Copper Catalyzed Oxidation of Organozinc Halides

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s Supporting Information

General Considerations

¹H NMR Spectra were recorded on Bruker DPX 400 or 500 spectrometers in deuterochloroform or deuterodimethyl sulfoxide operating at 400 and 500 MHz respectively. ¹³C NMR spectra ¹⁰ were recorded on Bruker 400 or 500 spectrometers operating at 100

- and 125 MHz respectively. Chemical shifts are quoted relative to residual solvent (7.26 ppm for CHCl₃ and 77.0 ppm for ¹³C of CDCl₃, 2.54 ppm for DMSO and 40.45 ppm for ¹³C of d_6 -DMSO) and coupling constants (*J*) are given in Hz. The following
- ¹⁵ abbreviations are used singularly or in combination to indicate the multiplicity of signals: s singlet, d doublet, t triplet, q quartet, m multiplet and b broad. NMR spectra were acquired at 300 K unless otherwise indicated. Assignments are supported by COSY and HMQC correlations where appropriate. High resolution mass
- ²⁰ spectroscopic (HRMS) analyses were measured on a Micromass Q-TOF or a Micromass LCT Premier spectrometer at the Department of Chemistry, University of Cambridge or on a Finnigan MAT 900 XLT or a Finnigan MAT 95XP spectrometer at the EPSRC National Mass Spectrometry Service Centre, Swansea.
- ²⁵ Low resolution mass spectroscopic (LRMS) analyses were measured on a Waters ZQ 4000 or an HP/Agilent MSD LC-MS. Infrared spectra were recorded on a Perkin Elmer 1 FT-IR Spectrometer fitted with an Attenuated Total Reflectance (ATR) sampling accessory as neat films. Selected absorption maxima
- $_{30}$ (v_{max}) are reported in wavenumbers (cm⁻¹). Optical rotations were recorded on a Perkin Elmer 343 polarimeter. α_D values are reported in 10^{-1} deg cm² g⁻¹ at 589 nm, concentration (*c*) is given in g(100mL)⁻¹. Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Elemental analyses were
- ³⁵ performed on an Exeter Analytical CE-440 Elemental Analyzer. Single crystal X-ray diffraction was performed on a Nonius Kappa CCD diffractometer. The structures were solved by direct methods (SHELXS-97) and refined by least squares (SHELXS-97).^[25] Reactions were carried out in oven-dried glassware under an
- ⁴⁰ atmosphere of nitrogen with dry, freshly distilled solvents. Tetrahydrofuran was distilled from LiAlH₄ with triphenylmethane as indicator. All chemicals were purchased from Sigma-Aldrich or Avocado. Copper(I) bromide-dimethyl sulfide complex was purified before use according to the procedure of House.^[1]
- ⁴⁵ Grignard reagent and alkyllithium solutions were titrated with 1,10penanthroline and menthol before use. All flash chromatography was carried out using slurry-packed Merck 9385 Kieselgel 60 silca gel. Oxidant 3 was prepared by the procedure that we have previously disclosed.^[2]

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General procedure

Aryl bromide (1.0 mmol) in THF (2 mL) was added to Rieke zinc (4 mL, 5g/100mL suspension in THF). After addition the reaction mixture was heated at reflux and then concentrated *in vacuo*. The ⁵⁵ aryl zinc was dissolved in DMA (4 mL) and transferred *via* cannula onto solid copper(I) bromide-dimethyl sulfide complex (20 mg, 0.1 mmol). Oxidant 3 (147 mg, 0.5 mmol) in DMA (2 mL) was then added and the solution was kept stirring for 1 h at room temperature. The reaction mixture was filtered through a plug of ⁶⁰ silica eluting with hexane and EtOAc. The filtrate was concentrated *in vacuo* and the residue purified by flash column chromatography on silica gel.

