Supporting Information
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Experimental Procedure and Analytical Data of Selected Compounds

**Compound 11**
To a solution of the methyl vanillate 10 (0.5 g, 2.75 mmol) in dry acetone (84 mL), under argon atmosphere, was added potassium carbonate (1.5 g, 10.98 mmol) and benzyl bromide (0.7 g, 4.10 mmol). The resulting mixture was refluxed overnight. The mixture was filtered and the solvent removed under reduced pressure. The resulting residue was acidified with HCl 1M. The solution was extracted with EtO. The ether extracts were dried over sodium sulphate and the solvent removed. The product was isolated as an oil (75%). Mp 110-112 °C (chloroform/hexane); νmax (KBr): 1677 cm⁻¹; 1H NMR (400 MHz, CDCl3): δ = 7.69 (d, J 8.4, 1H, ArH), 7.61 (s, 1H, ArH), 7.44 (d, J 7.2 Hz, 2 H, ArH), 7.38 (t, J 7.0 Hz, 2 H, ArH), 7.33 (t, J 7.1 Hz, 1 H, ArH), 6.93 (d, J 8.5 Hz, 1H, ArH), 5.23 (s 2 H, CH2) 3.95 (s, 3 H, Ar-OCH3).

**Compound 13**
To a solution of the acid 11 (0.5 g, 1.86 mmol) in dry THF (10 mL), under argon atmosphere, was added N-(1-methanesulfonyl)benzotriazole 12 (0.38 g, 1.95 mmol) (previously prepared according to the literature procedure), and dry triethylamine (0.4 mL). The resulting mixture was stirred at room temperature overnight. After THF removal, the resulting residue was dissolved in chloroform and washed with water. The organic layer was dried, filtered and the solvent removed under reduced pressure. The crude product was recrystallized from chloroform/hexane and the product 13 was isolated as a white solid (90%). Mp 110-112 °C (chloroform/hexane); νmax (KBr): 1694 cm⁻¹; 1H NMR (400 MHz, CDCl3) δ = 8.37 (d, J 8.2 Hz, 1H, Ar-H), 8.17 (d, J 8.1 Hz, 1H, Ar-H), 7.95 (d, J 8.2 Hz, 1H, ArH), 7.84 (s, 1H, ArH), 7.70 (t, J 7.6 Hz, 1H, CH2), 7.53 (t, J 7.6 Hz, 1H, CH2), 7.47-7.32 (m, 5H, ArH), 7.03 (d, J 8.4 Hz, 1H, ArH), 5.23 (s, 2 H, OCH3) 3.95 (s, 3H, Ar-OCH3); 13C NMR (100.6 MHz, CDCl3) δ = 165.5, 153.2, 149.2, 145.6, 135.9, 132.6, 130.2, 128.7, 128.2, 127.2, 126.9, 126.1, 123.6, 120.1, 114.9, 114.8, 114.6, 112.3, 70.9, 56.2; HRMS (ESI) m/z: 359.1268, (C12H13N3O requires 359.1270).

**Compound 15**
To a solution of the N-acylbenzotriazole derivative 13 (0.25 g, 0.67 mmol) in dry THF (1 mL) in an ice bath, was added a solution of the previously prepared Grignard reagent 8 (prepared from 0.37 g of the corresponding bromide in dry THF, according to the literature procedure). The reaction mixture was stirred at 0 °C for 40 min and then at room temperature for 3 h, till complete consumption of the starting material 13. Quenching was performed by addition of a saturated ammonium chloride solution followed by extraction with Et2O. The organic layer was dried, filtered, and the solvent removed. The crude product was purified by column chromatography (benzene/hexane/triethylamine, 10:1:0.5) and the ketone 15 was isolated as an oil (75%). νmax (NaCl): 1644 cm⁻¹; 1H NMR (400 MHz, CDCl3) δ = 7.74 (d, J 8.4 Hz, 2 H, ArH), 7.66-7.26 (s, 7H, ArH), 6.90 (m, 3H, ArH), 5.22 (s, 2H, OCH3), 4.14 (t, J 5.7 Hz, 2H, OCH2), 3.92 (s, 3H, OCH3), 2.93 (t, J 7.5 Hz, 2H, CH2=N), 2.71 (q, J 7.0 Hz, 4H, NCH2), 1.09 (t, J 7.0 Hz, 6H, CH3CH3); 13C NMR (100.6 MHz, CDCl3) δ = 194.4, 162.0, 151.7, 149.4, 136.4, 132.2, 131.0, 130.6, 128.6, 128.0, 127.2, 124.6, 113.9, 112.7, 111.9, 70.8, 66.6, 56.1, 51.5, 47.7, 11.6; HRMS (ESI) m/z: 433.2256, (C21H23N4O4 requires 433.2253).

