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Materials and Methods

Unless stated otherwise, reactions were performed in flame dried glassware under a nitrogen atmosphere, using freshly distilled solvents. Diethyl ether (Et₂O) and tetrahydrofuran (THF) were distilled from sodium/benzophenone. Methylene chloride (CH₂Cl₂), benzene, and triethylamine (Et₃N) were distilled from calcium hydride. All other commercially obtained reagents were used as received. All reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) using E. Merck silica gel 60 F254 pre-coated plates (0.25-mm). Column or flash chromatography (silica) was performed with the indicated solvents using silica gel (particle size 0.032-0.063 mm) purchased from Fisher Scientific. All melting points were obtained on a Gallenkamp variable temperature melting point apparatus (model: MPD350.BM2.1) and are uncorrected. Infrared spectra were recorded on a Midac M-1200 FTIR. ¹H and ¹³C NMR spectra were recorded on a Bruker AM-500 spectrometer. High resolution mass spectra were performed at The University of Illinois Mass Spectrometry Center. High performance liquid chromatography (HPLC) was performed on a Waters model 510 system using a Rainin Microsorb 80-199-C5 column, or a Rainen Dynamax SD-200 system with a Rainen Microsorb 80-120-C5 column. Single crystal X-ray analyses were performed by Susan DeGala (Yale University).
Preparation of enoate 7, ester 8 and acid 9.

All solvents used in this procedure were used as received. To a solution of ethyl triphenylphosphoranylidene acetate (74.6 g, 214 mmol, 1.05 equiv) in THF (244 mL) at 0 °C in a one-neck, 1L flask equipped with an addition funnel was added isatin (6) (30.0 g, 204 mmol) in THF (232 mL) rapidly via an addition funnel. The ice bath was removed and the solution was stirred until all starting material had been consumed and a new higher Rf spot appeared by TLC (ca. 30 min). In a separate 3-neck flask equipped with a mechanical stirrer and addition funnel was introduced isopropyl triphenylphosphonium iodide (212 g, 490 mmol, 2.4 equiv) and THF (613 mL). This suspension was cooled to 0 °C and was treated slowly via syringe with a 2.33 M solution of n-BuLi in hexanes (228 mL, 531 mmol, 2.6 equiv). After stirring at 0 °C for 30 min the derived red mixture was treated with the entire crude reaction containing enoate 7 (dropwise via addition funnel). The resultant mixture was stirred for 2.5 h (0 °C - rt) and then excess iodomethane (63.6 mL, 1.02 mol, 5 equiv) was added. After stirring for 1.5 h at rt, the reaction was vacuum filtered to separate the methyl triphenylphosphonium iodide salt and the solid was washed with 1 L diethyl ether. The filtrate was concentrated under reduced pressure to yield the cyclopropyl ester 8. Crude ester 8 was dissolved in THF (577 mL) and placed into a 2L, one-necked flask equipped with a condenser. To this solution was added 4.6N LiOH (577 mL, 2.65 mol, 13 equiv) and the two-phased reaction was heated to reflux overnight. After cooling, the THF was removed under reduced pressure and the aqueous layer was washed with CH₂Cl₂ (2 x 200 mL). After removing any remaining traces of CH₂Cl₂ in vacuo, the aqueous layer was acidified with conc. HCl at 0 °C to afford, after vacuum filtering and azeotropic drying with benzene, acid 9 (38.8 g, 79% yield, 4 steps) as a tan
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S3 solid.

Although generally carried directly through to acid 9, several intermediates were isolated and characterized. Thus, an analytical sample of enoate 7 can be obtained by purifying via silica gel flash chromatography (hexanes:EtOAc, 3:2) followed by recrystallization from EtOH. Enoate 7 was identical in all respects to data reported in the literature.

An analytically pure sample of ester 8 can be obtained by subjecting to silica gel chromatography (4:1 hexanes:EtOAc eluent). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.63 (d, J = 7.7 Hz, 1H), 7.29 (td, J = 1.2, 7.7 Hz, 1H), 7.05 (td, J = 1.0, 7.7 Hz, 1H), 6.90 (d, J = 7.6 Hz, 1H), 4.13 (m, 2H), 2.77 (s, 3H), 1.60 (s, 3H), 1.59 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 173.8, 168.7, 144.2, 127.0, 125.6, 124.9, 121.4, 107.7, 60.5, 41.7, 40.9, 34.8, 26.4, 20.5, 16.9, 14.1; IR (thin film/NaCl) 2945 (br w), 1708 (s), 1606 (m), 1465 (m), 1351 (m), 1263 (w), 1166 (m), 1102 (m), 1003 (w), 751 (m) cm$^{-1}$; HRMS (CI) m/z found: 274.1443, [calc'd for C$_{16}$H$_{19}$NO$_3$ (M+H): 274.1443]; m.p. 91-92$^\circ$ C.

To obtain an analytical sample of acid 9, the dry solid can be recrystallized from MeOH to yield white needles. $^1$H NMR (500 MHz, DMSO-d$_6$) δ 12.61 (s, 1H), 7.40 (d, J = 7.8 Hz, 1H), 7.28 (t, J = 7.9 Hz, 1H), 7.05 (d, J = 7.8 Hz, 1H), 7.00 (t, J = 7.9 Hz, 1H), 3.18 (s, 3H), 2.52 (s, 1H), 1.48 (s, 3H), 1.45 (s, 3H); $^{13}$C NMR (125 MHz, DMSO-d$_6$) δ 173.1, 169.2, 144.0, 127.0, 124.7, 124.6, 121.1, 108.3, 40.7, 40.6, 34.0, 26.4, 20.1, 16.8; IR (KBr pellet) 2932 (br m), 2673 (w), 1753 (s), 1661 (s), 1602 (s), 1418 (m), 1364 (s), 1191 (s), 1103 (s), 1094 (m), 755 (s), 697 (s) cm$^{-1}$; HRMS (CI) m/z found: 246.1129, [calc'd for C$_{14}$H$_{15}$NO$_3$ (M+H): 246.1130]; m.p. 168-169$^\circ$ C.
Preparation of α-diazo ketone 5.

To a 500 mL round bottom flask was added recrystallized acid 9 (9.00 g, 36.7 mmol) and CH₂Cl₂ (200 mL). The resulting white slurry was cooled to 0 °C and stirred. Oxalyl chloride (4.66 g, 38.5 mmol, 1.05 equiv) was added neat via syringe followed by DMF (100 μL, 1.3 mmol, 0.04 equiv). The ice bath was removed after 1 h and stirring continued for 90 min, at which time gas evolution had ceased and a clear, pale yellow solution remained. The solution was concentrated and azeotroped (3x) with benzene under reduced pressure to give acid chloride i as a yellow solid. The solid was then dried in vacuo for 45 min and used crude in the next step.

To a scratch-free 2L round bottom flask equipped with a 250 mL addition funnel was added triethylamine (4.36 g, 43.0 mmol, 1.2 equiv) and acetonitrile (25 mL) and the solution was cooled to 0 °C. Ethers diazomethane (450 mL, prepared from 32.2 g Diazald) was added to the flask through a plastic funnel. Dried acid chloride i was dissolved in THF (200 mL), transferred to the addition funnel via cannula, and added dropwise over 30-40 min to the diazomethane solution. The funnel was rinsed with THF (10 mL) and the resulting heterogeneous mixture was stirred for 1 h after which time 400 mL of 0.1N acetic acid was added slowly. After gas evolution ceased, the biphasic mixture was transferred to a separatory funnel. The aqueous layer was removed and washed with ethyl ether (100 mL). The combined organic layers were concentrated under reduced pressure to give a yellow oil which solidified upon cooling. The solid was purified via silica gel flash chromatography, eluting with a gradient of hexanes:EtOAc (1:4-1:1) to afford α-chloro ketone ii as a yellow solid (0.99 g, 9.7%) and α-diazo ketone 5 (8.36 g, 84% yield from acid 9) as a light yellow solid.

The first compound to elute was α-chloro ketone ii. 1H NMR (500 MHz, CDCl₃) δ 7.65 (d, J = 7.6 Hz, 1H), 7.30 (t, J = 7.7 Hz, 1H), 7.06 (t, J = 7.7 Hz, 1H), 6.89 (d, J =
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ... S5

7.8 Hz, 1H), 4.21 (d, J = 15.5 Hz, 1H), 4.09 (d, J = 15.5 Hz, 1H), 3.27 (s, 3H), 3.08 (s, 1H), 1.64 (s, 3H), 1.56 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 197.3, 173.4, 144.0, 127.4, 126.0, 124.2, 121.9, 107.9, 49.9, 45.0, 44.8, 37.6, 26.6, 20.6, 16.7; IR (thin film/NaCl) 2932 (br w), 1702 (s), 1609 (m), 1468 (m), 1375 (m), 1349 (m), 1266 (w), 1141 (w), 1091 (m), 1024 (w), 753 (m) cm⁻¹; HRMS (El) m/z found: 277.0867; [calc'd for C15H16ClNO2 (M+): 277.0870]; m.p. >135°C (dec).

The second compound to elute was the desired α-diazoketone 5: 1H NMR (500 MHz, CDCl3) δ 7.70 (br s, 1H), 7.29 (td, J = 1.57, 7.7 Hz, 1H), 7.06 (t, J = 6.7 Hz, 1H), 6.90 (dd, J = 1.3, 7.6 Hz, 1H), 5.37 (s, 1H), 3.27 (s, 3H), 2.67 (s, 1H), 1.63 (s, 3H), 1.59 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 189.2, 174.0, 144.0, 127.0, 126.0, 125.0, 121.7, 107.7, 57.1, 46.2, 36.9, 26.5, 20.8, 17.0; IR (thin film, NaCl) 3080 (br w), 2934 (br w), 2101 (s), 1702 (s), 1636 (m), 1469 (m), 1415 (m), 1348 (s), 1266 (m), 1146 (m), 1094 (s), 1029 (w), 753 (m), 695 (w) cm⁻¹; HRMS (El) m/z found: 269.1167; [calc'd for C15H15N3O2 (M+): 269.1164]; m.p. >133°C (dec).

