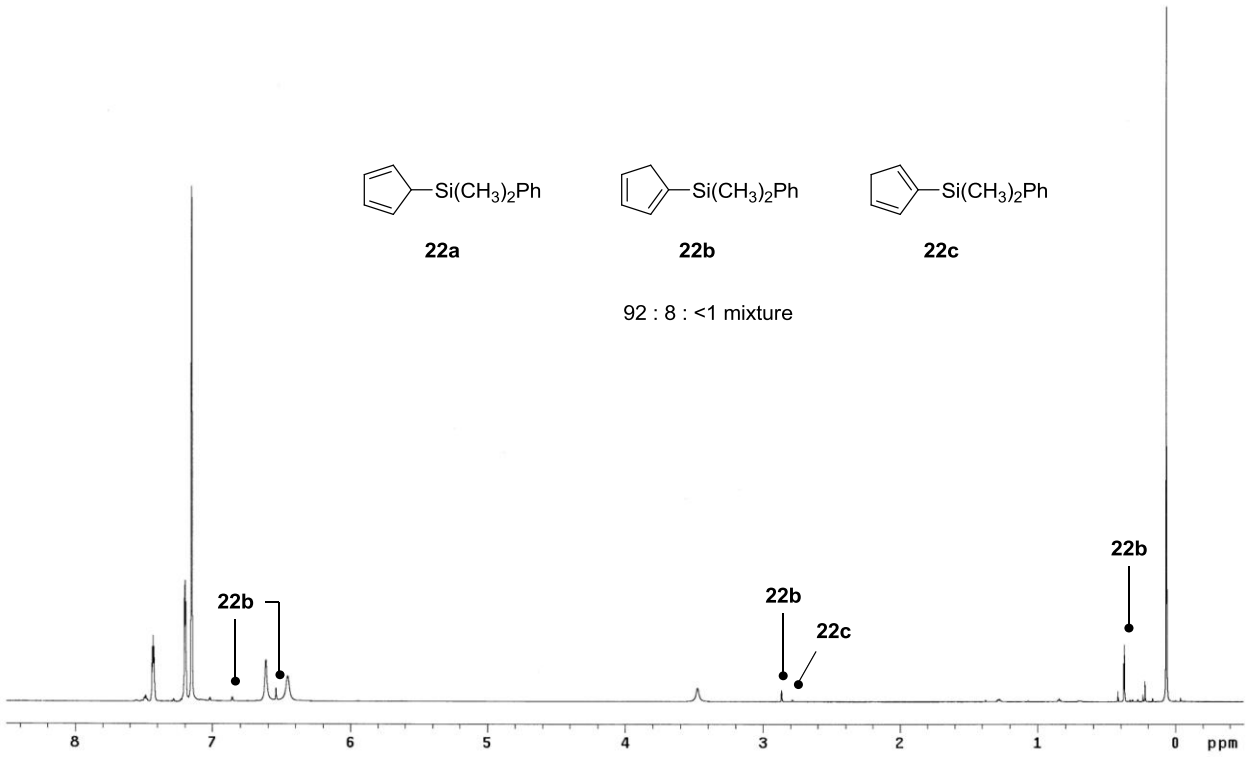
(12.8:1 mixture of **15** and **14**, not subject to purification)

