Regioselective Preparation of Iodinated Phloroglucinols

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Received December 20, 1991

Key Words: Resorcinols, methoxy-, monoprotected / Iodination, mild / Iodobenzenes, electron-rich

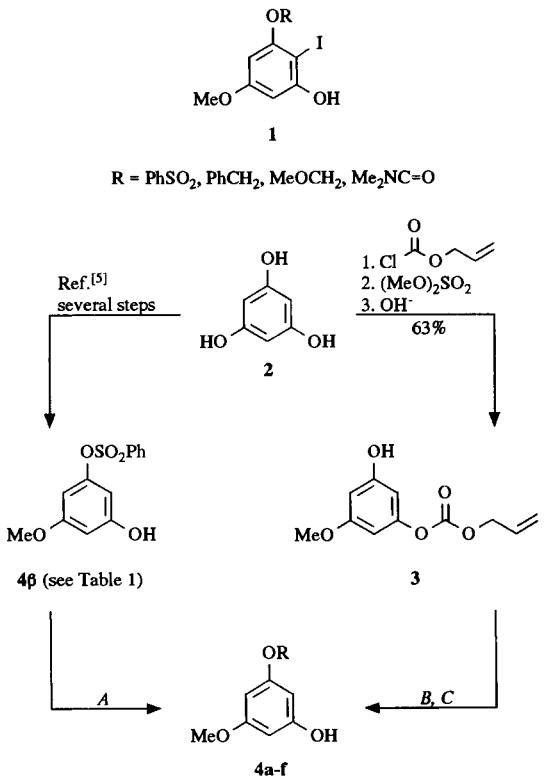
A range of mono- and diiodinated phloroglucinols with differential protection of two hydroxy groups has been prepared.

"A good general method for the *ortho*-iodination (of phenols) does not exist"[1,2]. Typical difficulties encountered in this reaction are lack of regiocontrol in that the *ortho* isomer is often accompanied by the *para* one. Furthermore, mixtures of mono- and polyiodinated products are difficult to separate. The resulting iodophenols are generally sensitive towards light, base, heat and oxygen.

In context with a synthetic project[3,4] we required monoiodinated 5-methoxyresorcinols such as **1** and also diiodinated derivatives, in which one hydroxy group was protected.

Thus, precursors for iodination were protected phloroglucinols (Scheme 1).

Scheme 1



A: 1. RX; 2. OH^-; (**4β**→**4a,b,c**). – *B*: 1. R_2NCOCl; 2. OH^- (**3**→**4d,e**). – *C*: 1. *N,N'*-Carbonyldiimidazole, piperidine; 2. $ZnCl_2 \cdot OEt_2$ (**3**→**4f**).

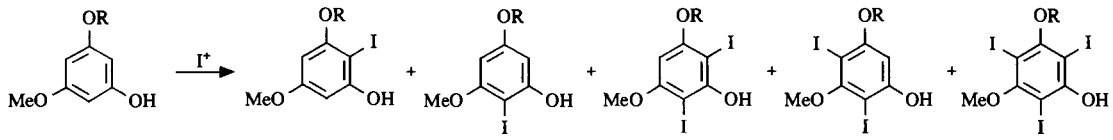
Whereas benzyl ether **4a**[5] as well as **4ß**[5] had been prepared previously, scale-up proved to be difficult. Nevertheless, we took advantage of compound **4ß** and converted it into **4b, c**. The difficulties in obtaining **4ß** on a 100-mmol scale prompted us to prepare allyloxycarbonyl (ALOC) derivative **3** by a simple and fast three-step/two-pot procedure.

Treatment of **3** with carbamoyl chlorides and hydrolysis of the carbonate furnished **4d, e**. In the case of **4f**, piperidinocarbonylation (piperidine, carbonyldiimidazolide) was followed by liberation of the phenolic OH group with $ZnCl_2 \cdot OEt_2$. The latter route from **3**→**4** was the method of choice. Transesterification, i.e. regeneration of the dicarbonate, in the urethane-forming step was avoided, and both steps were carried out at room temperature[6].

Conventionally, iodination is carried out with KI/KIO_3 and acid under two-phase conditions[1]. A milder procedure was introduced by Kajigaeshi[10], who used $PhCH_2Et_3N^+Cl_2I^-/MeOH/CH_2Cl_2/CaCO_3$ under neutral conditions. Except for the iodination of **4α**, the Kajigaeshi procedure was superior, especially for preparing the diiodo derivatives. The monoiodophloroglucinols were obtained with little regiocontrol[1,2] and tended to decompose on column chromatography. The desired diiodophloroglucinols **7** were formed with high regioselectivity. Thanks to the second iodine atom they were more lipophilic, i.e. less polar, having high R_f values on column chromatography. They tended to crystallize easily from $CHCl_3$ (**7α** was so sensitive that it had to be crystallized to avoid contact with a polar column). Regioisomers were identified by gated ^{13}C-NMR spectroscopy, requiring extended NMR time. The multiplicities of the ^{13}C-NMR signals due to long-range C–H coupling under gated decoupling conditions are characteristically different for the isomeric iodophenols. This was confirmed by the corresponding spectra of the diiodo derivatives. *o,o'*-Diiodophenols such as **7a**, which contains a sterically hindered hydroxy group, also showed a sharp, narrow OH band in the IR spectrum.

In conclusion, the problem of regioselective monoiodination of protected phloroglucinols has been circumvented by regioselective diiodination to **7** (see Table 1). The resulting diiodo aromatic compounds are useful in natural products synthesis, giving rise to an "*o,o'*-diiodine effect" in Heck-type olefinations[3,11]. Diiodo- and triiodoaromatics

Table 1. Iodination of monoprotected 5-methoxyresorcinols



4 5 6 7 8 9

Starting material	R	Method[b]	I⁺ [eq]	T [°C][c]	t [h]	Yields [%] 5	6	7	8	9
4α[a]	H	A	2.0	0	1			64		
4β	$PhSO_2$	B	1.1	r.t.	47	11	56	26		
4a	$PhCH_2$	B	2.3	r.t.	96			67[d]		
4b	$2\text{-}O_2NC_6H_4CH_2$	B	1.5	r.t.	2			25	14	
4c	$MeOCH_2$	B	1.5	r.t.	5	19		17		
4d	$CONMe_2$	B	2.4	-10→r.t.	4			59		
4e	$CONPh_2$	B	2.3	0→r.t.	29			68		20
4f	$CON[CH_2]_5$	B	2.3	-30→r.t.	2.5	12	11	65		

[a] Commercially available (Aldrich); iodination with I^-/IO_3^-, H^+, PTC. — [b] Method A: H^+, KI/KIO_3 in CH_2Cl_2/H_2O, $Bu_4N^+HSO_4^-$; method B: $PhCH_2Et_3N^+Cl_2I^-$, $CaCO_3$, CH_2Cl_2, MeOH[10]. — [c] r.t.: room temperature. — [d] 3-Benzyloxy-2,4-diiodo-5-methoxyphenol [**8a'** (≡**8a** with MeO replaced by RO and vice versa)] is formed also (4%).

are also used as a diagnostic aid for X-ray investigations and in pharmacology[12].

We thank Dr. *E. Hofer* for advice with the NMR spectra and the *Fonds der Chemischen Industrie* for support of our work.