Preparation of ketone 15, spirocycle 11, and heterocycle 14.

To a stirred solution of diazoketone 5 (100 mg, 0.37 mmol) in CH2Cl2 (4 mL) at rt was added rhodium trifluoroacetate (1 mg, 0.002 mmol, 0.4 mol %). After 20 min, nitrogen evolution ceased and the reaction turned from yellow to red. The reaction was adsorbed onto silica gel and purified via flash chromatography (4:1:2:1 hexanes:EtOAc) to provide ketone 15 (14 mg, 15% yield) as a yellow solid, spirocycle 11 (1 mg, 1% yield) as an off-white solid, and heterocycle 14 (14 mg, 15% yield) as a red solid.

The first compound to elute was ketone 15. 1H NMR (500 MHz, CDCl3) δ 7.23 (t, J = 7.8 Hz, 1H), 6.77 (d, J = 7.7 Hz, 2H), 3.51 (d, J = 21.5 Hz, 1H), 3.42 (d, J = 21.7 Hz, 1H), 3.26 (s, 3H), 2.76 (s, 1H), 1.62 (s, 3H), 1.37 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 203.4, 173.7, 142.2, 129.6, 127.9, 124.1, 120.4, 106.0, 44.9, 43.2, 42.7,
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S6

36.5, 26.6, 21.4, 18.7; IR (thin film/NaCl) 2931 (br w), 1706 (s), 1615 (m), 1468 (m), 1377 (w), 1330 (w), 1279 (w), 1224 (w), 1104 (w), 1033 (m), 870 (w), 766 (w) cm⁻¹; HRMS (EI) m/z found: 241.1102, [calc’d for C₁₅H₁₅NO₂ (M⁺): 241.1103]; m.p. 139-140°C.

The second compound to elute was spirocycle 11. The solid was recrystallized from ethyl acetate/hexanes to provide white crystals suitable for X-ray analysis (see Appendix for X-ray structure report). ¹H NMR (500 MHz, CDCl₃) δ 7.32 (t, J = 7.7 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 6.93 (d, J = 7.8 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 3.27 (s, 3H), 3.25-2.30 (comp m, 4H), 2.82 (s, 1H), 1.70 (s, 3); ¹³C NMR (125 MHz, CDCl₃) δ 211.3, 172.3, 144.9, 127.7, 125.0, 122.0, 121.3, 108.5, 48.9, 44.1, 41.0, 40.3, 27.8, 26.6, 15.6; IR (thin film/NaCl) 2934 (w), 1716 (s), 1605 (w), 1482 (m), 1462 (w), 1378 (m), 1255 (w), 1136 (m), 1067 (m), 750 (m), 624 (w) cm⁻¹; HRMS (EI) m/z found: 241.1104, [calc’d for C₁₅H₁₅NO₂ (M⁺): 241.1103]; m.p. 182-183°C.

The final compound to elute was ketone 14. An analytically pure sample of 14 was obtained via HPLC purification (5% MeOH/CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃) δ 7.66 (d, J = 9.0 Hz, 1H), 7.15 (t, J = 10.0 Hz, 1H), 6.86 (t, J = 9.5 Hz, 1H), 6.78 (d, J = 9.2 Hz, 1H), 3.56 (s, 3H), 2.71 (s, 2H), 1.44 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 198.7, 166.3, 146.4, 139.0, 134.5, 129.7, 126.6, 119.0, 109.9, 53.6, 33.9, 27.4, 26.2; IR (thin film/NaCl) 2956 (w), 1664 (s), 1615 (m), 1591 (m), 1548 (m), 1475 (m), 1456 (m), 1414 (w), 1361 (w), 1270 (w), 1201 (m), 1088 (w), 830 (w), 757 (m) cm⁻¹; HRMS (EI) m/z found: 241.1107, [calc’d for C₁₅H₁₅NO₂ (M⁺): 241.1103]; m.p. 193-198°C.
Preparation of ketone 15 and spirocycle 11: An improved aryl C-H insertion reaction.

Montmorillonite K-10 (10 g) was flame-dried under vacuum for 10 min, cooled to rt and then suspended in CH₂Cl₂ (100 mL). The vigorously stirred suspension was treated with Rh₂(TFA)₄ (10 mg, 0.02 mmol, 0.4 mol %) followed by a solution of α-diazo ketone 5 (1.0 g, 3.7 mmol) in CH₂Cl₂ (40 mL) (added over a 45 min period via an addition funnel). Immediately after addition, the reaction mixture was filtered through a pad of celite topped with a thin layer of silica gel. The filter pad was washed with EtOAc (500 mL) and MeOH (50 mL). The filtrate was concentrated and the crude material purified by silica gel column chromatography (hexane:EtOAc, 3:1) to afford cyclohexanone 15 (512 mg, 57% yield) as a yellow solid and spirocycle 11 (45 mg, 5% yield) as an off-white solid.

Preparation of alcohol iii: Confirmation of the aryl C-H insertion event via X-ray analysis.

To a solution of ketone 15 (30 mg, 0.12 mmol) in CH₂Cl₂/MeOH (8 mL, 1:1) was added NaBH₄ (15 mg, 0.40 mmol, 3.3 equiv). The reaction was stirred for 30 min in the open air, after which time the solvents were removed under reduced pressure. The flask was cooled to 0 °C, and the residue was treated with 1N HCl (5 mL). After stirring at 0 °C for 0.5 h, the reaction was extracted with CH₂Cl₂ (3 x 5 mL). The organic layers were combined, dried (Na₂SO₄), filtered, and concentrated. The product was purified via silica
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis

Gel flash chromatography (1:1 hexanes:EtOAc) to afford alcohol iii (28 mg, 93% yield) as a white solid. The solid was recrystallized from CH₂Cl₂/Et₂O/hexanes to provide white crystals suitable for X-ray analysis (see Appendix for X-ray structure report). ¹H NMR (500 MHz, CDCl₃) δ 7.19 (t, J = 7.7 Hz, 1H), 6.82 (d, J = 7.7 Hz, 1H), 6.73 (d, J = 7.7 Hz, 1H), 3.78 (m, 1H), 3.26 (s, 3H), 3.03 (dd, J = 7.3, 16.4 Hz, 1H), 2.80 (dd, J = 10.2, 16.4 Hz, 1H), 1.59 (s, 3H), 1.31 (s, 3); ¹³C NMR (125 MHz, CDCl₃) δ 176.1, 142.2, 130.1, 126.7, 125.8, 120.9, 105.6, 67.9, 40.2, 39.2, 38.0, 35.7, 26.6, 23.4, 19.1; IR (thin film/NaCl) 3054 (w), 2999 (w), 2936 (br m), 2880 (w), 2244 (w), 1688 (s), 1611 (s), 1469 (m), 1378 (m), 1339 (m), 1287 (m), 1175 (m), 1102 (m), 1041 (m), 961 (w), 914 (w), 760 (m), 732 (m) cm⁻¹; HRMS (EI) m/z found: 243.1261, [calc'd for C₁₅H₁₇NO₂ (M⁺): 243.1259]; m.p. 166-168°C.

Preparation of alcohol iv and ester v: Confirmation of the structure of ketone 14 via X-ray analysis.

To a solution of 14 (100 mg, 0.41 mmol) in CH₂Cl₂/MeOH (15 mL, 1:1) was added NaBH₄ (51 mg, 1.35 mmol, 3.3 equiv). After stirring for 45 min in the open air, the yellow reaction was concentrated, cooled to 0°C and treated with 1N HCl (5 mL). After stirring at 0°C for 20 min, the reaction was extracted with CH₂Cl₂ (3 x 10 mL), the organic layers were combined, dried (Na₂SO₄), filtered, and concentrated. The product was purified via silica gel flash chromatography using 3:2 hexanes:EtOAc to afford alcohol iv (73 mg, 73% yield) as a yellow solid.

To alcohol iv (52 mg, 0.21 mmol) in CH₂Cl₂ (10 mL) was added 4-bromobenzoyl chloride (52 mg, 0.24 mmol, 1.1 equiv), triethylamine (45μL, 0.32 mmol, 1.5 equiv), and finally DMAP (1 mg, 0.008 mmol, 0.04 equiv). The resulting solution was heated to reflux for 30 min. After cooling to rt, the reaction was cooled, adsorbed onto SiO₂ and
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...

chromatographed using hexanes:EtOAc (4:1). The derived benzoate v (60 mg, 67% yield) was recrystallized from ethyl acetate to furnish yellow crystals suitable for X-ray analysis (see Appendix for X-ray structure report).

Data for alcohol iv: \(^1\text{H NMR}\) (500 MHz, CDCl\(_3\)) \(\delta\) 7.34 (d, \(J = 8.5\) Hz, 1H), 6.93 (t, \(J = 9.5\) Hz, 1H), 6.84 (t, \(J = 9.9\) Hz, 1H), 6.76 (d, \(J = 8.8\) Hz, 1H), 4.84 (dd, \(J = 4.3, 11.2\) Hz, 1H), 3.51 (s, 3H), 2.17 (d, \(J = 5.6\) Hz, 1H), 2.08 (dd, \(J = 4.4, 8.0\) Hz), 1.86 (t, \(J = 11.9\) Hz, 1H), 1.52 (s, 3H), 1.38 (s, 1H); \(^{13}\text{C NMR}\) (125 MHz, CDCl\(_3\)) \(\delta\) 166.6, 142.4, 141.5, 137.3, 128.4, 127.4, 125.0, 120.7, 110.3, 68.8, 47.2, 31.9, 27.8, 27.4, 26.0; \(\text{IR}\) (thin film/NaCl) 3371 (br m), 2952 (w), 2862 (w), 2240 (w), 1646 (s), 1590 (m), 1546 (m), 1513 (m), 1446 (m), 1408 (m), 1358 (w), 1271 (w), 1188 (w), 1088 (m), 1035 (w), 915 (w), 732 (m) cm\(^{-1}\); HRMS (EI) m/z found: 243.1265, [calc'd for C\(_{15}\)H\(_{17}\)NO\(_2\) (M+)]: 243.1259]; m.p. 187-192\(^\circ\) C.

