Supporting Information

Toxic on Purpose: Ionic Liquid Fungicides as Combinatorial Crop Protecting Agents

1. General

All chemicals unless otherwise stated were purchased from Aldrich Chemical Company (Dorset, UK) and used without further purification. NMR data were recorded at 25 °C on a Bruker (Coventry, UK) 300 DRX spectrometer and the solvent peak was used as reference. Electrospray mass spectrometry was performed on a LCT Premier from Waters using an Advion nanomate injection system (Manchester, UK). Water content was measured by Karl-Fischer-titration with a Mettler Toledo Titrator (Hiranuma Sangyo, Japan). The water content of all dried ILs was found to be below 2000 ppm.

Thermogravimetric analysis was performed on a Mettler Toledo Star^e TGA/DSC (Leicester, UK) under nitrogen. Samples between 5 and 10 mg were placed in open alumina pans and were heated from 25 °C to 600 °C with a heating rate of 5 °C/min. Decomposition temperatures ($T_{5\%dec}$) were reported from onset to 5 wt% mass loss. Infrared spectra were recorded as neat samples from 4000-450 cm^{-1} on a Perkin-Elmer Spectrum 65 FT-IR spectrometer fitted with a Universal ATR Sampling Accessory.

Differential scanning calorimetry (DSC) was performed on a Mettler Toledo Star^e DSC (Leicester, UK) under nitrogen. Samples between 5 and 10 mg were heated from 25 °C to 110 °C at a heating rate of 5 °C/min followed by a 5 min isotherm. A cooling rate of 5 °C/min to -70 °C was followed by a 5 min isotherm at -70 °C, and the cycle was repeated twice. A melting transition was observed as single-event peak in the first run. Second and third cycles proved to be identical and gave a glass transition temperature only. Transitions above ambient temperature were confirmed optically on a Stuart SMP3 melting point apparatus.

2. Synthetic protocols

2.2. Thiabendazolium Docusate (3)

Thiabendazole (10.00 g, 0.05 mol) was suspended in 50 mL of distilled water and a solution of HCl (5.03 g, 0.05 mmol, ~37% in H_2O) was added. The suspension was stirred for 60 min at room temperature and the solvent was evaporated. The remaining white solid was dissolved in 100 mL of acetone/H_2O 1:1, sodium docusate (22.23 g, 0.05 mol) was added and stirred overnight at room temperature. Acetone was evaporated, and the remaining suspension was diluted with 100 mL of

H_2O. The crude mixture was repeatedly extracted with dichloromethane (200 mL). The combined organic layers were washed successively with water until no more chloride ions could be detected in the washings (checked by addition of $AgNO_3$ solution), dried over $MgSO_4$, filtered, and the solvent was evaporated. Remaining volatile material was removed under reduced pressure (0.01 mbar, 60 °C) with stirring to gave thiabendazolium docusate **3** in 91% yield as colourless gel.

^{1}H NMR (300 MHz, d_6-DMSO): δ 9.51 (d, J = 1.74 Hz, 1H), 8.91 (d, J = 1.77 Hz, 1H), 7.83 (m, 2H), 7.56 (m, 2H), 3.85 (m, 4H), 3.72 (m, 1H), 2.89 (m, 2H), 1.40 (m, 2H), 1.19 (m, 16H), 0.80 (m, 12H). ^{13}C NMR (75 MHz, d_6-DMSO): δ230.71, 229.86, 171.09, 168.37, 158.22, 143.77, 139.71, 131.81, 127.07, 126.08, 114.20, 66.35, 66.34, 61.61, 38.07, 33.99, 29.67, 29.52, 28.27, 23.09, 22.91, 22.35, 13.81, 10.67. IR (neat) ν = 3088, 2957, 2929, 1731, 1633, 1464, 1315, 1153, 1034, 886, 751, 618, 519 cm^{-1}. HRMS (ESI+) calc. for $C_{10}H_8N_3S$ 202.0433, found 202.0421, HRMS (ESI–) calc. for $C_{20}H_{37}O_7S$ 421.2265, found 421.2260. T_g -16.3 °C; mp 46.9 °C; $T_{5\%onset}$ 252.0 °C.

2.3. Imazalilium Docusate (4)

Imazalil sulfate (3.2178 g, 8.141 mmol), suspended in 20 mL chloroform and 3.594 g (8.141 mmol) sodium docusate, dissolved in 20 mL chloroform, were combined in a 50 mL round bottom flask and refluxed for 1 h. The resulting suspension was cooled to 0 °C and filtered over a batch of silica. The combined organic layers were washed once with H_2O (care must be taken in this step to avoid emulsion formation), dried over $MgSO_4$, filtered, and the solvent was evaporated. Any remaining volatile material was removed under reduced pressure (0.01 mbar, 60 °C) with stirring to give imazalilium docusate in 61% yield as yellow viscous liquid.