4,4'-Dimethoxybiphenyl (2a)

⁶⁵ Chromatographic purification (SiO₂, EtOAc-hexane, 1:6) yielded the title compound as a solid, mp 168-170 °C (lit.,^[3] 176-178 °C). ¹H and ¹³C NMR spectra were in accordance with those described in the literature.^[4]

70 Diethyl biphenyl-4,4'-dicarboxylate (2b)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:8) yielded the title compound as a solid, mp 108-110 °C (lit.,^[5] 110-112 °C). ¹H and ¹³C NMR spectra were in accordance with those described in the literature.^[6]

4,4'-Dibromo-biphenyl (2d)

75

100

Chromatographic purification (SiO₂, EtOAc-hexane, 1:10) yielded the title compound as needles, mp 162-165 °C (EtOH)(lit.,^[7] 168-169 °C); ¹³C NMR spectrum was in accordance with that described ⁸⁰ in the literature.^[8]

Diethyl biphenyl-2,2'-dicarboxylate (2e)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:9) yielded the title compound as a solid, mp 39-40 °C (lit,.^[9] 42 °C); $v_{max}(neat)/cm^{-1}$ 1706, 1286, 1250, 1127, 1079, 753, 706; $\delta_{H}(500 \text{ MHz; CDCl}_3)$ 8.03 (1 H, d, *J* 8.0), 7.53 (1 H, t, *J* 8.0), 7.44 (1 H, t, *J* 8.0), 7.22 (1 H, d, *J* 8.0), 4.06 (4 H, q, *J* 7.0), 0.99 (6 H, t, *J* 7.0); $\delta_{C}(125 \text{ MHz; CDCl}_3)$ 167.1, 143.3, 131.2, 130.2, 130.0, 129.9, 127.1, 60.6, 13.7; HRMS found ESI [M+Na]⁺ 321.1103, $0 [C_{18}H_{18}NaO_4]^+$ requires 321.1103.

1,1'-(Biphenyl-2,2'-diyl)diethanone (2f)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:6) yielded the title compound as a solid, mp 80-82 °C (lit, ^[10] 84 °C); $v_{max}(neat)/cm^{-1}$ 1668, 1275, 1263, 1233, 765; $\delta_{H}(400 \text{ MHz}; \text{CDCl}_3)$ 7.73 (2 H, dt, *J* 7.5, 1.0), 7.47 (2 H, td, *J* 7.0, 1.5), 7.45 (2 H, td, *J* 7.5, 1.5), 7.17 (2 H, td, *J* 7.5, 1.5), 2.26 (6 H, s); $\delta_{C}(100 \text{ MHz}; \text{CDCl}_3)$ CDCl₃) 202.9, 140.6, 138.7, 131.0, 130.7, 128.6, 127.6, 29.3.

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100 2,2'-Divinylbiphenyl (2g)

Chromatographic purification (SiO₂, hexane) yielded the title compound as a solid, mp 76-78 °C (lit.,^[11] 71 °C). ¹H and ¹³C NMR spectra were in accordance with those described in the literature.^[11]

2,2'-Bis-allyloxy-biphenyl (2h)

105

Chromatographic purification (SiO₂, EtOAc-hexane, 1:20) yielded the title compound as an oil (76%), $v_{max}(neat)/cm^{-1}$ 2863, 1593, 1502, 1480, 1440, 1263, 1218, 1117, 995, 923, 749; δ_{H} (400 MHz;

¹¹⁰ CDCl₃) 7.30 (4 H, m), 7.02 (2 H, dt, *J* 7.3, 1.0), 6.95 (2 H, d, *J* 8.0),5.90 (2 H, m), 5.25 (1 H, q, *J* 1.7), 5.21 (1 H, q, *J* 1.7), 5.15 (1 H, q, *J* 1.7), 5.13 (1 H, q, *J* 1.7), 4.51 (4 H, dt, *J* 4.5, 1.7); $\delta_{\rm C}$ (125 MHz; CDCl₃) 156.1, 133.6, 131.5, 128.4, 120.5, 116.3, 112.4, 69.0; HRMS found ESI [M+Na]⁺ 289.1217, [C₁₈H₁₈O₂Na]⁺ requires 115 289.1205.

