Supplementary Material (ESI) for Organic & Biomolecular Chemistry

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

SUPPORTING INFORMATION

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Contents

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

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indicated all the spectra were measured in DMSO-d_6 solutions and referenced to the residual DMSO signal. All ^1H and ^{13}C signals are given in ppm (δ scale). For ^{1}HNMR 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), Merck Kieselgel $60F_{254}$ analytical plates in the following systems: (A) CH_2Cl_2 , (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 nitrated with a mixture of fuming nitric acid and fuming sulphuric acid to give 5-iodo-2-nitrobenzaldehyde **33**[2] 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.

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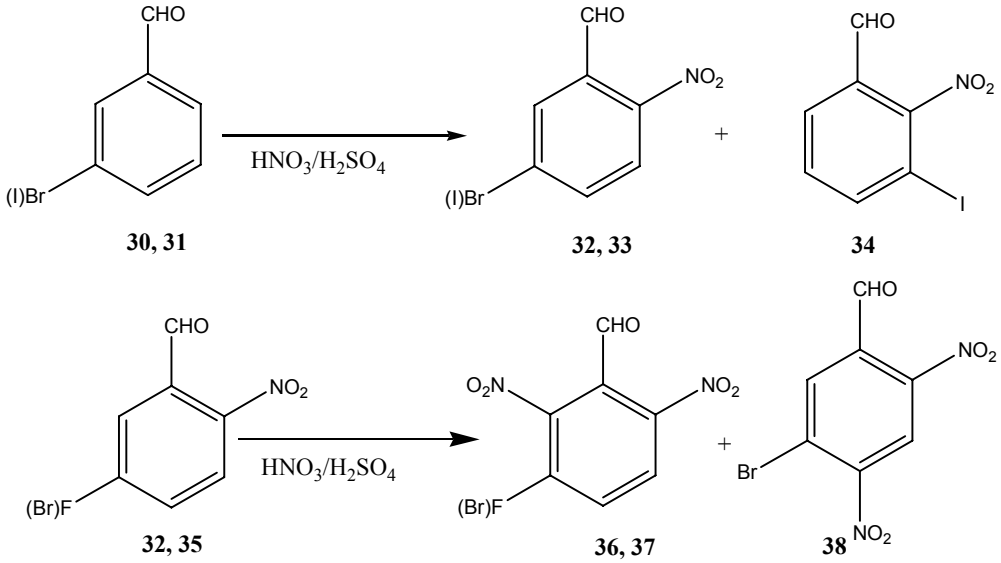
Scheme 1
Nitration of 2-nitro-5-halobenzaldehydes



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 ºC. 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 ºC 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 δ 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 δ 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_7H_5 I NO_3 $[M+H]^+$ 277.9314, found 277.9331 LR MS (ES mode) for C_7H_5 I NO_3 $[M+H]^+$ found 277.97. 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 δ 7.36 (t,1H, H-3) , 8.16 (d, J=7.9Hz, H-2) 8.35 (d, 1H, H, H-4), 9.81 (s, 1H, CHO). ^{13}C NMR δ 89.87 (C-5), 127.61 (C-1), 132.51 (C-3), 134.12 (C-2), 142.48(C-4), 145.19 (C-6), 188.94 (CHO); HRMS (ES mode, m/z) calcd. for C_7H_5 I NO_3 $[M+H]^+$ 277.9314, found 277.9319; LRMS (ES mode, m/z) for C_7H_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; ^{1}H-NMR δ 8.08 (m, 1H, H-4), 8.62 (m, 1H, H-3), 10.34 (s, 1H, CHO). ^{13}C 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 $C_7H_4FN_2O_5$ $[M+H]^+$ found 215.14; LRMS (ES mode) for $C_7H_2FN_2O_5$ $[M-H]^-$ 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% SO_3, 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; ^{1}H-NMR δ 8.41 (s, 2H, H-3, H-4), 10.22 (s, 1H, CHO). ^{13}C 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 $C_7H_3BrN_2O_5$ $[M+H]^+$ 275.09; LRMS (ES mode, m/z) for $C_7HBrN_2O_5$ $[M-H]^-$ found 273.03.
The minor 2,4-dinitro isomer **9** was obtained after the extraction of mother liquors with dichloromethane (0.075g, 5.4 %) ^{1}H-NMR δ 8.39 (s, 2H, H-3, H-4), 10.32 (s, 1H, CHO).

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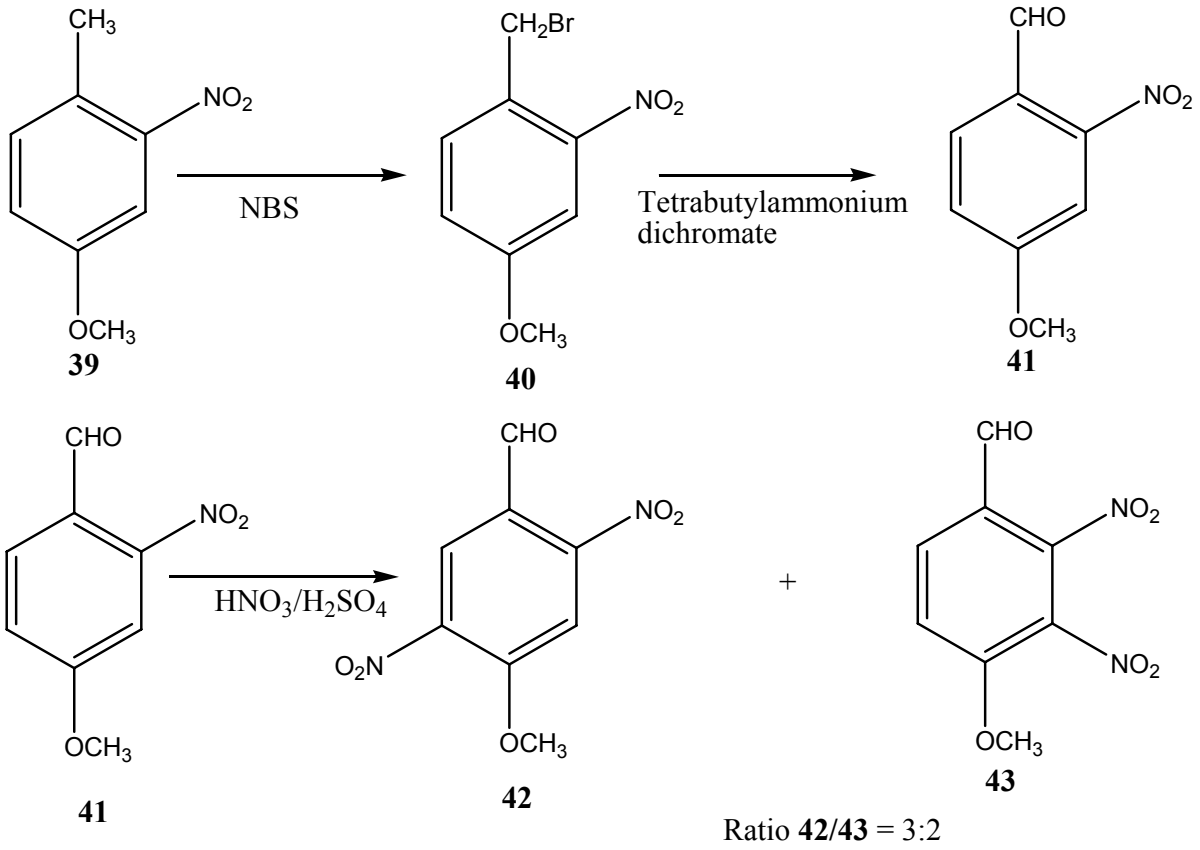
Scheme 2
Nitration of 2-nitro-4-methoxybenzaldehyde



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.[3] 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**[27] 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**.[4]

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[3], 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.

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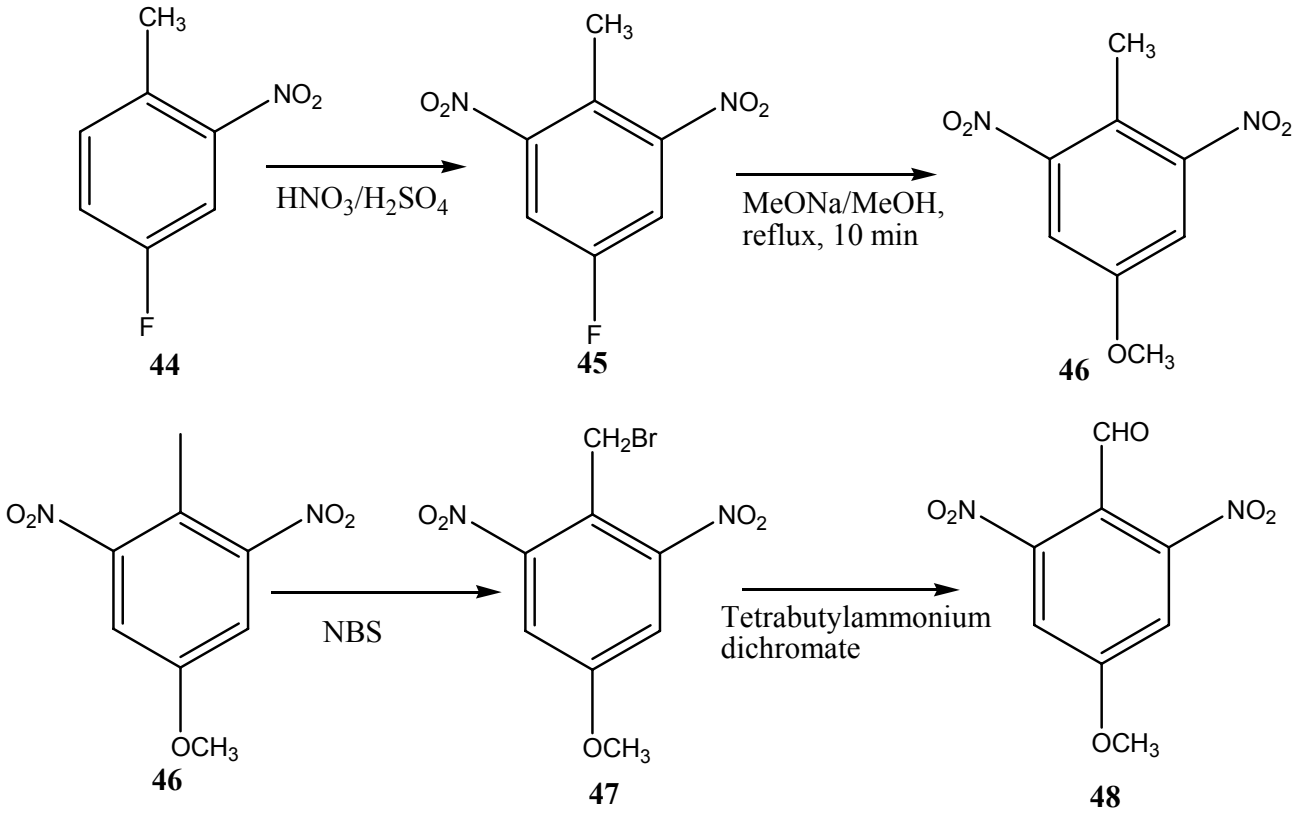
Scheme 3
Synthesis of 4-methoxy-2,6-dinitrobenzaldehyde



44 **45** **46** **46** **47** **48**

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**.[5]
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**.

