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Supporting Information

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o-Nitrobenzyl Photolabile Protecting Groups with Red-shifted Absorption: Syntheses and Uncaging Cross-sections for One- and Two-Photon Excitation

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Supporting Information

Syntheses

General Procedures

The commercially available chemicals were used without further purification. Anhydrous solvents were freshly distilled before use. Column chromatography (CC): silica gel 60 (0.040-0.063 mm) Merck. Analytical and thin layer chromatography (TLC): Merck silica gel 60 F_{254} precoated plates; detection by UV (254 nm). Melting point: Büchi 510. ^{1}H-NMR Spectra: AM-250 or 400 AVANCE Bruker; chemical shifts (δ) in ppm related to protonated solvent as internal reference (^{1}H: $CHCl_3$ in $CDCl_3$, 7.26 ppm; CHD_2COCD_3 in CD_3COCD_3, 2.20 ppm; CHD_2SOCD_3 in CD_3SOCD_3, 2.49 ppm. ^{13}C: $^{13}CDCl_3$ in $CDCl_3$, 77.0 ppm; $^{13}CD_3COCD_3$ in CD_3COCD_3, 29.8 ppm; $^{13}CD_3SOCD_3$ in CD_3SOCD_3, 39.6 ppm); Coupling constants J in Hz. Mass spectrometry (chemical ionization and high resolution with NH_3 or CH_4) was performed at the Service de Spectrométrie de masse de l'ENS. Microanalyses were obtained from the Service de Microanalyses de l'Université Pierre et Marie Curie, Paris.

5-Methoxy-2-nitro-benzyl alcohol 3a A mixture of 5-hydroxy-2-nitro-benzyl alcohol **2a** (900 mg, 5.3 mmol), methyl iodide (0.5 mL, 7.7 mmol, 1.5 equiv), dry potassium carbonate (1.33 g, 9.6 mmol, 1.8 equiv) in dry acetone (12 mL) was vigorously stirred under nitrogen at 35–40°C for 46 h. After cooling to room temperature, the suspension was filtered. The solvent was evaporated under a vacuum and the residue was dissolved in ether. The organic phase was washed with water, and then with saturated aqueous potassium carbonate. It was dried over magnesium sulfate and concentrated under reduced pressure to give **3a** as a pale yellow solid (484 mg, 50% yield). m.p. 122°C (methanol); ^{1}H NMR (400 MHz, CD_3COCD_3, 25°C): δ (ppm)= 8.30 (d, 1 H, J=9.0 Hz), 7.63 (d, 1 H, J=2.9 Hz), 7.16 (dd, 1 H, J=9.0 Hz and J=2.9 Hz), 5.17 (d, 2 H, J=5.5 Hz), 4.82 (t, 1 H, J=5.5 Hz), 4.10 (s, 3 H); ^{13}C NMR (62.8 MHz, $CDCl_3$, 25°C): δ (ppm)= 164.2, 149.0, 140.3, 127.9, 114.1, 113.2, 62.9, 55.9; MS (CI, NH_3): m/z 201, 152 (calcd av mass for $C_8H_9NO_4$: 183.05); MS (CI, CH_4, HR): m/z 184.0608 (calcd av mass for $C_8H_{10}NO_4$: 184.0610).

2,2,2-Trifluoro-1-(4,5-dimethoxy-2-nitrophenyl)ethanol 4Fa A catalytic amount of tetrabutylammonium fluoride (ca. 4.8 mg) was added to a mixture of 4,5-dimethoxy-2-nitrobenzaldehyde (490 mg, 2.32 mmol) and 0.5 M (trifluoromethyl)trimethylsilane in tetrahydrofuran (5 mL, 2.5 mmol, 1.1 equiv) cooled to 0°C, under nitrogen atmosphere. An orange color instantaneously appeared. The solution was stirred for 30 min at 0°C and was then warmed to room temperature. After stirring for 2 h, 1.2 M hydrochloric acid (3 mL) was added and the mixture was stirred overnight. After extraction with ether, the organic layers were washed with brine, dried over magnesium sulfate and evaporated. The crude residue was purified by column chromatography on silica gel with cyclohexane/ethyl acetate: 3/2 v/v as eluent. **4Fa** was obtained as a pale yellow solid (520 mg, 80% yield). m.p. 112°C (cyclohexane/ether: 4/1); ^{1}H NMR (400 MHz, CD_3COCD_3, 25°C): δ (ppm)= 7.82 (s, 1 H), 7.62 (s, 1 H), 6.47–6.41 (m, 2 H), 4.13 (s, 3 H), 4.13 (s, 3 H); ^{13}C NMR (100 MHz, CD_3COCD_3, 25°C): δ (ppm)= 153.8, 149.8, 141.5, 125.1 (q, ^{1}J=280.6 Hz), 124.6, 110.8, 108.4, 66.2 (q, ^{2}J=31.6 Hz), 56.2, 56.1; ^{19}F NMR (235 MHz, $CFCl_3$, CD_3COCD_3, 25°C): δ (ppm)= -77.1 (d, J=7.0 Hz); MS (CI, CH_4): m/z 282, 264, 252 (calcd av mass for $C_{10}H_{10}F_3NO_5$: 281.05); MS (CI, CH_4, HR): m/z 282.0583 (calcd av mass for $C_{10}H_{11}F_3NO_5$: 282.0589); elemental analysis calcd (%) for $C_{10}H_{10}F_3NO_5$ (281.19): C 42.71, H 3.58, N 4.98; found: C 43.23, H 3.86, N 5.27.

2,2,2-Trichloro-1-(4,5-dimethoxy-2-nitrophenyl)ethanol 4Cla Freshly distilled 1,8-diazabicyclo[5.4.0]undec-7-ene (0.35 mL, 2.36 mmol, 1 equiv) was added dropwise under nitrogen to a solution of 4,5-dimethoxy-2-nitrobenzaldehyde (500 mg, 2.36 mmol) in freshly distilled chloroform (0.4 mL, 4.8 mmol, 2 equiv). The mixture was stirred overnight at room temperature. After dilution with chloroform (10 mL), the organic phase was washed with hydrochloric acid aqueous solution (1.2 M, 3 × 10 mL), and dried over sodium sulfate. After solvent evaporation, **4Cla** was obtained as a yellow solid (762 mg, 98% yield). m.p. 158–159°C; ^{1}H NMR (400 MHz, CD_3COCD_3, 25°C): δ (ppm)= 7.75 (s, 1 H), 7.72 (s, 1 H), 6.98 (d, 1 H, J=6.0 Hz), 6.69 (d, 1 H, J=6.0 Hz), 4.12 (s, 3 H), 4.11 (s, 3 H); ^{13}C NMR (100 MHz, CD_3COCD_3, 25°C): δ (ppm)= 152.7, 149.8, 143.2, 125.0, 112.3, 108.0, 76.8, 67.0, 56.1, 56.1; MS (CI, CH_4): m/z 312, 182 (calcd av mass for $C_{10}H_{10}NCl_3O_5$: 328.96); MS (CI, CH_4, HR): m/z 329.9700 and 331.9672 (calcd av mass for $C_{10}H_{11}NCl_3O_5$: 329.9703, 331.9675).

2,2,2-Tribromo-1-(4,5-dimethoxy-2-nitrophenyl)ethanol 4Bra Tribromoacetic acid previously recrystallised in chloroform (1.05 g, 3.55 mmol, 1.5 equiv) was added to a solution of 4,5-dimethoxy-2-nitrobenzaldehyde (500 mg, 2.36 mmol) in freshly distilled dimethyl sulfoxide (12.5 mL). The mixture was stirred for 1 h at room temperature under nitrogen. Then it was poured into ice-cold water (125 mL). The solution was extracted with ether. The organic phase was washed with sodium hydrogenocarbonate solution (5% m/m), and dried over magnesium sulfate. After solvent evaporation, **4Bra** was obtained as a yellow solid (962 mg, 88%). m.p. 177–180°C; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 7.63 (s, 1 H), 7.53 (s, 1 H), 6.61 (s, 1 H), 4.01 (s, 3 H), 3.96 (s, 3 H), 3.65 (s, 1 H) ; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 151.9, 149.1, 142.9, 123.8, 111.7, 107.7, 77.9, 56.4, 56.3, 52.5; MS (CI, CH_4): m/z 208 (calcd av mass for $C_{10}H_{10}NBr_3O_5$: 460.81); MS (CI, CH_4, HR): m/z 465.8141, 463.8172 and 461.8192 (calcd av mass for $C_{10}H_{11}NBr_3O_5$: 461.82, 463.8167, 465.81).