Data for benzoate v: \(^1\text{H NMR}\) (500 MHz, CDCl\(_3\)) \(\delta\) 7.95 (d, \(J = 8.4\) Hz, 2H), 7.61 (d, \(J = 8.5\) Hz, 2H), 7.03 (d, \(J = 8.7\) Hz, 1H), 6.96 (t, \(J = 10.0\) Hz, 1H), 6.76 (m, 2H), 6.30 (t, \(J = 6.3\) Hz, 1H), 3.55 (s, 3H), 2.12 (d, \(J = 6.7\) Hz, 2H), 1.55 (s, 3H), 1.5 (s, 3H); \(^{13}\text{C NMR}\) (125 MHz, CDCl\(_3\)) \(\delta\) 166.6, 165.3, 143.0, 137.2, 135.7, 131.9, 131.3, 129.5, 128.9, 128.5, 127.4, 126.9, 121.0, 110.0, 72.4, 42.8, 31.4, 27.9, 27.4, 26.1; \(\text{IR}\) (thin film/NaCl) 2957 (w), 2930 (w), 2865 (w), 2242 (w), 1719 (m), 1669 (s), 1591 (m), 1551 (w), 1516 (w), 1480 (w), 1443 (w), 1418 (w), 1362 (w), 1267 (s), 1192 (w), 1098 (m), 1011 (m), 920 (w), 849 (w), 753 (m), 733 (m) cm\(^{-1}\); HRMS (EI) m/z found: 425.0625, [calc'd for C\(_{22}\)H\(_{20}\)NO\(_3\)Br (M+): 425.0627]; m.p. 177-178\(^\circ\) C.
Preparation of diketone 16 and α-diazo ketone 4.

To a solution of ketone 15 (1.5 g, 6.2 mmol) in benzene (100 mL) was added celite (15 g) and pyridinium chlorochromate (PCC) (6.7 g, 31 mmol, 5 equiv). The reaction mixture was heated to reflux for 1 h. After this time, isopropyl alcohol (approx. 50 mL) was added and heating was continued for an additional 0.5 h. After cooling to rt, the mixture was filtered through a pad of celite topped with a thin layer of silica gel and MgSO₄. The filter pad was washed with Et₂O and EtOAc (500 mL each). The filtrate was concentrated in vacuo and the resulting brown residue 16 was then dissolved in THF (60 mL). This solution was treated with p-toluenesulfonylhydrazide (1.0 g, 5.6 mmol, 0.9 equiv) followed by a catalytic amount of conc. HCl (4 drops). The reaction was heated to reflux for 1 h and concentrated in vacuo. To a stirring solution of the crude mixture in CHCl₃ (150 mL) was added basic alumina (III) (200 mg). The reaction mixture was then directly placed onto a flash column containing basic alumina (III) (450 g) and eluted with CHCl₃ to furnish a brown solid. Trituration of the brown solid with cold Et₂O afforded α-diazo ketone 4 (978 mg, 59% yield, 2 steps) as a yellow solid.

Although used crude in this reaction, diketone 16 can be purified via silica gel flash chromatography to obtain an analytically pure sample. ¹H NMR (500 MHz, CDCl₃) δ 7.57 (d, J = 8.0 Hz, 1H), 7.43 (t, J = 7.9 Hz, 1H), 7.12 (d, J = 7.7 Hz, 1H), 3.35 (s, 3H), 3.25 (s, 1H), 1.69 (s, 3H), 1.39 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 189.2, 178.6, 171.9, 142.9, 132.9, 129.0, 128.6, 119.3, 112.6, 43.6, 42.9, 40.4, 27.1, 21.2, 17.0; IR (thin film/NaCl) 3025 (w), 2959 (w), 1704 (s), 1604 (m), 1485 (m), 1416 (m), 1380 (m), 1330 (m), 1264 (m), 1127 (w), 1100 (m), 1058 (w), 1035 (m), 1015 (m), 948 (w), 863 (w), 786 (m), 765 (m) cm⁻¹; HRMS (EI) m/z found: 255.0895, [calc’d for C₁₅H₁₅NO₃ (M⁺): 255.0895]; m.p. >150º C(dec).

Data for α-diazo ketone 4: ¹H NMR (500 MHz, CDCl₃) δ 7.58 (d, J = 7.7 Hz, 1H),
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis... S11

7.37 (t, J = 7.8 Hz, 1H), 7.00 (d, J = 7.6 Hz, 1H), 3.29 (s, 3H), 3.20 (s, 1H), 1.65 (s, 3H), 1.07 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 181.4, 174.6, 143.1, 129.2, 128.3, 127.6, 117.5, 111.0, 36.4, 32.7, 31.9, 26.8, 19.4, 16.7; IR (thin film/NaCl) 2928 (w), 2247 (w), 2089 (s), 1711 (s), 1632 (m), 1602 (s), 1478 (m), 1419 (m), 1374 (m), 1339 (m), 1305 (m), 1244 (m), 1225 (w), 1192 (w), 1137 (m), 1104 (w), 1034 (m), 996 (m), 913 (w), 858 (w), 794 (m), 732 (m) cm⁻¹; HRMS (EI) m/z found: 267.1009, [calc'd for C15H13N3O2 (M+): 267.1008]; m.p. >134° C(dec).

Preparation of trifluoroacetate vi.

The following experiment was performed to support the intermediacy of an enol in the reactions of diazo ketone 4 with alcohols. Although enols derived from the coupling of tertiary allylic alcohols with diazo ketone 4 can be trapped, the derived products are difficult to handle due to rapid Claisen rearrangement (e.g., reaction of diazo ketone 4 with 2-methyl-3-buten-2-ol; see below). The experiment using t-butanol (illustrated below) was performed since trapping of the derived enol affords a stable product.

A solution of α-diazo ketone 4 (50 mg, 0.19 mmol) and t-butanol (54 µL, 0.56 mmol, 3.0 equiv) in CH₂Cl₂ (10 mL) was cooled to -78 °C and treated with Rh₂(TFA)₄ (1.2 mg, 0.002 mmol, 1 mol %). The cold bath was removed and the reaction was allowed to warm slightly (approx. 3 min) until nitrogen evolution commenced and the reaction turned brown. Immediately after gas evolution ceased (ca. 1 min), trifluoroacetic anhydride (134 µL, 0.95 mmol, 5 equiv) and Et₃N (132 µL, 0.95 mmol, 5 equiv) were added rapidly. The resulting yellow reaction was allowed to warm to rt at which time it was concentrated under reduced pressure. The resulting residue was chromatographed on silica gel using hexanes:EtOAc (3:1) to provide enol ether vi (20 mg, 27% yield) as a white solid, and...
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ... S12

diazo ketone 4 (30 mg). The yield of the desired trapped product was 90% based on recovered starting material. Data for trifluoroacetate vi: \textbf{\textsuperscript{1}H NMR} (500 MHz, CDCl\textsubscript{3}) \(\delta\) 7.28 (t, \(J = 7.8\) Hz, 1H), 6.82 (d, \(J = 7.7\) Hz, 1H), 6.79 (d, \(J = 8.0\) Hz, 1H), 3.27 (s, 3H), 3.06 (s, 1H), 1.71 (br s, 3H), 1.42 (s, 9H), 0.97 (br s, 3H); \textbf{\textsuperscript{13}C NMR} (125 MHz, CDCl\textsubscript{3}) \(\delta\) 175.4, 154.9 (q, \(J_{\text{CF}} = 42.6\) Hz), 142.7, 141.6, 132.2, 127.7, 126.0, 120.0, 114.7 (q, \(J_{\text{CF}} = 285.6\) Hz), 112.8, 106.7, 82.2, 43.4, 42.7, 29.4, 26.6 (3), 20.9, 19.7 (br), 16.2 (br); \textbf{IR} (thin film, NaCl) 2697 (m), 2929 (m), 1800 (w), 1712 (s), 1656 (m), 1606 (m), 1466 (m), 1367 (m), 1341 (m), 1298 (m), 1172 (m), 1148 (m), 1021 (m), 770 (w) cm\(^{-1}\); \textbf{HRMS} (El) \(m/\zeta\) found: 409.1496, [calc'd for C\textsubscript{21}H\textsubscript{22}F\textsubscript{3}N\textsubscript{2}O\textsubscript{4}(M+)]: 409.1501; m.p. 156-159\(^{\circ}\) C.