Experimental

Column chromatography (silica gel, 0.02–0.63 mm, Merck) was carried out under weak positive pressure. — TLC: Precoated plates, Macherey-Nagel, Merck. — Melting points: Büchi apparatus. — IR: Electrophotometer 580 and FT spectrometer 1710, Perkin-Elmer. — ^1H NMR: WP 80, WH 90, WP 200 SY and AM 300, Bruker. — ^{13}C NMR: WP 200 SY and AM 300, Bruker. — MS: Spectrometer MAT 312, Finnigan. — Elementary analyses: Microanalytical laboratory of the Department of Organic Chemistry. — Abbreviations: PE: petroleum ether; r.t.: room temperature.

3-Allyloxycarbonyloxy-5-methoxyphenol (**3**): **2** (1.27 g, 10 mmol) and dry K_2CO_3 (7 g, 50 mmol) are suspended in dry acetone (50 ml). The mixture is heated to reflux, and ALOC-Cl (3.8 ml, 4.34 g, 36 mmol) is injected under N_2. After 2 h, dimethyl sulfate (1 ml, 1.33 g, 11 mmol) is injected. Heating to reflux is continued for 3 h, finally the reaction mixture is cooled to r.t., filtered and concentrated under reduced pressure. The residue is dissolved in MeOH (10 ml) and cooled to −40°C. KOH (0.84 g, 15 mmol) in MeOH (10 ml) is added at this temperature within 10 min, stirring is continued for 10 min. The mixture is quenched with satd. aqueous NH_4Cl solution and rapidly warmed to r.t. The mixture is filtered through silica gel (ether) and concentrated under reduced pressure. The residue is purified by chromatography [Et_2O/PE (1:1)], giving the phenol as a colorless oil (1.41 g, 63%). — IR ($CHCl_3$): $\tilde{\nu}$ = 3600 cm^{-1}, 3290, 2850, 1760, 1620, 1600, 1500, 1474, 1455, 1435, 1365, 1294, 1158, 1050. — ^1H NMR ($CDCl_3$, 80 MHz): δ = 3.72 (s, 3H, OCH_3), 4.72 (ddd, ^3J = 5.5 Hz, ^4J = 1.5 Hz, ^4J = 1 Hz, 2H, OCH_2), 5.23–5.55 (m, 2H, 3'-H), 5.76–6.24 (m, 1H, 2'-H), 6.15 (br. s, 1H, OH), 6.2–6.3 (m, 3 arom. H). — MS (70 eV, 80°C): *m/z* (%) = 225 (5), 224 (38), 179 (12), 140 (21) [$M^+ - C_4H_4O_2$], 112 (25), 41 (100) [$C_3H_3^+$].

$C_{11}H_{12}O_5$ Calcd. 224.0685 Found 224.0685 (MS)

3-Benzyloxy-5-methoxyphenol (**4a**): See ref.[5].

1-Hydroxy-3-methoxy-5-(2-nitrobenzyloxy)benzene (**4b**): A solution of **4β**[5] (3.9 g, 14 mmol), K_2CO_3 (2.5 g, 18 mmol) and *o*-nitrobenzyl chloride (3.9 g, 21 mmol) in absol. acetone (50 ml) is heated to reflux for 5 h under N_2. The mixture is cooled to r.t. and filtered. The solvent is evaporated and the residue filtered through silica gel ($CHCl_3$). After removal of the solvent, the residue crystallizes from warm acetone/Et_2O. Recrystallization [$CHCl_3$/cyclohexane (1:1)] affords 5-benzenesulfonyloxy-3-methoxy-1-(2-nitrobenzyloxy)benzene (2.74 g, 48%).

A solution of 5-benzenesulfonyloxy-3-methoxy-1-(2-nitrobenzyloxy)benzene (2.74 g, 6.6 mmol) in absol. MeOH (5 ml) is treated with KOH (1.06 g, 19 mmol) in absol. MeOH (10 ml) and stirred for 19 h at room temperature under N_2. The mixture is poured into H_2O (200 ml), neutralized with HCl and extracted with EtOAc (3 × 50 ml). The combined organic layers are washed with aqueous $Na_2S_2O_3$ solution and dried ($MgSO_4$). The solvent is evaporated and the residue purified by column filtration ($CHCl_3$) to afford **4b** (1.20 g, 66%), m.p. 145°C. — IR (KBr): $\tilde{\nu}$ = 3475 cm^{-1}, 2924, 1730, 1605, 1578, 1524, 1496, 1341, 1205, 1156, 1068. — ^1H NMR ([D_6]acetone, 200 MHz): δ = 3.72 (s, 3H, OCH_3), 5.43 (s, 2H, OCH_2), 6.09, 6.12, 6.14 (3 t, 3H, 2-, 4-, 6-H), 7.59 (ddd, ^3J = ^3J = 8 Hz, ^4J = 1 Hz, 4-H), 7.74 (dd, ^3J = 8 Hz, ^4J = 1 Hz, 6-H), 7.89 (ddd, ^3J = ^3J = 8 Hz, ^4J = 1 Hz, 5'-H), 8.13 (dd, ^3J = 8 Hz, ^4J = 1 Hz, 3'-H), 8.44 (s, 1H, OH). — ^{13}C NMR ([D_6]acetone, 50.2 MHz, APT): δ = 55.45 (q, OCH_3), 67.34 (t, OCH_2), 93.72, 95.60, 95.68 (3 d, C-2, -4, -6), 125.55 (d, 4'-C), 129.55 (d, 3'-C), 129.81 (d, 5'-C), 134.13 (s, 1'-C), 134.62 (d, 6'-C), 148.41 [s, $C(NO_2)$], 160.13 [s, C(OBn)], 161.09 [s, C(OH)], 162.71 [s, C(OMe)]. — MS (70 eV,

170°C): *m/z* (%) = 275 (6), 229 (5) [$M^+ - NO_2$], 170 (1), 136 (75) [$C_7H_6NO_2^+$], 111 (17), 78 (100).

$C_{14}H_{13}NO_5$ (275.08)
Calcd. C 61.09 H 4.76 N 5.09
Found C 61.19 H 4.83 N 5.32
Calcd. 275.0794 Found 275.0789 (MS)

3-Methoxy-5-(methoxymethoxy)phenol (**4c**): To a suspension of NaH (90 mg, 3.75 mmol) in absol. THF (5 ml) is added **4β** (720 mg, 2.90 mmol) in absol. THF (10 ml). The mixture is stirred for 10 min under N_2, then MOM-Br (390 mg, 3.10 mmol) in absol. THF (1 ml) is added. After 60 min, the mixture is quenched with satd. aqueous NH_4Cl solution and extracted with Et_2O (2 × 100 ml). The combined organic layers are dried ($MgSO_4$), and the solvent is evaporated to give 3-benzenesulfonyloxy-5-(methoxymethoxy)anisole (850 mg, 90%) as a light yellow oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 1615 cm^{-1}, 1595, 1451, 1436, 1377, 1196, 1151, 1024, 852. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.40 (s, 3H, OCH_2OCH_3), 3.70 (s, 3H, OCH_3), 5.03 (s, 2H, OCH_2O), 6.22, 6.24, 6.47 (3 t, ^4J = 2 Hz, 3 arom. H), 7.45–7.90 (m, 5H, $PhSO_2O$). – MS (70 eV, 70°C): *m/z* (%) = 326 (6), 325 (14), 324 (76), 293 (10) [$C_{14}H_{13}O_5S^+$], 260 (20), 230 (26), 202 (23), 141 (36) [$PhSO_2^+$], 77 (100) [Ph^+].