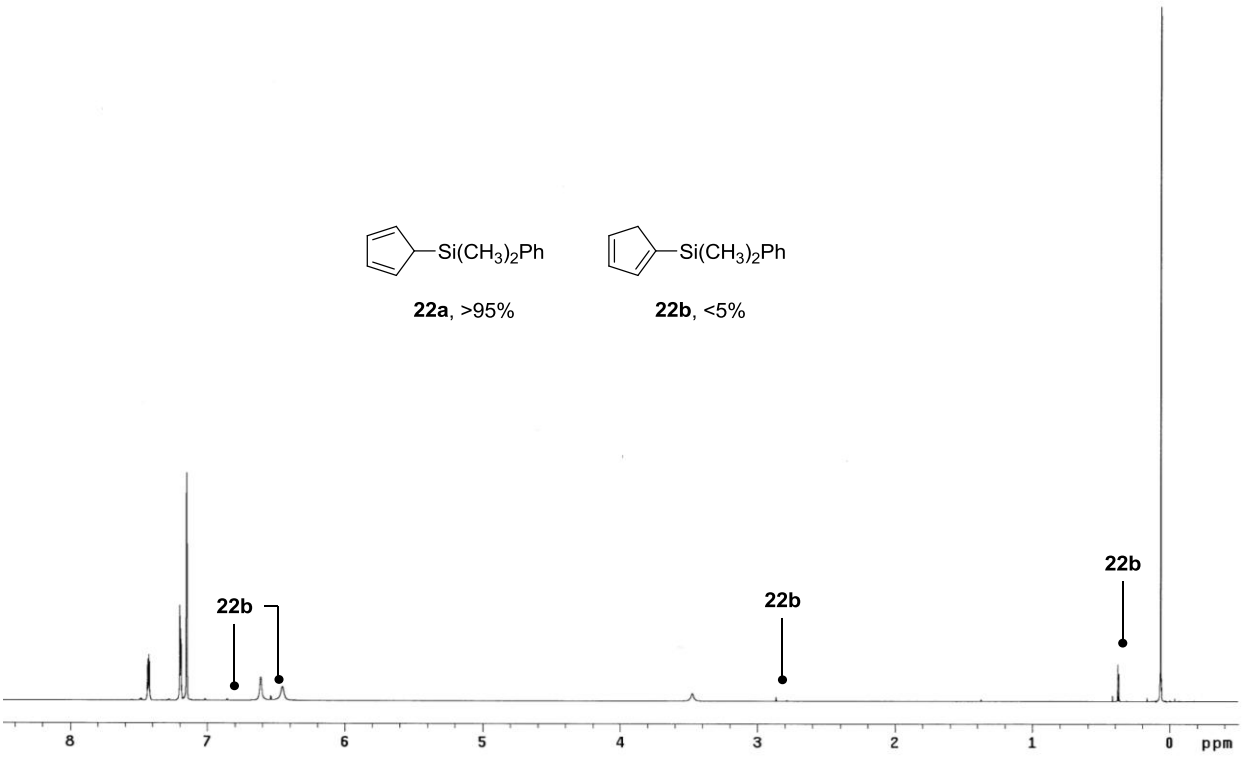


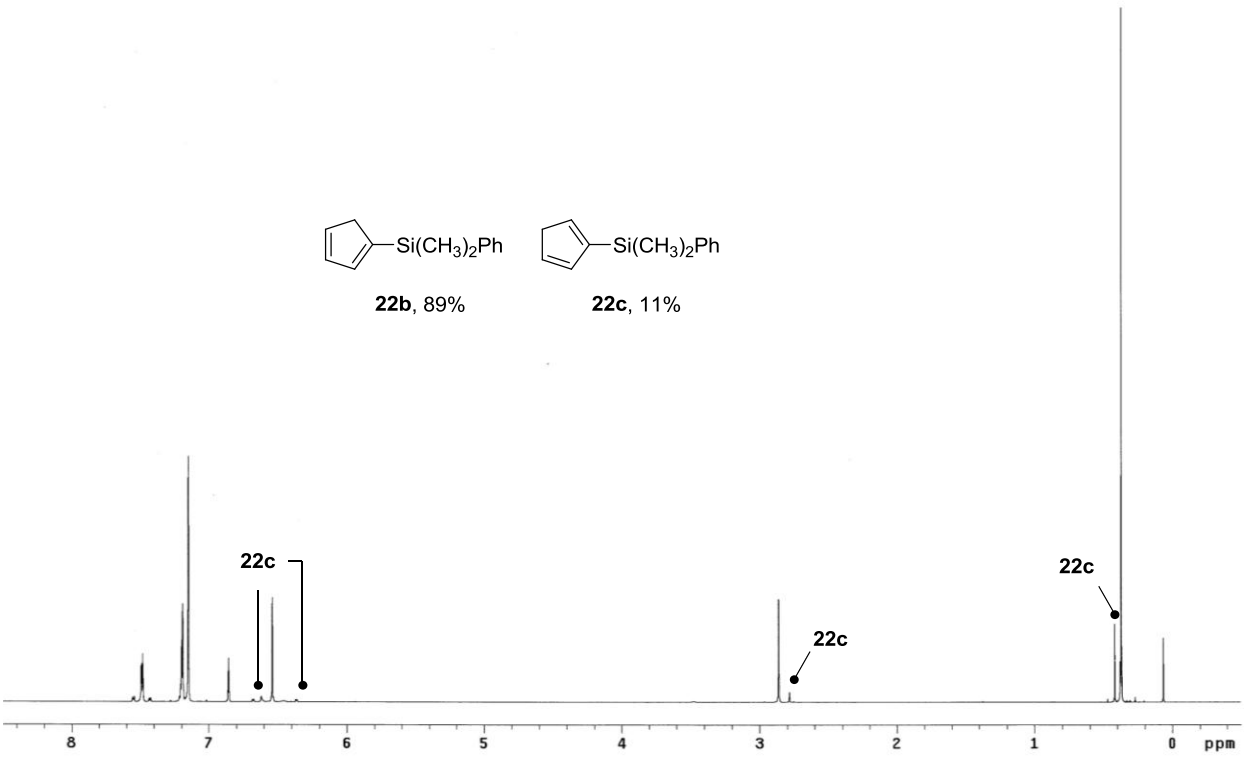


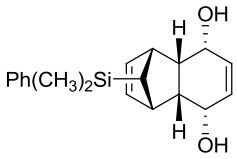
AB Enone **1**



