Supplementary Material for "Development of a Rhodium Carbenoid-Initiated Claisen Rearrangement for the Enantioselective Synthesis of α-Hydroxy Carbonyl Compounds"

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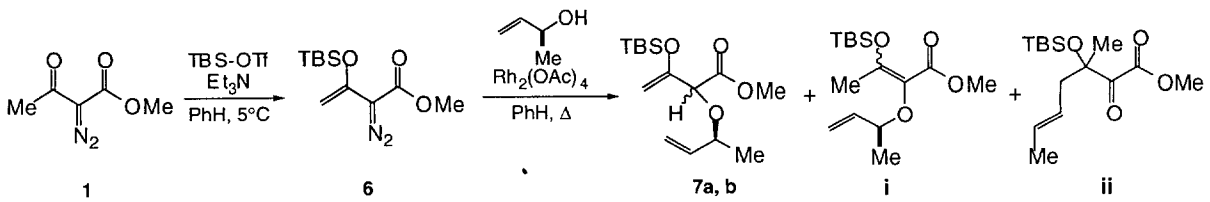
Materials and Methods

Unless otherwise stated, reactions were performed in flame-dried glassware under a nitrogen atmosphere using freshly distilled solvents. All commercially-obtained reagents were used as received. Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 precoated plates (0.25 mm). Silica gel (particle size 0.032-0.063 mm) was used for flash chromatography. High-performance liquid chromatography (HPLC) was performed with either a Rainin Microsorb 80-199-C5 or 80-120-C5 column. 1H and 13C NMR chemical shifts are reported as δ values relative to internal tetramethylsilane. Melting points are uncorrected. High resolution mass spectra were acquired at The University of Illinois Mass Spectrometry Center. Single crystal X-ray analyses were performed by Dr. Susan DeGala (Yale University) and Dr. Patrick Carroll (University of Pennsylvania).

Preparation of TBS-Enol Ether 6, OH-Insertion Products 7a,b, Enone i, and α-ketoester ii.



To a solution of methyl 2-diazo-3-oxobutanoate (**1**, 250 mg, 1.76 mmol, 1.0 equiv) and triethylamine (736 μL, 5.28 mmol, 3.0 equiv) in benzene (13 mL) at

5°C was added *t*-butyldimethylsilyltrifluoromethane sulfonate (TBSOTf, 405 μL, 1.76 mmol, 1.0 equiv) over 5 min. The resulting orange mixture was stirred for 15 min then flushed through a short column of silica gel (4:1 hexanes:EtOAc with 1% triethylamine eluent). Concentration under reduced pressure provided the crude TBS enol ether which was added to a mixture of *(S)*-(+)-3-buten-2-ol (183 μL, 2.11 mmol, 1.2 equiv) and $Rh_2(OAc)_4$ (1.0 mg, 0.0023 mmol, 0.0013 equiv) in benzene (15 mL). The mixture was heated under reflux for 15 min, cooled to room temperature and concentrated. Purification by flash chromatography (40:1 hexanes:Et_2O eluent) provided α-ketoester **ii** (50 mg, 9.5% yield) and a mixture of **7a,b** and enone **i** (450 mg, 85% yield) of which **7a,b** (1:1 mixture) were the major constituents. Partial separation of these compounds could be achieved by column chromatography (75:1 hexanes:Et_2O eluent). First to elute was diastereomer **7a**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.73 (m, 1H), 5.17 (m, 2H), 4.53 (m, 1H), 4.32 (s, 1H), 4.29 (d, *J*=1.5 Hz, 1H), 3.95 (quint, *J*=6.4 Hz, 1H), 3.75 (s, 3H), 1.31 (d, *J*=6.3 Hz, 3H), 0.91 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.8, 153.9, 139.1, 116.9, 92.0, 77.8, 76.6, 52.0, 25.5, 21.2, 18.0, -4.8, -5.0; **IR** (thin film/NaCl) 3080 (w), 2954 (s), 2932 (s), 2889 (m), 2859 (s), 1762 (s), 1640 (s), 1471 (m), 1436 (m), 1375 (m), 1363 (m), 1292 (s), 1254 (s), 1197 (m), 1170 (m), 1137 (w), 1101 (s), 1031 (s), 926 (m), 840 (s), 831 (s), 783 (s), 697 (w) cm^{-1}; **HRMS** (FAB) *m/z* found: 301.1834, [calc'd for $C_{15}H_{29}O_4Si$ (M+H): 301.1835].

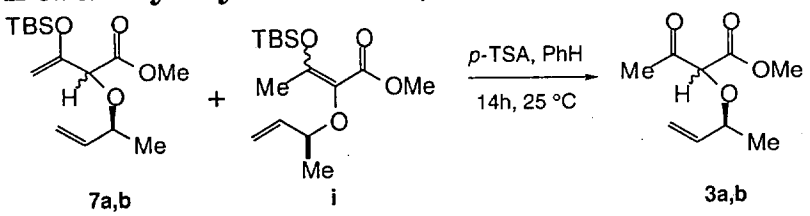
The second compound to elute was enone **i**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.84 (m, 1H), 5.13 (m, 2H), 4.23 (m, 1H), 3.74 (s, 3H), 1.99 (s, 3H), 1.34 (d, *J*=6.5 Hz, 3H), 0.96 (s, 9H), 0.78 (s, 3H), 0.17 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 164.5, 155.5, 139.2, 117.0, 79.4, 51.0, 25.7, 25.6, 20.7, 19.9, 18.3, -3.97, -3.99; **IR** (thin film/NaCl) 2953 (m), 2932 (m), 2896 (w), 2859 (m), 1723 (s), 1626 (m), 1470 (w), 1436 (m), 1380 (m), 1333 (m), 1233 (s), 1191 (m), 1168 (s), 1127 (w), 1060 (m), 1001 (m), 930 (m), 831 (s), 838 (s), 809 (m), 780 (s) cm^{-1}; **HRMS** (FAB) *m/z* found: 301.1834, [calc'd for $C_{15}H_{29}O_4Si$ (M+H): 301.1835].

The final compound to elute was diastereomer **7b**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.72 (ddd, *J*=7.8, 10.2, 17.3 Hz, 1H), 5.18 (m, 2H), 4.46 (s, 1H), 4.32 (d, *J*=1.5 Hz, 1H), 4.28 (s, 1H), 3.99 (m, 1H), 3.71 (s, 3H), 1.31 (d, *J*=6.3 Hz, 3H), 0.91 (s, 9H), 0.18 (s, 3H), 0.17 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.2, 153.3, 139.2, 117.1, 92.5, 78.2, 76.3, 52.0, 25.4, 21.3, 17.9, -4.8, -5.1; **IR** (thin film/NaCl) 3081 (w), 2954 (m), 2932 (m), 2890 (w), 2856 (m), 1758 (s),

1643 (m), 1471 (m), 1463 (w), 1436 (w), 1375 (m), 1363 (w), 1293 (m), 1254 (s), 1198 (m), 1173 (m), 1137 (m), 1102 (m), 1066 (w), 1030 (m), 928 (w), 832 (s), 814 (m), 783 (s), 700 (w) cm^{-1}; **HRMS** (FAB) *m/z* found: 301.1834, [calc'd for $C_{15}H_{29}O_4Si$ (M+H): 301.1835].

Data for TBS-protected α-keto ester **ii**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.51 (m, 1H), 5.34 (m, 1H), 3.83 (s, 3H), 2.53 (m, 2H), 1.66 (dd, *J*=1.3, 6.4 Hz, 3H), 1.46 (s, 3H), 0.87 (s, 9H), 0.15 (s, 3H), 0.13 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.0, 165.4, 129.8, 124.5, 81.5, 52.1, 43.8, 25.6, 24.8, 18.1, 18.0, -2.1, -2.4; **IR** (thin film/NaCl) 3031 (w), 2956 (m), 2932 (m), 2893 (w), 2858 (m), 1746 (s), 1733 (s), 1473 (w), 1463 (w), 1451 (w), 1435 (w), 1390 (w), 1371 (w), 1280 (m), 1256 (s), 1191 (w), 1158 (m), 1115 (w), 1089 (w), 1070 (w), 1039 (s), 1000 (m), 968 (w), 893 (w), 837 (s), 810 (m), 777 (s), 724 (w), 667 (w) cm^{-1}; **HRMS** (FAB) *m/z* found: 301.1834, [calc'd for $C_{15}H_{29}O_4Si$ (M+H): 301.1835].

Preparation of α-Allyloxy Ketones 3a,b.



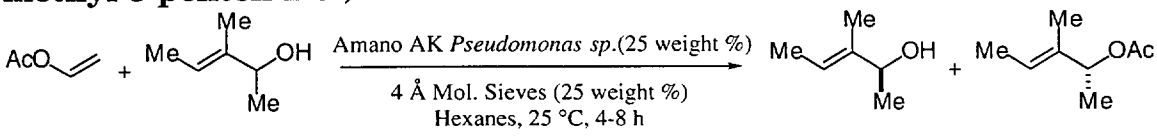
7a,b **i** **3a,b**

A mixture of **7a,b** (containing some enone **i**) (430 mg, 1.43 mmol, 1.0 equiv) and *p*-toluene sulfonic acid (272 mg, 1.43 mmol, 1.0 equiv) in benzene (15 mL) was stirred for 2 h at room temperature and then concentrated under reduced pressure. Purification by flash chromatography (4:1 hexanes:EtOAc eluent) afforded **3a,b** (223 mg, 84% yield of a 1:1 mixture of diastereomers) as a colorless liquid. Separation of the diastereomers was achieved by HPLC (15:1 hexanes:EtOAc eluent). The first diastereomer to elute was **3a**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.73 (ddd, *J*=7.7, 10.2, 17.3 Hz, 1H), 5.24 (m, 2H), 4.42 (s, 1H), 3.90 (m, 1H), 3.77 (s, 3H), 2.28 (s, 3H), 1.37 (d, *J*=6.3 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.0, 167.9, 138.3, 117.9, 83.1, 78.8, 52.6, 26.2, 21.0; **IR** (thin film/NaCl) 2982 (w), 2956 (w), 2933 (w), 1755 (s), 1728 (s), 1436 (w), 1357 (m), 1276 (m), 1202 (m), 1164 (m), 1141 (m), 1112 (s), 1064 (m), 995 (w), 936 (w),

839 (w), 751 (w), 694 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 185.0820, [calc'd for $C_9H_{13}O_4$ (M-H): 185.0814].

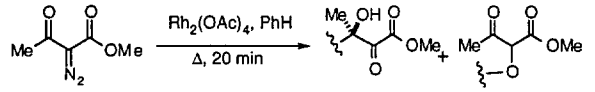
The second diastereomer to elute was **3b**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.68 (ddd, *J*=8.2, 10.1, 17.2 Hz, 1H), 5.23 (m, 2H), 4.47 (s, 1H), 3.93 (m, 1H), 3.80 (s, 3H), 2.27 (s, 3H), 1.37 (d, *J*=6.3 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.4, 168.2, 138.1, 118.7, 82.4, 78.0, 52.6, 26.6, 21.3; **IR** (thin film/NaCl) 3083 (w), 2981 (m), 2956 (m), 2931 (m), 2849 (w), 1755 (s), 1727 (s), 1660 (w), 1624 (w), 1437 (m), 1424 (w), 1377 (w), 1357 (m), 1319 (w), 1261 (s), 1201 (m), 1160 (m), 1141 (m), 1112 (s), 1064 (m), 1032 (w), 995 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 185.0812, [calc'd for $C_9H_{13}O_4$ (M-H): 185.0814].

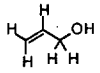
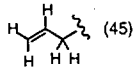
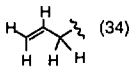
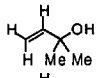
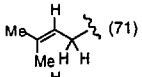
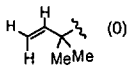
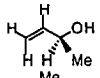
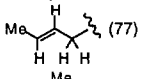
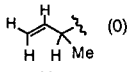
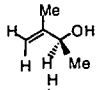
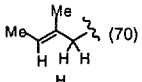
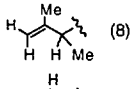
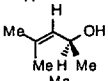
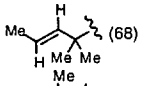
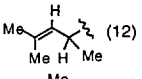
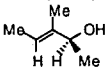
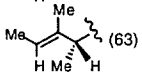
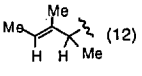
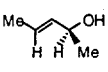
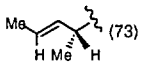
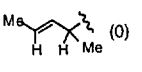
General Procedure for the Enzymatic Resolution of Allylic Alcohols (3-methyl-3-penten-2-ol).



To a stirred solution of (±)-3-methyl-3-penten-2-ol (10 g, 100 mmol, 1.0 equiv) and vinyl acetate (25 mL, 271 mmol, 2.7 equiv) in hexanes (500 mL) was added Amano AK® enzyme (2.5 g) and molecular sieves (2.5 g). The reaction was allowed to proceed at room temperature with periodic aliquotting and analysis by chiral gas chromatography (Astec Chiraldex TA column). Once the enantiomeric excess had plateaued (<2% change in 30 minutes, about 8 h, 47% conversion), the solids were removed by filtration and the mixture distilled to afford *(R)*-3-methyl-3-penten-2-ol acetate (6.68 g, 95% ee) and *(S)*-3-methyl-3-penten-2-ol (4.28 g, 43% recovery, 92% ee, configuration established by Mosher ester analysis).[1] Enantiomeric excess was determined by chiral GC analysis of the derived trifluoroacetate.