Biphenyl-2,2'-dicarbonitrile (2i)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:5) yielded the title compound as a solid, mp 158-160 °C (lit.,^[12] 177 °C);

¹²⁰ $v_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 2225, 1475, 764, 728; $\delta_{\text{H}}(400 \text{ MHz; CDCl}_3)$ 7.82 (2 H, dd, *J* 7.0, 1.5), 7.72 (2 H, td, *J* 7.0, 1.5), 7.57 (2 H, td, *J* 8.0, 1.0), 7.55 (2 H, dd, *J* 8.0, 1.0); $\delta_{\text{C}}(100 \text{ MHz; CDCl}_3)$ 141.6, 133.6, 132.8, 130.6, 129.2, 117.5, 112.4.

125 2,2'-Bithiophene (2j)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:5) yielded the title compound (0.076 g, 92%) as an oil. ¹H and ¹³C NMR spectra were in accordance with those described in the literature.^[13]

130 2,3-Diphenyl-1,3-butadiene (2k)

Chromatographic purification (SiO₂, Petroleum ether 40-60 °C) yielded the title compound as an oil. ¹H and ¹³C NMR spectra were in accordance with those described in the literature.^[14]

135 1,2-Bis(2-bromophenyl)ethane (21)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:8) yielded the title compound as a solid, mp 76-78 °C (lit,^[15] 78 °C); *ν*_{max}(neat)/cm⁻¹ 3053, 2930, 1469, 1453, 1437, 1153, 1095, 1018, 760; δ_H (400 MHz; CDCl₃) 7.55 (2 H, d, *J* 8.0), 7.19 (4 H, m), 7.06 ¹⁴⁰ (2 H, dt, *J* 8.0, 2.0), 3.04 (4 H, s); δ_C (125 MHz; CDCl₃) 140.6, 132.8,130.6, 127.8, 127.4, 124.5, 36.4.

1,2-Bis(2-cyanophenyl)ethane (2m)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:5) yielded ¹⁴⁵ the title compound as a solid, mp 138-140 °C (lit.,^[16] 138.5-141.5 °C); $v_{max}(neat)/cm^{-1}$ 2224, 1598, 1486, 1445, 1156, 759; $\delta_{\rm H}$ (400 MHz; CDCl₃) 7.63 (2 H, d, *J* 7.5), 7.51 (2 H, dt, *J* 7.5, 1.5), 7.33 (4 H, dt, *J* 7.5, 1.5), 3.20 (4 H, s); $\delta_{\rm C}$ (125 MHz; CDCl₃) 144.2, 133.0, 132.8, 129.9, 127.1, 117.8, 112.4, 35.7; HRMS found ESI [M+H]⁺ ¹⁵⁰ 233.1082, [C₁₆H₁₃N₂]⁺ requires 233.1079.

1,2-Bis(4-methoxyphenyl)ethane (2n)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:6) yielded the title compound as a solid, mp 120-122 °C (lit.,^[17] 123-125 °C); v_{max} (neat)/cm⁻¹ 3010, 2932, 1610, 1508, 1463, 1242, 1174, 1029, 830; $\delta_{\rm H}$ (400 MHz; CDCl₃) 7.08 (4 H, d, *J* 6.5), 6.80 (4 H, d, *J* 6.5),

3.78 (6 H, s), 2.82 (4 H, s); $\delta_{\rm C}$ (125 MHz; CDCl₃) 157.8, 134.0, 129.4, 113.7, 55.2, 37.2.

