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Synthesis and Alkylation of Cyclopentane β-Ketoxime Sulfones. α,α-Methylation-Alkynylation of Cyclopentanone

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Abstract: The synthesis and selected transformations of some cyclopentanoid β-ketoxime sulfone derivatives are reported. Utilization of the sulfone group to stabilize adjacent negative charge facilitates smooth alkylation. Subsequent 1,4-elimination of the sulfonyl moiety generates a vinyl nitroso species that is readily intercepted by lithium acetylides. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

In the course of a synthetic program directed towards the sesterpene retigeranic acid, we required an efficient method for the preparation of an α,α-dialkylated cyclopentanone, preferably from a β-keto sulfone. β-Keto sulfones are well established versatile intermediates in organic synthesis since stabilization of adjacent negative charge by the sulfonyl moiety allows a wide range of electrophiles to undergo alkylation at the α-carbon.[2)] After C-C bond formation, the sulfonyl group can be readily removed by either reductive or eliminative methods.[3)] Surprisingly, the related β-ketoxime sulfones have not received much attention.[4,5)] In contrast to the keto analogs, β-oxime sulfones have the potential to function both as soft nucleophiles via deprotonation, or as electrophiles, by 1,4-elimination of a sulfinic acid to produce a vinyl nitroso species.[6,7)] Combination of these two processes could lead to formation of two C-C bonds at the α-position of a ketone, a difficult transformation, leading to a solution to our synthetic problem. In this paper we report the results of some model studies that show that β-ketoxime sulfones can indeed function as soft nucleophiles and electrophiles, leading to an α-α dialkylation of cyclopentanone (Fig. 1).

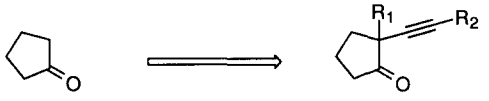
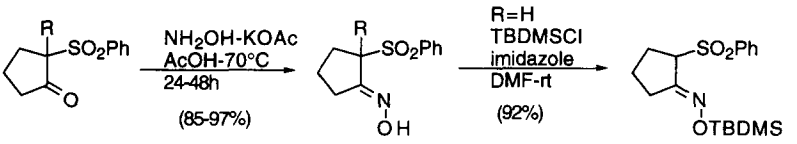


Figure 1

RESULTS AND DISCUSSION

β-Keto sulfone **1a** is readily obtained from cyclopentanone by sulfenylation-oxidation.[8,9)] Conversion to a single geometric isomer of oxime **2a** in 97% yield was readily accomplished by treatment with hydroxylamine hydrochloride in acetic acid in the presence of potassium acetate at 70°C. Compound **2a** has been reported in the patent literature[5)] to have a mp of 147°C, compared to 158°C in this work, although no

assignment of oxime geometry was presented. Denmark used similar conditions, although at ambient temperature, in order to prevent 1,4-elimination in a series of α-chloro ketones.[6b] In a similar manner, the β-keto sulfones **1b** and **1c** were smoothly converted to oximes **2b** and **2c** in 92 and 85% yields respectively as single isomers. The starting ketones **1b** and **1c** were readily obtained in high yield by cesium carbonate-mediated alkylation of **1a** with the appropriate alkyl halide (see Experimental Section). Chloro derivative **1d**, readily obtained by chlorination of **1a** with NCS in CCl_4 at reflux (71%), similarly afforded a single isomer of oxime **2d** in 91% yield. For examination of alkylation chemistry, we also required the silylated oxime **3**. Straightforward silylation of oxime **2a** gave the required *O*-silyl derivative **3** in 92% yield as a clear oil and as a single geometric isomer.



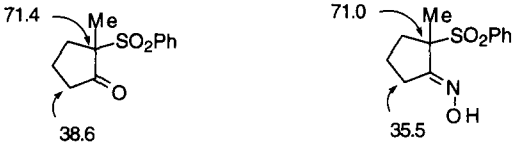
1a R = H
1b R = Me (95% from **1a**)
1c R = CH_2—≡—Me (98% from **1a**)
1d R = Cl (71% from **1a**)

2a R = H
2b R = Me
2c R = CH_2—≡—Me
2d R = Cl

3

Scheme 1

Assignment of the geometry of the oxime moiety was accomplished by analysis of the ^{13}C NMR signals of the α and α' carbons of the ketones and oximes utilizing the method of Fuchs.[10] For example, it was clear that oxime **2b** had the E-configuration since an upfield shift of the C5-carbon, presumably due to shielding via steric compression, was apparent. The C2-carbon signal was essentially unchanged (Fig.2). Unambiguous assignment of the appropriate signals for oximes **2a** and **2c-d** was complicated, however, given the formation of single isomers under the same reaction conditions, assignment of the E-configuration is reasonable.