Preparation of \(\alpha\)-hydroxy ketones 21 and vii: Reaction of \(\alpha\)-diazo ketone 4 with a tertiary allylic alcohol.

\[
\begin{align*}
\text{4} & \quad \text{Rh}_2(TFA)_4 \quad \text{CH}_2\text{Cl}_2 \quad \text{rt} \\
\text{Me} & \quad \text{Me} \\
\text{N} & \quad \text{H} \\
\text{O} & \quad \text{O} \\
\text{N} & \quad \text{N} \\
\text{OH} & \quad \text{OH} \\
\text{Me} & \quad \text{Me} \\
\text{M} & \quad \text{M} \\
\text{OH} & \quad \text{OH} \\
\text{Me} & \quad \text{Me} \\
\text{21} & + \\
\text{vii} & \\
\text{CH}_2\text{Cl}_2, \ 1.5 \text{d} \\
\end{align*}
\]

To \(\alpha\)-diazo ketone 4 (100 mg, 0.37 mmol) and 2-methyl-3-buten-2-ol (43 \(\mu\)L, 0.41 mmol, 1.1 equiv) in CH\textsubscript{2}Cl\textsubscript{2} (4 mL) at rt was added Rh\(_2\)(TFA)\(_4\) (2.4 mg, 0.004 mmol, 1 mol %). Gas evolution was noted and appeared to cease at which time the reaction was concentrated. NMR analysis of crude material indicated the presence of one compound, alcohol 21. The reaction was chromatographed on silica gel (5:1 hexanes:E\textsubscript{2}OAc) to yield alcohol 21 (99 mg, 81% yield) as a yellow residue, which now contained a trace of regioisomer vii. Upon stirring in CH\textsubscript{2}Cl\textsubscript{2} for 1.5 d or standing in CDCl\textsubscript{3}, alcohol 21 was completely converted to regioisomer vii (98 mg, 99% yield), a clear, pale yellow oil.

Alcohol 21 was triturated from Et\(_2\)O to furnish white crystals suitable for X-ray analysis (see Appendix for X-ray structure report). \textbf{\textsuperscript{1}H NMR} (500 MHz, CDCl\textsubscript{3}) \(\delta\) 7.32 (t, \(J = 7.9\) Hz, 1H), 7.17 (d, \(J = 7.8\) Hz, 1H), 6.81 (d, \(J = 7.6\) Hz, 1H), 4.37 (m, 1H), 3.45
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S13

(s, 1H), 3.30 (s, 3H), 3.02 (s, 1H), 2.51 (dd, J = 9.0, 13.3 Hz, 1H), 2.30 (dd, J = 6.7, 13.3 Hz, 1H), 1.53 (s, 3H), 1.50 (s, 3H), 1.32 (s, 3H), 1.11 (s, 3H); \(^{13}\text{C} \text{ NMR} \) (125 MHz, CDCl\(_3\)) \(\delta\) 208.6, 173.7, 141.6, 137.2, 133.9, 128.2, 123.5, 119.1, 115.3, 106.3, 77.7, 45.5, 45.1, 38.7, 37.9, 26.8, 22.6, 20.8, 18.3, 14.1; \text{IR} \) (thin film, NaCl) 3442 (br w), 2961 (w), 2932 (w), 2885 (w), 1703 (s), 1617 (m), 1478 (m), 1388 (m), 1338 (w), 1289 (m), 1080 (m), 1037 (m), 854 (w), 790 (m), 725 (m) cm\(^{-1}\); \text{HRMS} \text{ (EI) m/z} \) found: 325.1674, [calc'd for C\(_{20}\)H\(_{23}\)NO\(_3\)(M\(^+\)): 325.1678]; \text{m.p.} 120-123° C.

Data for alcohol vii: \(^{1}H \text{ NMR} \) (500 MHz, CDCl\(_3\)) \(\delta\) 7.37 (d, J = 7.4 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.03 (d, J = 7.3 Hz, 1H), 4.76 (m, 1H), 3.85 (br s, 1H), 3.30 (s, 3H), 2.60 (s, 1H), 2.11 (dd, J = 8.3, 14.2 Hz, 1H), 1.98 (dd, J = 7.4, 14.2 Hz, 1H), 1.58 (s, 3H), 1.49 (s, 3H), 1.30 (s, 3H), 1.04 (s, 3H); \(^{13}\text{C} \text{ NMR} \) (125 MHz, CDCl\(_3\)) \(\delta\) 199.1, 174.4, 142.5, 136.5, 133.2, 127.1, 125.4, 117.1, 116.1, 111.5, 77.6, 40.7, 39.0, 38.8, 36.5, 26.7, 25.7, 21.2, 17.7, 16.4; \text{IR} \) (thin film, NaCl) 2924 (br w), 1702 (s), 1613 (m), 1478 (w), 1377 (w), 1341 (w), 1285 (m), 1106 (w), 1027 (w) cm\(^{-1}\); \text{HRMS} \text{ (EI) m/z} \) found: 325.1680, [calc'd for C\(_{20}\)H\(_{23}\)NO\(_3\)(M\(^+\)): 325.1678].
Preparation of trifluoroacetate ix.

Due to the propensity of α-hydroxy ketone 21 to rearrange to vii, alcohol 21 was protected as the trifluoroacetate ix. Described below are two ways to access trifluoroacetate ix: first, by trapping the intermediate enol followed by Claisen rearrangement (Method A) and second by trapping alcohol 21 after Claisen rearrangement but prior to α-ketol rearrangement (Method B).

Method A: A solution of α-diazo ketone 4 (50 mg, 0.19 mmol) and 2-methyl-3-buten-2-ol (22 μL, 0.21 mmol, 1.1 equiv) in CH₂Cl₂ (5 mL) was cooled to -78°C and treated with Rh₂(TFA)₄ (1.2 mg, 0.002 mmol, 1 mol %). The cold bath was removed and the reaction was allowed to warm slightly (approx. 3 min) until nitrogen evolution commenced and the reaction turned brown. Immediately after gas evolution ceased, trifluoroacetic anyhydride (134 μL, 0.95 mmol, 5 equiv) followed by Et₃N (132 μL, 0.95 mmol, 5 equiv) were added rapidly. The resulting yellow reaction was allowed to warm to rt at which time it was concentrated and chromatographed on silica gel using hexanes:EtOAc (3:1) to yield an inseparable mixture of enol ether viii (assigned via NMR analysis) and ketone ix. Upon standing for 2 h in CDCl₃, the mixture of compounds undergoes complete conversion to ketone ix (55 mg, 69% yield) which can be isolated as a white solid.
Method B: A solution of α-diazo ketone 4 (50 mg, 0.19 mmol) and 2-methyl-3-buten-2-ol (22 μL, 0.21 mmol, 1.1 equiv) in CH₂Cl₂ (5 mL) at rt was treated with Rh₂(TFA)₄ (1.2 mg, 0.002 mmol, 1 mol %). After N₂ evolution ceased, the reaction was cooled to 0 °C and trifluoroacetic anhydride (134 μL, 0.95 mmol, 5 equiv) was added followed by the addition of triethylamine (132 μL, 0.95 mmol, 5 equiv). The reaction was stirred for 0.5 h (0 °C to rt) then concentrated in vacuo and subjected to silica gel chromatography (3:1 hexanes:EtOAc) to provide the protected alcohol ix (60 mg, 75% yield) as a white solid. 

**¹H NMR** (500 MHz, CDCl₃) δ 7.28 (t, J = 7.9 Hz, 1H), 7.04 (d, J = 7.7 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 4.59 (tt, J = 1.3, 7.9 Hz, 1H), 3.28 (s, 3H), 3.12 (s, 1H), 2.57 (dd, J = 7.8, 13.9 Hz, 1H), 2.50 (dd, J = 8.0, 13.9 Hz, 1H), 1.56 (s, 3H), 1.53 (s, 3H), 1.29 (s, 3H), 1.21 (s, 3H); 

**¹³C NMR** (125 MHz, CDCl₃) δ 197.3, 173.8, 154.9 (q, JCF = 43.0), 142.9, 138.9, 131.4, 128.6, 124.6, 117.0, 116.6 (q, JCF = 285.6), 113.9, 107.1, 87.7, 46.9, 41.4, 40.9, 38.7, 26.8, 25.8, 21.9, 18.8, 17.4; 

**IR** (thin film, NaCl) 2924 (w), 1794 (m), 1717 (s), 1616 (w), 1462 (w), 1372 (w), 1280 (w), 1223 (m), 1161 (m), 1046 (w), 983 (w), 777 (w) cm⁻¹; 

**HRMS (EI)** m/z found: 421.1505, [calc'd for C₂₂H₂₂F₃NO₄(M⁺): 421.1501]; 

**m.p.** 89-94°C.
Preparation of trifluoroacetate x.

Given the possibility that 21 could undergo isomerization to vii prior to acylation (to furnish x instead of the desired ix), an authentic sample of the potential end product x was prepared. Comparison of the data obtained for ix and x clearly indicated they are different.

A solution of alcohol vii (30 mg, 0.09 mmol) in CH$_2$Cl$_2$ (5 mL) at 0 °C was treated with trifluoroacetic anhydride (65 μL, 0.46 mmol, 5 equiv) and triethylamine (64 μL, 0.46 mmol, 5 equiv). The reaction was stirred for 0.5 h (0 °C to rt) and then concentrated in vacuo and chromatographed (3:1 hexanes:EtOAc) to provide ketone x (35 mg, 92% yield) as a clear colorless oil which solidified upon cooling. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.42 (d, $J = 7.8$ Hz, 1H), 7.37 (m, $J = 7.8$ Hz, 1H), 7.05 (d, $J = 7.5$ Hz, 1H), 4.61 (t, $J = 7.7$ Hz, 1H), 3.32 (s, 3H), 3.14 (s, 1H), 2.70 (d, $J = 7.8$ Hz, 2H), 1.57 (s, 3H), 1.40 (s, 3H), 1.35 (s, 3H), 1.12 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 189.5, 173.6, 155.9 (q, $J_{CF}$= 42.2 Hz), 142.5, 138.0, 131.7, 127.7, 126.1, 117.9, 114.4 (q, $J_{CF}$= 286.6 Hz), 114.2, 111.7, 89.2, 38.1, 37.5, 36.9, 36.4, 26.9, 25.5, 20.7, 17.7, 16.9; IR (thin film, NaCl) 2933 (br w), 1787 (m), 1713 (s), 1603 (m), 1358 (w), 1337 (m), 1159 (s), 1038 (m) cm$^{-1}$; HRMS (EI) m/z found: 421.1503, [calc'd for C$_{22}$H$_{22}$F$_3$NO$_4$(M+): 421.1501]; m.p. 64-68° C.
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S17

Reaction of α-diazo ketone 4 with a primary allylic alcohol: Preparation of ring-opened allylic enol ether 22.