Hydroxy-(4,5-dimethoxy-2-nitrophenyl)acetonitrile 4CNa Same as for **4Fa**. Tetrabutylammonium fluoride (ca. 4.8 mg), 4,5-dimethoxy-2-nitrobenzaldehyde (500 mg, 2.36 mmol), trimethylsilane cyanide (0.4 mL, 3.07 mmol, 1.3 equiv) in tetrahydrofuran (5 mL). After stirring for 2 h at room temperature, 1.2 M hydrochloric acid (3 mL) was added and the mixture was stirred for 1 h. The solution was extracted with ether. The organic layers were washed with brine, dried over magnesium sulfate and evaporated to yield **4CNa** as a brown solid (500 mg, 90%). m.p. 148-150°C (methanol); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 7.74 (s, 1 H), 7.36 (s, 1 H), 6.19 (s, 1 H), 4.04 (s, 3 H), 3.99 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 154.1, 149.5, 125.6, 117.6, 110.2, 108.5, 60.4, 56.7, 56.5; MS (CI, NH_3): m/z 229, 212, 182 (calcd av mass for $C_{10}H_{10}N_2O_5$: 238.06).

5-Amino-2-nitro-benzyl alcohol 5a [?] A 1 M borane solution in tetrahydrofuran (9 mL, 9 mmol, 1.33 equiv) was added dropwise to a solution of 5-amino-2-nitrobenzoic acid (Sigma-Aldrich, 1.0 g, 5.5 mmol) in tetrahydrofuran (3 mL) cooled to 0°C. The resulting mixture was warmed to room temperature and was then refluxed for 2 h. The mixture was cooled to 0°C and sodium hydroxide (3 M, 10 mL) was added. After stirring at room temperature for 12 h, the aqueous layer was extracted twice with ether. The combined organic layers were dried over sodium sulfate. After evaporation of the solvents, **5a** was obtained as a pale yellow solid (764 mg, 83% yield). m.p. 144.5-145.5°C (methanol); ^{1}H NMR (250 MHz, CD_3COCD_3, 25°C): δ (ppm)= 8.14 (d, 1 H, J=8.9 Hz), 7.30 (d, 1 H, J=2.5 Hz), 6.78 (dd, 1 H, J=8.9 Hz and J=2.5 Hz), 6.16 (s, 2 H), 5.10 (d, 2 H, J=5.6 Hz), 4.57 (t, 1 H, J=5.6 Hz); ^{13}C NMR (62.8 MHz, CD_3COCD_3, 25°C): δ (ppm)= 163.0, 155.0, 143.1, 128.4, 111.6, 111.5, 62.0; elemental analysis calcd (%) for $C_7H_8N_2O_3$ (168.15): C 50.00, H 4.80, N 16.66; found: C 50.30, H 4.74, N 16.42.

5-Iodo-2-nitrobenzoic acid I 5-amino-2-nitrobenzoic acid (Sigma-Aldrich, 2.0 g, 11 mmol) in tetrahydrofuran (22 mL) was added under nitrogen to neat boron trifluoride etherate (5.6 mL, 27 mmol, 2.5 equiv) cooled to -15°C. Then tert-butyl nitrite (3.5 mL, 29 mmol, 2.6 equiv) dissolved in tetrahydrofuran (5.5 mL) was added dropwise to the rapidly stirred solution. After complete addition, the mixture was stirred at -15°C for 10 min and was then allowed to warm to 5°C. A fine precipitate appeared. After stirring at 5°C for 20 min, cold ether (2 mL) was added. The precipitate was collected by filtration, washed with cold ether, and air-dried. The resulting diazonium tetrafluoroborate salt was added portionwise to a solution of sodium iodide (4.4 g, 29 mmol, 2.6 equiv) in acetone (110 mL). The mixture was stirred at room temperature for 12 h. After evaporation of the solvent, ether (140 mL) and water (140 mL) were added to the residue. The aqueous layer was made basic (pH=11) with sodium hydroxide pellets and the mixture was vigorously stirred for 30 min at room temperature. The aqueous phase was washed twice with ether, acidified (pH=1) by adding concentrated hydrochloric acid and stirred with additional ether (150 mL) for 30 min. The layers were separated and the aqueous layer was extracted twice with ether. The combined organic phases were dried over magnesium sulfate and then concentrated. Recrystallisation in hydrochloric acid solution (1.2 M) gave **I** as pale yellow crystals (2.1 g, 65% yield). m.p. 174-175°C (HCl 1.2 M, lit.: 174°C [**?**]); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.38 (d, 1 H, J=1.9 Hz), 8.34 (dd, 1 H, J=1.9 Hz and J=8.3 Hz), 7.91 (d, 1 H, J=8.3 Hz); ^{13}C NMR (100 MHz, CD_3COCD_3, 25°C): δ (ppm)= 164.2, 149.6, 141.6, 138.9, 129.0, 125.6, 99.1; elemental analysis calcd (%) for $C_7H_4NO_4I$ (293.02): C 28.69, H 1.37, N 4.78; found: C 28.86, H 1.25, N 4.57.

5-Iodo-2-nitrobenzyl alcohol II [**?**] 1 M borane in tetrahydrofuran (9 mL, 9 mmol, 1.33 equiv) was added dropwise to 5-Iodo-2-nitrobenzoic acid **I** (2.0 g, 6.8 mmol) in tetrahydrofuran (8 mL) at 0°C. The resulting mixture was warmed to room temperature and then stirred at reflux for 1 h. Excess hydride was carefully destroyed at 0°C with a saturated aqueous solution of ammonium chloride. The aqueous layer was extracted twice with ether. The combined organic layers were washed with a saturated aqueous solution of potassium carbonate and dried over magnesium sulfate. Removal of the solvents gave **II** as a pale yellow solid (1.7 g, 90% yield). m.p. 121-122°C (H_2O/Ethanol: 3/1 v/v); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.17 (s, 1 H), 7.82 (s, 2 H), 4.97 (s, 2 H), 2.41 (bs, 1 H); ^{13}C NMR (62.8 MHz, $CDCl_3$, 25°C): δ (ppm)= 167.8, 138.6, 138.4, 137.5, 126.2, 102.2, 61.8; elemental analysis calcd (%) for $C_7H_6NO_3I$ (279.03): C 30.13, H 2.16, N 5.02; found: C 30.13, H 2.11, N 4.88.

5-(4-Methoxy-phenyl)-2-nitro-benzyl alcohol 7a 5-iodo-2-nitrobenzyl alcohol **II** (400 mg, 1.43 mmol) in dry toluene (24 mL) was stirred at room temperature under nitrogen for 30 min with tetrakis(triphenylphosphine)palladium(0) (67 mg, 5.8 mmol, 4 mol %) and sodium carbonate (2.4 mL of 2 M aqueous solution). 4-methoxyphenylboronic acid (468 mg, 3.16 mmol, 2.1 equiv) dissolved in dry ethanol (2 mL) was added dropwise and the mixture was stirred at room temperature for 30 min. The mixture was refluxed for 2h30. After cooling to 5°C, 30% hydrogen peroxide was added. Dichloromethane (100 mL) was added. The organic phase was washed with water (2 x 70 mL) and saturated aqueous sodium hydrogen carbonate (2 x 70 mL). Then it was dried over magnesium sulfate and the solvent was evaporated. The crude residue was purified by column chromatography on silica gel with cyclohexane/ethyl acetate: 60/40 v/v as eluent to give **7a** as a pale yellow solid (280 mg, 78% yield). m.p. 102°C (cyclohexane/ethyl acetate: 94/6 v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.17 (d, 1 H, J=8.5 Hz), 7.91 (d, 1 H, J=2.0 Hz), 7.63 (dd, 1 H, J=8.5 Hz and J=2.0 Hz), 7.59 (AA'XX', 2 H, J=8.8 Hz), 7.00 (AA'XX', 2 H, J=8.8 Hz), 5.03 (s, 2 H), 3.86 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 160.4, 146.7, 145.6, 137.5, 130.8, 128.5, 127.7, 126.0, 125.9, 114.5, 62.9, 55.4; MS (CI, CH_4): m/z 260, 242 (calcd av mass for $C_{14}H_{13}NO_4$: 259.08); MS (CI, CH_4, HR): m/z 260.0924 (calcd av mass for $C_{14}H_{14}NO_4$: 260.0923).