$C_{15}H_{16}O_6S$ Calcd. 324.0668 Found 324.0667 (MS)

A solution of 3-benzenesulfonyloxy-5-(methoxymethoxy)anisole (810 mg, 2.50 mmol) in absol. MeOH (8 ml) is treated with KOH (2.20 g, 39.3 mmol) in absol. MeOH (10 ml) and stirred for 6.5 h at r.t. under N_2. The mixture is quenched with satd. aqueous NH_4Cl solution (20 ml) and NaCl (4 g) and extracted with Et_2O (40 ml). The aqueous layer is acidified (HCl) and extracted with EtOAc (2 × 40 ml). The combined organic layers are dried ($MgSO_4$), the solvent is evaporated, and the residue purified by column chromatography [Et_2O/PE (1:1)] to give **4c** (286 mg, 63%) as a colorless oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3598 cm^{-1}, 3325, 1603, 1496, 1473, 1441, 1147, 1081, 1059, 1033. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.47 (s, 3H, OCH_2OCH_3), 3.72 (s, 3H, OCH_3), 5.12 (s, 2H, OCH_2OMe), 6.08, 6.17, 6.19 (3 t, ^4J = 2 Hz, 3H, 2-, 4-, 6-H), 6.52 (br. s, 1H, OH). – ^{13}C NMR ($CDCl_3$, 50.2 MHz, APT): δ = 55.34 (q, OCH_3), 56.02 (q, OCH_3), 94.33 (t, OCH_2), 95.19, 95.68, 96.46 (3 d, C-2, -4, -6), 157.61 [s, C(OH)], 159.01 [s, C(OMOM)], 161.54 [s, C(OMe)]. – MS (70 eV): *m/z* (%) = 184 (16), 124 (13), 111 (7), 46 (100).

$C_9H_{12}O_4$ Calcd. 184.0736 Found 184.0736 (MS)

3-Hydroxy-5-methoxyphenyl N,N-Dimethylcarbamate (**4d**): To a solution of **3** (1.45 g, 6.47 mmol), K_2CO_3 (1.81 g, 13.1 mmol), and NaBr (870 mg, 8.50 mmol) in absol. acetone (40 ml) is added *N,N*-dimethylcarbamoyl chloride (1.20 ml, 13.0 mmol), and the mixture is heated to reflux for 7 h under N_2. After cooling to r.t., the mixture is filtered, the solvent evaporated, and the resulting residue purified by chromatography [Et_2O/PE (1:1)] to give 5-(allyloxycarbonyloxy)-3-(*N,N*-dimethylcarbamoyloxy)anisole (1.12 g, 59%) as a colorless oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 2942 cm^{-1}, 1762 (OCOO), 1719 (OCON), 1619, 1600, 1473, 1391, 1365, 1245, 1176, 1057, 964. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 2.97 (s, 3H, $NC\alpha H_3$), 3.04 (s, 3H, $NC\beta H_3$), 3.75 (s, 3H, OCH_3), 4.70 (ddd, ^3J = 6 Hz, ^4J = 1.5 Hz, ^4J = 1 Hz, 2H, OCH_2), 5.31 (ddt, $^3J_{cis}$ = 10.5 Hz, ^2J = 1.5 Hz, ^4J = 1 Hz, 3′-H^E), 5.40 (ddt, $^3J_{trans}$ = 17 Hz, ^4J = 1.5 Hz, ^2J = 1.5 Hz, 3′-H^Z), 5.97 (ddt, $^3J_{trans}$ = 17 Hz, $^3J_{cis}$ = 10.5 Hz, ^3J = 6 Hz, 2′-H), 6.60 (d, ^4J = 2 Hz, 2-, 6-H), 6.65 (dd, ^4J = 2 Hz, ^4J = 2 Hz, 4-H). – ^{13}C NMR ($CDCl_3$, 50.2 MHz): δ = 36.40 (q, $NC\alpha H_3$), 36.55 (q, $NC\beta H_3$), 55.63 (q, OCH_3), 69.17 (t, OCH_2), 104.33, 105.69, 107.45 (3 d, C-2, -4, -6), 119.46 (t, C-3′), 131.14 (d, C-2′), 151.91 (s, C-5), 152.66 (s, C-3), 153.00 [t, OC(O)N], 154.16 [s, OC(O)O], 160.64 (s, $COCH_3$, C-1). – MS (70 eV): *m/z* (%) = 297 (1), 296 (2), 295 (11) [M^+], 225 (1), 179 (4), 71 (100) [$C_2H_5NCO^+$].

$C_{14}H_{17}NO_6$ Calcd. 295.1056 Found 295.1057 (MS)

To a solution of 5-(allyloxycarbonyloxy)-3-(*N,N*-dimethylcarbamoyloxy)anisole (166 mg, 0.56 mmol) in absol. MeOH (1 ml) is added within 2 min a solution of KOH (63 mg, 1.1 mmol) in absol. MeOH (2 ml), and the mixture is stirred for 13 min under N_2. After the addition of satd. aqueous NH_4Cl solution (2 ml), the mixture is diluted with Et_2O (100 ml) and extracted with water (30 ml). The aqueous phase is reextracted with Et_2O (50 ml), and the combined organic layers are dried (Na_2SO_4). After removal of the solvent, **4d** (118 mg, 100%) is obtained as a colorless oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3600 cm^{-1}, 3318, 1713, 1616, 1473, 1393, 1270, 1176, 1157, 1058, 1000. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 2.97 (s, 3H, $NC\alpha H_3$), 3.04 (s, 3H, $NC\beta H_3$), 3.67 (s, 3H, OCH_3), 6.17 (s, 3 arom. H), 7.65 (br. s, 1H, OH). – ^{13}C NMR ($CDCl_3$, 50.2 MHz, APT): δ = 36.47 (s, $NC\beta H_3$), 36.70 (s, $NC\alpha H_3$), 55.30 (s, OCH_3), 99.18, 99.70, 102.40 (3 d, C-2, -4, -6), 152.57 (s, C-1), 155.49 (s, OCON), 158.07 [s, C(OH)], 161.00 [s, C(OMe)]. – MS (70 eV, 80°C): *m/z* (%) = 212 (4), 211 (32), 91 (22), 72 (100) [$C_3H_6NO^+$].

$C_{10}H_{13}NO_4$ Calcd. 211.0845 Found 211.0844 (MS)

3-(N,N-Diphenylcarbamoyloxy)-5-methoxyphenol (**4e**): To a solution of dry phloroglucinol (2.34 g, 18.6 mmol) and dry K_2CO_3 (14.0 g, 246 mmol) in absol. acetone (100 ml) is added ethyl chloroformate (5.74 ml, 60.0 mmol), and the mixture is heated to reflux (N_2). After 280 min, dimethyl sulfate (3.80 ml, 40.0 mmol) is added, and the mixture is heated to reflux for further 70 min. The mixture is cooled to room temperature, filtered, and the solvent is evaporated. The residue is diluted with Et_2O (200 ml) and washed with H_2O (50 ml). The aqueous phase is extracted with Et_2O (50 ml), and the combined organic layers are dried (Na_2SO_4). After removal of the solvent, the residue is purified by column chromatography [Et_2O/PE (1:2)] to afford 3,5-bis(ethoxycarbonyloxy)anisole (5.15 g, 98%) as a colorless oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 2988 cm^{-1}, 1763, 1620, 1600, 1477, 1371, 1240. – ^1H NMR ($CDCl_3$, 80 MHz): δ = 1.37 (t, *J* = 7 Hz, 6H, CH_3), 3.78 (s, 3H, OCH_3), 4.31 (q, *J* = 7 Hz, 4H, OCH_2), 6.65 (d, ^4J = 1.8 Hz, 2H, 2-, 6-H), 6.73 (dd, ^4J = 1.8 Hz, 1H, 4-H).