To a solution of diazo ketone 4 (2.2 g, 8.2 mmol) and allyl alcohol (2.8 mL, 41.2 mmol, 5 equiv) in CH₂Cl₂ (82 mL) at rt was added Rh₂(OAc)₄ (40 mg, 0.09 mmol, 1 mol %). The solution was stirred for 5 min and then concentrated under reduced pressure. The resulting residue was chromatographed (2:1 hexanes:EtOAc) to afford 22 (2.3 g, 95% yield) as a yellow solid. ¹H NMR (500 MHz, CDCl₃) δ 7.65 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 7.9 Hz, 1H), 6.99 (d, J = 7.7 Hz, 1H), 6.07-5.99 (comp m, 1H), 5.78 (s, 1H), 5.38 (dd, J = 1.5, 17.2 Hz, 1H), 5.23 (dd, J = 1.3, 10.4 Hz, 1H), 4.37 (dd, J = 1.3, 5.5 Hz, 2H), 3.74 (s, 1H), 3.25 (s, 3H), 1.73 (s, 3H), 0.85 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 184.7, 173.9, 148.8, 143.7, 133.3, 133.2, 133.1, 128.5, 126.6, 122.3, 117.9, 111.2, 70.7, 52.7, 37.9, 28.7, 26.4, 21.8; IR (thin film/NaCl) 2943 (w), 2872 (w), 1706 (s), 1689 (m), 1650 (s), 1462 (m), 1341 (m), 1299 (m) cm⁻¹; HRMS (EI) m/z found: 297.1371, [calc'd for C₁₈H₁₉NO₃ (M⁺): 297.1365]; m.p. 140-142°C.

Preparation of allylic alcohol 23.

To ethyl-3-methyl-4-oxocrotonate (xi) (1 g, 7.0 mmol) in CH₂Cl₂ and MeOH (70 mL, 1:1) was added NaBH₄ (530 mg, 14.0 mmol, 2 equiv). After stirring for 5 min, the solvents were removed in vacuo and the derived residue was cooled to 0°C and treated with 1N HCl (50 mL). The reaction was stirred for 15 min and then extracted with CH₂Cl₂ (3 x 100 mL). The combined organic layers were dried (MgSO₄), filtered, then
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S18

conzentrated to yield an oil which was used in the next step without further purification.

A solution of the derived alcohol in CH₂Cl₂ (70 mL) was treated with TBSCl (1.1 g, 7.4 mmol, 1.1 equiv) and imidazole (572 mg, 8.4 mmol, 1.2 equiv). A white precipitate rapidly formed and the reaction was stirred for 20 min. After this time, 1N HCl (50 mL) was added and the layers were separated. The organic layer was washed with 1N HCl (3 x 50 mL) then brine (3 x 50 mL). Drying (K₂CO₃), filtering, and concentrating afforded an oil which was used crude in the next step.

To a 1.4 M solution of methylmagnesium bromide in toluene/THF (25 mL, 35 mmol, 5 equiv) and ether (35 mL) was added a solution of the crude TBS-protected alcohol in ether (35 mL). After 5 minutes, the reaction was quenched with ice (750 mg). Extracting with ether (3 x 100 mL), drying (Na₂SO₄) and concentrating provided an oil which was subjected to silica gel chromatography (5:1 pentane:Et₂O) to yield tertiary alcohol 23 (1.1 g, 64% overall yield) as a clear, colorless oil. ³¹H NMR (500 MHz, CDCl₃) δ 5.51 (m, 1H), 3.89 (s, 2H), 2.00 (br s, 1H), 1.75 (s, 3H), 1.30 (m, 6H), 0.85 (s, 9H), 0.005 (s, 3H), 0.002 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 135.5, 131.1, 70.7, 68.7, 30.9, 25.8, 18.2, 13.9, -4.75; IR (thin film, NaCl) 3432 (br w), 2959 (s), 2934 (s), 2864 (s), 1693 (w), 1476 (m), 1463 (m), 1377 (m), 1358 (m), 1254 (s), 1144 (m), 1093 (s), 1008 (w), 843 (s), 774 (s) cm⁻¹; HRMS (EI) m/z found: 243.1774, [calc'd for C₁₃H₂₇SiO₂(M–H): 243.1780].
Preparation of diastereomeric alcohols 26 and 27.

To a solution of $\alpha$-diazo ketone 4 (50 mg, 0.19 mmol) and alcohol 23 (46 mg, 0.19 mmol, 1 equiv) in CH$_2$Cl$_2$ (5 mL) at rt was added Rh$_2$(TFA)$_4$ (1.2 mg, 0.002 mmol, 1 mol %). After 5 min, the reaction was concentrated under reduced pressure and chromatographed (10:1 hexanes:EtOAc) to yield a residue (75 mg) which contained a mixture of diastereomeric alcohols 24 and 25 (2:1, 24:25, 70% yield based on NMR integrations). Efforts to obtain analytically pure samples of 24 and 25 using HPLC (3:1 hexanes:EtOAc) resulted in the isolation of diastereomeric alcohols 26 and 27 (2:1 ratio, 26:27), which arise via $\alpha$-ketol rearrangement of alcohols 24 and 25, respectively.

The first compound to elute was alcohol 26, the $\alpha$-ketol rearrangement product of 24. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.37 (d, $J = 7.9$ Hz, 1H), 7.31 (t, $J = 7.7$ Hz, 1H), 6.99 (d, $J = 7.6$ Hz, 1H), 5.20 (s, 1H), 4.95 (s, 1H), 3.50 (d, $J = 10.1$ Hz, 1H), 3.46 (d, $J = 9.9$ Hz, 1H), 3.31 (s, 3H), 2.91 (s, 1H), 1.61 (s, 3H), 1.52 (s, 3H), 1.51 (s, 3H), 1.09 (s, 3H), 0.91 (s, 9H), 0.62 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 198.8, 174.6, 142.4, 134.0, 133.8, 128.5, 127.0, 124.8, 116.7, 110.8, 81.7, 69.2, 48.6, 38.8, 37.6, 37.5, 29.1, 26.8, 25.8, 21.9, 19.3, 18.3, 17.0, -4.3, -4.4; IR (thin film, NaCl) 3470 (br w), 2942 (m), 2870 (m), 2248 (w), 1704 (s), 1617 (m), 1474 (m), 1387 (w), 1346 (s, m), 1270 (m), 1072 (m), 1022 (m), 922 (w), 846 (m), 783 (m).
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ... S20

763 (m) cm⁻¹; HRMS (EI) m/z found: 483.2797, [calc'd for C_{28}H_{41}NO_{4}Si(M⁺): 483.2805].

The second compound to elute was alcohol 27, the α-ketol rearrangement product of 25. ¹H NMR (500 MHz, CDCl₃) δ 7.37 (d, J = 7.5 Hz, 1H), 7.32 (t, J = 7.7 Hz, 1H), 6.97 (d, J = 7.2 Hz, 1H), 4.86 (s, 1H), 3.74 (s, 1H), 3.41 (d, J = 10.0 Hz, 1H), 3.28 (s, 3H), 3.13 (d, J = 10.0 Hz, 1H), 2.78 (s, 1H), 1.62 (s, 3H), 1.54 (s, 3H), 1.39 (s, 3H), 1.11 (s, 3H), 1.05 (s, 3H), 0.94 (s, 9H), 0.11 (s, 3H), 0.04 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 199.2, 174.7, 142.4, 133.9, 133.7, 128.6, 126.9, 124.5, 116.4, 110.7, 82.4, 69.8, 48.6, 38.2, 37.6, 37.2, 28.7, 26.7, 25.8, 21.8, 19.3, 18.3, 18.2, 17.0, -4.2, -4.4; IR (thin film, NaCl) 3472 (br m), 2936 (m), 2851 (m), 1709 (s), 1687 (s), 1611 (m), 1468 (m), 1335 (m), 1284 (m), 1254 (m), 1069 (m), 1009 (m), 845 (m), 780 (m) cm⁻¹; HRMS (EI) m/z found: 483.2808, [calc'd for C_{28}H_{41}NO_{4}Si(M⁺): 483.2805].

Preparation of hemiacetal xii alcohol xiii: Confirmation of the [3,3]/[1,2] event via X-ray analysis.