Table 1



Entry	Allylic Alcohol [%ee]	[3,3] Product (yield) [%ee][a]	Insertion Product (yield)
1		 (45)	 (34)
2		 (71)	 (0)
3	 [98]	 (77) [95][a]	 (0)
4	 [82]	 (70) [77][b]	 (8)
5	 [75]	 (68) [54][c]	 (12)
6	 [92]	 (63) [90][d]	 (12)
7	 [98]	 (73) [98][d]	 (0)

[a] %ee Determined by Mosher ester analysis of the derived triol
[b] %ee Determined by Chiral GC analysis of the derived trifluoroacetate
[c] %ee Determined by Chiral GC analysis of the bis-trifluoroacetate of the derived diol
[d] %ee Determined by Chiral GC analysis of the derived methyl ester trifluoroacetate

Representative Procedure for the Preparation of β-Hydroxy-α-ketoesters and α-Allyloxy-β-ketoesters in Table 1 (Entry 3). To a stirred solution of methyl 2-diazo-3-oxobutanoate (**1**, 3.17 g, 22.3 mmol, 1.0 equiv) and *(S)*-(+)-3-buten-2-ol (**2**, 1.93 g, 26.8 mmol, 1.2 equiv) in benzene (75 mL) was added $Rh_2(OAc)_4$ (30 mg, 0.068 mmol, 0.003 equiv). The resulting mixture was immersed in a preheated oil bath and heated under reflux for 20 min. Once cooled to room temperature, the solvent was evaporated under reduced pressure and the residue purified by flash chromatography (4:1 hexanes:EtOAc eluent) to afford β-hydroxy-α-ketoester (3.20 g, 77% yield) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.57 (m, 1H), 5.35 (m, 1H), 3.88 (s, 3H), 3.28 (br s, 1H), 2.68 (dd, *J*=7.0, 14.0 Hz, 1H), 2.42 (dd, *J*=7.7, 14.0 Hz, 1H), 1.66 (d, *J*=6.4 Hz, 3H), 1.47 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 198.5, 162.7, 130.9, 123.5, 78.3, 52.5, 42.2, 24.1, 17.8; **IR** (thin film/NaCl) 3521 (m), 3029 (w), 2981 (m), 2957 (m), 2938 (m), 2920 (m), 2857 (w), 1743 (s), 1726 (s), 1452 (m), 1437 (m), 1376 (w), 1361 (w), 1289 (m), 1250 (m), 1193 (w), 1146 (w), 1116 (w), 1081 (w), 1060 (w), 1032 (s), 972 (m), 920 (w), 862 (w), 845 (w),

814 (w), 723 (w), 663 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 187.0966, [calc'd for $C_9H_{15}O_4$ (M+H): 187.0970]; $[\alpha]_D^{20}$ +14.7° (*c* 1.08, $CHCl_3$).

Entry 1 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (m, 1H), 5.19 (m, 2H), 3.89 (s, 3H), 3.18 (br s, 1H), 2.77 (dd, *J*=7.2, 14.0 Hz, 1H), 2.51 (m, 1H), 1.51 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 198.2, 162.4, 131.4, 120.2, 78.3, 52.9, 43.5, 24.5; **IR** (thin film/NaCl) 3528 (br m), 3081 (w), 2982 (w), 2957 (w), 1742 (s), 1727 (s), 1436 (m), 1366 (w), 1294 (m), 1117 (w), 1071 (w), 1033 (s), 925 (m), 814 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 173.0817, [calc'd for $C_8H_{13}O_4$ (M+H): 173.0813].

Entry 1 (OH-Insertion Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.92 (m, 1H), 5.30 (m, 2H), 4.42 (s, 1H), 4.18 (m, 1H), 4.06 (m, 1H), 3.80 (s, 3H), 2.28 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.1, 167.6, 132.8, 119.2, 84.1, 71.9, 52.7, 26.4; **IR** (thin film/NaCl) 2957 (w), 2889 (w), 1748 (s), 1651 (w), 1439 (m), 1359 (m), 1206 (m), 1166 (m), 1033 (w), 996 (w), 974 (w), 774 (w), 715 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 171.0663, [calc'd for $C_8H_{11}O_4$ (M-H): 171.0657].

Entry 2 ([3,3] Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.07 (m, 1 H), 3.88 (s, 3H), 3.13 (s, 1H), 2.69 (dd, *J*=7.4, 14.5 Hz, 1H), 2.48 (dd, *J*=7.8, 14.5 Hz, 1H), 1.72 (s, 3H), 1.62 (s, 3H), 1.49 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 198.6, 162.5, 137.3, 116.6, 78.9, 52.7, 37.9, 25.9, 24.4, 18.0; **IR** (thin film/NaCl) 3528 (br m), 2975 (m), 2933 (m), 2916 (m), 2861 (w), 2731 (w), 1744 (s), 1727 (s), 1441 (m), 1377 (m), 1293 (s), 1209 (w), 1124 (m), 1038 (s), 959 (w), 812 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 201.1133, [calc'd for $C_{10}H_{17}O_4$ (M+H): 201.1127].

Entry 4 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.32 (qd, *J*=1.1, 6.6 Hz, 1H), 3.88 (s, 3H), 3.13 (br s, 1H), 2.79 (d, *J*=13.8 Hz, 1H), 2.41 (d, *J*=13.7 Hz, 1H), 1.60 (t, *J*=1.0 Hz, 3H), 1.58 (d, *J*=6.6 Hz, 3H), 1.48 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 199.4, 162.9, 130.7, 125.5, 78.5, 52.7, 48.9, 25.5, 17.3, 13.6; **IR** (thin film/NaCl) 3529

(br m), 2980 (m), 2956 (m), 2922 (m), 2861 (w), 1742 (s), 1726 (s), 1436 (m), 1381 (w), 1293 (m), 1135 (m), 1040 (s), 958 (w), 813 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 199.0971, [calc'd for $C_{10}H_{15}O_4$ (M-H): 199.0970]; $[\alpha]_D^{20}$ +9.2° (*c* 1.00, $CDCl_3$).

Entry 4 (OH-Insertion Product)

First Diastereomer by HPLC (15:1 hexanes:EtOAc eluent)
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.96 (m, 1H), 4.90 (s, 1H), 4.38 (s, 1H), 3.96 (q, *J*=6.4 Hz, 1H), 3.79 (s, 3H), 2.27 (s, 3H), 1.68 (s, 3H), 1.35 (d, *J*=6.4 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.2, 168.3, 143.7, 114.9, 82.2, 80.1, 52.6, 26.5, 19.8, 16.3; **IR** (thin film/NaCl) 3076 (w), 2982 (m), 2955 (m), 2923 (w), 1754 (s), 1728 (s), 1651 (w), 1436 (m), 1357 (m), 1260 (m), 1202 (m), 1164 (m), 1143 (m), 1112 (s), 1080 (m), 1046 (w), 908 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 201.1127, [calc'd for $C_{10}H_{17}O_4$ (M+H): 201.1127].

Second Diastereomer by HPLC (15:1 hexanes:EtOAc eluent)
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.93 (t, *J*=1.5 Hz, 1H), 4.92 (s, 1H), 4.37 (s, 1H), 3.91 (q, *J*=6.4 Hz, 1H), 3.76 (s, 3H), 2.28 (s, 3H), 1.71 (s, 3H), 1.36 (d, *J*=6.4 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.4, 167.6, 144.2, 114.5, 82.8, 80.9, 52.6, 26.2, 19.6, 16.4; **IR** (thin film/NaCl) 2975 (m), 2930 (m), 1752 (s), 1726 (s), 1674 (w), 1438 (m), 1376 (m), 1355 (m), 1259 (m), 1208 (m), 1154 (m), 1121 (m), 1092 (w), 1067 (m), 1044 (w), 984 (w), 932 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 201.1132, [calc'd for $C_{10}H_{17}O_4$ (M+H): 201.1127].

Entry 5 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.49-5.60 (comp m, 2H), 3.84 (s, 3H), 3.20 (s, 1H), 1.71 (d, *J*=5.7 Hz, 3H), 1.46 (s, 3H), 1.11 (s, 3H), 1.08 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.1, 164.5, 135.8, 125.7, 82.5, 52.5, 43.2, 23.1, 21.8, 21.2, 18.2; **IR** (thin film/NaCl) 3529 (w), 3028 (w), 2968 (m), 2939 (w), 2919 (w), 2882 (w), 2856 (w), 1745 (s), 1725 (s), 1449 (m), 1438 (m), 1373 (m), 1284 (s), 1198 (w), 1174 (w), 1131 (m), 1071 (w), 1031 (s), 979 (m), 940 (w), 824 (w), 705 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 215.1278, [calc'd for $C_{11}H_{19}O_4$ (M+H): 215.1283]; $[\alpha]_D^{20}$ +1.2° (*c* 2.94, $CHCl_3$).

Entry 5 (OH-Insertion Product)

First Diastereomer by HPLC (20:1 hexanes:EtOAc eluent)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.01 (m, 1H), 4.42 (s, 1H), 4.32 (dq, *J*=6.2, 9.6 Hz, 1H), 3.79 (s, 3H), 2.25 (s, 3H), 1.74 (d, *J*=1.3 Hz, 3H), 1.62 (d, *J*=1.3 Hz, 3H), 1.30 (d, *J*=6.2 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.0, 168.5, 138.0, 125.3, 82.2, 72.3, 52.4, 26.4, 25.8, 21.6, 18.0; **IR** (thin film/NaCl) 2976 (m), 2955 (w), 2930 (m), 2918 (m), 2731 (w), 2254 (w), 1752 (s), 1727 (s), 1674 (w), 1622 (w), 1438 (m), 1376 (m), 1356 (m), 1320 (w), 1259 (m), 1207 (m), 1155 (m), 1124 (m), 1092 (w), 1066 (m), 1044 (w), 977 (w), 915 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 213.1126, [calc'd for $C_{11}H_{17}O_4$ (M-H): 213.1127].

Second Diastereomer by HPLC (20:1 hexanes:EtOAc eluent)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.07 (m, 1H), 4.36 (s, 1H), 4.27 (dq, *J*=6.3, 9.4 Hz, 1H), 3.76 (s, 3H), 2.28 (s, 3H), 1.73 (d, *J*=0.9 Hz, 3H), 1.64 (d, *J*=1.0 Hz, 3H), 1.32 (d, *J*=6.2 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.6, 168.2, 137.3, 125.6, 82.9, 73.4, 52.5, 26.1, 25.8, 21.3, 18.0; **IR** (thin film/NaCl) 2977 (m), 2933 (w), 2866 (w), 1753 (s), 1727 (s), 1673 (w), 1438 (m), 1376 (m), 1356 (m), 1319 (w), 1274 (m), 1259 (m), 1206 (m), 1156 (m), 1124 (m), 1091 (w), 1067 (m), 1044 (w), 977 (w), 931 (w), 869 (w), 846 (w), 753 (w), 557 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 213.1127, [calc'd for $C_{11}H_{17}O_4$ (M-H): 213.1127].

Entry 6 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.39 (q, *J*=6.6 Hz, 1H), 3.89 (s, 3H), 3.13 (s, 1H), 2.73 (q, *J*=7.1 Hz, 1H), 1.63 (d, *J*=1.0 Hz, 3H), 1.62 (d, *J*=7.0 Hz, 3H), 1.38 (s, 3H), 1.00 (d, *J*=7.1 Hz, 3H); **^{13}C NMR** (500 MHz, $CDCl_3$) δ 200.2, 163.2, 135.3, 123.8, 81.3, 52.8, 49.0, 24.0, 13.8, 13.5, 13.3; **IR** (thin film/NaCl) 3517 (br m), 2983 (m), 2937 (w), 2877 (w), 1743 (s), 1723 (s), 1451 (m), 1437 (m), 1373 (w), 1287 (m), 1139 (w), 1022 (m), 948 (w), 830 (w), 678 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 215.1292, [calc'd for $C_{11}H_{19}O_4$ (M+H): 215.1283]; $[\alpha]_D^{20}$ +22.1° (*c* 1.00, $CDCl_3$).

Entry 6 (OH-Insertion Product)

First Diastereomer by HPLC (25:1 hexanes:EtOAc eluent)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.52 (qd, *J*=1.2, 7.0 Hz, 1H), 4.55 (q, *J*=6.4 Hz, 1H), 4.30 (s, 1H), 3.80 (s, 3H), 2.27 (s, 3H), 1.63 (quint, *J*=1.4 Hz, 3H), 1.56 (dq, *J*=1.4, 7.0 Hz, 3H), 1.33 (d, *J*=6.4 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.5, 168.6, 133.7, 125.4, 82.0, 72.1, 52.5, 26.4, 19.0, 17.0, 12.7; **IR** (thin film/NaCl) 2982 (w), 2954 (w), 2889 (w), 2865 (w), 1754 (s), 1728 (s), 1437 (w), 1356 (m), 1274 (m), 1217 (m), 1164 (w), 1146 (m), 1114 (m), 1065 (m), 1003 (w), 973 (w), 879 (w), 826 (w), 753 (w), 511 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 215.1282, [calc'd for $C_{11}H_{19}O_4$ (M+H): 215.1283].

Second Diastereomer by HPLC (25:1 hexanes:EtOAc eluent)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.46 (m, 1H), 4.45 (q, *J*=6.5 Hz, 1H), 4.29 (s, 1H), 3.76 (s, 3H), 2.28 (s, 3H), 1.65 (t, *J*=1.5 Hz, 3H), 1.57 (dq, *J*=1.5, 7.0 Hz, 3H), 1.33 (d, *J*=6.5 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.7, 167.6, 134.4, 124.5, 82.7, 73.1, 52.5, 26.0, 18.9, 17.0, 12.8; **IR** (thin film/NaCl) 2979 (w), 2954 (w), 2926 (w), 1752 (s), 1727 (s), 1437 (m), 1376 (w), 1356 (m), 1261 (m), 1200 (m), 1145 (m), 1112 (m), 1091 (m), 1065 (m), 1035 (w), 1002 (w), 875 (w), 824 (w), 772 (w), 749 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 215.1277, [calc'd for $C_{11}H_{19}O_4$ (M+H): 215.1283].