5-(4-Methoxy-phenylethynyl)-2-nitro-benzyl alcohol 8a 4-Ethynylanisole (200 mg, 1.5 mmol, 1 equiv) was added to a solution of 5-iodo-2-nitrobenzyl alcohol **II** (422 mg, 1.5 mmol) in deoxygenated piperidine (6 mL) with copper(I) iodide (3 mg, 0.015 mmol, 1 mol %) and tetrakis(triphenylphosphine)-palladium(0) (44 mg, 0.04 mmol, 2.5 mol %) at 0°C. After stirring for 2 h at room temperature, saturated aqueous solution of ammonium chloride and ether were added. The aqueous layer was extracted twice with ether. The combined organic layers were washed with a hydrochloric acid solution (1.2 M) and dried over magnesium sulfate. After evaporation of the solvent, the brown crude residue was purified by column chromatography on silica gel with dichloromethane/cyclohexane: 95/5 as eluent to give **8a** as a pale yellow solid (376 mg, 89% yield). m.p. 90°C (cyclohexane/ethanol: 4/1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.11 (d, 1 H, J=8.5 Hz), 7.87 (d, 1 H, J=1.8 Hz), 7.54 (dd, 1 H, J=8.5 Hz and J=1.8 Hz), 7.49 (AA'XX', 2 H, J=8.8 Hz), 6.90 (AA'XX', 2 H, J=8.8 Hz), 5.00 (s, 2 H), 3.84 (s, 3 H); ^{13}C NMR (ppm, 100 MHz, $CDCl_3$, 25°C): δ (ppm)= 160.3, 145.0, 137.2, 133.4, 132.3, 130.8, 130.3, 125.3, 114.1, 114.0, 94.9, 86.6, 62.4, 55.3; elemental analysis calcd (%) for $C_{16}H_{13}NO_4$ (283.28): C 67.84, H 4.63, N 4.94; found: C 67.70, H 4.60, N 4.75.

5-(4-Methoxy-phenylethylene)-2-nitro-benzyl alcohol 9a Silver nitrate (311 mg, 1.8 mmol, 1 equiv) was added to a mixture of 5-iodo-2-nitrobenzyl alcohol **II** (500 mg, 1.8 mmol), palladium acetate (8 mg, 0.036 mmol, 0.02 equiv), triphenylphosphine (19 mg, 0.07 mmol, 0.04 equiv), 4-methoxystyrene (0.48 mL, 3.6 mmol, 2 equiv) and triethylamine (0.3 mL, 2.15 mmol, 1.2 equiv) in acetonitrile (5 mL). The solution was refluxed for 5 days. After cooling to room temperature, it was diluted with dichloromethane (5 mL) and filtered. The filtrate was washed with hydrochloric acid (1.2 M). The aqueous phase was extracted twice with dichloromethane. The combined organic layers were dried over magnesium sulfate. After solvent evaporation, the crude residue was purified by column chromatography on silica gel with cyclohexane/ethyl acetate: 80/20, 70/30 then 50/50 v/v as eluent. **9a** was obtained as a pale yellow solid (194 mg, 34% yield). m.p. 106°C (cyclohexane/ethanol: 5/1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.11 (d, 1 H, J=8.6 Hz), 7.79 (d, 1 H, J=1.7 Hz), 7.51 (dd, 1 H, J=8.6 Hz and J=1.7 Hz), 7.48 (AA'XX', 2 H, J=8.7 Hz), 7.23 (d, 1 H, J=17.0 Hz), 6.98 (d, 1 H, J=17.0 Hz), 6.92 (AA'XX', 2 H, J=8.7 Hz), 5.00 (s, 2 H), 3.84 (s, 3 H), 2.67 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 160.2, 145.4, 143.9, 137.6, 133.0, 128.9, 128.4, 127.1, 125.9, 125.4, 123.9, 114.3, 62.8, 55.3; MS (CI, CH_4): m/z 286 (calcd av mass for $C_{16}H_{15}NO_4$: 285.1); MS (CI, CH_4, HR): m/z 286.1074 (calcd av mass for $C_{16}H_{16}NO_4$: 286.1079).

3-Methyl-4-nitrobenzoic acid methyl ester III [?] A solution of 3-methyl 4-nitrobenzoic acid (9.05 g, 50 mmol) and concentrated sulfuric acid (9.8 g, 100 mmol, 2 eq) in methanol (50 mL) was refluxed for 3 h. After cooling, the precipitated solid was filtered and washed three times with cold methanol. After recrystallization in methanol, **III** was obtained as colourless crystals (7.73 g, 79%).

3-Bromomethyl-4-nitrobenzoic acid methyl ester IV [?] A mixture of **III** (7.73 g, 40 mmol), N-bromosuccinimid (10.57 g, 45 mmol, 1.15 eq) and benzoyle peroxid (338 mg, 1.39 mmol, 3.5% eq) in carbon tetrachloride (250 mL) was refluxed for 18 h. After filtration, the filtrate was concentrated until a solid appeared. **IV** was isolated as a colourless solid after filtration (3.28 g, 12 %). Evaporation of the remaining solution gave 7.93 g of a mixture of **IV** (42 %), methyl 3-dibromomethyl 4-nitrobenzoate (31 %) and **III** (27 %).

3-Hydroxymethyl-4-nitrobenzoic acid V A mixture of **IV** (2.11 g, 7.7 mmol), concentrated sulfuric acid (7.56 g, 77 mmol) and water (78 mL) was refluxed overnight [?]. The cooled solution was extracted with ethyl acetate to afford **V** that was used without further purification for the next step (1.28 g, 84%).

3-Acetoxymethyl-4-nitrobenzoic acid VI A solution of **V** (1.93 g, 9.79 mmol), acetic anhydride (2.0 g, 19.6 mmol, 2 eq) and DMAP (4 mg) in tetrahydrofurane (10 mL) was stirred at room temperature for 16 h. After solvent evaporation, ethyl acetate and water were added. The organic layer was acidified to pH=1 with concentrated hydrochloric acid, dried over magnesium sulfate. Essentially pure **VI** was obtained after solvent evaporation (2.17 g, 92%). It was used without further purification for the next step. ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.33 (s, 1 H), 8.32–8.12 (m, 2 H), 5.54 (s, 2 H), 2.44 (s, 1 H), 2.21 (s,3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 170.4, 169.2, 150.6, 139.5, 132.6, 131.0, 130.6, 125.4, 62.4, 20.8; MS (CI, C_4H_{10}): m/z (%) 257(39) ($M+H_2O$), 240 (19) $[M+H]^+$, 180 (100).

