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**Substituted 2-Nitrobenzyltrichloroacetate Esters for Photodirected Oligonucleotide Detritylation in Solid Films**

**SUPPORTING INFORMATION**

Pawel J. Serafinowski and Peter B. Garland

_Cancer Research UK Centre for Cancer Therapeutics_ & _Section of Molecular Carcinogenesis_

_The Institute of Cancer Research, Sutton, Surrey, SM2 5NG, UK_

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1 Chemical synthesis and characterization of photolabile esters

1.1 General experimental section

Melting points were determined on a Reichert micro-hot stage apparatus and are uncorrected.

UV spectra were measured in dichloromethane with a Pye-Unicam SP-8-150 UV-vis spectrophotometer, values for molar extinction coefficients are given in [m$^{-1}$ cm$^{-1}$].  $^1$H and $^{13}$C NMR spectra were recorded using Bruker Avance DPX 500MHz or 600MHz spectrometer. Unless otherwise
indicated all the spectra were measured in DMSO-d₆ solutions and referenced to the residual DMSO signal. All ¹H and ¹³C signals are given in ppm (δ scale). For ¹H NMR s = singlet, d = doublet, t = triplet, dd = double doublet, q = quadruplet, m = multiplet, br s = broad signal. Mass spectra in FAB mode were run on a VG ZAB-SE spectrometer with FAB ionisation. Accurate masses were determined with MNOBA+Na as the matrix.

The HRMS and LRMS (LCMS) in ES mode were run using Waters LCT with ESI Lockspray source and Alliance 2795 LC system. GC MS spectra were recorded on ThermoFinnigan Polaris Q instrument. Thin layer chromatography was run on HPTLC (high performance TLC), Merek Kieselgel 60F₂₅₄ analytical plates in the following systems: (A) CH₂Cl₂, (B) Hexane/ EtOAc (9:1), (C) Hexane/Acetone (7:3). Coarse ICN silicagel was used for short column chromatography.

A microwave reactor CEM Focused Microwave Synthesis System Model Discovery was used for the reactions of nucleophilic aromatic substitution and oxidation with chromium trioxide. Phenylmagnesium bromide and 5-fluoro-2-nitrobenzaldehyde were purchased from Aldrich and Fluorochem, respectively.

1.2 Preparation of precursors for the synthesis of photolabile esters

Synthesis of the target photolabile esters entailed prior preparation of various precursors with appropriate structural modifications to render the required properties of final products. (Scheme 1). These precursors included 2-nitro and 2,6-dinitro substituted benzaldehydes and α-phenyl-2-nitro and α-phenyl-2,6-dinitro benzyl alcohols obtained via the Grignard reaction of the benzaldehydes with phenyl magnesium bromide. Some of the resulting α-phenyl-2-nitrobenzyl alcohols were subjected to further transformations such as nucleophilic substitution with aliphatic and aromatic amines, coupling with nitrosobenzene or Suzuki coupling with various phenyl boronic acids to introduce electron donating 5-amino, 5-phenylazo or 5-phenyl substituents, respectively.

1.2.1 Synthesis of substituted benzaldehydes

5-bromo-2-nitrobenzaldehyde 32 was prepared by the nitration of a commercially available 3-bromo-benzaldehyde 30 as described earlier.¹ A commercially available 3-iodobenzaldehyde 31 was nitratred with a mixture of fuming nitric acid and fuming sulphuric acid to give 5-iodo-2-nitrobenzaldehyde 33² and the unreported 3-iodo-2-nitrobenzaldehyde 34 in the 2:1 ratio. Nitration of a commercially available 5-fluoro-2-nitrobenzaldehyde 35 with a mixture of fuming nitric acid and concentrated sulphuric acid gave 5-fluoro-2,6-dinitrobenzaldehyde 6. Compound 32 upon nitration with a mixture of fuming nitric acid and concentrated sulphuric acid gave a mixture of 5-bromo-2,6-dinitrobenzaldehyde 37 and 5-bromo-2,4-dinitrobenzaldehyde 38 in the ratio of 9:1.
Nitration of either 5-iodo-2-nitrobenzaldehyde 33 or 3-iodo-2-nitrobenzaldehyde 34 with a mixture of fuming nitric acid and concentrated sulphuric acid resulted in the isolation of unreacted starting material.

5-Bromo-2-nitrobenzaldehyde (30) was prepared following the literature procedure \(^1\) and the spectroscopic data were consistent with the structure.

5-iodo-2-nitrobenzaldehyde (33) \(^2\) and 5-iodo-6-nitrobenzaldehyde (34)
A commercially available 3-iodobenzaldehyde 31 (0.80 g, 3.44 mmol) was dissolved in fuming concentrated nitric acid (d =1.5 g/mL, 3 mL) at 0 °C. Sulphuric acid (30% SO\(_3\), 9 mL) was then added dropwise over 15 minutes at 0 °C. The mixture was stirred at rt for 18 h, and subsequently was poured onto crushed ice (100 mL) and left at 0 °C for 24 h. The resulting precipitate was filtered off to give the product as a yellowish solid; yield 0.50 g; TLC (B) indicated that the starting material (Rf = 0.18) was converted into two products: (Rf = 0.08, minor and (Rf= 0.15), major. The crude product was purified on a silicagel column eluting with hexane-ethyl acetate (9:1) to give compound 33 as a white solid (0.22 g, 28%); mp 77-80 °C; \(^1\)H-NMR \(\delta\) 7.94 (d, J=8.7Hz, 1H, H-4), 8.23 (d, J=1.9 Hz, 1H, H-6), 8.33 (dd, J=1.8Hz, 7.2Hz, 1H, H-3), 10.34 (s, 1H, CHO ); \(^{13}\)C NMR \(\delta\) 102.51(C-5), 125.85(C-3), 131.73 (C-1), 137.9 (C-6), 142.48(C-4 ), 148.41 (C-2), 188.80 (CHO); HRMS (ES mode, m/z) calcd. for C\(_7\)H\(_5\) I NO\(_3\) [M+H]\(^+\) 277.9314, found 277.9331 LR MS (ES mode) for C\(_7\)H\(_5\) I NO\(_3\) [M+H]\(^+\) found 277.95.

Further elution with hexane-ethyl acetate (9:1) gave compound 34 as a white solid (0.16 g, 23%); mp 59-60 °C; \(^1\)H-NMR \(\delta\) 7.36 (t,1H, H-3) , 8.16 (d, J=7.9Hz, H-2) 8.35 (d, 1H, H-4), 9.81 (s, 1H, CHO). \(^{13}\)C NMR \(\delta\) 89.87 (C-5), 127.61 (C-1), 132.51 (C-3), 142.48(C-4 ), 145.19 (C-6), 188.94 (CHO); HRMS (ES mode, m/z) calcd. for C\(_7\)H\(_5\) I NO\(_3\) [M+H]\(^+\) 277.9314, found 277.9319; LRMS (ES mode, m/z) for C\(_7\)H\(_5\) I NO\(_3\) [M+H]\(^+\) found 277.95.

5-Fluoro-2,6-dinitrobenzaldehyde (36)
A commercially available 5-fluoro-2-nitrobenzaldehyde 35 (1.69g, 10 mmol ) was dissolved in concentrated sulphuric acid (d = 1.84 g/mL, 7.5 mL) and fuming nitric acid (d = 1.5 g/mL, 1.28 mL)
was added dropwise over 5 min at rt. After the addition the mixture was stirred at 55-60 °C for 5 hours. Subsequently, it was cooled to rt and poured onto crushed ice (100 mL). After the ice had melted, dichloromethane (150 mL) was added and the organic layer was washed with water (2 x 25 mL), 3% aqueous sodium bicarbonate (4 x 25 mL), brine (30 mL), dried (sodium sulphate) and concentrated in vacuo. The residue was purified on a silicagel column eluting with hexane-ethyl acetate (3:1) to give compound 36 as a white solid (0.45 g, 25%); mp 74-76 °C; 1H-NMR δ 8.08 (m, 1H, H-4), 8.62 (m, 1H, H-3), 10.34 (s, 1H, CHO). 13C NMR δ 121.74 (C-4), 129.75 (C-1), 130.57 (C-3), 143.86 (C-6), 155.11(C-2), 157.25 (C-5), 187.31 (CHO); GC MS for C7H4FN2O5 [M+H]+ found 215.14; LRMS (ES mode) for C7H2FN2O5 [M-H]- found 213.0.

5-Bromo-2,6-dinitrobenzaldehyde (37) and 5-bromo-2,4-dinitrobenzaldehyde (38)

5-Bromo-2-nitrobenzaldehyde 32 (1.15g, 5 mmol) was dissolved in fuming nitric acid (d = 1.5g/mL, 4.4 mL) at 0 ºC. Sulphuric acid (30% SO3, 13.2 mL) was then added dropwise over 15 minutes at 0 ºC. The temperature was then raised to 50-55 ºC over 30 min and kept at that level for further 45 min. TLC (B) indicated that the starting material (Rf = 0.47) was converted into two products: Rf = 0.22, minor and Rf = 0.12, major. The mixture was cooled to 0 ºC and poured onto crushed ice (200 mL) and left at 0 ºC for 24 h. The resulting precipitate was filtered off to give product 8 as a yellowish solid; (0.66g, 48%); mp 78-80 ºC; 1H-NMR δ 8.41 (s, 2H, H-3, H-4), 10.22 (s, 1H, CHO). 13C NMR δ 120.28 (C-5), 126.57 (C-1), 127.83(C-3), 138.19 (C-4), 147.85 (C-2), 148.06 (C-6), 187.31 (CHO); GC MS for C7H3BrN2O5 [M+H]+ 275.09; LRMS (ES mode, m/z ) for C7H BrN2O5 [M-H]- found 273.03.

The minor 2,4-dinitro isomer 9 was obtained after the extraction of mother liquors with dichloromethane (0.075g, 5.4 %) 1H-NMR δ 8.39 (s, 2H, H-3, H-4), 10.32 (s, 1H, CHO).
Nitration of 2-nitro-4-methoxybenzaldehyde

\[ \text{CHO} \quad \text{HNO}_3/\text{H}_2\text{SO}_4 \quad \text{NO}_2 \quad \text{OCH}_3 \]

\[ \text{CHO} \quad \text{NO}_2 \quad \text{OCH}_3 \]

4-Methoxy-2-nitrobenzaldehyde 41 was prepared starting from a commercially available 4-methoxy-2-nitrotoluene 39 by successive reactions with N-bromosuccinimide and bis(tetrabutylammonium) dichromate as described earlier. Nitration of compound 41 with fuming nitric acid resulted in the mixture of 4-methoxy-2,5-dinitrobenzaldehyde 42 and 4-methoxy-2,3-dinitrobenzaldehyde 43 in the ratio of ~ 3:2. Both the compounds were isolated by column chromatography on silicagel. The desired 4-methoxy-2,6-dinitrobenzaldehyde 48 was not formed and it had to be made via an alternative route starting from a commercially available 4-fluoro-2-nitrotoluene 44. Nitration of the latter with the mixture of nitric acid and concentrated sulphuric acid gave 4-fluoro-2,6-dinitrotoluene 45. Subsequent reaction with sodium methoxide resulted in 4-methoxy-2,6-dinitrotoluene 46. Successive reactions of 4-methoxy-2,6-dinitrotoluene 46 with N-bromosuccinimide and bis(tetrabutylammonium)dichromate, similar to those described above for 4-methoxy-2-nitrotoluene, resulted in the expected 4-methoxy-2,6-nitrobenzaldehyde 48. The free radical bromination of the side chain with N-bromosuccinimide in 46 was, however, much slower than in the case of 4-methoxy-2-nitrotoluene. The oxidation also required very carefully controlled conditions.
4-(4-Methoxyphenyl)-2,6-nitrobenzaldehyde 53 was prepared starting from a commercially available 4-bromo-2-nitrotoluene 49. The nitration of compound 49 with the mixture of nitric acid and concentrated sulphuric acid afforded 4-bromo-2,6-dinitrotoluene 50.4 The subsequent Suzuki coupling 6 of the latter with 4-methoxyphenyl boronic acid gave 4-(4-methoxyphenyl)-2,6-nitrotoluene 51. The free radical bromination of 4-(4-methoxyphenyl)-2,6-nitrotoluene with N-bromosuccinimide gave 4-(4-methoxyphenyl)-2-(bromomethyl)-1,3-dinitrobenzene 28. This product could upon irradiation release hydrogen bromide and act as a photoacid generator in its own right as discussed in section 1.5. Finally, oxidation of 28 with bis(tetrabutylammonium) dichromate gave 4-(4-methoxyphenyl)-2,6-nitrobenzaldehyde 52.
Scheme 4
Synthesis of 4-(4-methoxyphenyl)-2,6-dinitrobenzaldehyde

4-Methoxy-2-nitrobenzaldehyde 41 was prepared starting from a commercially available 4-methoxy-2-nitrotoluene 39 by successive reactions with N-bromosuccinimide and bis(tetraethylamonium) dichromate as described earlier. 3

4-Methoxy-2,5-nitrobenzaldehyde (42) and 4-methoxy-2,3-nitrobenzaldehyde (43)
4-Methoxy-2-nitrobenzaldehyde 41 (0.36 g, 2 mmol) was cooled to 0 °C and fuming nitric acid (d=1.5 g/mL, 2 mL) was added dropwise over 5 min. After the addition the mixture was stirred at 0 °C until the ice had melted and then at rt for 20 min. Subsequently, the mixture was poured onto crushed ice (100 mL). After the ice had melted, dichloromethane (50 mL) was added and the organic layer was washed with water (2x25 mL), 3% aqueous sodium bicarbonate (4x25 mL), brine (30 mL), dried (sodium sulphate) and concentrated in vacuo. The residue was purified on a silicagel column eluting with hexane-ethyl acetate to give compound 42 as a yellow solid (0.13 g, 29%); mp 71-80 °C; Rf (B) 0.15; 1H-NMR δ 4.12 (OCH3), 8.09 (s, 1H, H-6), 8.57 (s, 1H, H-6), 10.03 (s, 1H, CHO). 13C NMR δ 58.50 (OCH3), 110.86 (C-3), 121.76 (C-1), 127.92 (C-6), 140.49 (C-2), 151.55 (C-5), 155.86 (C-4) 186.87 (CHO). HRMS (ES mode, m/z) calcd. for C8H6N2O6 [M+H]+ 227.0304, found 227.0296; LRMS (ES mode, m/z) for C8H6N2O6 [M+H]+ found 227.14.
Further elution with hexane-ethyl acetate (7:3) gave compound 43 as a yellow solid (0.09 g, 20%); mp 123-124 °C; Rf (B) 0.05; 1H-NMR δ 4.12 (OCH₃), 7.95 (d, 1H, H-6, J=8.72 Hz), 8.37 (d, 1H, H-5, J=8.72 Hz), 9.95 (s, 1H, CHO). 13C NMR δ 58.56 (OCH₃), 118.02 (C-5), 120.55 (C-1), 135.82 (C-6), 139.49 (C-3), 155.02 (C-4), 187.03 (CHO); HRMS (ES mode, m/z) calcd. for C₈H₇N₂O₆ [M+H]+ 227.0304, found 227.0301; LRMS (ES mode, m/z) for C₈H₆N₂O₆Na [M+Na]+ found 249.02.

5-Fluoro-2-methyl-1,3-dinitrobenzene 45 and 5-methoxy-2-methyl-1,3-dinitrobenzene 46 were prepared starting from a commercially available 4-fluoro-2-nitrotoluene 44 following a literature procedure.⁴

2-(Bromomethyl)-5-methoxy-1-nitrobenzene 40 and 4-methoxy-2-nitrobenzaldehyde 41 were prepared following the procedure of Mohan and Katzenellenbogen.⁶

4-Bromo-2,6-dinitrotoluene 50 was prepared following the procedure described by Segura et al.⁵

Condensation of 4-bromo-2,6-dinitrotoluene 50 with 4-methoxyphenylboronic acid to give 4-(4-methoxyphenyl)-2,6-dinitrotoluene 51 is described in section 1.2.4 (Suzuki cross couplings) below.

Bromination of 5-methoxy-2-methyl-1,3-dinitrobenzene (46) or 4-(4-methoxyphenyl)-2,6-dinitrotoluene (51) Compound 46 (0.093 g, 0.44 mmol) or 51 (0.13 g, 0.44 mmol), NBS (0.16 g, 0.88 mmol) and benzoyl peroxide (0.02 g, 0.08 mmol) were dissolved in dry carbon tetrachloride (5 mL), and the mixture was heated under reflux for 42 h. The solid was filtered off, the filtrate was concentrated in vacuo and the residue was coevaporated with coarse silicas (1 g) in dichloromethane (20 mL). Each residue was treated with hexane (20 mL) with some sonication and the resulting slurry was applied onto a silica gel column eluting with hexane/ethyl acetate to give products 47 and 28, respectively.

2-(Bromomethyl)-5-methoxy-1,3-dinitrobenzene (47) (0.091 g, 70%); light yellow gum; mp indef; 1H-NMR δ 4.81 (s, 2 H, CH₂Br), 4.01 (s, 3H, OCH₃) 7.99 (s, 2H, H-3, H-5); LRMS (ES mode, m/z) for C₈H₇BrN₂O₅ [M-H]- found 289.91.

5-(4-Methoxyphenyl)-2-(bromomethyl)-1,3-dinitrobenzene (28) (0.075, 46.5%); light yellow solid; mp 85-86 °C; 1H-NMR δ 4.81 (s, 2H, CH₂Br), 4.85 (s, 2H, CH₂Br), 7.12 (d, 2H, H-3', H-5'), 7.89 (d, 2H, H-2', H-4'), 123.00 (C-1), 124.27 (C-2', C-6') 128.26 (C-1'), 128.74 (C-3, C-5), 139.70 (C-4), 151.61 (C-2, C-6), 160.21 (C-4'); GC MS for C₁₄H₁₁BrN₂O₅ [M-Br]⁺ found 288.10; LRMS (ES mode, m/z) for C₁₄H₁₁BrN₂O₅Na [M+Na]+ found 391.24.