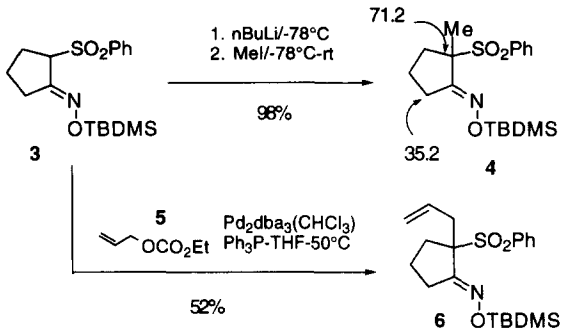


1b **2b**

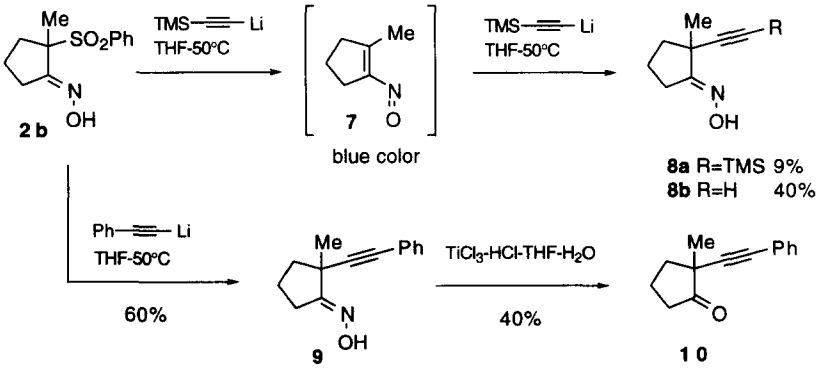
Figure 2

For exploration of alkylation chemistry, we initially envisaged a C-C bond formation α to the sulfone moiety of **2a** via a dianion, followed by monoalkylation with an electrophile. In the event, generation of a dianion and trapping with methyl iodide failed to afford any C-alkylation product. It is well known that an oxime anion activates the syn-protons towards deprotonation leading to regioselective dianion formation,[11] therefore it is possible that the E-configuration of **2a** is not conducive to clean dianion formation-alkylation. Formation of a monoanion from the silyl derivative **3** nicely solved this problem. Generation of a yellow anion solution (nBuLi/THF/-78°C/30min) followed by reaction with methyl iodide gave a 98% yield of **4** with retention of oxime configuration. Compound **3** could also participate as the nucleophilic partner in a Pd-

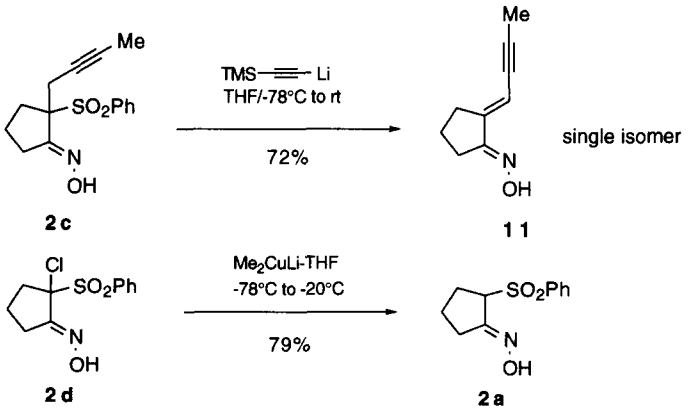
catalyzed allylic alkylation reaction. For example, reaction with carbonate **5** under standard alkylative conditions ($Pd_2dba_3(CHCl_3)$-Ph_3P-THF-50°C) led to C-allyl derivative **6** in 52% isolated yield.



Demonstration of the utility of β-ketoxime sulfones as precursors of vinyl nitroso species was achieved by reaction of oxime **2b** with acetylide anions. While no reaction occurred up to room temperature with an excess of lithium trimethylsilylacetylide in THF, increasing the temperature to 50°C led to the transient formation of a blue color, presumably due to **7**, a characteristic feature of vinyl nitroso species,[6] and interception by the acetylide to give a 49% isolated yield of two alkynylated products. The major product, **8b** (40%), had undergone *in situ* desilylation; the minor product, silylated acetylene **8a** was obtained in 9% isolated yield. A trace of the product resulting from β-elimination of sulfinate via deprotonation of the C2-methyl group, 2-methylene cyclopentanone oxime, was also obtained as a mixed fraction with **8a**. It is of note that compounds **8a** and **8b** were single isomers as indicated by ^{13}C NMR spectroscopy. Reaction with the lithium anion of phenylacetylene under similar conditions gave the alkynylated product **9** in ~60% yield. Characterization of the product was best achieved by deprotection of the oxime moiety[12] ($TiCl_3$, 40%); in this way α,α-dialkylated cyclopentanone **10** was obtained as an oil. In these alkynylations we have clearly demonstrated that a vinyl nitroso species can be generated from β-ketoxime sulfone **2b**, but only at elevated temperatures. These results suggest that the borohydride-mediated desulfonylation of β-ketoxime sulfones, as described by Fuchs in his synthesis of PGE_2,[4] did not proceed by a vinyl nitroso species, but instead by simple base-mediated β-elimination-reduction.



