Tetrahedron Vol. 47, No. 45, pp. 9357-9368, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00
Pergamon Press plc

On the Way to Aflatoxins and Related Structure Types. Regio-controlled Annulations by Application of Homogenous Palladium Catalysis, Urethane Tether and ortho,ortho'-Diiodine Effect

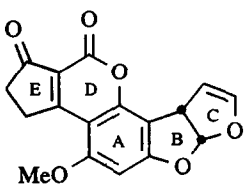
Boris Schmidt and H. Martin R. Hoffmann*

Department of Organic Chemistry, University of Hannover,
Schneiderberg 1 B, 3000 Hannover, Germany

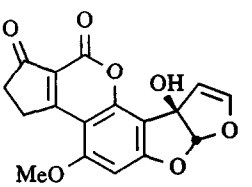
(*Received in Germany* 8 *July* 1991)

Abstract: Homogenous palladium catalyzed intramolecular hydroarylation of appropiately functionalized ortho-iodophenoxyfuranones afforded ABC substructures of AFM_1 and austocystine. The o,o'-diiodine effect, coupled with an appropiate urethane tether, allowed regio-controlled annulations.

Introduction. We have previously reported the synthesis of potential AFB_1 and AFM_1 precursors.[1-3] Specifically, the advanced precursor **5h** was obtained as outlined (Scheme 1). The annulation **4a** → **5h** was



1 AFB_1



2 AFM_1

not possible by free radical methodology (Bu_3SnH, hv or Δ, AIBN), but was accomplished by a palladium catalyzed intramolecular hydroarylation.

Results. Following this synthetic concept we have now prepared further model AC precycles **4** (Table 1) and investigated the generality of the intramolecular hydroarylation, exemplified by the transformation **4a** → **5h**. Primary goals were to optimize this step and to gain added mechanistic insight. Replacement of the benzenesulfonyloxy group in **4** by a methoxy group was desirable in order to save two potentially awkward protecting and deprotecting steps and thus provide an abbreviated access to the required ABC building blocks.

Scheme 1.

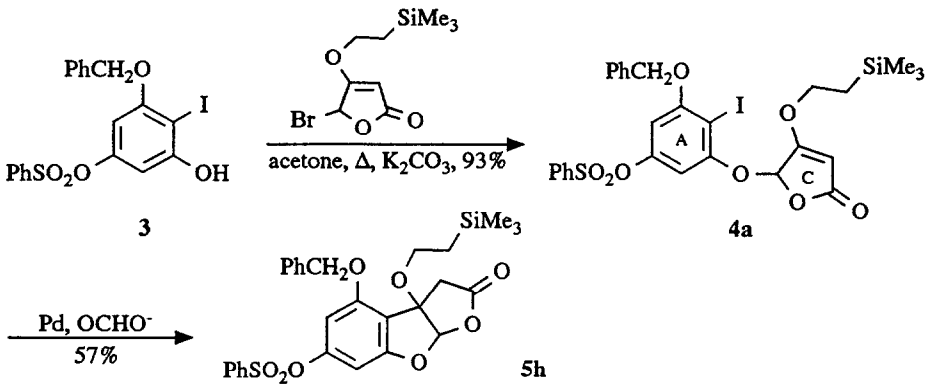
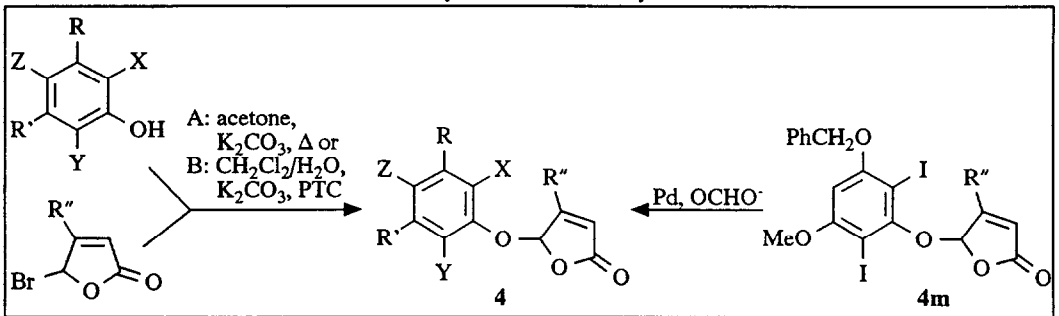


Table 1. Synthesis of AC Precycles.[a,b]

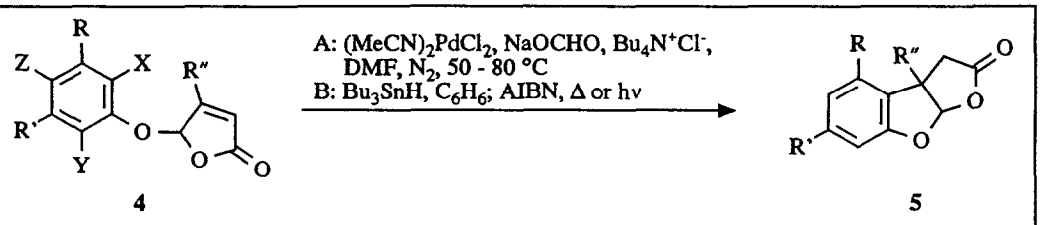


4	R	R'	R''	X	Y	Z	A/B	t [h]	Yield [%]
b	$PhCH_2O$	$PhSO_2O$	H	I	I	H	B	1.5	59
c	H	H	Me_3CCO_2	I	H	H	A	7.5	24
d	$PhCH_2O$	$PhSO_2O$	AcO	I	H	H	A	14	70
e	Me	H	TMSEO[c]	I	I	I	B	20	70
f	$PhSO_2O$	MeO	TMSEO	I	H	H	A	16	43
g	$PhSO_2O$	MeO	TMSEO	H	I	H	A	17	43
h	$2\text{-}O_2NC_6H_4CH_2O$	MeO	TMSEO	I	I	H	B	17	83
i	$2\text{-}O_2NC_6H_4CH_2O$	MeO	TMSEO	I	H	I	B	17	80
j	$2\text{-}O_2NC_6H_4CH_2O$	MeO	TMSEO	I	I	I	B	17	9
k	$PhCH_2O$	MeO	TMSEO	H	I	H	Pd	2.5	22
l	$PhCH_2O$	MeO	TMSEO	I	H	H	Pd	2.5	22[a]
m	$PhCH_2O$	MeO	TMSEO	I	I	H	B	7	65
n	Me_2NCO_2	MeO	TMSEO	I	I	H	A	19	62
o	$(CH_2)_5NCO_2$	MeO	TMSEO	I	I	H	A	14	41
p	Ph_2NCO_2	MeO	TMSEO	I	I	H	A	5	96

[a]Further iodophenoxyfuranones **4** have been reported[1,2] [b]A uniform numbering of the aromatic carbons attached to R and R' in **4** is, unfortunately, not possible, because the protective groups change the priority of substituents. See also EXPERIMENTAL [c]TMSEO = $Me_3CH_2CH_2O$

Synthesis of AC Precycles and Model Annulations. The coupling of o-iodophenols (e.g. **3**) with 5-bromofuranones to iodinated precycles **4** was accomplished by refluxing in acetone/solid K_2CO_3 (method A) or by a two phase reaction (method B). Compounds **4** could be handled readily, although they were polar and tended to appear as foams after evaporation of the solvent.

Table 2.



