The First Direct Chlorination of Iodoarenes – A Side-chain Directed Process

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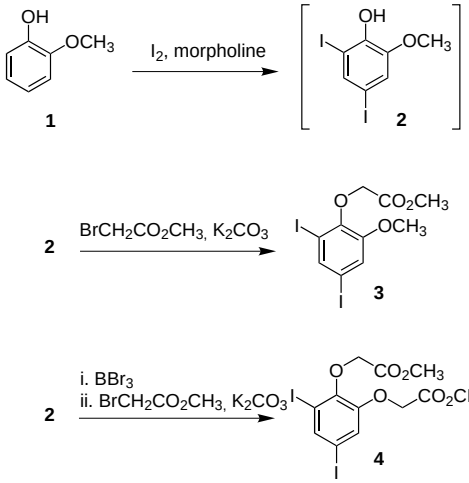
Abstract: The chlorination of electron rich iodoarenes with $MoCl_5$ proceeds with methoxycarbonylmethyl as the directing group. The transformation is selective and without loss of the valuable iodo substituent.

Key words: molybdenum, protective groups, iodoarenes, chlorination, radical reactions.

Based on their unique reactivity as substrates in transition metal catalysis, iodoarenes represent universal building blocks for organic synthesis. A direct installation of chloro substituents on a iodoarene is difficult since either an immediate multiple substitution occurs[1] or overoxidation leads to the loss of the valuable iodo moiety.[2] Most of these protocols require chlorine in combination with highly toxic heavy metals like thallium or lead.[3] The chlorination usually results in an isomeric mixture caused by the thermal decomposition of the initially formed hypervalent iodoarene dichloride, yielding an unselective chlorination of the aromatic core.[4]

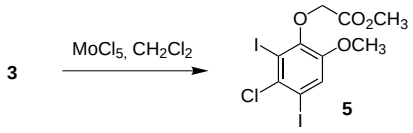
Older reports dealing with the conversion of arenes with $MoCl_5$ describe unselective and very sluggish chlorinations,[5] whereas the recently found oxidative coupling reaction mediated by $MoCl_5$ can be exploited for a direct access to complex structures in high efficacy.[6] Its synthetic power has been demonstrated in the total synthesis of (+)-5-detigloyloxysteganolide.[7] The compatibility of $MoCl_5$ towards many functional groups offers a broad variation in the substituents at the aromatic core as well as on the side chains.[8] The $MoCl_5$-mediated oxidative coupling reaction of iodobenzenes proceeds without loss of the precious iodo moiety to the corresponding biaryls.[9]

We describe a highly selective side-chain directed chlorination of iodoarenes, which is mediated by the easily available reagent $MoCl_5$. Remarkably, employment of a methoxycarbonylmethyl group instead of the simple methyl group on the phenolic oxygen changes the reaction outcome completely. A selective monochlorination of the aromatic core proceeds without formation of the corresponding biaryls or affecting the iodo moieties.



Scheme 1 Synthesis of the 3,5-diiodoveratrole derivatives.

The synthesis of the diiodobenzenes started with the known multiple iodination of guaiacol **1**,[10] providing in moderate yield the instable intermediate **2**, which did not allow further purification. The subsequent conversion with methyl bromoacetate gave **3** in 35% yield over all steps. Deprotection of the common intermediate, followed by an alkylation of both phenolic groups, provided **4** in a total yield of 27% (Scheme 1). The easily synthesized substrates **6**–**8** are known,[11] while the iodobenzenes **11** and **12** were obtained without any problems by using standard transformations.[12] All employed substrates were analytically pure.



Scheme 2

The conversion of the substituted 3,5-diiodoveratrole **3** with $MoCl_5$ resulted in the chlorinated compound **5** as the sole product, whose substitution pattern on the arene was verified by an X-ray analysis of a single crystal (see Figure 1). Despite the steric demand of both adjacent iodo moieties the introduction of the chloro substituent occurs exclusively at the 3-position and not in the more accessible position *ortho* to the methoxy group.