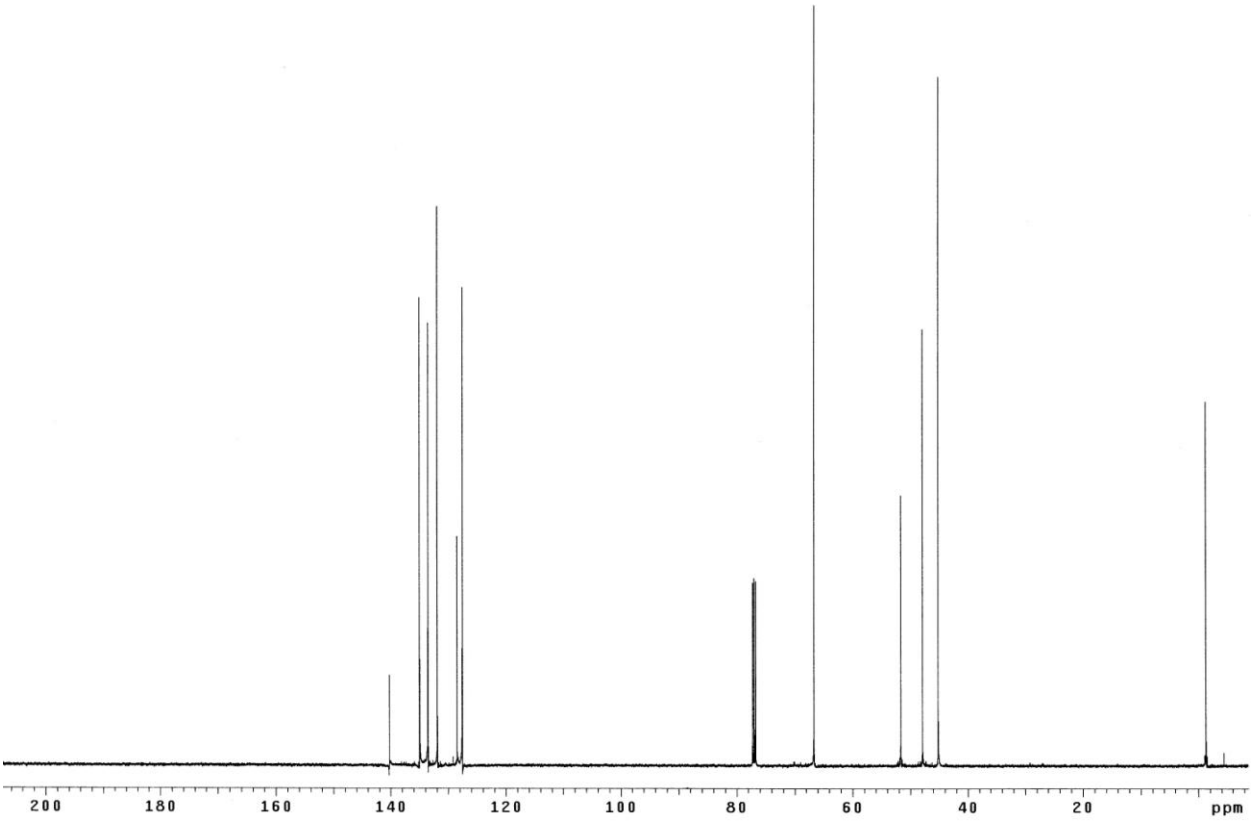

Si(CH3)2Ph
22a
Si(CH3)2Ph
22b
Si(CH3)2Ph
22c
92 : 8 : <1 mixture
22b
22b
22c
22b
8
7
6
5
4
3
2
1
0
ppm