Acetic acid 5-[2-(4-Methoxyphenyl)-2-oxo-ethylcarbamoyl]-2 -nitro-phenyl ester VIII A suspension of **VI** (2.15 g,9.0 mmol) in thionyl chloride (5 mL) was refluxed for 45 min. Crude acetic acid 5-chlorocarbonyl-2-nitrobenzyl ester **VII** was obtained after evaporation of the thionyl chloride in excess. Dichloromethane filtered over neutral alumina (150 mL) was added and the solution was cooled to 0°C. After addition of 4-methoxy-2'-aminoacetophenone chlorhydrate (1.64 g, 8.1 mmol, 0.9 eq) and potassium carbonate (3.10 g, 22.5 mmol, 2.5 eq), the mixture was stirred at room temperature for 15 h. After pouring onto ice, the organic layer was washed with water, dried over magnesium sulfate and evaporated to yield 3.02 g of crude product. The crude was purified by column chromatography over silica gel by using dichloromethane-ethyl acetate 95/5, then 90/10 as eluent. **VIII** was isolated as a white powder (203 mg, 71%). m. p. 145°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.19 (d, J=8.3 Hz, 1 H), 8.11 (s, 1 H), 8.02 (AA'XX', J=8.6 Hz, 2 H), 7.96 (d, J= 8.3 Hz, 1 H), 7.43 (t, J=3.9 Hz, 1 H), 7.01 (AA'XX', J=8.6 Hz, 2 H), 5.54 (s, 2 H), 4.91 (d, J=3.9 Hz, 2 H), 3.91 (s, 3 H), 2.21 (s, 3 H; ^{1}H NMR (250 MHz, CD_3SOCD_3, 25°C): δ (ppm)= 9.20 (t, J=3.2 Hz, 1 H), 8.26 (d, J=8.4 Hz, 1 H), 8.15 (s, 1 H), 8.13 (d, J=8.4Hz, 1 H), 8.08 (AA'XX', J=8.7 Hz, 2 H), 7.10 (AA'XX', J=8.6 Hz, 2 H), 5.46 (s, 2 H), 4.80 (d, J=3.2 Hz, 2 H), 3.88 (s, 3 H), 2.14 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 192.0, 170.3, 165.1, 164.6, 149.2, 138.7, 132.8, 130.4 (2), 128.3, 127.3, 127.1, 125.5, 114.3 (2), 62.6, 55.6, 46.5, 20.8; MS (CI, C_4H_{10}) m/z (%) 404 (14) (M+H_2O), 388(21), 387(100)[M+H]$^+$ (calcd av mass for $C_{19}H_{19}N_2$ O_7 387.36); elemental analysis calcd (%) for $C_{19}H_{18}N_2$ O_7 (386.36): C 59.07, H 4.70, N 7.25; found: C 59.28, H 4.72, N 7.43.

5-[5-(4-Methoxyphenyl)-2-oxazol-2-yl]-2-nitro-benzyl ester IX A solution of **VIII** (2.747 g, 7.1 mmol) in phosphoryl chloride (10 mL) was refluxed for 70 min. The solution was poured onto ice. The resulting supension was filtered and the precipitate was washed with water. After drying, the crude solid was purified by column chromatography over silica gel by using dichloromethane-ethyl acetate 90/10 as eluent. After recrystallization in ethanol, **IX** was obtained as yellow crystals (940 mg, 36%). m. p. 150°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.30 (d, ^{5}J=1.7 Hz, 1 H), 8,24 (d, J=8.7 Hz, 1 H), 8.16 (dd, J=8.7 Hz and ^{5}J=1.7 Hz, 1 H), 7.68 (AA'XX', J=8.8 Hz, 2 H), 7.42 (s, 1 H), 7.01 (AA'XX', J=8.8 Hz, 2 H), 5.58 (s, 2 H), 3.88 (s, 3 H), 2.23 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 170.3, 160.4, 158.1, 153.0, 147.7, 133.2, 132.2, 126.4, 126.1 (2), 126.0, 125.9, 122.9, 120.1, 114.6 (2), 62.9, 55.4, 20.8; MS (CI, C_4H_{10}) m/z (%) 370 (21), 369 (100) [M+H]$^+$ (calcd av mass for C_{19} $H_{17}N_2O_6$ MM=369.34), 309 (8); elemental analysis calcd (%) for $C_{19}H_{16}N_2O_6$ (368.34): C 61.95, H 4.38, N 7.60; found: C 61.39, H 4.37, N 7.63.

{5-[5-(4-Methoxyphenyl)-oxazol-2-yl]-2-nitrophenyl}-methanol 10a A solution of (5-(5'-(4-methoxyphenyl)oxazol-2'yl)-2-nitro-phenyl))methyle acetate **IX** (1.104 g, 3 mmol) and of 1 M sodium hydroxide (6 mL; 6 mmol, 2 eq) in tetrahydrofuran (27 mL) was stirred at room temperature for 16 h.

After solvent evaporation, water and ethyl acetate were added. The organic phase was washed with water, and dried over magnesium sulfate. After solvent evaporation, the crude residue was purified by column chromatography over silica gel by using dichloromethane/ethyle acetate 4/1 as eluent. After recrystallization in ethanol, **10a** was obtained as red-brown crystals (52 mg, 13%). m.p. 179°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.49 (s, 1 H), 8.23 (d, J=8.5 Hz, 1 H), 8.16 (d, J=8.5 Hz, 1 H), 7.69 (AA'XX', J=8.8 Hz, 2 H), 7.42 (s, 1 H), 7.01 (AA'XX', J=8.8 Hz, 2 H), 5.1 (bs, 2 H), 3.88 (s,3 H), 2.67 (bs, 1 H); ^{1}H NMR (250 MHz, CD_3SOCD_3, 25°C): δ (ppm)= 8.53 (s, 1 H), 8.26 (d, J=8.5 Hz, 1 H), 8.19 (d, J=8.5 Hz, 1 H), 7.86 (s, 1 H), 7.84 (d, J=8.8 Hz, 2 H), 7.12 (d, J=8.8 Hz, 2 H), 5.80 (t, J=5.6 Hz, 1 H), 4.93 (d, J=5.6 Hz, 2 H), 3.85 (s, 3 H); ^{13}C NMR (100 MHz, CD_3SOCD_3, 25°C): δ (ppm)= 159.2, 158.0, 152.2, 147.0, 139.7, 131.0, 126.0 (2), 125.6, 125.2, 124.7, 123.4, 119.6, 114.7 (2), 59.8, 55.3; MS (CI, C_4H_{10}) m/z (%) 328 (18), 327 (100) $[M+H]^+$ (calcd av mass for C_{17} $H_{15}N_2O_5$ (327.31)), 295 (22); elemental analysis calcd (%) for $C_{17}H_{14}N_2O_5$ (326.31): C 62.57, H 4.32, N 8.58; found: C 62.35, H 4.43, N 8.43.

1-(4-nitrophenoxymethyl)-5-chloro-2-nitro-benzene 1b Same as for **4b**. Diethyl azodicarboxylate (1.25 mL, 8 mmol, 1.5 equiv), 5-chloro-2-nitro-benzyl alcohol (Sigma-Aldrich 1.0 g, 5.33 mmol), triphenylphosphine (2.1 g, 8 mmol, 1.5 equiv) and 4-nitrophenol **11** (1.1 g, 8 mmol, 1.5 equiv) in tetrahydrofuran (30 mL). The mixture was refluxed for 15 h. After solvent evaporation, the residue was suspended in methanol (15 mL) and the mixture was stirred overnight at room temperature. The resulting precipitate was filtered, washed with cold methanol and dried under reduced pressure to give **1b** as a pale yellow powder (852 mg, 51% yield). m.p. 167–169°C (Tetrahydrofuran); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.22 (AA'XX', 2 H, J=9.2 Hz), 8.16 (d, 1 H, J=8.8 Hz), 7.84 (d, 1 H, J=2.3 Hz), 7.47 (dd, 1 H, J=8.8 Hz and J=2.3 Hz), 7.08 (AA'XX', 2 H, J=9.2 Hz), 5.53 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 162.4, 144.8, 142.3, 141.2, 134.4, 128.9, 128.3, 126.8, 126.1, 114.9, 66.8; elemental analysis calcd (%) for $C_{13}H_9ClN_2O_5$ (308.67): C 50.58, H 2.94, N 9.08; found: C 50.59, H 3.04, N 9.00.