160 (E)-1,4-diphenyl-1,5-hexadiene (20)

A mixture of three isomers (16:5:1 ratio) *i.e.* (*E*)-1,4-diphenyl-1,5-hexadiene, (*E*,*E*)-1,6-diphenyl-1,5-hexadiene, 3,4-diphenyl-1,5-hexadiene, was isolated in 92% yield by chromatographic purification (SiO₂, hexane) ¹H NMR spectra were in accordance ¹⁶⁵ with those described in the literature.^[18]

1,2,3,4-Tetraphenyl-butane-1,4-dione (2p)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:5) yielded the title compound as a solid, mp 250-252 °C (lit.,^[19] 254-256 °C); $_{70} v_{max}$ (neat)/cm⁻¹ 1666, 1597, 1579, 1496, 1448, 1289, 1236, 1197,

¹⁷⁰ $v_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 1666, 1597, 1579, 1496, 1448, 1289, 1236, 1197, 1176, 1075, 1012, 972, 764, 694; δ_{H} (400 MHz; CDCl₃) 7.97 (4 H, d, *J* 7.5), 7.46 (2 H, t, *J* 7.5), 7.38 (4 H, t, *J* 7.5), 7.10 (6 H, m), 7.02 (4 H, d, *J* 7.5), 5.39 (2 H, s); δ_{C} (125 MHz; CDCl₃) 199.5,198.4, 136.9, 136.8, 136.4, 136.3, 132.9, 132.8,129.1, 128.9, 128.8, 128.7, 128.6, 128.4, 127.5, 127.4, 127.2, 58.5, 56.2; HRMS found ESI [M+Na]⁺ 413.1512, [C₂₈H₂₂O₂Na]⁺ requires 413.1517.

1,4-Bis-(4-chloro-phenyl)-2,3-di-p-tolyl-butane-1,4-dione (2q)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:6) yielded the title compound as a solid, mp 217-219 °C (lit.,^[20] 232 °C); $v_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 1663, 1589, 1568, 1488, 1399, 1286, 1251, 1173, 1092, 1008, 976, 830, 777; δ_{H} (400 MHz; CDCl₃) 7.90 (4 H, d, J 8.5), 7.32 (4 H, t, J 8.5), 6.93 (4 H, d, J 8.0), 6.85 (4 H, d, J 8.0), 5.23 (2 H, s), 2.20 (6 H, s); δ_{C} (125 MHz; CDCl₃) 198.6, 139.2, 137.0, 134.7, 132.7, 130.3, 129.5, 128.8, 128.6, 58.0, 21.0. Crystal data for **2q**: C₃₀H₂₄Cl₂O₂, M_{w} =487.39, colourless block 0.46x0.10x0.07mm³, triclinic *P-I* (No. 2), *a*=9.9644(3), *b*=10.6247(4), *c*=12.3651(5)Å, *α*=72.322(20)°, *β*=77.493(2)°, γ =86.707(2)°, *V*=1217.6(1)Å³, *T* = 120(2)K, D_X = 1.329 g cm⁻³, λ =

- ¹⁹⁰ 0.71073 Å, $\mu = 0.293$ mm⁻¹, Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, $3.54^{\circ} < \theta < 27.46^{\circ}$, 15013 measured reflections, 5487 independent (R_{inf} =0.043), 4223 with $I > 4\sigma(I)$. The structure was solved by direct methods (*SHELXS*-97) and refined by least squares
- ¹⁹⁵ (*SHELXL*-97) using Chebyshev weights on F_0^2 to R1 = 0.050, wR2 = 0.102 [$I > 2\sigma(I)$], 309 parameters, goodness-of-fit on F^2 1.080, residual electron density 0.54 e Å⁻³. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary ²⁰⁰ publication no. CCDC-609161. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-

mail: deposit@ccdc.cam.ac.uk].



²⁰⁵ ORTEP plot of **2q** with thermal ellipsoids set at 50% probability shown above.