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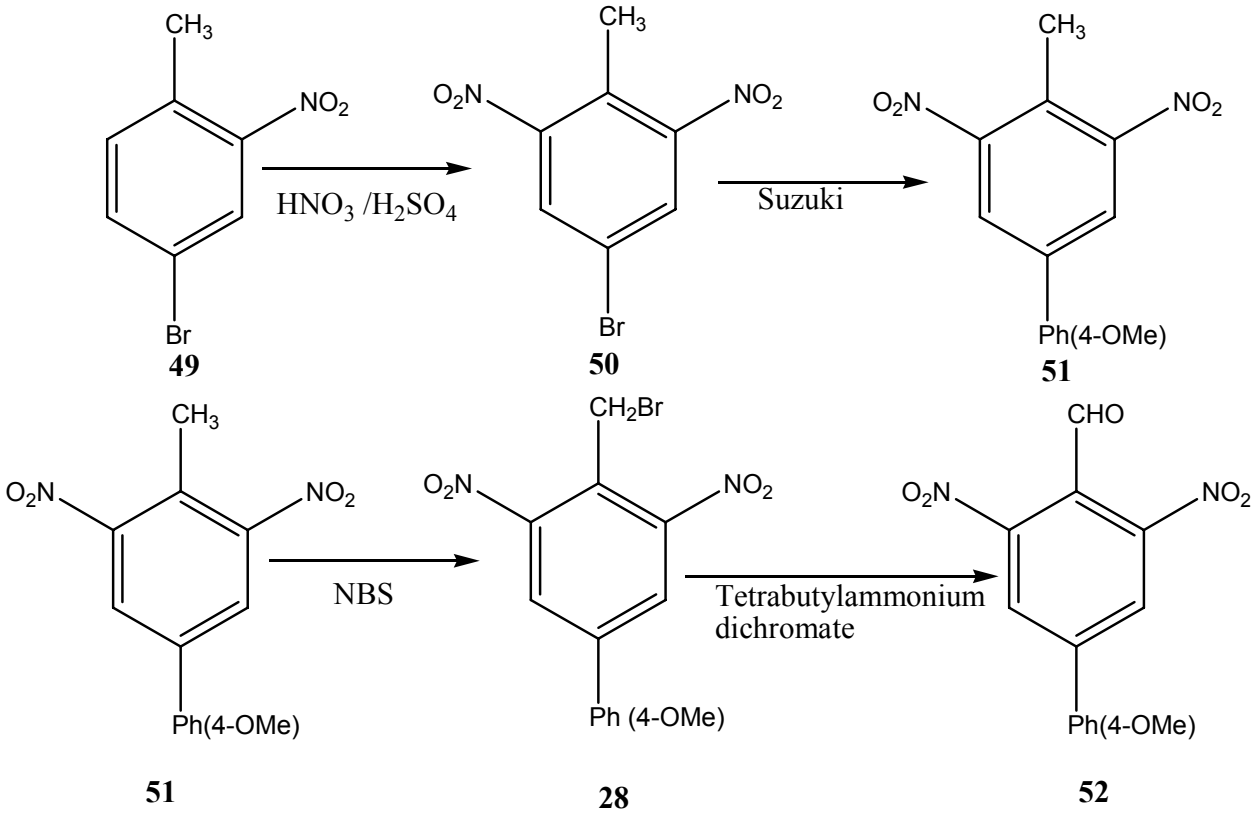
Scheme 4
Synthesis of 4-(4-methoxyphenyl)-2,6-dinitrobenzaldehyde



49 **50** **51**

51 **28** **52**

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. [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 (0.13g , 29%); mp 71-80 °C; Rf (B) 0.15; ^{1}H-NMR δ 4.12 (OCH_3), 8.09 (s, 1H, H-6), 8.57 (s, 1H, H-6), 10.03 (s, 1H, CHO). ^{13}C NMR δ 58.50 (OCH_3), 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 $C_8H_6N_2O_6$ $[M+H]^+$ 227.0304, found 227.0296; LR MS (ES mode, m/z) for $C_8H_6N_2O_6$ $[M+H]^+$ found 227.14.

Further elution with hexane-ethyl acetate (7:3) gave compound **43** as a yellow solid (0.09g, 20%); mp 123-124 °C; Rf (B) 0.05; ^{1}H-NMR δ 4.12 (OCH_3), 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). ^{13}C NMR δ 58.56 (OCH_3), 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 $C_8H_7N_2O_6$ $[M+H]^+$ 227.0304, found 227.0301; LRMS (ES mode, m/z) for $C_8H_6N_2O_6Na$ $[M+Na]^+$ 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-mehoxyphenylboronic 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** (0.093g, 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 (5mL) 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 silicagel (1g) in dichloromethane (20 mL). Each residue was treated with hexane (20mL) 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**) (0.091g, 70%); light yellow gum; mp indef; ^{1}H-NMR δ 4.81 (s, 2 H, CH_2Br) , 4.01 (s, 3H, OCH_3) 7.99 (s, 2H, H-3, H-5) , LRMS (ES mode, m/z) for $C_8H_7BrN_2O_5$ $[M-H]^-$ found 289.91.

5-(4-Methoxyphenyl)-2-(bromomethyl)- 1,3-dinitrobenzene (**28**) (0.075, 46.5%); light yellow solid; mp 85-86 ºC; ^{1}H-NMR δ 3.84 (s, 3H, OCH_3) 4.85 (s, 2 H, CH_2Br), (7.12, d, 2H, , H-3', H-5'), 7.89 (d, 2H, H-2', H-6') 8.58 (s, 2H, H-3, H-5); ^{13}C-NMR δ 13.76 (CH_2Br), 55.34 (OCH_3), 114.69(C-3', C-5'), 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 $C_{14}H_{11}N_2O_5$ $[M- Br]^+$ found 288.10; LRMS (ES mode, m/z) for $C_{14}H_{11}BrN_2O_5Na$ $[M+ Na]^+$ found 391.24.

4-Methoxy-2,6-dinitrobenzaldehyde (**48**)
2-(Bromomethyl)-5-methoxy-1,3-dinitrobenzene **47** (0.091g, 0.3 mmol) and bis(tetrabutyl-ammonium)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 silicagel (5g) eluting with methylene chloride to give product **48** as a light yellow solid (18 mg, 25%); mp 79-90 °C; ^{1}H-NMR δ 4.03 (s, 3H, OCH_3),

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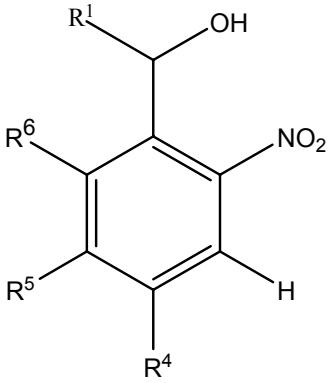
8.05 (s, 2H, H-3, H-5), 10.29 (s, 1H, CHO); ^{13}C-NMR δ 57.47 (OCH_3), 114.69 (C-3, C-5), 119.88 (C-1), 149.29 (C-2, C-6) 161.45 (C-4), 187.81 (CHO).

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 (0.19g, 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 δ 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 δ 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 $C_{14}H_{11}N_2O_6$ $[M+H]^+$ 303.0617, found 303.0613; LRMS (ES mode, m/z) for $C_{14}H_{11}N_2O_6$ $[M+H]^+$ found 303.0814.

Scheme 5
α–Phenyl-2-nitrobenzyl alcohols



53 R^1= C_6H_5 R^4= H R^5= Cl R^6= H
54 R^1= C_6H_5 R^4= H R^5= Cl R^6= NO_2
55 R^1= C_6H_5 R^4= H R^5= F R^6= H
56 R^1= C_6H_5 R^4= H R^5= F R^6= NO_2
57 R^1= C_6H_5 R^4= H R^5= Br R^6= H
58 R^1= C_6H_5 R^4= H R^5= Br R^6= NO_2
59 R^1= C_6H_5 R^4= H R^5= I R^6= H
60 R^1= C_6H_5 R^4= OCH_3 R^5= H R^6= H

61 R^1= C_6H_5 R^4= OCH_3 R^5= H R^6= NO_2
62 R^1= C_6H_5 R^4= p-$CH_3OC_6H_5$ R^5= H R^6= NO_2
63 R^1= C_6H_5 R^4= H R^5=$N(C_2H_5)_2$ R^6= NO_2
64 R^1= C_6H_5 R^4= H R^5=Pyrrolidin-1-yl R^6= NO_2
65 R^1= C_6H_5 R^4= H R^5=Piperidin-1-yl R^6=NO_2
66 R^1= C_6H_5 R^4= H R^5=Morpholin-4-yl R^6= NO_2
67 R^1= C_6H_5 R^4= H R^3=Pyrrolidin-1-yl R^6= H
68 R^1= C_6H_5 R^4= H R^5=NH_2 R^6=H
69 R^1= C_6H_5 R^4= H R^5=NH_2 R^6= NO_2
70 R^1= C_6H_5 R^4= H R^5= C_6H_5NH R^6= NO_2
71 R^1= C_6H_5 R^4= H R^5 = $CH_3OC_6H_5NH$ R^6= NO_2
72 R^1= C_6H_5 R^4= H R^5= p-$N(CH_3)_2C_6H_5$ R^6= NO_2
73 R^1= C_6H_5 R^4= H R^5= C_6H_5 R^6= NO_2
74 R^1= C_6H_5 R^4= H R^5= p- $CH_3OC_6H_5$ R^6= NO_2
75 R^1= C_6H_5 R^4= H R^5= o, p- $(CH_3O)_2C_6H_4$ R^6= NO_2
76 R^1= C_6H_5 R^4= H R^5=2-ethoxynaphtyl R^6= NO_2
77 R^1= C_6H_5 R^4= H R^5=Phenylazo R^6= H

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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**[28], **61** and **62** were prepared in high yields by condensation of aldehydes **32**, **33**, **35**, **36**, **37**, **41 48, 52** respectively, with phenylmagnesium bromide in anhydrous tetrahydrofuran at -78°C.
Compounds **53** and **54** were prepared us before 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-nitrobenzaldehyde* (**41**), *4-methoxy-2,6-dinitrobenzaldehyde* (**48**) and *4-(4-methoxyphenyl)-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=4.82Hz, 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). ^{13}C-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), 128.26 (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 $C_{13}H_9FNO_2$[M-OH]$^+$ 230.0609, found 230.0617; LRMS (ES mode, m/z)for $C_{13}H_9FNO_3K$ [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; ^{1}H-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); ^{13}C-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 $C_{13}H_8FN_2O_4$ [M-OH]$^+$ 275.0468, found 275.0464; LRMS (ES mode, m/z)for $C_{13}H_9FN_2O_5Na$ [M+Na]$^+$ found 315.17, for $C_{13}H_8FN_2O_5$ [M-H]$^-$ found 291.0.

(5-bromo-2-nitro-phenyl)-phenyl-methanol (**57**) (1.69 g, 55 %); yellowish oil; Rf (A) 0.23; ^{1}H-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). ^{13}C-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 $C_{13}H_9BrNO_2$ [M-OH]$^+$ 289.9849, found 289.9853, LRMS (ES mode, m/z) for $C_{13}H_9BrNO_2$ [M-OH]$^+$ 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 δ 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 δ 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 $C_{13}H_8BrN_2O_4$ $[M\text{-}OH]^+$ 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 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'), 7.69 (d, J=8.48 Hz, 1H, H-4), 7.93 (dd, 1.84 Hz, J=8.48 Hz, 1H, H-4), 8.17 (d, J=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 δ 3.83 (s, 3H, OCH_3), 6.11 (bs, 2H, CH, OH), 6.60 (dd, J=1.02Hz, J=4.37 Hz, 1H, H-5), 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 δ 3.92 (s, 3H, OCH_3), 6.02 (d, J=4.37 Hz, 1H, CH), 6.75 (d, J=8.09Hz), 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 δ 3.92 (s, 3H, OCH_3), 6.12 (d, J=4.32 Hz, 1H, CH), 6.75 (d, J=4.32Hz, 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 δ 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 $C_{20}H_{12}N_2O_6Na$ $[M+Na]^+$ 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.[9] 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 5μ C18-300A, were used for analytical and preparative scales. The mobile phases were (A) 0.05M aq. $[Et_3NH]^+$ $[HCO_3]^-$ (B) MeCN. Gradient elution; 5%(B) – 90% (B) over 30 minutes.

(*5-Diethylamino-2,6-dinitro-phenyl)-phenyl-methanol* (**63**) (2 x 90min, 90 ^oC); 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 ^oC) (0.17 g, 57%); yellow solid, mp indef; Rf (A) 0.25, Rf (B)- multiple development resolves the product and the starting material; ^{1}H-NMR δ 1.90 (m, 4H, $(CH_2)_2$), 3.25 (m, 4H, $(CH_2)_2$ 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 λ_{max} 393 nm, ε 17000; HRMS (FAB mode, m/z) calcd. for $C_{17}H_{17}N_3O_5Na$ $[M+Na]^+$ 366.1066, found 366.1067.

(*2,6-Dinitro-3-piperidin-1-yl-phenyl)-phenyl-methanol* (**65**) (2 x 15 min, 50 ^oC) (0.19 g, 52%); yellow solid, mp 85-95 ºC; %); Rf (C) 0.25; ^{1}H-NMR δ 1.53 (m, 6H, $(CH_2)_3$), 2.99 (m, 4H, $(CH_2)_2$), 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 λ_{max} 393nm, ε 13500; LRMS (ES mode, m/z) for $C_{18}H_{20}N_3O_5[M+H]^+$ found 358.3.