Entry 7 ([3,3]-Product) (12:1 Mixture of Diastereomers)

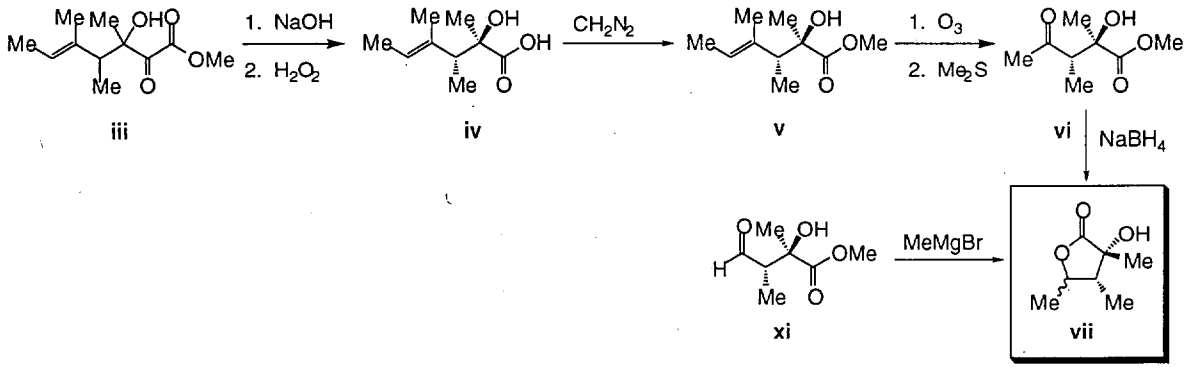
Major Diastereomer

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.50 (dq, *J*=6.5, 15.4 Hz, 1H), 5.31 (ddq, *J*=1.6, 8.7, 15.4 Hz, 1H), 3.87 (s, 3H), 3.07 (s, 1H), 2.82 (m, 1H), 1.63 (dd, *J*=1.5, 6.5 Hz, 3H), 1.43 (s, 3H), 1.07 (d, *J*=6.9 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 198.7, 162.4, 130.7, 128.4, 80.6, 52.7, 43.3, 22.1, 18.0, 14.0; **IR** (thin film/NaCl) 3529 (br w), 2981 (w), 2883 (w), 1741 (s), 1725 (s), 1449 (m), 1437 (m), 1291 (m), 1198 (w), 1137 (w), 1085 (w), 1038 (m), 1019 (m), 973 (m), 943 (w), 917 (w), 813 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 201.1135, [calc'd for $C_{10}H_{17}O_4$ (M+H): 201.1127]; $[\alpha]_D^{20}$ +16.0° (*c* 0.74, $CDCl_3$).

Minor Diastereomer

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.56 (dq, *J*=6.3, 15.2 Hz, 1H), 5.37 (m, 1H), 3.89 (s, 3H), 3.11 (s, 1H), 2.70 (dt, *J*=6.9, 15.8 Hz, 1H), 1.70 (dd, *J*=1.6, 6.4 Hz, 3H), 1.40 (s, 3H), 0.96 (d, *J*=6.9 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 199.3, 162.8, 130.3, 128.4, 80.8, 52.8, 44.3, 23.2, 18.0, 15.5; **IR** (thin film/NaCl) 3524 (br m), 3028 (m), 2977 (w), 2938 (w), 2881 (w), 1743 (s), 1724 (s), 1449 (m), 1437 (m), 1377 (w), 1290 (s), 1198 (w), 1167 (w), 1133 (w), 1031 (s), 1014 (s), 971 (m), 809 (w), 671 (w) cm^{-1}; **HRMS** (CI) *m/z* found: 201.1124, [calc'd for $C_{10}H_{17}O_4$ (M+H): 201.1127].

Determination of Relative Stereochemistry for Table 1, Entry 6, [3,3] Rearrangement Product.



Saponification and oxidative decarboxylation of β-hydroxy-α-ketoester **iii** provided the α-hydroxyacid **iv** which was treated with diazomethane to furnish α-hydroxyester **v**. Ozonolysis provided the β-hydroxyketone **vi**, which was reduced with sodium borohydride and cyclized, furnishing two diastereomeric (epimeric at the γ-position) lactones **viia,b**. The identical species could be prepared via addition of MeMgBr to aldehyde **xi** of established stereochemistry (vide infra), thus confirming that both **iii** and **xi** possess the same relative stereochemistry.

A. Preparation of α-Hydroxyacid (+)-iv

α-Keto ester (+)-**iii** (150 mg, 0.70 mmol) was suspended in 1N NaOH (7 mL) until the solution was homogeneous (about 1 h). To this yellow solution was

added 30% aqueous H_2O_2 (2 mL) and the reaction was allowed to stir for 12 h. The crude mixture was extracted with CH_2Cl_2 (7 mL). The organic layer was removed and the aqueous layer acidified to pH 1 with concentrated hydrochloric acid before being extracted with CH_2Cl_2 (5 x 7 mL). Combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (8:1 hexanes:EtOAc eluent) yielded acid (+)-**iv** (86 mg, 71% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.38 (q, J = 6.8 Hz, 1H), 2.55 (q, J = 6.4 Hz, 1H), 1.62 (d, J = 0.9 Hz, 3H), 1.56 (d, J = 6.5 Hz, 3H), 1.43 (s, 3H), 1.15 (d, J = 7.5 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 181.6, 136.6, 123.5, 77.4, 49.0, 23.8, 14.6, 13.3, 12.7; **IR** (thin film/NaCl) 3453 (br s), 2982 (s), 2939 (m), 1717 (s), 1454 (m), 1379 (m), 1260 (s), 1167 (s), 1101 (s), 1044 (w), 981 (w), 945 (m), 881 (w), 830 (w), 774 (w) cm^{-1}; **HRMS** (EI) m/z found: 172.1097, [calc'd for $C_9H_{16}O_3$ (M^+): 172.1099]; $[\alpha]^{20}_D$ +10.2° (c 0.50, $CDCl_3$).

B. Preparation of α-Hydroxyester (-)-v.

Acid (+)-**iv** (100 mg, 0.581 mmol) was dissolved in of Et_2O (6 mL) and cooled to 0°C. An ethereal solution of diazomethane was added dropwise until the reaction was complete (as signaled by a persistent yellow color). The mixture was adsorbed onto silica gel and chromatographed (15:1 hexanes:EtOAc eluent) to afford ester (-)-**v** (93 mg, 86% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.26 (m, 1H), 3.72 (s, 3H), 2.98 (br s, 1H), 2.46 (q, J = 7.2 Hz, 1H), 1.56 (t, J = 1.1 Hz, 3H), 1.53 (dd, J = 1.2, 6.8 Hz, 3H), 1.36 (s, 3H), 1.11 (d, J = 7.3 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.8, 137.3, 121.7, 77.7, 52.4, 49.7, 24.1, 14.1, 13.4, 12.6; **IR** (thin film/NaCl) 3524 (br s), 3027 (w), 2978 (m), 2880 (w), 2857 (w), 1733 (s), 1450 (m), 1376 (w), 1260 (m), 1245 (m), 1169 (m), 1129 (w), 1096 (w), 1049 (w), 1021 (w), 971 (m), 941 (w) cm^{-1}; **HRMS** (EI) m/z found: 186.1250, [calc'd for $C_{10}H_{18}O_3$ (M+): 186.1256]; $[\alpha]^{20}_D$ -27.1° (c 0.80 , $CDCl_3$).

C. Preparation of Ketone (-)-vi.

α-Hydroxy ester (-)-**v** (300 mg, 1.61 mmol) was dissolved in methanol (16 mL), cooled to -78 °C, and treated with a stream of ozone until a blue color persisted (about 10 min). The reaction mixture was purged with nitrogen, treated with dimethyl sulfide (5 mL), and allowed to warm to room temperature overnight with stirring. The mixture was adsorbed onto silica gel and chromatographed (4:1 hexanes:EtOAc eluent) affording ketone (-)-**vi** (270 mg, 96% yield): **^{1}H**

NMR (500 MHz, $CDCl_3$) δ 3.70 (s, 3H), 3.05 (q, J = 7.4 Hz, 1H), 2.16 (s, 3H), 1.29 (s, 3H), 1.22 (d, J = 7.2 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 214.1, 176.9, 75.4, 52.8, 52.0, 29.0, 24.8, 10.3; **IR** (thin film/NaCl) 3509 (br s), 2988 (m), 2953 (m), 1732 (s), 1706 (s), 1455 (m), 1436 (m), 1361 (m), 1331 (w), 1256 (s), 1198 (s), 1129 (s), 980 (w), 946 (w), 814 (w), 763 (w), 705 (w) cm^{-1}; **HRMS** (EI) m/z found: 175.0969, [calc'd for $C_8H_{15}O_4$ (M+H): 175.0970]; $[\alpha]^{20}_D$ -72.9° (*c* 1.70, $CDCl_3$).

D. Reduction/Lactonization of vi.

To a solution of ketone (±)-**vi** (100 mg, 0.581 mmol, 1.0 equiv) in 6:1 Et_2O:*i*PrOH (7 mL) at 0°C was added sodium borohydride (22 mg, 0.582 mmol 1.0 equiv) portionwise. After 30 min, the solvent was removed under reduced pressure, the remaining residue cooled to 0°C and treated with 1N HCl (7 mL). This aqueous solution was extracted with CH_2Cl_2 (4 x 7 mL) and the organic layer was dried over $MgSO_4$, concentrated, dissolved in $CHCl_3$ and allowed to sit at room temperature overnight to allow cyclization. Concentration under reduced pressure furnished a 2:1 mixture of diastereomeric lactones **viia/b** (72 mg, 86% yield).

(±)-**viia**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.32 (dq, J = 6.3, 9.7 Hz, 1H), 1.73 (dq, J = 6.9, 9.5 Hz, 1H), 1.42 (s, 3H), 1.39 (d, J = 6.3 Hz, 3H), 1.08 (d, J = 6.5 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.8, 80.5, 74.5, 48.5, 22.2, 18.3, 7.9; **IR** (thin film/NaCl) 3406 (br s), 2976 (m), 2939 (m), 2893 (w), 1759 (s), 1455 (m), 1389 (m), 1346 (w), 1320 (w), 1295 (m), 1241 (m), 1178 (s), 1128 (m), 1051 (s), 1028 (m), 978 (w), 936 (s), 867 (w), 759 (w), 651 (w) cm^{-1}; **HRMS** (EI) m/z found: 145.0870, [calc'd for $C_7H_{13}O_3$ (M+H): 145.0865].

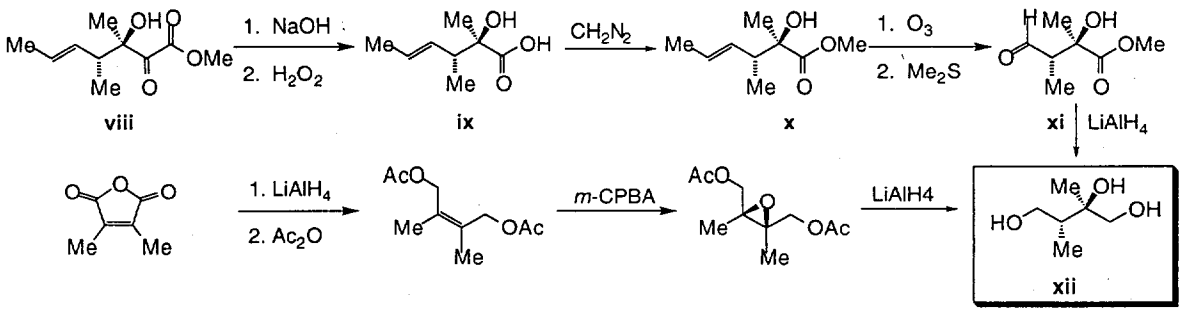
(±)-**viib**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.65 (m, 1H), 2.33 (m, 1H), 1.48 (s, 3H), 1.36 (d, J = 6.7 Hz, 3H), 1.00 (d, J = 7.5 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.3, 104.8, 76.6, 43.9, 24.0, 20.9, 16.1; **IR** (thin film/NaCl) 3464 (br m), 2979 (m), 2939 (w), 1763 (s), 1451 (w), 1386 (w), 1342 (w), 1201 (m), 1116 (m), 1063 (m), 1017 (w), 997 (w), 936m, 863 (w) cm^{-1}; **HRMS** (EI) m/z found: 145.0872, [calc'd for $C_7H_{13}O_3$ (M+H): 145.0865].

E. Grignard Addition/Lactonization of Aldehyde xi.

To a solution of aldehyde **xi** (7 mg, 0.044 mmol, 1.0 equiv) in Et_2O (1.5 mL) at -78 °C was added a 1.4 M solution of methyl magnesium bromide in ether (90 mL, 0.126 mmol, 2.9 equiv). The reaction mixture was allowed to stir for 15

min before 1 M HCl (184 mL) was added and the solution warmed to room temperature. The organic phase was separated, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was dissolved in $CHCl_3$ and allowed to stand at room temperature overnight to allow cyclization affording **viia,b** (5 mg, 79% yield) as a 3:2 mixture of diastereomers. Separation was achieved by flash column chromatography (20:1 hexanes:EtOAc eluent) affording the individual diastereomers which proved identical to those prepared from ketone **vi**.

Determination of Relative Stereochemistry for Table 1, Entry 7, [3,3] Rearrangement Product.



β-Hydroxy-α-ketoester **viii** was saponified and oxidatively decarboxylated to furnish α-hydroxyacid **ix**, which upon treatment with diazomethane provided the corresponding α-hydroxyester **x**. Reductive ozonolysis followed by exhaustive reduction furnished triol **xii**, which was spectroscopically identical to that prepared using the procedure of Masamune.[3]

A. Preparation of α-Hydroxyacid (+)-ix.

α-Keto ester (+)-**viii** (268 mg, 1.34 mmol) was suspended in 1N NaOH (15 mL) until the solution was homogeneous (about 1 h). To this yellow solution was added 30% aqueous H_2O_2 (2 mL) and the reaction allowed to stir for 12 h. The crude reaction mixture was extracted with CH_2Cl_2 (15 mL). The organic layer was removed; the aqueous acidified to pH 1 with concentrated hydrochloric acid and extracted with CH_2Cl_2 (5 x 15 mL). Combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was chromatographed (8:1 hexanes:EtOAc eluent) to yield acid (+)-**ix**

(80 mg, 37% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.54 (dq, *J* = 6.4, 15.3 Hz, 1H), 5.39 (ddd, *J* = 1.3, 8.5, 15.2 Hz, 1H), 2.48 (quint, *J* = 7.3 Hz, 1H), 1.63 (dd, *J* = 1.5, 6.3 Hz, 3H), 1.40 (s, 3H), 1.05 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 181.6, 131.1, 127.5, 77.2, 44.7, 23.2, 18.0, 13.8; **IR** (thin film/NaCl) 3440 (br s), 3030 (w), 2978 (s), 2939 (m), 2882 (w), 2859 (w), 1717 (s), 1451 (m), 1378 (m), 1335 (w), 1267 (m), 1244 (m), 1166 (s), 1021 (m), 970 (m), 942 (w), 901 (w), 867 (w), 803 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 158.0951, [calc'd for $C_8H_{14}O_3$ (M^+): 158.0943]; $[\alpha]^{20}_D$ +15.4° (*c* 1.60 $CDCl_3$).