**Compounds 17a and 17b**
To a solution of the chlorophosphonate 16 (3.46 mmol) (previously prepared in 2 steps from 5,5-dimethyl-1,3,2-dioxaphosphorinan-2-one, according to the Kumaraswammy et al. procedure) in dry THF (1.5 mL) at -78 °C was slowly added t-BuLi (2.54 mmol). The reaction mixture was stirred at -78 °C for 15 min and the temperature was then slowly increased till -50 °C, and then to room temperature. The mixture was then transferred under argon to a sealed tube and refluxed for 3 days. The reaction evolution was controlled by TLC (benzene/hexane/triethylamine, 7:3:1). After cooling the reaction mixture, the quenching was performed by addition of water, followed by extraction with Et2O. The ether layer was dried, filtered and the solvent removed under reduced pressure. The resulting residue was purified by column chromatography (benzene/hexane/triethylamine, 7:3:1) affording the desired chloro olefin as a yellow oil (70%). The NMR revealed that the product is a mixture of two isomers (17a/17b) in the ratio 60:40.  νmax (NaCl): 1602, 749 cm⁻¹; 1H NMR (400 MHz, CDCl3) δ = 7.46-7.17 (m, 7.2H of 17a + 4.8H of 17b, ArH), 6.94-6.84 (m, 1.2H of 17a + 1.2H of 17b, ArH), 6.63-6.59 (m, 0.6H of 17a + 0.8H of 17b, ArH), 6.44-6.43 (m, 1.2H of 17a, ArH), 5.17 (s, 0.8H of 17b, OCH2), 5.04 (s, 1.2H of 17a, OCH2), 4.07 (t, J 6.3 Hz, 1.2H of 17a, OCH2), 3.93 (t, J 6.3 Hz, 1.0H of 17a, OCH2).
Hz, 0.8H of 17b, OCH$_2$), 3.85 (s, 1.2H of 17b, OCH$_3$), 3.47 (s, 1.8H of 17a, OCH$_3$), 2.89 (t, J 6.3 Hz, 1.2H of 17a, CH$_2$-N$_2$), 2.80 (t, J 6.2 Hz, 0.8H of 17b, CH$_2$-N$_2$), 2.67-2.50 (m, 2.4H of 17a + 1.6H of 17b, CH$_2$CH$_2$); $^{13}$C NMR (100.6 MHz, CDCl$_3$) $\delta$ = 158.0, 157.7, 148.9, 148.6, 147.6, 147.3, 140.0, 139.8, 139.6, 137.1, 136.9, 135.2, 134.2, 133.6, 131.9, 131.3, 130.0, 129.9, 128.5, 128.0, 127.9, 127.8, 127.7, 127.3, 123.4, 122.7, 114.8, 113.9, 113.8, 113.1, 113.0, 70.9, 70.8, 66.0, 56.1, 55.6, 51.6, 51.5, 47.8, 11.5; HRMS (ESI$^-$) m/z: 541.2383, (C$_3$H$_5$NO$_2$, requires 541.2387).

Compounds 18a and 18b

To a solution of the compounds 17a/17b (40 mg, 0.07 mmol) in dry 1.2-dichloroethane (1.5 mL), cooled in an ice-bath, was added dropwise a solution of 1-chloroethyl chloroformate (40 µL, 0.37 mmol) in the same solvent. The resulting mixture was refluxed overnight (16 h). The solvent was removed and the obtained residue was dissolved in methanol (1 mL) and refluxed for 1 h. The solvent was removed and the crude was washed three times with hexane and dried under vacuum. Compounds 18a/18b were obtained as an oil in quantitative yield (37 mg) in a ratio 60:40. The stereoisomers were separated by preparative thin layer chromatography (benzene/hexane/triethylamine, 7:3:1).