4 **5**

Entry	R	R'	R''	X	Y	Z	A/B	Yield [%]	Product
1	Me	H	H	I	I	I	A	11	**5a**
2	H	H	Me_3CCO_2	I	H	H	A	---	
3	$PhCH_2O$	$PhSO_2O$	AcO	I	H	H	A/B	-/-	
4	$PhSO_2O$	MeO	TMSEO[a]	I	H	H	A/B	-/-	
5	MeO	$PhSO_2O$	TMSEO	I	H	H	A	20	**5b**
6	MeO	$PhCH_2O$	TMSEO	I	H	H	A/B	-/-	
7	$PhCH_2O$	$PhSO_2O$	H	I	I	H	A/B	71/--	**5c**[1,4]
8	$PhCH_2O$	$PhSO_2O$	H	I	H	H	A/B	51/51	**5d**[1,4]
9	H	H	MeO	I	H	H	A/B	57/58	**5e**[2b,4]
10	H	H	TMSEO	I	H	H	A/B	58/53	**5f**[1,2]
11	H	H	*n*-Pentyl-O	I	H	H	A	11	**5g**[2]
12	$PhCH_2O$	MeO	TMSEO	I	H	H	A/B	-/-	
13	HO	MeO	TMSEO	I	H	H	A/B	-/-	
14	AcO	MeO	TMSEO	I	H	H	A/B	-/-	
15	$PhCH_2O$	$PhSO_2O$	TMSEO	I	H	H	A/B	57/--	**5h**

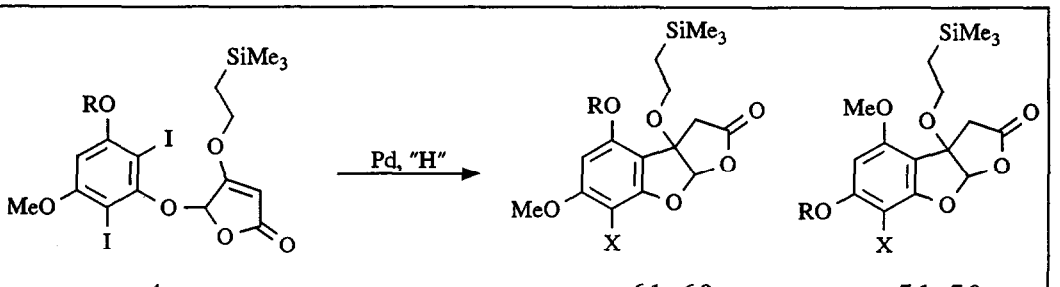
[a]TMSEO = $Me_3SiCH_2CH_2O$

Phenoxyfuranones with little additional functionality (Table 2, entries 1,2,9,10,11) were comparatively easy to annulate. However, more functionalized derivatives required a palladium catalyzed hydroarylation. Optimization was accomplished by variation of the hydride source (HCO_2H/NEt_3, LiOCHO, NaOCHO, KOCHO, TlOCHO, $Bu_4N^+OCHO^-$ and indoline[5]), variation of the ligand (Ph_3P, dppe, dppp, dppf[6]), the solvent (C_6H_6, DMF, MeOH, $MeNO_2$, MeCN, THF and DMF-H_2O) as well as addition of Bu_4NCl[7] and M_2CO_3. Best results were obtained with LiOCHO and NaOCHO, dppe, Bu_4NCl, Li_2CO_3 and Na_2CO_3 in DMF. The free radical Bu_3SnH method allowed cyclization of only the most simple precycles (entries 8 - 10). Whereas benzenesulfonyl activated p-iodophloroglucinols could be cyclized (entries 5, 7, 8, 15), the synthetically more advanced ethers (entries 4, 6, 12, 13, 14) failed to do so, also by palladium methodology (Table 2). As we found, reductive deiodination of Ar-I to Ar-H was kinetically favoured in the presence of donor substituents para to the reactive Ar-I bond. These disappointing results were backed by the reported

para-acceptor effect in Heck olefinations.[8] Apparently, the electron withdrawing para benzenesulfonyloxy group promotes internal coordination of the palladium to the butenolide. Thus the desired subsequent carbopalladation is also facilitated.

How can we get out of this impasse? Remarkably, introduction of a second iodine (Table 2, entries 7,8) was found to improve the yield of annulation product from 51%[1] to 71%, when using procedure A. This finding caused us to probe the nature of the **o,o'-diiodine effect** more thoroughly (Table 3).

Table 3. Diiodine Effect and Correct Placement of the Methoxy Group.



4 **6.1 - 6.8** **7.1 - 7.8**

Entry	R	X	Solvent	Reducing agent	eq	Pd [%]	T [°C]	t [h]	Products, Yield [%] 6	7	Regio-selectivity 6 : 7
1	$C_6H_5CH_2$	H	DMF	NaOCHO	2.2	13	85	4	20	21	0.95
2	$C_6H_5CH_2$	I	C_6H_6	Bu_3SnH	2.1	22	85	23	6	7	0.86
3	$C_6H_5CH_2$	H	C_6H_6	Bu_3SnH	2.4	10	81	2	31	34	0.91
4	$2\text{-}O_2NC_6H_4CH_2$	H	DMF	LiOCHO	2.6	10[a]	85	3	27	31	0.87
5	$CON(CH_2)_5$	H	PhMe	Bu_3SnH	3	100	110	4	27	40	0.68
6	$CONPh_2$	H	DMF	LiOCHO	6	100	120	22	---	15	< 0.07
7	$CONMe_2$	I	C_6H_6	Bu_3SnH	2.4	10	82	1+2[b]	11	27	0.41
8	$CONMe_2$	H	DMF	LiOCHO	2.6	10	110	12	30	---	> 10

Palladium complex: $(MeCN)_2PdCl_2$, coligand: dppe[6] [a]dppp was used instead of dppe[6] [b]ultrasound, 2 h

As it turned out, all diiodoarenes that were investigated and contained para-donor substituents (OMe and OCH_2Ph), gave tricyclic ABC derivatives! Initial experiments with the Pd°/formate system, furnished regioisomeric tricycles **6** and **7** (Table 3, entry 1) in a ratio almost 1:1. In order to differentiate attack at the two iodine atoms we tried a sterically demanding reducing agent, i.e. Pd°/Bu_3SnH. Control experiments (Bu_3SnH, AIBN, solvent benzene, Δ) showed that the Pd°/ Bu_3SnH procedure[9] was **not a free radical reaction.** As one might have expected, austocystine precursor **7** was now favoured over aflatoxin precursor **6**, on steric grounds (entry 2, 3). Thus, the sterically less demanding methoxy group rather than the benzyloxy group was preferentially placed next to the angular 2-trimethylsilylethoxy group. The isolation of monoiodinated tricycle, e.g. **6.2** and **7.2**, supports our assumption that the annulation *precedes* reductive removal of the second iodine atom, which terminates the reaction (e.g. **6.2** → **6.3**). Exchange of the benzyl group by an

o-nitrobenzyl group gave similar results (entry 4). Replacement of the passive ethers by a urethane tether led to high regioselectivities. Chelation was also indicated by a higher reaction temperature (85 vs 110 °C) and longer reaction times (4 vs 12 h, entry 1 vs 8). Furthermore, internal palladium complexation was evidenced by the absence of Bu_3SnH decomposition at 80 °C over a period of 16 h. A blank experiment on the reaction, suggested by Dr. Guibé:

$$2\ Bu_3SnH \xrightarrow[r.t.]{Pd^0\ (catal)} Bu_3SnSnBu_3 + H_2$$

showed spontaneous evolution of hydrogen, even at room temperature.

Whereas the piperidyl urethane (entry 5) showed moderate regioselection (**6.5** : **7.5**), the diphenyl substituted tether (entry 6) slowed down the reaction. On the other hand, regioselection was complete (**6.6** : **7.6** < 0.07). Application of the $Bu_3SnH/Pd^0/C_6H_6$ method to the dimethyl urethane tether (entry 7) favoured the austocystine precursor (**6.7** : **7.7** = 0.41). With the Pd^0/HCO_2^-/DMF method (entry 8), the same urethane afforded the desired aflatoxin precursor exclusively.

Conclusions and Summary. Previous attempts at annulating precycles AC to the ABC system using conventional methods (halogen/metal exchange) were not successful[10]. Disregarding model systems, recent free radical methodology (Bu_3SnH, AIBN, Δ or hv) also failed, although it is often stated and assumed that free radical chemistry is compatible with a wide variety of functional groups. The interference of various functional groups excluded the desired annulation. On the other hand, modern transition metal methodology provides suitable reagents. Specifically, Pd^0 allows a mild and chemoselective activation of the aryl-iodine bond. Unlike para-benzenesulfonyl protected iodophenols (Table 2), the synthetically more advanced p-methoxy substituted precycles required an additional iodine substituent to effect cyclization (o,o'-diiodine effect, Table 3). Thanks to this effect and palladium selectivity, the protection-deprotection sequence is now superfluous.