B. Preparation of α-Hydroxyester (-)-x.

Acid (+)-**ix** (80 mg, 0.056 mmol) was dissolved in of Et_2O (5 mL) and cooled to 0°C. An ethereal solution of diazomethane was added dropwise until the solution turned a persistant yellow color signalling completion. The reaction mixture was adsorbed onto silica gel and chromatographed (10:1 hexanes:EtOAc eluent) to afford ester (-)-**x** (84 mg, 96% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.43 (dq, *J* = 6.3, 15.0 Hz, 1H), 5.34 (ddq, *J* = 1.4, 8.7, 15.0 Hz, 1H), 3.72 (s, 3H), 2.39 (m, 1H), 1.61 (dd, *J* = 1.3, 6.3 Hz, 3H), 1.32 (s, 3H), 1.00 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.5, 131.9, 126.7, 77.1, 52.5, 45.1, 23.4, 18.0, 14.0; **IR** (thin film/NaCl) 3524 (br s), 3027 (w), 2978 (m), 2880 (w), 2857 (w), 1733 (s), 1450 (m), 1376 (w), 1260 (m), 1245 (m), 1169 (m), 1129 (w), 1096 (w), 1049 (w), 1021 (w), 971 (m), 941 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 173.1179, [calc'd for $C_9H_{17}O_3$ (M+H): 173.1178]; $[\alpha]^{20}_D$ -27.1° (*c* 0.80, $CDCl_3$).

C. Preparation of Aldehyde (-)-xi.

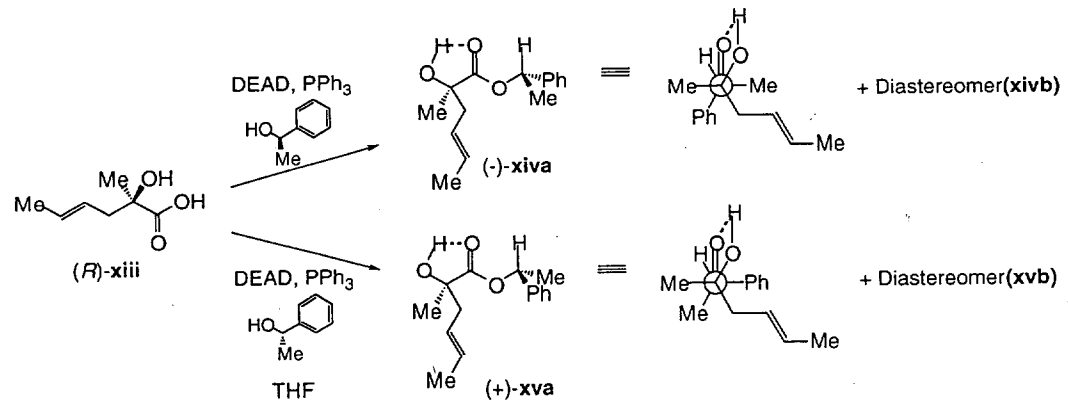
α-Hydroxy ester (-)-**x** (30 mg, 0.174 mmol) was dissolved in methanol (2 mL), cooled to -78 °C, and treated with a stream of ozone until a blue color persisted (about 10 min). The reaction mixture was purged with nitrogen and treated with dimethyl sulfide (1 mL). The solution was allowed to warm to room temperature and stirred overnight. Rotary evaporation onto silica gel and column chromatography (4:1 hexanes:EtOAc eluent) afforded aldehyde (-)-**xi** (20 mg, 72% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.62 (s, 1H), 3.79 (s, 3H), 3.33 (s, 1H), 2.82 (q, *J* = 7.5 Hz, 1H), 1.42 (s, 3H), 1.23 (d, *J* = 7.4 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.1, 176.7, 74.5, 53.3, 53.2, 24.3, 8.2; **IR** (thin film/NaCl) 3507 (br s), 2986 (m), 2955 (m), 2884 (w), 2846 (w), 2736 (w), 1726 (s), 1451 (m), 1377 (w), 1256 (s), 1168 (s), 1021 (w), 977 (w), 944 (w), 925 (w)

cm^{-1}; **HRMS** (EI) *m/z* found: 161.0813, [calc'd for $C_7H_{13}O_4$ (M+H): 161.0814]; $[\alpha]^{20}_D$ -37.7° (*c* 1.20, $CDCl_3$).

D. Preparation of Triol xii.

To a stirred solution of aldehyde **xi** (20 mg, 0.124 mmol, 1.0 equiv) in THF (2 mL) at 0°C was added $LiAlH_4$ (10 mg, 0.263 mmol, 2.1 equiv). The resulting mixture was allowed to warm to room temperature and then stirred for an additional 2 h, before being recooled to 0°C and subjected to the workup conditions described by Trost[4] to provide triol **xii** (12 mg, 66% yield).

Representative Procedure for Determination of Absolute Stereochemistry of [3,3] Rearrangement Products in Table 1.



Mosher[1] and Trost[2] have shown that esters of 2° alcohols exist in preferred conformations (wherein the proton and most electronegative group on the ester α-carbon eclipse the carbonyl). We have developed a variant of this method which has been applied to α-hydroxy acids derived from the [3,3]-rearrangement products in Table 1.[5] Coupling of enantioenriched α-hydroxyacid *R*-(+)-**xiii** of known absolute stereochemistry[6] with (*R*) and (*S*)-phenethyl alcohols under Mitsunobu conditions provided diastereomerically-enriched esters (-)-**xiva** and (+)-**xva**, respectively. Proton NMR analysis revealed chemical shift differences consistent with those predicted by the indicated conformations, enabling assignment of the (*R*) configuration to the tertiary hydroxylated center.

Preparation of Esters(-)-xiva and xivb.

To a solution of acid *R*-(+)-**xiii** (5 mg, 0.035 mmol 1.0 equiv), *R*-(+)-phenethyl alcohol (4.2 μL, 0.035 mmol, 1.,0 equiv), and triphenyl phosphine (9 mg, 0.034 mmol, 1.0 equiv) was added DEAD (5.5 μL, 0.035 mmol, 1.0 equiv). Triphenyl phosphine (0.1 equiv) or DEAD (0.1 equiv) was added alternately until no starting material remained. The crude reaction mixture was adsorbed onto silica gel and chromatographed (20:1 hexanes:EtOAc eluent) to afford ester (-)-**xiva** as the major component of a diastereomeric mixture (8:1, 3 mg, 34% overall yield).

(-)-**xiva**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35 (m, 5H), 5.92 (q, 6.6 Hz, 1H), 5.56 (m, 1H), 5.39 (m, 1H), 2.49 (dd, *J* = 13.8, 7.4 Hz, 1H), 2.34 (dd, *J* = 13.7, 7.2 Hz, 1H), 1.66 (dd, *J* = 1.5, 6.6 Hz, 3H), 1.56 (d, *J* = 6.6 Hz, 3H), 1.39 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 176.0, 141.2, 130.1, 128.7, 128.2, 126.0, 124.8, 74.0, 43.8, 25.5, 22.3, 18.2; **IR** (thin film/NaCl) 3518 (br m), 3032 (w), 2978 (m), 2963 (w), 1718 (s), 1496 (w), 1451 (m), 1375 (m), 1258 (s), 1235 (s), 1172 (m), 1138 (s), 1108 (m), 1061 (m), 1029 (w), 992 (m), 977 (m), 940 (w), 760 (n), 699 (s) cm-1; **HRMS** (CI) *m/z* found: 248.1418, [calc'd for $C_{15}H_{20}O_3$ (M^+): 248.1412]; $[\alpha]^{20}_D$ -46.2° (*c* 0.5, $CDCl_3$).

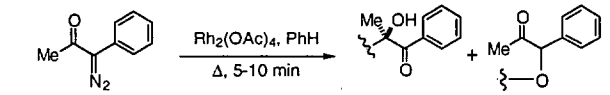
Preparation of Esters(+)-xva and xvb.

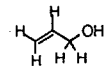
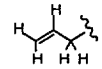
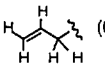
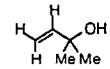
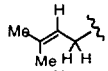
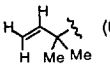
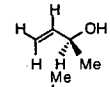
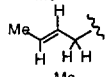
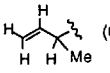
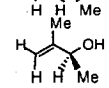
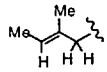
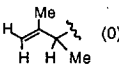
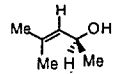
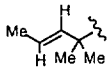
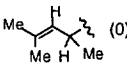
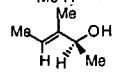
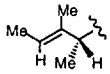
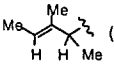
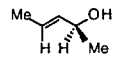
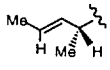
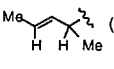
To a solution of acid *R*-(+)-**xiii** (5 mg, 0.035 mmol, 1.0 equiv), *S*-(-)-phenethyl alcohol (4.2 μL, 0.035 mmol, 1.0 equiv), and triphenyl phosphine (9 mg, 0.035 mmol, 1.0 equiv) was added DEAD (5.5 mL, 0.035 mmol, 1.0 equiv). Triphenyl phosphine (0.1 equiv) or DEAD (0.1 equiv) was added alternately until no starting material remained. The crude reaction mixture was adsorbed onto silica gel and chromatographed (20:1 hexanes:EtOAc eluent) to afford ester (+)-**xva** as the major constituent of a mixture of diastereomers (10:1, 6 mg, 70% overall yield) .

(+)-**xva**: **^{1}H NMR** (500 MHz, $CDCl_3$) d 7.30-7.38 (comp m, 5H), 5.92 (q, *J* = 6.6 Hz, 1H), 5.32 (dq, *J* = 6.3, 15.6 Hz, 1H), 5.18 (m, 1H), 2.40 (dd, *J* = 7.2, 13.9 Hz, 1H), 2.27 (dd, *J* = 7.4, 14.2 Hz, 1H), 1.58 (d, *J* = 6.7 Hz, 3H), 1.51 (dd, *J* = 1.2, 6.2 Hz, 3H), 1.43 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 176.1, 140.9, 130.2, 128.7, 128.3, 126.4, 124.4, 74.0, 43.6, 25.5, 22.0, 18.1; **IR** (thin film/NaCl) 3517 (br m), 3032 (w), 2978 (m), 2936 (w), 2879 (w), 1780 (w), 1717 (s), 1496 (w), 1451 (m), 1375 (m), 1258 (s), 1235 (s), 1173 (m), 1138 (s), 1108 (m), 1060

(m), 1029 (w), 992 (m), 977 (m), 940 (w), 760 (m), 699 (s) cm-1; ; **HRMS** (CI) *m/z* found: 248.1414, [calc'd for $C_{15}H_{20}O_3$ (M+): 248.1412]; $[\alpha]^{20}_{D}$ +39.0° (*c* 0.8, $CDCl_3$).

Table 2



Entry	Allylic Alcohol [ee]	[3,3] Product (yield) [% ee][a]	Insertion Product (yield)
1		 (77)	 (0)
2		 (72)	 (0)
3	 [98]	 (77) [94]	 (0)
4	 [82]	 (76) [79]	 (0)
5	 [75]	 (70) [45]	 (0)
6	 [92]	 (67) [91]	 (0)
7	 [98]	 (80) [97]	 (0)

[a] %ee Determined by Mosher ester analysis of derived diols

Representative Procedure for the Preparation of α-Hydroxyketones in Table 2 (Entry 3). A stirred mixture of 1-diazo-1-phenyl-2-propanone (**8**, 102 mg, 0.637 mmol, 1.0 equiv), *(S)*-(+)-3-buten-2-ol (**2**, 55 mg, 0.763 mmol, 1.2 equiv) and $Rh_2(OAc)_4$ (1.0 mg, 0.0023 mmol, 0.003 equiv) in benzene (7 mL) was immersed in a 100°C (preheated) oil bath and heated under reflux for 5 min. The mixture was cooled and concentrated and the residue purified by flash chromatography (10:1 hexanes:EtOAc eluent) affording α-hydroxyketone (120 mg, 77% yield) as a clear yellow oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.01 (m, 2H), 7.57 (m, 1H), 7.47 (m, 2H), 5.33-5.48 (comp m, 2H), 3.91 (s, 1H), 2.75 (dd, *J*=6.8, 14.1 Hz, 1H), 2.54 (dd, *J*=7.3, 14.1 Hz, 1H), 1.61 (m, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 204.4, 134.5, 132.8, 130.2, 129.5, 128.4, 124.5, 79.0, 44.3, 26.7, 18.0; **IR** (thin film/NaCl) 3466 (br m), 3061 (w), 3027 (w), 2976 (m), 2935 (m), 2917 (m), 2856 (w), 1672 (s), 1597 (m), 1578 (w), 1449 (m), 1374 (m), 1263 (m), 1160 (m), 973 (s), 946 (m), 716 (s), 697 (m) cm^{-1}; **HRMS** (EI) *m/z*

found: 205.1227, [calc'd for $C_{13}H_{17}O_2$ (M+H): 205.1229]; $[\alpha]_D^{20}$ +5.5° (*c* 1.20, $CHCl_3$).

Entry 1 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (m, 2H), 7.55 (m, 1H), 7.44 (m, 2H), 5.74 (m, 1H), 5.02 (m, 2H), 4.04 (s, 1H), 2.78 (dd, *J*=7.1, 14.1 Hz, 1H), 2.62 (dd, *J*=7.3, 14.1 Hz, 1H), 1.61 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 204.1, 134.2, 132.9, 132.2, 129.5, 128.3, 119.2, 78.7, 45.4, 26.7; **IR** (thin film/NaCl) 3458 (br m), 3075 (m), 2979 (m), 2933 (w), 1673 (s), 1597 (m), 1577 (w), 1448 (m), 1371 (m), 1268 (m), 1236 (m), 1222 (m), 1165 (m), 921 (m), 715 (m), 699 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 191.1070, [calc'd for $C_{12}H_{15}O_2$ (M+H): 191.1072].