1-(4-nitrophenoxymethyl)-5-methoxy-2-nitro-benzene 3b Same as for **4b**. Diethyl azodicarboxylate (0.25 mL, 1.4 mmol, 1.5 equiv), 5-methoxy-2-nitro-benzyl alcohol **3a** (200 mg, 1.1 mmol), triphenylphosphine (442 mg, 1.7 mmol, 1.5 equiv) and 4-nitrophenol **11** (228 mg, 1.6 mmol, 1.5 equiv) in tetrahydrofuran (16 mL). The mixture was refluxed for 40 h. After solvent evaporation, the residue was suspended in methanol (10 mL) and the mixture was stirred overnight at room temperature. The resulting precipitate was filtered, washed with cold methanol and dried under reduced pressure to give **3b** as a yellow powder (131 mg, 40% yield). m.p. 173°C; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.30 (d, 1 H, J=9.1 Hz), 8.24 (AA'XX', 2 H, J=9.2 Hz), 7.30 (d, 1 H, J=2.8 Hz), 7.09 (AA'XX', 2 H, J=9.2 Hz), 6.95 (dd, 1 H, J=2.8 Hz and J=9.1 Hz), 5.61 (s, 2 H), 3.91 (s, 3 H); ^{13}C NMR (100 MHz,

$CDCl_3$, 25°C): δ (ppm)= 164.2, 162.8, 142.1, 139.5, 135.5, 128.2, 126.0, 114.9, 113.4, 112.7, 67.6, 56.0; elemental analysis calcd (%) for $C_{14}H_{12}N_2O_6$ (304.25): C 55.27, H 3.98, N 9.21; found: C 55.30, H 4.09, N 9.06.

1-(4-nitrophenoxymethyl)-4,5-dimethoxy-2-nitro-benzene 4b [?] Diethyl azodicarboxylate (0.5 mL, 3.2 mmol, 1.35 equiv) was added dropwise to a solution of 4,5-dimethoxy-2-nitrobenzyl alcohol (Sigma-Aldrich, 500 mg, 2.3 mmol), 4-nitrophenol **11** (322 mg, 2.3 mmol, 1 equiv) and triphenylphosphine (832 mg, 3.2 mmol, 1.35 equiv) in tetrahydrofuran (40 mL) at 0°C, under nitrogen atmosphere. Upon completion of the addition, the solution was stirred at room temperature for 14 h and was subsequently refluxed for 6 h. After solvent evaporation, the residue was suspended in ether (30 mL) and was stirred overnight at room temperature. The resulting precipitate was filtered, washed with ether and dried under reduced pressure to give **4b** as a pale yellow solid (645 mg, 84% yield). m.p. 201-203°C (THF); ^1H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.24 (AA'XX', 2 H, J=9.2 Hz), 7.79 (s, 1 H), 7.25 (s, 1 H), 7.09 (AA'XX', 2 H, J=9,2 Hz), 5.59 (s, 2 H), 3.98 (s, 3 H), 3.97 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 162.8, 153.9, 148.2, 142.1, 139.1, 127.3, 126.0, 114.9, 109.2, 108.1, 67.6, 56.4, 56.4; elemental analysis calcd (%) for $C_{15}H_{14}N_2O_7$(334.28): C 53.89, H 4.22, N 8.38; found: C 53.90, H 4.27, N 8.43.

1-(4-nitrophenoxymethyl)-5-amino-2-nitro-benzene 5b Same as for **4b**. Diethyl azodicarboxylate (0.8 mL, 4.4 mmol, 1.35 equiv), 5-amino-2-nitro-benzyl alcohol **5a** (552 mg, 3.3 mmol), triphenylphosphine (1.16 g, 4.4 mmol, 1.35 equiv) and 4-nitrophenol **11** (460 mg, 3.3 mmol, 1 equiv) in tetrahydrofuran (35 mL). The mixture was refluxed for 25 h. After solvent evaporation, the residue was suspended in methanol (15 mL) and the mixture was stirred overnight at room temperature. The resulting precipitate was filtered, washed with cold methanol and dried under reduced pressure to give **5b** as a a brown powder (475 mg, 50% yield). m.p. 209-211°C; ^1H NMR (400 MHz, CD_3COCD_3, 25°C): δ (ppm)= 8.40 (AA'XX', 2 H, J=9.2 Hz), 8.23 (d, 1 H, J=8.9 Hz), 7.39 (AA'XX', 2 H, J=9.2 Hz), 7.16 (d, 1 H, J=2.5 Hz), 6.88 (dd, 1 H, J=8.9 Hz and J=2.5 Hz), 6.30 (s, 2 H), 5.79 (s, 2 H); ^{13}C NMR (100 MHz, CD_3COCD_3, 25°C): δ (ppm)= 163.9, 155.1, 142.2, 136.4, 135.8, 128.9, 126.1, 115.6, 112.3, 111.6, 68.7; elemental analysis calcd (%) for $C_{13}H_{11}N_3O_5$ (289.24): C 53.98, H 3.83, N 14.53; found: C 54.10, H 3.88, N 14.34.

1-(4-nitrophenoxymethyl)-5-(N-methylpiperazine)-2-nitro-benzene 6b 1-Methylpiperazine (0.8 mL, 7 mmol, 10 equiv) was added to a solution of 1-(4-nitrophenoxymethyl)-5-chloro-2-nitro-benzene **1b** (200 mg, 0.65 mmol) in dimethylformamide (8 mL). The solution was heated at 110°C for 2 h. After evaporation of the solvent under reduced pressure, the residue was dissolved in dichloromethane. The organic layer was washed with a saturated aqueous solution of potassium carbonate, and dried over sodium sulfate. After solvent evaporation, the crude residue was purified by column chromatography on silica gel with dichloromethane/ethanol: 3/2 v/v as eluent. **6b** was obtained as a pale yellow solid (187 mg, 78% yield). m.p. 168–169°C; ^{1}H NMR (400 MHz, CDCl$_3$, 25°C): δ (ppm)= 8.22 (AA'XX', 2 H, J=9.2 Hz), 8.21 (d, 1 H, J=9.5 Hz), 7.12 (d, 1 H, J=2.8 Hz, J=9.2 Hz), 7.09 (AA'XX', 2 H, J=9.2 Hz), 6.80 (dd, 1 H, J=9.5 Hz and J=2.8 Hz), 5.60 (s, 2 H), 3.44 (t, 4 H, J=5.1 Hz), 2.53 (t, 4 H, J=5.1 Hz), 2.34 (s, 3 H); ^{13}C NMR (100 MHz, CDCl$_3$, 25°C): δ (ppm)= 163.0, 154.3, 141.9, 136.1, 135.2, 128.3, 126.0, 114.9, 111.8, 110.8, 68.3, 54.4, 46.7, 46.0; MS (CI, CH$_4$): m/z 373 (calcd av mass for $C_{18}H_{20}N_4O_5$: 372.38); MS (CI, CH$_4$, HR): m/z 373.1505 (calcd av mass for $C_{18}H_{21}N_4O_5$: 373.1512).

1-(4-nitrophenoxymethyl)-5-(4-methoxy-phenyl)-2-nitro-benzene 7b Same as for **4b**. Diethyl azodicarboxylate (0.25 mL, 1.4 mmol, 1.35 equiv), 5-(4-methoxy-phenyl)-2-nitro-benzyl alcohol **7a** (274 mg, 1 mmol), triphenylphosphine (374 mg, 1.4 mmol, 1.35 equiv) and 4-nitrophenol **11** (147 mg, 1 mmol, 1 equiv) in tetrahydrofuran (25 mL). The mixture was refluxed for 24 h. After solvent evaporation, the residue was suspended in methanol (10 mL) and the mixture was stirred overnight at room temperature. The resulting precipitate was filtered, washed with cold methanol and dried under reduced pressure to give **7b** as a yellow powder (118 mg, 31% yield). m.p. 165-167°C; ^{1}H NMR (400 MHz, CDCl$_3$, 25°C): δ (ppm)= 8.29 (d, 1 H, J=8.6 Hz), 8.25 (AA'XX', 2 H, J=9.2 Hz), 7.98 (d, 1 H, J=2.0 Hz), 7.68 (dd, 1 H, J=8.6 Hz and J=2.0 Hz), 7.56 (AA'XX', 2 H, J=8.8 Hz), 7.12 (AA'XX', 2 H, J=9.2 Hz), 7.02 (AA'XX', 2 H, J=8.8 Hz), 5.65 (s, 2 H), 3.87 (s, 3 H); ^{13}C NMR (100 MHz, CDCl$_3$, 25°C): δ (ppm)= 162.9, 160.6, 146.9, 144.9, 142.1, 132.9, 130.7, 128.6, 126.4, 126.1, 126.0, 126.0, 114.9, 114.6, 67.6, 55.4; MS (CI, CH$_4$): m/z 409, 381, 242, 140 (calcd av mass for $C_{20}H_{16}N_2O_6$: 380.10); MS (CI, CH$_4$, HR): m/z 380.1012 and 381.1082 (calcd av mass for $C_{20}H_{16}N_2O_6$: 380.1008 and $C_{20}H_{17}N_2O_6$: 381.1087).