Does the second iodine exert an electronic effect on the annulation? HOMO-LUMO calculations on the appropriate mono- and diiodinated aromatic π system provided no evidence of any substantial change in π energies. Furthermore, ^{13}C NMR shifts of the aromatic carbon atoms stayed practically constant, irrespective of the number and position of the iodine atoms. Models suggest that the second iodine atom ensures proximity of the σ-aryl bonded palladium and the olefinic double bond of the furanone. MM2 calculations reveal that this double bond is always in the vicinity of either iodine atom, ensuring annulation, which in general does not proceed with monoiodoanisole derivatives. The second iodine introduces the problem of regiocontrol. This problem has been solved by the urethane link, which serves as a protecting group **and** a tether, at the same time.

EXPERIMENTAL

Coupling of the iodophenols with the bromobutenolides was carried out as follows: Method A. o-Iodophenol (1 mmol) in abs. acetone (5 ml) is treated with anhydrous K_2CO_3 (2 mmol). Bromobutenolide (1 mmol) in abs. acetone (5 ml) is injected under N_2 and the mixture is refluxed for 3 - 19 h, cooled to r.t. and filtered through silica gel (Et_2O or CH_2Cl_2). The concentrated filtrate is purified by column chromatography or crystallization. *Method B.* o-Iodophenol (1 mmol) is dissolved in CH_2Cl_2 (4 ml) and treated with n-$Bu_4N^+Cl^-$ (30 mg). Then the bromobutenolide (1 mmol) in CH_2Cl_2 (2.6 ml) is injected and K_2CO_3 (1.4

mmol) and H_2O (5.3 ml) are added. The mixture is stirred for 1 - 17 h under nitrogen. The layers are separated and the organic layer is extracted with CH_2Cl_2 (5 ml, 2x). The combined organic layers are dried ($MgSO_4$) and concentrated. The resulting crude product is purified by column chromatography or column filtration/crystallization.

5-[3-Hydroxy-2-iodo-5-methoxyphenoxy]-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)-furanone[2b]

5-(5-Benzenesulfonyloxy-2-iodo-3-benzyloxyphenoxy)-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4a**)[1,2]

5-(5-Benzenesulfonyloxy-3-benzyloxy-2,6-diiodophenoxy)-2(5H)furanone (**4b**). Method B,[4] 90 min, chromatography (PE/CH_2Cl_2, 1:3), 59%, amorphous solid, m.p. 156 °C. IR ($CHCl_3$) ν 1796, 1570, 1451, 1430, 1386, 1349, 1322, 1198, 1176, 1083, 1018 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ 5.27 (s, 2H, $PhCH_2$), 6.65-6.68 (m, 2H, H-3, H-5), 6.94 (s, 1H, H-4'), 7.35-8.05 (m, 11H, Ph, $PhSO_3$, H-4). 50.2 MHz ^{13}C NMR (DMF-D_7) δ 71.91 (t, $PhCH_2$), 80.21 (s, C-2'), 84.49 (s, C-6'), 104.22 (d, C-4'), 104.98 (d, C-5), 125.80 (d, C-3), 128.01, 128.71, 129.16, 129.40, 130.44, 136.00 (6 d, 10 arom. C), 135.57 (s, C-1'''), 136.54 (s, C-1''), 151.58 (d, C-4), 152.48 (s, C-3'), 157.90 (s, C-1'), 159.90 (s, C-5'), 170.44 (s, C-2). MS (250 °C) *m/z* 481 (7), 480 (6), 352 (6), 338 (7), 254 (8), 91 (100, $PhCH_2$). Anal. Calcd for $C_{23}H_{16}I_2O_7S$: C 40.02, H 2.34; found: C 40.25 H 2.69.

5-(o-Iodophenoxy)-4-(trimethylacetyloxy)-2(5H)furanone (**4c**). Method A, 7.5 h, chromatography (CH_2Cl_2), 24%, fine needles, m.p. 78 °C. IR ($CHCl_3$) ν 3005, 2990, 1790, 1640, 1470, 1440, 1375, 1295, 1265, 1070, 1020, 1000 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ 1.38 (s, 9H, CH_3), 6.26 (d, ^4J=0.5 Hz, 1H, H-3), 6.32 (d, ^4J=0.5 Hz, 1H, H-5), 6.90 (ddd, J=7 Hz, J=7 Hz, ^4J=1.5 Hz, 1H, H-4'), 7.26 (dd, J=7 Hz, ^4J=1.5 Hz, 1H, H-6'), 7.37 (ddd, J=7 Hz, J=7 Hz, ^4J=1.5 Hz, H-5'), 7.83 (dd, J=7 Hz, ^4J=1.5 Hz, 1H, H-3'). MS *m/z* 403 (1), 402 (5, M^+), 305 (1), 304 (2), 303 (18), 219 (38, C_6H_4IO), 190 (39), 57 (100, Me_3C). Anal. Calcd for $C_{15}H_{15}IO_5$: C 44.79, H 3.75 ; found: C 45.92, H 4.13.

5-(5-Benzenesulfonyloxy-3-benzyloxy-2-iodophenoxy)-4-acetoxy-2(5H)furanone (**4d**). 200 MHz ^1H NMR ($CDCl_3$) δ 2.3 (s, 3H, Ac), 5.02 (s, 2H, $PhCH_2$), 5.08 (s, 1H, H-3), 6.38 (d, ^4J=2 Hz, 1H, H-4'), 6.48 (d, J=2 Hz, 1H, H-6'), 6.58 (s, 1H, H-5), 7.38-8.0 (m, 10 arom. H). 50.2 MHz ^{13}C NMR ($CDCl_3$, APT) δ 21.06 (q, Me), 71.44 (t, OCH_2), 82.46 (s, C-I), 104.61, 104.91 (d, C-4', C-6'), 109.32, 109.94 (d, C-3, C-5), 127.07, 128.55, 128.62, 129.30, 129.60, 134.61 (d, 10 arom. C), 134.75 (s, CCH_2), 135.10 (s, CSO_3), 150.89 (s, C-1'), 152.60 (s, C-3'), 158.01 (s, C-5'), 167.74, 167.82 (s, C-4, MeCO), 168.53 (s, C-2).

5-[Tri-2,4,6-iodo-3-methylphenoxy]-4-[2-trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4e**). Method B, 20 h, chromatography (PE/CH_2Cl_2, 1:1), 70%, colourless oil. IR ($CHCl_3$) ν 2980, 1790, 1780 (Fermi resonance), 1640, 1410, 1295, 1150, 1065, 1020, 925, 860, 840 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ 0.11 (s, 9H, $SiCH_3$), 1.25 (dd, J=7 Hz, J=9 Hz, 2H, $SiCH_2$), 2.80 (s, 3H, CH_3), 4.26 (dd, J=7 Hz, J=9 Hz, 2H, OCH_2), 5.22 (s, 1H, H-3), 6.32 (s, 1H, H-5), 8.28 (s, 1H, H-5'). 50.2 MHz ^{13}C NMR ($CDCl_3$, APT) δ -1.4 (q, $SiCH_3$), 17.08 (t, $SiCH_2$), 35.76 (q, $ArCH_3$), 71.86 (t, OCH_2), 87.64 (s, C-6'), 90.42 (d, C-3), 95.63 (s, C-4'), 97.79 (d, C-5), 100.05 (s, C-2'), 145.88 (s, C-3'), 148.19 (d, C-5'), 154.32 (s, C-1'), 169.28 (s, C-4), 175. 08 (s, C-2). MS (180 °C) *m/z* 685 (1), 560 (2), 559 (5), 558 (29), 171 (33), 101 (9, TMSE), 73 (100, TMS).