4-Methoxy-2,6-dinitrobenzaldehyde (48) 2-(Bromomethyl)-5-methoxy-1,3-dinitrobenzene 47 (0.091 g, 0.3 mmol) and bis(tetramethylammonium)dichromate (0.11 g, 0.16 mmol) were dissolved in dry chloroform (5 mL) and the solution was heated under reflux for 20 hrs. The solvent was removed in vacuo and the residue was dried in vacuo over phosphorus pentoxide. The dried material was treated with methylene chloride (10 mL) and the resulting suspension was applied onto a column of silicas (5 g) eluting with methylene chloride to give product 48 as a light yellow solid (18 mg, 25%); mp 79-90 °C; 1H-NMR δ 4.03 (s, 3H, OCH₃),
$^{13}$C-NMR $\delta$ 57.47 (OCH$_3$), 114.69 (C-3, C-5), 119.88 (C-1), 149.29 (C-2, C-6) 161.45 (C-4), 187.81 (CHO).

4-(4-Methoxyphenyl)-2,6-dinitrobenzaldehyde (52)

5-(4-Methoxyphenyl)-2-(bromomethyl)-1,3-dinitrobenzene 28 (0.15 g, 0.4 mmol) and bis(tetrabutyl-ammonium)dichromate (0.19 g, 0.27 mmol) were dissolved in dry chloroform (10 mL) and the solution was heated under reflux for 18 hrs. The solvent was removed in vacuo and the residue was dried in vacuo over phosphorus pentoxide. The dried material was treated with methylene chloride (10 mL), silicagel coarse (1 g) was added and the suspension was evaporated in vacuo. The resulting white powder was treated with n-hexane (20 mL) and the resulting slurry was applied on to a silica gel column eluting with hexane/ethyl acetate to give product 52 as a light yellowish solid (0.019 g, 23%); mp 118-123 °C; Rf (A) 0.56; $^1$H-NMR $\delta$ 3.85 (s, 3H, OCH$_3$), 7.19 (d, J= 8.45 Hz, 2H, H-3', H-5'), 8.05 (d, , J= 8.45 Hz 2H, H-2', H-6') 8.74 (s, 2H, H-3, H-5), 10.49 (s, 1H, CHO); $^{13}$C-NMR $\delta$ 55.44 (OCH$_3$), 114.85 (C-3', C-5'), 125.88 (C-2', C-6') 126.31(C-1), 127.05 (C-1'), 128.96 (C-3, C-5), 143.96 (C-4), 148.43(C-2, C-6), 161.05 (C-4'), 188.74 (CHO); HRMS (ES mode, m/z) calcd. for C$_{14}$H$_{11}$N$_2$O$_6$ [M+H]$^+$ 303.0617, found 303.0613; LRMS (ES mode, m/z) for C$_{14}$H$_{11}$N$_2$O$_6$ [M +H]$^+$ found 303.0814.

**Scheme 5**

\[ \alpha-\text{Phenyl-2-nitrobenzyl alcohols} \]

\[
\begin{align*}
53 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = Cl \quad R^6 = H \\
54 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = Cl \quad R^6 = NO_2 \\
55 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = F \quad R^6 = H \\
56 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = F \quad R^6 = NO_2 \\
57 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = Br \quad R^6 = H \\
58 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = Br \quad R^6 = NO_2 \\
59 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = I \quad R^6 = H \\
60 \quad & R^1 = C_6H_5 \quad R^4 = OCH_3 \quad R^5 = H \quad R^6 = H \\
61 \quad & R^1 = C_6H_5 \quad R^4 = OCH_3 \quad R^5 = H \quad R^6 = NO_2 \\
62 \quad & R^1 = C_6H_5 \quad R^4 = p-CH_3OC_6H_5 \quad R^5 = H \quad R^6 = NO_2 \\
63 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = N(CH_3)_2 \quad R^6 = NO_2 \\
64 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = Pyrroldin-1-yl \quad R^6 = NO_2 \\
65 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = Piperidin-1-yl \quad R^6 = NO_2 \\
66 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = Morpholin-4-yl \quad R^6 = NO_2 \\
67 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = Pyrroldin-1-yl \quad R^6 = H \\
68 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = NH_2 \quad R^6 = H \\
69 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = NH_2 \quad R^6 = NO_2 \\
70 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = CH_3OC_6H_5NH \quad R^6 = NO_2 \\
71 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = CH_3OC_6H_5NH \quad R^6 = NO_2 \\
72 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = p-N(CH_3)_2C_6H_5 \quad R^6 = NO_2 \\
73 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = CH_3OC_6H_5NH \quad R^6 = NO_2 \\
74 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = p-CH_3OC_6H_5NH \quad R^6 = NO_2 \\
75 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = o, p- (CH_3O)2C_6H_4 \quad R^6 = NO_2 \\
76 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = 2-ethoxynaphtyl \quad R^6 = NO_2 \\
77 \quad & R^1 = C_6H_5 \quad R^4 = H \quad R^5 = Phenylazo \quad R^6 = H
\end{align*}
\]
1.2.2 Preparation of α-phenyl-2-nitrobenzyl and α-phenyl-2,6-dinitrobenzyl alcohols by condensation of substituted benzaldehydes with phenylmagnesium bromide

Introduction of the α-phenyl group enhancing the quantum yield was achieved by the condensation of various substituted benzaldehyde precursors with phenylmagnesium bromide.7, 8 Various substituted α-phenyl-2-nitro and α-phenyl-2,6-dinitrobenzyl alcohols such as 55, 56, 57, 58, 59, 60, 61 and 62 were prepared in high yields by condensation of aldehydes 32, 33, 35, 36, 41, 48, 52 respectively, with phenylmagnesium bromide in anhydrous tetrahydrofuran at -78°C. Compounds 53 and 54 were prepared in a similar way.7, 8

Condensation of 5-fluoro-2-nitrobenzaldehyde (35), 5-fluoro-2,6-dinitrobenzaldehyde (36), 5-bromo-2-nitrobenzaldehyde (32), 5-bromo-2,6-dinitrobenzaldehyde (37), 5-iodo-2-nitrobenzaldehyde (31), 4-methoxy-2,6-dinitrobenzaldehyde (52) with phenylmagnesium bromide (General Procedure)

A benzaldehyde (10 mmol) was dissolved in anhydrous tetrahydrofuran (40 mL) and the solution was cooled to –78°C. Phenylmagnesium bromide (1M solution in THF, 11 mL, 11 mmol) was added to the stirred solution by syringe during 15 minutes. After 15 minutes at -78°C the mixture was stirred at –10°C to -15°C for 15 minutes. 2% Aqueous hydrochloric acid (100 mL) was added dropwise over 20 minutes followed by dichloromethane (100 mL). The organic layer was washed with water (50 mL), 3% aqueous sodium bicarbonate (4 x 50 mL), water (50 mL), brine (50 mL), dried (sodium sulphate) and concentrated in vacuo. The residue was chromatographed on a silicagel column eluting with dichloromethane to give required products.

(5-Fluoro-2-nitro-phenyl)-phenyl-methanol (55) (1.35 g, 55 %); colourless solid; mp 64-65 °C; Rf (A) 0.42; NMR δ 6.25 (d, J=4.82 Hz, 1H, CH,), 6.36 (d, 1H, OH, J=4.82 Hz), 7.29 (m, 5H, H-2'-H-6’), 7.40 (m, 1H, H-6), 7.66 (m, 1H, H-4), 8.04 (m, 1H, H-3). 13C-NMR 69.46 (CHOH), 115.16 (C-4), 115.35 (C-6), 127.07 (C-2’, C-6’), 127.52 (C-4’), 127.67 (C-3, C-5’), 142.49 (C-1’), 143.35 (C-1), 143.94 (C-2), 164.15 (C-5). HRMS (ES mode, m/z) calcd. for C13H9FNO2[M-OH]+ 230.0609, found 230.0617; LRMS (ES mode, m/z) for C13H9FNO3K [M+K]+ 286.0.

(3-Fluoro-2,6-dinitro-phenyl)-phenyl-methanol (56) colourless solid; (1.35 g, 55 %; mp 66-67 °C; Rf (A) 0.35; 1H-NMR δ 6.21 (d, J=5.03 Hz, 1H, CH,), 6.85 (d, J=5.03 Hz, 1H, OH), 7.24 (m, 2H, H-2’, H-6’), 7.31 (m, 3H, H-3’, H-5’), 7.93 (m, 1H, H-4), 8.31 (m, 1H, H-3); 13C-NMR 69.29 (CHOH), 117.95 (C-4), 126.69 (C-2’, C-6’), 128.11 (C-4’), 128.81 (C-3’, C-5’), 128.80 (C-3), 133.81 (C-1), 138.44 (C-6), 140.93 (C-1’), 144.98 (C-2), 156.05 (C-5); HRMS (ES mode, m/z) calcd. for C13H9FNO2 [M-OH]+ 275.0468, found 275.0464; LRMS (ES mode, m/z) for C13H9FNO3Na [M+Na]+ found 315.17, for C13H9FNO2 [M-H]- found 291.0.

(5-bromo-2-nitro-phenyl)-phenyl-methanol (57) (1.69 g, 55 %); yellowish oil; Rf (A) 0.33; 1H-NMR δ 6.21 (d, J=4.87 Hz, 1H, CH), 6.38 (d, J=4.87 Hz, 1H, OH), 7.30 (m, 5H, H-2’-H-6’), 7.65 (dd, J=2.12 Hz, J=8.63 Hz, 1H, H-4), 7.88 (d, J=8.63 Hz 1H, H-3), 7.99 (d, J=2.12 Hz, 1H, H-6). 13C-NMR 69.32 (CH,), 126.32 (C-3), 126.95 (C-3’, C-5’), 127.59 (C-4’), 128.03 (C-2’, C-6’), 131.22 (C-4), 132.99 (C-6), 138.21 (C-5), 141.36 (C-1’), 142.43 (C-1), 146.81 (C-2); HRMS (ES mode, m/z)calcd. for C13H9BrNO2 [M-OH]+ 289.9849, found 289.9853, for C13H9BrNO2 [M-H]- found 290.01.
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(3-bromo-2,6-dinitro-phenyl)-phenyl-methanol (58) (2.99 g, 85.2 %); yellowish oil; RF (A) 0.46; $^1$H-NMR $\delta$ 6.08 (d, $J=4.94$ Hz, 1H, CH), 6.38 (d, $J=4.94$ Hz, 1H, OH), 7.18 - 7.40 (m, 5H, H-2', H-6'), 8.10 (d, $J=8.79$ Hz 1H, H-4'), 8.19 (d, $J=8.79$ Hz, 1H, H-3'). $^{13}$C-NMR $\delta$ 69.06 (CHOH), 118.41(C-5), 124.26 (C-5) 126.50 (C-3', C-5'), 127.09 (C-4'), 127.87(C-3), 128.11 (C-2', C-6'), 131.28 (C-1), 134.51(C-4), 140.84 (C-1'), 148.46 (C-2), 149.64 (C-6); HRMS(ES mode, m/z) calcd. for C$_{13}$H$_8$BrN$_2$O$_4$ [M-OH]$^+$ 334.966, found 334.9673.

(5-iodo-2-nitro-phenyl)-phenyl-methanol (59) (3.33 g, 94 %) a yellowish oil; RF (A) 0.23; $^1$H-NMR $\delta$ 6.21 (d, $J=4.87$ Hz, 1H, CH), 6.38 (d, $J=4.87$ Hz, 1H, OH), 7.30 (m, 5H, H-2', H-6'), 7.69 (d, $J=8.48$ Hz, 1H, H-4), 7.93 (dd, 1.84 Hz, $J=8.48$ Hz, 1H, H-4), 8.17 (d, 1.84 Hz, 1H, H-6).

(4-methoxy-2-nitrophenyl)-phenyl-methanol (60) (2.32 g, 89 %); colourless oil; RF (A) 0.25; $^1$H-NMR $\delta$ 3.83 (s, 3H, OCH$_3$), 6.11 (bs, 2H, CH, OH), 6.60 (d, $J=4.37$ Hz, 1H, H-3'), 7.26 (m, 5H, H-2', H-6'), 7.43 (d, $J=1.02$ Hz, 1H, H-3), 7.63 (d, $J=4.37$ Hz, 1H, H-4).

(4-methoxy-2,6-dinitrophenyl)-phenyl-methanol (61) (2.97 g, 98 %); light brown solid; mp indef; RF (A) 0.25; $^1$H-NMR $\delta$ 3.92 (s, 3H, OCH$_3$), 6.02 (d, $J=4.32$ Hz, 1H, CH), 6.75 (d, $J=4.32$ Hz, 1H, OH), 7.19 (m, 5H, H-2', H-6'), 7.79 (s, 2H, H-3, H-5).

2,6-dinitro-4-(4-methoxyphenyl)-phenyl-phenyl-methanol (62) (3.72 g, 98 %); light brown solid; mp indef; RF (A) 0.31; $^1$H-NMR $\delta$ 3.92 (s, 3H, OCH$_3$), 6.12 (d, $J=4.32$ Hz, 1H, CH), 6.75 (d, $J=4.32$ Hz, 1H, OH), 6.80 (d, $J=7.16$ Hz, 2H, H-3', H-5'), 7.15-7.40 (m, 5H, H-2', H-6'), 7.93 (d, 2H, H-2', H-6'), 8.50 (s, 2H, H-3, H-5); $^{13}$C-NMR $\delta$ 55.36 (OCH$_3$ ), 74.57 (CHOH), 114.71 (C-3'', C-5''), 123.92 (C-2'',C-6''), 126.44 (C-3',C-5'), 127.15 (C-4'), 127.90 (C-2', C-6') 128.42 (C-3, C-5), 150.23 (C-2, C-6), 159.75 (C-4''); LRMS (ES mode, m/z) for C$_{20}$H$_{12}$N$_2$O$_6$ Na [M + Na]$^+$ found 403.0906.

1.2.3 Nucleophilic aromatic substitution of α-phenyl-5-chloro(fluoro)-2-nitrobenzyl alcohols with various amines

Initially, introduction of various electron donating amino groups was achieved by nucleophilic aromatic substitution of 5-chloro-2,6-dinitrobenzyl alcohol 54 with appropriate amines to give the expected products 63-66 (Scheme 5). The reactions were carried out in a microwave reactor. In order to facilitate the substitution with less reactive nucleophiles, such as ammonia or substituted phenylamines, compound 54 was replaced as the starting material by 5-fluoro-(2-nitro-phenyl)-phenyl-methanol 55 and 5-fluoro-(2,6-dinitro-phenyl)-phenyl-methanol 56. It was expected that the fluorine atom, as opposed to the chlorine atom, should be a better leaving group in the SN$_{AR}$ substitution. The desired products 67-71 were obtained in good yields. The reactions were carried out in a microwave reactor.

Reaction of (5-chloro-2,6-dinitro-phenyl)-phenyl-methanol 54 with diethylamine, pyrrolidine, piperidine and morpholine (General Procedure). Compound 54 (0.308 g, 1 mmol) was treated with 2M solution of diethylamine (0.5 mL) in ethanol or isopropanol (2.5 mL), pyrrolidine(0.5 mL) in methanol (2.5 mL), piperidine (0.5 mL) in methanol (2.5 mL) or morpholine(0.5 mL) in methanol (2.5 mL). Each solution was irradiated in a microwave reactor (50W, 100psi) at different temperatures for a required period as specified below in brackets. The solvent was removed in vacuo and each residue was co-evaporated with dichloromethane (2 x 10 mL) and applied onto a column of silicagel. The column was eluted with dichloromethane/ethanol.
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(49:1) to give compounds 63-66. Reverse phase HPLC was performed using a Waters chromatography system with a variable wavelength detector set at 254 nm and 280 nm. Columns, Waters Delta Pak 5 μ C18-300A, were used for analytical and preparative scales. The mobile phases were (A) 0.05M aq. [Et3NH]+ [HCO3]- (B) MeCN. Gradient elution; 5%(B) – 90% (B) over 30 minutes.

(5-Diethylamino-2,6-dinitro-phenyl)-phenyl-methanol (63) (2 x 90min, 90 °C); this compound could not be obtained pure and was used in the esterification step without characterisation.

(2,6-Dinitro-3-pyrrolidin-1-yl-phenyl)-phenyl-methanol (64) (15 min, 50 °C) (0.17 g, 57%); yellow solid, mp indef; Rf (A) 0.25, Rf (B)- multiple development resolves the product and the starting material; 1H-NMR δ 1.90 (m, 4H, (CH2)2), 3.25 (m, 4H, (CH2)2 6.09 (d, J=5.07 Hz, 1H, CH), 6.49 (d J=5.07Hz, 1H, OH), 7.05 (d, 1H, J=9.31Hz, H-4), 7.26 ( m, 5H, H-2'-H-6'), 7.99 (d, 1H, J=9.31 Hz, H-3); UV λmax 393 nm, ε 17000; HRMS (FAB mode, m/z) calcd. for C17H17N3O5Na [M+Na]+ 366.1066, found 366.1067.

(2,6-Dinitro-3-piperidin-1-yl-phenyl)-phenyl-methanol (65) (2 x 15 min, 50  °C) (0.19 g, 52%); yellow solid, mp 85-95 °C; %); Rf (C) 0.25; 1H-NMR δ 1.53 (m, 6H, (CH2)3), 2.99 (m, 4H, (CH2)2), 5.98 (d, J=5.01 Hz, 1H, CH), 6.58 (d, J=5.01Hz, 1H, OH), 7.28 ( m, 5H, H-2'-H-6', H-4), 751 (d, J=8.97 Hz, 1H, H-4); 8.04 (d, J=8.97 Hz, 1H, H-3); UV λmax 393nm, ε 13500; LRMS (ES mode, m/z) for C18H20N3O5 [M+H]+ found 358.3.