(*2,6-Dinitro-3-morpholin-4-yl-phenyl)-phenyl-methanol* (**66**) (2 x 20 min, 60 ^oC)(0.24 g, 67%);; yellow solid, mp 58-60 ˚C; Rf (A) 0.07, (C) 0.17; ^{1}H-NMR δ 3.01 (t, 4H, J=5.48Hz $(CH_2)_2$), 3.63 (t, 4H, J=5.48Hz, $(CH_2)_2$, 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 λ_{max} 361.5 nm, ε 13120; HRMS (FAB mode, m/z) calcd. for $C_{17}H_{17}N_3O_6Na$ $[M+Na]^+$ 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_2O_5, 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 ˚C; Rf (A) 0.24; ^{1}H-NMR δ 2.02 (m, 4H, $(CH_2)_2$, 3.40 (m, 4H, $(CH_2)_2$, 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 λ_{max} 393 nm, ε 17000; LRMS (ES mode, m/z) for $C_{17}H_{19}N_2O_3$ $[M+H]^+$ 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 NH_3/MeOH (1 mL) and concentrated aqueous NH_4OH (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 ^{o}C; Rf (A) 0.1; ^{1}H-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, NH_2), 7.11 (s, 1H, H-6), 7.23 (m, 5H, H-2'- H-6'), 8.04 (d, J=9.06Hz, 1H, H-3). ^{13}C-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) $C_{13}H_{13}N_2O_3$ $[M+H]^+$ 244.0; HRMS (ES mode, m/z) calc. for $C_{13}H_{11}N_2O_2$ 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 ^{o}C; Rf (A) 0.1; ^{1}H-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, NH_2), 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). ^{13}C-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 $C_{13}H_{10}N_3O_4$ $[M-OH]^+$ 272.0671, found 272.0674; LRMS (ES mode, m/z) for $C_{13}H_{10}N_3O_5[M-H]^-$ 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 ^{o}C; Rf (B) 0.20; ^{1}H-NMR δ 3.73 (s, 3H, OCH_3), 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 $C_7H_3BrClN_2O_4$ $[M-H]^-$ found 292.9256; for $C_7H_4BrClN_2O_4$ $[M]^+$ 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[6] with various phenylboronic acids including 4-N,N-dimethylaminophenylboronic acid, phenylboronic acid, 4-methoxyphenylboronic acid, 3,4-dimethoxyphenylboronic acid and 2-ethoxynaphtylboronic 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**).

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A commercially available 4-N,N-Dimethylaminophenylboronic acid, phenylboronic acid, 4-methoxyphenylboronic acid, 3,4-dimethoxyphenylboronic acid, 2-ethoxynaphtylboronic 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 tetrakis 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 (Na_2SO_4) 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; Rf (B) = 0.19; ^{1}H-NMR δ 2.44 (m, 3H, CH_3), 3.83 (m, 3H, OCH_3), 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); ^{13}C NMR 13.76 (CH_3), 55.31(OCH_3), 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 $C_{14}H_{13}N_2O_5$ $[M+H]^+$ found 288.09; LRMS (ES mode, m/z) for $C_{14}H_{12}N_2O_5$ 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; Rf (A) = 0.51; ^{1}H-NMR δ 2.96 (s, 6H, $N(CH_3)_2$) 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). ^{13}C-NMR 39.72 [N $(CH_3)_2$] 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-3), 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 $C_{21}H_{20}N_3O_5$ $[M+H]^+$ 394.1403, found 394.1407.

(2,6-Dinitro-3-(phenyl)phenyl)(phenyl)methanol (**73**) (0.17 g, 50%); off white solid; mp indef; Rf (A) = 0.51 ^{1}H-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).
^{13}C-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), 141.41(C-1'), 148.66 (C-2, C-6). HRMS (ES mode, m/z) calc. for $C_{19}H_{13}N_2O_4$, $[M-OH]^+$ 333.0873, found 333.0874; LRMS (ES mode, m/z) for $C_{19}H_{14}N_2O_5Na$ $[M+Na]^+$, found 373.0555.

(2,6-Dinitro-3-(4-methoxyphenyl)phenyl)(phenyl)methanol (**74**) (0.23 g, 61%); light yellow solid; mp 85-87ºC; Rf (A) = 0.48; ^{1}H-NMR δ 3.79 (s, 3H, OCH_3), 6.08 (d, J= 5.04 Hz, 1H, CH), 6.80 (d, J= 5.04 Hz, 1H, OH), 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); ^{13}C NMR 55.28 (OCH_3) 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), 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 $C_{21}H_{18}N_2O_7Na$ $[M+Na]^+$ 403.0906, found 403.0904 LRMS (ES mode, m/z) for $C_{20}H_{15}N_2O_6$ $[M-H]^-$ found 379.1143; for $C_{20}H_{15}N_2O_5$ $[M-OH]^+$ found 363.0528.

(2,6-Dinitro-3-(3,4-dimethoxyphenyl)phenyl)(phenyl)methanol (**75**) (0.15 g, 37%); light yellow solid; mp 69-72ºC; Rf (A) = 0.28; ^{1}H-NMR δ 3.77 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 6.08 (d, J= 5.09 Hz, 1H, CH), 6.80 (d, J= 5.09 Hz, 1H, OH), 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); ^{13}C NMR 55.57 (OCH_3), 55.64 (OCH_3) 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 $C_{21}H_{18}N_2O_7Na$ $[M+Na]^+$ 433.1012, found 433.1029; LRMS (ES mode, m/z) for $C_{21}H_{18}N_2O_7$ Na $[M+Na]^+$ found 433.0781for $C_{21}H_{17}N_2O_6$ $[M-OH]^+$ found 393.0484.

(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; ^{1}H-NMR δ 1.14 (m, 3H, $OCH_2\underline{CH_3}$), 4.18 (m, 2H, $O\underline{CH_2}CH_3$), 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). ^{13}C-NMR δ 13.28 (CH_3), 57.63 (CH_2) , 67.07 (<u>CH</u>OH), 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), 143.25.13 (C-2), 156.42 (C-2"). 127.53 (C-10"), 128.29 (C-8"), 128.88 (C-4'), 135.34135.43(C-5), 135.98 (C-1'), HRMS (ES mode, m/z) calcd. for $C_{25}H_{19}N_2O_5$[M-OH]$^+$ 427.1294, found 427.1310; LRMS (ES mode, m/z) for $C_{25}H_{20}N_2O_6Na$ [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 acid[10] gave predominantly 2-nitro-5-phenylazo-phenyl)-phenyl-methanol **77** in 37% yield together with only a small amount of compound **90**.

(2-Nitro-5-phenylazo-phenyl)-phenyl-methanol (**77**) and *acetic acid (2-nitro-5-phenylazo-phenyl)-phenyl-methyl ester* (**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 °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 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 92-96 ^{o}C; ^{1}H-NMR δ 2.12 (s, 3H, CH_3CO), 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); ^{13}CNMR 20.63 (CH_3), 77.14 (CH), 121.89(C-4), 123.16 (C-2"-C-6"), 123.23 (C-3), 126.65 C-6, 127.48 (C-2'-C-6'), 128.55 (C-4'), 128.73 (C-3"-C-5"), 129.62 (C-3'-C-5'),132.81 (C-4"), 135.96 (C-1), 137.72 (C-1'), 148.04 (C-2), 151.76 (C-1"), 154.54 (C-5), 160.51 (CO); HRMS (ES mode, m/z) calcd. for $C_{19}H_{13}N_3O_2$ $[M-CH_3COO]^+$ 316.1086, found 316.1113; LR MS (ES mode, m/z) for $C_{21}H_{17}N_3O_4Na$ $[M+Na]^+$, found 398.2. Further elution with dichloromethane afforded product **77** as an orange solid; yield 0.031g (31%); mp indef; Rf (A) = 0.35; ^{1}H-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 $C_{21}H_{18}N_3O_4$ $[M+H]^+$ found 333. 0.

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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 405nm. (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 410-420nm 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). ^{13}C 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 ºC; Rf (A) = 0.90; ^{1}H-NMR δ 3.89 (s, 3H, OCH_3), 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)); ^{13}C-NMR 56.14 (OCH_3), 76.88 (CH), 81.06 (CCl_3), 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 $C_{14}H_{12}NO_3$ $[M\text{-}Cl_3CCOO]^+$ 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 ºC; Rf (A) = 0.89; ^{1}H-NMR δ 3.98 (s, 3H, OCH_3), 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); ^{13}C-NMR 57.16 (OCH_3), 74.11 (CH), 81.06 (CCl_3), 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 $\lambda_{shoulder}$ 314 nm ε 3176; HRMS (ES mode, m/z) calcd. for $C_{14}H_{11}N_2O_5$$[M\text{-}Cl_3CCOO]^+$ 287.0668, found 287.0699; LRMS (ES mode, m/z) for $[C_{16}H_{11}Cl_3N_2O_7 +H]^+$ found 449.63.

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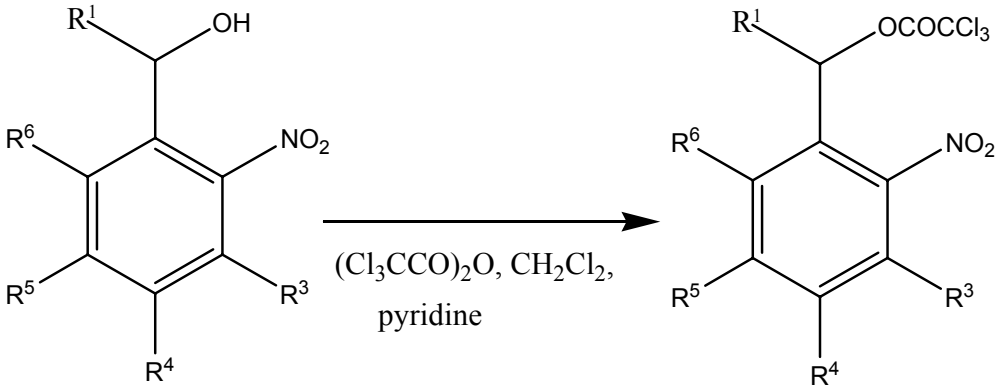
Scheme 6
Synthesis of α-phenyl-2-nitrobenzyltrichloroacetates



3 R^1= C_6H_5 R^3= H R^4= OCH_3 R^5=H R^6= H
4 R^1= C_6H_5 R^3= H R^4= OCH_3 R^5=H R^6= NO_2
5 R^1= C_6H_5 R^3= H R^4= H R^5= F R^6= NO_2
6 R^1= C_6H_5 R^3= H R^4= H R^5= Cl R^6= H
7 R^1= C_6H_5 R^3= H R^4= H R^5= Cl R^6= NO_2
8 R^1= C_6H_5 R^3= H R^4= H R^5=Br R^6= H
9 R^1= C_6H_5 R^3= H R^4= H R^5=Br R^6= NO_2
10 R^1= C_6H_5 R^3= H R^4= H R^5=I R^6= H
12 R^1= C_6H_5 R^3 = H R^4= H R^5 = $N(C_2H_5)_2$ R^6= NO_2
13 R^1= C_6H_5 R^3 = H R^4= H R^5 = Morpholin-4-yl R^6= NO_2
14 R^1= C_6H_5 R^3 = H R^4= H R^5 = Pyrrolidin-1-yl R^6=H
15 R^1= C_6H_5 R^3 = H R^4= H R^5 = Pyrrolidin-1-yl R^6= NO_2
16 R^1= C_6H_5 R^3 = H R^4= H R^5 = Piperidin-1-yl R^6= NO_2
17 R^1= C_6H_5 R^3= H R^4= H R^5=4-methoxyphenylamino R^6= NO_2
18 R^1= C_6H_5 R^3= H R^4= H R^5=phenylamino R^6= NO_2
19 R^1= C_6H_5 R^3= H R^4= H R^5=phenylazo R^6= H
20 R^1= C_6H_5 R^3= H R^4= H R^5= 4-(N,N-dimethylamino)phenyl R^6= NO_2
21 R^1= C_6H_5 R^3= H R^4= H R^5= phenyl R^6= NO_2
22 R^1= C_6H_5 R^3= H R^4= H R^5= 4-methoxyphenyl R^6= NO_2
23 R^1= C_6H_5 R^3= H R^4= H R^5=3,4-dimethoxyphenyl R^6= NO_2
24 R^1= C_6H_5 R^3= H R^4= 4-methoxyphenyl R^5=H R^6= NO_2
25 R^1= C_6H_5 R^3= H R^4= H R^5=2-ethoxynaphtalen-1-yl R^6= NO_2