To a solution of 3,5-bis(ethoxycarbonyloxy)anisole (1.39 g, 4.50 mmol) in absol. MeOH (7 ml) is added within 10 min a solution of KOH (476 mg, 8.50 mmol) in absol. MeOH (5 ml) at −45° under N_2. After 10 min, satd. aqueous NH_4Cl solution is added, and the mixture is allowed to warm up to room temperature. The suspension is diluted with Et_2O (150 ml) and washed with H_2O (70 ml). The aqueous phase is extracted with Et_2O (70 ml), and the combined organic phases are dried (Na_2SO_4). After removal of the solvent, the residue is chromatographed [Et_2O/PE (1:1)] to give starting material (244 mg) and 3-ethoxycarbonyl-5-methoxyphenol (681 mg, 79%) as a yellow oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3600 cm^{-1}, 3300, 2986, 2844 (OMe), 1761, 1621, 1496, 1474, 1440, 1395, 1372, 1347, 1255, 1157, 1055, 1000, 888, 840. – ^1H NMR ($CDCl_3$, 80 MHz): δ = 1.38 (t, ^3J = 7 Hz, 3H, CH_3), 3.74 (s, 3H, OCH_3), 4.31 (q, ^3J = 7 Hz, 2H, OCH_2), 5.70 (s, 1H, OH), 6.25 (d, ^4J = 2 Hz, 2H, 2-, 6-H), 6.29 (dd, ^4J = 2 Hz, 1H, 4-H). – MS (70 eV): *m/z* (%) = 214 (4), 213 (24), 212 (88) [M^+], 183 (5) [$M^+ - C_2H_5$], 140 (100) [$M^+ - C_3H_4O_2$], 111 (89), 110 (81).

To a solution of 3-ethoxycarbonyloxy-5-methoxyphenol (628 mg, 2.96 mmol), NaBr (450 mg, 4.37 mmol) and K_2CO_3 (820 mg, 5.85 mmol) in absol. acetone (15 ml) is added *N,N*-diphenylcarbamoyl chloride (1.02 g, 4.40 mmol). The mixture is heated to reflux for 4 h (N_2), then further carbamoyl chloride (500 mg, 2.16 mmol) is added, and heating to reflux is continued for 14 h. After cooling to room

temperature, filtration and removal of the solvent, the residue is diluted with Et_2O (200 ml) and washed with H_2O (100 ml). The aqueous phase is extracted with Et_2O (100 ml), and the combined organic layers are dried (Na_2SO_4). Removal of the solvent and column chromatography [Et_2O/PE (1:2)] give 5-(*N,N*-diphenylcarbamoyloxy)-3-(ethoxycarbonyloxy)anisole (707 mg, 59%) as a colorless wax. – IR ($CHCl_3$): $\tilde{\nu}$ = 2840 cm^{-1}, 1761 (OCO_2), 1729 (NCO_2), 1619, 1598, 1493, 1476, 1347, 1302, 1206, 1156, 1136, 1056, 1039, 1022. – ^1H NMR ($CDCl_3$, 80 MHz): δ = 1.36 (t, *J* = 7 Hz, 3H, CH_3), 3.75 (s, 3H, CH_3), 4.28 (q, *J* = 7 Hz, 2H, OCH_2), 6.55–6.70 (m, 3 arom. H), 7.32 (br. s, 10 arom. H, NPh). – MS (70 eV, 180°C): *m/z* (%) = 407 (11), 369 (10), 368 (13), 262 (11), 230 (19), 195 (30) [$C_{13}H_9NO^+$], 151 (37), 123 (100).

$C_{23}H_{21}NO_6$ Calcd. 407.1369 Found 407.1370 (MS)

5-(*N,N*-Diphenylcarbamoyloxy)-3-(ethoxycarbonyloxy)anisole (641 mg, 1.57 mmol) is allowed to react as described for 3-ethoxycarbonyloxy-5-methoxyphenol to give after chromatography [Et_2O/PE (1:1)] starting material (190 mg) and **4e** (249 mg, 67%) as an amorphous solid, m.p. 150° (dec.). – IR ($CHCl_3$): $\tilde{\nu}$ = 3600 cm^{-1}, 3300, 2840, 1719, 1630, 1600, 1494, 1354, 1303, 1157, 1132, 1057, 1042, 1024. – ^1H NMR ($CDCl_3$, 80 MHz): δ = 3.68 (s, 3H, OCH_3), 5.96 (br. s, 1H, OH), 6.13, 6.20, 6.23 (3 t, ^4J = 2 Hz, 3H, 2-, 4-, 6-H), 7.2–7.4 (m, 10 arom. H, NPh). – MS (70 eV, 130°C): *m/z* (%) = 336 (8), 335 (32), 197 (16), 196 (100) [$(Ph)_2NCO^+$], 168 (41) [$(Ph)_2N^+$].

$C_{20}H_{17}NO_4$ Calcd. 335.1158 Found 335.1158 (MS)

3-Hydroxy-5-methoxyphenyl N-Piperidylcarbamate (**4f**): A solution of **3** (540 mg, 2.40 mmol) in absol. acetone (20 ml) is treated with K_2CO_3 (500 mg, 3.60 mmol) and carbonyldiimidazolide (600 mg, 3.60 mmol). After 90 min at r.t. under N_2, absol. piperidine (1.0 ml, 10 mmol) is added. The mixture is stirred for 19 h, then $ZnCl_2 \cdot OEt_2$ (0.5 ml of a 2.2 M solution in CH_2Cl_2, 1.1 mmol) is added. After 10 min, the mixture is treated with EtOAc (100 ml) and washed with satd. aqueous NH_4Cl solution. The organic phase is filtered without delay through silica gel (15 g; EtOAc). The solvent is evaporated and the residue purified by column chromatography [Et_2O/PE (1:1)]. First *N*-(allyloxycarbonyl)piperidine (colorless liquid), then the phenol is eluted (455 mg, 75%) as colorless needles, instable, m.p. 64°C. – IR ($CHCl_3$): $\tilde{\nu}$ = 3600 cm^{-1}, 3333, 2944, 2861, 1702, 1606, 1494, 1469, 1428, 1355, 1257, 1236, 1152, 1058, 1025, 1008. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.60 (br. s, 6H, $[CH_2]_3$), 3.47 (br. s, 2H, NCH_2^Z), 3.56 (br. s, 2H, NCH_2^E), 3.65 (s, 3H, OCH_3), 6.16, 6.18, 6.20 (3 t, ^4J = 1.5 Hz, 3H, 2-, 4-, 6-H), 7.23 (br. s, 1H, OH). – ^{13}C NMR ($CDCl_3$, 50.2 MHz, APT): δ = 24.13 (t, C-4′), 25.41, 25.77 (2 t, C-3′, -5′), 45.26, 45.60 (2 t, C-2′, -6′), 55.37 (q, OCH_3), 99.27, 100.13, 102.59 (3 d, C-2, -4, -6), 152.52 (s, C-1, *C*OCON], 154.35 (s, OCON), 157.73 [s, C-3, C(OH)], 160.97 [s, C-5, C(OMe)]. – MS (70 eV, 120°C): *m/z* (%) = 252 (27), 251 (54), 140 (69) [$M^+ - C_5H_{10}NCO$], 112 (100) [$C_5H_{10}NCO^+$], 69 (74).