(2,6-Dinitro-3-morpholin-4-yl-phenyl)-phenyl-methanol (66) (2 x 20 min, 60 °C)(0.24 g, 67%); yellow solid, mp 58-60 ºC; Rf (A) 0.25; 1H-NMR δ 3.01 (t, 4H, J=5.48Hz (CH 2)2), 3.63 (t, 4H, J=5.48Hz, (CH2)2, 6.00 (d, J=5.02 Hz, 1H, CH), 6.64 (d, J=5.02Hz, 1H, OH), 7.23 ( m, 5H, H-2'-H-6'), 7.61 (d, J=8.91Hz, H-4), 7.99 (d, J=8.91 Hz, 1H, H-3); UV λmax 361.5 nm, ε 13120; HRMS (FAB mode, m/z) calcd. for C17H17N3O6Na [M+Na]+ 382.1015, found 382.1005.

Reaction of (5-fluoro-2-nitro-phenyl)-phenyl-methanol (55) with pyrrolidine. Compound 55 (0.125 g, 0.5 mmol) was dissolved in methanol (2.5 mL) and pyrrolidine  (0.7 mL) was added. The solution was irradiated in a microwave reactor at 60 °C for 50min (150W, 100Psi).  The solvent was removed in vacuo and the residue was dried in a desiccator over P 2O5, dissolved  in dichloromethane (3 mL) and applied onto a column of silicagel. The column was eluted with dichloromethane/ethanol (97:3) to give product 67 as a yellow solid.

(2-Nitro-5-pyrrolidin-1-yl-phenyl)-phenyl-methanol (67) (0.12 g, 77.2 %); mp 149-150 ºC; Rf (A) 0.24; 1H-NMR δ 2.02 (m, 4H, (CH2)2), 3.40 (m, 4H, (CH2)2), 5.98 (d, 1H, J=5.19 Hz, CH), 6.49 (d, 1H, J=5.19Hz, OH), 6.55 (d, 1H, J=9.14Hz, H-4), 7.22 ( m, 5H, H-2'-H-6'), 8.00 (d, 1H, J=9.14 Hz, H-3); UV λmax 393 nm, ε 17000; LRMS (ES mode, m/z) for C17H19N2O3 [M+H]+ found 299.0.

Reaction of (5-fluoro-2-nitro-phenyl)-phenyl-methanol (55) and (3-fluoro-2,6-dinitro-phenyl)-phenyl-methanol 56 with aqueous ammonia. Compound 55 or 56 (0.5mmol) was dissolved in 8M NH3/MeOH (1 mL) and concentrated aqueous NH4OH (3 mL). Each solution was irradiated in a microwave reactor at 90 °C for 2 x 50 min (150W, 100Psi). The solvent was removed by freeze drying and each residue was co-evaporated with toluene (2x10mL) and applied onto a column of silicagel eluting with dichloromethane/ethanol (97:3) to give products 68 and 69.
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(5-Amino-2-nitro-phenyl)-phenyl-methanol (68) (0.090 g, 67%); yellowish solid; mp 51-52 °C; Rf (A) 0.1; 1H-NMR δ 5.94 (d, J=4.49 Hz, 1H, OH), 6.44 (d, J=4.49 Hz, 1H, CH), 6.52 (d, J=9.06Hz, 1H, H-4), 6.65 (bs, 2H, NH2), 7.11 (s, 1H, H-6), 7.23 (m, 5H, H-2'- H-6'), 8.04 (d, J=9.06Hz, 1H, H-3). 13C-NMR 69.75 (CHOH), 111.24 (C-4), 111.71 (C-6), 126.84 (C-3), 127.08 (C-2', C-6'), 128.10 (C-3', C-5'), 128.21 (C-4'), 128.80 (C-4'), 134.74 (C-1), 143.75 (C-1'), 144.16 (C-2), 159.44 (C-5). LRMS (ES mode) C13H13N2O3 [M+H]+ 244.0; HRMS (ES mode, m/z) calc. for C13H11N2O2 227.0821 [M-OH]+ found 227.0819.

(3-Amino-2,6-dinitro-phenyl)-phenyl-methanol (69) (0.096 g (73.7%); yellowish solid, mp 82-85 oC; Rf (A) 0.1; 1H-NMR δ 6.24 (d, 1H, CH, J=4.78 Hz), 6.47(d, 1H, OH, J=4.78 Hz), 6.52 (d, J=9.06Hz, 1H, H-4), 6.84 (bs, 2H, NH2), 6.94 (d, J=8.89 Hz 1H, H-4), 7.22 (m, 5H, H-2'- H-6'), 7.98 (d, J=8.89 Hz, 1H, H-3). 13C-NMR 69.05 (CHOH), 115.63 (C-4), 126.40 (C-2', C-6'), 127.65 (C-4'), 128.23 (C-3', C-5'), 128.80 (C-3), 135.05 (C-1), 135.12 (C-1'), 136.19 (C-6 ), 142.28 (C-2), 146.02 (C-5); HRMS (ES mode, m/z) calc. for C13H10N3O4 [M-OH]+ 272.0671, found 272.0674; LRMS (ES mode, m/z) for C13H10N3O5 [M-H]- found 288.0.

Reaction of compound 56 with aniline or p-anisidine.

Compound 56 (0.125 g, 0.5 mmol) and aniline or p-anisidine (1.5 mmol) were dissolved in methanol (5 mL) and each solution was irradiated in a microwave reactor at 60 °C for 3 x 59 min (50W, 100Psi). The solvent was removed in vacuo. The residue after the reaction with aniline containing the expected product 2,6-dinitro-3-(phenylamino)-phenyl-phenyl-methanol 70 contaminated with the unreacted starting material was used in the trichloroacetylation without further purification or characterisation. The residue after the reaction with anisidine was purified by column chromatography on silica gel eluting with dichloromethane to give product 71 as a colourless glass.

3-(4-methoxyphenylamino)-2,6-dinitrophenyl-phenyl-methanol (71) (0.11 g, 78%); mp 74-76 °C; Rf (B) 0.20; 1H-NMR δ 3.73 (s, 3H, OCH3), 6.35 (d, J= 4.84 Hz, 1H, CH), 6.57 (d, J= 4.84 Hz, 1H, OH), 7.09 (m, 2H, ) 6.90 -7.40 (m, 10H, H-4, H-2'-H-6', H-3'', H-5'', H-2'', H-6''), 8.01 (d, J=9.42 Hz, 1H, H-3); LRMS (ES mode, m/z) for C13H3BrClN2O4 [M-H]+ found 292.9256; for C13H4BrClN2O4 [M]+ found 293.9166.

1.2.4 Suzuki cross-couplings

Introduction of various phenyl substituents into the 5-position was envisaged to extend the conjugation system of the 2-nitrobenzyl aromatic rings.

Compound 58 was used in Suzuki cross-couplings with various phenylboronic acids including 4-N,N-dimethylaminophenylboronic acid, phenylboronic acid, 4-methoxyphenylboronic acid, 3,4-dimethoxyphenylboronic acid and 2-ethoxynaphthylboronic acid. The condensations were carried out in 1,2-dimethoxyethane in the presence of palladium tetrakistriphenylphosphine to provide 5-phenyl substituted derivatives 72-76 which were isolated in good yields.

Suzuki condensation of 2,6-dinitro-4-bromotoluene (50) with 4-methoxyphenylboronic acid gave 4-(4-methoxyphenyl)-2,6-dinitrotoluene (51) used in further transformations as described in section 1.2.1.

Suzuki coupling of 2,6-dinitro-4-bromotoluene (50) and (3-bromo-2,6-dinitro-phenyl)-phenyl-methanol (58) with various boronic acids (General Procedure).
A commercially available 4-N,N-Dimethylaminophenylboronic acid, phenylboronic acid, 4-methoxyphenylboronic acid, 3,4-dimethoxyphenylboronic acid, 2-ethoxynaphthylboronic acid, (1mmol) and compound 50 (0.26g, 1mmol) or 58 (0.35 g, 1 mmol) were dissolved in dimethoxyethane (53 mL). The mixture was stirred for 20 min at rt under argon. Catalyst, Pd[P(Ph)3]4 (palladium tetakis triphenylphosphine) ( 0.19 g ) followed by 0.2 M aqueous potassium carbonate (48 mL) were then added and the mixture was stirred at 90-100 ºC for 3 hrs under argon. Dichloromethane (300 mL) was added and the organic layer was washed with brine (2 x 60 mL), dried (Na2SO4) and concentrated in vacuo. The residue was applied on to a silicagel column eluting with dichloromethane to give the required products.

5-(4-Methoxyphenyl)-2-methyl-1,3-dinitrobenzene (51) (0.26 g, 89%); yellow solid; mp 155-165 ºC dec;  
1H-NMR δ 2.44 (m, 3H, CH3), 3.83 (m, 3H, OCH3), 7.09 (d, J= 6.75 Hz, 2H, H-3’,H-5’), 7.81 (d, J= 6.75 Hz, 2H, H-2’, H-6’), 8.47 (s, 2H, H-3, H-5 );  
13C NMR  13.76 (CH 3), 55.31(OCH3), 114.71 (C-3’, C-5’), 123.01 (C-1), 124.28 (C-3, C-5), 127.88 (C-1’), 128.28 (C-2’, C-6’), 139.71 (C-4), 151.66 (C-2, C-6), 160.30 (C-4’)  
GC MS for C14H13N2O5 [M+H]+  found 288.09; LRMS (ES mode, m/z) for C14H12N2O5 Na [M+Na]+  found 311.13.  

(2,6-Dinitro-3-(4-N,N-dimethylaminophenyl)phenyl)(phenyl)methanol (72) (0.25 g, 64%); orange solid; mp slow dec> 150 ºC;  
1H-NMR δ 2.96 (s, 6H, N(CH3)2) 6.02 (d, 1H, CH, J=4.53 Hz), 6.72 (d, 1H, OH, J=4.53 Hz), 6.78 (d, 2H, H-3”,H-5”), J=8.83Hz), 7.19 (d, 2H, H-2”, H-6”) J=8.83 Hz) 7.30 (m, 5H, H-2’-H-6’), 7.73 (d, 1H, H-4, J= 8.11 (d, 1H, H-3, 8.43 Hz ).  
13C-NMR 68.83 (CHOH ), 112.14 (C-2”-C-6”), 125.95 (C-4’), 126.05 (C-3’,C-5’), 126.36 (C-4), 127.19 (C-3”, C-5”), 127.93 (C-1’), 128.50(C-2’, C-6’), 129.51 (C-1”) 138.24 (C-1’), 141.58 (C-5) 147.65 (C-2), 148.36 (C-2’), C-6), 150.77 (C-5); HRMS (ES mode, m/z) calcd. for C21H20N3O5 [M+H]+ 394.1403, found 394.1407.  

(2,6-Dinitro-3-(phenyl)phenyl)(phenyl)methanol (73) (0.17 g, 50%); off white solid; mp indef;  
1H-NMR δ 6.04 (d, 1H, CH, J=4.11 Hz), 6.72 (d, 1H, OH, J=4.11 Hz), 7.20-7.52 (m, 10H, H-2’-H-6’, H-2”-H-6”) 7.79 (d, 1H, H-4, J=8.39 Hz), 8.20 (d, 1H, H-3, 8.39 Hz ).  
13C-NMR 68.99 (CHOH ), 126.05 (C-4’), 126.44 (C-2”-C-6”), 127.33 (C-4), 127.85 (C-3”, C-5”), 127.99 (C-3’, C-5’), 128.89 (C-2’, C-6’), 129.35 (C-3), 131.95 (C-4”), 133.39 (C-1), 134.76 (C-1”), 137.85 (C-5), 144.11(C-1’), 148.66 (C-2, C-6).  
HRMS (ES mode, m/z) calcd. for C19H13N2O4, [M-OH] 333.0873, found 333.0874; LRMS (ES mode, m/z) for C19H14N2O5Na [M+Na]+, found 373.0555.  

(2,6-Dinitro-3-(4-methoxyphenyl)phenyl)(phenyl)methanol (74) (0.23 g, 61%); light yellow solid; mp 85-87ºC;  
1H-NMR δ 3.79 (s, 3H, OCH3), 6.08 (d, J= 5.04 Hz, 1H, CH), 6.80 (d, J= 5.04 Hz, 1H, CH), 7.09 (m, 2H, H-3”-H-5”), 7.35 (m, 7H, H-2’-H-6’, H-2”, H-6”), 7.80 (d, J=8.36 Hz, 1H, H-4), 8.19 (d, 1H, H-3, 8.36 Hz );  
13C NMR 55.28 (OCH3) 68.87 (CHOH ), 114.45 (C-2”, C-6”), 125.97 (C-4”), 126.41 (C-3’-C-5”) 126.80 (C-1”), 127.28 (C-3, C-5”), 127.91 (C-3”, C-5”), 129.24 (C-2’, C-6’), 131.91 (C-4’), 137.62 (C-5’), 141.45 (C-1’),148.30 (C-2), 148.63 (C-6), 160.08 (C-4”); HRMS (ES mode) calcd. for C21H18N2O7Na [M+Na]+ 403.0906, found 403.0904 LRMS (ES mode, m/z) for C20H15N2O6 [M-H]- found 379.1143; for C20H15N2O5 [M-OH]+ found 363.0528.  

(2,6-Dinitro-3-(3,4-dimethoxyphenyl)phenyl)(phenyl)methanol (75) (0.15 g, 37%); light yellow solid; mp 69-72ºC;  
1H-NMR δ 3.77 (s, 3H, OCH3), 3.70 (s, 3H, OCH3), 6.08 (d, J= 5.09 Hz, 1H, CH), 6.80 (d, J= 5.09 Hz, 1H, CH), 6.95-7.40 (m, 9H, H-2’-H-6’, H-3”, H-5”, H-2”, H-6”) 7.86 (d,
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J=8.43 Hz, 1H, H-4), 8.21 (d, 8.43 Hz, 1H, H-3); 13C NMR 55.57 (OCH3), 55.64 (OCH3) 68.68 (CHOH ), 111.52 (C-2''), 112.26 (C-5''), 120.33 (C-6''), 125.90 (C-4'), 126.37 (C-2'-C-6'), 127.23 (C-4), 127.90 (C-3', C-5'), 129.27 (C-1''), 131.98 (C-3), 133.16 (C-1), 137.68 (C-5), 141.52(C-1'), 148.10 (C-6), 148.33 (C-2), 149.01(C-4'), 149.72 (C-3''); HRMS (ES mode, m/z) calcd. for C21H18N2O7Na [M+Na] + 433.1012, found 433.1029; LRMS (ES mode, m/z) for C21H17N2O6 Na [M+Na]+ found 433.0781 for C21H18N2O7 Na [M+Na]+ found 398.2.

(3-(2-ethoxynaphthalen-1-yl)-2,6-dinitrophenyl)(phenyl)methanol (76) (0.13 g, 29%); light yellow powder; mp 145-147 ºC; Rf (A) = 0.33; 1H-NMR δ 1.14  (m, 3H, OCH2CH3), 4.18 (m, 2H, OCH2CH3), 5.94 (d, J= 5.14 Hz, 1H, CH), 6.79 (d, J= 5.14 Hz, 1H, OH), 7.20-7.60 (m, 11H, H-2'-H-6', H-3'', H-4'', H-7'', H-10'') 7.86 (d, J=7.89 Hz, 1H, H-4), 8.21 (d, 7.89 Hz, 1H, H-3). 13C-NMR δ 13.28 (CH3), 57.63 (CH2), 67.07 (CHOH), 113.43 (C-3''), 116.41 (C-1''), 126.13 (C-6''), 126.32 (C-4), 127.89 (C-3', C-5'), 128.24 (C-4''), 128.90 (C-2'', C-6''), 129.33 (C-7''), 131.25 (C-3), 134.95 (C-9''), 140.39 (C-1') 140.67 (C-5), 141.77 (C-6), 146.42 (C-2''), 147.71 (C-6), 148.29 (C-2'), 152.35 (C-5), 153.43, 155.26 (C-1'), HRMS (ES mode, m/z) calcd. for C25H19N2O5[M-OH]+ 427.1294, found 427.1310; LRMS (ES mode, m/z) for C25H20N2O6Na [M+Na]+ found 467.9832.

1.2.5 Synthesis of α-phenyl-5-phenylazo-2-nitrobenzyl alcohol

The synthesis of 5-phenylazo derivatives is described in detail in section 1.4.1 In this paragraph only the synthesis of α-phenyl-5-phenylazo-2-nitrobenzyl alcohol is highlighted since this 2-nitrobenzyl alcohol precursor was required for the trichloroacetylation.

Reaction of compound 68 with nitrosobenzene in acetic acid10 gave predominantly 2-nitro-5-phenylazo-phenyl)-phenyl-methanol 77 in 37% yield together with only a small amount of compound 90.