We briefly explored the scope of this alkynylation process. The outcome of the reaction of alkyne derivative **2c** with a lithium acetylide at -78°C to room temperature, in which a single isomer of enyne derivative **11** was the only product in 72% yield, supports the proposition that β-elimination is a competing process, leading to limitations in the range of possible substrates. Furthermore, highly functionalized oxime **2d**, a substrate for a postulated sequential double alkylation, afforded only reduction product **2a** upon treatment with a cuprate.



In summary, we have shown for the first time that cyclopentyl β-ketoxime sulfones can participate as soft nucleophiles in alkylation reactions and can function as electrophiles via 1,4-elimination of benzenesulfinic acid to yield a vinyl nitroso intermediate that is intercepted by acetylide anions, leading to α,α-dialkylation of cyclopentanone (Fig. 3). We believe that the model studies outlined herein indicate new possibilities for sulfone chemistry.

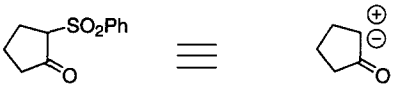


Figure 3

Acknowledgments

We thank the NSF and NIH for their generous support of our programs.

EXPERIMENTAL SECTION

General Procedures.

Anhydrous reactions were performed in oven-dried or flame-dried glassware under nitrogen. Solvents were distilled: methylene chloride from calcium hydride, tetrahydrofuran from sodium benzophenone ketyl. Flash chromatography was performed using Kieselgel 60. NMR spectra were obtained on a Varian XL-400 (^{1}H: 400 MHz; ^{13}C: 100 MHz). Infrared spectra were obtained on a Perkin Elmer 1420 in solution or as thin films.

Mass spectra were provided by the NIH Mass Spectrometry Facility, University of California-San Francisco. Melting points were obtained on a Thomas Hoover apparatus in open capillary tubes and are uncorrected. Unless otherwise stated, yields refer to homogeneous material (TLC/NMR or TLC/GC/NMR).

Preparation of ß-Ketosulfones (1b and 1c).

Alkylations were performed using a mixture of sulfone **1a** (1eq), methyl iodide or bromobut-2-yne(1.1-2.0eq), and cesium carbonate(1.2eq) in acetone (~0.2-0.5M concentration) at room temperature or reflux. Extractive work-up, flash chromatography and recrystallization gave white crystalline solids.

2-Methyl-2-phenylsulfonylcyclopentan-1-one (1b).

95% yield, 23 mmol scale. R_f 0.30 (CH_2Cl_2); mp 85-86°C (CH_2Cl_2-hexane); IR($CDCl_3$) 3070, 2985, 2930, 1745, 1450, 1410, 1380, 1305, 1190, 1150, 1085, 1060, 1025, 805, 635 cm^{-1}; ^1H NMR($CDCl_3$) δ=7.81 (2H, d, *J* = 7.2Hz), 7.68 (1H, t, *J* = 7.6Hz), 7.55 (2H, t, *J* = 7.8Hz), 3.00 (1H, dt, *J* = 14, 7.3Hz), 2.57 (1H, dt, *J* = 18.7, 8.5Hz), 2.39-2.30 (1H, m), 2.28-2.17 (1H, m), 2.03 (1H, dt, *J* = 14.3, 7.1Hz), 1.92-1.84 (1H, m), 1.30 (3H, s); ^{13}C NMR($CDCl_3$) δ=211.3, 135.4, 134.1, 130.5, 128.7, 71.4, 38.6, 32.4, 19.5, 18.6; MS(EI) *m/z* (relative intensity) 238 ($\underline{M}^+$, 28.4%), 183(2.9), 143(11.3), 125(7.6), 113(7.6), 105(3.6), 97(100). Found: $\underline{M}^+$, 238.0664. Calcd for $C_{12}H_{14}O_3S$: 238.0664.

2-Phenylsulfonyl-2-but-2'-ynylcyclopentan-1-one (1c).