(3-Fluoro-2,6-dinitrophenyl)(phenyl)methyl-2,2,2-trichloroacetate(**5**) (0.29 g, 67%); red-brown solid; mp 135-138 ºC; Rf (A) 0.76; ^{1}H-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-3), 8.58 (m, 1H, H-4); ^{13}C-NMR 74.97 (CH), 88.67 (CCl_3), 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); λ_{max} 255 nm ε 8900 λ_{max} 232 nm ε 15600; HRMS (ES mode, m/z) calcd. for $C_{15}H_7FN_2O_4$ $[M\text{-}Cl_3COO]^+$ 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; ^{1}H-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), 7.85 (dd, J=2.23 Hz, J= 8.78Hz, 1H, H-4), 8.12 (d, J=8.78 Hz, 1H, H-3); ^{13}C-NMR 76.69 (CH), 88.99 (CCl_3), 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-6), 134.51 (C-1'), 135.48 (C-1), 139.04 (C-5), 146.21 (C-2), 159.78 (CO); UV λ_{max} 270 nm ε 6200; HRMS (ES mode, m/z) calcd. for $C_{13}H_9ClNO_2$ $[M\text{-}Cl_3COO]^+$ 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 ºC dec; Rf (A) 0.85; ^{1}H-NMR δ 7.32 (m, 2H, H-4', CH), 7.44 (m, 4H, H-2', H-6', H-3', H-5'), 8.24(d, 1H, J=8.94Hz, H-4), 8.41 (d, 1H, J=8.94 Hz, H-3); ^{13}C-NMR 75.14 (CH), 89.29 (CCl_3), 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 λ_{max} 256 nm ε 7500; LR MS HRMS (ES mode, m/z) for $C_{15}H_9Cl_4N_2O_6$ $[M+H]^+$ 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; ^{1}H-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), 7.96 (dd, J=2.06 Hz, J=8.74 Hz, 1H, H-4), 8.12 (d, J=8.74 Hz, 1H, H-3); ^{13}C-NMR 76.37 (CH), 89.00 (CCl_3), 127.10 (C-3), 127.55 (C-2', C-6'), 127.64 (C-5) 128.94 (C-3', C-5'), 129.35 (C-4'), 130.99 (C-4) 132.99 (C-6), 134.41 (C-1'), 134.60 (C-1) , 135.40 (C-5), 146.65 (C-2), 159.76 (CO); λ_{max} 276 nm ε 6600; HRMS (ES mode, m/z) calcd. for $C_{13}H_9NO_2$ $[M\text{-}Cl_3COO]^+$ 289.9817, found 289.9838, LRMS (ES mode, m/z) for $C_{13}H_9NO_2$ $[M\text{-}Cl_3COO]^+$ found 290.00, for $C_{15}H_{10}BrCl_3NO_4$ $[M+H]^+$ 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 ºC; Rf (A) 0.86; ^{1}H-NMR δ 7.37 (m, 2H, H-2', H-6'), 7.47(m, 3H, H-3'-H-5'), 7.54 (s, 1H, CH), 8.35 (d, J=8.72 Hz, 1H, H-4), 8.42 (d, J=8.72 Hz, 1H, H-3); ^{13}C-NMR δ 74.74 (CH), 88.61 (CCl_3), 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'), 136.59 (C-4), 148.69 (C-2), 149.67 (C-6), 160.53 (CO); UV λ_{max} 255 nm ε 8900; HRMS (ES mode, m/z) calcd. for $C_{13}H_8BrN_2O_4$ $[M\text{-}Cl_3COO]^+$ 334.9667, found 334.9682.

(5-Iodo-2-nitrophenyl)(phenyl)methyl-2,2,2-trichloroacetate (**10**) (0.28 g, 57%); colourless oil; mp indef.; Rf (A) 0.90; ^{1}H-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 (dd, J=1.79 Hz, J= 8.64 Hz, 1H, H-4,); ^{13}C-NMR 76.60 (CH), 88.43 (CCl_3), 103.01 (C-5), 126.98 (C-3), 127.60 (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 λ max 296 nm ε 6500; HRMS (ES mode, m/z) calcd. for $C_{13}H_9INO_2$ $[M\text{-}Cl_3CCOO]^+$ 337.9678, found 337.9716; LRMS (ES mode, m/z) for $C_{15}H_8Cl_3INO_2$ $[M\text{-}NO_2\text{-}H]^-$ found 452.1105; for $C_{15}H_{10}Cl_3INO_2$ $[M\text{-}NO_2+H]^+$ found 454.2730.

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Trichloro-acetic acid (5-diethylamino-2,6-dinitro-phenyl)-phenyl-methyl ester (**12**) (0.39 g, 80%); colourless glass, mp indef; Rf (A) 078;UV λ_{max} 380 nm ε 8000; R_t = 15.35min (triethylammonium bicarbonate buffer); HRMS (FAB mode, m/z) calcd. for $C_{19}H_{19}Cl_3N_3O_6$ $[M+H]^+$ 490.0335; found 490.0337; LRMS (ES mode, m/z) for $C_{19}H_{19}Cl_3N_3O_6$ $[M+H]^+$ 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 δ 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 δ 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 λ_{max} 359 nm ε 6450;
HRMS (FAB mode, m/z) calcd. for $C_{19}H_{18}Cl_3N_3O_7$ $[M+H]^+$ 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; ^{1}HNMR 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 δ 24.87 $[(CH_2)_2]$, 47.46 $[(CH_2)_2N]$, 79.16 (CCl_3), 105.75 (CH), 116.87 (C-4), 125.98 (C-3', C-5'), 126.61(C-4'), 128.17 (C-2', C-6'), 128.81 (C-1), 133.21 (C-1'), 136.63 (C-2, C-6) 143.89 (C-5), 160.85 (CO); UV λ_{max} 403 nm ε 22700; HRMS (ES mode, m/z) calcd. for $C_{17}H_{17}N_2O_2[M\text{-}Cl_3CCOO]^+$ 281.1290, found 281.1300; LRMS (ES mode, m/z) for $C_{19}H_{16}Cl_3N_2O_4$ $[M-H]^-$ 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 δ 1.92 [bs, 4H, $(CH_2)_2$], δ 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', CH), 8.16 (d, J=9.55 Hz, 1H, H-3); ^{13}C-NMR δ 24.54 $[(CH_2)_2]$, 49.04 $[(CH_2)_2]$, 75.73 (CH), 88.25 (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'), 136.63 (C-1), (C-6) 143.89 (C-5), 160.85 (CO); UV λ_{max} 380 nm ε 14600; HRMS (FAB mode, m/z) calcd. for $C_{19}H_{17}Cl_3N_3O_6$ $[M+H]^+$ 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 δ 1.54 [bs, 6H, $(CH_2)_3$], 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 δ 25.38 $[(CH_2)_2]$, 51.58 $[N(CH_2)_2]$, 75.34 (CHOH), 88.77 (CCl_3), 123.15 (C-4), 124. 54 (C-1), 126.27 (C-3', C-5'), 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 λ_{max} 380 nm ε 13120; HRMS (FAB mode, m/z) calcd. for $C_{20}H_{20}Cl_3N_3O_6$ $[M+H]^+$ 502.0339, found 502.0355.

(*3-(4-Methoxyphenylamino)-2,6-dinitrophenyl)(phenyl)methyl-2,2,2*-trichloroacetate (**17**) (0.36 g, 67%); reddish solid; mp 54-56 ºC; Rf (A) 0.82; ^{1}H-NMR δ 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); λ_{max} 370 nm ε 8200; HRMS (ES mode, m/z) calcd. for $C_{20}H_{16}N_3O_5[M\text{-}Cl_3CCOO]^+$ 378.1090, found 378.1109

(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), 88.86 (CCl_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"), 138.57 (C-1'), 143.90 (C-2 C-6), 157.39 (C-5), 160.85 (CO); λ_{max} 363 nm ε 6600; HRMS (ES mode, m/z) calcd. for $C_{19}H_{14}N_3O_4$[M-Cl_3CCOO]$^+$, 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); 8.39 (d, J=8.67 Hz, 1H, H-3); ^{13}CNMR 77.14 (CH), 89.12 (CCl_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_{max} 334.5 nm ε 22000, 454 nm ε 1000; HRMS (ES mode, m/z) calcd. for $C_{21}H_{15}Cl_3N_3O_4$[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), 8.38 (d, 8.63Hz, 1H, H-3); ^{13}C-NMR 39.67 [N (CH_3)$_2$] 75.18 (CH), 88.86 (CCl_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_{max} 410 nm ε 7100; HRMS (ES mode, m/z) calcd. for $C_{23}H_{19}Cl_3N_3O_6$ [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 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-4), 8.42 (d, 8.49 Hz, 1H, H-3); ^{13}C-NMR 75.08 (CH), 88.70 (CCl_3), 126.49 (C-2", C-6"), 127.40 (C-4), 127.93 (C-2', C-6'), 128.40 (C-4'), 128.42 (C-3', C-5'), 128.78 (C-4") 128.98 (C-3", 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); $\lambda_{shoulder}$ 280 nm ε 7600; HRMS (ES mode, m/z) calcd. for $C_{19}H_{13}N_2O_4$ [M-Cl_3CCOO]$^+$ 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 indef.; Rf (A) 0.85; ^{1}H-NMR δ 3.91 (s, 3H, OCH_3), 7.16 (m, 2H, H-3", H-5"), 7.40-7.65 (m, 6H, CH, H-2'- H-6'), 7.96 (pseudo t, J=8.78 Hz, 2H, H-2", H-6"), 8.65 (dd, J=2.56 Hz, J=4.90 Hz, 2H, H-3, H-5);^{13}C-NMR δ 53.03 (OCH_3), 72.36 (<u>CH</u>O$COCCl_3$), 89.33 (CCl_3), 112.82 (C-3", C-5"), 123.97(C-4'), 124.29 (C-2', C-6'), 125.06 (C-1"), 125.97(C-2", C-6") 126.52(,C-3, C-5), 127.97(C-3', C-5'), 133.16 (C-1), 136.09 (C-4), 140.88(C-1'), 148.40 (C-2, C-6), 157.99(C-4"), 158.43 (CO); UV λ_{max} 334 nm ε 4100; HRMS (ES mode, m/z) calcd. for $C_{20}H_{15}N_2O_5$ [M-Cl_3CCOO]$^+$ 363.0981, found 363.1030.

(2,6-Dinitro-3-(3,4-dimethoxyphenyl)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 4.20 (s, 3H, OCH_3), 4.23 (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);^{13}C NMR 55.62 (OCH_3) 55.68 (OCH_3) 75.13 (CH), 88.71 (CCl_3), 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"), 133.82 (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_{max} 343 nm ε 4750; HRMS (ES mode, m/z) calcd. for $C_{21}H_{17}N_2O_6$ $[M\text{-}Cl_3CCOO]^+$ 393.1087, found 393.1086; LRMS (ES mode, m/z) for $C_{23}H_{17}Cl_3N_2O_8Na$ $[M+Na]^+$ 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; ^{1}H-NMR δ 3.81 (s, 3H, OCH_3), 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); ^{13}C NMR 55.31 (OCH_3) 75.11 (CH), 88.72 (CCl_3), 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-5), 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_{max} 324 nm ε 4430; HRMS (ES mode, m/z) calcd. for $C_{20}H_{15}N_2O_5$ $[M\text{-}Cl_3CCOO]^+$ 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; ^{1}H-NMR δ 1.21 (m, 3H, $OCH_2\underline{CH_3}$), 4.20 (m, 2H, $O\underline{CH_2}CH_3$), 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);^{13}C-NMR δ 14.43 (CH_3), 64.48 (CH_2) , 75.53 ($\underline{CH}OCOCCl_3$), 88.73 (CCl_3), 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_{max} 334 nm ε 4100; HRMS (ES mode, m/z) calcd. for $C_{25}H_{19}N_2O_5$ $[M\text{-}Cl_3CCOO]^+$ 427.1294, found 427.1295; LRMS (ES mode, m/z) for $C_{27}H_{20}Cl_3N_2O_7$ $[M+H]^+$ 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. [11]

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.[10]

Thus 5-amino-2-nitrobenzylalcohol **82** was prepared following the literature procedure,[12] starting from commercially available 3-aminobenzyl alcohol **78**. Acetylation of the latter gave 3-acetylaminobenzylacetate **79**. Subsequent nitration resulted in 5-acetylamino-2-nitrobenzylacetate **80**.[13] Deprotection of compound **80** was carried out with 8M methanolic ammonia during 48 hours at room temperature and resulted in compound **82**. Partially deacetylated product **81** 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 **68** and **69**, were prepared via nucleophilic aromatic substitution of the corresponding 5-fluoro derivatives as described in section **1.2.3**.