Entry 2 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (m, 2H), 7.54 (m, 1H), 7.44 (t, *J*=7.4 Hz, 2H), 5.07 (tq, *J*=1.3, 6.0 Hz, 1H), 3.95 (s, 1H), 2.73 (dd, *J*=7.4, 14.7 Hz, 1H), 2.59 (dd, *J*=7.4, 14.8 Hz, 1H), 1.63 (s, 3H), 1.61 (s, 3H), 1.48 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 204.7, 135.9, 134.5, 132.7, 129.4, 128.3, 117.6, 79.3, 39.7, 26.8, 25.8, 17.9; **IR** (thin film/NaCl) 3470 (br m), 3059 (w), 2975 (m), 2930 (m), 2859 (w), 1672 (s), 1597 (m), 1577 (w), 1449 (m), 1375 (m), 1269 (m), 1231 (m), 1156 (m), 1088 (m), 971 (m), 945 (m), 718 (s), 697.0 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 219.1383, [calc'd for $C_{14}H_{19}O_2$ (M+H): 219.1385].

Entry 4 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (m, 2H), 7.56 (m, 1H), 7.46 (t, *J*=7.8 Hz, 2H), 5.21 (q, *J*=6.6 Hz, 1H), 3.83 (br s, 1H), 2.83 (d, *J*=13.9 Hz, 1H), 2.56 (d, *J*=13.9 Hz, 1H), 1.60 (s, 3H), 1.59 (s, 3H), 1.52 (d, *J*=6.7 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 205.0, 134.9, 132.6, 131.4, 129.7, 128.3, 124.5, 79.3, 50.6, 27.6, 17.5, 13.5; **IR** (thin film/NaCl) 3469 (m), 3060 (w), 2977 (m), 2919 (m), 2861 (w), 1671 (s), 1597 (m), 1578 (w), 1449 (m), 1268 (m), 1228 (m), 1155 (m), 967 (m), 718 (m), 697 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 218.1308, [calc'd for $C_{14}H_{18}O_2$ (M+): 218.1307]; $[\alpha]_D^{20}$ +5.6° (*c* 1.77, $CHCl_3$).

Entry 5 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (m, 2H), 7.47 (m, 1H), 7.37 (m, 2H), 5.43 (dq, *J*=1.4, 15.6 Hz, 1H), 5.35 (dq, *J*=6.2, 15.6 Hz, 1H), 3.56 (s, 1H), 1.59 (s, 3H), 1.55 (dd, *J*=1.4, 6.1 Hz, 3H), 1.07 (s, 3H), 1.02 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 206.9, 138.5, 137.1, 131.7, 129.4, 127.8, 124.6, 83.9, 43.5, 23.1, 22.9, 22.3, 18.1; **IR** (thin film/NaCl) 3475 (br s), 3060 (w), 3026 (w), 2970 (s), 2938 (m), 2878 (w), 1666 (s), 1596 (m), 1447 (m), 1370 (m), 1255 (m), 1233 (m), 1133 (m), 977 (s), 714 (s), 695 (s) cm^{-1}; **HRMS** (EI) *m/z* found: 233.1549, [calc'd for $C_{15}H_{21}O_2$ (M+H): 233.1542]; $[\alpha]_D^{20}$ -9.1° (*c* 1.35, $CHCl_3$).

Entry 6 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (m, 2H), 7.53 (m, 1H), 7.43 (m, 2H), 4.94 (m, 1H), 4.15 (s, 1H), 2.86 (q, *J*=7.0 Hz, 1H), 1.58 (s, 3H), 1.49 (s, 3H), 1.33 (dd, *J*=0.8, 6.7 Hz, 3H), 1.23 (d, *J*=7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 204.8, 136.7, 134.9, 132.6, 129.6, 128.2, 122.3, 81.5, 50.1, 25.7, 14.0, 13.5, 13.0; **IR** (thin film/NaCl) 3457 (br m), 3060 (w), 2979 (m), 2933 (m), 2878 (s), 1667 (s), 1597 (m), 1577 (w), 1449 (m), 1376 (m), 1253 (m), 1164 (s), 961 (m), 712 (s), 690 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 233.1546, [calc'd for $C_{15}H_{21}O_2$ (M+H): 233.1542]; $[\alpha]_D^{20}$ +11.2° (*c* 1.25, $CHCl_3$).

Entry 7 ([3,3]-Product) (7:1 Mixture of Diastereomers)

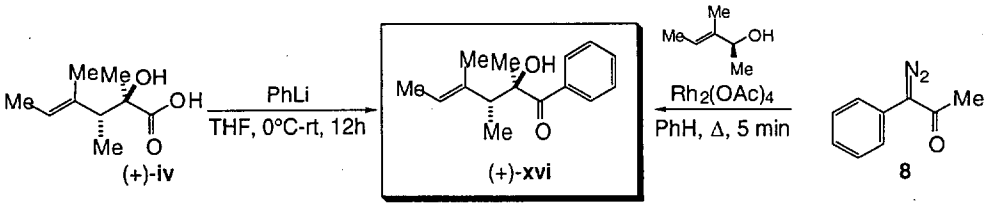
Major diastereomer

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (m, 2H), 7.56 (m, 1H), 7.45 (m, 2H), 5.27 (ddq, *J*=1.5, 8.5, 15.3 Hz, 1H), 5.14 (dq, *J*=6.3, 15.3 Hz, 1H), 2.81 (m, 1H), 1.58 (s, 3H), 1.50 (dd, *J*=1.5, 6.3 Hz, 3H), 1.15 (d, *J*=6.8 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 204.8, 134.9, 132.6, 131.2, 129.5, 128.3, 127.0, 80.9, 44.9, 24.4, 17.9, 14.4; **IR** (thin film/NaCl) 3456 (br m), 3061 (w), 3026 (w), 2976 (m), 2936 (m), 2878 (w), 2855 (w), 1668 (s), 1597 (w), 1576 (w), 1448 (m), 1257 (m), 1240 (m), 1165 (m), 971 (m), 714 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 219.1381, [calc'd for $C_{14}H_{19}O_2$ (M+H): 219.1385]; $[\alpha]_D^{20}$ +3.2° (*c* 1.20, $CHCl_3$).

Minor diastereomer

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (m, 2H), 7.59 (m, 1H) 7.48 (m, 2H), 5.51-5.63 (comp m, 2H), 2.78 (m, 1H), 1.74 (d, *J*=4.9 Hz, 3H), 1.55 (s, 3H), 0.83 (d, *J*=6.7 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 205.2, 134.4, 132.9, 131.6, 129.4, 128.5, 127.3, 80.8, 45.7, 26.1, 18.0, 15.5; **IR** (thin film/NaCl) 3462 (br m), 3027 (w), 2975 (m), 2933 (m), 2856 (w), 1666 (s), 1597 (m), 1577 (w), 1448 (m), 1374 (m), 1258 (s), 1237 (m), 1166 (s), 970 (s), 715 (s), 690 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 219.1391, [calc'd for $C_{14}H_{19}O_2$ (M+H): 219.1385].

General Procedure for Determination of Relative and Absolute Stereochemistry of [3,3] Rearrangement Products in Table 2.

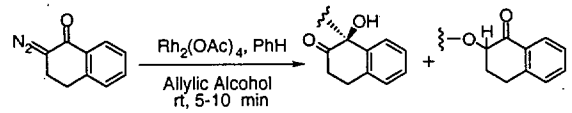


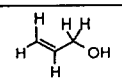
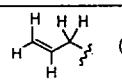
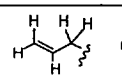
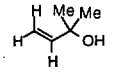
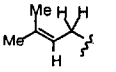
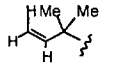
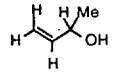
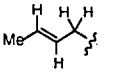
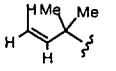
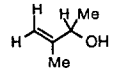
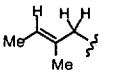
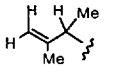
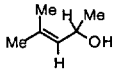
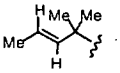
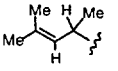
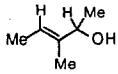
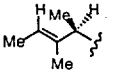
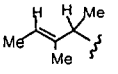
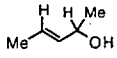
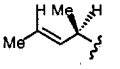
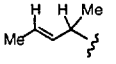
Addition of phenyllithium to α-hydroxyacid (+)-**iv** of established relative and absolute stereochemistry (vide supra) provided α-hydroxyketone (+)-**xvi**. This compound was spectroscopically identical to that derived from Claisen rearrangement with diazoketone **8** and 3-methyl-3-penten-2-ol. Comparison of optical rotation data established that (+)-**xvi** prepared by both routes shared the same absolute stereochemistry as well.

Preparation of α-hydroxyketone (+)-xvi from α-hydroxyacid (+)-iv. To a stirred solution of α-hydroxyacid (+)-**iv** (394 mg, 2.29 mmol, 1.0 equiv) in THF (20 mL) at 0°C was added dropwise a solution of phenyllithium (1.8M, 4.2 mL, 7.56 mmol, 3.3 equiv). The resulting mixture was allowed to warm to room temperature and stirred for 12 h after which it was recooled to 0°C, quenched with H_2O (10 mL), and acidified with 4N HCl (2 mL). The heterogeneous mixture was extracted with CH_2Cl_2 (3 x 25 mL) and the combined organic layers dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography (10:1 hexanes:EtOAc eluent) afforded α-hydroxyketone (+)-**xvi** (77 mg, 14% yield) that was identical spectroscopically to that obtained

by Claisen rearrangement with α-diazoketone **8**. Absolute stereochemistry was assigned by optical rotation: $[\alpha]_D^{20}$ +11.0° (*c* 3.4, $CHCl_3$).

Table 3



Entry	Allylic Alcohol	[3,3] Product (yield)	Insertion Product (yield)
1		 (42)	 (7)
2		 (60)	 (0)
3		 (73)	 (0)
4		 (52)	 (0)
5		 (66)	 (0)
6		 (52)	 (0)
7		 (66)	 (0)

Representative Procedure for the Preparation of α-Hydroxyketones in Table 3 (Entry 3). To a stirred solution of β-diazo-α-tetralone (100 mg, 0.58 mmol, 1.0 equiv) and 3-buten-2-ol (65 mg, 0.90 mmol, 1.5 equiv) in benzene (5 mL) was added $Rh_2(OAc)_4$ (2.0 mg, 0.0045 mmol, 0.008 equiv). Once gas evolution had ceased (5 min), the reaction mixture was concentrated under reduced pressure. The residue was purified by flash chromatography (10:1 hexanes:EtOAc eluent) to provide α-hydroxyketone (92 mg, 73% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (dd, *J*=1.2, 7.4 Hz, 1H), 7.32 (t, *J*=7.6 Hz, 1H), 7.26 (td, *J*=1.6, 7.3 Hz, 1H), 7.16 (d, *J*=7.4 Hz, 1H), 5.50 (m, 1H), 5.33 (m, 1H), 3.97 (s, 1H), 3.35 (quint, *J*=8.3 Hz, 1H), 3.08 (ddd, *J*=3.9, 7.7, 16.5 Hz, 1H), 2.87 (ddd, *J*=4.2, 7.9, 17.8 Hz, 1H), 2.66 (m, 1H), 2.53 (m, 2H), 1.65 (dd, *J*=1.5, 6.2 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 211.8, 139.9, 133.7, 130.4, 127.6, 127.6, 127.2, 125.8, 124.0, 79.0, 43.5, 33.7, 27.8, 18.0; **IR** (thin film/NaCl) 3481 (br m), 3074 (w), 2933 (m), 2864 (w), 1685 (s), 1639 (w), 1603 (s), 1482

(w), 1456 (m), 1381 (w), 1289 (s), 1233 (s), 1191 (w), 1156 (m), 1093 (m), 1057 (m), 995 (s), 939 (m), 917 (m), 742 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 216.1150, [calc'd for $C_{14}H_{16}O_2$ (M^+): 216.1150].

Entry 1 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J*=7.7 Hz, 1H), 7.41 (t, *J*=7.5 Hz, 1H), 7.35 (tt, *J*=1.4, 7.5 Hz, 1H), 7.26 (d, *J*=7.6 Hz, 1H), 5.81 (m, 1H), 5.18 (m, 2H), 4.10 (s, 1H), 3.45 (quint, *J*=8.4 Hz, 1H), 3.17 (ddd, *J*=4.1, 7.5, 16.3 Hz, 1H), 2.97 (dddd, *J*=1.6, 4.0, 8.0, 18.0 Hz, 1H), 2.64-2.80 (comp m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 211.6, 140.0, 133.7, 131.8, 127.7, 127.3, 125.9, 119.1, 78.8, 44.5, 33.6, 27.8; **IR** (thin film/NaCl) 3481 (br m), 3075 (w), 3018 (m), 2979 (w), 2945 (w), 2915 (w), 2861 (w), 2251 (w), 1715 (s), 1640 (w), 1484 (m), 1456 (m), 1370 (w), 1348 (w), 1216 (m), 1173 (m), 1124 (m), 1070 (s), 990 (m), 915 (s), 842 (w), 761 (br s) cm^{-1}; **HRMS** (EI) *m/z* found: 202.0993, [calc'd for $C_{13}H_{14}O_2$ (M^+): 202.0994].

Entry 1 (OH-Insertion Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J*=7.9 Hz, 1H), 7.49 (t, *J*=7.6 Hz, 1H), 7.33 (t, *J*=7.6 Hz, 1H), 7.25 (d, *J*=7.7 Hz, 1H), 5.98 (m, 1H), 5.35 (dd, *J*=2.0, 17.2 Hz, 1H), 5.21 (dd, *J*=1.2, 10.5 Hz, 1H), 4.40 (dd, *J*=5.5, 12.8 Hz, 1H), 4.19 (dd, *J*=6.2, 12.5 Hz, 1H), 4.11 (dd, *J*=4.3, 10.7 Hz, 1H), 3.16 (dt, *J*=4.8, 16.9 Hz, 1H), 3.04 (ddd, *J*=4.5, 9.7, 16.9 Hz, 1H), 2.38 (dq, *J*=4.7, 13.4 Hz, 1H), 2.21-2.29 (comp m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 196.9, 143.5, 134.6, 133.5, 131.9, 128.6, 127.6, 126.7, 79.2, 71.4, 30.0, 27.4; **IR** (thin film/NaCl) 3072 (w), 3024 (w), 2932 (m), 2870 (w), 2248 (w), 1696 (s), 1601 (m), 1456 (m), 1432 (w), 1297 (w), 1270 (w), 1224 (m), 1158 (m), 1138 (m), 1101 (m), 1021 (m), 997 (m), 927 (m), 748 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 202.0993, [calc'd for $C_{13}H_{14}O_2$ (M^+): 202.0994].