1-(4-nitrophenoxymethyl)-5-(4-methoxy-phenylethynyl)-2-nitro-benzene 8b Same procedure as for **4b**. Diethyl azodicarboxylate (0.1 mL, 0.69 mmol, 1.35 equiv), 5-(4-methoxy-phenylethynyl)-2-nitro-benzyl alcohol **8a** (145 mg, 0.5 mmol), triphenylphosphine (181 mg, 0.69 mmol, 1.35 equiv) and 4-nitrophenol **11** (71 mg, 0.5 mmol, 1 equiv) in tetrahydrofuran (12 mL). After precipitation in ether (8 mL), **8b** was obtained as a pure pale yellow powder (150 mg, 75% yield). m.p. 169°C (THF); ^{1}H NMR (400 MHz, CDCl$_3$, 25°C): δ (ppm)= 8.26 (AA'XX', 2 H, J=9.2 Hz), 8.21 (d, 1 H, J=8.5 Hz), 7.93 (d, 1 H, J=1.8 Hz), 7.61 (dd, 1 H, J=8.5 Hz and J=1.8 Hz), 7.50 (AA'XX', 2 H, J=8.8 Hz), 7.12 (AA'XX', 2 H, J=9.2 Hz), 6.90 (AA'XX', 2 H, J=8.8 Hz), 5.58 (s, 2 H), 3.84 (s, 3 H); ^{13}C NMR (100 MHz, CDCl$_3$, 25°C): δ (ppm)= 162.8, 160.5, 145.0, 142.1, 133.5, 132.7, 131.2, 130.7, 130.5, 126.0, 125.5, 114.9, 114.2, 113.8, 95.4, 86.5, 67.2, 55.3; elemental analysis calcd (%) for $C_{22}H_{16}N_2O_6$ (404.37): C 65.34, H 3.99, N 6.93; found: C 65.4, H 3.96, N 6.93.

1-(4-nitrophenoxymethyl)-5-(4-methoxy-phenylethylene)-2-nitro-benzene 9b Same as for **4b**. Diethyl azodicarboxylate (0.21 mL, 1.35 mmol, 1.5 equiv), 5-(4-methoxy-phenylethylene)-2-nitro-benzyl alcohol **9a** (232 mg, 0.9 mmol), triphenylphosphine (335 mg, 1.35 mmol, 1.5 equiv) and 4-nitrophenol **11** (187 mg, 1.35 mmol, 1.5 equiv) in tetrahydrofuran (7 mL). The mixture was refluxed for 48 h. After solvent evaporation, the residue was suspended in methanol (10 mL) and the mixture was stirred overnight at room temperature. The resulting precipitate was filtered, washed with cold methanol and dried under reduced pressure. After purification by column chromatography on silica gel with cyclohexane/ethyl acetate: 7/3 v/v as eluent, **9b** was obtained as a pale yellow solid (114 mg, 30% yield). m.p. 190-192°C; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.26 (AA'XX', 2 H, J=9.2 Hz), 8.23 (d, 1 H, J=8.6 Hz), 7.84 (d, 1 H, J=1.8 Hz), 7.61 (dd, 1 H, J=1.8 Hz and J=8.6 Hz), 7.49 (AA'XX', 2 H, J=8.7 Hz), 7.23 (d, 1 H, J=16.3 Hz), 7.13 (AA'XX', 2 H, J=9.2 Hz), 7.00 (d, 1 H, J=16.3 Hz), 6.92 (AA'XX', 2 H, J=8.7 Hz), 5.62 (s, 2 H), 3.84 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 162.9, 160.3, 144.6, 144.1, 142.1, 133.5, 133.0, 128.7, 128.5, 126.1, 126.1, 125.7, 125.4, 123.8, 114.9, 114.3, 67.6, 55.3; MS (CI, CH_4): m/z 407, 270, 140 (calcd av mass for $C_{22}H_{18}N_2O_6$: 406.12); MS (CI, CH_4, HR): m/z 407.1242 (calcd av mass for $C_{22}H_{19}N_2O_6$: 407.1243).

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid 12 [?] **12** was prepared according to the literature procedure from Knoevenagel condensation between 4-diethylamine salicylaldehyde and diethylmalonate and additional hydrolysis of the resulting ethyl ester. The carboxylic acid was purified by precipitation in ether. Yield: 65%.

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid 4,5-dimethoxy-2-nitrobenzyl ester 4c Dicyclohexycarbodiimide (78.4 mg, 0.38 mmol, 1 equiv) was added at 0°C under nitrogen to a stirred solution of 7-diethylamino-2-oxo-2H-chromene-3-carboxylic acid **12** (100 mg, 0.38 mmol), 4,5-dimethoxybenzyl alcool (81 mg, 0.38 mmol, 1 equiv) and 4-dimethylaminopyridine (47 mg, 0.38 mmol, 1 equiv) in anhydrous dichloromethane (10 mL). The mixture was stirred for 10 min at 0°C and for 12 h at 20°C. The organic phase was washed with 1.2 M hydrochloric acid (2 x 10 mL) and with saturated aqueous solution of sodium hydrogen carbonate (2 x 10 mL). It was subsequently dried over magnesium sulfate and evaporated. The resulting residue was suspended in methanol. The precipitate was filtered, washed with cold methanol and dried under reduced pressure to give **4c** as a yellow powder (136 mg, 78%). m.p. 243°C ; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.60 (s, 1 H), 8.04 (s, 1 H), 7.77 (s, 1 H), 7.40 (d, 1 H, J=9.0 Hz), 6.63 (dd, 1 H, J=2.4 Hz and J=9.0 Hz), 6.48 (d, 1 H, J=2.4 Hz), 5.79 (s, 2 H), 4.12 (s, 3 H), 3.96 (s, 3 H), 3.45 (q, 4 H, J=7.1 Hz), 1.24 (t, 6 H, J=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 164.4, 158.7, 158.6, 154.4, 153.2, 150.6, 147.6, 138.6, 131.3, 128.5, 110.5, 109.7, 108.0, 107.9, 107.7, 96.6, 64.3, 57.1, 56.3, 45.2, 12.4; MS (CI, CH_4): m/z 457 (calcd av mass for $C_{23}H_{24}N_2O_8$: 456.46); MS (CI, NH_3, HR): m/z 457.1608 (calcd for $C_{23}H_{25}N_2O_8$: 457.1611).

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid 2,2,2-trifluoro-1- (4,5-dimethoxy-2-nitrophenyl)-ethyl ester 4Fc Same procedure as for **4c**. 7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid **12** (100 mg, 0.38 mmol), 2,2,2-trifluoro-1-(4,5-dimethoxy-2-nitrophenyl)ethanol **4Fa** (135 mg, 0.48 mmol, 1.25 equiv), 4-dimethylaminopyridine (47 mg, 0.38 mmol, 1 equiv) and dicyclohexycarbodiimide (78.4 mg, 0.38 mmol, 1 equiv). **4Fc** as a yellow powder (126 mg, 63%). m.p. 178–180°C; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.52 (s, 1 H), 7.88 (s, 1 H), 7.76 (s, 1 H), 7.76 (q, 1 H, J=6.0 Hz), 7.43 (d, 1 H, J=9.0 Hz), 6.67 (dd, 1 H, J=2.4 Hz and J=9.0 Hz), 6.50 (d, 1 H, J=2.4 Hz), 4.12 (s, 3 H), 4.01 (s, 3 H), 3.50 (q, 4 H, J=7.2 Hz), 1.28 (t, 6 H, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 162.9, 158.9, 157.9, 153.7, 153.5, 150.9, 149.4, 140.7, 131.5, 124.4, 121.4, 111.9, 109.9, 108.1, 107.8, 106.7, 96.6, 67.3 (q, ^{2}J=33 Hz), 57.0, 56.4, 45.2, 29.7, 12.4; MS (CI, CH_4): m/z 525 (calcd av mass for $C_{24}H_{23}F_3N_2O_8$: 524.44); MS (CI, CH_4, HR): m/z 525.1483 (calcd for $C_{24}H_{24}F_3N_2O_8$: 525.1485); elemental analysis calcd (%) for $C_{24}H_{23}F_3N_2O_8$ (524.44): C 54.97, H 4.42, N 5.34; found: C 54.48, H 4.78, N 5.23.