Compounds 6a and 6b

To a solution of 0.18 mmol of 18a/18b (60/40) in 2.8 mL of glacial acetic acid was added 28 mg of Pd on charcoal. The mixture was shaken under 20 psi of H$_2$ for 4 h. Then the mixture was filtered over celite and the solvent removed after addition of toluene. The crude was purified by HPLC performed on a Luna C$_18$ semi-preparative column (5 µm particle size, 250 mm x 10 mm I.D.) coupled to a guard C$_18$ precolumn (Phenomenex, Cheshire, UK); UV detection at 254 nm. A gradient was used for the mobile phase with the system: mobile phase A (H$_2$O, pH 2.5 with TFA)/mobile phase B (MeCN) delivered at 4 mL/min; A:B 60:40 (min 20:80), (min 20:80 (17 min); 60:40 (20 min), to afford 6a/6b (ca. 21 mg, t$_r$ 6.9 min). The yield was calculated on the basis of the peak area (70%). Compounds 6a/6b were isolated as an oil in the ratio 60:40. $\nu$ max (NaCl): 3052, 1681, 1514, 1202, 752 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 9.47-9.39 (bs, 0.6H of 6a + 0.4H of 6b, OH), 7.34-7.15 (m, 4.2H of 6a + 2.8H of 6b, ArH), 6.89-6.77 (m, 1.2H of 6a + 1.2H of 6b, ArH), 6.63-6.40 (m, 0.6H of 6a + 0.8H of 6b, ArH), 3.67-3.51 (m, 1.2H of 6a, ArH), 4.20 (m, 0.6H of 6a, OCH$_3$), 4.05 (m, 0.8H of 6b, OCH$_3$), 3.83 (s, 1.2H of 6b, OCH$_3$), 3.46 (s, 1.8H of 6a, OCH$_3$), 3.31 (m, 1.2H of 6a, CH$_2$N$_2$), 3.23 (m, 0.8H of 6b, CH$_2$N$_2$), 3.10-3.04 (m, 1.2H of 6a + 0.8 H of 6b, CH$_2$CH$_2$); $^{13}$C NMR (100.6 MHz, CDCl$_3$) $\delta$ = 156.7, 156.3, 156.3, 146.1, 145.7, 145.1, 144.8, 139.9, 139.5, 135.4, 134.8, 133.9, 132.9, 131.9, 131.4, 129.8, 128.5, 128.0, 124.1, 123.8, 113.8, 113.7, 62.8, 55.9, 55.6, 46.3, 43.2, 10.9; HRMS (ESI$^-$) m/z: 423.1602, (C$_{13}$H$_9$NO$_2$, requires 423.1601). MS (ESI$^-$) m/z (%): 424.2 (11.8 [M$^+$]), 423.2 (37.7 [M$^-$]), 352.1 (64.9), 317.1 (2.8), 71.6 (40.8), 57.4 (100).

The crude 6a/6b and the clomiphene urine sample were submitted to LC-MS analysis performed on a Waters Quattro Micro LCMS system, operated in the positive ESI mode. For ESI analysis, the cone voltage was set to 60V and the capillary voltage was set to 3kV. The following MRM transitions were monitored: m/z 424-71, 424-224, 424-257, 424-317, 424-352. The LC-MS was performed on a C18 XTerra analytical column (5 µm, 150 x 2.1 mm). A gradient was used for the mobile phase with the system: mobile phase A (95:5 MeCN:H$_2$O with 0.1% formic acid)/mobile phase B (5:95 MeCN:H$_2$O with 0.1% formic acid) delivered at 0.3 mL/min; A:B 25:75 (1 min); A:B 40:60 (9 min); A:B 80:20 (14 min). 6a/6b was detected at m/z 424 with t$_r$ 7.5 min in both the crude sample and the urine sample.