2,3-Diphenyl-succinic acid dimethyl ester (2r)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:5) yielded the title compound as a solid, mp 150-152 °C (lit.,^[21] 169-172 °C); v_{max} (neat)/cm⁻¹ 1731, 1492, 1454, 1434, 1253, 1230, 1153, 969, 854, 791, 739, 699; $\delta_{\rm H}$ (400 MHz; CDCl₃) 7.13 (2 H, d, *J* 1.7), 7.10 (4 H, d, *J* 2.1), 7.01 (4 H, m), 4.25 (2 H, s), 3.70 (6 H, s); $\delta_{\rm C}$ (125 MHz; CDCl₃) 173.6, 135.6, 128.5, 128.3, 127.4, 54.7, 52.4; HRMS found ESI [M+Na]⁺ 321.1104, [C₂₈H₂₂O₂Na]⁺ requires 321.1103.

²¹⁵ Crystal data for **2r**: $C_{18}H_{18}O_4$, M_w =298.32, colourless block 0.35x0.23x0.12mm³, monoclinic $P_{2/n}$ (No. 14), a=8.9596(2), b=17.7193(6), c=10.0126(3)Å, β =104.631(2)°, V=1538.03(8)Å³, T= 120(2)K, D_X = 1.288 g cm⁻³, λ = 0.71073 Å, μ = 0.091 mm⁻¹, Nonius Kappa CCD diffractometer equipped with an Oxford

- ²²⁰ Cryosystems Cryostream cooling apparatus, $3.57^{\circ} < \theta < 27.49^{\circ}$, 11178 measured reflections, 3503 independent (R_{int} =0.043), 2739 with $I > 4\sigma(I)$. The structure was solved by direct methods (*SHELXS*-97) and refined by least squares (*SHELXL*-97) using Chebyshev weights on F_0^2 to R1 = 0.041, wR2 = 0.088 [$I > 2\sigma(I)$],
- ²²⁵ 201 parameters, goodness-of-fit on F^2 1.021, residual electron density 0.23 e Å⁻³. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-609162. Copies of the data can be obtained free of charge
- ²³⁰ on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].



ORTEP plot of **2r** with thermal ellipsoids set at 50% probability shown above.

Ethane-1,2-diyl bis(2-bromobenzoate) (1s)

Based on a literature procedure.^[22] A solution of a 2-bromobenzoic acid in thionyl chloride was heated at reflux for 30 min. The solution was allowed to cool and excess thionyl chloride removed under reduced pressure and by azeotropic distillation with toluene. The residue was dissolved in CH₂Cl₂ and added to a solution of diol, triethylamine and 4-(dimethylamino)pyridine in CH₂Cl₂ at 0 °C and stirred at RT for 12 h. The reaction mixture was washed
²⁴⁵ with water, the organic layer separated, dried (MgSO₄) and concentrated under reduced pressure. Chromatographic purification (SiO₂, EtOAc-hexane, 1:3) yielded the title compound (2.03 g, 95%); v_{max}(neat)/cm⁻¹ 1720, 1468, 1245, 1113, 1029, 739; δ_H(400 MHz; CDCl₃) 7.84-7.81 (2 H, m), 7.67-7.64 (2 H, m), 7.38-7.30 (4
²⁵⁰ H, m), 4.68 (4 H, s); δ_C(125 MHz; CDCl₃) 165.8, 134.4, 132.8,

131.6, 131.5, 127.2, 121.9, 63.0; HRMS found ESI $[M+NH_4]^+$ 443.9436, $[C_{16}H_{16}Br_2NO_4]^+$ requires 443.9441.