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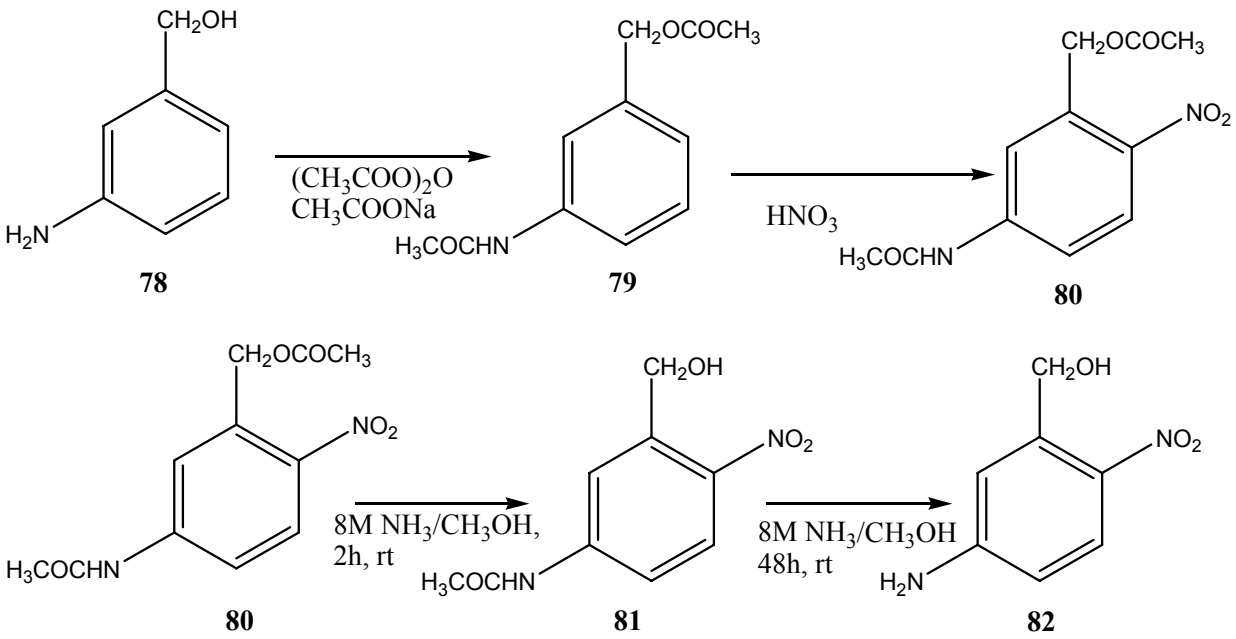
Scheme 7
Synthesis of 5-amino-2-nitrobenzylalcohol



Reaction of compound **82**, with nitrosobenzene in acetic acid gave corresponding 5-amino-2-nitrobenzyl acetate **83**.[14] 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); ^{1}H-NMR δ 2.01(s, 3H, CH_3COO), 2.13 (s, 3H, CH_3CONH), 5.03 (s, 2H, CH_2), 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).

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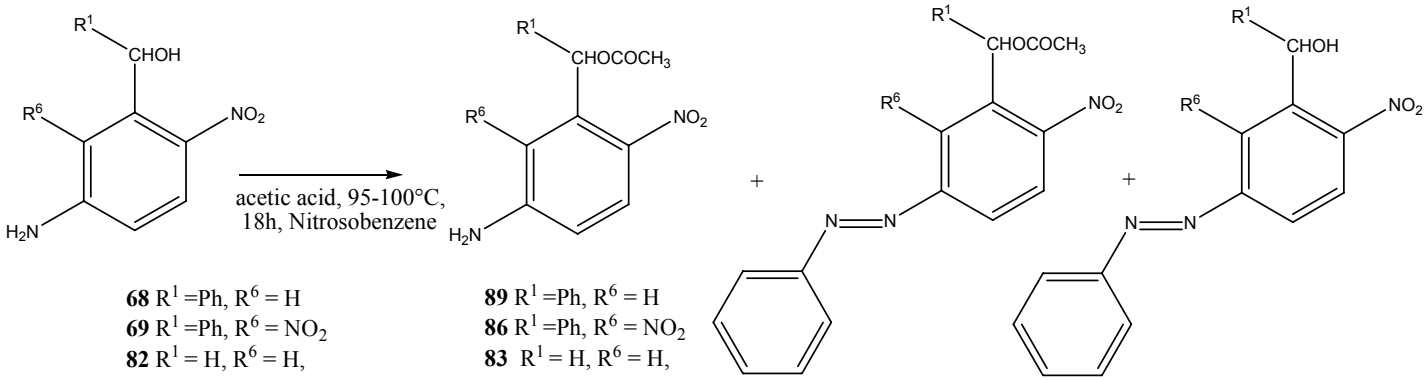
Scheme 8
Acetic acid 2-nitro-5-phenylazo-benzyl esters



68 R^1 =Ph, R^6 = H
69 R^1 =Ph, R^6 = NO_2
82 R^1 = H, R^6 = H,

89 R^1 =Ph, R^6 = H
86 R^1 =Ph, R^6 = NO_2
83 R^1 = H, R^6 = H,

90 R^1 = Ph, R^6 = H,
87 R^1 = Ph, R^6 =NO_2
84 R^1 = H, R^6=H

77 R^1 = Ph, R^6 = H,
88 R^1 = Ph, R^6 = NO_2
85 R^1 = H , R^6 = H

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 ^oC; Rf = 0.37 (A); ^{1}H-NMR δ 2.06 (s, 3H, CH_3COO), 2.10 (s, 3H, CH_3CONH), 5.15 (s, 2H, CH_2), 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 λ_{max} 355nm ε 5340; LRMS (ES mode, m/z) found for $C_{11}H_{13}N_2O_5[M+H]^+$ 252.7.

(5-Amino-2-nitro-phenyl)-methanol (**82**)
Compound **80** (1.37 g, 5.4 mmol) was treated with 8 M NH_3/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 (94:6) to give **82**[12] as a white solid (0.69 g, 76%); R_f (A) = 0.1; mp 108-110 ^oC; ^{1}H-NMR 4.44 (d, J=6.60 Hz, 2H, CH_2), 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, NH_2), 7.89 (d, J=8.84 Hz, 1H, H-3); ^{13}C-NMR 62.06 (CH_2OH), 113.45 (C-6), 115.30 (C-4), 125.20 (C-3), 128.96 (C-1), 146.33 (C-2), 151.12 (C-5); LRMS (ES mode, m/z) for $C_7H_9N_2O_3$ $[M+H]^+$ found 169.0.

N-(3-Hydroxymethyl-4-nitro-phenyl)-acetamide (**81**)[12]
Compound **80** (1.37g, 5.4 mmol) was treated with 8 M NH_3/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 (95.5:4.5) to give compound **81** as a white solid (0.94 g, 83%); mp indef.; Rf (A) = 0.21; ^{1}H-NMR 2.06 (s, 3H, CH_3CONH), 4.56 (d,

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J=5.69 Hz, 2H, CH_2), 5.48 (t, J=5.69 Hz, 1H, OH), 7.24 (d, J=6.84 Hz, 1H, H-4), 7.61(s, 1H, H-6), 7.90 (d, J=6.84 Hz, 1H, H-2), 10.23 (s, 1H, NHCO)

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 silicagel. 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 ^oC; ^{1}H-NMR 2.06 (s, 3H, CH_3CO), 5.02 (s, 2H, CH_2), 6.56 (d, J=8.99 Hz, 1H, H-4), 6.95 (s, 1H, H-6), 7.46 (bs, 2H, NH_2), 7.94(d, J=8.99 Hz, 1H, H-3); ^{13}C 20.58 (CH_3), 64.15 (CH_2O), 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 λ_{max} 396nm ε 5710; LRMS (ES mode, m/z) for $C_9H_9N_2O_5$ $[M-H]^-$ 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 silicagel. The column was eluted with dichloromethane to give product **84** as an orange solid (0.004 g, 2.6 %); mp 83-87 ^oC; Rf (A) 0.82; ^{1}H-NMR 2.12 (s, 3H, CH_3CO), 5.26 (s, 2H, CH_2), 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=8.31Hz, 1H, H-3); ^{13}CNMR 20.61 (CH_3), 64.09 ($\underline{C}HOCOCH_3$), 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 λ_{max} 322 nm ε 14230, λ_{max} 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 silicagel. The column was eluted with dichloromethane to give product **87** as an orange solid (0.004 g, 2.6 %); Rf (A) =0.57; ^{1}H-NMR δ 2.03 (s, 3H, CH_3CO), 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=8.11Hz, 1H, H-4), 8.26 (d, J=8.11 Hz, 1H, H-3); UV λ_{max} 318 nm ε 10500. Further elution with dichloromethane afforded product **86** as a yellow solid (0.031 g, 31%); mp 187-190 ^oC; Rf (A)=0.22; ^{1}H-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); ^{13}C NMR 20.24 (CH_3), 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-1), 134.31(C-6), 135.89(C-2), 137.23(C-1'), 146.37(C-5), 169.77 (CO); UV λ_{max} 328nm ε 9200; HRMS (ES mode, m/z) calcd. for $C_{13}H_{10}N_3O_4$ $[M-CH_3COO]^+$ 272.0685, found 272.0678; LRMS (ES mode, m/z) for $C_{15}H_{12}N_3O_6$ $[M-H]^-$ found 330.0.

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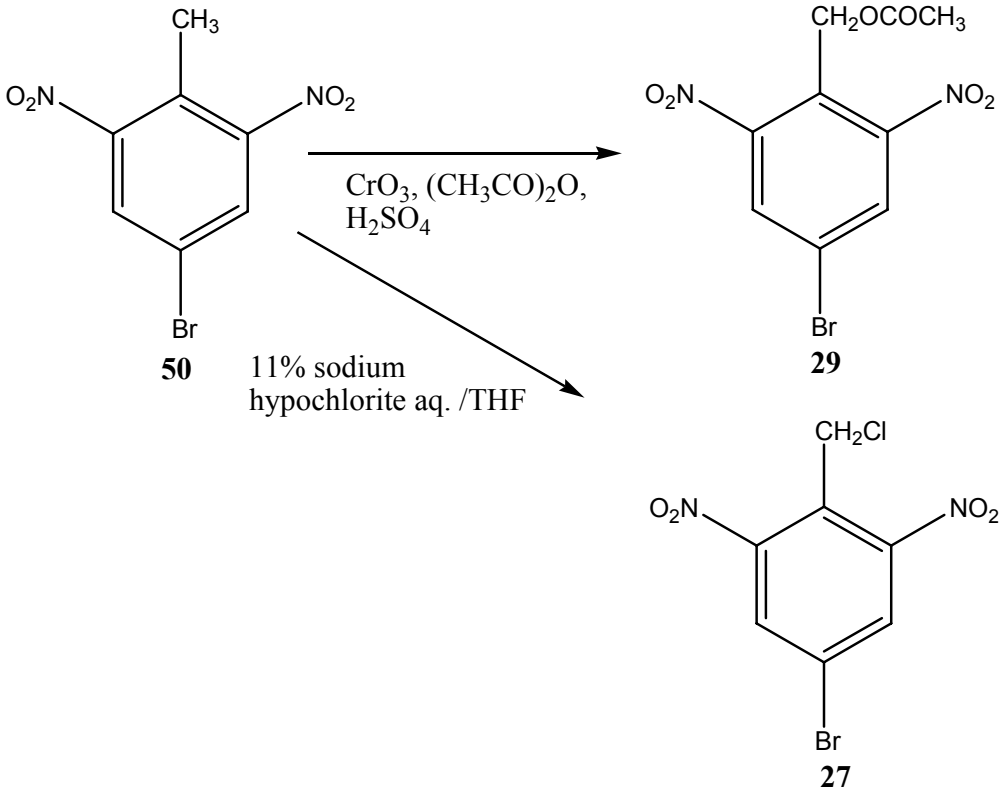
1.4.2 Synthesis of 4-bromo-2,6-dinitrobenzyl acetate 29

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[15] 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% SO_3, 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 P_2O_5 and purified by column chromatography on silica gel eluting with dichloromethane to give

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product **29** as a white gum (0.035 g, 11%); mp indef; Rf=0.6(A); ^{1}H-NMR δ 1.95 (s, 3 H, CH_3CO) , 5.30(s, 2H, CH_2) 8.62 (s, 2H, H-3, H-5). ^{13}C NMR δ 18.82 ($CH_2OCO\underline{CH_3}$), 57.38 ($\underline{CH_2}OCOCH_3$), 123.33 (C-4), 128.90 (C-1), 130.34 (C-3, C-5), 150.57 (C-2, C-6), 169.56 (CO); UV λ_{max} 247 nm ε 7000; GCMS for $C_6H_2BrN_2O_5$ $[M\text{-}CH_2COCH_3]^+$ found 243.01; LRMS (ES mode, m/z) for $C_9H_6BrN_2O_6$ $[M\text{-}H]^-$ 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 α-methyl-4,5-dimethoxy-2-nitrobenzyl alcohol **93**[24] with p-toluene sulphonic acid anhydride, p-toluenesulphonyl chloride or mesitylenesulphonyl acid 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 α-pheny-4,5-dimethoxy-2-nitrobenzyl alcohol **95**[7, 8] with p-toluenesulphonic acid anhydride resulted in the formation of 4,5-dimethoxy-2-nitrobenzophenone (**96**), the photoproduct isolated previously during the irradiation of α-pheny-4,5-dimethoxy-2-nitrobenzyl trichloroacetate.[7,8] No product of tosylation such as **97** was detected. Reaction of α-pheny-4,5-dimethoxy-2,6-dnitrobenzyl alcohol **98** [7,8] with p-toluenesulphonic acid anhydride resulted in the formation of a mixture of α-pheny-4,5-dimethoxy-2,6-dnitrobenzyl tosylate **100** and 4,5-dimethoxy-2-nitroso 6-nitrobenzophenone **99**, the photoproduct isolated previously during the irradiation of α-pheny-4,5-dimethoxy-2,6-dinitrobenzyl trichloroacetate **2**.[7,8] Attempts to isolate pure compound **100**, formed only in a small amount, were unsuccessful due to its rearrangement to photoproduct **99** during the purification on silicagel.