98% yield, 6.67 mmol scale. R_f 0.76 (Et_2O); mp 68°C (Et_2O-hexane); IR($CDCl_3$) 1740, 1445, 1305, 1170, 1140, 1075, 680 cm^{-1}; ^1H NMR($CDCl_3$) δ=7.78 (2H, d, *J* = 7.3Hz), 7.71 (1H, t, *J* = 7.5Hz), 7.56 (2H, t, *J* = 7.6Hz), 2.98-2.91 (1H, m), 2.64-2.48 (4H, m), 2.35-2.17 (2H, m), 2.06-1.96 (1H, m), 1.69 (3H, t, *J* = 2.4Hz); ^{13}C NMR($CDCl_3$) δ=210.3, 135.1, 134.4, 130.6, 128.8, 79.6, 73.5, 71.8, 39.0, 29.1, 23.7, 19.2, 3.4; MS(EI) *m/z* (relative intensity) 276 ($\underline{M}^+$, 1.7%), 258(5.2), 211(20.6), 135(89.8), 91(61). Found: $\underline{M}^+$, 276.0831. Calcd for $C_{15}H_{16}O_3S$: 276.0820.

2-Chloro-2-phenylsulfonylcyclopentan-1-one (1d).

Obtained by reaction of ß-ketosulfone **1a** (1eq) with NCS (1.2eq) in CCl_4 in the presence of catalytic AIBN at reflux followed by extractive work-up and purification. White solid, 71% yield, 0.446 mmol scale. R_f 0.59 (CH_2Cl_2). IR($CDCl_3$) 1760, 1450, 1405, 1325, 1310, 1280, 1160, 1150, 1130, 1080, 995, 815, 680, 635, 630, 625 cm^{-1}; ^1H NMR($CDCl_3$) δ=7.95-7.92 (2H, m), 7.76-7.71 (1H, m), 7.61-7.57 (2H, m), 3.25 (1H, dt, *J* = 15.2, 7.6Hz), 2.66 (1H, dt, *J* = 19.2, 8.8Hz), 2.58-2.46 (2H, m), 2.37-2.27 (1H, m), 2.15-2.03 (1H, m); ^{13}C NMR($CDCl_3$) δ=203.7, 134.9, 133.8, 131.5, 128.6, 80.8, 37.1, 35.3, 18.3; MS(EI) *m/z* (relative intensity) 260 ($\underline{M}^+$, 38.1%), 259(12.6), 258($\underline{M}^+$, 100%), 220(6.6), 205(2.4), 191(3.9), 177(3.6), 163(8.0), 158(1.8), 149(28.7), 143(10.1), 142(17.3), 135(80.2), 126(15.6), 125(39.7), 121(36.4). Found: $\underline{M}^+$, 260.0060, 258.0107. Calcd for $C_{11}H_{11}{}^{37}ClO_3S$: 260.0087. Calcd for $C_{11}H_{11}{}^{35}ClO_3S$: 258.0117.

General Procedure for Synthesis of Oximes.

A mixture of ß-ketosulfone (1eq), hydroxylamine hydrochloride (4eq) and KOAc (4eq) in AcOH (~0.5M concentration) was heated at 70°C for 24-48 h. Extractive work-up and recrystallization gave single geometric isomers of the oximes as white solids.

2-Phenylsulfonylcyclopentan-1-one, Oxime (2a).

97% yield, 8.93 mmol scale. R_f 0.13 (50% Et_2O-hexane); mp 158°C (dec.) (CH_2Cl_2-hexane); IR($CDCl_3$) 3555, 3325, 3065, 2975, 1445, 1420, 1360, 1305, 1230, 1200, 1145, 1115, 1085, 1045, 1025, 975, 680 cm^{-1}; ^1H NMR($CDCl_3$) δ=8.76 (1H, s), 7.90-7.88 (2H, m), 7.68-7.64 (1H, m), 7.57 (2H, d, *J* = 8Hz), 4.10 (1H, dd, *J* = 8.5, 4Hz), 2.62-2.39 (3H, m), 2.14-2.09 (1H, m), 1.97-1.90 (1H, m), 1.80-1.75 (1H, m); ^{13}C NMR($CDCl_3$) δ=159.0, 137.6, 133.9, 129.1, 66.9, 27.4, 27.3, 22.1; MS(EI) *m/z* (relative intensity) 240 ($\underline{MH}^+$, 0.7%), 239(0.2), 223(3.4), 175(77), 158(16.1), 143(21.8), 125(20.3), 98(99.8), 97(100). Found: $\underline{M}^+$, 239.0617. Calcd for $C_{11}H_{13}NO_3S$: 239.0616.

2-Methyl-2-phenylsulfonylcyclopentan-1-one, Oxime (2b).