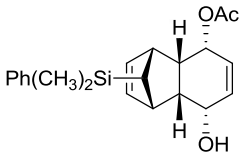

Si(CH3)2Ph
22a, >95%
Si(CH3)2Ph
22b, <5%
22b
22b
22b
8
7
6
5
4
3
2
1
0
ppm


Si(CH3)2Ph
Si(CH3)2Ph
22b, 89%
22c, 11%
22c
22c
22c
8
7
6
5
4
3
2
1
0
ppm

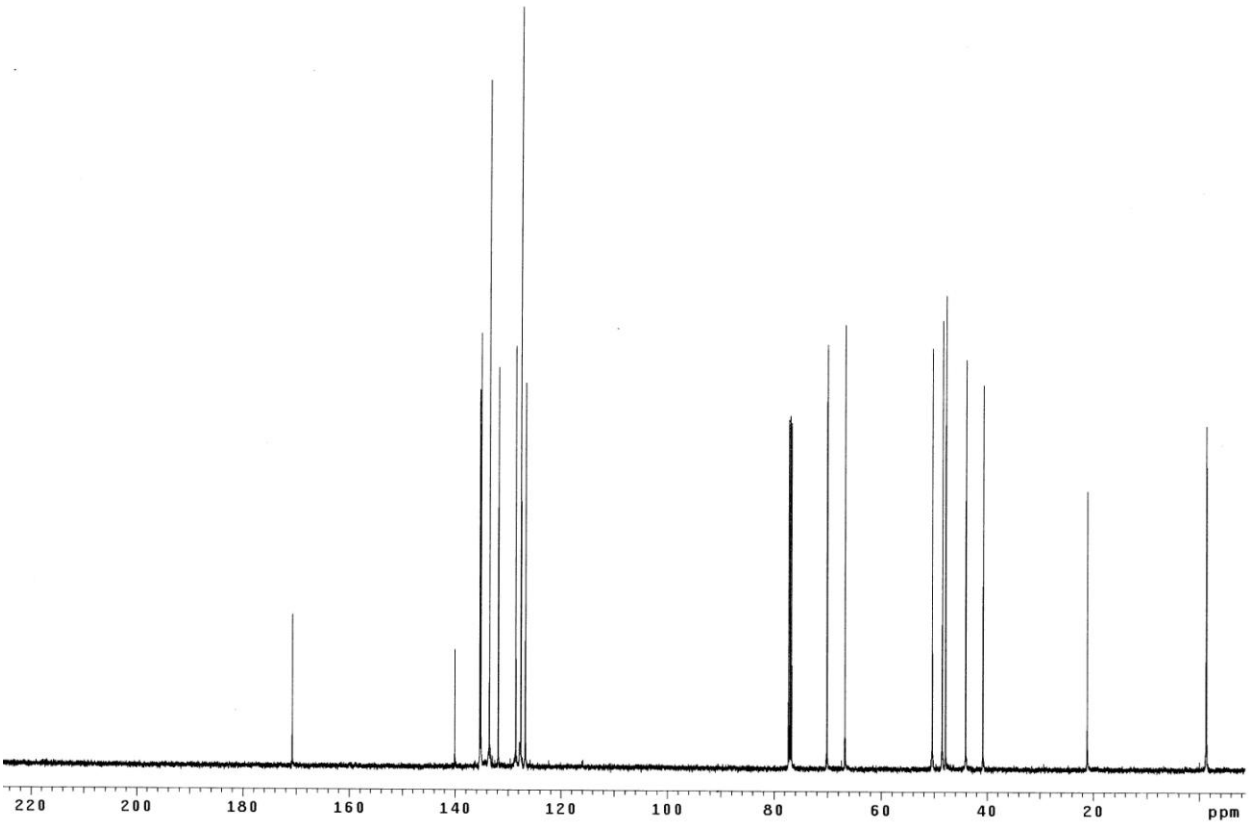


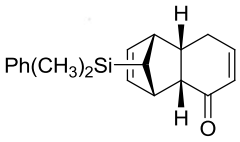
23