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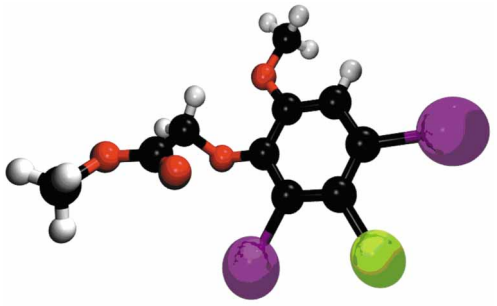


Figure 1 Crystal structure of **5**.

Table 1 Influence of the Reaction Conditions on the Conversion of **3**

Entry	Time (h)	$MoCl_5$ (equiv)	Yield[a] **5** (%)
1	3	2.0	49
2	6	2.0	60
3	20	2.0	39
4	1	3.0	55
5	2	3.0	63
6	3	3.0	60[b]
7	3	4.0	53

[a] Refers to analytically pure product.
[b] No starting material or by-product detected.

Using that particular transformation (Scheme 2), the reaction conditions were optimised. If less than two equivalents of $MoCl_5$ were employed or the transformation was performed below room temperature, only moderate conversions were observed (Table 1). Applying three equivalents of $MoCl_5$ allows short reaction times combined with synthetically interesting yields. In contrast, prolonged reaction times or elevated temperatures resulted in a decomposition of the target molecule. A significant increase in the amount of reagent turned out to be disadvantageous as doubly chlorinated species appear. When treating **3** with 5 equivalents of $MoCl_5$, **5** was isolated in 50% yield, besides 19% of the dichlorinated derivative **17**. Employment of 10 equivalents of chlorinating agent pushes the reaction towards 37% of **17** as sole product.

The conversion of the monoiodo derivatives **6** and **7** was smoothly performed in good yields and provided colourless solids analytically pure (Table 2). The individual substitution patterns were verified by NMR techniques. The chlorination reaction and work-up of **4** turned out to be difficult. Therefore, **15** was only obtained in modest quantities. Even triply iodinated systems like **8** are susceptible to the transformation. The installation of the chloro substituent now proceeds at the remaining *meta*-position to the electron rich substituent.

The pivotal role of the methoxycarbonylmethyl group in the reaction is clearly demonstrated by subjecting the analogous anisole derivatives **9** and **10** to the same process. These substrates should exhibit the same electronic properties as **6** and **7**, respectively. But under the applied reaction conditions no conversion was observed; not even traces of chlorinated products were detected. Presumably, the initial step, the chlorination reaction, involves a complex formation by the oxygen atoms of the phenoxyacetate moiety conducting the reagent $MoCl_5$ to the reaction partner. The acceleration of the reaction for substrates exhibiting an alkoxycarbonylmethyl group supports the hypothesis. The reaction may start with a single electron transfer. The resulting radical cation then becomes susceptible to an attack of the abundantly present chloride anions. The steric influence of the bulky iodo substituents and the absence of good organic nucleophiles, e.g. very electron rich aromatic systems, favours the chloro-adduct. Subsequent oxidation and extrusion of a proton accomplishes the transformation. The hypothesis is confirmed by the abscene of any conversion products on treatment of **11**, which can not form a reagent complex anymore. The 4-phenoxybutyric acid derivative **12** should only form an entropically disfavored precomplex, which results in less and isomerically impure product.[13] A detailed investigation of the reaction mixtures indicates that no hypervalent iodo species are present.

The first direct and selective chlorination of electron rich iodoarenes can be performed by $MoCl_5$. The employment of the alkoxycarbonylmethyl group on the phenolic oxygen is of pivotal significance since it induces the reaction by activating the reagent. The presented methodology works without the loss of the valuable iodo moieties and avoids the formation of hypervalent iodo intermediates.