Entry 2 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J*=7.8 Hz, 1H), 7.33 (t, *J*=7.4 Hz, 1H), 7.27 (td, *J*=1.0, 7.3 Hz, 1H), 7.18 (d, *J*=7.6 Hz, 1H), 5.08 (tt, *J*=1.0, 7.3 Hz, 1H), 4.00 (s, 1H), 3.38 (quint, *J*=8.2 Hz, 1H), 3.09 (ddd, *J*=4.0, 7.6, 16.3 Hz, 1H),

2.89 (ddd, J=4.0, 7.8, 17.9 Hz, 1H), 2.66 (m, 1H), 2.58 (s, 1H), 2.57 (s, 1H), 1.71 (s, 3H), 1.53 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 212.0, 139.9, 136.1, 133.7, 127.5, 127.5, 127.1, 125.9, 116.9, 79.0, 38.8, 33.5, 27.8, 25.8, 17.8; **IR** (thin film/NaCl) 3483 (br m), 3019 (m), 2973 (w), 2916 (w), 2858 (w), 2401 (w), 1714 (s), 1484 (w), 1456 (m), 1378 (w), 1348 (w), 1216 (s), 1118 (w), 1069 (m), 984 (w), 909 (w), 838 (w), 784 (br m), 668 (m) cm^{-1}; **HRMS** (EI) m/z found: 230.1309, [calc'd for $C_{15}H_{18}O_2$ (M^+): 230.1307].

Entry 4 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J=7.8 Hz, 1H), 7.31 (t, J=7.4 Hz, 1H), 7.25 (td, J=1.2, 7.3 Hz, 1H), 7.17 (d, J=7.3 Hz, 1H), 5.22 (q, J=7.6 Hz, 1H), 3.96 (s, 1H), 3.36 (quint, J=8.3 Hz, 1H), 3.07 (ddd, J=3.6, 7.4, 16.3 Hz, 1H), 2.90 (ddd, J=3.6, 7.6, 18.3 Hz, 1H), 2.65 (m, 1H), 2.54 (s, 2H), 1.57 (s, 3H), 1.55 (d, J=6.9 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 212.2, 140.2, 133.8, 130.8, 127.6, 127.5, 125.8, 124.4, 79.8, 50.0, 33.9, 27.7, 17.3, 13.6; **IR** (thin film/NaCl) 3482 (br m), 3064 (w), 3032 (w), 2916 (m), 2859 (w), 1714 (s), 1483 (w), 1456 (m), 1380 (w), 1206 (w), 1172 (w), 1119 (m), 1067 (m), 986 (w), 784 (w), 755 (m) cm^{-1}; **HRMS** (EI) m/z found: 230.1307, [calc'd for $C_{15}H_{18}O_2$ (M^+): 230.1307].

Entry 5 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (dd, J=1.9, 7.5 Hz, 1H), 7.27 (m, 2H), 7.12 (d, J=6.6 Hz, 1H), 5.39 (dq, J=6.2, 15.7 Hz, 1H), 5.26 (dd, J=1.5, 16.0 Hz, 1H), 4.22 (s, 1H), 3.33 (quint, J=8.5 Hz, 1H), 2.98 (ddd, J=4.8, 7.9, 17.2 Hz, 1H), 2.75 (m, 1H), 1.65 (dd, J=1.5, 6.2 Hz, 3H), 1.03 (s, 3H), 1.03 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 212.9, 137.6, 136.8, 135.2, 128.8, 127.5, 127.5, 126.1, 123.4, 82.0, 45.4, 34.4, 27.7, 23.5, 21.4, 18.2; **IR** (thin film/NaCl) 3470 (br m), 3027 (w), 2969 (m), 2936 (m), 2878 (w), 2251 (w), 1703 (s), 1486 (w), 1451 (m), 1383 (m), 1359 (m), 1177 (m), 1119 (m), 1055 (s), 989 (m), 909 (s), 736 (s), 649 (w) cm^{-1}; **HRMS** (EI) m/z found: 244.1463, [calc'd for $C_{16}H_{20}O_2$ (M+): 244.1463].

Entry 6 ([3,3]-Product) (4:1 Mixture of Diastereomers)

Major Diastereomer

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (dd, *J*=1.4, 7.4 Hz, 1H), 7.30 (t, *J*=7.6 Hz, 1H), 7.25 (td, *J*=1.3, 7.5 Hz, 1H), 7.17 (d, *J*=7.7 Hz, 1H), 5.37 (qd, *J*=1.4, 6.6 Hz, 1H), 3.89 (s, 1H), 3.48 (quint, *J*=8.6 Hz, 1H), 3.01 (ddd, *J*=1.4, 8.3, 16.4 Hz, 1H), 2.82 (ddd, *J*=1.5, 8.1, 19.6 Hz, 1H), 2.73 (q, *J*=7.7 Hz, 1H), 2.61 (m, 1H), 1.63 (s, 3H), 1.56 (dd, *J*=0.9, 6.6 Hz, 3H), 1.00 (d, *J*=6.9 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 212.9, 139.6, 137.7, 134.1, 127.8, 127.4, 126.8, 126.7, 121.3, 82.8, 48.0, 32.9, 27.0, 13.2, 12.3; **IR** (thin film/NaCl) 3477 (br m), 3021 (w), 2969 (m), 2913 (m), 2863 (w), 2253 (w), 1710 (s), 1479 (m), 1455 (s), 1382 (m), 1347 (m), 1287 (w), 1236 (w), 1205 (w), 1176 (m), 1120 (s), 1071 (s), 985 (m), 913 (s), 750 (s), 649 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 244.1463, [calc'd for $C_{16}H_{20}O_2$ (M^+): 244.1463].

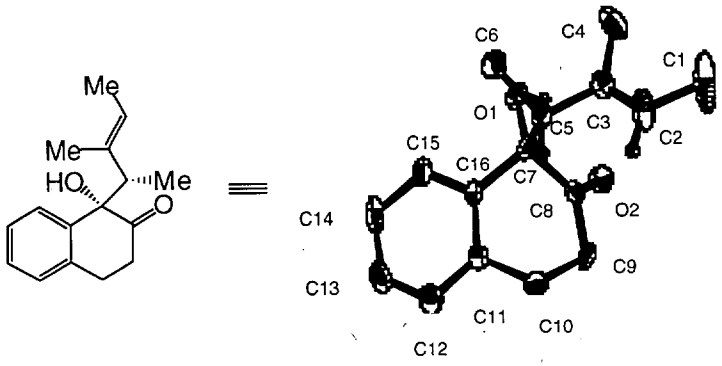
Entry 7 ([3,3]-Product) (5:1 Mixture of Diastereomers)

Major Diastereomer

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (dd, *J*=1.5, 7.6 Hz, 1H), 7.30 (tt, *J*=1.1, 7.4 Hz, 1H), 7.25 (td, *J*=1.4, 7.3 Hz, 1H), 7.16 (d, *J*=7.5 Hz, 1H), 5.50 (dq, *J*=6.3, 15.8 Hz, 1H), 5.42 (ddq, *J*=1.4, 7.9, 15.3 Hz, 1H), 3.96 (s, 1H), 3.46 (quint, *J*=8.7 Hz, 1H), 3.02 (ddd, *J*=2.4, 8.4, 16.6 Hz, 1H), 2.80 (ddd, *J*=2.0, 8.6, 19.0 Hz, 1H), 2.67 (m, 2H), 1.65 (dd, *J*=1.5, 6.2 Hz, 3H), 0.92 (d, *J*=6.9 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 211.8, 138.9, 134.0, 131.6, 127.7, 127.5, 126.8, 126.4, 81.8, 42.3, 32.8, 27.0, 17.9, 14.1; **IR** (thin film/NaCl) 3470 (br m), 3069 (w), 3024 (w), 2974 (m), 2934 (m), 2917 (m), 2872 (w), 1713 (s), 1454 (m), 1367 (m), 1346 (m), 1205 (w), 1175 (m), 1119 (m), 1075 (m), 1012 (m), 971 (m), 925 (w), 786 (w), 758 (m), 699 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 231.1389, [calc'd for $C_{15}H_{19}O_2$ (M+H): 231.1385].

Determination of Relative Stereochemistry for Table 3, Entry 6 [3,3] Rearrangement Product.

Relative stereochemistry was determined by single crystal X-RAY analysis. The relevant crystallographic data follows.



X-RAY STRUCTURE REPORT

Data Collection

A colorless plates crystal of $C_{16}H_{20}O_2$ having approximate dimensions of 0.10 x 0.27 x 0.35 mm was mounted on a glass fiber. All measurements were made on an Enraf-Nonius CAD4 diffractometer with graphite monochromated Mo-KALPHA radiation.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the setting angles of 25 carefully centered reflections in the range $7.36 < 2\theta < 18.12^o$ corresponded to a primitive triclinic cell with dimensions: a = 7.356(2) Å, b = 8.883(1) Å, c = 11.509(2) Å, α = 75.74(1)°, β = 75.95(2)°, γ = 78.07(1), and V = 698.3(2) Å^3. For Z = 2 and F.W. = 244.33, the calculated density is 1.16 g/cm^3. Based on a statistical analysis of intensity distribution,and the successful solution and refinement of the structure, the space group was determined to be:

$P\bar{1}$ (#2)

The data were collected at a temperature of 23 ± 1°C using the ω-2θ scan technique to a maximum 2θ value of 52.6°. Omega scans of several intense reflections, made prior to data collection, had an average width at half-height of 0.00° with a take-off angle of 2.8°. Scans of (1.06 + 1.00 tan θ)° were made at a speed of 0.0°/min (in omega). Moving-crystal moving counter background measurements were made by scanning an additional 25 above and below the scan range. The counter aperture consisted of a variable horizontal slit with a width ranging from 2.0 to 2.5 mm and a vertical slit set to 2.0 mm. The diameter of the incident beam collimator was 0.7 mm and the crystal to

detector distance was 21 cm. For intense reflections an attenuator was automatically inserted in front of the detector.

Data Reduction

Of the 3005 reflections which were collected, 2819 were unique (R_{int} = 0.076). The intensities of three representative reflection were measured after every 0 minutes of X-ray exposure time. No decay correction was applied.

The linear absorption coefficient, μ, for Mo-KALPHA radiation is 0.7 cm^{-1}. An empirical absorption correction based on azimuthal scans of several reflections was applied which resulted in transmission factors ranging from 0.80 to 1.00. The data were corrected for Lorentz and polarization effects. A correction for secondary extinction was applied (coefficient = 4.11839e-06).

Structure Solution and Refinement

The structure was solved by direct methods[1] and expanded using Fourier techniques[2]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement[3] was based on 856 observed reflections (I > 3.00sigma(I)) and 163 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R = S \, | \, |Fo| - |Fc| \, | \, / \, S \, |Fo| = 0.064$$

$$R_w = [(\Sigma \, w \, (|Fo| - |Fc|)^2 / \Sigma \, w \, Fo^2)]^{1/2} = 0.065$$

The standard deviation of an observation of unit weight[4] was 2.01. The weighting scheme was based on counting statistics and included a factor (p = 0.025) to downweight the intense reflections. Plots of $\Sigma \, w \, (|Fo| - |Fc|)^2$ versus |Fo| reflection order in data collection, sin θ/λ and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.23 and -0.20 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber[5]. Anomalous dispersion effects were included in Fcalc[6]; the values for DELTAf

and DELTAf' were those of Creagh and McAuley[7]. The values for the mass attenuation coefficients are those of Creagh and Hubbel[8]. All calculations were performed using the teXsan[9] crystallographic software package of Molecular Structure Corporation.

References

(1) SIR92: Altomare, A., Burla, M.C., Camalli, M., Cascarano, M., Giacovazzo, C., Guagliardi, A., Polidori, G. (1994). J. Appl. Cryst., in preparation.

(2) DIRDIF94: Beurskens, P.T., Admiraal, G., Beurskens, G., Bosman, W.P., de Gelder, R., Israel, R. and Smits, J.M.M.(1994). The DIRDIF-94 program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands.

(3) Least-Squares:

Function minimized: $Sw(|F_o|-|F_c|)^2$

where $w = 4F_o^2/\sigma^2(F_o^2) = [s^2(F_o) + (pF_o/2)^2]^{-1}$

$F_o^2 = S(C-RB)/Lp$

and $s^2(F_o^2) = [S^2(C+R^2B) + (pF_o^2)^2]/Lp^2$

S = Scan rate

C = Total integrated peak count

R = Ratio of scan time to background counting time

B = Total background count

Lp = Lorentz-polarization factor

p = p-factor

(4) Standard deviation of an observation of unit weight:

$[Sw(|F_o|-|F_c|)^2/(N_o-N_v)]^{1/2}$

where: N_o = number of observations and N_v = number of variables

(5) Cromer, D. T. & Waber, J. T.; "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

(6) Ibers, J. A. & Hamilton, W. C.; Acta Crystallogr., 17, 781 (1964)

(7) Creagh, D. C. & McAuley, W.J .; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219-222 (1992).

(8) Creagh, D. C. & Hubbell, J.H..; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).

(9) teXsan: Crystal Structure Analysis Package, Molecular Structure Corporation (1985 & 1992).