^{1}H NMR (300 MHz, d_6-DMSO): δ14.32 (br s, 1H), 8.97 (s, 1H), 7.71 (d, J = 2.10 Hz, 2H), 7.63 (dt, J_1 = 12.61 Hz, J_2 = 1.58 Hz, 1H), 7.51 (dd, J_1 = 8.40 Hz, J_2 = 2.27 Hz, 1H), 7.32 (d, J = 8.58 Hz, 1H), 5.74 (m, 1H), 5.11 (m, 3H), 4.50 (m, 2H), 3.88 (m, 6H), 3.64 (m, 1H), 2.86 (m, 2H), 1.49 (m, 2H), 1.26 (m, 16H), 0.83 (m, 12H). ^{13}C-NMR (75 MHz, d_6-DMSO): δ171.06, 168.37, 136.27, 133.99, 133.93, 133.15, 129.30, 129.20, 128.03, 122.83, 120.19, 117.16, 69.48, 66.08, 66.06, 61.43, 51.71, 38.15, 34.13, 29.63, 29.53, 28.33, 23.19, 23.35, 22.98, 22.44, 13.96, 11.80. IR (neat) ν = 2958, 2929, 2859, 1720, 1586, 1458, 1253, 1199, 1168, 1034, 853, 788, 643, 538 cm^{-1}. HRMS (ESI+) calc. for $C_{14}H_{15}Cl_2N_2O$ 297.0556, found 297.0561, HRMS (ESI–) calc. for $C_{20}H_{37}O_7S$ 421.2265, found 421.2260. T_g -28.0 °C; mp 70.0 °C; $T_{5\%onset}$ 208.8 °C.

3. Biological testing

3.1. Origin of the Isolates

All isolates were obtained from naturally infected potato tubers as indicated below. All except *F. sambucinum* ex SASA were isolated in the lab of Dr. Louise R. Cooke (Applied Plant Science and Biometrics Division, Agri-Food and Biosciences Institute, Newforge Lane, Belfast, BT9 5PX, UK). *F. sambucinum* ex SASA was supplied by SASA (Science and Advice for Scottish Agriculture, Roddinglaw Road, Edinburgh, EH12 9F, UK).

Isolate	Origin (year of isolation)
F. sambucinum ex SASA	SASA, Scotland (2004)
F. sambucinum L'gall 10	AFBI, Northern Ireland (2009)
F. sambucinum L'gall 11	AFBI, Northern Ireland (2009)
F. sambucinum L'gall 53	AFBI, Northern Ireland (2009)
F. coeruleum ex B7/06 T8	AFBI, Northern Ireland (2006)
F. coeruleum ex B16/08 P31	AFBI, Northern Ireland (2008)
F. culmorum P13	AFBI, Northern Ireland (pre-2000)
Phoma exigua 9.1	AFBI, Northern Ireland (1999)
Phoma foveata BL2 05 T3	AFBI, Northern Ireland (2005)
P. erythroseptica BL2/08 P31	AFBI, Northern Ireland (2008)
P. erythroseptica Rooster Eire	AFBI, tubers from Republic of Ireland (2008)

3.2. *In vitro* testing

In each test three replicate plates for each organism per concentration were used and tests were repeated at least once.

For tests with thiabendazole (TBZ), TBZ docusate and TBZ stearate, TBZ (0.5 g, drug pure, MSD Agvet) was dissolved in water (10 ml) by adding the minimum required volume (*c.* 0.5 ml) of hypophosphorous acid and heating gently with stirring, then made up to 100 ml with water to give a stock solution (25 mM). TBZ docusate (0.155 g) or TBZ stearate (0.121 g) were dissolved in ethanol (100 ml) to give stock solutions (25 mM). A ten-fold dilution of each of these stock solutions was prepared (in water for TBZ and in ethanol for TBZ docusate and stearate). Each solution was added to separate aliquots of either

potato dextrose agar (PDA) or malt agar (MA), depending on the species to be tested, at the rate of 10 ml per litre and mixed thoroughly to give final concentrations of 250 and 25 μM of each compound in agar. In addition, agar with 1% v/v ethanol and unamended agar was prepared (ethanol and unamended controls). The agar was poured into Petri plates (9 cm) and allowed to set.

For tests with imazalil sulphate and imazalilium docusate, imazalil sulphate (0.5 g, drug pure, Janssen) was dissolved in sterile water (100 ml) to give a stock solution (12.7 mM). Imazalilium docusate (0.91 g) was dissolved in ethanol (100 ml) to give a stock solution (12.7 mM). Dilutions (alternately five-fold and two-fold) of each of these stock solutions were prepared (in water for imazalil sulphate and in ethanol for imazalilium docusate) to produce a dilution series (12.7, 2.54, 1.27, 0.25 and 0.13 mM). Each solution was added to separate aliquots of either potato dextrose agar (PDA) or malt agar (MA), depending on the species to be tested, at the rate of 10 ml per litre and mixed thoroughly to give final concentrations of at 127, 25, 12.7, 2.5 and 1.27 μM of each compound in agar. In addition, agar with 1% v/v ethanol and unamended agar was prepared (ethanol and unamended controls). The agar was poured into Petri plates (9 cm) and allowed to set.

Isolates of the appropriate potato tuber pathogens were grown on PDA for *Fusarium* spp. and *Phytophthora erythroseptica* or on MA for *Phoma* spp. Each isolate to be tested was inoculated onto three replicate plates of the two concentrations of each compound and onto ethanol and unamended agar controls using plugs (6 mm diameter) cut from the margins of actively growing cultures. Plates were incubated in darkness at 20 °C and mycelial growth measured (two measurements at right-angles for each plate) after 5-7 days (depending on the growth rates). The percentage reduction in growth in the presence of the test compounds was calculated with respect to the appropriate control. In the case of imazalil and imazalilium docusate, log-probability plots of the percentage reduction in growth against the concentration were used to estimate EC_{50} values (the concentration required to reduce mycelial growth by 50%).