A solution of compound 68 (0.08 g, 0.3 mmol) and nitrosobenzene (0.035g, 0.23 mmol) in glacial acetic acid (1.5 mL) was heated at 90-95 ºC for 18 hours. The solvent was removed by freeze drying and the residue was dissolved in dichloromethane (2 mL) and applied onto a column of silicagel. The column was eluted with dichloromethane to give product 90 as an orange solid; yield (0.004 g, 2.6%); Rf=0.64 (A); mp 145-147 ºC; 1H-NMR δ 2.12 (s, 3H, CH3CO), 7.33 (s, 1H, CH), 7.40 (m, 5H, H-2'- H-6') 7.65 (m, 3H, H-3''-H-5''), 7.98 (m, 2H, H-2'', H-6''), 8.06 (m, 2H, H-4, H-6), 8.25 (d, J=8.51 Hz, 1H, H-3); 13C-NMR δ 13.85 (CH3), 57.63 (CH2), 67.07 (CHOH), 113.43 (C-3''), 116.41 (C-1''), 126.13 (C-6''), 126.32 (C-4), 127.89 (C-3', C-5'), 128.24 (C-4''), 128.90 (C-2'', C-6''), 129.33 (C-7''), 131.25 (C-3), 134.95 (C-9''), 140.39 (C-1') 140.67 (C-5), 141.77 (C-6), 143.25 (C-12'), 152.42 (C-2''), 156.42 (C-5'). 127.53 (C-10''), 128.29 (C-8''), 128.88 (C-4'), 135.4135.43(C-5), 135.98 (C-1'), HRMS (ES mode, m/z) calcd. for C25H19N2O5[M+Na]+398.2. Further elution with dichloromethane afforded product 77 as an orange solid; yield 0.031g (37%); mp indef; Rf (A) = 0.35; 1H-NMR δ 6.29 (d, 1H, CH, J=4.86 Hz), 6.44 (d, 1H, OH, J=4.86 Hz), 7.30 (m, 5H, H-2'- H-6'), 7.65 (m, 3H, H-3''-H-5''), 7.98 (m, 2H, H-2'', H-6''), 8.13 (d, J=8.89 Hz, 1H, H-3'), 8.29 (m, 2H, H-4, H-6) LRMS (ES mode, m/z) for C25H20N2O6Na [M+H]+ found 467.9832.

(2-Nitro-5-phenylazo-phenyl)-phenyl-methanol (77) and acetic acid (2-nitro-5-phenylazo-phenyl)-phenyl-methyl ester (90).

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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1.3 Synthesis of substituted 2-nitrobenzyl esters of trichloroacetic acid

Substituted α-phenyl-2-nitro and α-phenyl-2,6-dinitrobenzyl alcohols 60, 61, 55, 53, 54, 56, 57, 58, 59, 63, 66, 67, 64, 65, 71, 70, 77, 72, 73, 74, 75, 62 and 76 were acylated with trichloroacetic acid in pyridine to give the corresponding trichloroacetate esters 3-10, 12-25 (Table 1) (Scheme 6) which were isolated in excellent yields. Compound 11 was prepared by us previously.7

Esters substituted with various electron donating amino groups at the 5-position have their absorption maxima at 360-405 nm with molar extinction coefficients approaching 8000 m⁻¹ cm⁻¹ at 405 nm. (See spectroscopic data in the experimental section). The 5-phenylazo substituted esters, on the other hand, have their main absorption maxima at 320-340 nm with molar extinction coefficients about 23000 m⁻¹ cm⁻¹ as well as maxima at 410-420 nm of considerably lower intensity which is consistent with literature reports.11 All the synthesized compounds were characterized by high resolution mass spectroscopy (HRMS), ultraviolet spectroscopy (UV) and nuclear magnetic resonance spectroscopy (NMR). 13C NMR proved particularly diagnostic to confirm the presence of the trichloroacetate residue at ~ 80-90 ppm. The MS spectra often showed the presence of stable substituted diphenylmethyl carbocations resulting from the fragmentation involving the loss of trichloroacetic acid.

Reaction of trichloroacetic anhydride with substituted 2-nitro and 2,6-dinitrobenzyl alcohols (General Procedure). The substituted benzyl alcohol precursors 60, 61, 55, 53, 54, 56, 57, 58, 59, 63, 66, 67, 64, 65, 71, 70, 77, 72, 73, 74, 75, 62 and 76 (1 mmol) and trichloroacetic anhydride (5 mmol) were dissolved in dry dichloromethane (5 mL) and pyridine (0.1 mL, 0.12 mmol) was added by syringe under argon. Each mixture was stirred at room temperature for 6 hours and subsequently dichloromethane (25 mL) was added. Each solution was washed with water (5 mL), 3% aqueous sodium bicarbonate (4 x 5 mL), water (5 mL), brine (5 mL), dried with sodium sulphate and concentrated in vacuo. Each residue was chromatographed on silicagel eluting with dichloromethane to give products 3-10 and 13-25. Compound 12 was obtained by HPLC purification.

(4-Methoxy-2-nitrophenyl)(phenyl)methyl-2,2,2-trichloroacetate (3) (0.19 g, 56%); light brown solid; mp 83-85 °C; Rf (A) = 0.90; 1H-NMR δ 3.89 (s, 3H, OCH₃), 7.37 (m, 2H, H-5, H-6), 7.45 (s, 6H, H-2',H-6', CH), 7.65 (1H, d, J=2.42Hz, H-3); 13C-NMR 56.14 (OCH₃), 76.88 (CH), 81.06 (CCl₃), 110.06 (C-5), 120.07 (C-3), 123.73 (C-1), 127.13 (C-2', C-6'), 128.81 (C-3', C-5'), 128.94 (C-4'), 130.14 (C-6), 136.52 (C-1'), 148.92 (C-2), 159.76 (C-4), 159.95 (CO); UV λ_max 329 nm ε 2750; HRMS (ES mode, m/z) calcd. for C₁₄H₁₂NO₃ [M-Cl₃CCOO]+ 242.0817, found 242.0822.

(4-Methoxy-2,6-dinitrophenyl)(phenyl)methyl-2,2,2-trichloroacetate (4) (0.2 g, 44%); yellow solid; mp 95-97 °C; Rf (A) = 0.89; 1H-NMR δ 3.98 (s, 3H, OCH₃), 7.27 (m, 2H, H-2',H-6'), 7.41 (m, 4H, H-3',H-5', CH), 7.96 (s, 2H, H-3, H-5); 13C-NMR 57.16 (OCH₃), 74.11 (CH), 81.06 (CCl₃), 114.56 (C-3, C-5), 120.59 (C-4'), 126.04 (C-2', C-6'), 128.19 (C-3', C-5'), 130.15 (C-1), 135.70 (C-1'), 151.14 (C-2, C-6), 160.37 (C-4), 160.63 (CO); UV λ_shoulder 314 nm ε 3176; HRMS (ES mode, m/z) calcd. for C₁₄H₁₁N₂O₇[Cl₃CCOO]+H⁺ 242.0817, found 242.0822.
Scheme 6
Synthesis of α-phenyl-2-nitrobenzyltrichloroacetates

\[
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{OCH3} \quad \text{R5} = \text{H} \quad \text{R6} = \text{H} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{OCH3} \quad \text{R5} = \text{H} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{F} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{Cl} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{Br} \quad \text{R6} = \text{H} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{Br} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{I} \quad \text{R6} = \text{H} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{N(C2H5)2} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{Morpholin-4-yl} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{Pyrroldin-1-yl} \quad \text{R6} = \text{H} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{Pyrroldin-1-yl} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{Piperidin-1-yl} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = 4-\text{methoxyphenylamino} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{phenylamino} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{phenylazo} \quad \text{R6} = \text{H} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = 4-(\text{N,N-dimethylamino})\text{phenyl} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = \text{phenyl} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = 4\text{-methoxyphenyl} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = 3,4\text{-dimethoxyphenyl} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = 2\text{-ethoxynaphtalen-1-yl} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = 2\text{-ethoxynaphtalen-1-yl} \quad \text{R6} = \text{NO2} \\
\text{R1} = \text{C6H5} \quad \text{R3} = \text{H} \quad \text{R4} = \text{H} \quad \text{R5} = 2\text{-ethoxynaphtalen-1-yl} \quad \text{R6} = \text{NO2}
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(3-Fluoro-2,6-dinitrophenyl)(phenyl)methyl-2,2,2-trichloroacetate (5) (0.29 g, 67%); red-brown solid; mp 135-138 °C; Rf (A) 0.76; 1H-NMR δ 7.38 (m, 2H, H-2', H-6'), 7.48 (m, 3H, H-3',H-5'), 7.51 (s, 1H, CH), 8.14 (pseudo triplet, J=9.02 Hz, 1H, H-4); 13C-NMR 74.97 (CH), 88.67 (CCl3), 120.15 (C-4), 126.64 (C-2', C-6'), 128.76 (C-3', C-5'), 128.96 (C-4'), 130.18 (C-3), 134.75 (C-1'), 138.48 (C-1), 145.47 (C-6), 154.45 (C-2), 156.64 (C-5), 159.78 (CO); λmax 255 nm ε 8900; HRMS (ES mode, m/z) calcd. for C15H7FN2O4 [M-Cl3COO]+ 275.0468, found 275.0497.

(5-Chloro-2-nitrophenyl)(phenyl)methyl-2,2,2-trichloroacetate (6) (0.34 g, 83%); yellowish oil, solidifies on cooling; Rf (A) 0.92; 1H-NMR δ 7.47 (s, 5H, H-2', H-6'), 7.53 (s, 1H, CH), 7.60 (d, J=2.23 Hz, 1H, H-6), 7.84 (d, J=8.94 Hz, H-4), 8.41 (d, J=8.94 Hz, H-3); 13C-NMR 76.69 (CH), 88.99 (CCl3), 127.06 (C-3), 127.66 (C-2', C-6'), 128.07 (C-4'), 128.94 (C-3', C-5'), 129.35 (C-4'), 132.92 (C-1'), 135.48 (C-1), 139.04 (C-5), 146.21 (C-2), 159.78 (CO); UV λmax 270 nm ε 6200; HRMS (ES mode, m/z) calcd. for C13H9ClNO2 [M-Cl3COO]+ 246.0322, found 246.0323.

Trichloro-acetic acid (3-chloro-2,6-dinitro-phenyl)-phenyl-methyl ester (7) (0.36 g, 80%); yellow solid; mp 125-140 °C dec; Rf (A) 0.85; 1H-NMR δ 7.32 (m, 2H, H-4', CH), 7.44 (m, 4H, H-2', H-6', H-3', H-5'), 8.24 (d, J=8.94 Hz, 1H, H-4), 8.41 (d, J=8.94 Hz, H-3); 13C-NMR 75.14 (CH), 89.29 (CCl3), 124.95 (C-4'), 126.83 (C-2', C-6'), 128.89 (C-3', C-5'), 129.26 (C-4), 130.50 (C-1), 133.84 (C-3), 134.90 (C-1'), 148.15 (C-5), 148.57 (C-2, C-6), 160.90 (CO); UV λmax 256 nm ε 7500; LRMS HRMS (ES mode, m/z) for C15H9Cl4N2O6 [M+H]+ found 453.2.

(5-Bromo-2-nitrophenyl)(phenyl)methyl-2,2,2-trichloroacetate (8) (0.37 g, 83%); yellowish oil solidifies on cooling; Rf (A) 0.92; 1H-NMR δ 7.47 (s, 5H, H-2', H-6'), 7.53 (s, 1H, CH), 7.65 (d, J=2.06 Hz, 1H, H-6), 7.92 (d, J=8.64 Hz, 2H, H-3, H-6), 8.12 (d, J=8.64 Hz, 1H, H-4); 13C-NMR 76.37 (CH), 89.00 (CCl3), 127.10 (C-3), 127.55 (C-2', C-6'), 127.64 (C-2', C-6'), 128.07 (C-4'), 128.94 (C-3', C-5'), 129.35 (C-4'), 131.92 (C-2', C-6'), 128.89 (C-3', C-5'), 129.26 (C-4'), 139.04 (C-5), 146.21 (C-2), 159.76 (CO); UV λmax 276 nm ε 6600; HRMS (ES mode, m/z) calcd. for C13H9NO2 [M-Cl3COO]+ 289.9817, found 289.9838, LRMS (ES mode, m/z) for C13H9NO2 [M-Cl3COO]+ found 290.00, for C15H10BrCl3NO4 [M+H]+ found 454.2700.

(3-Bromo-2,6-dinitrophenyl)(phenyl)methyl-2,2,2-trichloroacetate (9) (0.27 g, 55%); light yellow solid; mp 128-131 °C; Rf (A) 0.85; 1H-NMR δ 7.37 (m, 2H, H-2', H-6'), 7.47 (s, 1H, CH), 7.65 (d, J=2.06 Hz, 1H, H-6), 7.92 (d, J=8.64 Hz, 1H, H-4); 13C-NMR 74.74 (CH), 88.61 (CCl3), 119.71 (C-5), 124.26 (C-1), 126.40 (C-3', C-5'), 128.20 (C-4'), 128.50 (C-2', C-6'), 129.00 (C-3), 134.59 (C-1'), 148.69 (C-2), 149.67 (C-6), 160.53 (CO); UV λmax 255 nm ε 8900; HRMS (ES mode, m/z) calcd. for C13H9NO2 [M-Cl3COO]+ 334.9667, found 334.9682.

(5-Iodo-2-nitrophenyl)(phenyl)methyl-2,2,2-trichloroacetate (10) (0.28 g, 57%); colourless oil; mp indet.; Rf (A) 0.90; 1H-NMR δ 7.46 (s, 5H, H-2', H-6'), 7.49 (s, 1H, CH), 7.92 (d, J=8.64 Hz, 2H, H-3, H-6), 8.12 (d, J=1.79 Hz, J=8.64 Hz, 1H, H-4); 13C-NMR 76.60 (CH), 88.43 (CCl3), 103.02 (C-5), 126.98 (C-3), 127.20 (C-2', C-6'), 128.94 (C-3', C-5'), 129.31 (C-4'), 133.79 (C-1'), 135.58 (C-1), 136.85 (C-4), 139.10 (C-6), 146.21 (C-2), 159.78 (CO); UV λmax 296 nm ε 6500; HRMS (ES mode, m/z) calcd. for C13H9INO2 [M-Cl3CCOO]+ 337.9716; for C15H10Cl3INO2 [M-H]+ found 454.2730.
Trichloro-acetic acid (5-diethylamino-2,6-dinitro-phenyl)-phenyl-methyl ester (12) (0.39 g, 80%); colourless glass, mp indef; Rf (A) 0.78; UV $\lambda_{max}$ 380 nm $\in$ 8000; R$_e$ = 15.35 min (triethylammonium bicarbonate buffer); HRMS (FAB mode, m/z) calcd. for C$_{19}$H$_{15}$Cl$_3$N$_3$O$_6$ [M+H]$^+$ 490.0335; found 490.0337; LRMS (ES mode, m/z) for C$_{19}$H$_{15}$Cl$_3$N$_3$O$_6$ [M+H]$^+$ found 490.0.

Trichloro-acetic acid (3-morpholin-4-yl-2,6-dinitro-phenyl)-phenyl-methyl ester (13) (0.36 g, 72.2 %); yellow solid, mp 165-167 ºC; Rf (A) 0.47; $^1$H-NMR $\delta$ 3.08 [bs, 4H, N(CH$_2$)$_2$], 3.63 [bs, 4H, O(CH$_2$)$_2$], 7.30 (m, 2H, H-2',H-6'), 7.40 (m, 4H, H-3',H-5', CH), 7.68 (d, J=9.19Hz, 1H, H-3), 8.28 (d, J=9.19 Hz, 1H, H-3); $^{13}$C-NMR $\delta$ 51.07 [N(CH$_2$)$_2$], 65.61 [O(CH$_2$)$_2$], 75.24 (CHOH), 88.77 (CCl$_3$), 123.71 (C-4), 124.75 (C-1), 126.33 (C-3', C-5'), 128.31 (C-2', C-6'), 128.53 (C-4', C-3), 135.47 (C-1'), 142.64 (C-6), 143.43 (C-2) 148.51 (C-5), 160.71 (CO); UV $\lambda_{max}$ 359 nm $\varepsilon$ 6450; HRMS (FAB  mode, m/z) calcd. for C$_{19}$H$_{18}$Cl$_3$N$_3$O$_7$ [M+H]$^+$ 504.0132, found 504.0147.

Trichloro-acetic acid (2-nitro-5-pyrrolidin-1-yl-phenyl)-phenyl-methyl ester (14) (0.35 g, 80%); yellow solid; mp 129-130 ºC; Rf (A) 0.62; 1HNMR 1.98 (m, 4H, (CH$_2$)$_2$), 3.35 (m, 4H, (CH$_2$)$_2$), 6.69 (d, J=5.19 Hz, 1H, CH), 6.55 (d, J=9.02 Hz, 1H, H-4), 7.40 ( m, 6H, CH, H-2'-H-6'), 7.73 (s, 1H, H-6), 8.15 (d, J=9.02 Hz, 1H, H-3); NMR $\delta$ 24.87 [(CH$_2$)$_2$], 47.46 [(CH$_2$)$_2$N], 79.16 (CCl$_3$), 105.75 (CH), 116.87 (C-4), 125.98 (C-2', C-6'), 126.61(C-4'), 128.17 (C-3', C-5'), 128.81 (C-2), 133.21 ( C-1'), 136.63 (C-1), (C-6) 143.89 (C-5), 160.85 (CO); UV $\lambda_{max}$ 403 nm $\varepsilon$ 22700; HRMS (ES mode, m/z) calcd. for C$_{17}$H$_{17}$N$_2$O$_2$[M-Cl$_3$CCOO]$^+$ 281.1290, found 281.1300; LRMS (ES mode, m/z ) for C$_{19}$H$_{16}$Cl$_3$N$_2$O$_4$ [M-H]$^-$ found 443.7

Trichloro-acetic acid (2,6-dinitro-3-pyrrolidin-1-yl-phenyl)-phenyl-methyl ester (15) (0.37 g, 75%); yellow solid, mp 78-81 ºC; Rf (A) 0.76; $^1$H-NMR $\delta$ 1.92 [bs, 4H, (CH$_2$)$_2$], $\delta$ 3.30 [bs, 4H, (CH$_2$)$_2$], 7.20 (d, J=9.55 Hz, 1H, H-3); 7.36 ( m, 6H, H-2'-H-6', H-3'', H-5'', H-2'', H-6'', CH), 8.18  (d, J=9.51 Hz, 1H, H-3), 8.88 (bs, 1H, NH); 13C-NMR 55.32 (OCH$_3$) 75.62 (CH ), 88.90 (CCl$_3$), 115.10 (C-3'', C-5''), 115.50 (C-4), 126.61(C-2'-C-6''), 128.28 (C-2', C-6'), 128.41 (C-3), 128.51(C-4') 135.64( C-1''), 141.48(C-6), 142.77 (C-2), 149.15 (C-5), 160.51 (CO); UV $\lambda_{max}$ 380 nm $\in$ 14600; HRMS (FAB mode, m/z) calcd. for C$_{19}$H$_{15}$N$_3$O$_6$ [M+H]$^+$ 488.0183, found 488.0164.