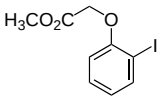
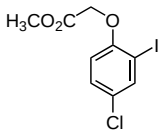
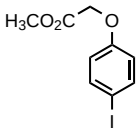
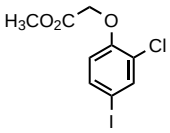
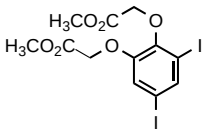
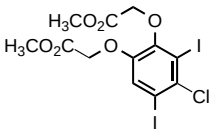
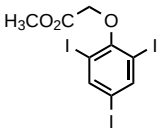
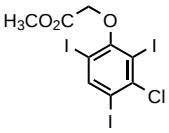
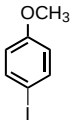
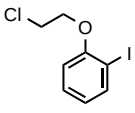
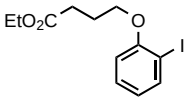
All reagents were used in analytical grades. Solvents were desiccated if necessary by standard methods. Column chromatography was performed on silica gel 60 (particle size 63–200 μm) using mixtures of cyclohexane and EtOAc as eluents. Melting points were determined on a MFB 595 Gallenkamp apparatus (UK) and were uncorrected. Microanalyses were performed using a Vario EL III (Elementar-Analysensysteme, Hanau, D). NMR spectra were recorded at 25 °C on a Bruker ARX 300 or AMX 400 using TMS as an internal standard. Mass spectra were obtained on a MAT8200 system (Finnigan-MAT, Bremen, D). Exact mass was determined with a GC-TOF (Micromass, Manchester, UK).

(2,4-Diiodo-6-methoxy-phenoxy)acetic Acid Methyl Ester (3)

I_2 (46 g, 181 mmol) was dissolved in EtOH (200) mL and treated dropwise with morpholine (48 mL, 360 mmol). After stirring for an additional hour guaiacol (**1**) (5 mL, 45.1 mmol) was added. The reaction mixture was stirred at 25 °C over night and then concentrated in vacuum. Sat. NH_4Cl solution (400 mL) was added and the aqueous phase was extracted with Et_2O (3 × 200 mL). The combined organic layers were washed with $Na_2S_2O_3$ solution (250 mL) and brine, dried over anhyd $MgSO_4$ and concentrated in vacuum.

Without further purification the crude product **2** was dissolved in DMF (120 mL). K_2CO_3 (25 g, 180 mmol) and bromoacetic acid methyl ester (6.4 mL, 76 mmol) were added. The reaction mixture was stirred at 25 °C over night, diluted with water (300 mL) and extracted EtOAc (2 × 200 mL). The combined organic layers were washed several times with water, brine and anhyd $MgSO_4$ and concentrated in vacuum. After purification by column chromatography, 7.1 g

Table 2 Chlorination by $MoCl_5$

Entry	Substrate	Product	Yield [a] (%)
1	 **6**	 **13**	77
2	 **7**	 **14**	80
3	 **4**	 **15**	28
4	 **8**	 **16**	48
5	 **9**	---	0
6	 **10**	---	0
7	 **11**	---	0
8	 **12**	---	31[b]

[a] Refers to analytically pure product.
[b] Isomeric mixture in a ratio of 10:9:2.

(15.9 mmol, 35%) of **3** were obtained as colourless crystals; mp 91–92 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, OCH_3), 3.79 (s, 3 H, $ArOCH_3$), 4.56 (s, 2 H, $ArOCH_2$), 7.11 (d, 1 H, $^4J_{3,5}$ = 1.9 Hz, 5-H), 7.64 (d, 1 H, $^4J_{3,5}$ = 1.9 Hz, 3-H).

^{13}C NMR (75MHz, $CDCl_3$): δ = 52.02 (OCH_3), 56.26 ($ArOCH_3$), 68.96 ($ArOCH_2$), 88.04 (C-2), 92.75 (C-4), 122.16 (C-5), 138.44 (C-3), 147.20 (C-6), 152.17 (C-1), 168.82 (CO).

MS (EI, 70 eV): *m/z* (%) = 448 (100) [M^+], 375 (50) [M^+ – $CH_2CO_2CH_3$], 321 (9) [M^+ – I].

Anal. Calcd for $C_{10}H_{10}I_2O_4$ (447.99): C, 26.81; H, 2.25. Found: C, 26.93; H, 2.25.