To a solution of TBS-alcohol 26 (246 mg, 0.51 mmol) in THF (5 mL) at 0 °C was slowly added excess HF/Py (~5 mL of a 23% HF/Py solution). After stirring for 3 h and warming from 0 °C to rt, a saturated aqueous solution of NaHCO₃ was added until CO₂ evolution ceased (~250 mL). The reaction was extracted with EtOAc (10 x 50 mL) and the combined organic layers were washed with CuSO₄ solution (3 x 20 mL), dried (Na₂SO₄), filtered and concentrated. The derived oil was purified via silica gel chromatography (3:1 hexanes:EtOAc) to yield a white solid (114 mg, 61% yield) which was recrystallized from methanol to provide white crystals suitable for X-ray analysis (see Appendix for X-ray structure report). Although recrystallization provided hemiacetal xii for X-ray analysis, both xii and xiii were observed in the ¹H and ¹³C NMR spectra in a 1:1.5 ratio. ¹H
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S21

NMR (500 MHz, CDCl₃) δ 7.39-7.25 (comp m, 4H), 7.02 (d, J = 7.3 Hz, 1H), 6.77 (d, J = 7.3 Hz, 1H), 5.42 (s, 1H), 4.95 (br s, 1H), 4.56 (s, 1H), 4.40 (br s, 1H), 4.25 (d, J = 8.1 Hz, 1H), 3.95 (d, J = 8.1 Hz, 1H), 3.88 (d, J = 11.4 Hz, 1H), 3.45 (d, J = 11.4 Hz, 1H), 3.30 (s, 3H), 3.25 (s, 3H), 2.95 (br s, 1H), 2.87 (s, 1H), 2.43 (s, 1H), 1.81 (s, 3H), 1.63 (s, 3H), 1.61 (s, 3H), 1.56 (s, 3H), 1.42 (s, 3H), 1.37 (s, 3H), 1.32 (s, 3), 1.26 (s, 1H), 1.06 (s, 3H), 0.87 (s, 3H), 0.67 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 198.8, 175.1, 174.4, 142.5, 141.6, 136.7, 135.2, 134.3, 134.2, 127.7, 127.5, 127.2, 124.3, 124.0, 123.5, 117.7, 116.7, 111.3, 106.6, 102.5, 83.8, 82.3, 75.2, 68.2, 53.8, 49.4, 38.9, 38.6, 37.8, 37.6, 36.5, 36.4, 29.0, 27.9, 26.8, 26.6, 22.8, 21.9, 21.1, 19.5, 19.1, 18.6, 18.4, 16.8; IR (thin film, NaCl) 3398 (br w), 2930 (br w), 2248 (w), 1689 (s), 1611 (m), 1470 (m), 1378 (m), 1340 (m), 1288 (m), 1058 (m), 1039 (m), 976 (w), 914 (m), 783 (m), 732 (m) cm⁻¹; HRMS (EI) m/z found: 369.1945, [calc'd for C₂₂H₂₇NO₄(M⁺): 369.1940]; m.p. 151-153° C(dec).

Preparation of alcohol xiv.

To a stirred solution of ketone 22 (1.92 g, 6.5 mmol) in benzene (64 mL) at 0 °C was added 16.2 mL of a 1.0 M solution of ethynyl Grignard in THF (16.2 mmol, 2.5 equiv). After stirring for 10 minutes, the reaction was diluted with H₂O (250 mL) and extracted with ethyl acetate (4 × 100 mL). The organic layers were combined, washed with brine (100 mL), dried (Na₂SO₄), concentrated and chromatographed (3:1 hexanes:EtOAc) to provide xiv (1.9 g, 91% yield) as a white solid. ¹H NMR (500 MHz, CDCl₃) δ 7.51 (d, J = 8.1 Hz, 1H), 7.34 (t, J = 7.9 Hz, 1H), 6.80 (d, J = 7.7 Hz, 1H), 6.06-5.99 (comp m, 1H), 5.39 (dq, J = 1.4, 17.3 Hz, 1H), 5.31 (dq, J = 1.2, 10.4 Hz, 1H), 4.53 (s, 1H), 4.46 (s, 1H), 4.40 (dd, J = 5.6, 12.2 Hz, 1H), 4.31 (dd, J = 5.6, 12.2 Hz, 1H), 3.97 (s, 1H), 3.22 (s, 3H), 2.51 (s, 1H), 1.6 (s, 3H), 0.68 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.8, 148.4, 144.1, 138.0, 132.4, 128.4, 124.2, 118.4, 117.5, 113.2,
Preparation of alcohols 28 and 29.

A solution of enol ether xiv (900 mg, 2.8 mmol) in xylenes (50 mL) was submersed into an oil bath that had been preheated to 145 °C. The solution was refluxed for 10 minutes, cooled, and concentrated. The resulting residue was chromatographed (2:1 hexanes:EtOAc) to afford ketone 28 (860 mg, 96% yield) and ketone 29 (25 mg, 2% yield) as white solids.

The first compound to elute was ketone 28. $^1$H NMR (500 MHz, CDCl₃) δ 7.47 (dd, $J = 1.0$, 8.0 Hz, 1H), 7.43 (t, $J = 7.8$ Hz, 1H), 6.84 (d, $J = 7.5$ Hz, 1H), 5.69-5.61 (comp m, 1H), 5.07 (dd, $J = 1.2$, 17.0 Hz, 1H), 4.98 (d, $J = 10.0$ Hz, 1H), 3.26 (s, 1H), 3.20 (s, 3H), 3.03 (dd, $J = 2.7$, 11.6 Hz, 1H), 2.78 (s, 1H), 2.73 (q, $J = 12.1$ Hz, 1H), 2.19 (dd, $J = 4.9$, 12.4 Hz, 1H), 1.43 (s, 3H), 0.78 (s, 3H); $^{13}$C NMR (125 MHz, CDCl₃) δ 203.3, 175.1, 144.1, 135.9, 135.7, 129.5; 122.1, 120.0, 117.1, 108.0, 81.1, 78.1, 76.4, 55.1, 51.8, 41.0, 31.2, 26.2, 21.8, 20.6; IR (thin film, NaCl) 2972 (bw), 2936 (w), 1693 (s), 1609 (s), 1467 (s), 1347 (m), 1310. w, 915 (w), 732 (m) cm⁻¹; HRMS (EI) m/z found: 323.1526, [calc'd for C₂₉H₂₁NO₃ (M+): 323.1521]; m.p. 194-196°C (dec).

The second compound to elute was ketone 29. The solid was recrystallized from CH₂Cl₂/hexanes to furnish crystals suitable for X-ray analysis (see Appendix for X-ray structure report). $^1$H NMR (500 MHz, CDCl₃) δ 7.44 (d, $J = 8.1$ Hz, 1H), 7.36 (t, $J = 7.9$ Hz, 1H), 6.79 (d, $J = 7.7$ Hz, 1H), 5.74-5.68 (comp m, 1H), 5.12 (dd, $J = 1.2$, 8.0 Hz, 1H), 4.97 (d, $J = 10.0$ Hz, 1H), 3.28 (s, 1H), 3.20 (s, 3H), 2.90 (dd, $J = 4.9$, 12.4 Hz, 1H), 1.43 (s, 3H), 0.78 (s, 3H); $^{13}$C NMR (125 MHz, CDCl₃) δ 203.3, 175.1, 144.1, 135.9, 135.7, 129.5; 122.1, 120.0, 117.1, 108.0, 81.1, 78.1, 76.4, 55.1, 51.8, 41.0, 31.2, 26.2, 21.8, 20.6; IR (thin film, NaCl) 2972 (bw), 2936 (w), 1693 (s), 1609 (s), 1467 (s), 1347 (m), 1310. w, 915 (w), 732 (m) cm⁻¹; HRMS (EI) m/z found: 323.1526, [calc'd for C₂₉H₂₁NO₃ (M+): 323.1521]; m.p. 194-196°C (dec).
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S23

17.1 Hz, 1H), 5.04 (d, J = 10.3 Hz, 1H), 4.40 (s, 1H), 4.12 (dd, J = 2.7, 11.1 Hz, 1H), 3.82 (s, 1H), 3.20 (s, 3H), 2.80 (s, 1H), 2.65-2.59 (comp m, 1H), 2.49-2.44 (comp m, 1H), 1.72 (s, 3H), 0.47 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 204.4, 174.5, 144.3, 135.8, 135.4, 129.4, 123.2, 117.0, 116.8, 108.0, 81.2, 76.8, 76.2, 58.4, 55.4, 44.4, 29.8, 26.4, 24.3, 16.4; IR (thin film/NaCl) 2973 (w), 1702 (s), 1604 (m), 1468 (m), 1340 (m), 765 (s) cm⁻¹; HRMS (EI) m/z found: 323.1521, [calc'd for C₂₀H₂₃NO₃ (M⁺): 323.1521]; m.p. 189-192° C.

Preparation of diene xv.

To a solution of acetylene 28 (500 mg, 1.5 mmol) in EtOAc (30 mL) was added Lindlar's catalyst (100 mg) and the mixture was placed under 1 atmosphere of H₂. The reaction was carefully monitored by TLC (3:1 hexanes:EtOAc) and upon completion (ca. 15 min) was filtered through celite. The filtrate was evaporated and the residue purified by silica gel chromatography (3:1 hexanes:EtOAc) to afford diene xv (495 mg, 99% yield) as a white solid. 1H NMR (500 MHz, CDCl₃) δ 7.38 (t, J = 7.9 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 6.79 (d, J = 7.7 Hz, 1H), 6.20 (dd, J = 10.8, 17.2 Hz, 1H), 5.71-5.63 (comp m, 1H), 5.29 (d, J = 10.8 Hz, 1H), 5.24 (d, J = 17.2 Hz, 1H), 5.12 (dd, J = 1.1, 16.9 Hz, 1H), 4.98 (d, J = 10.0 Hz, 1H), 3.20 (s, 3H), 3.13 (brs, 1H), 3.08 (dd, J = 2.4, 11.6 Hz, 1H), 2.68-2.61 (compm, 1H), 2.14-2.13 (br s, 1H), 1.41 (s, 3H), 0.80 (s, 3H); 13C NMR (125 MHz, CDCl₃) δ 208.1, 175.3, 144.1, 138.1, 136.5, 136.4, 129.2, 122.6, 120.3, 116.9, 115.3, 107.3, 82.1, 52.1, 41.1, 30.9, 29.7, 26.1, 21.7, 20.5; IR (thin film/NaCl) 2969 (w), 2242 (w), 1717 (s), 1691 (s), 1614 (s), 1464 (m), 1335 (m), 908 (m), 738 (m) cm⁻¹; HRMS (EI) m/z found: 325.1677, [calc'd for C₂₀H₂₃NO₃ (M⁺): 325.1678]; m.p. 148-149° C.
Preparation of olefin 3.