5-(3-Benzenesulfonyloxy-2-iodo-5-methoxyphenoxy)-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4f**). Method A, 16 h, chromatography (PE/MTB, 1:1), 43%, colourless oil. IR (CCl_4) ν 2960, 1795, 1750, 1640, 1595, 1455, 1450, 1410, 1385, 1365, 1290, 1250, 1220, 1195, 1150, 1120, 1000, 860, 840 cm^{-1}. 200 MHz ^1H-NMR ($CDCl_3$) δ 0.1 (s, 9H, $SiCH_3$), 1.23 (dd, J=10 Hz, J=8 Hz, 2H, $SiCH_2$), 3.81 (s, 3H, OCH_3),

4.22 (dd, *J*=10 Hz, *J*=8 Hz, 2H, OCH_2CH_2), 5.15 (s, 1H, H-3), 5.83 (s, 1H, H-5), 6.40+6.41 (2 d, ^4J=1 Hz, 2H, H-4', H-6'), 7.5-7.9 (m 5H, $PhSO_3$). 50.2 MHz ^{13}C-NMR ($CDCl_3$) δ -0.07 (q, $SiMe_3$), 18.72 (t, $SiCH_2$), 58.26 (q, OCH_3), 72.57 (s, C-3'), 73.46 (t, OCH_2), 91.73 (d, C-3), 98.48 (d, C-5), 102.88, 104.90 (d, C-4', C-6'), 130.00, 130.83, 136.11 (3 d, 5C, C-2'', C-3'', C-4''), 136.32 (s, C-1''), 152.68 (s, C-1'), 158.10 (s, C-3'), 161.31 (s, C-5'), 170.76 (s, C-4), 175.86 (s, C-2). MS *m/z* 278 (2), 121 (26), 119 (96), 117 (100, TMSE), 73 (49, TMS).

5-(5-Benzenesulfonyloxy-2-iodo-3-methoxyphenoxy)-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4g**) Method A, 17 h, chromatography (PE/MTB, 1:1), 43%, yellow oil. IR ($CHCl_3$) ν 2955, 1791, 1760, 1645, 1600, 1580, 1462, 1451, 1416, 1381, 1297, 1203, 1194, 1122, 1094, 1003, 842 cm^{-1}. 200 MHz ^{1}H NMR ($CDCl_3$) δ 0.09 (s, 9H, $SiCH_3$), 1.17-1.28 (m, 2H, $SiCH_2$), 3.76 (s, 3H, OCH_3), 4.23 (dd, *J*=9 Hz, *J*=8 Hz, 2H, OCH_2CH_2), 5.18 (s, 1H, H-3), 5.86 (s, 1H, H-5), 6.36, 6.42 (2 d, ^4J=2.5 Hz, 2H, H-4', H-6'), 7.52-7.92 (m, 5H, $PhSO_3$). 50.2 MHz ^{13}C NMR ($CDCl_3$, APT) δ 1.42 (q, $SiCH_3$), 18.68 (t, $SiCH_2$), 58.23 (q, OMe), 73.48 (t, OCH_2), 74.25 (s, C-2'), 91.71 (d, C-3), 98.44 (d, C-5), 102.76, 104.82 (d, C-4', C-6'), 129.98, 130.86, 136.15 (3 d, 5C, C-2'', C-3'', C-4''), 136.25 (s, C-1''), 152.67 (s, C-1'), 158.10 (s, C-5'), 161.30 (s, C-3'), 170.81 (s, C-4), 175.95 (s, C-2). MS *m/z* 477 (0.5, M^+-I), 462 (0.5), 461 (1), 409 (0.5), 408 (1), 407 (3), 406 (12, $C_{13}H_{11}IO_5S$), 342 (3), 265 (3), 264 (8), 246 (7), 101 (9, $Me_3SiC_2H_4$), 73 (100, Me3Si). HRMS calcd for $C_{13}H_{11}IO_5S$ 405.9372, found 405.9371.

5-[2,6-Diiodo-3-methoxy-5-o-nitrobenzyloxyphenoxy]-4-[2-(trimethylsilyl)eth-1-oxy)-2(5H)furanone (**4h**). Method B, 17 h, chromatography (Et_2O/PE, 1:1), 83%, light yellow oil. IR ($CHCl_3$) ν 2960, 2940, 2860, 1785, 1750, 1720, 1640, 1570, 1525, 1380, 1290, 1100, 1015, 860, 840 cm^{-1}. 200 MHz ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 9H, $SiCH_3$), 1.20-1.30 (m, 2H, $SiCH_2$), 3.92 (s, 3H, OCH_3), 4.20-4.35 (m, 2H, OCH_2CH_2), 5.21 (s, 1H, H-3), 5.56 (s, 2H, $ArCH_2O$), 6.40 (s, 1H, H-5), 6.49 (s, 1H, H-4'), 7.5-8.3 (m, 4H, $ArNO_2$). 50.2 MHz ^{13}C NMR ($CDCl_3$, APT) δ -1.36 (q, $SiCH_3$), 17.22 (t, SiCH2), 56.99 (q, OCH_3), 68.19 (t, OCH_2Ar), 71.94 (t, OCH_2CH_2), 74.47, 74.61 (2 s, C-2', C-6'), 90.50 (d, C-3), 94.24 (d, C-4'), 98.14 (d, C-5), 124.94 (d, C-4''), 128.59 (d, C-3''), 129.05 (d, C-5''), 132.57 (s, C-1''), 134.45 (d, C-6''), 146.41 (s, C-2''), 155.51 (s, C-1'), 158.99 (s, C-5'), 160.69 (s, C-3'), 169.86 (s, C-4), 175.44 (s, C-2). MS (340 °C) *m/z* 728 (11), 727 (36), 726 (100), 600 (19), 599 (51, M^+-I), 464 (41), 448 (23), 280 (8), 149 (88). HRMS calcd for $C_{23}H_{25}I_2NO_8Si$ 724.9439, found 724.9439.

5-[2,4-Diiodo-5-methoxy-3-o-nitrobenzyloxyphenoxy]-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4i**). Method B, 17 h, thick layer chromatography (PE/CH_2Cl_2, 1:1), 80%, colourless oil. IR ($CHCl_3$) ν 2956, 1790, 1760, 1641, 1568, 1529, 1366, 1344, 1295, 1110, 1015, 860, 840 cm^{-1}. 200 MHz ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 9H, $SiCH_3$), 1.26 (dd, *J*=7 Hz, *J*=9 Hz, 2H, $SiCH_2$), 3.88 (s, 3H, OCH_3), 4.26 (dd, *J*=7 Hz, *J*=9 Hz, 2H, OCH_2CH_2), 5.21 (s, 1H, H-3), 5.55 (s, 2H, $ArCH_2$), 6.09 (s, 1H, H-5), 6.71 (s, 1H, H-6'), 7.54-8.2 (m, 4H, $ArNO_2$). MS (220 °C) *m/z* 725 (2, M^+), 724 (5, M^+-1), 598 (12, M^+-I), 527 (1), 463 (8), 391 (1), 321 (3), 171 (11), 136 (100, $O_2NC_7H_6$), 73 (83, TMS). HRMS calcd for $C_{25}H_{25}I_2NO_8Si$ 724.9439, found 724.9458.

5-[2,4,6-Triiodo-5-methoxy-3-o-nitrobenzyloxyphenoxy]-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4j**). Method B, 17 h, chromatography (PE/acetone, 4:1), 9%, light yellow oil. IR ($CHCl_3$) ν 2960, 1785, 1760, 1640, 1525, 1360, 1290, 1085, 1080, 1020, 980, 940, 925, 910, 860, 840 cm^{-1}. 200 MHz ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 9H, $SiCH_3$), 1.20-1.33 (m, 2H, $SiCH_2$), 3.92 (s, 3H, OCH_3), 4.22-4.33 (m, 2H, OCH_2CH_2), 5.22 (s, 1H, H-3), 5.47 (s, 2H, $ArCH_2$), 6.42 (s, 1H, H-5), 7.53-8.2 (m, 4H, $ArNO_2$). MS (200 °C) *m/z* 850 (0.1), 849 (0.2), 788 (0.1), 787 (0.3), 760 (0.3), 759 (0.1), 758 (0.4), 136 (100, $O_2NC_6H_4CH_2$), 73 (100,

$SiMe_3$).