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid 2,2,2-trichloro-1-(4,5-dimethoxy-2-nitrophenyl)-ethyl ester 4Clc Same as for **4c**. 7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid **12** (100 mg, 0.38 mmol), 2,2,2-trichloro-1-(4,5-dimethoxy-2-nitrophenyl)ethanol **4Cla** (159 mg, 0.48 mmol, 1.25 equiv), 4-dimethylaminopyridine (47 mg, 0.38 mmol, 1 equiv) and dicyclohexycarbodiimide (78.4 mg, 0.38 mmol, 1 equiv). **4Clc** as a yellow powder (118 mg, 54%). m.p. 190–194°C; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.49 (s, 1 H), 8.11 (s, 1 H), 7.99 (s, 1 H), 7.63 (s, 1 H), 7.39 (d, 1 H, J=9.0 Hz), 6.62 (dd, 1 H, J=2.4 Hz and J=9.0 Hz), 6.45 (d, 1 H, J=2.4 Hz), 4.07 (s, 3 H), 3.96 (s, 3 H), 3.46 (q, 4 H, J=7.1 Hz), 1.23 (t, 6 H, J=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 162.8, 158.9, 157.9, 153.4, 152.5, 150.7, 149.3, 142.2, 131.5, 122.3, 113.4, 109.8, 107.9, 107.8, 107.0, 96.6, 77.3, 56.9, 56.4, 45.2, 29.7, 12.4; MS (CI, CH_4): m/z 573 (calcd av mass for $C_{24}H_{23}Cl_3N_2O_8$: 573.82); MS (CI, CH_4, HR): m/z 573.0596 and 575.0565 (calcd for $C_{24}H_{24}Cl_3N_2O_8$: 573.0598 and 575.0573); elemental analysis calcd (%) for $C_{24}H_{23}Cl_3N_2O_8$ (573.82): C 50.24, H 4.04, N 4.88; found: C 49.95, H 4.30, N 4.68.

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid 2,2,2-tribromo-1- (4,5-dimethoxy-2-nitrophenyl)-ethyl ester 4Brc Same procedure as for **4c**. 7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid **12** (100 mg, 0.38 mmol), 2,2,2-tribromo-1-(4,5-dimethoxy-2-nitrophenyl)ethanol **4Bra** (232 mg, 0.5 mmol, 1.3 equiv), 4-dimethylaminopyridine (47 mg, 0.38 mmol, 1 equiv) and dicyclohexycarbodiimide (78.4 mg, 0.38 mmol, 1 equiv). **4Brc** as a yellow powder (161 mg, 60%). m.p. 260–262°C; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.55 (s, 1 H), 8.17 (s, 1 H), 8.13 (s, 1 H), 7.68 (s, 1H), 7.43 (d, 1 H, J=9.0 Hz), 6.66 (dd, 1 H, J=2.4 Hz and J=9.0 Hz), 6.50 (d, 1 H, J=2.4 Hz), 4.12 (s, 3 H), 4.01 (s, 3 H), 3.50 (q, 4 H, J=7.2 Hz), 1.28 (t, 6 H, J=7.2 Hz); ^{13}C NMR (100 MHz,

$CDCl_3$, 25°C): δ (ppm)= 162.6, 158.9, 157.9, 153.4, 152.4, 150.6, 149.3, 142.5, 131.5, 123.2, 113.5, 109.8, 107.9, 107.8, 107.2, 96.6, 77.5, 56.9, 56.4, 45.2, 29.7, 12.4; MS (CI, NH_3): m/z 707 and 709 (calcd av mass for $C_{24}H_{23}Br_3N_2O_8$: 707.90); MS (CI, NH_3, HR): m/z 706.9060 and 708.9030 (calcd for $C_{24}H_{24}Br_3N_2O_8$: 706.9064 and 708.9046).

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid cyano- (4,5-dimethoxy-2-nitrophenyl)-methyl ester 4CNc Same procedure as for **4c**. 7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid **12** (52 mg, 0.20 mmol), 2,2,2-trichloro-1-(4,5-dimethoxy-2-nitrophenyl)ethanol **4CNa** (60 mg, 0.25 mmol, 1.25 equiv), 4-dimethylaminopyridine (24.5 mg, 0.20 mmol, 1 equiv) and dicyclohexycarbodiimide (41.3 mg, 0.20 mmol, 1 equiv). **4CNc** as a yellow powder (60 mg, 62%). m.p. 219–222°C ; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.63 (s, 1 H), 8.20 (s, 1 H), 7.86 (s, 1 H), 7.47 (d, 1 H, J=9.1 Hz), 7.28 (s, 1 H), 6.69 (dd, 1 H, J=2.4 Hz and J=9.1 Hz), 6.52 (d, 1 H, J=2.4 Hz), 4.20 (s, 3 H), 4.04 (s, 3 H), 3.52 (q, 4 H, J=7.2 Hz), 1.29 (t, 6 H, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 162.9, 159.1, 158.1, 154.6, 153.8, 151.7, 149.4, 138.8, 131.8, 122.9, 115.3, 111.0, 110.1, 108.1, 108.0, 105.8, 96.6, 60.4, 57.3, 56.5, 45.3, 12.4; MS (CI, NH_3): m/z 482 (calcd av mass for $C_{24}H_{23}N_3O_8$: 481.45).

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid 5-amino-2-nitro-benzyl ester 5c Same procedure as for **4c**. 7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid **12** (115 mg, 0.4 mmol), 5-amino-2-nitrobenzyl alcohol **5a** (74 mg, 0.4 mmol, 1 eq), 4-dimethylaminopyridine (45 mg, 0.4 mmol, 1 eq) and dicyclohexycarbodiimide (91 mg, 0.4 mmol, 1 eq). **5c** as a yellow powder (130 mg, 65%). m. p. 235–237°C (methanol); ^{1}H NMR (400 MHz, CD_3SOCD_3, 25°C): δ (ppm)= 8.89 (s, 1 H), 8.24 (d, 1 H, J=9.1 Hz), 7.90 (d, 1 H, J=9.1 Hz), 7.02 (dd, 1 H, J=9.1 Hz and J=2.3 Hz), 6.99 (d, 1 H, J=2.3 Hz), 6.79 (m, 2 H), 5.80 (s, 2 H), 3.71 (q, 4 H, J=7.0 Hz), 1.36 (t, 6 H, J=7.0 Hz); ^{13}C NMR (100 MHz, CD_3SOCD_3, 25°C): δ (ppm)= 162.8, 158.2, 157.0, 155.1, 153.0, 149.7, 136.4, 133.9, 132.0, 128.7, 111.5, 111.5, 109.9, 107.0, 106.4, 95.8, 63.5, 44.3, 12.3; MS (CI, NH_3): m/z 412 (calcd av mass for $C_{21}H_{21}N_3O_6$: 411.41); MS (FAB, HR): m/z 412.1514 (calcd for $C_{21}H_{22}N_3O_6$: 412.1509).