92% yield, 18.4 mmol scale. R_f 0.65 (Et_2O); mp 175°C (dec.) (CH_2Cl_2-hexane); IR($CDCl_3$) 3560, 3315, 2985, 1445, 1420, 1375, 1355, 1300, 1175, 1135, 1085, 1070, 965, 955, 680 cm^{-1}; ^1H NMR($CDCl_3$) δ=8.43 (1H, s), 7.87-7.85 (2H, m), 7.65 (1H, t, *J* = 7.3Hz), 7.54 (2H, d, *J* = 7.9Hz), 2.75-2.62 (2H, m), 2.50 (1H, ddd, *J* = 18.6, 5.5, 8.9Hz), 1.99-1.90 (1H, m), 1.88-1.80 (1H, m), 1.78-1.70 (1H, m), 1.51 (3H, s); ^{13}C NMR($CDCl_3$) δ=162.6, 135.7, 133.8, 130.6, 128.6, 71.0, 35.5, 27.7, 21.4, 21.0; MS(EI) *m/z* (relative intensity) 254 ($\underline{MH}^+$, 0.3%), 253(0.1), 190(0.5), 189(3.5), 172(3.2), 143(3.3), 131(8.2), 125(7.6), 119(7.0), 112(100). Found: $\underline{M}^+$, 253.0762. Calcd for $C_{12}H_{15}NO_3S$: 253.0773.

2-Phenylsulfonyl-2-but-2'-ynylcyclopentan-1-one, Oxime (2c).

85% yield, 1.81 mmol scale. R_f 0.76 (Et_2O); mp 195°C (dec.) (CH_2Cl_2-hexane); IR($CDCl_3$) 3570, 3340, 3070, 2970, 2930, 1450, 1425, 1365, 1310, 1285, 1170, 1145, 1085, 685 cm^{-1}; ^1H NMR($CDCl_3$) δ=8.34 (1H, s), 7.86-7.84 (2H, m), 7.66 (1H, t, *J* = 7.3Hz), 7.55 (2H, t, *J* = 7.9Hz), 2.83 (2H, brq, *J* = 2.5Hz), 2.64-2.43 (4H, m), 2.37 (1H, dt, *J* = 14.4, 8.4Hz), 1.88-1.82 (1H, m), 1.71 (3H, t, *J* = 2.5Hz); ^{13}C NMR($CDCl_3$) δ=161.3, 135.5, 134.0, 130.7, 128.7, 79.0, 73.2, 72.6, 31.9, 28.1, 24.8, 21.5, 3.5; MS(EI) *m/z* (relative intensity) 292 ($\underline{MH}^+$, 0.2%), 274(1), 227(1.5), 217(3.2), 151(10.7), 150(100). Found: $\underline{MH}^+$, 292.0999. Calcd for $C_{15}H_{18}NO_3S$: 292.1008.

2-Chloro-2-phenylsulfonylcyclopentan-1-one, Oxime (2d).

91% yield, 0.31 mmol scale. R_f 0.10 (CH_2Cl_2); IR($CDCl_3$) 3560, 3340, 1450, 1440, 1425, 1365, 1330, 1315, 1160, 1145, 1085, 980, 965, 685 cm^{-1}; ^1H NMR($CDCl_3$) δ=8.67 (1H, s), 8.00-7.98 (2H, m), 7.71 (1H, t, *J* = 7.6Hz), 7.58 (2H, t, *J* = 8Hz), 3.00 (1H, quintet, *J* = 7.2Hz), 2.82 (1H, ddd, J = 19.2, 8.8, 5.6Hz), 2.64 (1H, ddd, *J* = 18.8, 8.4, 7.6Hz), 2.27 (1H, quintet, *J* = 7.2Hz), 2.20-2.09 (1H, m), 2.02-1.91 (1H, m); ^{13}C NMR($CDCl_3$) δ=159.9, 134.6, 134.0, 131.6, 128.6, 83.9, 30.1, 27.3, 20.9; MS(EI) *m/z*

(relative intensity) 211 and 209 ($\underline{M}^+$-O_2S, 6.6 and 20.2%), 156(2.0), 143(2.9), 134(8.6), 132(26.6), 125(15.2), 114(8.9), 96(16.4). Found: 211.0578, 209.0607. Calcd for $C_{11}H_{12}NO^{37}Cl$ and $C_{11}H_{12}NO^{35}Cl$: 211.0574 and 209.0608.

2-Phenylsulfonylcyclopentan-1-one, Oxime-*O*-TBDMS Ether (3).