5-(5-Benzyloxy-2-iodo-3-methoxyphenoxy)-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4k**). 5-(3-Benzyloxy-2,6-diiodo-5-methoxyphenoxy)-4-[2-(trimethylsilyl)eth-1-oxy]-2(5*H*)furanone (**4m**) (116 mg, 0.17 mmol), TBACl (81 mg), NaOCHO (25 mg) and PPh_3 (12 mg) are treated with a solution of $(MeCN)_2PdCl_2$ in abs. DMF (0.7 ml). The mixture is stirred for 2.5 h at 68°C under nitrogen and then cooled to r.t. After filtration through silica gel (Et_2O), the solvent is removed. The resulting residue is purified by chromatography PE/CH_2Cl_2, 2:1). The desired tricycle and the monoiodo-isomers are obtained as yellow oils, 22%. IR (CCl_4) ν 2956, 1796, 1646, 1599, 1367, 1294, 1158, 1013, 878, 860, 840 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ 0.11 (s, 9H, $SiCH_3$), 1.15-1.27 (m, 2H, $SiCH_2$), 3.78 (s, 3H, OCH_3), 4.15-4.25 (m, 2H, OCH_2CH_2), 5.03 (s, 2H, OCH_2Ph), 5.18 (s, 1H, H-3), 6.06 (s, 1H, H-5), 6.3-6.42 (m, 2H, H-4', H-6'), 7.3-7.5 (m, 5H, Ph). MS (180 °C) *m/z* 462 (0.5, M^+-C_7H_8), 430 (0.1), 429 (1), 428 (3), 91 (100, $PhCH_2$).

5-(3-Benzyloxy-2-iodo-5-methoxyphenoxy)-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4l**).[1,2b]

5-(3-Benzyloxy-2,6-diiodo-5-methoxyphenoxy)-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4m**). Method B, 7 h, chromatography (E/PE, 1:1), 65%, colourless prisms (recrystallized from CCl_4), m.p. 156 °C. IR ($CHCl_3$) ν 2950, 1790, 1760, 1640, 1569, 1498, 1456, 1433, 1387, 1362, 1294, 1249, 1222, 1204, 1151, 1108, 1014, 862, 840 cm^{-1}. 300 MHz ^1H NMR ($CDCl_3$) δ 0.1 (s, 9H, $SiCH_3$), 1.22-1.3 (m, 2H, $SiCH_2$), 3.84 (s, 3H, OCH_3), 4.2-4.3 (m, 2H, OCH_2CH_2), 5.18 (s, 2H, $PhCH_2$), 5.20 (s, 1H, H-3), 6.34 (s, 1H, H-5), 6.49 (s, 1H, H-4'), 7.3-7.52 (m, 5H, Ph). 75.5 MHz ^{13}C NMR ($CDCl_3$) δ -1.406 (q, $SiCH_3$), 17.190 (t, $SiCH_2$), 56.791 (q, OMe), 71.587 (t, $PhCH_2O$), 71.837 (t, OCH_2CH_2), 74.219, 74.461 (2 s, C-2', C-6'), 90.435 (d, C-3), 94.741 (d, C-4'), 98.700 (d, 5), 127.033, 128.083, 128.610 (3d, 5C, C-2'', C-3'', C-4''), 135.887 (s, C-1''), 152.5 (s, C-1'), 159.625 (s, C-3'), 160.431 (s, C-5'), 169.782 (s, C-4), 176.0 (s, C-2). MS (160 °C) *m/z* 681 (0.1), 680 (0.3), 679 (1), 678 (2), 586 (1), 552 (3, M^+-HI), 460 (3), 426 (4, M^+-2 I), 337 (3), 335 (4), 170 (6), 91 (100, $PhCH_2$), 73 (44, TMS). HRMS calcd for $C_{23}H_{26}I_2O_6Si$ 679.9557, found 679.9588 Anal. Calcd for $C_{23}H_{26}I_2O_6Si$: C 40.61, H 3.85; found: C 42.66, H 4.43.

5-(2,6-Diiodo-3-[N,N-dimethylcarbamoyloxy]-5-methoxyphenoxy)-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4n**). Method A, 19 h, chromatography (E/PE, 3:1), 62%. IR ($CHCl_3$) ν 1792, 1729, 1641, 1575, 1395, 1381, 1362, 1340, 1319, 1159, 1103, 1018, 860, 840 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ 0.11 (s, 9H, $SiCH_3$), 1.21-1.32 (m, 2H, $SiCH_2$), 3.04 (s, 3H, $NCH_{3\alpha}$), 3.19 (s, 3H, $NCH_{3\beta}$), 3.88 (s, 3H, OCH_3), 4.20-4.30 (m, 2H, OCH_2CH_2Si), 5.20 (s, 1H, H-3), 6.43 (s, 1H, H-5), 6.72 (s, 1H, H-4'). 50.2 MHz ^{13}C NMR ($CDCl_3$, APT) δ -1.38 (q, $SiCH_3$), 17.07 (t, $SiCH_2$), 36.77, 36.83 (2 q, $NCH_{3\alpha+\beta}$), 56.94 (q, OCH_3), 71.89 (t, $SiCH_2$), 78.90, 80.20 (2 s, C-2', C-6'), 90.43 (d, C-3), 98.11 (d, C-4'), 103.85 (d, C-5), 152.99 (s, C-1'), 153.87 (s, C-3'), 155.14 (s, OC(O)N), 159.87 (s, C-5'), 169.63 (s, C-4), 175.30 (s, C-2). MS (100 °C) *m/z* 663 (2), 662 (3, $^{13}C^{12}C_{18}$), 536 (3), 535 (8, $M^+[^{13}C]$-I), 410 (3), 409 (6), 408 (22, $M^+[^{13}C]$-2 I), 336 (5), 335 (5), 73 (38, TMS), 72 (100, Me_2NCO). HRMS calcd 660.9490, found 660.9500.

5-((2,6-Diiodo-3-N-piperidylcarbamoyloxy)-5-methoxyphenoxy)-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)-furanone (**4o**). Method A, 14 h, chromatography (E/PE, 3:2), 41%, yellow foam. IR ($CHCl_3$) ν 1791, 1758, 1719, 1641, 1575, 1417, 1363, 1263, 1253, 1232, 1197, 1142, 1080, 1019, 860, 840 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ 0.10 (s, 9H, $SiCH_3$), 1.2-1.3 (m, 2H, $SiCH_2$), 1.67 (br. s, 6H), 3.52 (br. s, 2H), 3.70 (br. s, 2H), 3.88 (s, 3H, OCH_3), 4.20-4.30 (m, 2H, OCH_2), 5.20 (s, 1H, H-3), 6.42 (s, 1H, H-5), 6.70 (s, 1H, H-4'). MS (220 °C) *m/z* 701 (2, M^+), 576 (2), 575 (9), 503 (1), 448 (6), 447 (19, M^+-2 I), 376 (3), 171 (10), 112 (100, $C_6H_{10}NO$), 73 (TMS, 57). HRMS calcd 700.9803, found 700.9794.

5-(2,6-Diiodo-3-[N,N-diphenylcarbamoyloxy]-5-methoxyphenoxy)-4-[2-(trimethylsilyl)eth-1-oxy]-2(5H)furanone (**4p**). Method A, 5 h, chromatography (E/PE, 3:1), 96%. IR ($CHCl_3$) ν 1788, 1734, 1640, 1575, 1491, 1383, 1351, 1334, 1296, 1196, 1175, 1152, 1102, 1073, 1047, 1019, 860, 840 cm^{-1}. 200 MHz ^{1}H-NMR ($CDCl_3$) δ 0.10 (s, 9H, $SiCH_3$), 1.2-1.3 (m, 2H, $SiCH_2$), 3.88 (s, 3H, OCH_3), 4.18-4.28 (m, 2H, OCH_2), 5.19 (s, H-3), 6.39 (s, H-5), 6.72 (s, H-4'), 7.3-7.5 (m, 10H, NPh_2). MS (200 °C) *m/z* 786 (4), 785 (5, M^+), 688 (4), 587 (4), 532 (10), 196 (100, Ph_2NCO), 73 (88, TMS).