7,8-Dihydro-6,9-dioxa-dibenzo[a,c]cyclodecene-5,10-dione

Chromatographic purification (SiO₂, EtOAc-hexane, 1:9) yielded the title compound as a solid, mp 160-162 °C. ¹H and ¹³C NMR spectra were in accordance with those described in the literature.^[22] Crystal Data for **2s**: Crystal data: $C_{16}H_{12}O_4$, M_w =268.3, colourless block 0.32x0.16x0.05mm³, orthorhombic Aba2 (No. 41), 260 $a=9.7780(7), b=13.5482(10), c=9.4858(8)\text{Å}, V=1256.6(2)\text{Å}^3, T=1256.6(2)\text{Å}^3$ 180(2)K, $D_{\rm X} = 1.418$ g cm⁻³, $\lambda = 0.71073$ Å, $\mu = 0.102$ mm⁻¹ Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, $3.66^{\circ} < \theta < 27.46^{\circ}$, 265 5041 measured reflections, 764 independent (Rint=0.045), 671 with $I > 4\sigma(I)$. The structure was solved by direct methods (SHELXS-97) and refined by least squares (SHELXL-97) using Chebyshev weights on F_0^2 to R1 = 0.039, wR2 = 0.074 $[I > 2\sigma(I)]$, 91 parameters, goodness-of-fit on F^2 1.123, residual electron density 270 0.12 e Å⁻³. 655 Friedel pairs were averaged for the refinement. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-609163. Copies of the data can be obtained free of charge on application to the CCDC, 275 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].



ORTEP plot of **2s** with thermal ellipsoids set at 50% probability shown above.

1,2-Phenylene bis(2-iodobenzoate) (1t)

A solution of a 2-bromobenzoic acid in thionyl chloride was heated at reflux for 30 min. The solution was allowed to cool and excess thionyl chloride removed under reduced pressure and by azeotropic 285 distillation with toluene. The residue was dissolved in CH₂Cl₂ and added to а solution of diol, triethylamine and 4-(dimethylamino)pyridine in CH₂Cl₂ at 0 °C and stirred at RT for 12 h. The reaction mixture was washed with water, the organic layer separated, dried (MgSO₄) and concentrated under reduced pressure. Chromatographic purification (SiO₂, EtOAc-hexane, 1:3) 290 yielded the title compound (2.19 g, 92%); $v_{max}(neat)/cm^{-1}$ 1746, 1493, 1233, 1074, 1019, 733; $\delta_{\rm H}$ (400 MHz; CDCl₃) 7.96-7.94 (2 H, m), 7.68-7.65 (2 H, m), 7.42-7.25 (8 H, m); δ_C(125 MHz; CDCl₃) 163.2, 142.2, 134.7, 133.4, 132.2, 130.2, 127.2, 127.0, 123.6, ²⁹⁵ 122.7; HRMS found ESI $[M+NH_4]^+$ 491.9440, $[C_{20}H_{16}Br_2NO_4]^+$ requires 491.9441.

Product (2t)

Chromatographic purification (SiO₂, EtOAc-hexane, 1:2) yielded ³⁰⁰ the title compound as a solid, mp 163-165 °C. We have previously disclosed spectroscopic data for this compound.^[2] Crystal data for

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2t: C₂₀H₁₂O₄, M_w =316.30, colourless block 0.28x0.21x0.07mm³, monoclinic $P2_1/c$ (No. 14), a=9.3998(2), b=11.4953(3), c=13.9452(4)Å, β =97.273(1)°, V=1494.7(1)Å³, T = 180(2)K, D_X = ³⁰⁵ 1.406 g cm³, λ = 0.71073 Å, μ = 0.098 mm⁻¹, Nonius Kappa CCD

diffractometer equipped with an Oxford Cryosystems Cryosystems cooling apparatus, $3.54^{\circ} < \theta < 27.47^{\circ}$, 11656 measured reflections, 3415 independent (R_{ini} =0.037), 2715 with $I > 4\sigma(I)$. The structure was solved by direct methods (*SHELXS*-97) and refined by least

squares (*SHELXL*-97) using Chebyshev weights on F_0^2 to R1 = 0.044, wR2 = 0.095 [$I > 2\sigma(I)$], 217 parameters, goodness-of-fit on F^2 1.034, residual electron density 0.18 e Å⁻³. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary ³¹⁵ publication no. CCDC-609164. Copies of the data can be obtained

free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; Email: deposit@ccdc.cam.ac.uk].

³²⁰ ORTEP plot of **2t** with thermal ellipsoids set at 50% probability shown above.

Synthesis of Buflavine (2u)

2-(2-Bromophenyl)-N-methylethanamine was prepared according ³²⁵ to a literature procedure.^[23] 6-Bromoveratraldehyde is commercially available and was used as received.