Silylation was performed using a mixture of oxime (1eq), TBDMSCl (1.2eq), and imidazole (1.2eq) in DMF at room temperature. Extractive workup and flash chromatography gave the silyl oxime **3** as an oil in 92% yield, 2.93 mmol scale. R_f 0.67 (CH_2Cl_2); IR(neat film) 3050, 2940, 2920, 2880, 2850, 1580, 1465, 1460, 1445, 1415, 1390, 1360, 1305, 1245, 1225, 1205, 1145, 1115, 1080, 1065, 1040, 1020, 995, 940, 840, 780, 755, 725, 680, 655, 610 cm^{-1}; ^1H NMR($CDCl_3$) δ=7.87-7.84 (2H, m), 7.65-7.61 (1H, m), 7.55 (2H, t, *J* = 7.6Hz), 4.10 (1H, dd, *J* = 8, 3.2Hz), 2.72-2.66 (1H, m), 2.58 (2H, t, *J* = 7.6Hz), 2.22-2.05 (2H, m), 1.87-1.76 (1H, m), 0.82 (9H, s), -0.02 (3H, s), -0.06 (3H, s); MS(EI) *m/z* (relative intensity) 354 ($\underline{MH}^+$, 0.1%), 338(3.3), 296(100), 200(21.2), 154(13.6), 135(86.4), 125(63.3). Found: $\underline{MH}^+$, 354.1566. Calcd for $C_{17}H_{28}NO_3SSi$: 354.1560.

2-Methyl-2-phenylsulfonylcyclopentan-1-one, Oxime-*O*-TBDMS Ether (4).

To a solution of oxime **3** (71 mg, 0.201 mmol) in THF (1.0 mL) at -78°C was added nBuLi (0.166 mL of a 1.37M solution in hexane, 0.221 mmol) dropwise. After 30 min, methyl iodide (251 mg, 1.77 mmol) was added dropwise to the yellow solution. After 5 h at -78°C, the solution was allowed to warm slowly to room temperature overnight (17 h). The reaction was then quenched with water and extracted with ether (2x). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* and the residue purified by flash chromatography (20% Et_2O-hexane) to yield oxime **4** (72 mg, 98%) as a clear oil. R_f 0.71 (CH_2Cl_2); IR(neat film) 3060, 2960, 2930, 2890, 2860, 1590, 1460, 1450, 1420, 1390, 1380, 1365, 1305, 1255, 1180, 1140, 1090, 1070, 1000, 960, 935, 900, 860, 840, 785, 755, 725, 690, 660, 620 cm^{-1}; ^1H NMR($CDCl_3$) δ=7.78-7.76 (2H, m), 7.60-7.56 (1H, m), 7.46 (2H, t, *J* = 8Hz), 2.87 (1H, ddd, *J* = 14, 8, 3.7Hz), 2.68-2.53 (2H, m), 2.14-2.02 (1H, m), 1.82 (1H, dt, *J* = 14.3, 8.6Hz), 1.76-1.66 (1H, m), 1.37 (3H, s), 0.79 (9H, s), 0.00 (3H, s), -0.06 (3H, s); ^{13}C NMR($CDCl_3$) δ=166.3, 135.7, 133.5, 130.7, 128.4, 71.2, 35.2, 28.0, 25.9, 21.7, 21.0, 18.0, -5.2; MS(EI) *m/z* (relative intensity) 352 ($\underline{M}^+$-CH_3, 1.1%), 310(30.9), 292(1.2), 227(3.8), 226(18.2), 210(1.8), 200(4.1), 185(9.9), 168(10.7), 135(7.8), 125(8.1), 94(8.1), 71(100). Found: 352.1396. Calcd for $C_{17}H_{26}NO_3SSi$: 352.1403.

2-Allyl-2-phenylsulfonylcyclopentan-1-one, Oxime-*O*-TBDMS Ether (6).

To $Pd_2dba_3(CHCl_3)$ (29.4 mg, 5 mol%) and triphenylphosphine (59.4 mg, 40 mol%) was added THF (1.0 mL) and the mixture stirred 10 min to give a yellow solution. Oxime **3** (200 mg, 0.567 mmol) in THF (1.0 mL) was then added, followed by allyl carbonate **5** (176.8 mg, 1.36 mmol) in THF (1.6 mL). After 10 min at room temperature and 30 h at 50°C, the reaction was concentrated *in vacuo* and the residue purified by flash chromatography (20% Et_2O-hexane) to give allylated oxime sulfone **6** (115 mg, 52%) as a clear oil. R_f 0.49 (30% Et_2O-hexane); IR(neat film) 3060, 2950, 2920, 2880, 2855, 1640, 1585, 1470, 1460, 1445, 1390, 1360, 1305, 1250, 1210, 1165, 1140, 1080, 1045, 1010, 1000, 955, 940, 850, 835, 780, 755, 725, 690,