Experimental Details

A. Crystal Data	
Empirical Formula	$C_{16}H_{20}O_2$
Formula Weight	244.33
Crystal Color, Habit	colorless, plates
Crystal Dimensions	0.10 X 0.27 X 0.35 mm
Crystal System	triclinic
Lattice Type	Primitive
No. of Reflections Used for Unit Cell Determination (2θ range)	25 (7.4 - 18.1°)
Omega Scan Peak Width at Half-height	0.00°
Lattice Parameters	a = 7.356(2)Å b = 8.883(1) Å c = 11.509(2) Å α = 75.74(1)° β = 75.95(2)° γ = 78.07(1)° V = 698.3(2) Å^3
Space Group	$P\bar{1}$ (#2)
Z value	2
D_{calc}	1.162 g/cm^3
F_{000}	264.00
m(MoKa)	0.75 cm^{-1}
B. Intensity Measurements	
Diffractometer	CAD4
Radiation	MoKa (λ= 0.71069 Å) graphite monochromated
Attenuator	Zr foil (factor = 20.40)
Take-off Angle	2.8°
Detector Aperture	2.0 - 2.5 mm horizontal 2.0 mm vertical

Crystal to Detector Distance	21 mm
Temperature	23.0°C
Scan Type	ω-2θ
Scan Rate	0.0°/min (in ω) (up to 0 scans)
Scan Width	$(1.06 + 1.00 \tan \theta)^{o}$
$2\theta_{max}$	52.6°
No. of Reflections Measured	Total: 3005
Unique:	2819 (R_{int} = 0.076)
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.7966 - 1.0000)
	Secondary Extinction
	(coefficient: 4.11839e-06)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares
Function Minimized	$\Sigma w (\|Fo\| - \|Fc\|)^2$
Least Squares Weights	$1/^2\Sigma(Fo) = 4Fo^2/\Sigma^2(Fo^2)$
p-factor	0.0250
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>3.00sigma(I))	856
No. Variables	163
Reflection/Parameter Ratio	5.25
Residuals: R; Rw	0.064 ; 0.065
Goodness of Fit Indicator	2.01
Max Shift/Error in Final Cycle	0.00
Maximum peak in Final Diff. Map	0.23 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.20 $e^-/Å^3$

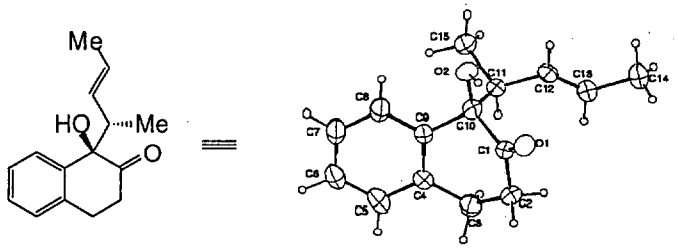
Atomic coordinates and B_{iso}/B_{eq}

atom	x	y	z	B_{eq}
O(1)	0.9701(6)	0.1569(5)	0.6304(4)	3.4(1)
O(2)	0.7679(7)	0.0095(5)	0.5458(4)	4.0(1)
C(1)	0.698(2)	-0.357(1)	0.9444(8)	9.6(4)
C(2)	0.671(1)	-0.1787(9)	0.9066(7)	5.5(3)
C(3)	0.801(1)	-0.0924(9)	0.8470(6)	3.5(2)
C(4)	1.005(1)	-0.1622(9)	0.8047(8)	6.1(3)
C(5)	0.7516(9)	0.0864(8)	0.8230(6)	2.9(2)
C(6)	0.859(1)	0.1621(8)	0.8879(6)	4.5(2)
C(7)	0.7757(9)	0.1636(8)	0.6857(6)	2.6(2)
C(8)	0.6790(10)	0.0802(8)	0.6240(6)	2.6(2)
C(9)	0.467(1)	0.0925(8)	0.6590(7)	3.6(2)
C(10)	0.3632(10)	0.2353(9)	0.7193(7)	4.2(2)
C(11)	0.479(1)	0.3684(9)	0.6858(6)	3.5(2)
C(12)	0.388(1)	0.523(1)	0.6701(7)	4.7(3)
C(13)	0.488(1)	0.6432(10)	0.6410(8)	5.0(3)
C(14)	0.683(1)	0.6151(9)	0.6213(7)	5.0(3)
C(15)	0.779(1)	0.4589(9)	0.6352(7)	4.1(2)
C(16)	0.676(1)	0.3362(8)	0.6686(6)	3.0(2)
H(1)	0.5796	-0.3902	0.9843	11.4712
H(2)	0.7479	-0.4016	0.8738	11.4712
H(3)	0.7842	-0.3915	0.9988	11.4712
H(4)	0.5462	-0.1245	0.9286	6.5549
H(5)	1.0116	-0.2260	0.7482	7.2712
H(6)	1.0550	-0.2246	0.8732	7.2712
H(7)	1.0781	-0.0800	0.7661	7.2712
H(8)	0.6206	0.1097	0.8578	3.4967
H(9)	0.8359	0.1174	0.9731	5.3675
H(10)	0.9912	0.1431	0.8549	5.3675
H(11)	0.8160	0.2722	0.8756	5.3675
H(12)	1.0066	0.0965	0.5569	6.5173
H(13)	0.4374	-0.0012	0.7154	4.3002
H(14)	0.4205	0.1016	0.5871	4.3002
H(15)	0.3388	0.2002	0.8058	5.0395

H(16)	0.2465	0.2740	0.6928	5.0395
H(17)	0.2538	0.5451	0.6801	5.6945
H(18)	0.4229	0.7482	0.6339	6.0257
H(19)	0.7526	0.7004	0.5986	5.9969
H(20)	0.9137	0.4382	0.6216	4.8907

Determination of Relative Stereochemistry for Table 3, Entry 7 [3,3] Rearrangement Product.

Relative stereochemistry was determined by single crystal X-RAY analysis. The relevant crystallographic data follows.



X-RAY STRUCTURE REPORT

Compound 9039, $C_{15}H_{18}O_2$, crystallizes in the triclinic space group $P\bar{1}$ with a=8.9047(8)Å, b=11.7642(12)Å, c=7.3543(8)Å, α=96.258(6)°, β=115.372(8)°, γ=106.118(11)°, V=645.27(11)Å^3, Z=2 and d_{calc}=1.185 g/cm^3. X-ray intensity data were collected on an Rigaku R-AXIS IIc area detector employing graphite-monochromated Mo-K_α radiation (λ=0.71069 Å) at a temperature of 200°K. Indexing was performed from a series of 1° oscillation images with exposures of 200 seconds per frame. A hemispere of data was collected using 10° oscillation angles with exposures of 100 seconds per frame and a crystal-to-detector distance of 82 mm. Oscillation images were processed using bioteX[1], producing a listing of unaveraged F^2 and $\sigma(F^2)$ values which were then passed to the teXsan[2] program package for further processing and structure solution on a Silicon Graphics Indigo R4000 computer. A total of 4747 reflections were measured over the ranges: $5.36 \leq 2\theta \leq 50.90°$, $-10 \leq h \leq$

10, $-14 \le k \le 14$, $-8 \le l \le 8$ yielding 2122 unique reflections ($R_{int} = 0.0400$). The intensity data were corrected for Lorentz and polarization effects but not for absorption.

The structure was solved by direct methods (SIR92[3]). Refinement was by full-matrix least squares based on F^2 using SHELXL-93[4]. All reflections were used during refinement (F^2's that were experimentally negative were replaced by $F^2 = 0$). The weighting scheme used was $w=1/[\sigma^2(F_o^2)+ 0.1008P^2 + 0.2384P]$ where $P = (F_o^2 + 2F_c^2)/3$. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined isotropically. Refinement converged to $R_1=0.0634$ and $wR_2=0.1787$ for 1825 reflections for which $F > 4\sigma(F)$ and $R_1=0.0730$, $wR_2=0.1896$ and GOF = 1.088 for all 2122 unique, non-zero reflections and 227 variables[5]. The maximum Δ/σ in the final cycle of least squares was 0.006 and the two most prominent peaks in the final difference Fourier were +0.186 and -0.216 e/Å^3.

References

1. bioteX: A suite of Programs for the Collection, Reduction and Interpretation of Imaging Plate Data, Molecular Structure Corporation (1995).

2. teXsan: Crystal Structure Analysis Package, Molecular Structure Corporation (1985 & 1992).

3. SIR92: Altomare, A., Burla, M.C., Camalli, M., Cascarano, M., Giacovazzo, C., Guagliardi, A., Polidoro, G. (1994). *J. Appl. Cryst.*, **27**, 435.

4. SHELXL-93: Program for the Refinement of Crystal Structures, Sheldrick, G.M. (1993), University of Göttingen, Germany.

5. $R_1 = \sum ||F_o| - |F_c|| / \sum |F_o|$
$wR_2 = \{ \sum w (F_o^2 - F_c^2)^2 / \sum w(F_o^2)^2\}^{1/2}$
$GOF = \{ \sum w (F_o^2 - F_c^2)^2 / (n - p)\}^{1/2}$ where n = the number of reflections and p = the number of parameters refined.

6. "ORTEP-II: A Fortran Thermal Ellipsoid Plot Program for Crystal Structure Illustrations". C.K. Johnson (1976) ORNL-5138.

Experimental Details

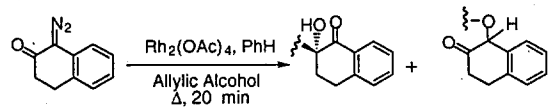
Formula:	$C_{15}H_{18}O_2$
Formula weight:	230.29
Crystal class:	triclinic
Space group:	$P\bar{1}$ (#2)
Z	2
Cell constants:	
a	8.9047(8)Å
b	11.7642(12)Å
c	7.3543(8)Å
α	96.258(6)°
β	115.372(8)°
γ	106.118(11)°
V	645.27(11)Å^3
μ	0.77 cm^{-1}
crystal size, mm	0.47 x 0.28 x 0.10
D_{calc}	1.185 g/cm^3
F(000)	248
Radiation:	Mo-K_α (λ=0.71069Å)
2q range	5.36–50.90°
hkl collected:	-10≤ h ≤10; -14≤ k ≤14; -8≤ l ≤8
No. reflections measured:	4747
No. unique reflections:	2122 (R_{int}=0.0400)
No. observed reflections	1825 (F>4σ)
No. reflections used in refinement	2122
No. parameters	227
R indices (F>4σ)	R_1=0.0634
	wR_2=0.1787
R indices (all data)	R_1=0.0730
	wR_2=0.1896
GOF:	1.088
Final Difference Peaks, e/Å^3	+0.186, -0.216

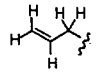
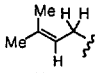
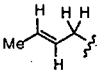
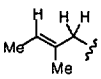
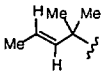
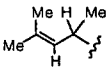
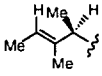
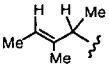
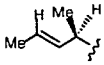
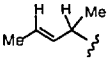
Refined Positional Parameters

Atom	x	y	z	U_{eq}, Å^2
C1	0.2070(3)	0.1495(2)	0.8364(4)	0.0444(6)
C2	0.2894(4)	0.1888(3)	1.0700(4)	0.0523(7)
C3	0.4932(4)	0.2396(3)	1.1843(4)	0.0567(7)
C4	0.5750(3)	0.1961(2)	1.0596(4)	0.0506(7)
C5	0.7345(4)	0.1755(3)	1.1577(6)	0.0660(8)
C6	0.8137(4)	0.1404(3)	1.0463(6)	0.0716(9)
C7	0.7310(5)	0.1212(3)	0.8304(7)	0.0723(10)
C8	0.5702(4)	0.1382(2)	0.7292(5)	0.0570(7)
C9	0.4927(3)	0.1777(2)	0.8425(4)	0.0444(6)
C10	0.3203(3)	0.2024(2)	0.7344(4)	0.0420(6)
C11	0.3557(3)	0.3415(2)	0.7635(4)	0.0416(6)
C12	0.1834(3)	0.3651(2)	0.6882(4)	0.0499(7)
C13	0.1361(4)	0.4246(3)	0.8036(5)	0.0565(7)
C14	-0.0366(5)	0.4473(4)	0.7264(7)	0.0750(10)
C15	0.4580(4)	0.3936(3)	0.6478(5)	0.0531(7)
O1	0.0568(2)	0.0756(2)	0.7310(3)	0.0550(6)
O2	0.2304(2)	0.1474(2)	0.5175(2)	0.0503(5)
H2	0.134(5)	0.077(4)	0.492(6)	0.099(12)
H2a	0.242(5)	0.119(3)	1.112(6)	0.086(11)
H2b	0.238(5)	0.250(3)	1.099(6)	0.086(11)
H3a	0.545(4)	0.332(3)	1.227(5)	0.064(8)
H3b	0.535(4)	0.211(3)	1.312(5)	0.074(9)
H5	0.790(4)	0.186(3)	1.304(5)	0.064(8)
H6	0.930(6)	0.125(4)	1.113(6)	0.107(13)

H7	0.779(5)	0.094(3)	0.748(6)	0.099(12)
H8	0.501(4)	0.116(3)	0.573(5)	0.078(10)
H11	0.429(3)	0.384(2)	0.919(4)	0.048(7)
H12	0.104(4)	0.329(3)	0.536(5)	0.058(8)
H13	0.217(4)	0.455(3)	0.959(5)	0.068(9)
H14b	-0.099(5)	0.401(4)	0.778(6)	0.093(13)
H14c	-0.108(6)	0.409(4)	0.553(8)	0.13(2)
H14a	-0.013(5)	0.530(4)	0.758(6)	0.093(12)
H15a	0.575(4)	0.376(2)	0.690(4)	0.056(7)
H15b	0.491(4)	0.484(3)	0.689(5)	0.068(8)
H15c	0.381(4)	0.362(3)	0.492(5)	0.060(8)

Table 4



Entry	Allylic Alcohol	[3,3] Product (yield)	Insertion Product (yield)
1		 (72)	 (0)
2		 (67)	 (0)
3		 (67)	 (0)
4		 (72)	 (0)
5		 (74)	 (0)
6		 (66)	 (0)
7		 (63)	 (0)

Representative Procedure for the Preparation of α-Hydroxyketones in Table 4 (Entry 3). To a stirred solution of α-diazo-β-tetralone (100 mg, 0.58 mmol, 1.0 equiv) and 3-buten-2-ol (64 mg, 0.89 mmol, 1.5 equiv) in benzene (5 mL) was added $Rh_2(OAc)_4$ (2.0 mg, 0.0045 mmol, 0.008 equiv). The reaction mixture was immersed in an oil bath preheated to 100°C, stirred at reflux for 15 min, and finally cooled to room temperature. Concentration under reduced pressure followed by flash column chromatography (20:1 hexanes:EtOAc eluent) afforded α-hydroxyketone (84 mg, 67% yield) as a colorless oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.02 (dd, *J*=1.0, 7.7 Hz, 1H), 7.51 (td, *J*=1.5, 7.7 Hz, 1H), 7.34 (t, *J*=7.7 Hz, 1H), 7.26 (d, *J*=7.7 Hz, 1H), 5.48-5.52 (comp m, 2H), 3.76 (br s, 1H), 3.10 (m, 1H), 2.98 (ddd, *J*=2.2, 5.6, 17.6 Hz, 1H), 2.28-2.39 (comp m, 3H), 2.15 (td, *J*=5.8, 13.0 Hz, 1H), 1.68 (d, *J*=5.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.2, 143.4, 134.0, 130.2, 129.9, 129.0, 127.9, 126.9, 124.2, 75.5, 39.0, 33.4, 26.2, 18.1; **IR** (thin film/NaCl) 3489 (br m), 3065 (w), 3026 (w), 2934 (m), 2855 (w), 1685 (s), 1603 (s), 1482 (w), 1455 (m), 1387 (w), 1290 (s), 1228 (s), 1146 (w), 1094 (m), 997 (m), 970 (m), 946 (m), 908 (w), 741

(s), 649 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 216.1150, [calc'd for $C_{14}H_{16}O_2$ (M^+): 216.1150].