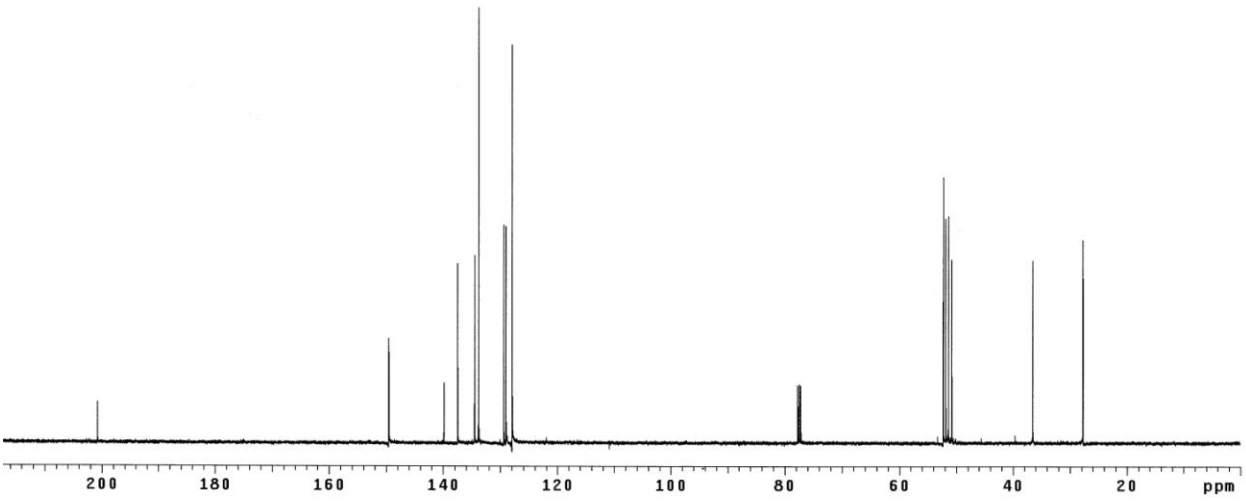
24

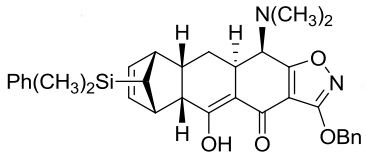




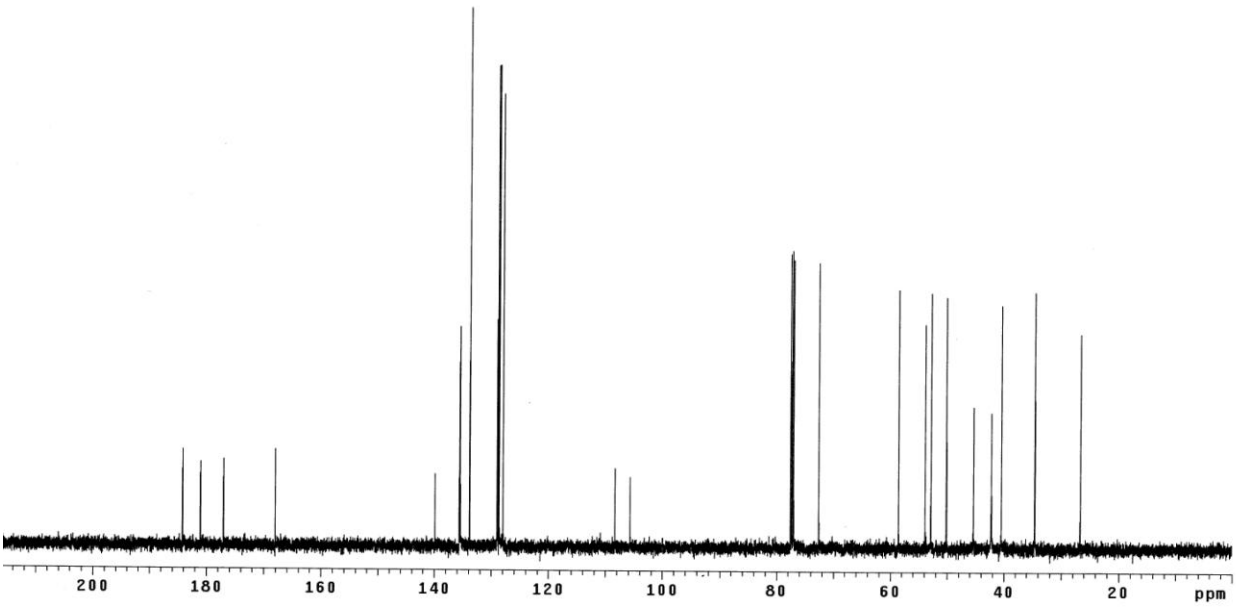
25

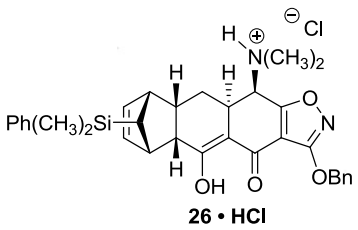
(not subject to purification, est. >90% purity)





26





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