Trichloro-acetic acid (2,6-dinitro-3-piperidin-1-yl-phenyl)-phenyl-methyl ester (16) (0.40 g; 80%); yellow solid, mp 52-54 ºC; Rf (A) 0.89; $^1$H-NMR $\delta$ 1.54 [bs, 6H, (CH$_2$)$_3$], $\delta$ 3.08 [bs, 4H, (CH$_2$)$_2$], 7.28 (m, 2H, H-2',H-6'), 7.40 (m, 4H, H-3',H-5', CH), 7.59 (d, J=9.18 Hz, 1H, H-3); 8.22 (d, J =9.18 Hz, 1H, H-3); $^{13}$C-NMR $\delta$ 25.38 [(CH$_2$)$_2$], 51.58 [N(CH$_2$)$_2$], 75.34 (CHOH), 88.77 (CCl$_3$), 116.87 (C-4), 125.98 (C-2', C-6'), 126.61(C-4'), 128.17 (C-3', C-5'), 128.81 (C-2), 133.21 ( C-1'), 136.36 (C-2, C-6) 143.89 (C-5), 160.85 (CO); UV $\lambda_{max}$ 380 nm $\in$ 14600; HRMS (FAB mode, m/z) calcd. for C$_{20}$H$_{20}$Cl$_3$N$_3$O$_6$ [M+H]$^+$ found 443.7

Trichloro-acetic acid (2,6-dinitro-3-picolinoyl-1-yl)-phenyl-methyl ester (17) (0.36 g, 67%); reddish solid; mp 54-56 ºC; Rf (A) 0.82; $^1$H-NMR $\delta$ 3.82 (s, 3H, OCH$_3$), 6.90-7.60  (m, 11H, H-4, H-2',H-6', H-3'', H-5'', H-2'', H-6'', CH), 8.18 (d, J=9.51 Hz, 1H, H-3), 8.88 (bs, 1H, NH); $^{13}$C-NMR 55.32 (OCH$_3$) 75.62 (CH ), 88.90 (CCl$_3$), 115.10 (C-3'', C-5''), 115.50 (C-4), 126.61(C-2',C-6''), 126.64 (C-2'-C-6''), 128.13(C-3', C-5'), 128.27 (C-4'), 128.41 (C-3), 130.94 (C-1''), 135.74 (C-1), 136.28 (C-1'), 137.67 (C-2. C-6), 143.90 (C-5), 157.43 (C-4''), 160.50 (CO); UV $\lambda_{max}$ 370 nm $\in$ 8200; HRMS (ES mode, m/z) calcd. for C$_{20}$H$_{16}$N$_3$O$_5$[M-Cl$_3$CCOO]$^+$ 378.1090, found 378.1109

S-19
(2,6-Dinitro-3-(phenylamino)phenyl)(phenyl)methyl-2,2,2-trichloroacetate (18) (0.29 g, 57%); yellowish gum; mp indef.; Rf (A) 0.86; $^1$H-NMR δ (7.2-7.7m, 12H, H-4, H-2'-H-6', H-2''-H-6', CH), 8.22 (d, J=9.47Hz, 1H, H-3), 9.03 (bs, 1H, NH); $^{13}$C-NMR 75.63 (CH$_3$), 88.86 (C($\text{Cl}_3$)), 114.85 (C-2'', C-6''), 115.39 (C-4''), 121.42 (C-4), 126.44 (C-3', C-5''), 126.64 (C-3'', C-5''), 128.26(C-2'', C-6''), 128.40 (C-4''), 128.94 (C-3), 137.12 (C-1), 137.58 (C-1''), 143.90 (C-2 C-6), 157.39 (C-5), 160.85 (CO); λ$_{\text{max}}$ 363 nm ε 6600; HRMS (ES mode, m/z) calcd. for C$_{19}$H$_{14}$N$_3$O$_4$[M-Cl$_3$CCOO]$^+$ 348.0984, found 348.0985.

Trichloro-acetic acid (2-nitro-5-phenylazo-phenyl)-phenyl-methyl ester (19) (0.38 g, 80%; yellow solid; mp 129-130 ºC; Rf (A) 0.85; $^1$H-NMR δ 7.49 (m, 6H, H-2'- H-6', CH), 7.65 (m, 3H, H-3''-H-5''), 7.95 (m, 2H, H-2'', H-6''), 8.08 (s, 1H, H-6), 8.16 (d, J=8.67 Hz, 1H, H-3); 13C-NMR  77.14 (CH), 89.12 (C($\text{Cl}_3$)), 122.10 (C-3), 123.22 (C-2''-C-6''), 123.60 (C-3), 127.44 C-6, 127.78 (C-2'-C-6''), 128.97 (C-3''-C-5''), 129.36 (C-4'), 129.70 (C-3'-C-5'),133.05 (C-4''), 134.09 (C-1), 135.74 (C-1''), 148.29 (C-2), 151.65 (C-1''), 153.90 (C-5), 159.89 (CO); UV λ$_{\text{max}}$ 334.5 nm ε 22000, 454 nm ε 1000; HRMS (ES mode, m/z) calcd. for C$_{21}$H$_{15}$Cl$_3$N$_3$O$_4$[M+H]$^+$ 478.0128 found 478.0121.

(2,6-Dinitro-3-(4-N,N-dimethylaminophenyl)phenyl)(phenyl)methyl-2,2,2-trichloroacetate (20) (0.36 g, 67 %; red-brown solid; mp 68-75 ºC; Rf (A) 0.91; $^1$H-NMR δ 3.02 (s, 6H, N(CH$_3$)$_2$) 6.83 (d, 2H, H-3'',H-5'', J=8.81 Hz),  7.28 (d, J=8.81 Hz, 2H, H-2'', H-6''), 7.39 (m, 3H, H-3'- H-5'), 7.49 (m, 3H, H-2', H-6', CH), 7.98 (d, J=8.63 Hz, 1H, H-4),  8.39 (d, 8.63Hz,  1H, H-3); 13C-NMR  39.67 [N (CH$_3$)$_2$] 75.18 (CH$_3$), 88.86 (C($\text{Cl}_3$)), 112.16 (C-2'', C-6''), 122.83 (C-1''), 126.45 (C-2'-C-6') 127.24 (C-4'), 128.38 (C-2'', C-6''), 128.52(C-3', C-5'), 128.65 (C-3) 133.64 (C-4) 135.33 (C-1) 139.40 (C-1'), 147.29 (C-2, C-6), 150.93 (C-5), 160.67 (CO) λ$_{\text{max}}$ 410 nm ε 7100; HRMS (ES mode, m/z) calcd. for C$_{23}$H$_{19}$Cl$_3$N$_3$O$_6$ [M+H]$^+$ 538.0339, found 538.0329.

(2,6-Dinitro-3-(phenyl)phenyl)(phenyl)methyl-2,2,2-trichloroacetate (21) (0.31 g, 63 %); light yellow solid; mp 129-130 ºC; Rf (A) 0.85; $^1$H-NMR δ 7.49 (m, 6H, H-2'- H-6', CH), 7.65 (m, 3H, H-3''-H-5''), 7.95 (m, 2H, H-2'', H-6''), 8.08 (s, 1H, H-6), 8.16 (d, J=8.67 Hz, 1H, H-3); 8.39 (d, J=8.67 Hz, 1H, H-3); $^{13}$C-NMR 75.08 (CH$_3$), 89.70 (C($\text{Cl}_3$)), 121.7 (C-3'), 123.22 (C-2'-C-6''), 123.60 (C-3), 127.44 C-6, 127.78 (C-2'-C-6''), 128.97 (C-3''-C-5''), 129.36 (C-4'), 129.70 (C-3'-C-5'),133.05 (C-4''), 134.09 (C-1), 135.74 (C-1''), 148.29 (C-2), 151.65 (C-1''), 153.90 (C-5), 159.89 (CO); UV λ$_{\text{max}}$ 334.5 nm ε 22000, 454 nm ε 1000; HRMS (ES mode, m/z) calcd. for C$_{19}$H$_{13}$N$_2$O$_4$ [M-Cl$_3$CCOO]$^+$ 333.0875, found 333.0873.

(4-(4-methoxyphenyl)-2,6-dinitrophenyl)(phenyl)methyl-2,2,2-trichloroacetate (22) (0.32 g, 61%); yellowish solid; mp 50-52 ºC; Rf (A) = 0.88; $^1$H-NMR δ 7.20-7.60 (m, 11H, CH, H-2'-H-6', H-2''-H-6'') 7.99 (d, J=8.49 Hz, 1H, H-3), 8.42 (d, 8.49 Hz, 1H, H-3'); $^{13}$C-NMR 75.08 (CH$_3$), 88.70 (C($\text{Cl}_3$)), 112.82 (C-2', C-6'), 123.97(C-4'), 124.29 (C-2', C-6'), 128.42 (C-3'-C-5'), 128.78 (C-4'-C-5'), 129.62 (C-3), 134.05 (C-1) 135.09 (C-1''), 136.20 (C-5), 139.03 (C-1'), 148.50 (C-6) 148.75 (C-2), 160.63 (CO); λ$_{\text{shoulder}}$ 280 nm ε 7600; HRMS (ES mode, m/z) calcd. for C$_{19}$H$_{13}$N$_2$O$_5$ [M-C$_3$CCOO]$^+$ 333.0875, found 333.0873.

(2,6-Dinitro-3-(4-N,N-dimethylaminophenyl)phenyl)(phenyl)methyl-2,2,2-trichloroacetate (23) (0.21 g, 37%); yellow solid; mp 58-61 ºC; Rf (A) = 0.72; $^1$H-NMR δ 3.91 (s, 3H, OCH$_3$), 4.20 (s, 3H, OCH$_3$), 7.33 (m, 1H, H-2''), 7.46(m, 2H, H-5'', H-6'') 7.7-7.9 (m, 6H, H-2''-H-6', CH) 8.41 (d, J=8.52 Hz, 1H, H-4),
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8.80 (d, 8.52 Hz, 1H, H-3); 13C NMR 55.62 (OCH3) 55.68 (OCH3) 75.13 (CH), 88.71 (CCl3), 111.59 (C-2''), 111.96(C-5''), 120.30 (C-6''), 126.46 (C-3', C-5'), 127.15 (C-4'), 128.42 (C-2'-C-6'), 128.75 (C-4), 130.14 (C-1'), 134.06 (C-3), 135.41 (C-5), 138.81 (C-1'), 148.12 (C-6), 148.68 (C-2), 148.92(C-3''), 149.99 (C-4''), 160.63 (CO); UV λ<sub>max</sub> 343 nm ε 4750; HRMS (ES mode, m/z) calcd. for C<sub>21</sub>H<sub>17</sub>N<sub>2</sub>O<sub>6</sub> [M-Cl<sub>3</sub>COO]<sup>+</sup> 393.1087, found 393.1086; LRMS (ES mode, m/z) for C<sub>23</sub>H<sub>17</sub>Cl<sub>3</sub>N<sub>2</sub>O<sub>8</sub>Na [M+Na]<sup>+</sup> found 554.75.

(2,6-Dinitro-3-(4-methoxyphenyl)phenyl)(phenyl)methyl-2,2,2-trichloroacetate (24) (0.38 g, 73 %); yellow solid; mp 55-57 ºC; Rf (A) 0.85; 1H-NMR δ 3.81 (s, 3H, OCH<sub>3</sub>), 7.03 (m, 2H, H-3''-H-5'') 7.35  (m, 8H, H-2'-H-6', H-2'', H-6'', CH) 7.94 (d, J=8.55 Hz, 1H, H-4), 8.37 (d, 8.55 Hz, 1H, H-3); 13C NMR 55.31 (OCH3) 75.11 (CH), 88.72 (CCl3), 114.45 (C-2'', C-6''), 122.55 (C-4), 126.36(C-1''), 126.47 (C-2'-C-6') 127.26 (C-4'), 128.40 (C-2'', C-6''), 128.72 (C-4'), 129.26 (C-3), 133.94 (C-1), 135.41 (C-1''), 138.81 (C-1') 147.29 (C-2, C-6), 160.64 (C-4'), 162.05 (CO) λ<sub>max</sub> 324 nm ε 4430; HRMS (ES mode, m/z) calcd. for C<sub>20</sub>H<sub>15</sub>N<sub>2</sub>O<sub>5</sub> [M-Cl<sub>3</sub>COO]<sup>+</sup> 363.098, found 363.1035.

(3-(2-Ethoxynaphthalen-1-yl)-2,6-dinitrophenyl)(phenyl)methyl 2,2,2-trichloroacetate (25) (0.17 g, 29%); yellowish solid; 65-68 ºC; Rf (A) = 0.92; 1H-NMR δ 1.21  (m, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 4.20 (m, 2H, OCH<sub>2</sub>CH3), 7.30-7.60  (m, 12H, H-2'-H-6', H-3'', H-4'', H-7'', H-10'', CH), 7.93 (d, J=8.50 Hz, 1H, H-4), 8.46 (d, 8.50 Hz, 1H, H-3); 13C-NMR δ 14.43 (CH<sub>3</sub>), 64.48 (CH<sub>2</sub>), 75.53 (CHOCOCCl<sub>3</sub>), 88.73 (CCl3), 114.18 (C-3''), 116.41 (C-1''), 123.54 (C-6''), 123.92 (C-4'), 126.32 (C-4), 126.79 (C-3', C-5'), 127.12 (C-7''), 127.48 (C-4'), 127.53 (C-10''), 128.14 (C-2'', C-6''), 128.29 (C-8''), 128.88 (C-4'), 135.34(C-9''), 135.43(C-5), 135.98 (C-1'), 148.92 (C-6), 150.13 (C-2), 154.32 (C-2''), 160.67 (CO); UV λ<sub>max</sub> 334 nm ε 4100; HRMS (ES mode, m/z) calcd. for C<sub>25</sub>H<sub>19</sub>N<sub>2</sub>O<sub>5</sub> [M-Cl<sub>3</sub>COO]<sup>+</sup> 427.1295, found 427.1294; LRMS (ES mode, m/z) for C<sub>27</sub>H<sub>20</sub>Cl<sub>3</sub>N<sub>2</sub>O<sub>7</sub> [M+H]<sup>+</sup> found 588.03.

1.4. Synthesis of substituted 2-nitrobenzyl esters of acetic acid

1.4.1. Synthesis of 5-amino and 5-phenylazo-2-nitrobenzyl acetates

It was expected that the 5-phenylazo group would extend the conjugation of the benzene ring resulting in the red shift of the absorption maximum. The synthesis of various 5-phenylazo substituted-2-nitrobenzylalcohols entailed prior preparation of the appropriate 5-amino-2-nitrobenzyl alcohol precursors required for the condensation with nitrosobenzene in acetic acid. Thus 5-amino-2-nitrobenzylalcohol was prepared following the literature procedure, starting from commercially available 3-aminobenzyl alcohol. Acetylation of the latter gave 3-acetylaminobenzylacetate. Subsequent nitration resulted in 5-acetylamino-2-nitrobenzylacetate. Deprotection of compound was carried out with 8M methanolic ammonia during 48 hours at room temperature and resulted in compound. Partially deacetylated product was formed, almost quantitatively, when the reaction was quenched after 2 hours (Scheme 7). Further precursors required for the condensation with nitrosobenzene, such as 5-amino substituted compounds, were prepared via nucleophilic aromatic substitution of the corresponding 5-fluoro derivatives as described in section 1.2.3.
Scheme 7
Synthesis of 5-amino-2-nitrobenzylalcohol

Reaction of compound 82, with nitrosobenzene in acetic acid gave corresponding 5-amino-2-nitrobenzyl acetate 83. 5-Phenylazo-2-nitrobenzyl acetate 84 was isolated only in a low yield and the formation of 5-phenylazo-2-nitrobenzyl alcohol 85 was not detected. Similarly, the reaction of α-phenyl-5-amino-2,6-dinitrobenzylalcohol (69) with nitrosobenzene in acetic acid gave α-phenyl-5-amino-2,6-dinitrobenzyl acetate 86. α-Phenyl-5-phenylazo-2,6-dinitrobenzyl acetate 87 was isolated only in a very low yield whereas α-phenyl-5-phenylazo-2,6-dinitrobenzyl alcohol 88 was not detected.

On the other hand, the similar reaction of α-phenyl-5-amino-2-nitrobenzylalcohol 68 with nitrosobenzene in acetic acid gave predominantly α-phenyl-5-phenylazo-2-nitrobenzyl alcohol 77 in 37% yield together with only a small amount of α-phenyl-5-phenylazo-2-nitrobenzyl acetate 90. The formation of α-phenyl-5-amino-2-nitrobenzyl acetate 89 was not observed.