Entry 1 ([3,3]-Product)[7]

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (dd, *J*=1.2, 7.8 Hz, 1H), 7.53 (td, *J*=1.4, 7.5 Hz, 1H), 7.35 (t, *J*=7.5 Hz, 1H), 7.27 (d, *J*=7.8 Hz, 1H), 5.84-5.93 (comp m, 1H), 5.17 (dq, *J*=0.9, 11.1 Hz, 1H), 5.10 (dq, *J*=1.8, 17.1 Hz, 1H), 3.82 (s, 1H), 3.11 (ddd, *J*=5.2, 12.6, 17.9 Hz, 1H), 3.00 (ddd, *J*=2.2, 5.4, 17.7 Hz, 1H), 2.45 (dd, *J*=8.3, 14.3 Hz, 1H), 2.36 (m, 2H), 2.18 (td, *J*=5.6, 13.0, 19.2 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.0, 143.4, 134.1, 132.1, 129.0, 128.0, 126.9, 119.1, 75.3, 40.3, 33.4, 26.1; **IR** (thin film/NaCl) 3486 (br m), 3074 (w), 2933 (w), 2864 (w), 1685 (s), 1603 (s), 1430 (m), 1382 (w), 1289 (s), 1232 (s), 1156 (m), 1092 (m), 1057 (m), 996 (s), 940 (m), 918 (m), 784 (m), 742 (s) cm^{-1}.

Entry 2 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J*=8.3 Hz, 1H), 7.52 (t, *J*=7.6 Hz, 1H), 7.34 (t, *J*=7.6 Hz, 1H), 7.26 (d, *J*=7.7 Hz, 1H), 5.22 (m, 1H), 3.78 (s, 1H), 3.10 (ddd, *J*=5.0, 12.6, 17.6 Hz, 1H), 3.00 (dd, *J*=5.5, 17.6 Hz, 1H), 2.43 (dd, *J*=7.9, 14.7 Hz, 1H), 2.29-2.38 (comp m, 2H), 2.16 (td, *J*=5.6, 13.0 Hz, 1H), 1.73 (s, 3H), 1.52 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.3, 143.4, 135.9, 133.9, 130.2, 128.9, 127.9, 117.1, 76.0, 34.4, 33.7, 26.4, 26.0, 18.0; **IR** (thin film/NaCl) 3409 (br m), 2906 (w), 2928 (m), 2861 (w), 1685 (s), 1603 (m), 1482 (w), 1454 (m), 1377 (w), 1287 (m), 1233 (m), 1157 (w), 1086 (m), 996 (m), 839 (w), 789 (w), 783 (w), 741 (m), 651 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 230.1307, [calc'd for $C_{15}H_{18}O_2$ (M^+): 230.1309].

Entry 4 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J*=7.8 Hz, 1H), 7.53 (td, *J*=1.1, 7.5 Hz, 1H), 7.35 (t, *J*=7.5 Hz, 1H), 7.26 (d, *J*=7.8 Hz, 1H), 5.23 (q, *J*=6.7 Hz, 1H), 3.80 (s, 1H), 3.16 (ddd, *J*=5.4, 12.8, 18.0 Hz, 1H), 2.99 (ddd, *J*=1.8, 5.6, 18.0 Hz, 1H), 2.37 (s, 2H), 2.32 (ddd, *J*=2.2, 5.3, 13.4 Hz, 1H), 2.17 (td, *J*=5.6, 13.0 Hz, 1H), 1.64 (s, 3H), 1.60 (d, *J*=6.8 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.6, 143.2, 133.9, 131.0, 130.5, 129.0, 127.8, 126.9, 124.2, 76.1, 45.5, 34.1, 26.4,

17.6, 13.6; **IR** (thin film/NaCl) 3489 (br s), 3060 (w), 3025 (w), 2925 (m), 2861 (w), 1685 (s), 1602 (m), 1480 (w), 1452 (m), 1382 (m), 1288 (s), 1229 (s), 1157 (w), 1096 (m), 994 (m), 948 (w), 914 (w), 764 (w), 739 (m), 653 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 230.1307, [calc'd for $C_{15}H_{18}O_2$ (M^+): 230.1309].

Entry 5 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (dd, *J*=1.1, 7.6 Hz, 1H), 7.46 (td, *J*=1.3, 7.5 Hz, 1H), 7.31 (t, *J*=7.7 Hz, 1H), 7.17 (d, *J*=7.8 Hz, 1H), 5.32-5.40 (comp m, 1H), 3.68 (s, 1H), 3.09 (ddd, *J*=5.4, 11.7, 17.4 Hz, 1H), 2.92 (ddd, *J*=4.1, 6.3, 17.7 Hz, 1H), 2.50 (ddd, *J*=3.7, 5.4, 14.3 Hz, 1H), 2.11 (ddd, *J*=6.3, 11.6, 14.1 Hz, 1H), 1.41 (d, *J*=4.9 Hz, 3H), 1.13 (s, 3H), 1.00 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.1, 143.7, 136.4, 133.4, 133.3, 128.5, 126.9, 126.6, 123.4, 78.2, 43.3, 32.2, 26.6, 23.4, 22.6, 17.9; **IR** (thin film/NaCl) 3504 (br m), 3026 (w), 2966 (m), 2935 (m), 2878 (w), 2855 (w), 2251 (w), 1678 (s), 1455 (s), 1381 (m), 1366 (m), 1289 (s), 1233 (m), 1193 (w), 1158 (m), 1126 (w), 1103 (m), 1084 (m), 987 (s), 940 (m), 911 (m), 826 (w), 762 (m), 737 (s), 693 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 244.1463, [calc'd for $C_{16}H_{20}O_2$ (M^+): 244.1463].

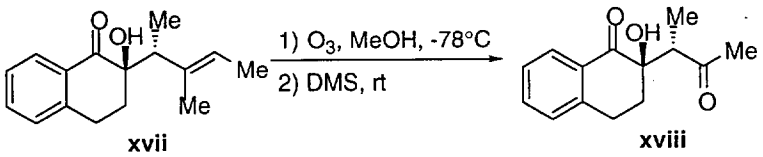
Entry 6 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J*=8.0 Hz, 1H), 7.51 (td, *J*=1.3, 7.6 Hz, 1H), 7.33 (t, *J*=7.5 Hz, 1H), 7.25 (d, *J*=7.7 Hz, 1H), 4.83 (m, 1H), 3.70 (s, 1H), 3.11 (ddd, *J*=5.2, 12.6, 17.9 Hz, 1H), 2.99 (dd, *J*=5.4, 18.0 Hz, 1H), 2.56 (q, *J*=6.9 Hz, 1H), 2.44 (ddd, *J*=2.0, 5.3, 13.8 Hz, 1H), 2.04 (td, *J*=5.8, 13.4 Hz, 1H), 1.50 (s, 3H), 1.45 (d, *J*=6.6 Hz, 3H), 1.21 (d, *J*=7.1 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.1, 142.8, 136.2, 133.5, 131.6, 128.9, 127.7, 126.8, 121.8, 78.3, 43.9, 32.7, 26.3, 14.9, 13.2, 13.0; **IR** (thin film/NaCl) 3487 (br m), 3060 (w), 2967 (m), 2929 (m), 2863 (w), 1687 (s), 1604 (m), 1456 (m), 1437 (w), 1370 (w), 1281 (s), 1238 (m), 1216 (w), 1152 (w), 1096 (m), 991 (m), 943 (m), 784 (w), 741 (m), 651 (m), 630 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 244.1463, [calc'd for $C_{16}H_{20}O_2$ (M^+): 244.1465].

Entry 7 ([3,3]-Product)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J*=7.9 Hz, 1H), 7.50 (tt, *J*=1.6, 7.5 Hz, 1H), 7.32 (t, *J*=7.6 Hz, 1H), 7.24 (d, *J*=7.7 Hz, 1H), 5.29 (m, 1H), 5.12 (m, 1H), 3.68 (s, 1H), 3.09 (ddd, *J*=5.0, 12.5, 17.7 Hz, 1H), 2.98 (m, 1H), 2.41-2.51 (comp m, 2H), 2.08 (m, 1H), 1.56 (dt, *J*=1.5, 6.1 Hz, 3H), 1.16 (dd, *J*=1.6, 6.9 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.7, 143.0, 133.5, 131.1, 130.6, 128.8, 127.8, 126.8, 126.5, 77.6, 39.0, 32.2, 26.1, 17.9, 14.1; **IR** (thin film/NaCl) 3484 (br m), 3067 (w), 3026 (w), 2971 (m), 2932 (m), 1688 (s), 1603 (s), 1454 (m), 1437 (m), 1370 (m), 1283 (s), 1236 (m), 1152 (m), 1096 (s), 1009 (m), 992 (s), 969 (m), 943 (m), 907 (w), 774 (m), 741 (s) cm^{-1}; **HRMS** (EI) *m/z* found: 231.1382, [calc'd for $C_{15}H_{19}O_2$ (M+H): 231.1385]; **m.p.** 64-66° C.

Determination of Relative Stereochemistry for Table 4, Entry 6 [3,3] Rearrangement Product.



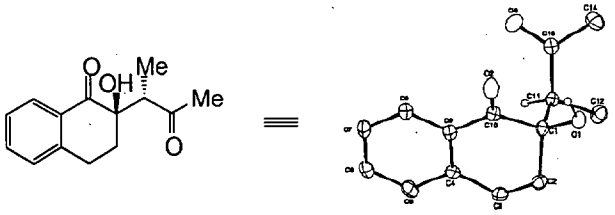
xvii **xviii**

Reductive ozonolysis of α-hydroxyketone **xvii** afforded the diketone **xviii** which was suitable for single crystal X-ray analysis. The relevant crystallographic data follows.

Preparation of Ketone xviii.

To a solution of α-hydroxyketone **xvii** (300 mg, 1.2 mmol, 1.0 equiv.) in methanol (15 mL) was added Sudan red (1 mg). The solution was cooled to -78° C and treated with ozone until colorless (about 5 min). The cold reaction mixture was purged with nitrogen for 10 min, treated with dimethyl sulfide (10 mL), warmed to room temperature and stirred overnight. Solvent was removed *in vacuo* and the crude product was purified by column chromatography (9:1 CH_2Cl_2:MeOH eluent) to afford **xviii** (251 mg, 90% yield) as a clear, colorless solid suitable for single crystal x-ray analysis: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.7 Hz, 1H), 5.02 (s, 1H), 3.3 (ddd, *J* = 5.3, 9.2, 17.1

Hz, 1H), 2.8 (m, 2H), 2.33 (s, 3H), 2.3 (m, 1H), 2.0 (m, 1H), 1.25 (dd, J = 0.8, 7.3 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 215.2, 198.5, 143.4, 133.6, 130.8, 128.5, 128.2, 126.8, 77.8, 47.3, 32.4, 30.2, 24.9, 10.8; **IR** (thin film/NaCl) 3386 (br m), 3066 (w), 2934 (m), 2882 (w), 1684 (s), 1602 (m), 1457 (m), 1424 (m), 1357 (m), 1228 (m), 1169 (m), 1098 (m), 1058 (w), 990 (w), 943 (m), 899 (m), 852 (w), 745 (m) cm^{-1}; **m.p.** 121-124° C.



X-RAY STRUCTURE REPORT

Compound 9040, $C_{14}H_{16}O_3$, crystallizes in the triclinic space group P$\bar{1}$ with a=9.4945(5)Å, b=10.7412(5)Å, c=6.8970(3)Å, α=107.921(2)°, β=101.917(3)°, γ=110.873(3)°, V=584.46(5)Å^3, Z=2 and d_{calc}=1.320 g/cm^3. X-ray intensity data were collected on an Rigaku R-AXIS IIc area detector employing graphite-monochromated Mo-K_α radiation (λ=0.71069 Å) at a temperature of 200°K. Indexing was performed from a series of 1° oscillation images with exposures of 300 seconds per frame. A hemispere of data was collected using 10° oscillation angles with exposures of 200 seconds per frame and a crystal-to-detector distance of 82 mm. Oscillation images were processed using bioteX[1], producing a listing of unaveraged F^2 and σ(F^2) values which were then passed to the teXsan[2] program package for further processing and structure solution on a Silicon Graphics Indigo R4000 computer. A total of 4614 reflections were measured over the ranges: $6.28 \le 2\theta \le 50.68°$, $-11 \le h \le 11$, $-12 \le k \le 12$, $-8 \le l \le 8$ yielding 1956 unique reflections (R_{int} = 0.0246). The intensity data were corrected for Lorentz and polarization effects but not for absorption.

The structure was solved by direct methods (SIR92[3]). Refinement was by full-matrix least squares based on F^2 using SHELXL-93[4]. All reflections were used during refinement (F^2's that were experimentally negative were