Reaction of α-pheny-5-bromo-2,6-dnitrobenzyl alcohol **58** with toluenesulphonic acid anhydride resulted in the initial formation of the expected α-pheny-5-bromo-2,6-dnitrobenzyl 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-nitrobenzophenone **101**.

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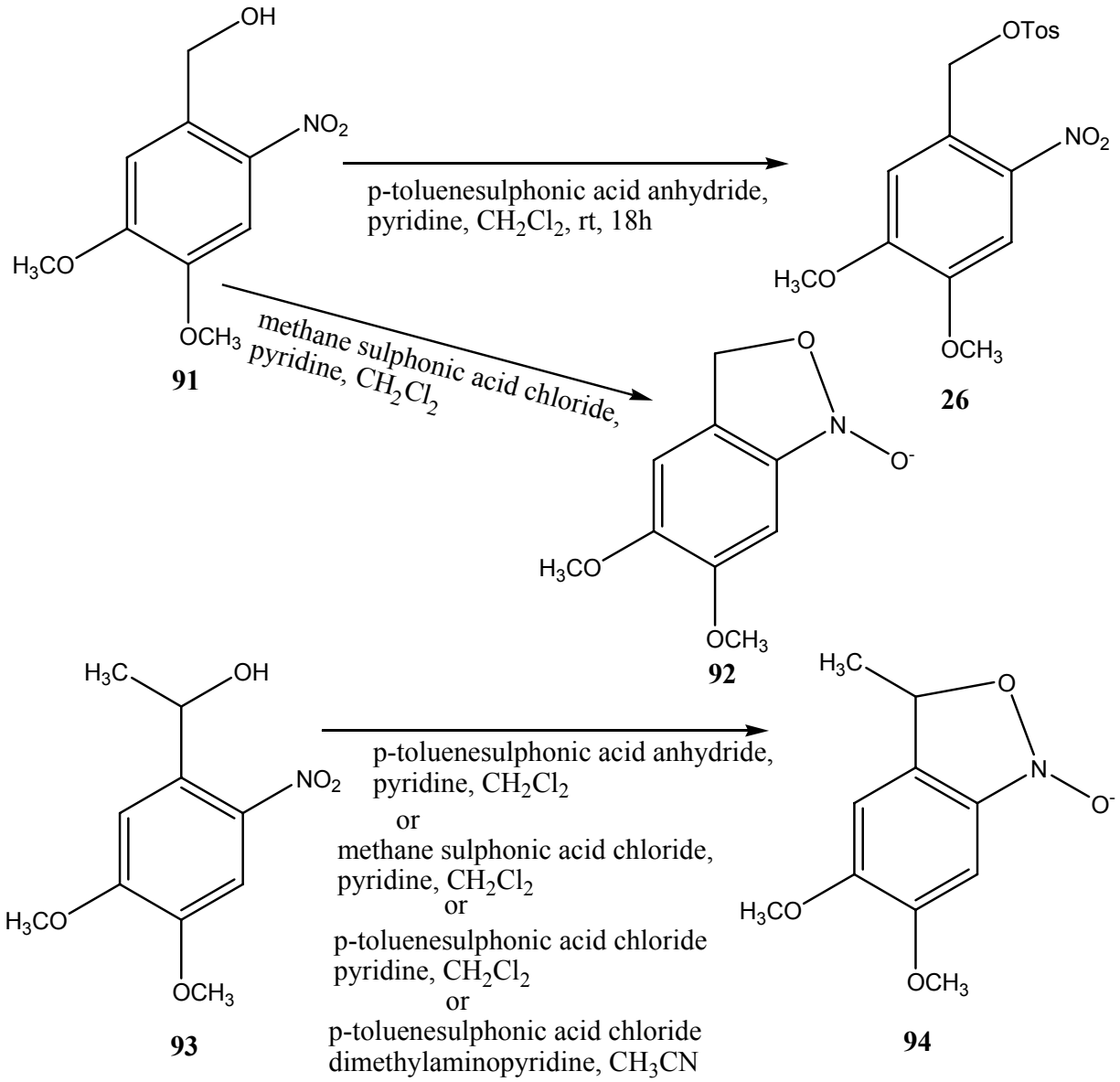
Scheme 10
Tosylation of 4,5-dimethoxy-2-nitrobenzylalcohol
and a-methyl- 4,5-dimethoxy-2-nitrobenzylalcohol



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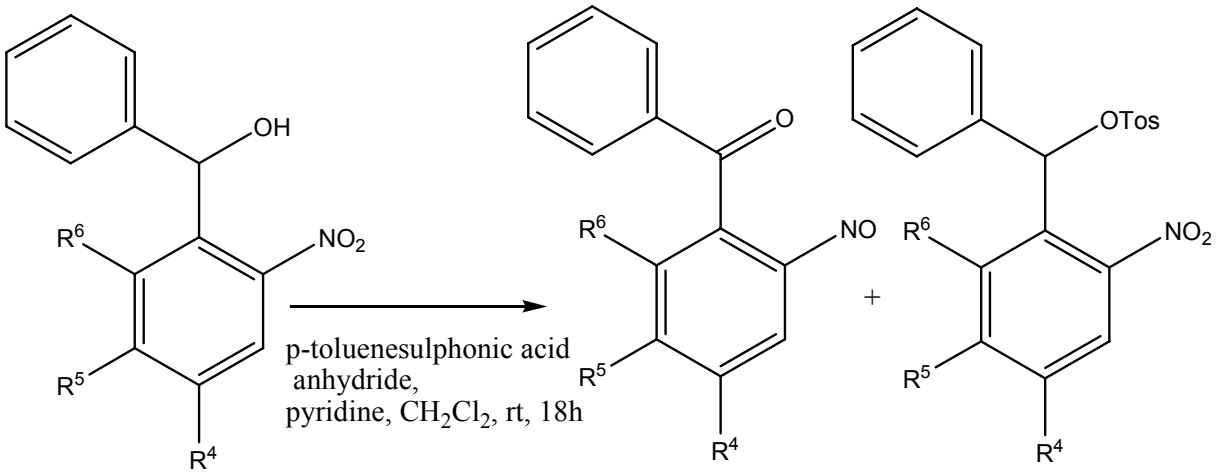
Scheme 11
Tosylation of α-phenyl-2-nitrobenzalcohols



95 R^4 = OCH_3 R^5 = OCH_3 R^6= H
98 R^4 = OCH_3 R^5 = OCH_3 R^6= NO_2
58 R^4 = H R^5 = Br R^6= NO_2

96 R^4 = OCH_3 R^5 = OCH_3 R^6= H
99 R^4 = OCH_3 R^5 = OCH_3 R^6= NO_2
101 R^4 = H R^5 = Br R^6= NO_2

97 R^4 = OCH_3 R^5 = OCH_3 R^6= H
100 R^4 = OCH_3 R^5 = OCH_3 R^6= NO_2
102 R^4 = H R^5 = Br R^6= NO_2

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** wheras 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, 1mmol) 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 **26** as a light pink solid (0.058 g, 16%); mp 100-103 ºC; Rf (A) = 0.32; ^{1}H-NMR δ 2.48 (s,3H, CH_3) 3.90 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 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); ^{13}C-NMR δ 20.72 (CH_3), 56.25 (OCH_3), 56.50 (OCH_3), 73.80 (CHOSO$_2$), 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 λ_{max} 347 nm ε 8500; HRMS (ES mode, m/z) calcd. for $C_{16}H_{17}N_7O_7SNa$ $[M+Na]^+$ 390.0623, found 390.0638

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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; ^{1}H-NMR δ 3.84 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 4.97 (s, 2H, CH_2), 7.27 (s, 1H, H-6), 7.67 (s, 1H, H-3), ^{13}C-NMR δ 43.25 (CH_2) 56.15 (OCH_3), 56.38 (OCH_3), 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} 344 nm ε 4077; HRMS (ES mode, m/z) calcd. for $C_9H_{10}NO_4$ $[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; ^{1}H-NMR δ 2.48 (d, J=6.71 Hz, 3H, CH_3), 3.90 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 5.87 (q, J=6.71 Hz, 1H, CH) 7.33 (s, 1H, H-6), 7.56 (s, 1H, H-3); ^{13}C-NMR δ 43.25 (CH_3) 56.15 (OCH_3), 56.38 (OCH_3), 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 $C_{10}H_{12}NO_4$ $[M]^-$ 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)[7,8] 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. [8]

4,5-Dimethoxy-2-nitroso-6-nitrobenzophenone (**99**)
Compound **98**[7,8] (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

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**; ^{1}H-NMR δ 2.45 (s, 3H, CH_3), 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, 2H, H-2'', H6'') 8.25 (d, J=8.84 Hz, 1H, H-4), 8.33 (d, J=8.84 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 |^{1}HNMR 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); ^{1}H-NMR δ 2.45 (s, 3H, CH_3), 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 ^{1}HNMR was consistent with the photoproduct **101**; ^{1}H-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 $CHOSO_2$ and the CH_3 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; ^{1}H-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); ^{13}C 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 $C_{13}H_8BrN_2O_4$ $[M+H]^+$ 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 imtermediate, **104**[26], 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

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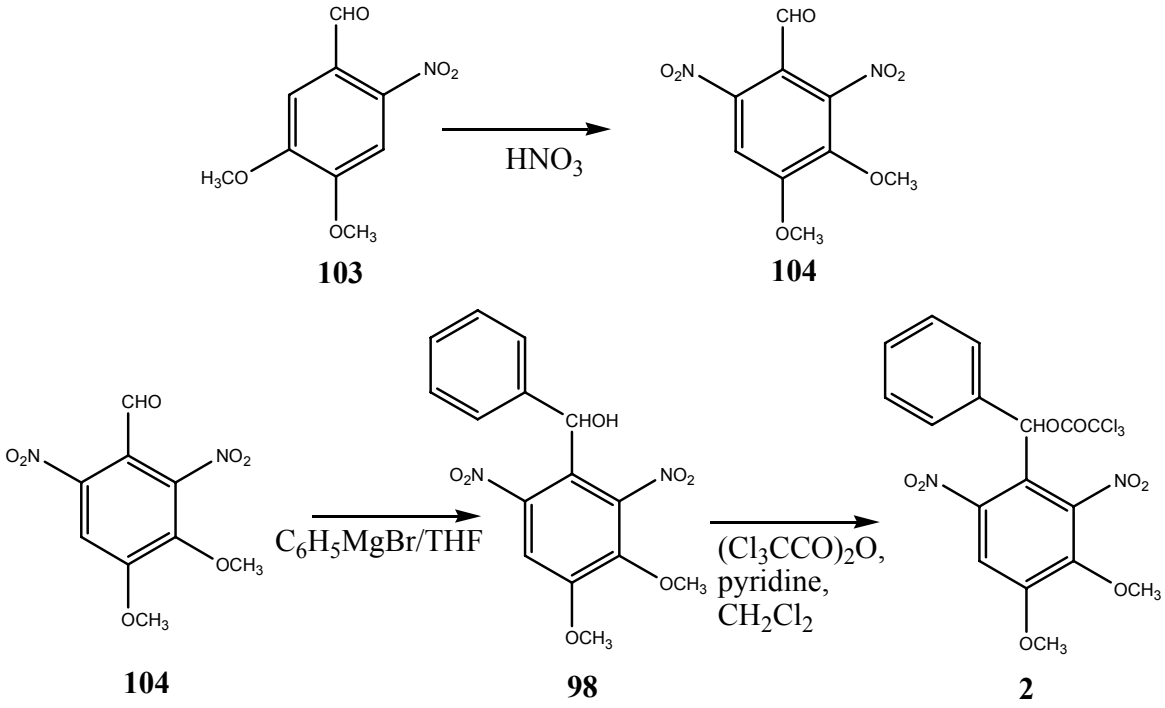
gave 4,5-dimethoxy-2,6-dinitrobenzaldehyde **104** together with some non-aldehyde side products having similar Rf values in several solvent systems.