$C_{13}H_{17}NO_4$ (251.12)
Calcd. C 62.14 H 6.82 N 5.57
Found C 58.46 H 6.36 N 4.10
Calcd. 251.1158 Found 251.1157(MS)

2,4-Diiodo-5-methoxyresorcinol[3] (**7α**): Concd. HCl (0.64 ml) is added to a solution of **4α** (562 mg, 4.00 mmol) and $nBu_4N^+HSO_4^-$ (20 mg) in CH_2Cl_2 (30 ml) at 0°C (N_2). Within 1 h, a solution of KI (890 mg, 5.30 mmol) and KIO_3 (565 mg, 2.60 mmol) in H_2O (25 ml) is added, then the mixture is allowed to reach r.t. The layers are separated, the aqueous phase is extracted with CH_2Cl_2 (2 × 10 ml), the combined organic phases are washed with satd. aqueous $Na_2S_2O_3$ solution and dried ($MgSO_4$). After removal of the solvent and fast column filtration (CH_2Cl_2), the residual solid is crystallized from $CHCl_3$ to give light-sensitive **7α** (998 mg, 64%; ref.[3] 9%) as colorless needles, m.p. 127°C (dec.). – ^1H NMR ([D_6]acetone): δ = 3.81 (s, 3H, OCH_3), 6.32 (s, 6-H), 7.62 (br. s, OH), 9.19 (br. s, OH). – ^{13}C NMR ([D_6]acetone): δ = 56.86 (q, OCH_3), 64.16 (s, C-2), 64.74 (s, C-4), 92.39 (d, C-6), 157.04 (s, C-3), 159.48 (s, C-1), 160.84 (s, C-5). – MS (70 eV, 40°C): *m/z* (%) = 392 [M^+].

3-Benzenesulfonyloxy-2-iodo-5-methoxyphenol (**5β**), *5-Benzenesulfonyloxy-2-iodo-3-methoxyphenol* (**6β**), *and 3-Benzenesulfonyloxy-2,6-diiodo-5-methoxyphenol* (**7β**): To a solution of **4β** (90 mg, 0.32 mmol) and $CaCO_3$ (100 mg, 1.00 mmol) in absol. CH_2Cl_2 (1.7 ml) and absol. MeOH (0.7 ml) is added $PhCH_2Et_3N^+Cl_2I^-$ [10] (130 mg, 0.33 mmol), and the mixture is stirred for 47 h under N_2. After column filtration and removal of the solvent, the resulting residue is purified by column chromatography [PE/CH_2Cl_2 (2:1)]. First **7β**, then **5β** and **6β** are eluted.

5β: 14 mg (11%) of an oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3300 cm^{-1}, 2930, 1670, 1610, 1595, 1585, 1470, 1450, 1430, 1380, 1180, 1160, 1095, 1080, 1060, 1010, 840. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.80 (s, 3H, OCH_3), 6.2 (br. s, 1H, OH), 6.38 (d, ^4J = 3 Hz, 1 arom. H), 6.56 (d, ^4J = 3 Hz, 1 arom. H), 7.48–8.0 (m, 5 arom. H, $PhSO_3$). – MS (70 eV, 60°C): *m/z* (%) = 406 (1), 318 (1), 281 (0.5), 280 (1), 279 (8), 278 (5), 215 (9), 187 (6), 166 (11), 148 (27), 77 (39), 73 (100).

$C_{13}H_{11}IO_5S$ Calcd. 405.9372 Found 405.9371 (MS)

6β: 73 mg (56%) of an oil. – IR (film): $\tilde{\nu}$ = 3450 cm^{-1}, 1599, 1583, 1462, 1450, 1421, 1372, 1340, 1313, 1216, 1191, 1177, 1093, 1000, 843. 788, 755, 723. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.74 (s, 3H, OCH_3), 6.00 (br. s, 1H, OH), 6.10, 6.28 (2 d, ^4J = 2.5 Hz, 2H, 4-, 6-H), 7.5–7.9 (m, 5H, $PhSO_3$). – ^{13}C NMR ($CDCl_3$, 50.2 MHz, APT {gated decoupling}): δ = 56.69 (q, OCH_3), 75.77 (s {t}, *J* = 7, C-2), 98.01 (d {dd}, C-4), 101.97 (d {dd}, C-6), 128.53, 129.25, 134.43 (3 d, C-2′, -3′, -4′), 135.14 (s, C-1′), 151.81 [s {t}, $C(OSO_2)$], 156.44 [s {d}, C(OH)], 159.09 [s {quint}, C(OMe)]. – MS (70 eV, 50°C): *m/z* (%) = 407 (1), 406 (4), 313 (2), 265 (1) [$M^+ - PhSO_2$], 264 (2), 249 (2) [$M^+ - PhSO_3$], 86 (74), 84 (100).

$C_{13}H_{11}IO_5S$ Calcd. 405.9372 Found 405.9371 (MS)

7β: 45 mg (26%) of hexagonal plates, m.p. 128°C. – IR ($CHCl_3$): $\tilde{\nu}$ = 3460 cm^{-1}, 2930, 1610, 1580, 1570, 1560, 1460, 1450, 1400, 1380, 1330, 1100, 1010. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.83 (s, 3H, OCH_3), 6.04 (br. s, 1H, OH), 6.53 (s, 1H, 4-H), 7.52–8.0 (m, 5H, $PhSO_3$). – ^{13}C-NMR ($CDCl_3$, 50.2 MHz, APT {gated decoupling}): 56.94 (q, OCH_3), 69.12, 73.04 (2 s {dd}, C-2, -6), 98.60 (d {d}, C-4), 128.89, 129.30, 134.75 (3 d, C-2′, -3′, -4′), 135.57 (s, C-1′), 151.53 (s {d}, C-3), 155.45 [s {s}, C(OH)], 159.52 [s {dq}, C(OMe)]. – MS (70 eV, 50°C): *m/z* (%) = 532 (0.5), 531 (3), 442 (1), 441 (5), 439 (19), 408 (0.5), 407 (10), 406 (100), 263 (23), 146 (70), 118 (63).