To a solution of diene xv (25 mg, 0.08 mmol) in CH₂Cl₂ (30 mL) was added Grubbs' catalyst (13 mg, 0.015 mmol, 20 mol%). The resulting solution was refluxed for 24 h, cooled and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (2:1 hexanes:EtOAc) to afford recovered diene xv (5.2 mg, 21%) and the desired olefin 3 (12.9 mg, 56% yield) as a white solid (71% yield based on recovered starting material).

The first compound to elute was diene xv.

The second compound to elute was olefin 3. **¹H NMR** (500 MHz, CDCl₃) δ 7.45 (d, J = 8.1 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 6.77 (d, J = 7.7 Hz, 1H), 5.94-5.91 (comp m, 1H), 5.61 (dd, J = 2.6, 9.7 Hz, 1H), 4.24 (s, 1H), 3.78 (s, 1H), 3.20 (s, 3H), 3.03-2.98 (comp m, 1H), 2.80-2.74 (comp m, 2H), 1.56 (s, 3H), 0.62 (s, 3H); **¹³C NMR** (125 MHz, CDCl₃) δ 208.6, 175.2, 144.1, 135.8, 130.0, 129.0, 126.3, 123.9, 117.9, 107.6, 72.1, 49.7, 40.8, 29.5, 26.3, 26.2, 22.8; **IR** (thin film/NaCl) 3032 (w), 2930 (w), 2248 (w), 1708 (2), 1597 (m), 1471 (m), 1340 (m), 1146 (m), 725 (m) cm⁻¹; **HRMS** (EI) m/z found: 197.1362, [calc'd for C₁₈H₁₉NO₃ (M+)]: 297.1365; **m.p. >235° C(dec).**
Preparation of diol xvi: Confirmation of the structure of olefin 3 via X-ray analysis.

A solution of olefin 3 (16 mg, 0.05 mmol) in methanol and CH₂Cl₂ (1 mL, 1:1) was treated with sodium borohydride (1.9 mg, 0.08 mmol, 1.7 equiv) at 0 °C. The resulting slurry was stirred for 10 min when the reaction was quenched by the addition of silica gel (ca. 100 mg). The mixture was concentrated under reduced pressure and chromatographed (EtOAc) to yield alcohol xvi (15.2 mg, 95% yield) as a white crystalline solid. Recrystallization from Et₂O/hexanes provided crystals suitable for single crystal X-ray analysis (see Appendix for X-ray structure report). \(^1\)H NMR (500 MHz, CDCl₃) δ 7.40 (dd, \(J = 1.0, 8.0 \) Hz, 1H), 7.34 (t, \(J = 7.6 \) Hz, 1H), 6.76 (d, \(J = 7.7 \) Hz, 1H), 5.86 (ddd, \(J = 9.8, 5.4, 2.0 \) Hz, 1H), 5.42 (dd, \(J = 2.8, 9.9 \) Hz, 1H), 4.31 (t, \(J = 4.0 \) Hz, 1H), 3.60 (s, 1H), 3.18 (s, 3H), 2.74 (dd, \(J = 5.4, 19.2 \) Hz, 1H), 2.57 (s, 1H), 2.55-2.49 (comp m, 1H), 2.16 (t, \(J = 5.7 \) Hz, 1H), 2.10 (d, \(J = 4.0 \) Hz, 1H), 1.47 (s, 3H), 0.86 (s, 3H); \(^13\)C NMR (125 MHz, CDCl₃) δ 176.3, 144.0, 138.5, 128.5, 128.1, 127.3, 124.8, 119.4, 107.0, 80.0, 75.3, 51.4, 49.8, 37.1, 29.1, 28.3, 26.2, 24.6; IR (thin film/NaCl) 3413 (bw), 2969 (w), 1682 (s), 1598 (m), 1469 (m), 1351 (m), 1036 (w) cm⁻¹; HRMS (EI) \(m/z\) found: 299.1508, [calc’d for C₁₈H₂₁NO₃ (M⁺): 299.1521]; m.p. >235° C(dec).
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ... S26

APPENDIX

X-RAY STRUCTURE REPORT

Data Collection

A colorless prism crystal of C_{15}H_{15}NO_{2} having approximate dimensions of 0.21 x 0.38 x 0.40 mm was mounted on a glass fiber. All measurements were made on a Nonius KappaCCD diffractometer with graphite monochromated Mo-Kα radiation.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using ten (1° in ω, 10s exposure, de-zingered) data frames, corresponded to a primitive monoclinic cell with dimensions: a = 7.282(1) Å, b = 16.256(1) Å, β = 91.46(1)°, c = 10.196(1) Å, V = 1206.6(2) Å³. For Z = 4 and F.W. = 241.29, the calculated density is 1.33 g/cm³. The systematic absences of: h0l: l = 2n+1; 0k0: k = 2n+1, uniquely determine the space group to be: P2₁/c (#14).

The data were collected at a temperature of 23 ± 1° C to a maximum 2θ value of 52.7°. One phi scan consisting of 163 data frames and one omega scan consisting of 85 data frames, respectively, were collected with a scan width of 1° and a detector-to-crystal distance, Dx, of 35mm. Each frame was exposed twice (for the purpose of de-zingering) for 60s. The data frames were processed and scaled using the DENZO software package. (Z. Otwinowski and W. Minor, “Processing of X-Ray Diffraction Data Collected in Oscillation Mode,” Methods in Enzymology, vol. 276: Macromolecular Crystallography,
**Data Reduction**

A total of 2439 reflections was collected. No decay correction was applied. The linear absorption coefficient, \( \mu \), for Mo-K\( \alpha \) radiation is 0.9 cm\(^{-1} \) and no absorption correction was applied. The data were corrected for Lorentz and polarization effects.

**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. In the case of the methyl group hydrogen atoms, one hydrogen was located in the difference map and included at an idealized distance to set the orientation of the other two hydrogen atoms. The final cycle of full-matrix least-squares refinement\(^3 \) was based on 1988 observed reflections (I > 3.00\( \sigma \)(I)) and 163 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

\[
R = \frac{\sum |F_{o} - |F_{c}| |}{\sum |F_{o}|} = 0.044
\]

\[
R_{w} = \left[ \frac{\sum w (|F_{o}| - |F_{c}|)^2}{\sum w |F_{o}|^2} \right]^{1/2} = 0.068
\]

The standard deviation of an observation of unit weight\(^4 \) was 4.05. The weighting scheme was based on counting statistics and included a factor (p = 0.010) to downweight the intense reflections. Plots of \( \sum w (|F_{o}| - |F_{c}|)^2 \) versus \( |F_{o}| \), reflection order in data collection, \( \sin \theta/\lambda \) and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.21 and -0.15 e/Å\(^3 \), respectively.

Neutral atom scattering factors were taken from Cromer and Waber\(^5 \). Anomalous dispersion effects were included in Fcalc; the values for \( \Delta f' \) and \( \Delta f'' \) 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.
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S28

References


(3) Least-Squares:

Function minimized $\sum w(|F_{o}|-|F_{c}|)^2$

where $w = 4F_{o}^2/\sigma^2(F_{o})$

and $\sigma^2(F_{o}) = [S^2(C+R^2B)+(pF_{o})^2]/Lp^2$

$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:

$[\sum w(|F_{o}|-|F_{c}|)^2/(N_{o}-N_{v})]^{1/2}$

where $N_{o} = $ number of observations

$N_{v} = $ number of variables


Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S29

Experimental Details

A. Crystal Data

Empirical Formula \( \text{C}_{15}\text{H}_{15}\text{NO}_{2} \)

Formula Weight 241.29

Crystal Color, Habit colorless, prism

Crystal Dimensions 0.21 X 0.38 X 0.40 mm

Crystal System monoclinic

Lattice Parameters

\[ a = \ 7.282(1)\text{Å} \]

\[ b = \ 16.256(1) \text{Å} \]

\[ c = \ 10.196(1) \text{Å} \]

\[ \beta = \ 91.46(1)^{\circ} \]

\[ V = \ 1206.6(2) \text{Å}^3 \]

Space Group \( \text{P2}_1/c \) (#14)

Z value 4

\( \text{D}_{\text{calc}} \) 1.328 g/cm\(^3\)

\( F(000) \) 512.00

\( \mu(\text{MoK\alpha}) \) 0.88 cm\(^{-1}\)

B. Intensity Measurements

Diffractometer Nonius KappaCCD

Radiation MoK\( \alpha \) (\( \lambda = 0.71069 \) Å)

graphite monochromated

Crystal to Detector Distance 35 mm

Temperature 23.0\(^\circ\)C

Scan Type \( \omega \)

Scan Rate 60s/frame

Scan Width 1\(^\circ\)/frame

2\( \theta \)max 52.7\(^\circ\)

No. of Reflections Measured Total: 2439

Corrections Lorentz-polarization

C. Structure Solution and Refinement

Structure Solution Direct Methods (SIR92)

Refinement Full-matrix least-squares
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S30

Function Minimized
Least Squares Weights
p-factor
Anomalous Dispersion
No. Observations (I>3.00σ(I))
No. Variables
Reflection/Parameter Ratio
Residuals: R; Rw
Goodness of Fit Indicator
Max Shift/Error in Final Cycle
Maximum peak in Final Diff. Map
Minimum peak in Final Diff. Map

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Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S31

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Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S32

X-RAY STRUCTURE REPORT

Data Collection

A colorless prism crystal of C₁₅H₁₇NO₂ having approximate dimensions of 0.21 X 0.39 X 0.48 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC5S diffractometer with graphite monochromated Mo Kα 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 5.81 < 2θ < 20.97° corresponded to a monoclinic cell with dimensions: a = 8.849 (3)Å, b = 16.577 (3)Å, c = 9.522 (2)Å, β = 115.34 (2)°, and V = 1262 (1)Å³. For Z = 4 and F.W. = 243.30 the calculated density is 1.280 g/cm³. Based on the systematic absences of: h0l: l = 2n+1; 0k0: k = 2n+1; and the successful solution and refinement of the structure the space group was determined to be: P2₁/c (#14).