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 a-phenyl-4,5-dimethoxy-2,6-dinitrobenzyltrichloroacetate - ester 2
Alternative Route



103 **104** **104** **98** **2**

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 P_2O_5. to give a yellowish solid (9.5 g); its ^{1}H-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 ardgon, and the solution was cooled to –78 °C. 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 °C, the mixture was stirred at –10 - (- 15 °C) for a further 15 minutes. 2% Aqueous hydrochloric acid (100 mL) was added dropwise over 30 minutes followed by dichloromethane (250

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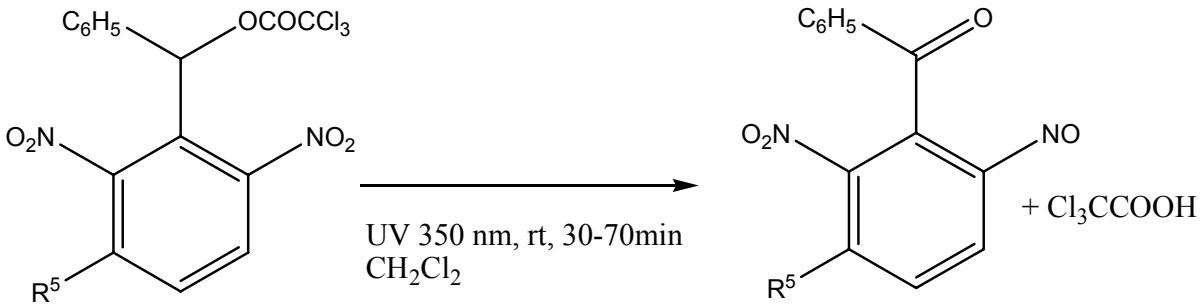
mL). The organic layer was washed with water (50 mL), 3% aqueous sodium bicarbonate (4 x 50 mL), water (50 mL), brine (50 mL), dried (sodium sulphate) and concentrated in vacuo. The residue was chromatographed on a silicagel column eluting with dichloromethane to give compound **98** as a light brown 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 [8]
This product was used in the subsequent trichloroacetylation step.

Scheme 13
Irradiation of Photolabile Esters



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. $[Et_3NH]^+$ $[CH_3COO]^-$ (B) MeCN. Gradient elution; 5%(B) – 90% (B) over 30 minutes.

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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_t) = 17.65min, and the photoproduct, R_t = 15.62min. The estimated degree of photoconversion, peak areas, was 80%. Preparative HPLC resulted in two fractions, fraction 1, Rt= 15.62 min and fraction 2, Rt=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 $C_{13}H_8ClN_2O_4$ $[M+H]^+$ 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 Rt in brackets) and their identity was confirmed by mass spectroscopy.

Trichloro-acetic acid-(3-chloro-2,6-dinitro-phenyl)-phenyl-methyl ester (**7**) (Rt 17.65 min)

Trichloro-acetic acid-(2,6-dinitro-3-morpholin-4-yl-phenyl)-phenyl-methyl ester (**13**)((Rt 17.12 min)

Trichloro-acetic acid-(2,6-dinitro-3-pyrrolidin-1-yl-phenyl)-phenyl-methyl ester (**15**)(Rt 17.92 min)

Trichloro-acetic acid-(2,6-dinitro-3-piperidin-1-yl-phenyl)-phenyl-methyl ester (**16**) (Rt 18.68min)

3-Chloro-2-nitro-6-nitrosobenzophenone (**105**) **(**90%), LRMS (ES mode, m/z) for $C_{13}H_8ClN_2O_4$ $[M+H]^+$ found 291.4 (Rt 15.62 min)

2-Nitro-6-nitroso-3-(pyrrolidin-1-yl)-benzophenone (**106**) (28%); LRMS (ES mode, m/z) for $C_{17}H_{16}N_3O_4$ $[M+H]^+$ found 326.3 (Rt 15.18 min).

2-Nitro-6-nitroso-3-(piperidin-1-yl)-benzophenone (**107**)(23%)(LRMS (ES mode, m/z) for $C_{18}H_{18}N_3O_4$ $[M+H]^+$ found 340.3 (Rt 13.42 min)

3-(Morpholin-4-yl)-2-nitro-6-nitrosobenzophenone (**108**)(19%) LRMS (ES mode, m/z) for $C_{17}H_{16}N_3O_5$ $[M+H]^+$ found 342.3 (Rt 14.57min)

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) (2mL) and freeze-dried to give photoproduct **105** as a yellow solid (0.011 g, 80%); Rf (A) 0.74; mp indef; ^{1}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 $C_{13}H_8ClN_2O_4$ $[M+H]^+$ 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, 0.05mmol), 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) (2mL) and freeze-dried to give photoproduct **107** as a yellowish glass (0.0021 g, 17%); Rf (A) 0.47; mp indef; ^{1}H-NMR δ 1.91 [bs, 4H, $(CH_2)_2$], δ

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3.30 [bs, 4H, $(CH_2)_2$], 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).

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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 2–3mm. These two beams are propagated in opposite directions.

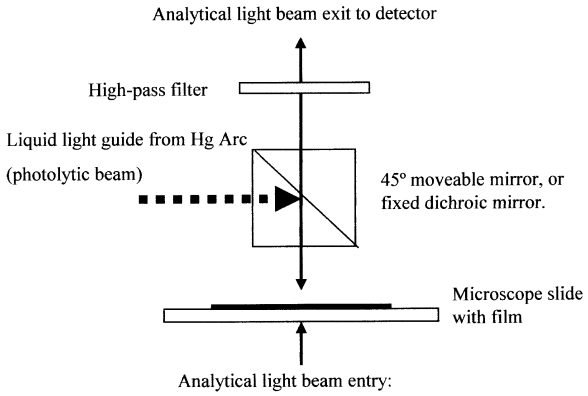

Figure 8. Outline of optical paths for combined photolysis and UV-vis spectrophotometry of films on microscope slides**.** The analytical beam entered and exited through fibre optic guides connecting to the light source and spectrometer respectively. The 45° mirror shown in the Figure was either a 100% 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 ≤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 ±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 ±0.0001 in the 510 nm region, corresponding to a change in DMT^+ density of ±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[a] in films to support photoacid-induced detritylation[b] and increased intra-film proton activity[c]. 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 **2**, 6-7 mM DMT-T and 0.2-0.3m M BG. Photolysis of ester **2** was at 365 nm for 30s at 50mW cm^{-2}. Detritylation was assessed by appearance of the 510 nm absorption peak of DMT^+, 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^+ 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^+ 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^+. 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)
1. Polystyrene
2. Poly(α-methylstyrene). M_w = 15k
3. Poly(styrene-*co*-α-methylstyrene).
4. Poly(4-methylstyrene). M_w = 70k
5. Poly(acenaphthalene). M_w = 5 - 10k
6. Poly(methylstyrene-*co*-indene), hydrogenated. M_n=0.8k
7. Polylimonene or poly(dipentene).
8. Poly(styrene-*block*-polyisoprene-*block*-polystyrene)[d] 14% styrene by wt.
9. Poly(carbomethylsilane)[e]. M_w = 2k
10. Poly(indene-*co*-coumarone). Ratio = 9:1. M_w = 0.7k
11. Poly(chlorostyrene). 60:40 mix of 3- & 4-isomers. M_w=100k

(ii) 45-70% detritylation (30-60% fall in BG absorption)
12. Poly(4-chlorostyrene). M_w = 75k
13. Poly(4-bromostyrene). M_w = 65k
14. Poly(4-tert-butylstyrene). M_w = 100-200k
15. Poly(4-hydroxystyrene). M_w = 20k
16. Poly(2-vinylnaphthalene). M_w = 100k
17. Polystyrene-*block*-polyisoprene-*block*-polystyrene Styrene content 22% by wt.

(iii) 5-10% detritylation (5-15% fall in BG absorption)
18. Poly(acrylonitrile-*co*-butadiene-*co*-styrene. Molar ratio 2:1:2
19. Poly(carbonate-urethane). M_w=256k
20. Poly(vinylchloride). M_w = 43k
21. Poly(bisphenol A carbonate).
22. Poly(vinylchloride-*co*-vinylacetate-*co*-2-hydroxy-propyl-acrylate. Wt ratio 81:4:15. .M_n = 15k

(iv) <5% detritylation (<5% fall in BG absorption)
23. Cellulose acetate butyrate. (acetate 2%, butyrate 52%)
24. Ethyl cellulose. (Ethoxy content 52% by wt.)
25. Sucrose octabenzoate[f].
26. Poly(caprolactone). M_w = 10k
27. Poly(2,6-dimethyl-1,4-phenylene-oxide. M_w = 244k.
28. Poly(oxyethylene) M_n =1.5k
29. Poly(oxyethylene) M_w=100k
30. Poly(1,3-propylene-glutarate) M_w = 7.1k
31. Poly(styrene-*co*-acrylonitrile) Wt ratio = 7:3. M_w = 185k
32. Poly(styrene-*co*-maleic anhydride), cumene terminated. Wt. ratio = 3:1. M_n = 1.9k
33. Poly(styrene-*co*-allyl alcohol) Molar ratio = 2:1. M_w=2.3k
34. Poly(styrene-*co*-methyl-methacrylate) Wt. ratio = 40:60. M_w = 100-150k
35. Poly(methylmethacrylate) M_w = 15k
36. Poly(benzylmethacrylate) M_w = 70k
37. Poly(cyclohexylmethacrylate) M_w = 65k
38. Poly(vinylacetate). M_w = 83k
39 Poly(9-vinylcarbazole) M_w = 83k
40. Poly(vinylphenylketone)
41. Poly(2-vinylpyridine) M_w=11k,
42. Poly(vinylpyrrolidine) M_w = 10k
43. Poly(propylenecarbonate) M_w =50k

(a) Data for composition, M_w (weight average mol. wt.) and M_n (number average mol. wt.) are those given by the supplier (Aldrich). (b) As shown by the DMT^+ 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^+ with the silyl hydride groups of the polymer. (f) Sucrose octabenzoate 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 pK_a 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. 9 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**.

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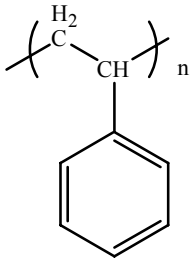
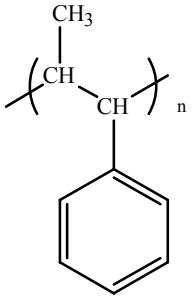
4.3 Chemical structures of polymers. Polymers **1-43** are those referred to in Table 2. Polymers **A-K** were inadequately soluble in the low boiling point solvents used for film formation, and could not be tested further.

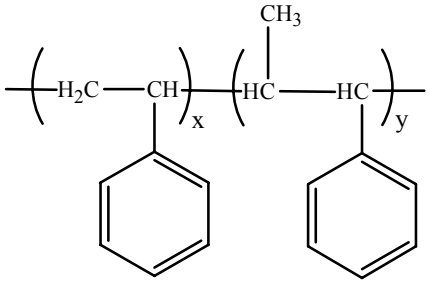
1. Polystyrene



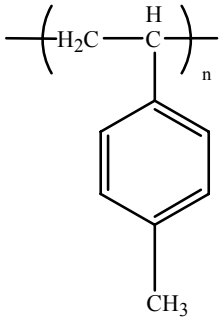
2. Poly(α-methylstyrene)



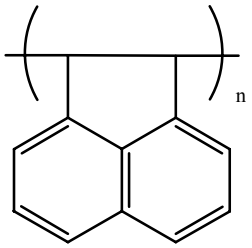
3. Poly(styrene-*co*-α-methylstyrene)



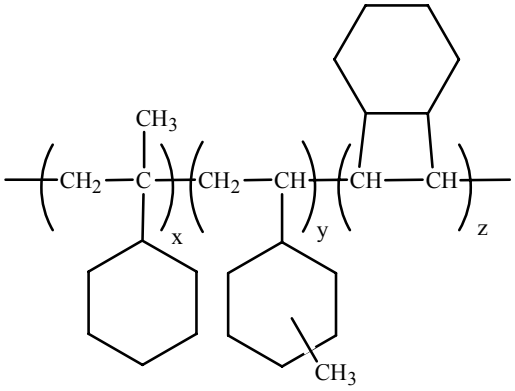
4. Poly(4-methy[styrene)



5. Poly(acenaphthalene)



6. Poly(methylstyrene-*co*-indene), hydrogenated



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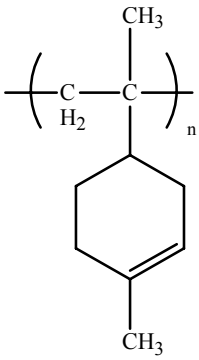
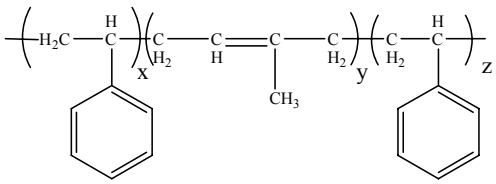
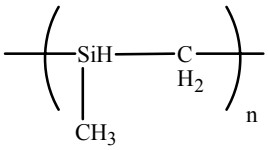
7. Poly(limonene) or Poly(dipentene)



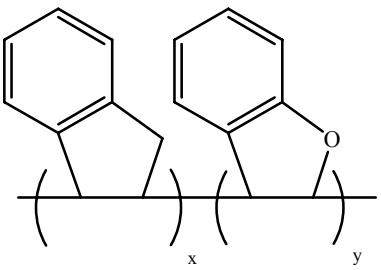
8. Poly(styrene-*block*-polyisoprene-*block*-polystyrene)
14% styrene by wt.