(2,4-Diiodo-6-methoxycarbonylmethoxy-phenoxy)acetic Acid Methyl Ester (4)

The iodination of guaiacol (**1**) (3.5 mL, 31.6 mmol) was done analogously to the synthesis of compound **3**. The crude product **2** was dissolved in anhyd CH_2Cl_2 (150 mL) and cooled to –78 °C. BBr_3 (3.5 ml, 38 mmol) was injected dropwise. The mixture was stirred for 30 min at –78 °C and 4 h at –12 °C. After addition of Et_2O (100 mL), the temperature was raised to 25 °C, water (200 mL) was added and the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with sat. $Na_2S_2O_3$ solu-

tion, brine, dried over anhyd $MgSO_4$ and concentrated in vacuum. The crude product was treated with bromoacetic acid methyl ester (8.0 mL, 95 mmol) and K_2CO_3 (26.5 g, 190 mmol) as described for compound **3**. After standard work-up and purification by column chromatography, 4.3 g (8.5 mmol, 27%) of **4** were obtained as colourless crystals; mp 119–120 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.75 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 4.60 (s, 2 H, $ArOCH_2$), 4.68 (s, 2 H, $ArOCH_2$), 7.04 (d, 1 H, $^4J_{3,5}$ = 2.0 Hz, 5-H), 7.70 (d, 1 H, $^4J_{3,5}$ = 2.0 Hz, 3-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 51.96 (OCH_3), 52.28 (OCH_3), 66.04 ($ArOCH_2$), 69.03 ($ArOCH_2$), 87.61 (C-2), 93.19 (C-4), 123.76 (C-5), 139.93 (C-3), 147.78 (C-6), 150.21 (C-1), 168.04 (CO), 168.76 (CO).

MS (EI, 70 eV): *m*/*z* (%) = 506 (100) [M^+], 433 (16) [M^+ – $CH_2CO_2CH_3$], 374 (28) [433 – CO_2CH_3].

Anal. Calcd for $C_{12}H_{12}I_2O_6$ (506.03): C, 28.48; H, 2.39. Found: C, 28.57; H, 2.45.

1-(2-Chloro-ethoxy)-2-iodo-benzene (11)

NaH (355 mg, 8.9 mmol; 60% in paraffin) was suspended in anhyd DMF (30 mL) and 2-iodophenol (1.5 g, 6.8 mmol) was added. After stirring at 25 °C for 1 h, (2-chloro-ethyl)tosylate (1.6 mL, 8.9 mmol) was injected. The reaction mixture was stirred at 90 °C for 7 h. After cooling to 25 °C, EtOAc (30 mL) were added and the mixture was washed with water (100 mL) and brine, dried over anhyd $MgSO_4$ and concentrated in vacuum. Purification by column chromatography yielded 1.9 g (6.7 mmol, 98%) of **11** as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.82 (t, 2 H, $^3J_{7,8}$ = 6.0 Hz, CH_2Cl), 4.22 (t, 2 H, $^3J_{7,8}$ = 6.0; $ArOCH_2$), 6.71 (ddd, 1 H, $^3J_{3,4}$ = 7.8 Hz, $^3J_{4,5}$ = 7.4 Hz, $^4J_{4,6}$ = 1.4 Hz, 4-H), 6.78 (d, 1 H, $^3J_{5,6}$ = 8.2 Hz, 6-H), 7.26 (ddd, 1 H, $^3J_{4,5}$ = 7.4 Hz, $^3J_{5,6}$ = 8.2 Hz, $^4J_{3,5}$ = 1.6 Hz, 5-H), 7.75 (dd, 1 H, $^3J_{3,4}$ = 7.8 Hz, $^4J_{3,5}$ = 1.6 Hz, 3-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.47 (CH_2Cl), 69.28 ($ArOCH_2$), 86.79 (C-2), 112.80 (C-6), 123.23 (C-4), 129.40 (C-5), 139.55 (C-3), 156.78 (C-1)

MS (EI, 70 eV): *m*/*z* (%) = 282, 284 (100, 27) [M^+], 233 (5) [M^+ – CH_2Cl], 220 (100) [M^+ – CH_2CH_2Cl].

HRMS: *m*/z calcd for C_8H_8ClIO (M^+): 281.9308. Found: 281.9307.