N-(2-Bromo-4,5-dimethoxybenzyl)-2-(2-bromophenyl)-*N*-methylethanamine (1u)

- ³³⁰ Borane-pyridine complex (8 M solution of borane, 6.5 mL, 52 mmol) was added to a stirred solution of 6-bromoveratraldehyde (10.8 g, 44.2 mmol) and 2-(2-bromophenyl)-N-methylethanamine (5.57 g, 26.0 mmol) in CH₂Cl₂ (10 mL) and methanol (10 mL) at room temperature. After 11 h the solution was warmed to 30 °C
- ³³⁵ and maintained at this temperature for a further 9 h. The solution was then acidified with hydrochloric acid (3 M) and maintained at room temperature for 0.5 h. The solution was concentrated under reduced pressure, diluted with water and washed with ether. The aqueous layer was then made basic by addition of aqueous sodium
- ³⁴⁰ hydroxide (10% w/w solution) and extracted with CH₂Cl₂. These organic extracts were washed with brine, dried (K₂CO₃) and concentrated under reduced pressure to give the title compound (80%) as an oil, v_{max} (neat)/cm⁻¹ 2933, 1503, 1463, 1436, 1380, 1251, 1208, 1155, 1027; δ_{H} (400 MHz; CDCl₃) 7.50 (1 H, d, *J* 8.0),
- $\begin{array}{l} {}_{345} 7.24\text{-}7.18 \ (2 \ H, \ m), \ 7.04 \ (1 \ H, \ m), \ 6.98 \ (2 \ H, \ s), \ 3.85 \ (3 \ H, \ s), \ 3.82 \\ (3 \ H, \ s), \ 3.60 \ (2 \ H, \ s), \ 2.97 \ (2 \ H, \ t, \ J \ 8.0), \ 2.71 \ (2 \ H, \ t, \ J \ 7.5), \ 2.36 \\ (3 \ H, \ s); \ \delta_C(100 \ MHz; \ CDCl_3) \ 148.4, \ 148.3, \ 139.8, \ 132.7, \ 130.8, \\ 130.5, \ 127.6, \ 127.3, \ 124.5, \ 115.2, \ 114.0, \ 113.1, \ 60.7, \ 57.2, \ 56.1, \\ 56.0, \ 42.2, \ 33.9. \end{array}$

350 Buflavine (2u)

Aryl bromide 1u (0.221 g, 0.5 mmol) in THF (2 mL) was added to Rieke zinc (4 mL, 5g/100mL suspension in THF). After addition the reaction mixture was heated at reflux overnight and then transferred via cannula onto solid copper (I) bromide-dimethyl sulfide complex (0.020 g, 0.1 mmol). Oxidant 3 (0.147 g, 355 0.5 mmol) in DMA (2 mL) was then added and the solution was kept stirring for 1 h at room temperature. The reaction mixture was washed with water and then extracted with CH₂Cl₂. The organic layer was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel (CHCl₃-360 MeOH, 9:1) to give the title compound (0.113 g, 80%), $\delta_{\rm H}(400$ MHz; CDCl₃) 7.36-7.23 (4 H, m), 6.92 (1 H, s), 6.80 (1 H, s), 3.94 (3 H, s), 3.88 (3 H, s), 3.60 (1 H, d, J13.5), 3.31 (1 H, q, J13.5), 3.15 (1 H, d, J 13.5), 2.74 (1 H, q, J 13.5), 2.61-2.49 (2 H, m), 2.54 365 (3 H, s); δ_C(125 MHz; CDCl₃) 148.5, 148.2, 140.8, 139.9, 133.2, 129.5, 129.1, 128.0, 126.3, 113.8, 112.2, 58.4, 58.1, 55.9, 45.4,

129.5, 129.1, 128.0, 120.5, 115.8, 112.2, 38.4, 38.1, 55.9, 43.4, 32.0. ¹H and ¹³C NMR spectra were in accordance with those described in the literature.^[24]

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