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid 5-iodo-2-nitrobenzyl ester IIc Same procedure as for **4c**. 7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid **12** (439 mg, 1.7 mmol), 5-iodo-2-nitrobenzyl alcohol **II** (585 mg, 2.1 mmol, 1.25 equiv), 4-dimethylaminopyridine (205 mg, 1.7 mmol, 1 equiv) and dicyclohexycarbodiimide (347 mg, 1.7 mmol, 1 equiv). **IIc** as a yellow powder (460 mg, 52%). m.p. 117.5–178°C; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.50 (m, 2 H), 7.84 (s, 2 H), 7.39 (d, 1 H, J=9.0 Hz), 6.62 (dd, 1 H, J=2.4 Hz and J=9.0 Hz), 6.47 (d, 1 H, J=2.4 Hz), 5.73 (s, 2 H), 3.46 (q, 4 H, J=7.1 Hz), 1.24 (t, 6 H, J=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 163.9, 158.7, 158.2, 153.2, 150.2, 146.3, 138.3, 137.7, 134.3, 131.3, 126.0, 109.7, 107.8, 107.6, 102.3, 96.6, 62.8, 45.1, 12.4; MS (CI, CH_4): m/z 523, 279, 262 (calcd av mass for $C_{21}H_{19}IN_2O_6$: 522.29).

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid 5- (4-methoxy-phenylethynyl)-2-nitrobenzyl ester 8c 4-Ethynylanisole (0.44 mL, 0.34 mmol, 1.2 equiv) was added to a solution of 7-diethylamino-2-oxo-2H-chromene-3-carboxylic acid 5-iodo-2-nitrobenzyl ester **IIc** (150 mg, 0.29 mmol) in deoxygenated piperidine (1 mL) with copper(I) iodide (2.7 mg, 0.014 mmol, 5 mol %) and tetrakis(triphenylphosphine)palladium(0) (33 mg, 0.03 mmol, 10 mol %) at 0°C. After stirring for 4 h at room temperature, saturated aqueous solution of ammonium chloride and ether were added. The aqueous layer was extracted twice with dichloromethane. The combined organic layers were washed with a hydrochloric acid solution (1.2 M) and dried over magnesium sulfate. After evaporation of the solvent, the brown crude residue was purified by column chromatography on silica gel with cyclohexane/ethyl acetate: 3/2 v/v as eluent to give **8c** as a pale yellow solid (92 mg, 61% yield). m.p. 193–194°C (ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.50 (s, 1 H), 8.13 (d, 1 H, J=8.5 Hz), 8.02 (s, 1 H), 7.56 (d, 1 H, J=8.5 Hz), 7.50 (d, 2 H, J=8.7 Hz), 7.38 (d, 1 H, J=9.0 Hz), 6.88 (d, 2 H, J=8.7 Hz), 6.61 (dd, 1 H, J=2.2 Hz and J=9.0 Hz), 6.48 (d, 1 H, J=2.2 Hz), 5.77 (s, 2 H), 3.83 (s, 3 H), 3.45 (q, 4 H, J=7 Hz), 1.24 (t, 6 H, J=7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 163.9, 160.3, 158.7, 158.1, 153.1, 150.1, 145.6, 133.5, 133.0, 131.8, 131.3, 131.0, 130.2, 125.2, 114.2, 114.0, 109.6, 107.8, 96.6, 94.9, 86.7, 63.4, 63.3, 55.3, 45.1, 12.4; MS (CI, CH_4): m/z 527 (calcd av mass for $C_{30}H_{26}N_2O_7$: 526.24); MS (CI, CH_4, HR): m/z 527.1815 (calcd for $C_{30}H_{27}N_2O_7$: 527.1818).

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid 5-(4-Methoxy-phenylethylene)-2-nitrobenzyl ester 9c Silver nitrate (89 mg, 0.53 mmol, 1 equiv) was added to a mixture of 7-diethylamino-2-oxo-2H-chromene-3-carboxylic acid 5-iodo-2-nitrobenzyl ester **IIc** (275 mg, 0.53 mmol), palladium acetate (2.7 mg, 0.01 mmol, 0.02 equiv), triphenylphosphine (5.5 mg, 0.02 mmol, 0.04 equiv), 4-methoxystyrene (0.48 mL, 3.6 mmol, 2 equiv) and triethylamine (0.1 mL, 0.63 mmol, 1.2 equiv) in acetonitrile (3 mL). The solution was refluxed for 6 days, then diluted with dichloromethane (5 mL) and filtered. The filtrate was washed with hydrochloric acid (1.2 M). The aqueous phase was extracted twice with dichloromethane. The combined organic layers were dried over magnesium sulfate and evaporated. The resulting residue was purified by column chromatography on silica gel with cyclohexane/ethyl acetate: 3/2 v/v then dichloromethane as eluent. **9c** was obtained as a yellow solid (120 mg, 43% yield). m. p. 203–205°C (ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.52 (s, 1 H), 8.29 (d, 1 H, J=1.4 Hz), 8.15 (d, 1 H, J=8.5 Hz), 7.54–7.49 (m, 3 H), 7.39 (d, 1 H, J=16.3 Hz), 7.38 (d, 1 H, J=9.0 Hz), 7.01 (d, 1 H, J=16.3 Hz), 6.90 (AA'XX', 2 H, J=8.7 Hz), 6.61 (dd, 1 H, J=2.4 Hz and J=9.0 Hz), 6.48 (d, 1 H, J=2.4 Hz), 5.8 (s, 2 H), 3.83 (s, 3 H), 3.45 (q, 4 H, J=7.0 Hz), 1.24 (t, 6 H, J=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): δ (ppm)= 164.2, 160.0, 158.7, 158.3, 153.1, 150.2, 144.6, 144.0, 133.5, 133.3, 131.3, 129.1, 128.5, 126.4, 125.7, 125.2, 124.0, 114.1, 109.6, 108.0, 107.8, 96.6, 63.9, 55.3, 45.1, 12.4; MS (CI, CH_4): m/z 529 (calcd av mass for $C_{30}H_{28}N_2O_7$: 528.57); MS (CI, CH_4, HR): m/z 529.1970 (calcd for $C_{30}H_{29}N_2O_7$: 529.1975).

7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid 5-[5-(4-methoxy-phenyl)-oxazol-2-yl]-2-nitro-benzyl ester 10c Same procedure as for **4c**. 7-Diethylamino-2-oxo-2H-chromene-3-carboxylic acid **12** (64 mg, 0.24 mmol), 5-[5-(4-methoxy-phenyl)-oxazol-2-yl]-2-nitro-phenyl-methanol **10a** (100 mg, 0.31 mmol, 1.25 eq), 4-dimethylaminopyridine (30 mg, 0.24 mmol, 1 eq) and dicyclohexycarbodiimide (50 mg, 0.24 mmol, 1 eq). **10c** as a yellow powder (53 mg, 40%). m. p. 207–209°C (methanol); ^{1}H NMR (ppm, 400 MHz, $CDCl_3$, 25°C): δ (ppm)= 8.81 (s, 1 H), 8.54 (s, 1 H), 8.26 (d, 1 H, J=8.6 Hz), 8.18 (dd, 1 H, J=8.6 Hz and J=1.6 Hz), 7.76 (AA'XX', 2 H, J=8.8 Hz), 7.40 (s, 1 H), 7.39 (d, 1 H, J=8.9 Hz), 6.96 (AA'XX', 2 H, J=8.8 Hz), 6.62 (dd, 1 H, J=2.3 Hz and J=8.9 Hz), 6.46 (d, 1 H, J=2.3 Hz), 5.86 (s, 2 H), 3.94 (s, 3 H), 3.46 (q, 4 H, J=7.1 Hz), 1.25 (t, 6 H, J=7.1 Hz); ^{13}C NMR (ppm, 100 MHz, $CDCl_3$, 25°C): δ (ppm)= 164.0, 160.1, 158.8, 158.2, 158.1, 153.1, 152.9, 150.1, 147.0, 133.9, 132.5, 131.4, 126.6, 126.2, 125.8, 125.6, 122.8, 120.3, 114.5, 109.7, 108.0, 107.8, 96.6, 63.5, 55.3, 45.1, 12.4; MS (CI, CH_4): m/z 570 (calcd av mass for $C_{31}H_{27}N_3O_8$: 569.56); MS (CI, CH_4, HR): m/z 570.1873 (calcd for $C_{31}H_{28}N_3O_8$: 570.1876).