3-Acetylaminobenzylacetate 79 was prepared by acetylation of a commercially available 3-aminobenzylalcohol 78 with acetic anhydride in the presence of sodium acetate, following the literature procedure 12 (92%); Rf = 0.19 (A); 1H-NMR δ 2.01 (s, 3H, CH3COO), 2.13 (s, 3H, CH3CONH), 5.03 (s, 2H, CH2), 7.03 (m, 1H, H-6), 7.22 (m, 1H, H-5), 7.52 (m, 1H, H-4), 7.57 (m, 1H, H-2) 8.22 (s, 1H, H-3), 8.93 (s, 1H, H-4), 9.95 (s, 1H, NHCO).
Acetic acid 5-acetylamino-2-nitro-benzyl ester (80)
3-Acetylaminobenzylacetate 79 (4.0g, 19.3 mmol) was placed in a 100 mL flask immersed in an ice bath (0 – 5 °C). Fuming nitric acid (d = 1.5g/mL, 8 mL) was added dropwise to the stirred solution over 15min. The stirring was continued at 0-5 °C for 30 min and then at room temperature for 90 min. Subsequently, the mixture was cooled to rt and poured onto crushed ice (100 mL). Dichloromethane (150 mL) was added and the organic layer was washed with water (2 x 25mL), 3% aqueous sodium bicarbonate (4 x 25mL), brine (30 mL), dried (sodium sulphate) and concentrated in vacuo. The residue was purified by column chromatography on silicagel eluting with dichloromethane to give compound 80 as a yellowish solid (1.37g 28%); mp 65-67 °C; Rf = 0.37 (A); 1H-NMR δ 2.06 (s, 3H, CH3COO), 2.10 (s, 3H, CH3CONH), 5.15 (s, 2H, CH2), 7.33 (d, J=8.44Hz, 1H, H-4), 7.59 (s, 1H, H-6), 7.93 (d, J=8.44Hz, 1H, H-2), 10.30 (s, 1H, NHCO); UV λmax 355nm ε 5340; LRMS (ES mode, m/z) found for C11H13N2O5 [M+H]+ 252.7.

(5-Amino-2-nitro-phenyl)-methanol (82)
Compound 80 (1.37g, 5.4 mmol) was treated with 8 M NH3/MeOH (50 mL) and the solution was stirred at rt for 48 hours. The solvent was removed in vacuo and the residue was purified on a silicagel column eluting with dichloromethane/methanol to give 82 as a white solid (0.69 g, 76%); Rf (A) = 0.37; 1H-NMR δ 2.06 (s, 3H, CH3CONH), 4.44 (d, J=6.60 Hz, 2H, CH2), 5.37 (t, J=6.60 Hz, 1H, OH), 6.52 (d, J=8.84 Hz, 1H, H-4), 6.99 (s, 1H, H-6), 7.44 (bs, 2H, NH2), 7.89 (d, J=8.84 Hz, 1H, H-3); LRMS (ES mode, m/z) for C7H9N2O3 [M+H]+ found 169.0.

N-(3-Hydroxymethyl-4-nitro-phenyl)-acetamide (81)
Compound 80 (1.37g, 5.4 mmol) was treated with 8 M NH3/MeOH (50 mL) and the solution was stirred at rt for 2 hours. The solvent was removed in vacuo and the residue was purified by column chromatography on silicagel eluting with dichloromethane/methanol to give 81 as a white solid (0.94 g, 83%); Rf (A) = 0.21; 1H-NMR δ 2.06 (s, 3H, CH3CONH), 4.56 (d,
Reactions of 5-amino substituted 2-nitrobenzylalcohols with nitrosobenzene

**Acetic acid 5-amino-2-nitro-benzyl ester (83)**

A solution of compound 82 (0.167 g, 1 mmol) and nitrosobenzene (0.11 g, 1 mmol) in glacial acetic acid (4 mL) was heated at 95-100 °C for 5 hours. The solvent was removed by freeze drying and the residue was dissolved in dichloromethane (2 mL) and applied onto a column of silica gel. The column was eluted with dichloromethane to give product 83 as a yellowish solid (0.065 g, 28%); Rf (A) = 0.32; mp 118-122 °C; 1H-NMR 2.06 (s, 3H, CH3CO), 5.02 (s, 2H, CH2), 6.56 (d, J=8.99 Hz, 1H, H-4), 6.95 (s, 1H, H-6), 7.46 (bs, 2H, NH2), 7.94 (d, J=8.99 Hz, 1H, H-3); 13C 20.58 (CH3), 64.15 (CH2O), 114.20 (C-6), 116.75 (C-3), 125.73 (C-4), 129.58 (C-1), 144.35 (C-2), 146.09 (C-5), 170.01 (CO); UV λmax 396nm ε 5710; LRMS (ES mode, m/z) for C9H9N2O5 [M-H]- found 209.1.

**Acetic acid 2-nitro-5-phenylazo-benzyl ester (84)**

A solution of compound 82 (0.085 g, 0.5 mmol) and nitrosobenzene (0.11 g, 1 mmol) in glacial acetic acid (2.5 mL) was heated at 105-110 °C for 18 hours. The solvent was removed by freeze drying and the residue was dissolved in dichloromethane (2 mL) and applied onto a column of silica gel. The column was eluted with dichloromethane to give product 84 as an orange solid (0.004 g, 2.6 %); mp 83-87 °C; Rf (A) = 0.82; 1H-NMR 2.12 (s, 3H, CH3CO), 5.26 (s, 2H, CH2), 7.66 (m, 4H, H-3', H-4', H-5', H-6), 7.75 (d, J=8.31 Hz, 1H, H-4), 7.90 (m, 2H, H-2', H-6'), 8.16 (d, J=8.31 Hz, 1H, H-3); 13CNMR 20.61 (CH3), 64.09 (CHOCOCH3), 117.32 (C-3), 123.07 (C-2', C-6'), 124.59 (C-4), 124.92 (C-6), 129.70 (C-3', C-5'), 130.16 (C-1), 132.87 (C-4'), 142.69 (C-2), 144.44 (C-1'), 151.82 (C-5), 170.13 (CO); UV λmax 322 nm ε 14230, λmax 431nm ε 1966.

**α-Phenyl-5-(phenylazo)-2-nitrobenzylalcohol 77 and α-phenyl-5-(phenylazo)-2-nitrobenzylacetate 90**

were synthesised as described in section 1.2.5.

**Acetic acid (3-amino-2,6-dinitro-phenyl)-phenyl-methyl ester (86) and acetic acid (2,6-dinitro-3-phenylazo-phenyl)-phenyl-methyl ester (87)**

A solution of compound 69 (0.08 g, 0.3 mmol) and nitrosobenzene (0.035 g, 0.23 mmol) in glacial acetic acid (1.5 mL) was heated at 90-95 °C for 18 hours. The solvent was removed by freeze drying and the residue was dissolved in dichloromethane (2 mL) and applied onto a column of silica gel. The column was eluted with dichloromethane to give product 87 as an orange solid (0.004 g, 2.6 %); mp 83-87 °C; Rf (A) = 0.57; 1H-NMR δ 2.03 (s, 3H, CH3), 7.26 (s, 1H, CH), 7.38 (m, 5H, H-2'- H-6'), 7.56 (m, 3H, H-3''-H-5''), 7.67 (m, 2H, H-2'', H-6''), 8.09 (d, J=8.11 Hz, 1H, H-4), 8.26 (d, J=8.11 Hz, 1H, H-3); UV λmax 318 nm ε 10500. Further elution with dichloromethane afforded product 86 as a yellow solid (0.031 g, 31%); mp 187-190 °C; Rf (A) = 0.22; 1H-NMR δ 6.21 (d, J=5.39 Hz, 1H, CH), 6.85 (d, J=5.39 Hz, 1H, OH), 7.24 (m, 3H, H-3''-H-5''), 7.39 (m, 5H, H-2'- H-6'), 7.89 (m, 2H, H-2'', H-6''), 8.13 (d, J=8.89 Hz, 1H, H-4), 8.29 (d, J=8.89 Hz, 1H, H-3); 13CNMR 20.24 (CH3), 70.58 (CH), 116.59 (C-4'), 126.90 (C-3, C-5'), 127.93 (C-4'), 128.06 (C-2', C-6'), 128.81 (C-3'), 129.53 (C-3'), 129.73 (C-3), 130.06 (C-2', C-6'), 134.31 (C-1), 134.89 (C-1), 135.89 (C-1'), 137.23 (C-1'), 137.47 (C-5), 169.77 (CO); UV λmax 328nm ε 9200; HRMS (ES mode, m/z) calcd. for C13H10N3O4 [M-CH3COO]+ 272.0685, found 272.0678; LRMS (ES mode, m/z) for C16H12N3O6 [M-H] found 330.0.
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1.4.2 Synthesis of 4-bromo-2,6-dinitrobenzyl acetate 29

Oxidation of 4-bromo-2,6-dinitrotoluene 50 with chromium VI trioxide in a mixture of glacial acetic acid and acetic anhydride in the presence of sulphuric acid resulted in the formation of 4-bromo-2,6-dinitrobenzyl acetate 29. This compound could act as a photoacid generator in its own right releasing acetic acid upon irradiation as discussed earlier in this article.

Scheme 9

Oxidation of 2,6-dinitro-4-bromotoluene

4-bromo-2,6-dinitrobenzyl acetate (29)

4-Bromo-2,6-dinitrotoluene 50 (0.44 g, 1.63 mmol) was suspended in a mixture of glacial acetic acid (0.7 mL) and acetic anhydride (1 mL). Sulphuric acid (30% SO₃, 0.25 mL) was carefully added and the resulting solution was cooled to 0 °C. A solution of chromium trioxide (0.45 g, 4.5 mmol) in water (0.27 mL) and glacial acetic acid (1.78 mL) were then added. After 5 min at 0 °C and 10 min at rt the mixture was heated at 115-120 °C for 18 hrs and then irradiated in a microwave reactor at 100 °C for 4 x 59 min (200W, 400psi). The solvent was removed in vacuo and the residue was dried in vacuo over P₂O₅ and purified by column chromatography on silica gel eluting with dichloromethane to give
product 29 as a white gum (0.035 g, 11%); mp indef; \(^1\)H-NMR \(\delta\) 1.95 (s, 3 H, CH\(_3\)CO), 5.30 (s, 2H, CH\(_2\)), 8.62 (s, 2H, H-3, H-5). \(^{13}\)C NMR \(\delta\) 18.82 (CH\(_2\)OCOCH\(_3\)), 57.38 (CH\(_2\)OCOCH\(_3\)), 123.33 (C-4), 128.90 (C-1), 130.34 (C-3, C-5), 150.57 (C-2, C-6), 169.56 (CO); UV \(\lambda_{max}\) 247 nm \(\varepsilon\) 7000; GCMS for C\(_6\)H\(_2\)BrN\(_2\)O\(_5\) [M-CH\(_2\)COCH\(_3\)]\(^+\) found 243.01; LRMS (ES mode, m/z) for C\(_9\)H\(_6\)BrN\(_2\)O\(_6\) [M-H]\(^-\) found 315.0112.

1.5 The synthesis of 5-(4-methoxyphenyl)-2-(bromomethyl)-1,3-dinitrobenzene 28

The synthesis of compound 28 is described in section 1.2.1. This product could upon irradiation release hydrogen bromide and act as a photoacid generator in its own right as discussed earlier in this article.

1.6 Synthesis of substituted 2-nitrobenzyl tosylates

Some 2-nitrobenzyl esters of strong acids, such as p-toluenesulphonic acid or hydrochloric acid, were required to compare their performance with the corresponding esters of trichloroacetic acid in solid films.

It has been reported that the neighbouring 2-nitro group in 2-nitrobenzyl esters can potentially act as an internal nucleophile.\(^{18-23}\) In the case of esters of a strong acid a good leaving group such as tosyl, mesyl or chlorine is present and it is likely to result in the formation of products of intramolecular cyclisation.\(^{20}\)

These reports were confirmed by our investigation of the reaction of various 2-nitrobenzyl alcohols with p-toluenesulphonic acid anhydride. Thus a commercially available 4,5-dimethoxy-2-nitrobenzyl alcohol 91 pyridine gave the expected 4,5-dimethoxy-2-nitrobenzyl tosylate 26. The product was formed in a good yield and was sufficiently stable to be purified by column chromatography on silicagel. Similar reaction of compound 91 with mesyl chloride gave, however, a cyclic product, 5,6-dimethoxybenzo[c]isoxazol-1(3H)-olate 92, resulting from the intramolecular nucleophilic attack of the 2-nitro group. Reaction of \(\alpha\)-methyl-4,5-dimethoxy-2-nitrobenzyl alcohol 93 with p-toluene sulphonyl chloride under various conditions resulted in the nearly quantitative formation of the same cyclic product, 5,6-dimethoxy-3-methylbenzo[c]isoxazol-1(3H)-olate 94.

Reaction of \(\alpha\)-pheny-4,5-dimethoxy-2-nitrobenzyl alcohol 95 with p-toluene sulfonic acid anhydride resulted in the formation of 4,5-dimethoxy-2-nitrobenzophenone (96), the photoproduce isolated previously during the irradiation of \(\alpha\)-pheny-4,5-dimethoxy-2-nitrobenzyl trichloroacetate.\(^7,8\) No product of tosylation such as 97 was detected. Reaction of \(\alpha\)-pheny-4,5-dimethoxy-2,6-dinitrobenzyl alcohol 98 with p-toluene sulfonic acid anhydride resulted in the formation of a mixture of \(\alpha\)-pheny-4,5-dimethoxy-2,6-dinitrobenzyl tosylate 100 and 4,5-dimethoxy-2-nitroso 6-nitrobensophenone 99, the photoproduce isolated previously during the irradiation of \(\alpha\)-pheny-4,5-dimethoxy-2,6-dinitrobenzyl trichloroacetate.\(^7,8\) Attempts to isolate pure compound 100, formed only in a small amount, were unsuccessful due to its rearrangement to photoproduce 99 during the purification on silicagel.

Reaction of \(\alpha\)-pheny-5-bromo-2,6-dinitrobenzyl alcohol 58 with toluenesulphonic acid anhydride resulted in the initial formation of the expected \(\alpha\)-pheny-5-bromo-2,6-dinitrobenzyl tosylate 102 which was confirmed by its \(^1\)HNMR spectrum. During the purification on silicagel the product was, however, unstable rearranging to 5-bromo-2-nitroso 6-nitrobensophenone 101.
Scheme 10
Tosylation of 4,5-dimethoxy-2-nitrobenzylalcohol and α-methyl-4,5-dimethoxy-2-nitrobenzylalcohol

91 → OTos

p-toluenesulphonic acid anhydride, pyridine, CH$_2$Cl$_2$, rt, 18h

91 → 92 → 26

methane sulphonic acid chloride, pyridine, CH$_2$Cl$_2$

92 → 93 → 94

p-toluenesulphonic acid anhydride, pyridine, CH$_2$Cl$_2$

93 → 94

or methane sulphonlic acid chloride, pyridine, CH$_2$Cl$_2$

or p-toluenesulphonic acid chloride pyridine, CH$_2$Cl$_2$

or p-toluenesulphonic acid chloride dimethylaminopyridine, CH$_3$CN
Scheme 11
Tosylation of α-phenyl-2-nitrobenzalcohols

\[
\begin{align*}
\text{R}^4 & = \text{OCH}_3 \quad \text{R}^5 = \text{OCH}_3 \quad \text{R}^6 = \text{H} \\
\text{R}^4 & = \text{OCH}_3 \quad \text{R}^5 = \text{OCH}_3 \quad \text{R}^6 = \text{NO}_2 \\
\text{R}^4 & = \text{H} \quad \text{R}^5 = \text{Br} \quad \text{R}^6 = \text{NO}_2
\end{align*}
\]

In summary, the reaction of 4,5-dimethoxy-2-nitrobenzyl alcohol 91 with p-toluenesulphonic acid anhydride resulted in the formation of the expected 4,5-dimethoxy-2-nitrobenzyl tosylate 26 but reaction of 91 with methanesulphonic acid chloride (mesyl chloride) gave a cyclic product 92. Likewise, compound 93 gave exclusively a cyclic product 94 under various conditions. Similar reaction of α-phenyl-4,5-dimethoxy-2-nitrobenzyl alcohol 95 resulted in the formation of a photoproduct 96 whereas compounds 98 and 58 gave a mixture tosylates 100 and 102 and photoproducts 99 and 101, respectively.

4,5-dimethoxy-2-nitrobenzyl-4-methylbenzenesulfonate (26)

Compound 91 (0.21 g, 1 mmol) and p-toluenesulphonic acid anhydride (0.32 g, 1 mmol) were dissolved in dry dichloromethane (5 mL) and pyridine (0.12 mL, 0.15 mmol) was added by syringe under argon. The mixture was stirred at room temperature for 18 hours and subsequently dichloromethane (25 mL) was added. The solution was washed with water (5 mL), 3% aqueous sodium bicarbonate (4 × 5 mL), water (5 mL), brine (5 mL), dried with sodium sulphate and concentrated in vacuo. The residue was chromatographed on silicagel eluting with dichloromethane/methanol (99:1) to give product 26 as a light pink solid (0.058 g, 16%); mp 100-103 ºC; RF (A) = 0.32; 1H-NMR δ 2.48 (s, 3H, CH₃) 3.90 (s, 3H, OCH₃), 3.92 (s, 3H, OCH₃), 7.13 (s, 1H, H-5, H-6), 7.52 (d, 2H, H-3',H-5') 7.70 (s, 1H, H-3) 7.84 (d, 2H, H-2', H-6') 7.45  (s, 6H, H-2'-H-6', CH), 7.65 (d, 2.43 Hz, 1H, H-3); 13C-NMR δ 20.72 (CH₃), 56.25 (OCH₃ ), 56.50 (OCH₃ ), 73.80 (CHOSO₂), 108.40 C-3), 113.07 (C-6), 123.85 (C-1), 125.45 (C-2', C-6') 127.99(C-3', C-5'), 137.54 (C-1'), 140.11 (C-2), 145.77 (C-4'), 148.93 (C-4), 153.21 (C-5); UV λmax 347 nm ε 8500; HRMS (ES mode, m/z) calcd. for C₁₆H₁₇N₂O₇SNa [M+Na]+ 390.0623, found 390.0638
5,6-dimethoxybenzo[c]isoxazol-1(3H)-olate (92)
4,5-Dimethoxy-2-nitrobenzyl alcohol 91 (0.21 g, 1 mmol) and mesyl chloride (0.33 g, 3 mmol) were dissolved in dry dichloromethane (5 mL) and pyridine (0.12 mL, 0.15 mmol) was added by syringe under argon. The mixture was stirred at room temperature for 18 hours and subsequently dichloromethane (25 mL) was added. The solution was washed with water (5 mL), 3% aqueous sodium bicarbonate (4 x 5 mL), water (5 mL), brine (5 mL), dried with sodium sulphate and concentrated in vacuo. The residue was chromatographed on silicagel eluting with dichloromethane/methanol (99:1) to give product 92 (0.031 g, 16%); light yellow powder; mp 84-86 ºC; Rf (A) = 0.73; 1H-NMR δ 3.84 (s, 3H, OCH₃), 3.87 (s, 3H, OCH₃), 4.97 (s, 2H, CH₂), 7.27 (s, 1H, H-6), 7.67 (s, 1H, H-3); 13C-NMR δ 43.25 (CH₂) 56.15 (OCH₃), 56.38 (OCH₃), 108.58 (OCH₃), 114.21 (C-3) 126.44 (C-1) 140.20 (C-5), 148.57 (C-4), 152.84 (C-2); UV λ max 344 nm ε 4077; HRMS (ES mode, m/z) calcd. for C₉H₁₀NO₄ [M]-196.0610, found 196.0619.