$C_{13}H_{10}I_2O_5S$ (532.09)
Calcd. C 29.34 H 1.89
Found C 28.01 H 2.19
Calcd. 530.8260 Found 530.8260(MS)

3-Benzyloxy-2,6-diiodo-5-methoxyphenol (**7a**) *and 3-Benzyloxy-2,4-diiodo-5-methoxyphenol* (**8a′**): To a suspension of **4a** (485 mg, 2.10 mmol) and $CaCO_3$ (660 mg, 6.60 mmol) in absol. MeOH (4.2 ml) is added $PhCH_2Et_3N^+Cl_2I^-$ (1.90 g, 4.80 mmol) in absol. CH_2Cl_2 (11 ml), the mixture is stirred for 96 h at r.t. (N_2) and then filtered through silica gel (CH_2Cl_2). The filtrate is washed with satd. aqueous $Na_2S_2O_3$ solution and dried ($MgSO_4$). Removal of the solvent and chromatography [PE/CH_2Cl_2 (1:1)] gives first **7a**, then **8a′**.

7a: 678 mg (67%) of colorless, hexagonal crystals, m.p. 129.5°C. – IR ($CHCl_3$): $\tilde{\nu}$ = 3468 cm^{-1}, 1575, 1463, 1404, 1341, 1303, 1231, 1180, 1114, 1076, 1039. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.83 (s, 3H, OCH_3), 5.17 (s, 2H, OCH_2), 6.00 (s, 1H, OH), 6.10 (s, 1H, 4-H), 7.3–7.52 (m, 5H, Ph). – ^{13}C NMR ([D_7]DMF, 50.2 MHz, APT {gated decoupling}): δ = 57.04 (q {q}, OCH_3), 67.51, 67.83 (2 s {d}, C-2, -6), 71.35 (t {tt}, $PhCH_2$), 90.92 (d {d}, C-4), 127.75, 128.22, 128.82 (3 d {m}, C-2′, -3′, -4′), 137.20 (s {m}, C-1′), 157.26 [s {s}, C(OH)], 159.62 [s {q}, C(OBn)], 160.52 [s {quint}, C(OMe)]. – MS (70 eV, 80°C): *m/z* (%) = 483 (0.5), 482 (3), 481 (18), 391 (1) [M^+ – Bn], 357 (1), 356 (3), 355 (22) [M^+ – I], 263 (2), 262 (1), 91 (100) [Bn^+].

$C_{14}H_{12}I_2O_3$ (482.06)
Calcd. C 34.88 H 2.51
Found C 34.78 H 2.55
Calcd. 481.8880 Found 481.8874(MS)

8a′: 44 mg (4.3%) of a colorless oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3485 cm^{-1}, 3300, 1672, 1580, 1563, 1498, 1456, 1426, 1414, 1379, 1291, 1209, 736. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 2.95 (br. s, 1H, OH), 3.86 (s, 3H, OCH_3), 5.01 (s, 2H, OCH_2Ph), 6.57 (s, 1H, 6-H), 7.36–7.77 (m, 5H, Ph). – ^{13}C NMR ([D_6]acetone, 50.2 MHz, APT {gated decoupling}): δ = 56.96 (q {q}, OCH_3), 71.68, 71.73 (2 s {d}, C-2, -4), 74.48 (t {tt}, $PhCH_2$), 96.19 (d {d}, C-6), 128.92, 129.05, 129.23 (3 d {m}, C-2′, -3′, -4′), 137.67 (s {m}, C-1′), 159.88 [s {dd}, C(OH)], 160.05 [s {m}, C(OBn)], 161.25 [s {dq}, C(OMe)]. – MS (70 eV, 60°C): *m/z* (%) = 482 (0.5), 481 (2), 480 (8), 356 (1), 355 (6) [M^+ – I], 354 (21) [M^+ – HI], 263 (3), 91 (100) [Bn^+], 83 (89).

$C_{14}H_{11}O_3I_2$ Calcd. 480.8798 Found 480.9643 (MS)

2,6-Diiodo-3-methoxy-5-(2-nitrobenzyloxy)phenol (**7b**) *and 2,4-Diiodo-3-methoxy-5-(2-nitrobenzyloxy)phenol* (**8b**): Compound **4b** (1.17 g, 4.23 mmol) is allowed to react as described for **7a**, **8a′**. Chromatography [CH_2Cl_2/PE (3:1)] gives first **7b**, then **8b**.

7b: 568 mg (25%) of fine, yellow needles, m.p. 170°C (dec.). – IR (KBr): $\tilde{\nu}$ = 3453 cm^{-1}, 2926, 1613, 1575, 1524, 1462, 1447, 1404, 1381, 1338, 1308, 1212, 1116, 786, 728. – ^1H NMR ([D_7]DMF, 200 MHz): δ = 3.94 (s, 3H, OCH_3), 4.55 (br. s, 1H, OH), 5.66 (s, 2H, OCH_2), 6.57 (s, 1H, 4-H), 7.70 (ddd, ^3J = ^3J = 7.5 Hz, ^4J = 1 Hz, 1H, 4′-H), 7.89 (ddd, ^3J = ^3J = 7.5 Hz, ^4J = 1 Hz, 1H, 5′-H), 8.11 (dd, ^3J = 7.5 Hz, ^4J = 1 Hz, 1H, 6′-H), 8.22 (dd, ^3J = 7.5 Hz, ^4J = 1 Hz, 3′-H). – ^{13}C NMR ([D_7]DMF, 50.2 MHz, APT {gated decoupling}): δ = 57.15 (q {q}, OCH_3), 67.81 (s {d}, CI), 68.71 (t {td}, OCH_2), 68.72 (s {d}, CI), 90.89 (d {d}, C-4), 125.51 (d {ddd}, C-4′), 128.81 (d {dd}, C-3′), 130.26 (d {ddd}, C-5′), 132.91 (s {m}, C-1′), 134.67 (d {dd}, C-6′), 148.02 (s {t}, CNO_2, C-2′), 157.72 (s {s}, C(OH), C-1), 159.42 (s {m}, $COCH_2$, C-5), 160.86 (s {dq}, COMe, C-3). – MS (70 eV, 160°C): *m/z* (%) = 528 (1), 527 (6), 392 (4), 391 (1), 363 (2), 264 (5) [M^+ – I – $C_7H_6NO_2$], 221 (4), 136 (100) [$C_7H_6NO_2^+$].

$C_{14}H_{11}I_2NO_5$ (527.05)
Calcd. C 31.90 H 2.10 N 2.65
Found C 31.58 H 2.24 N 3.14
Calcd. 526.8727 Found 526.8753(MS)

8b: 307 mg (14%) of an amorphous solid, m.p. 147°C. – IR (KBr): $\tilde{\nu}$ = 3458 cm^{-1}, 2933, 2851, 1570, 1522, 1451, 1392, 1338, 1228, 1103, 1063, 728. – ^1H NMR ([D_7]DMF, 200 MHz): δ = 3.83 (s, 3H, OCH_3), 4.9 (br. s, 1H, OH), 5.56 (s, 2H, OCH_2), 6.67 (s, 6-H), 7.71 (ddd, ^3J = ^3J = 8 Hz, ^4J = 1.5 Hz, 5′-H), 7.93 (ddd, ^3J = ^3J = 8 Hz, ^4J = 1.5 Hz, 4′-H), 8.15 (dd, ^3J = 8 Hz, ^4J = 1.5 Hz, 6′-H), 8.26 (dd, ^3J = 8 Hz, ^4J = 1.5 Hz, 3′-H). – ^{13}C NMR ([D_7]DMF, 50.2 MHz, APT {gated decoupling}): δ = 60.61 (q {q}, OCH_3), 68.56 (t {td}, OCH_2), 70.08 (s {d}, CI), 71.20 (s {d}, CI), 97.16 (d {d}, C-6), 125.66 (d {dd}, C-3′), 129.70, 129.71 (2 d {td}, C-4′, -5′), 134.34 (s {m}, C-1′), 134.97 (d {dd}, C-6′), 147.70 (s {m}, CNO_2), 159.25 (s {dt}, C-5), 160.61 [s {d}, C(OH)], 161.25 [s {q}, C(OMe)]. – MS (70 eV, 140°C): *m/z* (%) = 528 (2), 527 (8), 393 (1), 392 (4), 264 (4) [M^+ – I – $C_7H_6NO_2$], 249 (5), 221 (4), 136 (100) [$C_7H_6NO_2^+$].