4-Methyl-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydro-[2,3b]-benzofuran-2(3H)-one (**5a**). Iodophenoxyfuranone **4e** (862 mg, 1.26 mmol), NaOCHO (282 mg, 4.15 mmol), K_2CO_3 (590 mg, 4.21 mmol, 3.3 eq) and *n*-$Bu_4N^+Cl^-$ (1150 mg) are dissolved in abs. DMF (8 ml). The mixture is heated to 85°C under nitrogen. $(MeCN)_2PdCl_2$ (17.5 mg, 63 mmol) and dppp (26 mg, 63 mmol) are dissolved in abs. DMF (1 ml) and half of the solution is added to the reaction mixture. After 45 min the other half of the catalysator is added and the mixture is stirred for 20 h at 85°C. The black suspension is cooled to r.t. and filtered. After further filtration through silica gel (10g, Et_2O) and removal of the solvent the resulting residue is chromatographed ($CHCl_3$). Yield: 40.7 mg (11%), yellow oil and other unidentified, iodinated products. IR ($CHCl_3$) ν 2960, 2930, 1800, 1715, 1615, 1595, 1450, 1330, 1270, 1250, 1180, 1080, 1060, 1000, 860, 840 cm^{-1}. 200 MHz ^{1}H NMR ($CDCl_3$) δ -0.045 (s, 9, $SiCH_3$), 1.8-1.93 (m, 2H, $SiCH_2$), 2.34 (s, 3H, CH_3), 3.04-3.42 (m, 4H, OCH_2CH_2, $H_{\alpha,\beta}$-3), 6.27 (s, 1H, H-8a), 6.77-7.30 (m, ^3J=7.5 Hz, ^4J=1.5 Hz, 3 arom. H). MS *m/z* 307 (3, $M^+[^{13}C]$), 306 (9), 305 (33), 278 (4, M^+-CO), 263 (5), 250 (6), 249 (18), 207 (28), 145 (24), 83 (52) 73 (100, TMS). HRMS calcd 306.1287, found 306.1290.

3a-[2-(Trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one[2b]

6-Benzenesulfonyloxy-4-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydro-furo[2,3b]benzofuran-2(3H)-one (**5b**). Iodophenoxyfuranone **4g** (265 mg, 0.43 mmol), *n*-$Bu_4N^+Cl^-$ (225 mg), $(MeCN)_2PdCl_2$ (10.5 mg) and NaOCHO (59 mg) are allowed to react as described for **5a**. Yield: 43 mg (20%). IR (CCl_4) ν 1814, 1620, 1615, 1493, 1450, 1428, 1391, 1251, 1196, 1118, 1092, 1057, 1004, 983, 847 cm^{-1}. 200 MHz ^{1}H NMR ($CDCl_3$) δ -0.04(s, 9H, $SiCH_3$), 0.84 (m, 2H, $SiCH_2$), 3.07 (d, ^2J=18 Hz, H_α-3), 3.22, 3.36 (2 dt, ^2J=8.5 Hz, ^3J=8 Hz, 2H, $OCH_AH_BCH_2$), 3.38 (d, ^2J=18, H_β-3), 3.78 (s, 3H, OMe), 6.15 (s, H-8a), 6.20 (d, ^4J=1.5 Hz, H-5), 6.30 (d, ^4J=1.5 Hz, H-7), 7.52-7.94 (m, 5H, $PhSO_2$). 50.2 MHz ^{13}C NMR ($CDCl_3$) δ -1.43 (q, $SiCH_3$), 18.15 (t, $SiCH_2$), 38.93 (t, C-3), 55.87 (q, OMe), 63.05 (t, OCH_2), 86.69 (s, C-3a), 99.15 (d, C-5), 100.30 (d, C-7), 109.99 (s, C-3b), 110.16 (d, C-8a), 128.47, 129.30, 134.53 (3 d, 5 arom. C, $PhSO_2$), 135.18 (s, CSO_3), 153..30 (s, C-6), 157.44 (s, C-7a), 160.07 (s, C-4), 171.66 (s, C-2). MS (180 °C) *m/z* 480 (1), 479 (4), 478 (9, M^+), 477 (28, M^+-1), 449 (12, M^+-HCO), 435 (12), 421 (7), 406 (11), 393 (11), 379 (15), 361 (42, M^+-TMSEO), 316 (22), 77 (70, Ph), 73 (100, TMS). HRMS calcd for $C_{22}H_{26}O_8SSi$ 478.1118, found 478.1116.

6-Benzenesulfonyloxy-4-benzyloxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one[1] (**5h**). Iodophenoxyfuranone **3**[1] (510 mg, 0.75 mmol), *n*-$Bu_4N^+Cl^-$ (420 mg), $(MeCN)_2PdCl_2$ (30 mg), NaOCHO (60 mg) and triethylamine (0.2 ml) are allowed to react as described for **5a**. Chromatography affords starting material (224 mg) and **5h**, 128 mg (55%, 56% with respect to recovered starting material). For IR and ^{1}H NMR data see ref. 1. 50.2 MHz ^{13}C NMR ($CDCl_3$) δ -1.49 (q, $SiMe_3$), 18.2 (t, $SiCH_2$), 39.9 (t, 3), 70.49 (t, OCH_2CH_2), 71.97 (t, OCH_2Ph), 86.63 (s, C-3a), 99.23 (s, C-5), 101.27 (s, C-7), 110.21 (d, C-8a), 110.31 (s, C-3b), 126.95-134.48 (6 d, 10 arom. C), 135.2 (s, OCH_2CH_2), 135.5 (s, CSO_3), 151.09 (s, C-6) 153.1 (s, C-4), 156.44 (s, C-7a), 174.39 (s, C-2). HRMS calcd for $C_{23}H_{17}O_7S$ 437.0695, found

437.0694.

4-Benzyloxy-6-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one (**6.1**) and *6-Benzyloxy-4-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one* (**7.1**). Diiodophenoxyfuranone (**4m**) (205 mg, 0.3 mmol), 100 mg K_2CO_3 (100 mg), mg NaOCHO (57 mg, 0.8 mmol), *n*-$Bu_4N^+Cl^-$ (250 mg) and dppe (6 mg) are treated under nitrogen with a solution of $(MeCN)_2PdCl_2$ (10 mg, 38 mmol, 13%) in abs. DMF (1.6 ml). The mixture is stirred for 4 h at 85°C. After cooling to r.t., the reaction mixture is filtered through silica gel (CH_2Cl_2). The solvent is evaporated and the residue chromatographed (CH_2Cl_2) to give a mixture of the tricycles. Thick layer chromatography (CH_2Cl_2) affords **6.1** (26 mg, 20%) and **7.1** (27 mg, 21%). Spectroscopic data of **6.1**: IR (CCl_4) ν 2956, 1811, 1630, 1603, 1501, 1150, 1005, 860, 839 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ -0.03 (s, 9H, $SiCH_3$), 0.82-0.89 (m, 2H, $SiCH_2$), 3.06 (d, ^2J=18 Hz, 1H, H_α-3), 3.25-3.45 (m, 2H, OCH_2CH_2), 3.42 (d, ^2J=18 Hz, 1H, H_β-3), 3.82 (s, 3H, OCH_3), 5.04 (s, 2H, OCH_2Ph), 6.16, 6.22 (2 d, ^4J=0.7 Hz, 2H, H-5, H-7), 6.16 (s, H-8a), 7.38-7.46 (m, 5H, Ph). MS (100 °C) *m/z* 429 (1), 428 (3), 400 (1, M^+-CO), 310 (3), 91 (100, Ph). HRMS calcd for $C_{23}H_{28}O_6SSi$ 428.1655, found 428.1656. Spectroscopic data of **7.1**: IR (CCl_4) ν 2956, 1810, 1630, 1603, 1500, 1150, 1005, 860 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ -0.08 (s, 9H, $SiMe_3$), 0.80-0.88 (m, 2H, $SiCH_2$), 3.07 (d, ^2J=18 Hz, 1H, H_α-3), 3.25-3.45 (m, 2H, OCH_2CH_2), 3.46 (d, ^2J=18 Hz, 1H, H_β-3), 3.78 (s, 3H, OCH_3), 5.09 (s, 2H, OCH_2Ph), 6.15 (s, H-8a), 6.17, 6.21 (2 d, ^4J=0.7 Hz, 2H, H-5, H-7), 6.15 (s, H-8a), 7.37 (br. s, 5H, Ph). MS (100 °C) *m/z* 430 (0.25), 429 (1), 428 (3), 400 (1, M^+-CO), 310 (3), 274 (5), 91 (100, Ph). HRMS calcd for $C_{23}H_{28}O_6SSi$ 428.1655, found 428.1688.