5,6-Dimethoxy-3-methylbenzo[c]isoxazol-1(3H)-olate (94)
α-Methyl-4,5-Dimethoxy-2-nitrobenzyl alcohol 93 (0.23 g, 1 mmol) and toluenesulphonic acid anhydride (1.6 g, 5 mmol) were dissolved in dry dichloromethane (5 mL) and pyridine (0.3 mL, 0.38 mmol) was added by syringe under argon. The mixture was stirred at room temperature for 16 hours and subsequently dichloromethane (25 mL) was added. The solution was washed with water (5 mL), 3% aqueous sodium bicarbonate (4 x 5 mL), water (5 mL), brine (5 mL), dried with sodium sulphate and concentrated in vacuo. The residue was chromatographed on silicagel eluting with dichloromethane/methanol (99:1) to give product 94 (0.099 g, 47%); yellowish solid; mp 72-74 ºC; Rf (A) = 0.56; 1H-NMR δ 2.48 (d, J=6.71 Hz, 3H, CH₃), 3.90 (s, 3H, OCH₃), 3.92 (s, 3H, OCH₃), 5.87 (q, J=6.71 Hz, 1H, CH) 7.33 (s, 1H, H-6), 7.56 (s, 1H, H-3); 13C-NMR δ 43.25 (CH₃) 56.15 (OCH₃), 56.38 (OCH₃), 108.58 (C-6), 114.21 (C-3) 126.44 (C-1) 140.20 (C-5), 148.57 (C-4), 152.84 (C-2); UV λ max 347 nm ε 8500; HRMS (ES mode, m/z) calcd. for C₁₀H₁₂NO₄ [M] 210.0766, found 210.0767.

The identical product was obtained when the reaction was carried out with p-toluenesulphonic acid anhydride or p-toluenesulphonyl chloride in the presence of 4-N,N-dimethylaminopyridine in acetonitrile.

4,5-Dimethoxy-2-nitrosobenzophenone (96)
Compound 95 (0.29 g, 1 mmol) and p-toluenesulphonic acid anhydride (0.64 g, 2 mmol) were dissolved in dry dichloromethane (7 mL) and pyridine (0.3 mL, 0.38 mmol) was added by syringe under argon. The mixture was stirred at room temperature for 18 hours and subsequently dichloromethane (25 mL) was added. The solution was washed with water (5 mL), 3% aqueous sodium bicarbonate (4 x 5 mL), water (5 mL), brine (5 mL), dried with sodium sulphate and concentrated in vacuo. The residue was chromatographed on silicagel eluting with dichloromethane/methanol (99:1) to give product 96 (0.19 g, 68.5%); light green solid; Rf (A) = 0.43; the spectroscopic and analytical data were consistent with those reported by us earlier.

4,5-Dimethoxy-2-nitroso-6-nitrobenzophenone (99)
Compound 98 (0.33 g, 1 mmol) and p-toluenesulphonic acid anhydride (0.64 g, 2 mmol) were dissolved in dry dichloromethane (10 mL) and pyridine (0.4 mL, 0.5 mmol) was added by syringe under argon. The mixture was stirred at room temperature for 18 hours and subsequently dichloromethane (25 mL) was added. The solution was washed with water (5 mL), 3% aqueous sodium bicarbonate (4 x 5 mL), water (5 mL), brine (5 mL), dried with sodium sulphate and
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concentrated in vacuo. The residue was chromatographed on silicagel eluting with dichloromethane to give product 99 (0.18 g, 58 %); light green solid; Rf (A) = 0.67; further data consistent with the literature.8

α-Phenyl-5-bromo-2,6-nitrobenzyl tosylate (102)

α-Phenyl-5-bromo-2,6-nitrobenzyl alcohol 58 (0.35 g, 1 mmol) and p-toluenesulphonyl chloride (0.28 g, 1.5 mmol), 4-N,N-dimethylaminopyridine (0.24 g, 2 mmol) were dissolved in dry acetonitrile (10 mL) and the mixture was stirred under argon at room temperature for 18 hours. The solvent was removed in vacuo, the residue was dissolved in the mixture ethyl acetate-3% aqueous sodium bicarbonate (3:1, 40 mL). The organic layer was washed with water (15 mL), cold 0.1M hydrochloric acid (3 x 15 mL), water (15 mL), 3% aqueous sodium bicarbonate (4 x 15 mL), brine (15 mL), dried with sodium sulphate and concentrated in vacuo. The crude product before the purification did not seem to contain photoproduct 101; 1H-NMR δ 2.45 (s, 3H, CH3), 6.85 (s, 1H, CH), 7.15 (m, 2H, H-3'', H-5''), 7.40 (m, 3H, H-3', H-4', H-5'). 7.50 (m, H-2', H-6'), 7.76 (m, H-2'', H6'') 8.25 (d, J=8.8 Hz, 1H, H-4), 8.33 (d, J=8.8 Hz, 1H, H-3) was consistent with product 102.

The mixture was purified by column chromatography on silicagel eluting with dichloromethane, the appropriate fractions were combined and concentrated in vacuo to give the purified product which seemed to contain more contaminants and additional signals in the 1H-NMR spectrum at 8.69ppm and a different pattern of the aromatic protons at 7.40 and 7.50 ppm. While showing only one spot in dichloromethane, its tlc in hexane/ethyl acetate (7:3) indicated the presence of two products. Rf=0.42 (minor) and Rf= 0.31 (major); 1H-NMR δ 2.45 (s, 3H, CH3), 6.85 (s, 1H, CH), 7.15 (m, 2H, H-3'', H-5''), 7.40 (m, H-2', H6''). 7.59 (m, H-2'', H-6''), 7.76 (m, H-3', H-4', H-5' CH), 8.25 (d, J=8.84 Hz, 1H, H-4), 8.33 (d, J=8.84 Hz, 1H, H-3), 8.69 (s, 2H, H-3, H-4)

The mixture was applied onto column chromatography on silicagel eluting with in hexane/ethyl acetate. The amount of the minor product being eluted was getting increased and it turned out to be virtually the single product eluted from the column. Its 1H-NMR was consistent with the photoproduce 101; 1H-NMR δ 7.50 (m, 2H, H-2', H-6'), 7.70 (m, 3H, H-3'-H-5'), 8.69 (s, 2H, H-3, H-4) no signals corresponding to the CHOSO2 and the CH3 group of the toluene ring.

The residue was re-chromatographed on silicagel eluting with dichloromethane to give product 101 (68.5 %); light green solid; Rf (A) = 0.78; 1H-NMR δ 7.50 (m, 2H, H-2', H-6'), 7.70 (m, 3H, H-3'-H-5'), 8.69 (s, 2H, H-3, H-4); 13C NMR 120.85 (C-5), 127.66 (C-3', C-5'), 128.17 (C-2', C-6'), 133.33 (C-3), 134.21 (C-4'), 134.76 (C-1'), 136.84 (C-1') 137.85 (C-4'), 146.14 (C-6), 158.97 (C-2) 190.23 (CO); HRMS (ES mode, m/z) calcd. for C13H8BrN2O4 [M+H]+ 334.9718, found 334.9734.

1.7 Improved synthesis of α-phenyl-4,5-dimethoxy-2,6-dinitrobenzyltrichloroacetate (ester 2)

Ester 2, α-phenyl-4,5-dimethoxy-2,6-dinitrobenzyltrichloroacetate, displays superior photochemical characteristics both in solution and in solid films (Table 1).

Initially, the compound was prepared via the condensation of 4,5-dimethoxy-2,6-dinitrobenzaldehyde 104 with phenylmagnesium bromide and subsequent trichloroacetylation of the resulting α-phenyl-4,5-dimethoxy-2,6-dinitrobenzyl alcohol 98.7,8 The literature route employed for the synthesis of a key intermediate, 10426, involved, however, five steps making a large scale preparation of ester 2 rather difficult and time consuming.

The improved, alternative, route employs a commercially available 4,5-dimethoxy-2-nitrobenzaldehyde 103 as the starting material (Scheme 12). Nitration with concentrated nitric acid
gave 4,5-dimethoxy-2,6-dinitrobenzaldehyde 104 together with some non-aldehyde side products having similar Rf values in several solvent systems.

Since the product was very difficult to purify at that stage, the impure compound 104 was condensed with phenylmagnesium bromide. The resulting α-phenyl-4,5-dimethoxy-2,6-dinitrobenzyl alcohol 98 formed as a result and being much more polar than the carried over non-aldehyde contaminants, proved quite easy to purify by column chromatography on silicagel and could be used in the final step of trichloroacetylation. This methodology was applied successfully to the synthesis of gram quantities of a high purity ester 2.

**Scheme 12**

**Synthesis of α-phenyl-4,5-dimethoxy-2,6-dinitrobenzyltrichloroacetate - ester 2**

**Alternative Route**

4,5-Dimethoxy-2,6-dinitrobenzaldehyde (104)

4,5-Dimethoxy-2-nitrobenzaldehyde 103 (9 g, 42.6 mmol) was cooled to 0 ºC and fuming nitric acid (d=1.5g/mL, 65 mL, 1.55 mol) was added dropwise over 30 minutes at 0 ºC. After 30 min at rt, the mixture was poured onto crushed ice (1000 mL) and left at 0 ºC for 24 h. The resulting precipitate was filtered off, washed well with distilled water and dried in a desiccator over P₂O₅ to give a yellowish solid (9.5 g); its ¹H-NMR confirmed the formation of impure product 104; Rf (A)=0.50.

α-Phenyl-4,5-dimethoxy-2,6-dinitrobenzyl alcohol (98)
The impure material obtained as described above (5g) was dissolved in anhydrous tetrahydrofuran (100 mL), under argon, and the solution was cooled to −78 ºC. Phenylmagnesium bromide (1 M solution in THF, 25 mL, 25 mmol) was added to the stirred solution by syringe during 15 minutes. After 15 minutes at -78 ºC, the mixture was stirred at −10 - (- 15 ºC) for a further 15 minutes. 2% Aqueous hydrochloric acid (100 mL) was added dropwise over 30 minutes followed by dichloromethane (250
The organic layer was washed with water (50 mL), 3% aqueous sodium bicarbonate (4 x 50 mL), water (50 mL), brine (50 mL), dried (sodium sulphate) and concentrated in vacuo. The residue was chromatographed on a silicagel column eluting with dichloromethane to give compound 98 as a light brown solid (1.85 g, 24.7%) (calculated for the two steps - nitration and condensation with phenyl magnesium bromide). The spectroscopic data were in agreement with those quoted by us earlier. This product was used in the subsequent trichloroacetylation step.

**Scheme 13**

Irradiation of Photolabile Esters

![Scheme 13](image)

7 $R^5$= Chloro,
13 $R^5$= Morpholin-4-yl
15 $R^5$= Pyrrolidin-1-yl
16 $R^5$= Piperidin-1-yl

105 $R^5$= Chloro,
106 $R^5$= Morpholin-4-yl
107 $R^5$= Pyrrolidin-1-yl
108 $R^5$= Piperidin-1-yl

**2 Irradiation of some photolabile esters in the photoreactor**

Compounds 7 and 13-15 were irradiated in a semi-micro photochemical reactor provided by Photochemical Reactors Ltd. Irradiations were carried out using a four watt UV lamp with peak emission at 350 nm. The progress of photolysis was monitored by HPLC and TLC. Reverse phase HPLC was performed using a Waters chromatography system with a variable wavelength detector set at 254 nm and 280 nm. Columns, Waters Delta Pak 5µ C18-300A, were used for analytical and preparative scales. The mobile phases were (A) 0.05M aq. [Et$_3$NH]$^+$ [CH$_3$COO]$^-$ (B) MeCN. Gradient elution; 5%(B) – 90% (B) over 30 minutes.
Example: Irradiation of *trichloro-acetic acid (3-chloro-2,6-dinitro-phenyl)-phenyl methyl ester* (7)

Compound 7, 11mM solution in dichloromethane (4 mL), in a 1 cm quartz cuvette, was irradiated in the photoreactor at 350 nm for 30 minutes. The irradiated solution was analysed by HPLC showing the presence of the starting material, retention time (R<sub>t</sub>) = 17.65 min, and the photoproduct, R<sub>t</sub> = 15.62 min. The estimated degree of photoconversion, peak areas, was 80%. Preparative HPLC resulted in two fractions, fraction 1, R<sub>t</sub> = 15.62 min and fraction 2, R<sub>t</sub> = 17.65 min. Each fraction was analysed by MS; the photoproduct, *3-chloro-2-nitro-6-nitrosobenzophenone* (105), was found in fraction 1; LRMS (ES mode, m/z) for C<sub>13</sub>H<sub>8</sub>ClN<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup> found 291.4.

Similarly, esters 13, 15, 16 were irradiated in the photoreactor at 350 nm giving a varying degree of photoconversion. Photoproducts 106-108 were isolated by preparative HPLC (retention times R<sub>t</sub> in brackets) and their identity was confirmed by mass spectroscopy.

*Trichloro-acetic acid-(3-chloro-2,6-dinitro-phenyl)-phenyl-methyl ester* (7) (R<sub>t</sub> 17.65 min)

*Trichloro-acetic acid-(2,6-dinitro-3-morpholin-4-yl-phenyl)-phenyl-methyl ester* (13) (R<sub>t</sub> 17.12 min)

*Trichloro-acetic acid-(2,6-dinitro-3-pyrrolidin-1-yl-phenyl)-phenyl-methyl ester* (15) (R<sub>t</sub> 17.92 min)

*Trichloro-acetic acid-(2,6-dinitro-3-piperidin-1-yl-phenyl)-phenyl-methyl ester* (16) (R<sub>t</sub> 18.68 min)

3-Chloro-2-nitro-6-nitrosobenzophenone (105) (90%), LRMS (ES mode, m/z) for C<sub>13</sub>H<sub>8</sub>ClN<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup> found 291.4 (R<sub>t</sub> 15.62 min)

2-Nitro-6-nitroso-3-(pyrrolidin-1-yl)-benzophenone (106) (28%); LRMS (ES mode, m/z) for C<sub>17</sub>H<sub>16</sub>N<sub>3</sub>O<sub>4</sub> [M+H]<sup>+</sup> found 326.3 (R<sub>t</sub> 15.18 min).

2-Nitro-6-nitroso-3-(piperidin-1-yl)-benzophenone (107) (23%); LRMS (ES mode, m/z) for C<sub>18</sub>H<sub>18</sub>N<sub>3</sub>O<sub>4</sub> [M+H]<sup>+</sup> found 340.3 (R<sub>t</sub> 13.42 min)

3-(Morpholin-4-yl)-2-nitro-6-nitrosobenzophenone (108) (19%); LRMS (ES mode, m/z) for C<sub>17</sub>H<sub>16</sub>N<sub>3</sub>O<sub>5</sub> [M+H]<sup>+</sup> found 342.3 (R<sub>t</sub> 14.57 min)

Preparative scale irradiation of *trichloro-acetic acid (3-chloro-2,6-dinitro-phenyl)-phenyl-methyl ester* (7)

Ester 7, 0.5% solution in dichloromethane (3.5 mL, 0.05 mmol), was irradiated in the photoreactor at 350 nm for 30 min. The degree of photoconversion could be conveniently monitored by TLC. The solution was concentrated to a half of its volume and applied onto a column of silicagel. The column was eluted with dichloromethane, appropriate fractions were combined and the solvent was removed in vacuo. The residue was dissolved in water/ethanol (1:1) (2 mL) and freeze-dried to give photoproduct 105 as a yellow solid (0.011 g, 80%); R<sub>f</sub> (A) 0.74; mp indef; <sup>1</sup>H-NMR δ 7.53 (m, 2H, H-3', H-5'), 7.63 (m, 1H, H-4'), 7.86 (m, 2H, H-2', H-6'), 8.24 (d, 1H, J=9.06 Hz, H-4); 8.32 (d, 1H, J=9.06 Hz, H-3); LRMS (ES mode, m/z) for C<sub>13</sub>H<sub>8</sub>ClN<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup> found 291.5.