$C_{14}H_{11}I_2NO_5$ (527.05)
Calcd. C 31.90 H 2.10 N 2.65
Found C 31.74 H 2.23 N 2.89
Calcd. 526.8727 Found 526.8718(MS)

2-Iodo-5-methoxy-3-(methoxymethoxy)phenol (**5c**) *and 2,6-Diiodo-3-methoxy-5-(methoxymethoxy)phenol* (**7c**). Compound **4c** (85 mg, 0.46 mmol) is allowed to react as described for **7a**, **8a′**. Chromatography [Et_2O/PE (1:1)] gives first **7c**, then **5c**.

5c: 27 mg (19%) of an oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3592 cm^{-1}, 3317, 1588, 1466, 1404, 1338, 1240, 1230, 1156, 1115, 1078, 1040, 1027. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.53 [t, *J* = 0.5 Hz, 3H, OCH_2OCH_3 (*o*-iodinated)], 3.85 (s, 3H, OCH_3), 5.22 (s, 2H, OCH_2OMe), 5.55 [br. s, 1H, OH (*o*-iodinated)], 6.15, 6.33 (2 s, ^4J = 2.5 Hz, 4-, 6-H). – MS (70 eV, 100°C): *m/z* (%) = 310 (3), 309 (24) [M^+ – H], 278 (10) [M^+ – CH_3OH], 183 (12) [M^+ – I], 85 (40), 83 (62), 46 (100) [$C_2H_6O^+$].

$C_9H_{11}IO_4$ Calcd. 309.9702 Found 309.9701 (MS)

7c: 33 mg (17%) of crystals, m.p. 94°C. – IR ($CHCl_3$): $\tilde{\nu}$ = 3468 cm^{-1}, 1578, 1464, 1402, 1337, 1155, 1110, 1052, 1035. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.51 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 5.27 (s, 2H, OCH_2), 6.00 (br. s, 1H, OH), 6.36 (s, 1H, 4-H). – ^{13}C NMR ([D_7]DMF, 50.2 MHz): δ = 56.70 (qt, CH_2OCH_3), 57.06 (q, OCH_3), 68.69, 69.10 (2 d, C-2, -6), 92.50 (d, C-4), 95.92 (tq, CH_2OMe), 157.73 [s, C(OH)], 158.74 [dt, C(OMOM)], 160.76 [dq, C(OMe)]. – MS (70 eV): *m/z* (%) = 436 (22), 354 (16), 323 (38), 308 (19) [M^+ – HI], 232 (100), 202 (72).

$C_9H_{10}I_2O_4$ (435.98)
Calcd. C 24.79 H 2.31
Found C 29.84 H 3.38
Calcd. 435.8669 Found 435.8670(MS)

3-(N,N-Dimethylcarbamoyloxy)-2,6-diiodo-5-methoxyphenol (**7d**): Compound **4d** (419 mg, 1.98 mmol) is allowed to react as described for **7a**, **8a′**. Chromatography (CH_2Cl_2) gives 540 mg (59%) of colorless crystals, m.p. 121°C. – IR ($CHCl_3$): $\tilde{\nu}$ = 3472 cm^{-1}, 2941, 1729, 1582, 1463, 1394, 1334, 1163, 1101, 1041. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.05 (s, 3H, NCH_3), 3.19 (s, 3H, NCH_3), 3.86 (s, 3H, OCH_3), 6.04 [s, 1H, OH (*o,o*-diiodinated)], 6.44 (s, 1H, 4-H). – ^{13}C NMR ($CDCl_3$, 50.2 MHz): δ = 36.81, 36.93 [2 q, $N(CH_3)_2$], 56.80 (q, OCH_3), 69.74, 71.32 (2 s, C-2, -6), 99.10 (d, C-4), 153.27 [s, C(OH)], 153.56 [s, *C*OC(O)N], 155.00 [s, OC(O)N], 159.52 [s, C(OMe)]. – MS (70 eV, 140°C): *m/z* (%) = 463 (14), 462 (34), 335 (44) [M^+ – HI], 264 (14) [M^+ – HI – C_3H_5NO], 221 (18), 72 (100) [$C_3H_6NO^+$].

$C_{10}H_{11}I_2NO_4$ (463.01)
Calcd. C 25.94 H 2.39 N 3.04
Found C 24.56 H 2.37 N 3.16
Calcd. 462.8778 Found 462.8783(MS)

5-(N,N-Diphenylcarbamoyloxy)-2,6-diiodo-3-methoxyphenol (**7e**) *and 5-(N,N-Diphenylcarbamoyloxy)-2,4,6-triiodo-3-methoxyphenol* (**9e**): Compound **4e** (180 mg, 0.54 mmol) is allowed to react as described for **7a**, **8a′**. Chromatography [$CHCl_3$/PE (3:1)] gives first **7e**, then the triiodide **9e**.

7e: 214 mg (68%) of a yellow wax. – IR ($CHCl_3$): $\tilde{\nu}$ = 3467 cm^{-1}, 1734, 1582, 1491, 1464, 1404, 1357, 1320, 1301, 1197, 1104. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.85 (s, 3H, OCH_3), 6.45

(s, 4-H), 7.35 (br. s, 1H, OH), 7.35–7.50 (m, 10 arom. H, NPh_2). – ^{13}C NMR ($CDCl_3$, 50.2 MHz, APT): δ = 56.82 (q, OMe), 69.50, 71.54 (2 s, C-2, -6), 98.86 (d, C-4), 126.85, 129.11 (2 d, 10 arom. C, C-2′, -3′, -4′), 141.80 (s 2 arom. C, C-1′), 151.52 (s, C-5), 153.46 (s, OCON), 155.07 [s, C(OH)], 159.38 [s, C(OMe)]. – MS (170°C): *m/z* (%) = 588 (7), 587 (17) [M^+], 461 (5), 460 (8) [$M^+ - I$], 232 (5), 230 (8), 197 (18), 196 (100) [Ph_2NCO^+], 168 (52) [Ph_2N^+].

9e: 75 mg (20%) of a colorless, amorphous solid, m.p. 195°C (dec.). – IR (KBr): $\tilde{\nu}$ = 3446 cm^{-1}, 1735, 1592, 1542, 1492, 1350, 1300, 1194, 758, 695. – ^1H NMR ([D_6]DMSO, 200 MHz): δ = 3.35 (s, 3H, OCH_3), 3.73 (s, 1H, OH), 7.25–7.70 (m, 10 arom. H, NPh_2). – ^{13}C NMR ($CDCl_3$, 50.2 MHz APT): δ = 78.64, 80.78, 81.84 (3 s, C-2, -4, -6), 141.51, 142.18 (2 s, 2 arom. C, C-1′), 150.03 (s, C-3), 152.93 (s, OCON), 158.25 [s, C(OH)], 160.41 [s, C(OMe)]; error in APT parameters deletes all signals > s. – MS (70 eV, 350°C): *m/z* (%) = 714 (33), 713 (66) [M^+], 712 (36) [$M^+ - H$], 586 (66) [$M^+ - I$], 459 (56) [$M^+ - 2\,I$], 196 (100) [Ph_2NCO^+], 168 (70) [Ph_2N^+].