4-Benzyloxy-7-iodo-6-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one (**6.2**) and *6-Benzyloxy-7-iodo-4-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]-benzofuran-2(3H)-one* (**7.2**). Diiodide **4m** (221 mg, 0.32 mmol) is dissolved in abs. benzene (4 ml), $(MeCN)_2PdCl_2$ (20 mg, 22%) and dppe (130 mg) in abs. benzene (2 ml) are added and the mixture is heated to 85°C. Within 4 h (perfusor) Bu_3SnH (200 mg) in benzene (10 ml) is added. After stirring for 19 h at 85°C, the dark brown mixture is cooled to r.t. and filtered through silica gel (Et_2O). The solvent is evaporated and the residue purified by chromatography (PE/Et_2O, 3:1) to give the tricycles as colourless oils (10 and 11%), then the easy seperable monoiodinated tricycles as amorphous solid or, respectively, the 4-benzyl-7-iodid as light yellow needles. In another approach diiodide (1.27 mmol) is allowed to react with $(MeCN)_2PdCl_2$ (10%), dppe (10%) and Bu_3SnH in benzene (30 ml) for 2 h at 81°C. Chromatography gives the deiodinated tricycles, 34% (4-OMe) and 31% (6-OMe). **6.1**, yield 6%, m.p. 104 °C. IR ($CHCl_3$) ν 2957, 1800, 1643, 1612, 1490, 1409, 1386, 1360, 1300, 1250, 1167, 1125, 1100, 1073, 1003 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ -0.04 (s, 9H, $SiCH_3$), 0.8-0.97 (m, 2H, SiCH2), 3.05 (d, ^2J=18 Hz, 1H, H_α-3), 3.20-3.26 (m, 2H, OCH_2CH_2), 3.38 (d, ^2J=18 Hz, H_β-3), 3.82 (s, 3H, OCH_3), 5.19 (s, 2H, OCH_2Ph), 6.16 (s, H-8a), 6.22 (s, H-5), 7.33-7.53 (m, 5H, Ph). MS (190 °C) *m/z* 556 (2), 555 (4), 554 (12, M^+), 437 (2), 436 (6, M^+-$C_5H_{14}SiO$), 429 (2), 428 (6), 427 (3), 426 (16, M^+-HI), 281 (5), 131 (3), 91 (100, $PhCH_2$), 73 (100, TMS). HRMS calcd for $C_{23}H_{27}IO_6Si$ 554.0622, found 554.0616. Anal. Calcd for $C_{23}H_{27}IO_6Si$: C 49.82, H 4.91; found: C 50.96, H 5.47. **7.2**, yield 7%, m.p. 111 °C. IR ($CHCl_3$) ν 3022, 2956, 1800, 1613, 1490, 1463, 1443, 1408, 1359, 1259, 1123, 1098, 1055, 1003, 910, 862, 840 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ -0.07 (s, 9H, $SiCH_3$), 0.81-0.96 (m, 2H, $SiCH_2$), 3.08 (d, ^2J=18 Hz, 1H, H_α-3), 3.23-3.44 (m, 2H, OCH_2CH_2), 3.43 (d, ^2J=18 Hz, H_β-3), 3.85 (s, 3H, OCH_3), 5.16 (s, 2H, CH_2Ph), 6.17 (s, H-8a), 6.23 (s, H-5), 7.3-7.4 (m, 5H, Ph). MS (160 °C) *m/z* 555 (2), 554 (6, M^+), 553 (4, M^+-H), 437 (2), 436 (2, M^+-$C_5H_{14}OSi$), 391 (2), 347 (5), 302 (1), 91 (100, $PhCH_2$). HRMS

calcd for $C_{23}H_{27}IO_6Si$ 554.0622, found 554.0613. Anal. Calcd for $C_{23}H_{27}IO_6Si$: C 49.82, H 4.91; found: C 51.97, H 5.47.

4-o-Nitrobenzyloxy-6-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one (**6.4**) and *6-o-Nitrobenzyloxy-4-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy)-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one* (**7.4**). Diiodide **4h** (99 mg, 0.136 mg), LiOCHO (19 mg), Li_2CO_3 (26.4 mg), $Bu_4N^+Cl^-$ (120 mg) and dppp (11.3 mg) are dissolved in abs. DMF (2 ml) under nitrogen and the mixture is treated at 85°C with $(MeCN)_2PdCl_2$ (0.1 eq) in DMF (1 ml) at 85°C. After stirring for 3 h at the same temperature, the mixture is cooled to r.t. and filtered through flash gel. The solvent is removed and the residue purified by chromatography (PE/CH_2Cl_2, 3:1). The 6-methoxybenzofurofuranone is eluated first, followed by the 4-methoxy isomer. 6-Methoxy isomer **7.4**, yield 20 mg (31%), oil. IR ($CHCl_3$) ν 2860, 1797, 1632, 1604, 1529, 1344, 1151, 1125, 1095, 1004 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ -0.07 (s, 9H, $SiCH_3$), 0.86 (t, J=8 Hz, 2H, $SiCH_2$), 3.07 (d, ^2J=18 Hz, H_α-3), 3.25-3.45 (m, 2H, OCH_2CH_2), 3.42 (d, ^2J=18, H_β-3), 3.82 (s, 3H, OMe), 5.49 (s, 2H, $ArCH_2$), 6.20 (s, 1H, H-8a), 6.22, 6.25 (2 d, ^4J=1.5 Hz, 2H, H-5, H-7), 7.5-8.3 (m, 4H, $PhNO_2$). MS (110 °C) *m/z* 474 (2), 473 (3, M^+), 356 (2, M^+-$C_5H_{13}SiO_2$), 337 (2, M^+-$C_6H_4NO_2CH_2$), 236 (3, M^+-$C_7H_6NO_2$, -$C_5H_{13}Si$), 83 (100). 4-Methoxy isomer **6.4**, yield 17 mg (27%), oil. IR ($CHCl_3$) ν 2860, 1801, 1613, 1529, 1344, 1125, 1102, 1004 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ -0.03 (s, 9H, $SiCH_3$), 0.86 (t, J=8 Hz, 2H, $SiCH_2$), 3.15 (d, ^2J=18 Hz, H_α-3), 3.25 -3.45 (m, 2H, OCH_2CH_2), 3.42 (d, ^2J=18 Hz, H_β-3), 3.92 (s, 3H, OCH_3), 5.56 (s, 2H, $ArCH_2$), 6.22, 6.28 (2 d, ^4J=1.5 Hz, 2H, H-5, H-7), 6.28 (s, H-8a), 7.5-8.3 (m, 4H, $PhNO_2$). MS (110 °C) *m/z* 337 (3, M^+-$C_7H_6NO_2$), 236 (3, M^+-$C_7H_6NO_2$, -$SiMe_3$), 57 (100).

4-N-Piperidylcarbamoyloxy-6-methoxy-3a-[2-(trimethylsilyl)-eth-1-oxy]-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one (**6.5**) and *6-N-Piperidylcarbamoyloxy-4-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one* (**7.5**). Diiodide **4o** (63 mg, 89 mmol), $(MeCN)_2PdCl_2$ (23.3 mg, 89 mmol) and dppe (36 mg, 89 mmol) are dissolved in toluene (2 ml) and stirred for 4 min at 110°C (nitrogen). Within 3 h Bu_3SnH (77.7 mg, 2.97 eq) in toluene (3 ml) is added in 0.1 ml portions. The deep black reaction mixture is stirred for 1 h at 110°C, then cooled down to r.t. and filtered through silica gel (Et_2O). After removal of the solvent and chromatography (PE/Et_2O, 1:3) the tricyclic isomers (**6.5**:**7.5** = 3:2) are obtained as a light yellow oil, 27 mg (67%). 200 MHz ^1H NMR ($CDCl_3$) δ -0.03, 0.08 (2 s, 9H, 3:2 isomer ratio, $SiCH_3$), 0.92 (t, ^3J=7 Hz, 2H, $SiCH_2$), 1.2-1.7 (m, 6H), 3.0-3.9 (m, 8H, NCH_2, OCH_2, H-3), 3.83, 3.84 (2 s, 3H, OCH_3), 6.15-6.55 (m, 3H, H-4, H-6, H-8a).