Preparative scale irradiation of *trichloro-acetic acid (2,6-dinitro-3-pyrrolidin-1-yl-phenyl)-phenyl-methyl ester* (15)

Ester 15, 0.5% solution in dichloromethane (3.5 mL, 0.05 mmol), was irradiated in the photoreactor at 350 nm for 70 min. The degree of photoconversion could be conveniently monitored by TLC. The solution was concentrated to a half of its volume and applied onto a column of silicagel. The column was eluted with dichloromethane, appropriate fractions were combined and the solvent was removed in vacuo. The residue was dissolved in water/ethanol (1:1) (2 mL) and freeze-dried to give photoproduct 107 as a yellowish glass (0.0021 g, 17%); R<sub>f</sub> (A) 0.47; mp indef; <sup>1</sup>H-NMR δ 1.91 [bs, 4H, (CH<sub>2</sub>)<sub>2</sub>], δ
3.30 [bs, 4H, (CH₂)₂], 7.41 (d, J=6.76 Hz, 1H, H-4); 7.51 (m, 2H, H-3', H-5'), 7.54 (m, 1H, H-4'), 7.57 (m, 2H, H-3', H-5'), 8.28 (d, J=6.76 Hz, 1H, H-3).

3 References


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4 Further experimental methods: UV-visible spectrophotometry

4.1 Apparatus for photolysis and spectrophotometry. Figure 8 gives an outline of the optical apparatus used for measurement of absorption spectra of photosensitive films on glass slides and their response to photolysis. Construction was mainly by assembly of commercially available components from Linos (Microbench opto-mechanical system: www.linos.com) and Avantes (fibre-optic spectrophotometer system (www.avantes.com). The analytical and photolytic light beams are coaxial at the slide and orthogonal to it. The diameter of the photolytic beam was ca. 1 cm, whereas that of the analytical beam was 2–3 mm. These two beams are propagated in opposite directions.

Figure 8. Outline of optical paths for combined photolysis and UV-vis spectrophotometry of films on microscope slides. The analytical beam entered and exited through fibre optic guides connecting to the light source and spectrometer respectively. The 45° mirror shown in the Figure was either a 100% mirror in which case it was slid into position for the duration of photolysis and then removed, or the mirror was dichroic, reflecting below 380–390 nm and transmitting above, and left in position along with a high pass filter (>390 nm) to provide further protection against reflected photolytic light selected with a 365 nm interference filter from a 150 W Hg arc lamp (Hamamatsu). These two arrangements allowed for either spectroscopic measurement from 30–650 nm before and after but not during photolysis, or continuously but restricted to >390 nm. Averaged spectra were collected at \( \leq 0.5 \) Hz. For most purposes a low power UV-vis source and a 2000 element CCD detector was used, giving a noise level (in absorption units) of \( \pm 0.001 \) in the region from 450–550 nm. Their replacement with a high power light source and a deep-well photodiode detector spectrometer DW1024 lowered the noise level to \( \pm 0.0001 \) in the 510 nm region, corresponding to a change in DMT\(^+\) density of \( \pm 1.25 \) pmol cm\(^{-2}\). The DW1024 spectrometer is no longer available, having been replaced by model HAM 1024 with a CMOS array detector.
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4.2 Selection of film – forming polymers

Table 2. Ability of solid polymers<sup>a</sup> in films to support photoacid-induced detritylation<sup>b</sup> and increased intra-film proton activity<sup>c</sup>. Selection was on the basis of commercial availability, solubility in low boiling point solvents such as DCM, ability to form optically transparent films from solution, and chemical composition including absence of strongly acidic groups. Films were cast from a DCM solution containing 2% (w/v) polymer, 6.3m M ester<sup>2</sup>, 6-7 mM DMT-T and 0.2-0.3m M BG. Photolysis of ester<sup>2</sup> was at 365 nm for 30s at 50mW cm<sup>-2</sup>. Detritylation was assessed by appearance of the 510 nm absorption peak of DMT<sup>T</sup>, and intrafilm acidification from fall of the BG peak at 640 nm. Under these conditions detritylation of intrafilm DMT-T was ca. 80% complete. The anticipated height of the DMT<sup>T</sup> peak after 100% detritylation was obtained by addition of TCA (final conc 50 mM) to diluted casting solution and calculating the ratio of the heights of the post-acidification DMT<sup>T</sup> peak to the pre-acidification BG peak. The same ratio was then used to multiply the height of the pre-photolysis BG peak of the film to calculate the anticipated DMT<sup>T</sup>. This use of BG as internal marker assumes that the peak height ratios are the same in both solution and in polymer film, despite peak broadening and small red shifts in the maxima. They may not be, but high accuracy was not critical for these screening experiments.

| (i) 70-80% detritylation (>70% fall in BG absorption) | 22. Poly(vinylchloride-co-vinylacetate-co-2-hydroxy-propyl-acrylate). Wt ratio 81:4:15. Mn<sub>n</sub> = 15k |
| (ii) 45-70% detritylation (30-60% fall in BG absorption) | (iv) <5% detritylation (<5% fall in BG absorption) |
| (iii) 3-10% detritylation (5-15% fall in BG absorption) | 23. Cellulose acetate butyrate. (acetate 2%, butyrate 52%) |
| (iv) <5% detritylation (<5% fall in BG absorption) |
| Polystyrene | 24. Ethyl cellulose. (Ethoxy content 52% by wt.) |
| Poly(styrene-co-a-methylstyrene). M<sub>n</sub> = 15k | 25. Sucrose octabenzoyl<sup>e</sup>. |
| Poly(4-methylstyrene). M<sub>n</sub> = 70k | 26. Poly(caprolactone). M<sub>n</sub> = 10k |
| Poly(4-tert-butylstyrene). M<sub>n</sub> = 100k | 27. Poly(2,6-dimethyl-1,4-phenylene-oxide. M<sub>n</sub> = 244k |
| Poly(methyl methacrylate). M<sub>n</sub> = 65k | 28. Poly(oxyethylene). M<sub>n</sub> = 1.5k |
| Poly(benzyl methacrylate). M<sub>n</sub> = 2.3k | 29. Poly(oxyethylene). M<sub>n</sub> = 100k |
| Poly(2-vinyl naphthalene). M<sub>n</sub> = 100k | 30. Poly(1,3-propylene-glutarate). M<sub>n</sub> = 7.1k |
| Poly(4-hydroxy styrene). M<sub>n</sub> = 20k | 31. Poly(styrene-co-acrylonitrile) Wt ratio = 7:3. M<sub>n</sub> = 185k |
| Poly(2-vinyl pyridine). M<sub>n</sub> = 11k, | 32. Poly(styrene-co-maleic anhydride), cumene terminated. Wt. ratio = 3:1. M<sub>n</sub> = 1.9k |
| Polystyrene-block-polyisoprene-block-polystyrene<sup>d</sup> | 33. Poly(styrene-co-allyl alcohol) Molar ratio = 2:1. M<sub>n</sub> = 2.3k |
| 14% styrene by wt. | 34. Poly(styrene-co-methyl-methacrylate) Wt. ratio = 40:60. M<sub>n</sub> = 100-150k |
| Poly(carboxylsilane)<sup>f</sup>. M<sub>n</sub> = 2k | 35. Poly(methyl methacrylate). M<sub>n</sub> = 15k |
| Poly(indene-co-coumarone). Ratio = 9:1. M<sub>n</sub> = 0.7k | 36. Poly(benzyl methacrylate). M<sub>n</sub> = 70k |
| Poly(chlorostyrene). 60:40 mix of 3- & 4-isomers. M<sub>n</sub> = 100k | 37. Poly(cyclohexylmethacrylate). M<sub>n</sub> = 65k |
| Poly(4-tert-butylstyrene). M<sub>n</sub> = 100-200k | 38. Poly(vinylacetate). M<sub>n</sub> = 83k |
| Poly(4-hydroxy styrene). M<sub>n</sub> = 20k | 39. Poly(9-vinyl carbazole). M<sub>n</sub> = 83k |
| Poly(2-vinyl naphthalene). M<sub>n</sub> = 100k | 40. Poly(vinylphenylketone) |
| Poly(styrene-co-acrylonitrile) Wt ratio = 7:3. M<sub>n</sub> = 185k | 41. Poly(2-vinylpyridine) M<sub>n</sub> = 11k, |
| Polystyrene-block-polyisoprene-block-polystyrene | 42. Poly(vinyl pyrrolidone). M<sub>n</sub> = 10k |
| Styrene content 22% by wt. | 43. Poly(propylene carbonate) M<sub>n</sub> = 50k |

(a) Data for composition, M<sub>n</sub> (weight average mol. wt.) and M<sub>s</sub> (number average mol. wt.) are those given by the supplier (Aldrich). (b) As shown by the DMT<sup>T</sup> absorption peak at 510 nm. (c) As shown by the fall in the 640 nm peak of BG on protonation. (d) Not recommended due to risk of cross-linking on irradiation. (e) Detritylation underestimated due to reaction of DMT<sup>T</sup> with the silyl hydride groups of the polymer. (f) Sucrose octabenzoyl is included because it readily forms solid and optically clear films.

The polymers fell into four sets defined by their varying ability as solid films to support photoacid-induced detritylation of incorporated DMT-T. (i) Polymers 1-11 supported >70% photoacid-induced falls in the 640nm peak of BG, and >90% detritylation of DMT-T
nucleotide. The first eight were devoid of heteroatoms, the next three were not. The silicon heteroatom in polymer 9 is not electronegative. Polymer 10 contained oxygen, but the ratio of oxygen to carbon atoms of 0.006 was low and unlikely to have significant effect on the pKₐ of photogenerated TCA. For comparison, the oxygen:carbon atom ratio in poly-(methyl-methacrylate) is 0.4. Polymer 11 contained aryl chlorine atoms at the 3- or 4-position. Nine of the first eleven had aromatic structures, polymers 6, 7 and 9 did not. We were unable to test any polyalkyl compounds (e.g. polyethylene) because of their poor solubility in suitable casting solvents. (ii) Polymers of the second set (12-17) all supported detritylation, but only to 45-70%. Apart from 12 and 13 which are 4-halo-substituted polystyrenes, and 15 which has a phenolic hydroxyl, there were no other heteroatom-containing polymers in this group (iii) The third set (18-22) exhibited low but detectable detritylation. All members of this group contained O or N atoms, or Cl as an alkyl chloride.

(iv) The fourth set, Polymers 23–43, did not support detectable detritylation, nor was there any response of BG to photoacid generation. Polymers in this group included four polymethacrylates (34–37) five other ester-containing polymers (23, 25, 26, 30, 38), three polymers with numerous ether groups (24, 27, 29), four copolymers of styrene with heteroatom-containing subunits (31–34), two polymeric nitrogenous bases (41, 43) a poly(arylketone) (40) and a polycarbonate (43). Molecular weight was not a significant determinant of polymer behavior. A common feature of the poorly performing polymers 18-43 was the presence of oxygen or nitrogen, or chlorine as an alkyl chloride. We would not expect that the presence of electronegative heteroatoms is the only determinant of hydrogen bonding ability. Chlorine atoms may be less electronegative as aryl- rather than alkyl-chlorides, steric effects may interfere with the ability of polymer heteroatoms to interact with photoacid, and aryl rings may be capable of weak hydrogen bonding. For convenience structures of the polymers are shown in section 4.3.
4.3 Chemical structures of polymers. Polymers 1-43 are those referred to in Table 2. Polymers A-K were inadequately soluble in the low boiling point solvents used for film formation, and could not be tested further.

1. Polystyrene

2. Poly(α-methylstyrene)

3. Poly(styrene-co-α-methylstyrene)

4. Poly(4-methylstyrene)

5. Poly(acenaphthalene)

6. Poly(methylstyrene-co-indene), hydrogenated
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7. Poly(limonene) or Poly(dipentene)

\[
\begin{align*}
\text{CH}_3 & \quad \text{C} \quad \text{C} \quad \vdots \quad \text{C} \quad \vdots \quad \text{C} \\
\text{H}_2 & \quad \vdots \\
\text{CH}_3 & \quad \text{C} \quad \text{CH}_3 \\
\end{align*}
\]

8. Poly(styrene-block-polysoprene-block-polystyrene)

14% styrene by wt.

\[
\begin{align*}
\text{H}_2 \text{C} & \quad \text{H} \quad \text{C} \quad \text{H} \quad \text{C} \quad \vdots \quad \text{C} \quad \vdots \quad \text{C} \quad \text{H}_2 \\
\text{C} & \quad \text{H} \quad \text{C} \quad \text{H} \quad \text{C} \quad \vdots \\
\text{H}_2 \text{C} & \quad \text{H} \quad \text{C} \quad \text{H} \quad \text{C} \quad \vdots \\
\text{CH}_3 & \quad \vdots \\
\end{align*}
\]

9. Poly((methylsilylene)methylene) or poly(carbomethylsilane)

\[
\begin{align*}
\text{SiH} & \quad \text{C} \quad \vdots \quad \text{H} \\
\text{CH}_3 & \quad \vdots \\
\end{align*}
\]

10. Poly(indene-co-coumarone)

\[
\begin{align*}
\text{H}_2 \text{C} & \quad \text{C} \quad \vdots \quad \text{O} \\
\text{H}_2 \text{C} & \quad \vdots \\
\end{align*}
\]

11. Poly(3-chlorostyrene-co-4-chlorostyrene)

\[
\begin{align*}
\text{H}_2 \text{C} & \quad \text{H} \quad \text{C} \quad \text{C} \quad \text{H} \\
\text{Cl} & \quad \vdots \\
\end{align*}
\]

12 & 13. Poly(4-halostyrene). X = Cl or Br

\[
\begin{align*}
\text{H}_2 \text{C} & \quad \text{H} \quad \text{C} \quad \text{C} \quad \text{H} \\
\text{Cl} & \quad \vdots \\
\end{align*}
\]

14. Poly(4-t-butyl-styrene)

\[
\begin{align*}
\text{H}_2 \text{C} & \quad \text{H} \\
\text{t-But} & \quad \vdots \\
\end{align*}
\]

15. Poly(4-hydroxy-styrene)

\[
\begin{align*}
\text{H}_2 \text{C} & \quad \text{H} \\
\text{OH} & \quad \vdots \\
\end{align*}
\]
16. Poly(2-vinylnaphthalene)

17. Poly(styrene-\textit{block}-polysoprene-\textit{block}-polystyrene) 22\% styrene by wt. See 8.

18. Poly(acrylonitrile-\textit{co}-butadiene-\textit{co}-styrene)

19. Poly(carbonate-urethane). \textit{This is a co-polymer of (1,6-hexyl-1,2-ethylcarbonate)dial with 4,4'-methylenebis(phenylisocyanate) and 1,4-butenediol.}

20. Polyvinylchloride

21. Poly(bisphenol A carbonate)

22. Poly(vinylchloride-\textit{co}-vinylacetate-\textit{co}-hydroxypropylacrlate

23. Cellulose acetate butyrate (R= CH\textsubscript{3}(CH\textsubscript{2})\textsubscript{2}CO- or CH\textsubscript{3}CO-)

24. Ethylcellulose

25. Sucrose benzoate (benzoyl groups not shown)

26. Polycaprolactone
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27. Poly(2,6-dimethyl-1,4-phenylene oxide)

28, 29. Poly(oxyethylene)

30. Poly(1,3-propenylglutarate)

31. Poly(styrene-co-acrylonitrile)

32. Poly(styrene-co-maleic anhydride), cumene terminated.

33. Poly(styrene-co-allyl alcohol)

35. Poly(styrene-co-methylmethacrylate)

35. Poly(methylmethacrylate)

36. Poly(benzylmethacrylate)

37. Poly(cyclohexylmethacrylate)
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38. Poly(vinylacetate)

\[
\begin{array}{c}
\text{O} \\
\text{C} \\
\text{C} \\
\text{H}_2 \\
\text{C} \\
\text{O.C.CH}_3 \\
n 
\end{array}
\]

39. Poly(9-vinylcarbazole)

\[
\begin{array}{c}
\text{H}_2 \\
\text{C} \\
\text{CH} \\
n 
\end{array}
\]

40. Poly(vinylphenylketone)

\[
\begin{array}{c}
\text{H}_2 \\
\text{C} \\
\text{H} \\
\text{C} \\
\text{CO} \\
n 
\end{array}
\]

41. Poly(2-vinylpyridine)

\[
\begin{array}{c}
\text{H}_2 \\
\text{C} \\
\text{C} \\
n 
\end{array}
\]

42. Poly(vinylpyrrolidine)

\[
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{C} \\
\text{H} \\
\text{CH}_2 \\
n 
\end{array}
\]

43. Poly(propylenecarbonate)

\[
\begin{array}{c}
\text{CH}_3 \\
\text{C} \\
\text{C} \\
\text{O} \\
\text{O} \\
n 
\end{array}
\]

Insoluble Polymers

A. Polyethylene

\[
\begin{array}{c}
\text{C} \\
\text{C} \\
\text{H}_2 \\
\text{H}_2 \\
n 
\end{array}
\]

B. Polypropylene

\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{C} \\
\text{H}_2 \\
\text{CH}_3 \\
n 
\end{array}
\]

C. Polyacrylonitrile

\[
\begin{array}{c}
\text{C} \\
\text{H}_2 \\
\text{H} \\
\text{C} \\
\text{CN} \\
n 
\end{array}
\]

D. Poly (1,4-butylene-terephthalate)

\[
\begin{array}{c}
\text{(CH}_2\text{)}_4 \\
\text{O} \\
\text{C} \\
\text{C} \\
\text{O} \\
n 
\end{array}
\]

E. Poly(1,3-cyclopentane vinylene) or poly(norbornene)

\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{C} \\
n 
\end{array}
\]

F. Poly(methylene oxide, acetate end-capped)

\[
\begin{array}{c}
\text{H}_3\text{C} \\
\text{C} \\
\text{O} \\
\text{C} \\
\text{O} \\
\text{C} \\
\text{CH}_3 \\
n 
\end{array}
\]
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G. Poly(phenylenesulphone)

H. Poly(1,4-phenylenesulphide)

I. Poly(4-methyl-1-pentene)

J. Poly(ethylene-co-vinylacetate)