4-(2-Iodo-phenoxy)butyric Acid Ethyl Ester (12)

2-Iodophenol (5.0 g, 22.7 mmol), K_2CO_3 (6.3 g, 45.4 mmol) and 4-bromobutyric acid ethyl ester (3.3 ml, 22.7 mmol) were combined in cyclohexanone (40 mL) and refluxed for 6 h. After cooling to 25 °C, water (250 mL) and Et_2O (100 mL) were added and the aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic layers were subsequently treated with brine and anhyd $MgSO_4$ and concentrated in vacuum. After removal of the cyclohexanone, the crude product was purified by distillation in high vacuum to give 6.9 g (20.6 mmol, 91%) of **12** as a colourless oil; bp 104 °C (2.7×10^{-2} mbar).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, 3 H, $^3J_{11,12}$ = 7.2 Hz, CH_3), 2.14 (tt, 2 H, $^3J_{7,8}$ = 6.0 Hz, $^3J_{8,9}$ = 7.3 Hz, $CH_2CH_2CH_2$), 2.61 (t, 2 H, $^3J_{8,9}$ = 7.3, CH_2COO), 4.05 (t, 2 H, $^3J_{7,8}$ = 6.0 Hz, $ArOCH_2$), 4.14 (q, 2 H, $^3J_{11,12}$ = 7.2 Hz, $COOCH_2$), 6.69 (ddd, 1 H, $^3J_{3,4}$ = 7.7 Hz, $^3J_{4,5}$ = 7.7 Hz, $^4J_{4,6}$ = 1.2 Hz, 4-H), 6.78 (dd, 1 H, $^3J_{5,6}$ = 8.2 Hz, $^4J_{4,6}$ = 1.2 Hz, 6-H), 7.24–7.29 (m, 1 H, 5-H), 7.75 (dd, 1 H, $^3J_{3,4}$ = 7.7 Hz, $^4J_{3,5}$ = 1.7 Hz, 3-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.13 (CH_3), 24.39 ($CH_2CH_2CH_2$), 30.63 (CH_2COO), 60.30 ($COOCH_2$), 67.72 ($ArOCH_2$), 86.53 (C-2), 111.97 (C-6), 122.42 (C-4), 129.31 (C-5), 139.25 (C-3), 157.10 (C-1), 173.05 (CO).

MS (EI, 70 eV): *m*/*z* (%) = 334 (19) [M^+], 289 (14) [M^+ – OCH_2CH_3], 220 (33) [M^+ – $(CH_2)_3CO_2CH_2CH_3$], 115 (100) [$(CH_2)_3CO_2CH_2CH_3^+$].

HRMS: *m*/*z* calcd for $C_{12}H_{15}IO_3$ (M^+): 344.0066. Found: 344.0018.

(3-Chloro-2,4-diiodo-6-methoxy-phenoxy)acetic Acid Methyl Ester (5)

To a solution of **3** (807 mg, 1.8 mmol) was in CH_2Cl_2 (25 mL) at 25 °C was added $MoCl_5$. The reaction mixture was diluted with EtOAc (100 mL) and washed with water (100 mL). Subsequent treatment with brine, anhyd $MgSO_4$, and concentration of the organic phase provided the crude product, which was purified by column chromatogaphy yielding **5** as colourless crystals; mp 95–96 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.74 (s, 3 H, OCH_3), 3.75 (s, 3 H, $ArOCH_3$), 4.54 (s, 2 H, $ArOCH_2$), 7.32 (s, 1 H, ArH).

^{13}C NMR (75MHz, $CDCl_3$): δ = 52.10 (OCH_3), 56.55 ($ArOCH_3$), 68.99 ($ArOCH_2$), 89.71 (C-2), 96.11 (C-4), 123.63 (C-5), 138.47 (C-3), 148.71 (C-6), 150.04 (C-1), 168.61 (CO).

MS (EI, 70 eV): *m*/*z* (%) = 482, 484 (100, 33) [M^+], 448 (38) [M^+ – Cl], 409, 411 (53, 18) [M^+ – $CH_2CO_2CH_3$], 375 (20) [M^+ – Cl – $CH_2CO_2CH_3$].