650, 615 cm^{-1}; ^1H NMR($CDCl_3$) δ=7.81 (2H, d, *J* = 8.4Hz), 7.63 (1H, t, *J* = 7.6Hz), 7.50 (2H, t, *J* = 7.6Hz), 5.58-5.48 (1H, m), 5.12-5.07 (2H, m), 2.76-2.70 (1H, m), 2.60-2.55 (4H, m), 2.15-2.01 (2H, m), 1.74-1.64 (1H, m), 0.86 (9H, s), 0.05 (3H, s), 0.00 (3H, s); ^{13}C NMR($CDCl_3$) δ=165.1, 135.6, 133.6, 131.7, 130.9, 128.5, 120.1, 74.1, 38.1, 30.5, 28.6, 25.9, 21.1, 17.9, -5.0, -5.1; MS(EI) *m/z* (relative intensity) 393 (M^+, 0.3%), 379(0.3), 378(1.3), 338(5.3), 337(11), 336(44.9), 330(1.7), 329(6.7), 296(2.4), 254(6.4), 253(23.7), 252(100), 211(21.7), 210(23.0), 200(20.1), 194(17.1), 135(34.0), 125(20.8), 122(10.2), 120(38.4). Found: M^+, 393.1762. Calcd for $C_{20}H_{31}NO_3SSi$: 393.1793.

Reaction of Oxime (2b) with Lithium TMS-Acetylide.

To a solution of 1-trimethylsilylacetylene (2.03 g, 20.75 mmol) in THF (41.5 mL) at -78°C was added 1.52M nBuLi (13 mL, 19.76 mmol) and the solution stirred 30 min then warmed to 0°C and treated with **2b** (500 mg, 1.98 mmol) in THF (10 mL). After heating at 50°C for 48 h, the reaction was cooled, quenched with brine and extracted with methylene chloride (4x). The combined organic layers were washed with water, dried ($MgSO_4$), concentrated *in vacuo*, and the residue purified by flash chromatography (10% Et_2O-hexane) to give 3 fractions. The first-eluted material (38 mg, 9%) was 1-trimethylsilylacetylene **8a** as a white solid. The second-eluted material (25 mg) was a mixture of **8a** and 2-methylenecyclopentanone, oxime. The third-eluted material (108.3 mg, 40%) was the alkyne **8b** as a white solid.

Data for Acetylene **8a**. R_f 0.53 (50% Et_2O-hexane); mp 105-106°C (unrecrystallized); IR($CDCl_3$) 3570, 3300, 2970, 2900, 2170, 1450, 1425, 1375, 1355, 1250, 1210, 1200, 1180, 1095, 1000, 955, 860, 850 cm^{-1}; ^1H NMR($CDCl_3$) δ=8.94 (1H, bs), 2.69-2.52 (2H, m), 2.10-2.04 (1H, m), 1.96-1.87 (1H, m), 1.84-1.67 (2H, m), 1.40 (3H, s), 0.13 (9H, s); ^{13}C NMR($CDCl_3$) δ=167.5, 109.3, 85.3, 41.4, 41.3, 26.0, 25.3, 21.1, -0.06; MS(EI) *m/z* (relative intensity) 208 (M^+-H, 2.1%), 194(24.8), 192(20.4), 178(13.0), 176(33.2), 166(21.7), 153(14.4), 135(10.5), 123(30.8), 99(31.8), 97(100). Found: 208.1146. Calcd for $C_{11}H_{18}NOSi$: 208.1158.

Data for Acetylene **8b**. R_f 0.45 (50% Et_2O-hexane); IR($CDCl_3$) 3540, 3270, 2940, 2900, 1445, 1420, 1370, 1350, 1305, 1250, 1225, 1195, 1175, 1135, 1090, 1065, 955, 850, 630 cm^{-1}; ^1H NMR($CDCl_3$) δ=8.85 (1H, bs), 2.72-2.43 (2H, m), 2.24 (1H, s), 2.14-2.05 (1H, m), 2.00-1.90 (1H, m), 1.86-1.71 (2H, m), 1.43 (3H, s); ^{13}C NMR($CDCl_3$) δ=167.5, 87.3, 69.5, 41.0, 40.4, 26.1, 25.3, 21.1; MS(EI) *m/z* (relative intensity) 137 (M^+, 4.2%), 136(8.7), 135(5.2), 120(100), 92(17.4), 91(39.7). Found: M^+, 137.0836. Calcd for $C_8H_{11}NO$: 137.0841.

Sequential Reaction of Oxime (2b) with Lithium Phenylacetylide-$TiCl_3$.