6-N,N-Diphenylcarbamoyloxy-4-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one (**7.6**). Diiodophenoxyfuranone **4p** (72.3 mg, 92 mmol), $(MeCN)_2PdCl_2$ (24 mg, 1 eq), dppe (37 mg), Li_2CO_3 (18 mg), LiCl (54 mg, 10 eq) and *n*-$Bu_4N^+Cl^-$ (60 mg) are dissolved in abs. DMF (2 ml) and heated to 120°C (nitrogen). After 3 min at 120°C LiOCHO (4x7 mg) is added in 15 min intervals. After 21 h at 120°C the mixture is cooled to r.t. and filtered through silica gel (Et_2O). The solvent is evaporated and the orange residue is purified by chromatography (Et_2O/PE, 3:2) to give the tricyclus as light brown wax, 7 mg (15%). IR ($CHCl_3$) ν 1799, 1730, 1627, 1594, 1493, 1338, 1296, 1125, 1094, 1057, 1004 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ -0.04 (s, 9H, $SiCH_3$), 0.88-0.95 (m, 2H, $SiCH_2$), 3.06 (d, ^2J=18 Hz, 1H, H_α-3), 3.22-3.40 (m, 2H, OCH_2), 3.38 (d, ^2J=18 Hz, 1H, H_β-3), 3.84 (s, 3H, OCH_3), 6.17 (s, 1H, H-8a), 6.42, 6.43 (2d, ^4J=1 Hz, 2H, H-5, H-7), 7.2-7.4 (m, 10 arom. H). MS (90 °C) *m/z* 205 (2), 170 (13), 169 (100, Ph_2NH), 168 (39).

4-Dimethylcarbamoyloxy-7-iodo-6-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]-

benzofuran-2(3H)-one (**6.7**) and *6-Dimethylcarbamoyloxy-7-iodo-4-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]benzofuran-2(3H)-one* (**7.7**). Diiodide **4n** (306 mg, 0.46 mmol) is dissolved in abs. benzene (15 ml), treated with dppe (18 mg) and $(MeCN)_2PdCl_2$ (12 mg) and heated to reflux (nitrogen). Within 1 h (perfusor) Bu_3SnH (2.4 eq) in abs. benzene (5 ml) is added and the mixture is refluxed for 40 min. After further 2 h in an ultrasonic bath the mixture is filtered through silica gel (5 g, Et_2O) and the solvent is evaporated. The residue is chromatographed to give the tricyclic, isomeric iodides (6-methoxy isomer/ 4-methoxy isomer, 7:2) and the acyclic monoiodide yellow oils. Starting material is also isolated (203 mg). **6.7**, yield 11%. 200 MHz ^1H NMR ($CDCl_3$) δ 0.00 (s, 9H, $SiCH_3$), 0.83-0.95 (m, 2H, $SiCH_2$), 3.06 (s, 3H, $NCH_{3\alpha}$), 3.12 (s, 3H, $NCH_{3\beta}$) 3.3-3.48 (m, 2H, $H_{\alpha+\beta}$-3), 3.93 (s, 3H, OCH_3), 6.33 (s, 1H, H-8a), 6.55 (s, 1H, H-5). **7.7**, yield 27%. IR ($CHCl_3$) ν 1801, 1729, 1612, 1483, 1440, 1408, 1393, 1359, 1320, 1250, 1166, 1124, 1101, 1066, 1003, 864, 842 cm^{-1}. ^1H-NMR 200 MHz ($CDCl_3$) δ 0.01 (s, 9H, $SiCH_3$), 0.83-0.95 (m, 2H, $SiCH_2$), 3.08 (s, 3H, $NCH_{3\alpha}$), 3.22 (s, 3H, a $NCH_{3\beta}$), 3.3-3.5 (m, 2H, $H_{\alpha+\beta}$-3), 3.98 (s, 3H, OCH_3), 6.27 (s, 1H, 8a-H), 6.61 (s, 1H, 5-H). MS *m/z* 536 (60), 535 (95), 418 (100), 408 (70), 154 (65), 72 (100).

4-N,N-Dimethylcarbamoyloxy-6-methoxy-3a-[2-(trimethylsilyl)eth-1-oxy]-3a,8a-dihydrofuro[2,3b]-benzofuran-2(3H)-one (**6.8**). To a solution of diiodide **4n** (203 mg, 0.31 mmol), n-$Bu_4N^+Cl^-$ (270 mg), Li_2CO_3 (60 mg), LiOCHO (42 mg) and LiCl (180 mg) in abs. DMF (5 ml) are added $(MeCN)_2PdCl_2$ (8 mg, 30 mmol) and dppe (12.2 mg) in abs. DMF (0.5 ml) at 85°C (nitrogen). The reaction mixture is stirred for 12 h at 110°C. After cooling to r.t. the mixture is filtered through silica gel (5 g, Et_2O). The solvent is evaporated and the residue purified by chromatography (Et_2O/PE, 1:1) to afford 4-[2-trimethylsilyl)eth-1-oxy]-2(5*H*)-furanone[1] (5 mg, 8%) and the tricyclus, 37.8 mg (30%), semicrystalline. IR ($CHCl_3$) ν 2956, 1798, 1730, 1629, 1607, 1500, 1390, 1318, 1253, 1147, 1122, 1056, 1003, 861, 840 cm^{-1}. 200 MHz ^1H NMR ($CDCl_3$) δ 0.01 (s, 9H, $SiCH_3$), 0.83-0.92 (m, 2H, $SiCH_2$), 3.05 (s, 3H, $NCH_{3\alpha}$), 3.12 (s, 3H, $NCH_{3\beta}$), 3.12 (d, ^2J=18 Hz, 1H, H_α-3), 3.36 (t, ^3J=8 Hz, 2H, OCH_2), 3.37 (d, ^2J=18 Hz, H_β-3), 3.83 (s, 3H, OCH_3), 6.26 (s, 1H, H-8a), 6.41, 6.54 (2 d, ^4J=2 Hz, 2H, H-5, H7). NOE: OMe zu H-7 (4%) und H-5 (4%), $NCH_{3\alpha}$ zu OCH_2 (7%). MS (50 °C) *m/z* 409 (5, M^+), 231 (3), 169 (3), 85 (65), 83 (100). HRMS calcd 409.1557, found 409.1514.

Acknowledgements. We thank the Fonds der Chemischen Industrie, the Deutsche Forschungsgemeinschaft and Hoechst AG for support of our work.

REFERENCES

1. Hoffmann, H.M.R.; Schmidt, B.; Wolff, S. *Tetrahedron* **1989**, *45*, 6113.
2. a) Hoffmann, H.M.R.; Schmidt, B. *J.Toxic.: Toxin Reviews* **1989**, *8* (1&2), 299; b) Schmidt, B. Diploma thesis, University of Hannover, **1989**.
3. For the pioneering work in this area see Büchi, G.; Weinreb, S.M. *J.Am.Chem.Soc.* **1969**, *91*, 5048; Büchi, G.; Weinreb, S.M. *J.Am.Chem.Soc.* **1971**, *93*, 746; Büchi, G.; Liesch, J.M.; Francisco, M.A.; Schuda, P.F. *J.Am.Chem.Soc.* **1981**, *103*, 3497.
4. Wolff, S. PhD thesis, University of Hannover, **1988**.
5. Imai, H.; Nishiguchi, T.; Tanaka, M.; Fukuzumi, K. *J.Org.Chem.* **1977**, *42*, 2309; Imai, H.; Nishiguchi, T.; Tanaka, M.; Fukuzumi, K. *Chem.Lett.* **1976**, 855.
6. Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J.Am.Chem.Soc.* **1984**, *106*, 158.
7. Jeffery, T. *Synthesis* **1987**, 70; *Tetrahedron Lett.* **1985**, *26*, 2667; *J.Chem.Soc., Chem.Commun.* **1984**, 1287.
8. Heck, R.F.: Palladium Reagents in Organic Syntheses, Academic Press, London 1985.
9. Dangles, O.; Guibé, F.; Balavoine, G. *J.Org.Chem.* **1987**, *52*, 4984.
10. Schmidt, B. PhD thesis, University of Hannover, **1991**.