Anal. Calcd for $C_{10}H_9ClI_2O_4$ (482.42): C, 24.90; H, 1.88. Found: C, 25.27; H, 1.83.

X-Ray Structure Analysis

$C_{10}H_9ClI_2O_4$: colorless crystals, crystal dimension $0.45 \times 0.20 \times 0.20$ mm^3; M = 482.42; monoclinic, space group $P2_1/c$ (No. 14), a = 9.354(1), b = 9.693(1), c = 14.806(1) Å, β = 96.60(1)°, V = 1333.5(2) Å^3, Z = 4, λ = 0.71073 Å, T = 198 K, ρcalc = 2.403 g cm^{-3}, μ = 49.16 cm^{-1}, empirical absorption correction via SORTAV ($0.216 \le T \le 0.440$), ω and φ scans, 10438 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.68 Å^{-1}, 3251 independent (R_{int} = 0.021) and 3090 observed reflections [$I \ge 2\,\sigma(I)$], 156 refined parameters, R = 0.020, wR_2 = 0.046, max. residual electron density 0.48 (–0.60) e Å^{-3}, hydrogens calculated and refined as riding atoms.

Data set was collected with an Nonius KappaCCD diffractometer in combination with a Nonius FR591 (rotating anode) as X-ray source. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN,[14] absorption correction SORTAV,[15] structure solution SHELXS-97,[16a] structure refinement SHELXL-97,[16b] graphics POV-Ray 3.2.[17]

Chlorination by $MoCl_5$ (Table 2); General Procedure

Substrate (1.5 mmol) was dissolved in anhyd CH_2Cl_2 (25 mL) and treated for 3 h at 25 °C with 3 equivalents $MoCl_5$. Then the reaction mixture was diluted with EtOAc (100 mL) and washed with water (100 mL). Subsequent treatment with brine, anhyd $MgSO_4$, and concentration of the organic phase provided the crude product, which was purified by column chromatography yielding the desired products. All chlorinated compounds formed colourless crystalline compounds immediately upon evaporation of the solvents. The products were dried in high vacuum.

(4-Chloro-2-iodo-phenoxy)acetic Acid Methyl Ester (13)

Mp 36–37 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, OCH_3), 4.67 (s, 2 H, $ArOCH_2$), 6.64 (d, 1 H, $^3J_{5,6}$ = 8.7 Hz, 6-H), 7.24 (dd, 1 H, $^3J_{5,6}$ = 8.7 Hz, $^4J_{3,5}$ = 2.5 Hz, 5-H), 7.76 (d, 1 H, $^4J_{3,5}$ = 2.5 Hz, 3-H).

^{13}C NMR (75MHz, $CDCl_3$): δ = 52.33 (OCH_3), 66.55 ($ArOCH_2$), 86.76 (C-2), 112.99 (C-6), 127.63 (C-4), 129.17 (C-5), 138.97 (C-3), 155.67 (C-1), 168.40 (CO).

MS (EI, 70 eV): *m*/*z* (%) = 326, 328 (76, 25) [M^+], 292 (5) [M^+ – Cl], 267, 269 (26, 9) [M^+ – CO_2CH_3], 253, 255 (22, 7) [M^+ – $CH_2CO_2CH_3$], 199, 201 (100, 33) [M^+ – I].

Anal. Calcd for $C_9H_8ClIO_3$ (326.52): C, 33.11; H, 2.47. Found: C, 33.35; H, 2.35.

(2-Chloro-4-iodo-phenoxy)acetic Acid Methyl Ester (14)
Mp 60–63 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.79 (s, 3 H, OCH_3), 4.68 (s, 2 H, $ArOCH_2$), 6.59 (d, 1 H, $^3J_{5,6}$ = 8.6 Hz, 6-H), 7.47 (dd, 1 H, $^3J_{5,6}$ = 8.6 Hz, $^4J_{3,5}$ = 2.1 Hz, 5-H), 7.69 (d, 1 H, $^4J_{3,5}$ = 2.1 Hz, 3-H).