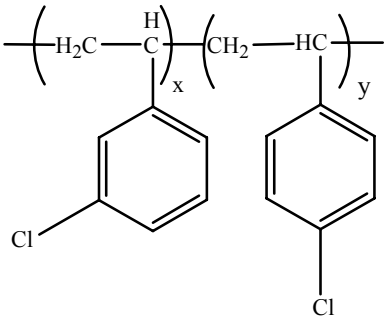
9. Poly((methylsilylene)methylene) or
poly(carbomethylsilane)



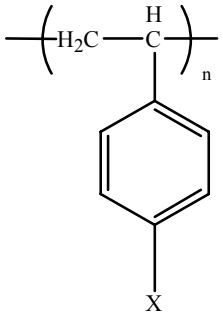
10. Poly(indene-*co*-coumarone)



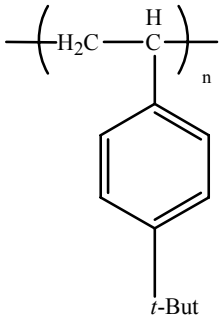
11. Poly(3-chlorostyrene-*co*-4-chlorostyrene)



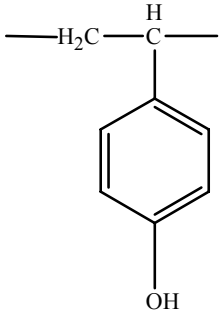
12 & 13. Poly(4-halostyrene). X = Cl or Br



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



15. Poly(4-hydroxy-styrene)



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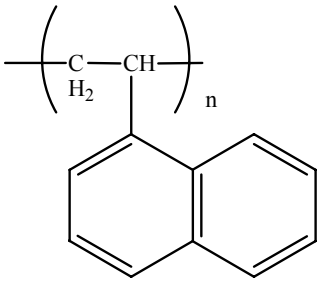
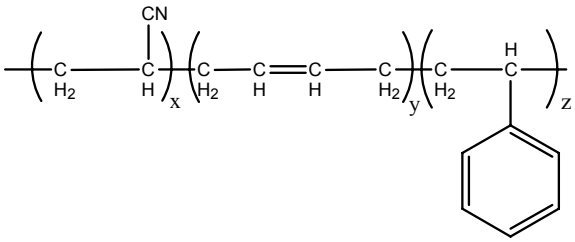
16. Poly(2-vinylnaphthalene)



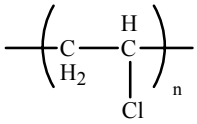
17. Poly(styrene-*block*-polyisoprene-*block*-polystyrene) 22% styrene by wt. See **8**.

18. Poly(acrylonitrile-*co*-butadiene-*co*-styrene)

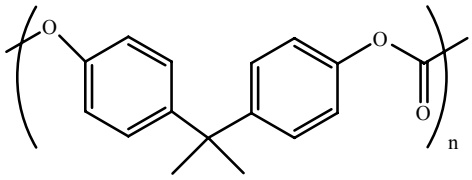


19. Poly(carbonate-urethane). *This is a co-polymer of (1,6-hexyl-1,2-ethylcarbonate)diol with 4,4'-methylenebis(phenylisocyanate) and 1,4-butenediol.*

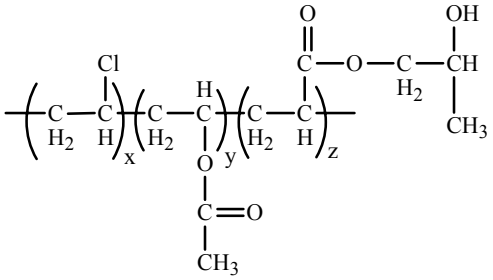
20. Polyvinylchloride



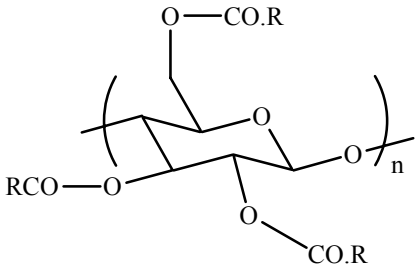
21. Poly(bisphenol A carbonate)



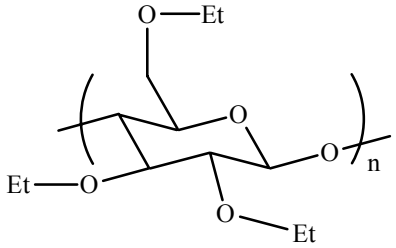
22. Poly(vinylchloride-*co*-vinylacetate-*co*-hydroxypropylacrlate



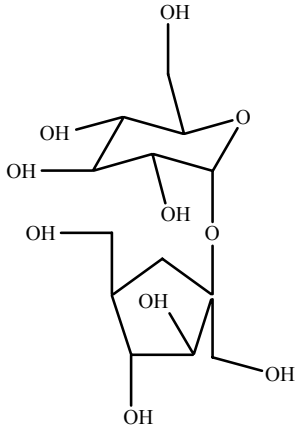
23. Cellulose acetate butyrate (R= $CH_3(CH_2)_2CO$- or CH_3CO-)



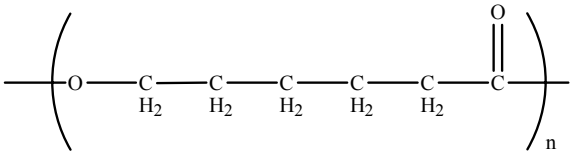
24. Ethylcellulose



25. Sucrose benzoate (benzoyl groups not shown)



26. Polycaprolactone



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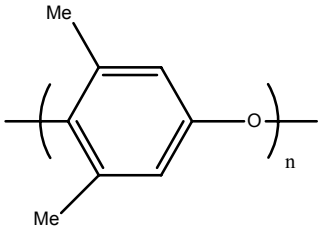
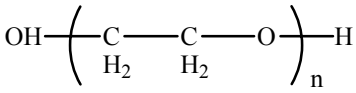
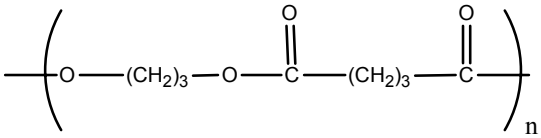
27. Poly(2,6-dimethyl-1,4-phenylene oxide)



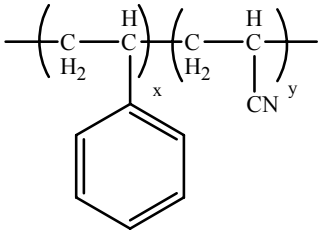
28, 29. Poly(oxyethylene))



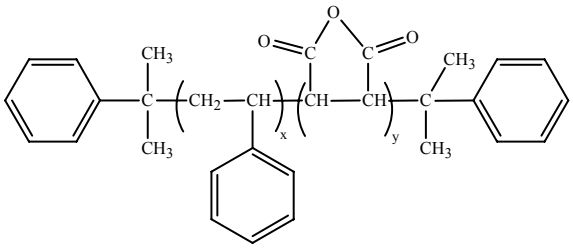
30. Poly(1,3-propyleneglutarate)



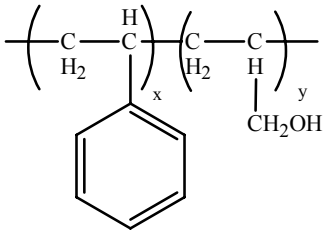
31. Poly(styrene-*co*-acrylonitrile)



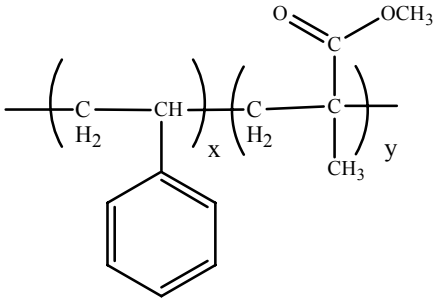
32. Poly(styrene-*co*-maleic anhydride), cumene terminated.



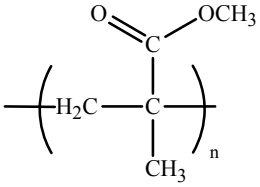
33. Poly(styrene-*co*-allyl alcohol)



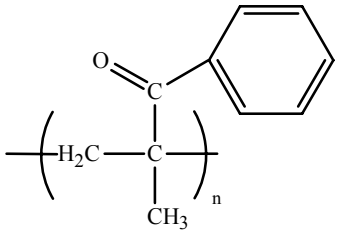
35. Poly(styrene-*co*-methylmethacrylate)



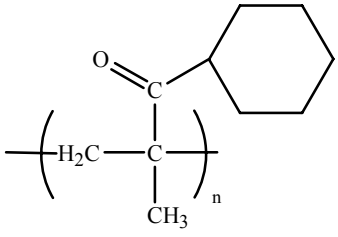
35. Poly(methylmethacrylate)



36. Poly(benzylmethacrylate)



37. Poly(cyclohexylmethacrylate



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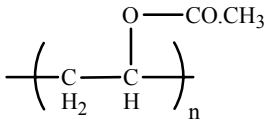
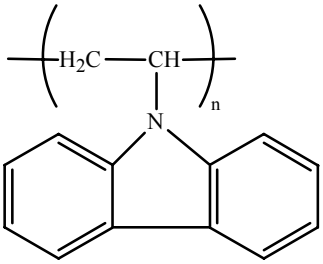
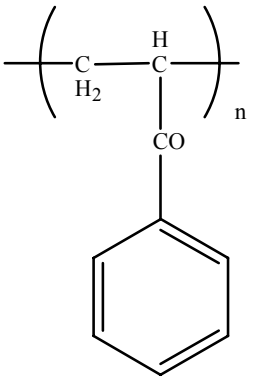
38. Poly(vinylacetate)



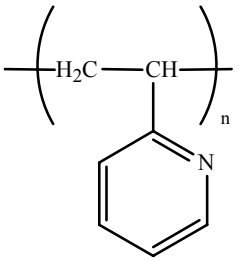
39. Poly(9-vinylcarbazole)



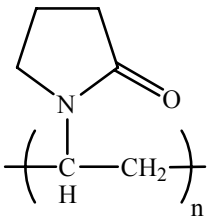
0. Poly(vinylphenylketone)



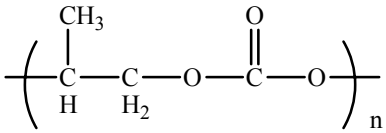
41. Poly(2-vinylpyridine)



42. Poly(vinylpyrrolidine)

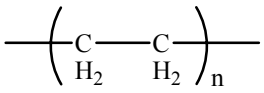


43. Poly(propylenecarbonate)

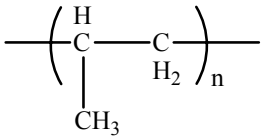


Insoluble Polymers

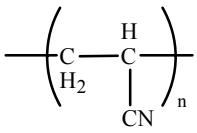
A. Polyethylene



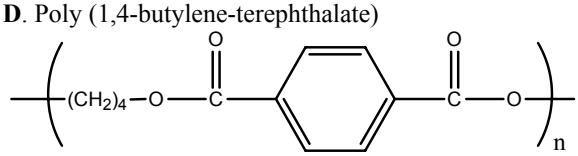
B. Polypropylene



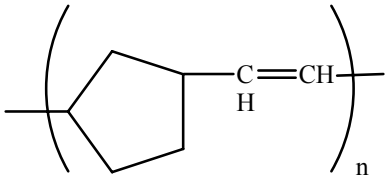
C. Polyacrylonitrile



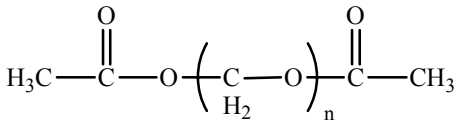
D. Poly (1,4-butylene-terephthalate)



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



F. Poly(methylene oxide, acetate end-capped



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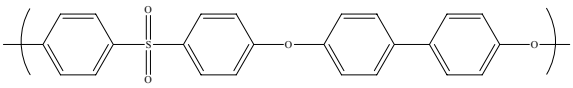
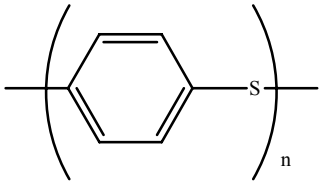
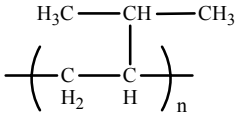
G. Poly(phenylenesulphone)



H. Poly(1,4-phenylenesulphide)



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



J. Poly(ethylene-*co*-vinylacetate)