The data were collected at a temperature of 23 ± 1°C using the ω-2θ scan technique to a maximum 2θ value of 50.0°. Omega scans of several intense reflections made prior to data collection had an average width at half-height of 0.19° with a take-off angle of 6.0°. Scans of (1.57 + 0.30 tan θ)° were made at a speed of 8.0° /min (in omega). The weak reflections (I < 10.0σ(I)) were rescanned (maximum of 2 rescans) and the counts were accumulated to assure good counting statistics. Stationary background counts were recorded on each side of the reflection. The ratio of peak counting time to background counting time was 2:1. The diameter of the incident beam collimator was 0.5 mm and the crystal to detector distance was 285.0 mm.
Data Reduction

Of the 2478 reflections which were collected 2323 were unique ($R_{int} = 0.031$). The intensities of three representative reflections which were measured after every 150 reflections remained constant throughout data collection indicating crystal and electronic stability (no decay correction was applied).

The linear absorption coefficient for Mo Kα is 0.8 cm$^{-1}$. Azimuthal scans of several reflections indicated no need for an absorption correction. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods$^1$. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were located in subsequent difference maps and refined isotropically. The final cycle of full-matrix least-squares refinement$^2$ was based on 1023 observed reflections ($I > 3.00\sigma(I)$) and 231 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R = \frac{\sum |F_o| - |F_c|}{\sum |F_o|} = 0.038$$
$$R_w = \left\{ \frac{\sum w(F_o - F_c)^2}{\sum w(F_o)^2} \right\}^{1/2} = 0.040$$

The standard deviation of an observation of unit weight$^3$ was 1.39. The weighting scheme was based on counting statistics and included a factor ($p = 0.02$) to downweight the intense reflections. Plots of $\sum w(F_o - F_c)^2$ versus $F_o$, reflection order in data collection, sin $\theta/\lambda$, and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.15 and -0.14 e-/Å$^3$ respectively.

Neutral atom scattering factors were taken from Cromer and Waber$^4$. Anomalous dispersion effects were included in Fcalc$^5$; the values for $\Delta f$ and $\Delta f''$ were those of Cromer$^6$. All calculations were performed using the TEXSAN$^7$ crystallographic software package of Molecular Structure Corporation.
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S34

References

(1) Structure Solution Methods:
    MITHRIL

(2) Least-Squares:
    Function minimized: $\Sigma w (|F_{o}\omega| - |F_{c}\omega|)^2$
    where: $w = 4F_0^2/\sigma^2(F_0^2)$
    $\sigma^2(F_0^2) = [S^2(C+R^2B) + (pF_0^2)^2]/Lp^2$
    $S$ = 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

(3) Standard deviation of an observation of unit weight:
    $[\Sigma w(|F_{o}\omega| - |F_{c}\omega|)^2/(N_0 - N_v)]^{1/2}$
    where: $N_0$ = number of observations $N_v$ = number of variables


Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S35

Experimental Details

A. Crystal Data

Empirical Formula  \( \text{C}_{15}\text{H}_{17}\text{NO}_{2} \)

Formula Weight  243.30

Crystal Color/Habit  colorless prisms

Crystal Dimensions (mm)  0.21 X 0.39 X 0.48

Crystal System  monoclinic

No. Reflections Used for Unit  25(5.8 - 21.0°)

Cell Determination (\( \theta \) range)  0.19

Omega Scan Peak Width at Half-height

Lattice Parameters:

\( a = 8.849 \text{ (3Å)} \)

\( b = 16.577 \text{ (3Å)} \)

\( c = 9.522 \text{ (2Å)} \)

\( \beta = 115.34 \text{ (2°)} \)

\( V = 1262 \text{ (1Å}^3 \text{)} \)

Space Group  \( P2_1/c \text{ (#14)} \)

Z value  4

Dcalc  1.280 g/cm³

F000  520

\( \mu(\text{MoK}\alpha) \)  0.79 cm⁻¹

B. Intensity Measurements

Diffractometer  Rigaku AFC5S

Radiation  MoK\( \alpha \text{(λ)} \)

\( = 0.71069 \text{ Å} \)

Temperature  23° C

Attenuator  Zr foil (factors: 2.3, 5.2, 11.7)

Take-off Angle  6.0°

Detector Aperture  6.0 mm hor./6.0 mm vert.

Crystal to Detector Distance  285 mm

Scan Type  \( \omega-\theta \)
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis

Scan Rate
8.0°/min (in omega)
(2 rescans)

Scan Width
(1.57 + 0.30 tanθ)°

2θ max
50.0°

No. of Reflections Measured
Total: 2478

Unique:
2323 (R int = 0.031)

Corrections
Lorentz-polarization

C. Structure Solution and Refinement

Structure Solution
Direct Methods
Refinement
Full-matrix least-squares
Function Minimized
Σ w (|Fol - IFcl|)²
Least-squares Weights
4Fo²/σ²(Fo²)
p-factor
0.02

Anomalous Dispersion
All non-hydrogen atoms

No. Observations (I>3.00σ(I))
1023

No. Variables
231

Reflection/Parameter Ratio
4.43

Residuals:
R; Rw  0.038; 0.040

Goodness of Fit Indicator
1.39

Max Shift/Error in Final Cycle
0.00

Maximum Peak in Final Diff. Map
0.15 e-/Å³

Minimum Peak in Final Diff. Map
-0.14 e-/Å³

Positional parameters and B(eq)

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<tr>
<th>atom</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>B(eq)</th>
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<td>C12</td>
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<tr>
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**X-RAY STRUCTURE REPORT**

**Data Collection**

An orange prism crystal of C$_{22}$H$_{20}$NO$_3$Br having approximate dimensions of 0.15 x 0.23 x 0.29 mm was mounted on a glass fiber. All measurements were made on a Nonius KappaCCD diffractometer with graphite monochromated Mo-K$_\alpha$ radiation.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using ten ($^\circ$ in $\omega$, 10s exposure, de-zingered) data frames, corresponded to a primitive triclinic cell with dimensions:

\[
\begin{align*}
a &= 8.1052(3) \text{ Å} & \alpha &= 101.220(2)^\circ \\
b &= 9.4180(2) \text{ Å} & \beta &= 107.306(2)^\circ \\
c &= 13.4027(4) \text{ Å} & \gamma &= 97.417(2) \\
V &= 938.82(6) \text{ Å}^3
\end{align*}
\]

For $Z = 2$ and F.W. = 426.31, the calculated density is 1.51 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$_1$ (#2).

The data were collected at a temperature of 23 ± 1° C to a maximum 2θ value of
Supplementary Material for Wood et al. Application of Reactive Enols in Synthesis ...S39

61.0°. One phi scan consisting of 183 data frames and one omega scan consisting of 120 data frames were collected with a scan width of 1° and a detector-to-crystal distance, Dx, of 35 mm. Each frame was exposed twice (for the purpose of de-zinging) for 20s. The data frames were processed and scaled using the DENZO software package. (Z. Otwinowski and W. Minor, “Processing of X-Ray Diffraction Data Collected in Oscillation Mode,” Methods in Enzymology, vol. 276: Macromolecular Crystallography, part A, 307-326, 1997, C.W. Carter, Jr. & R.M. Sweet, Eds., Academic Press).

Data Reduction

Of the 9204 reflections which were collected, 5071 were unique (R_int = 0.035). No decay correction was applied. The linear absorption coefficient, μ, for Mo-Kα radiation is 22.2 cm⁻¹ and a SORTAV absorption correction was applied. (MaXus: Mackay, S., Edwards, C., Henderson, A., Gilmore, C., Stewart, N., Shankland, K. and Donald, A. (1998) Chemistry Department, The University of Glasgow, Scotland.). The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods¹ and expanded using Fourier techniques². The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined.

In the case of the methyl group hydrogen atoms, one hydrogen was located in the difference map and included at an idealized distance to set the orientation of the other two hydrogen atoms. The final cycle of full-matrix least-squares refinement³ was based on 1978 observed reflections (I > 3.00σ(I)) and 244 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

\[ R = \frac{\Sigma |F_{o}|-|F_{c}|}{\Sigma |F_{o}|} = 0.035 \]
\[ R_w = \left(\frac{\Sigma w (|F_{o}|-|F_{c}|)^2}{\Sigma w |F_{o}|^2}\right)^{1/2} = 0.031 \]

The standard deviation of an observation of unit weight⁴ was 1.57. The weighting scheme was based on counting statistics and included a factor (p = 0.020) to downweight
the intense reflections. Plots of $\Sigma w (|F_{o}| - |F_{c}|)^2$ versus $|F_{o}|$, reflection order in data collection, $\sin \theta/\lambda$ and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.32 and -0.31 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 $\Delta f'$ and $\Delta f''$ 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


(3) Least-Squares:

Function minimized $\Sigma w(|F_{o}|-|F_{c}|)^2$

where $w = 4|F_{o}|^2/\sigma^2(|F_{o}|)$

and $\sigma^2(|F_{o}|) = [S^2(C+R^2B) + (p|F_{o}|)^2]/Lp^2$

$S$ = Scan rate

$C$ = Total integrated peak count

$R$ = Ratio of scan time to background count

$B$ = Total background count

$Lp$ = Lorentz-polarization factor

$p$ = p-factor

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

$[\Sigma w(|F_{o}|-|F_{c}|)^2/(No-Nv)]^{1/2}$

where $No$ = number of observations

$Nv$ = number of variables