To a solution of phenylacetylene (1.11 g, 10.81 mmol) in THF (22 mL) at -78°C was added nBuLi (6.5 mL of a 1.52M solution in hexanes, 9.88 mmol) and the solution then stirred 30 min then warmed to 0°C and treated with a solution of sulfone **2b** (500 mg, 1.98 mmol) in THF (10 mL) and the solution heated at 50°C for 3 h. After cooling, brine was added and the mixture extracted with methylene chloride (4x). The combined organic layers were washed with water (3x), dried ($MgSO_4$), concentrated *in vacuo* and the residue purified by flash chromatography (10% Et_2O-hexane elution) to give a white solid (293.3 mg) that was a 10.7:2.5:1 mixture of alkyne **9**, α-methylenecyclopentanone oxime, and 2-methyl cyclopentenone oxime. Calculated yield = 60% of

9, 20% of by-products. R_f 0.47 (50% Et_2O-hexane); ^{13}C NMR($CDCl_3$) signals for **9** δ=167.9, 131.7, 128.0, 127.7, 123.4, 92.6, 81.6, 41.4, 41.3, 26.2, 25.2, 21.3. Additional signals appeared at δ=107.6, 32.9, 29.0, 27.7, 22.0 for the by-products. This mixture was then dissolved in THF (3 mL), cooled to 0°C and treated with titanium trichloride (433.5 mg, 2.81 mmol) in water (3 mL). After 1 h at 0°C, a further batch of $TiCl_3$ (433.5 mg) in 10% hydrochloric acid (2 mL) was added and the mixture stirred 90 h at room temperature. The reaction was diluted with water and extracted with methylene chloride (4x), and the combined organic extracts washed with water, dried ($MgSO_4$), concentrated *in vacuo* and the residue purified by flash chromatography (10% Et_2O-hexane elution) to give ketone **10** (94 mg, 40%) as a clear oil. R_f 0.47 ($CHCl_3$); IR(neat film) 2960, 2920, 2850, 1740, 1670, 1590, 1485, 1440, 1400, 1365, 1300, 1270, 1150, 1135, 1060, 940, 915, 750, 685 cm^{-1}; ^1H NMR($CDCl_3$) δ=7.40-7.38 (2H, m), 7.29-7.26 (3H, m), 2.56-2.48 (1H, m), 2.41-2.36 (1H, m), 2.28 (1H, dt, *J* = 19.2, 8 Hz), 2.20-2.10 (1H, m), 2.02-1.86 (2H, m), 1.41 (3H, s); ^{13}C NMR($CDCl_3$) δ=215.3, 131.7, 128.1, 128.0, 123.0, 90.0, 82.9, 44.9, 39.0, 36.3, 22.3, 19.2.

Reaction of Oxime (2c) with Lithium TMS-Acetylide.

To a solution of 1-trimethylsilylacetylene (556 mg, 5.67 mmol) in THF (11.3 mL) at -78°C was added nBuLi (3.4 mL of a 1.52M solution in hexanes, 5.15 mmol) and the solution stirred 30 min. Oxime **2c** (300 mg, 1.03 mmol) in THF (4 mL) was then added. After 15 min at -78°C, the solution was allowed to warm to room temperature. After 4 h the reaction was quenched by the addition of brine and the mixture extracted with methylene chloride (4x). The combined organic layers were washed with water, dried ($MgSO_4$), concentrated *in vacuo*, and the residue purified by flash chromatography (25% Et_2O-hexane) to yield enyne **11** (110.2 mg, 72%) as a white solid and as a single geometric isomer. Starting **2c** (12.5 mg) was also recovered from the column. R_f 0.73 (Et_2O); mp 107°C (hexane); IR($CHCl_3$) 3560, 3360, 2990, 2940, 2900, 2870, 2830, 1640, 1600, 1460, 1430, 1420, 1355, 1275, 1240, 1160, 1040, 930, 840 cm^{-1}; ^1H NMR($CDCl_3$) δ=9.04 (1H, bs), 6.09 (1H, q, *J* = 2.8Hz), 2.63 (4H, t, *J* = 7.2Hz), 2.02 (3H, t, *J* = 2Hz), 1.80 (2H, quintet, *J* = 7.6Hz); ^{13}C NMR($CDCl_3$) δ=161.4, 147.1, 103.4, 93.6, 78.1, 31.5, 28.0, 21.4, 4.7; MS(EI) *m/z* (relative intensity) 149 ($\underline{M}^+$, 67.2%), 132(100), 117(25.6), 105(18.9), 91(22.2). Found: $\underline{M}^+$, 149.0834. Calcd for $C_9H_{11}NO$: 149.0841.

Reaction of Chlorooxime (2d) with Dimethylcopperlithium.

Reaction of **2d** (60 mg, 0.219 mmol) in ether (0.4 mL) with dimethylcopperlithium {prepared from CuI (125 mg) and MeLi (0.877 mL of a 1.5M solution) at -40°C, in ether (0.33 mL)} at -78°C to -20°C over 45 min gave after work-up and purification 41.3 mg (79%) of oxime **2a** (NMR/TLC).

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