$C_{20}H_{14}I_3NO_4$ (713.05)
Calcd. C 33.69 H 1.98 N 1.96
Found C 29.59 H 1.89 N 2.06

3-Hydroxy-2-iodo-5-methoxyphenyl N-Piperidylcarbamate (**5f**), *3-Hydroxy-4-iodo-5-methoxyphenyl N-Piperidylcarbamate* (**6f**), *and 3-Hydroxy-2,4-diiodo-5-methoxyphenyl N-Piperidylcarbamate* (**7f**): Compound **4f** (294 mg, 1.16 mmol) is allowed to react as described for **7a**, **8a′**. Chromatography [$CHCl_3$/PE (7:2)] gives first the diiodide **7f**, then the monoiodophenols.

5f: 52 mg (12%) of a yellow oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3483 cm^{-1}, 3300, 1708, 1596, 1466, 1425, 1256, 1148, 1101, 1020. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.63 (br. s, 6H), 3.52 (br. s, 2H), 3.56 (br. s, 2H), 3.58 (br. s, 1H, OH), 3.85 (s, 3H, OCH_3), 6.23, 6.42 (2 d, ^4J = 2.5 Hz, 2H, 2-, 6-H). – ^{13}C NMR ($CDCl_3$, 50.2 MHz, APT): δ = 24.23, 25.51, 25.88 (3 t, C-3′, -4′, -5′), 45.22, 45.55 (2 t, C-2, -6), 56.61 (q, OMe), 73.18 (s, C-2), 97.22, 101.91 (2 d, C-4, -6), 152.44 (s, COCON), 153.64 (s, OCON), 156.47 [s, C(OH)], 158.99 [s, C(OMe)]. – MS (70 eV, 90°C): *m/z* (%) = 378 (3), 377 (7) [M^+], 112 (37) [$C_5H_{10}NCO^+$], 83 (100) [$C_5H_9N^+$].

$C_{13}H_{16}INO_4$ Calcd. 377.0124 Found 377.0124 (MS)

6f: 46 mg (11%) of a yellow oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3287 cm^{-1}, 2944, 2861, 1969, 1592, 1467, 1445, 1422, 1264, 1255, 1235, 1157, 1147, 1101. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.69 (br. s, 6H), 3.56 (br. s, 2H), 3.70 (br. s, 2H), 3.74 (s, 3H, OCH_3), 5.86, 6.26 (2 d, ^4J = 2.5 Hz, 2H, 2-, 6-H), 7.7 (br. s, 1H, OH). – ^{13}C NMR ($CDCl_3$, 50.2 MHz, APT): δ = 24.24, 25.60, 25.93 (3 t, C-3′, -4′, -5′), 45.45, 45.91 (2 t, C-2′, -6′), 56.48 (q, OMe), 70.89 (s, C-4), 97.40 (d, C-6), 104.85 (d, C-2), 152.12 (s, COCON), 153.12 (s, OCON), 158.90 [s, C(OH)], 159.90 [s, C(OMe)]. – MS (70 eV, 220°C): *m/z* (%) = 377 (5) [M^+], 376 (2) [$M^+ - H$], 266 (2), 251 (12), 250 (27) [$M^+ - I$], 112 (100) [$C_5H_{10}NCO^+$].

$C_{13}H_{16}INO_4$ Calcd. 377.0124 Found 377.0113 (MS)

7f: 377 mg (65%) of a yellow oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3470 cm^{-1}, 2943, 2860, 1713, 1581, 1569, 1464, 1426, 1405, 1342, 1199, 1171, 1143, 1103, 1078, 909. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.69 (br. s, 6H), 3.53 (br. s, 2H), 3.69 (br. s, 2H), 3.86 (s, 3H, OCH_3), 6.10 (br. s, 1H, OH), 6.43 (s, 1H, 4-H). – ^{13}C NMR ($CDCl_3$, 50.2 MHz): δ = 24.20, 25.54, 25.97 (3 t, C-3′, -4′, -5′), 45.38, 45.88 (2 t, C-2′, -6′), 56.82 (q, OMe), 68.78, 71.32 (2 s, C-2, -4), 99.24 (d, C-6), 152.03 (s, COCON), 153.47 (s, OCON), 155.47 [s, C(OH)], 159.28 [s, C(OMe)]. – MS (70 eV, 80°C): *m/z* (%) = 503 (1) [M^+], 376 (4) [$M^+ - I$], 112 (7) [$C_5H_{10}NCO^+$], 83 (100) [$C_5H_9N^+$].

$C_{13}H_{15}I_2NO_4$ Calcd. 502.9091 Found 502.9158 (MS)

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CAS Registry Numbers

2: 108-73-6 / **3**: 140410-40-8 / **4α**: 2174-64-3 / **4β**: 3753-56-8 / **4a**: 105381-42-8 / **4b**: 140410-27-1 / **4c**: 140410-28-2 / **4d**: 140410-29-3 / **4e**: 140410-30-6 / **4f**: 140410-31-7 / **5β**: 139220-54-5 / **5c**: 140410-32-8 / **5f**: 140410-33-9 / **6β**: 139220-55-6 / **6f**: 140410-34-0 / **7α**: 134810-56-3 / **7β**: 140410-35-1 / **7a**: 139220-59-0 / **7b**: 139220-56-7 / **7c**: 140410-36-2 / **7d**: 139220-60-3 / **7e**: 139220-62-5 / **7f**: 139220-61-4 / **8a′**: 140410-37-3 / **8b**: 140410-38-4 / **9e**: 140410-39-5 / $H_2C{=}CHCH_2OCOCl$: 2937-50-0 / $2\text{-}O_2NC_6H_4CH_2Cl$: 612-23-7 / $MeOCH_2Br$: 13057-17-5 / Me_2NCOCl: 79-44-7 / Ph_2NCOCl: 83-01-2 / $H_2C{=}CHCH_2OCON[CH_2]_5$: 17738-04-4 / KI: 7681-11-0 / KIO_3: 7758-05-6 / $PhCH_2Et_3N^+Cl_2I^-$: 140410-47-5 / *N,N′*-carbonyldiimidazole: 530-62-1 / piperidine: 110-89-4 / 5-benzenesulfonyloxy-3-methoxy-1-(2-nitrobenzyloxy)benzene: 140410-41-9 / 3-benzenesulfonyloxy-5-(methoxymethoxy)anisole: 140410-42-0 / 5-(allyloxycarbonyloxy)-3-(*N,N*-dimethylcarbamoyloxy)anisole: 140410-43-1 / 3,5-bis(ethoxycarbonyloxy)anisole: 140410-44-2 / 3-ethoxycarbonyloxy-5-methoxyphenol: 140410-45-3 / 5-(*N,N*-diphenylcarbamoyloxy)-3-(ethoxycarbonyloxy)anisole: 140410-46-4