^{13}C NMR (75MHz, $CDCl_3$): δ = 52.33 (OCH_3), 66.12 ($ArOCH_2$), 83.64 (C-4), 115.69 (C-6), 124.72 (C-2), 136.48 (C-5), 138.62 (C-3), 153.61 (C-1), 168.39 (CO).

MS (EI, 70 eV): *m*/*z* (%) = 326, 328 (100, 33) [M^+], 291 (32) [M^+ – Cl], 267, 269 (27, 9) [M^+ – CO_2CH_3], 253, 255 (31, 10) [M^+ – $CH_2CO_2CH_3$].

Anal. Calcd for $C_9H_8ClIO_3$ (326.52): C, 33.11; H, 2.47; Found: C, 33.20; H, 2.47.

(3-Chloro-2,4-diiodo-6-methoxycarbonylmethoxy-phenoxy)acetic Acid Methyl Ester (15)
Mp 143–144 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.72 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 4.58 (s, 2 H, $ArOCH_2$), 4.67 (s, 2 H, $ArOCH_2$), 7.28 (s, 1 H, ArH).

^{13}C NMR (75MHz, $CDCl_3$): δ = 52.00 (OCH_3), 52.35 (OCH_3), 66.24 ($ArOCH_2$), 68.97 ($ArOCH_2$), 89.41 (C-2), 96.59 (C-4), 125.39 (C-5), 139.86 (C-3), 148.06 (C-6), 149.34 (C-1), 167.99 (CO), 168.55 (CO).

MS (EI, 70 eV): *m*/*z* (%) = 540, 541 (100,33) [M^+], 467, 469 (13, 4) [M^+ – $CH_2CO_2CH_3$], 409, 411 (25, 8) [467 – CO_2CH_3].

Anal. Calcd for $C_{12}H_{11}ClI_2O_6$ (540.47): C, 26.67; H, 2.05; Found: C, 26.75; H, 1.96.

(3-Chloro-2,4,6-triiodo-phenoxy)acetic Acid Methyl Ester (16)
Mp 137–139 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.87 (s, 3 H, OCH_3), 4.59 (s, 2 H, $ArOCH_2$), 8.29 (s, 1 H, ArH).

^{13}C NMR (75MHz, $CDCl_3$): δ = 52.37 (OCH_3), 68.52 ($ArOCH_2$), 87.97 (C-6), 92.75 (C-2), 95.62 (C-4), 147.42 (C-3), 148.56 (C-5), 158.70 (C-1), 167.42 (CO).

MS (EI, 70 eV): *m*/*z* (%) = 578, 580 (36, 12) [M^+], 505, 507 (14, 5) [M^+ – $CH_2CO_2CH_3$], 451, 453 (100, 33) [M^+ – I], 378, 380 (24, 8) [M^+ – I – $CH_2CO_2CH_3$].

Anal. Calcd for $C_9H_6ClI_3O_3$ (578.31): C, 18.69; H, 1.05; Found: C, 18.95; H, 1.06.

(3,5-Dichloro-2,4-diiodo-6-methoxy-phenoxy)acetic Acid Methyl Ester (17)
Mp 155–157 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 3.87 (s, 3 H, $ArOCH_3$), 4.67 (s, 2 H, $ArOCH_2$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.19 (OCH_3), 61.37 ($ArOCH_3$), 69.27 ($ArOCH_2$), 94.48 (C-2), 97.45 (C-4), 135.53 (C-5), 139.00 (C-3), 146.24 (C-6), 153.37 (C-1), 168.17 (CO).

MS (EI, 70 eV): *m*/*z* (%) = 516, 518, 520 (100, 66, 11) [M^+], 443, 445, 447 (34, 23, 4) [M^+ – $CH_2CO_2CH_3$], 389, 391, 393 (54, 36, 6) [M^+ – I].

Anal. Calcd for $C_{10}H_8Cl_2I_2O_4$ (516.88): C, 23.24; H, 1.56; Found: C, 23.23; H, 1.53.

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(17) Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 211377. Copies of the data can be obtained free of charge on application to The Director CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk].