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TETRAHEDRON

Transition Metal Catalysed Cross-Coupling Between Benzylic Halides and Aryl Nucleophiles. Synthesis of some Toxicologically Interesting Tetrachlorobenzyltoluenes.

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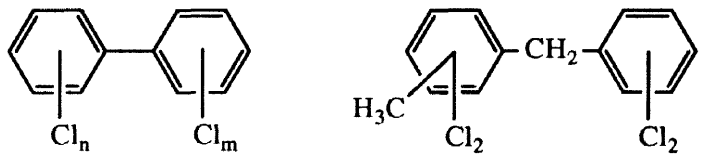
Abstract: The aryl-benzyl cross-coupling in the presence of copper-, nickel- and palladium-catalysts has been investigated with a number of chlorine- and methyl-substituted arylmetal compounds ArM (M= MgBr, ZnCl) and (substituted) benzylic halides $ArCH_2X$. The results have been applied in the selective synthesis of some toxicologically interesting tetrachlorobenzyltoluenes.

INTRODUCTION

Tetrachlorobenzyltoluenes (TCBTs, formal IUPAC-name tetrachloromethyl diphenylmethanes) are used as substitutes for polychlorinated biphenyls (PCBs, **Scheme 1**) in, among others, flame-resistant hydraulic fluids, especially in underground mining in Germany. The estimated losses amounted up to 700 ton/year, and, probably via pit water and mine outputs, significant levels (ranging from 0.1 to 25 mg/kg edible portion) of TCBTs have been detected in fish in the rivers Lippe and Ruhr (Germany) and in the Dutch rivers Meuse (Maas) and Rhine.[1-5]



PCB TCBT

Scheme 1. PolyChloroBiphenyls and TetraChloroBenzylToluenes.

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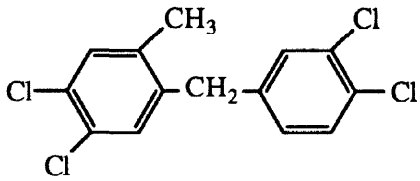
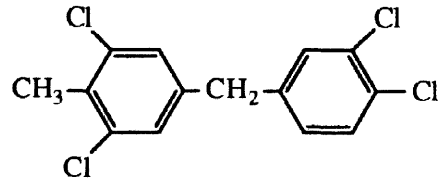
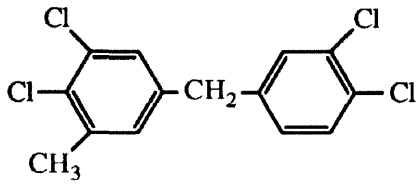
In spite of their resemblance to PCBs, only a few toxicological investigations have been carried out with TCBTs. However, these were carried out with the commercially available isomeric mixtures such as Ugilec-141,[6-9] a technical mixture consisting of 69 previously identified isomers.[10] A recent molecular modelling study earmarked a few of the TCBTs as particularly interesting because they were expected to have a dioxin-type toxicity.[11] Verification of these hypotheses with toxicological research and verification of theoretical models, required the availability of several of these compounds in a pure state (**Scheme 2**). For our investigations, we needed four of the 69 isomeric TCBTs, with a purity > 99 %.



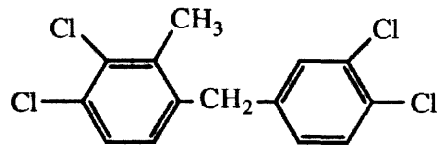
3', 4, 4', 5-tetrachloro-2-methyldiphenylmethane
(TCBT-89)



3, 3', 4', 5-tetrachloro-4-methyldiphenylmethane
(TCBT-94)



3, 3', 4, 4'-tetrachloro-2-methyldiphenylmethane
(TCBT-87)



3', 4, 4', 5-tetrachloro-3-methyldiphenylmethane
(TCBT-88)

Scheme 2. The desired TetraChloroBenzylToluenes.

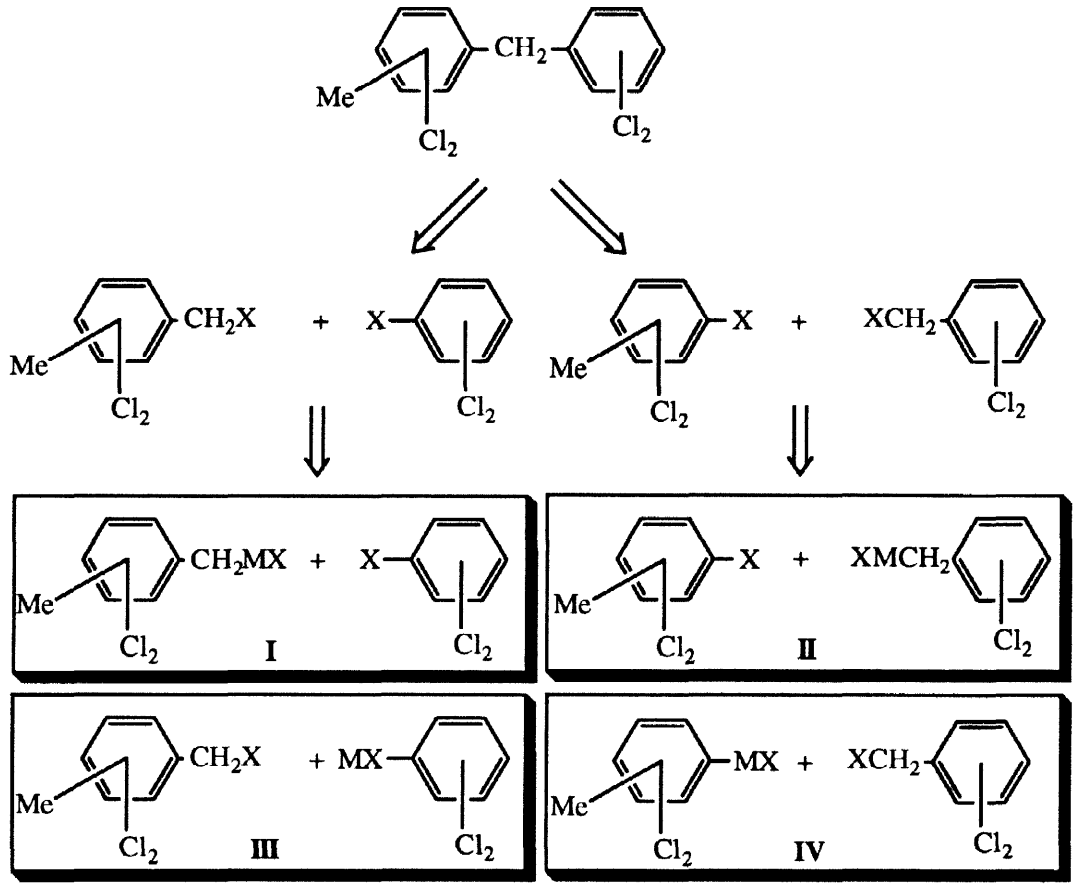
A retrosynthetic approach (**Scheme 3**) suggested four different combinations of organometallic compounds and aryl- or benzyl halides, which could be realised under the influence of a transition-metal catalyst. Combination IV seemed the most likely candidate for the preparation of the designated benzyltoluenes. The others were thought to have less potential either because the starting compound is tedious to prepare (combinations I and II) or because the reactivity of the substrate is not sufficiently delineated, with the possibility to give a mixture of difficultly separable isomeric coupling products (combination II).[12-15]

RESULTS AND DISCUSSION

A. Cross-couplings with various arylmetal compounds and benzylic halides- Investigation of the scope.

It was decided first to investigate the scope of the cross-coupling involved in the synthesis of **TCBTs-87, -88, -89,** and **-94** applying Cu(I)Br-, $NiCl_2(PPh_3)_2$- and $PdCl_2(PPh_3)_2$-catalysts mentioned in the literature on the preparation of unsymmetrical diarylmethanes.[16-21] Thus, a number of transition metal-catalysed cross-couplings between readily available aryl nucleophiles and benzylic halides were carried out (**Scheme 4**). The results are summarised in **Table 1.**

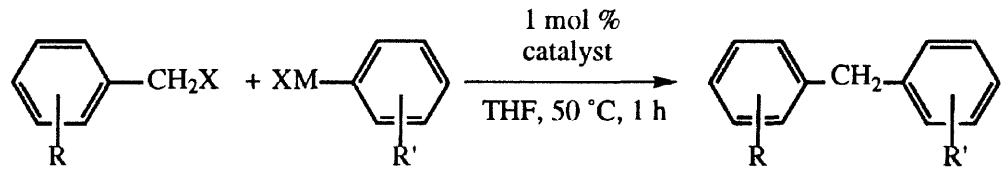
The reaction of benzyl bromide **2a** and benzyl chloride **2b** (**Scheme 4, Table 1**) with phenylmagnesium bromide **1a** proceeded to completion with all of the three catalysts applied, but only with CuBr was the



X = halogen, MX = MgBr, ZnCl, $SnBu_3$

Scheme 3. Possible combinations (I-IV) of a benzyl- and a tolyl-moiety for the preparation of TetraChloroBenzylToluenes.

selectivity satisfactory. The Ni- and Pd-catalysed reactions gave considerable amounts of homocoupled products (PhPh and $PhCH_2CH_2Ph$).



X = Cl, Br; R, R' = H, Cl, CH_3; MX = MgBr, ZnCl

Scheme 4. Transition metal-catalysed aryl-benzyl cross-coupling.

The reactions of the phenylmagnesium bromide **1a** with *ortho*-chlorobenzyl chloride **2c** were found to proceed with insufficient selectivities, irrespective of whether a Cu-, Ni-, or Pd-catalyst was used, but with zinc derivative **1b** these were excellent in the cases of the Ni- and Pd-catalyst. In the presence of CuBr no reaction at all occurred: presumably the obligatory zinc-to-copper transmetallation did not proceed due to the higher electropositivity of the zinc compound compared to copper. The results of the various copper catalysed reactions (entries 1, 2, 3, 4, 5, and 13) show that Cu(I)Br can be an efficient catalyst for the cross-coupling of

Table 1. Cross-Coupling of Aryl Nucleophiles With Benzyl Halides.[a]

entry	RMX[b]	Benzyl halide[b]	Product	Cu(I)Br		$NiCl_2(PPh_3)_2$		$PdCl_2(PPh_3)_2$	
			No.	C.[c]	S.[c]	C.	S.	C.	S.
1	**1a**	**2a**	**3**	>99[d] (98)[e]	94	>99	20	>99	59
2	**1a**	**2b**		>99	94	>99	23	>99	50
3	**1a**	**2c**		>99	57	>99	27	>99	24
4	**1b**	**2a**		0	0	>99	97	>99	>99
5	**1b**	**2c**	**4**	0	0	>99	83	>99 (82)	84
6	**1c**	**2c**	**5**			98	32	>99 (92)	94
7	**1d**	**2c**	**6**			42	92	>96 (74)	>99
8	**1e**	**2c**	**7**			90	99	>99 (97)	>99
9	**1f**	**2c**	**8**			77	25	97 (46)	85
10	**1f**	**2d**	**9**			80	83	98 (89)	95
11	**1g**	**2d**				0[f]		0[f]	
12	**1h**	**2d**	**10**			93 (62)	94	>99	67
13	**1i**	**2d**	**11**	6	23	93 (55)	96	80	56
14	**1j**	**2d**	**12**			66	99	87 (70)	99
15	**1k**	**2d**	**13**			67	63	98 (91)	96

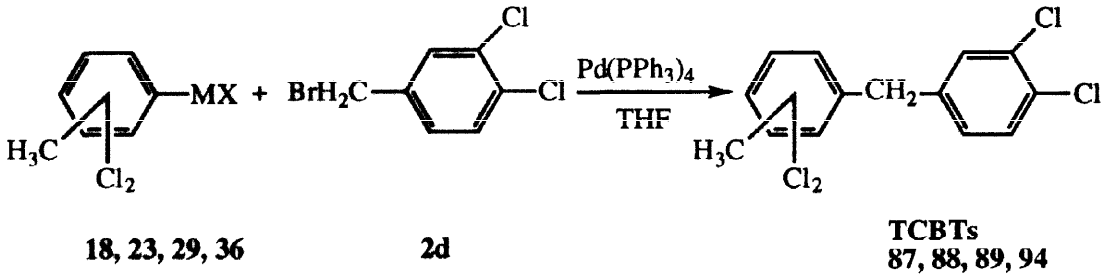
[a] For procedures, see the experimental part. [b] **1a**: PhMgBr; **1b**: PhZnCl; **1c**: 2-Me-C_6H_4ZnCl; **1d**: 2,6-Me_2-C_6H_3ZnCl; **1e**: 3-Cl-2-Me-C_6H_3ZnCl; **1f**: 2,4,6-Me_3-C_6H_2ZnCl; **1g**: 2-Cl-C_6H_4ZnCl; **1h**: 3-Cl-C_6H_4ZnCl; **1i**: 4-Cl-C_6H_4ZnCl; **1j**: 2,6-Cl_2-C_6H_3ZnCl; **1k**: 2,3-Cl_2-C_6H_3ZnCl; **2a**: $PhCH_2Br$; **2b**: $PhCH_2Cl$; **2c**: 2-Cl-$C_6H_4CH_2Cl$; **2d**: 3,4-Cl_2-$C_6H_3CH_2Br$. [c] Conversion (C.) and Selectivity (S.) determined by GLC after 1h. [d] Without catalyst: mainly homo-coupling. [e] Isolated yields in parentheses. [f] After 3 days.

arylmagnesium bromides with benzyl halides but that it is not suitable for the cross-coupling of arylzinc chlorides with chlorine-substituted benzyl halides. Entries 11, 12 and 13 of Table 1 shows that *meta*- and *para*-chlorophenylzinc chloride **1h** and **1i** couple satisfactorily with **2d** under the influence of $NiCl_2(PPh_3)_2$ but that, remarkably, with *ortho*-chlorophenylzinc chloride **1g** no reaction occurred, irrespective of whether $NiCl_2(PPh_3)_2$ or $PdCl_2(PPh_3)_2$ was used as the catalyst. This inertness may be ascribed to an intramolecular coordination of the chlorine towards the zinc, resulting in a lower nucleophilicity so that the reduction to the zerovalent catalytically active Ni- or Pd-species cannot occur. This explanation is supported by the fact that $Pd(PPh_3)_4$ has been reported to effectively catalyse the coupling of *ortho*-chlorophenylzinc chloride with aromatic halides.[22] Comparison of entries 14 and 15 shows that in reaction with dichlorosubstituted arylzinc halides **1j** and **1k** $PdCl_2(PPh_3)_2$ worked with higher selectivity than did the Ni-catalyst. In these reactions we did not observe any retarding effect of the neighbouring chlorine(s) on the reactivity of the zinc chloride.

For the reaction of methyl-substituted aryl nucleophiles (entries 6, 7 and 9) with **2c**, $PdCl_2(PPh_3)_2$ was shown to be the best catalyst. Increasing methylsubstitution had no influence on the reaction. No significant difference in reactivity was found between the reactions with **2c** and **2d**.

From these results we conclude that: 1. Cu(I)Br is a suitable catalyst for the benzyl-aryl cross-coupling when arylmagnesium halides are used, 2. $NiCl_2(PPh_3)_2$ is the most selective catalyst for the cross-coupling of

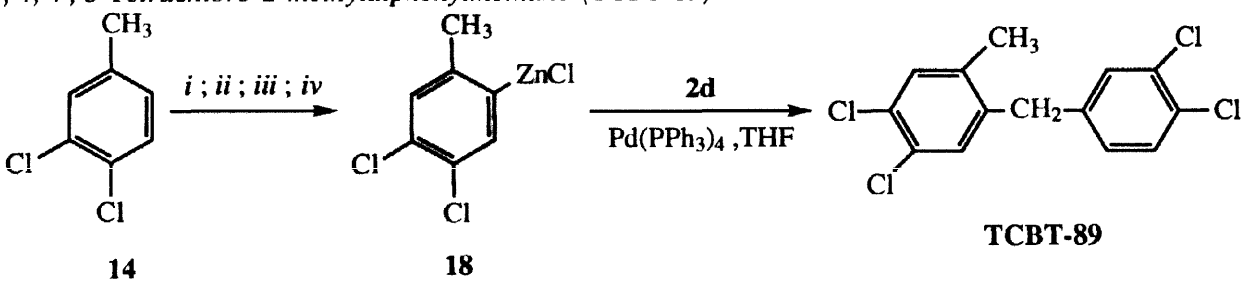
mono-chlorophenylzinc chlorides, 3. The use of more sterically hindered nucleophiles does not seem to have a profound influence on the Pd-catalysed reaction, but the Ni-catalysed reaction is severely hampered, 4. An increasing degree of substitution requires the use of more selective catalysts, nucleophiles with lower polarity of the carbon metal bond and longer reaction times. Based on the above mentioned experiences, the Pd-catalysed cross-coupling was applied for the preparation of the aforementioned TCBTs (**Scheme 5**).



Scheme 5. Pd-catalysed cross-coupling of dichlorobenzyl bromide with metallated dichlorotoluene.

B. Synthesis of the four tetrachloromethyldiphenylmethanes.

3', 4, 4', 5-Tetrachloro-2-methyldiphenylmethane (TCBT-89).



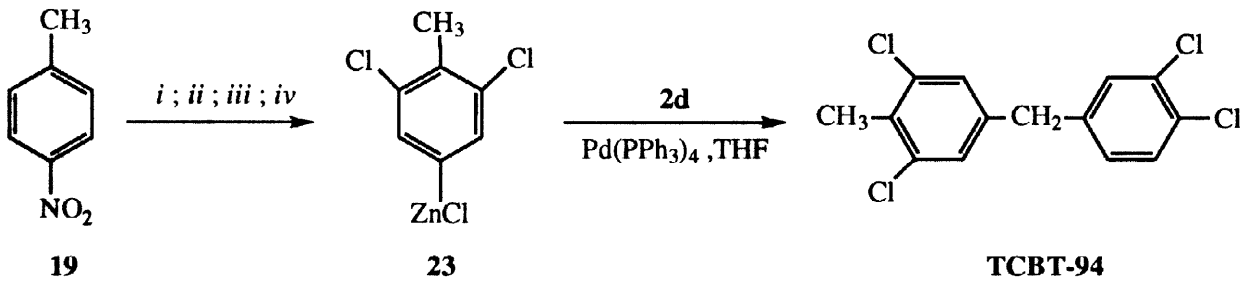
i. HNO_3, H_2SO_4; *ii*. Fe/HCl,H_2O; *iii*. $NaNO_2$/CuBr, HBr, H_2O; *iv*. BuLi/THF, $ZnCl_2$.

Scheme 6. The route to **TCBT-89.**

In the first step (**Scheme 6**) the commercially available 3,4-dichlorotoluene **14** was nitrated with a mixture of nitric and sulfuric acid at a slightly elevated temperature. Repeated crystallisation resulted in 22 % yield of the desired *o*-nitro-derivative **15**.[23] Reduction of the nitrogroup with Fe/HCl gave, after steam distillation, the expected toluidine **16** in a 60 % yield.[24] Another method for the reduction of the nitrogroup, employing hydrazine monohydrate, and Ru/C as the catalyst gave **16** in 98% yield.[25] When **16** was subjected to Sandmeyer's reaction (diazotation of the aniline and subsequent reaction with copper bromide), the bromide **17** was obtained in an 88 % yield. The nucleophilic reaction partner, 4, 5-dichloro-2-tolylzinc chloride **18**, was prepared from **17** by a lithium-bromine exchange at low temperatures with *n*-BuLi, followed by a transmetallation with anhydrous zinc chloride. Palladium-catalysed cross-coupling with the benzylic bromide **2d** gave, after repeated crystallisation, the desired **TCBT-89** in a 36 % yield.

3, 3', 4', 5-Tetrachloro-4-methyldiphenylmethane (TCBT-94).

The first step in the synthesis of **TCBT-94** (**Scheme 7**) is the chlorination of the starting compound *p*-nitrotoluene **19** with chlorine gas by a method described by Weinstock *et al.* using antimony(V)chloride as a



19 **23** **TCBT-94**

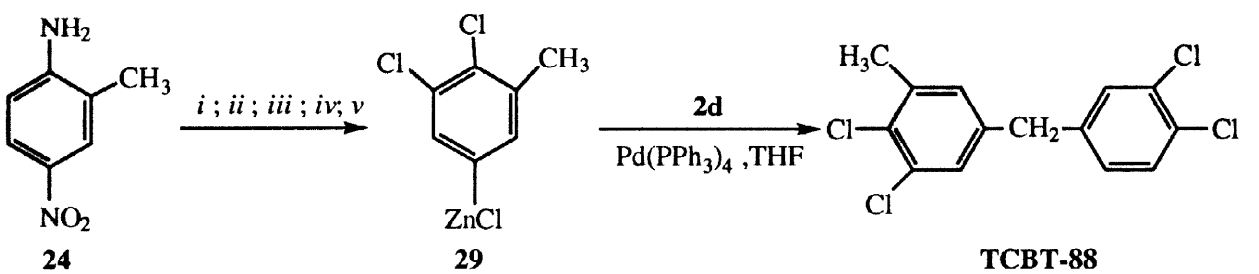
i. $SbCl_5/Cl_2$, H_2O, Cu/CH_3COOH/PhCl; *ii*. Fe/HCl, H_2O; *iii*. $NaNO_2$/CuBr, HBr, H_2O; *iv*. BuLi/THF, $ZnCl_2$.

Scheme 7. The route to **TCBT-94.**

catalyst/activator.[26] The resulting mixture of di-, tri-, and tetrachlorinated products was selectively dechlorinated to 2,6-dichloro-4-nitrotoluene **20** with copper powder and glacial acetic acid in 65 % yield.[27] Reduction of the nitro group with Fe/HCl, followed by a Sandmeyer reaction with copper bromide, of toluidine **21** gave the desired bromo dichloroderivative **22** in an 62 % yield. Cross-coupling of the resulting 4, 5-dichloro-2-tolylzinc chloride **23** with dichlorobenzyl bromide **2d** using 5 mol % $Pd(PPh_3)_4$ gave, after crystallisation, the expected **TCBT-94** in a 41 % yield.

3', 4, 4', 5-Tetrachloro-3-methyldiphenylmethane (TCBT-88).

The starting compound, 2-methyl-4-nitroaniline **24** was chlorinated to yield, after crystallisation from acetonitrile, compound **25** (**Scheme 8**). By a Sandmeyer reaction with copper(I)chloride the amino group was converted into the corresponding chlorine in **26**, subsequent reduction of the nitro group gave aniline **27**. This compound was converted into **28** by another Sandmeyer reaction with copper(I)bromide in a 63 % yield. In order to synthesise the target compound **TCBT-88**, bromide **28** was subjected to a lithium-bromine exchange with *n*-butyllithium in THF, followed by a transmetallation to the corresponding 4, 5-dichloro-3-tolylzinc chloride **29** The reaction of **29** with benzyl bromide **2d** in the presence of a catalytic amount of $Pd(PPh_3)_4$, afforded the depicted tetrachlorobenzyltoluene **TCBT-88** in a 41 % yield.



24 **29** **TCBT-88**

i. Cl_2; *ii*. $NaNO_2$/CuCl, HCl, H_2O; *iii*. Fe/HCl, H_2O; *iv*. $NaNO_2$/CuBr, HBr, H_2O; *v*. BuLi/THF, $ZnCl_2$.

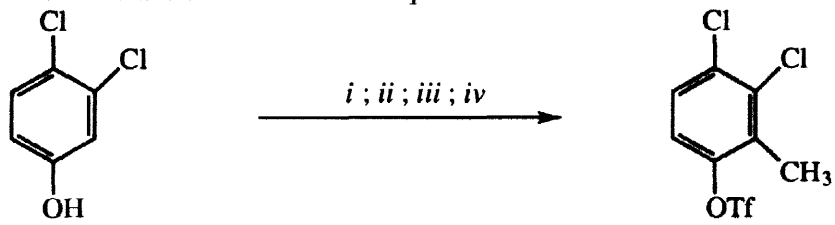
Scheme 8. The route to **TCBT-88.**

3, 3', 4, 4'-Tetrachloro-2-methyldiphenylmethane (TCBT-87).

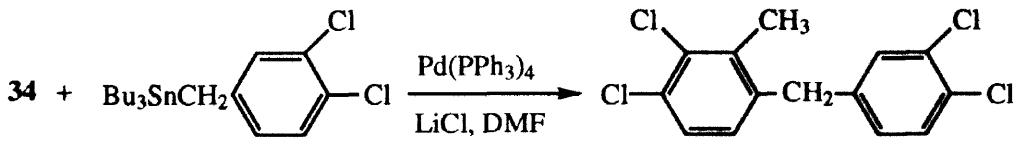
As we did not succeed after numerous attempts to synthesise the necessary 6-bromo-2,3-dichlorotoluene, a completely different strategy (**Scheme 9**) was chosen for the preparation of **TCBT-87**. The phenolic

OH-group in 3,4-dichlorophenol **30** was protected using *N, N*-diethylcarbamoyl chloride in pyridine.[28]

The so protected phenolic OH-group in **31** functions as a DMG (Directed Metallation Group).[29] Metallation of **31** with *sec*-butyllithium-TMEDA at low temperature, resulted in *ortho*-metallation at the position between the DMG and the chlorine. Subsequent functionalisation with excess methyl iodide gave compound **32**



30 **34**



35 **TCBT-87**

i. $Et_2N(CO)Cl$, pyridine; *ii*. *s*-BuLi/TMEDA, THF, CH_3I; *iii*. $LiAlH_4$/THF; *iv*. Tf_2O, pyridine.

Scheme 9. The route to **TCBT-87.**

in excellent yields. Removal of the carbamoyl moiety with $LiAlH_4$ afforded the phenol **33**.[30,31] By reaction with triflic anhydride in pyridine the corresponding triflate **34** was obtained in excellent yields. The target compound (**TCBT-87**) was obtained by an unprecedented Stille coupling of the aromatic triflate (**34**) with 3,4-dichlorobenzyltributyltin **35** with $Pd(PPh_3)_4$ in DMF.[32,33]

CONCLUSIONS

Starting from commercially available materials, the aryl moieties of the desired tetrachlorobenzyltoluenes are preparable. The latter can be used in the form of dichlorotolylzinc chlorides in palladium-catalysed cross-couplings with 3, 4-dichlorobenzyl chloride **2d** to give the desired compunds **TCBT-89**, **TCBT-94**, and **TCBT-88** with excellent purities and reasonable yields. The fourth TCBT, **TCBT-87** can be prepared by the synthesis of the dichlorotolyltriflate **34** and subsequent Stille cross-coupling with 3,4-dichlorobenzyl tributyltin **35**, which seems to be without precedent. In all cross-coupling reactions small amounts of homo-coupling products are found, but sufficiently pure end products can be obtained by repeated crystallisations. Preliminary toxicologic investigations have shown that **TCBT-87** indeed shows dioxin-type toxicity, further toxicological research being currently in progress.

EXPERIMENTAL

General. All ^1H- and ^{13}C-NMR spectra were recorded on a Bruker AC-300 spectrometer (^1H: 300 MHz, ^{13}C: 75 MHz) at room temperature, using $CDCl_3$ as solvent and internal standard unless otherwise stated.

Chemical shifts are given in ppm downfield from TMS, coupling constants are given in Herz. $NiCl_2(PPh_3)_2$[34], $PdCl_2(PPh_3)_2$[35] and $Pd(PPh_3)_4$[36] were prepared by literature procedures. THF was dried by distillation from $LiAlH_4$/ benzophenone, DMF by distillation from calciumhydride and stored under nitrogen over molsieve 4Å. Diethyl ether was dried over powdered KOH and subsequently filtered, hexane was distilled from sodium sand/ benzophenone. Zinc chloride was dried by azeotropic distillation with toluene. Phenylmagnesium bromide was prepared from bromobenzene and magnesium in THF. After titration with ethanol, using 1,10-phenantroline as indicator, a solution of 1.43 M phenylmagnesium bromide in THF was obtained, which was stored under nitrogen and used as such. All other reagents were commercially available and were used as such.

3, 4-Dichlorobenzyl bromide (2d, Scheme 5). Following the procedure for *para*-nitrobenzyl bromide[24] **2d** was prepared from 3,4-dichlorotoluene **14** and bromine in a 66% yield. B.p. 84-86°C/ 0.3 mm Hg ^{1}H-NMR: δ= 7.47 (d, *J*= 2.1, 1H, C_2(H)), 7.38 (d, *J*= 8.2, 1H, C_5(H)), 7.20 (dd, *J*= 8.2, 2.1, 1H, C_6(H)), 4.39 (s, 2H, C_{CH2}(H)). ^{13}C-NMR: δ= 137.9 (C_1), 132.7 (C_3), 132.5 (C_4), 130.8 (C_2), 130.7 (C_5), 128.4 (C_6), 31.5 (C_{CH2}).

Diphenylmethane (3, Scheme 5, Table 1). Yield 98%, from 4.3 g (25 mmole) of benzyl bromide (**2a**) and 18 mL of a solution of 1.43 M (26 mmole) phenylmagnesium bromide (**1a**) in 50 mL of dry THF. ^{1}H-NMR: δ= 7.81-7.70(m, 10H, $C_{arom.}$(H)), 4.47 (s, 2H, CH_2). ^{13}C-NMR: δ= 141.0 (C_1), 128.8 (C_2), 128.3 (C_3), 126.2 (C_4), 41.7 (C_{CH2}).

2-Chlorodiphenylmethane (4, Scheme 5, Table 1). Yield 82%, from 4.0 g (25 mmole) 2-chlorobenzyl chloride (**2c**) and 26 mmole of phenylzinc chloride prepared from 18 mL of a solution of 1.43 M (26 mmole) phenylmagnesium (**1a**) bromide in 50 mL of dry THF to which 3.4 g (25 mmole) $ZnCl_2$ was added. ^{1}H-NMR: δ= 7.58-7.10 (m, 9H, $C_{arom.}$(H)), 4.21 (s, 2H, CH_2). ^{13}C-NMR: δ= 139.4 ($C_{1'}$), 138.6 (C_1), 134.1 (C_2), 130.9 (C_5), 129.4 (C_6), 128.8 ($C_{2',6'}$), 128.4 ($C_{3',5'}$), 127.5 (C_3), 126.7 (C_4), 126.1 ($C_{4'}$), 39.1 (C_{CH2}).

Typical Cross-Coupling Procedure. Preparation of 2'-Chloro-2, 6-dimethyldiphenylmethane (6, Scheme 5, Table 1). A 100 mL three-necked round-bottomed flask equipped with a gas inlet, a thermometer and a reflux condenser was charged with 50 mL of dry THF and 4.6 g (25 mmole) of 2,6-dibromoxylene . The air in the flask was completely replaced with nitrogen and the mixture was cooled at -80°C. Subsequently 17 mL of a solution of 1.6 M *n*-BuLi in hexane was added over a few min. The mixture was stirred for 30 minutes at -80°C after which 3.4 g (25 mmole) of $ZnCl_2$ was added. The reaction mixture was stirred for another 15 min and allowed to reach 0°C. The mixture was cooled at < -90°C after which 4.0 g (25 mmole) of 2-chlorobenzyl chloride (**2c**) was added, immediately followed by 0.25 mmole of the catalyst (140 mg $NiCl_2(PPh_3)_2$, 180 mg $PdCl_2(PPh_3)_2$ or 40 mg copper(I)bromide, respectively). The reaction mixture was warmed to 50°C and stirred for 1 hr. The reaction mixture was poured into 100 mL of 2 M HCl and extracted three times with 25 mL portions of pentane. The combined organic fractions were dried over $MgSO_4$, the solvent removed and the resulting oil flash chromatographed over a short silica column (3 cm) using pentane as the eluens. The desired product was obtained in a 74 % yield. ^{1}H-NMR: δ= 7.43 (d, *J* = 7.7, 1H, C_5(H)), 7.19 - 7.05 (m, 5H, $C_{3'...6'}$(H)), 6.60 (d, *J* = 7.7, 2H, $C_{4,6}$(H)), 4.12 (s, 2H, CH_2), 2.23 (s, 6H, $C_{2,6}(CH_3)$). ^{13}C-NMR: δ= 137.4 ($C_{2,6}$), 137.2 (C_1), 135.7 ($C_{1'}$), 134.4 ($C_{2'}$), 129.1 ($C_{6'}$), 128.1 ($C_{3'}$), 127.2 ($C_{4'}$), 126.8 ($C_{5'}$), 126.6 (C_4), 128.2 ($C_{3,5}$), 32.6 (C_{CH2}), 19.9 (C_{CH3}). HRMS found: 230.0872 calculated: 230.0862

The following compounds were prepared by analogous procedures:

2'-Chloro-2-methyldiphenylmethane (5, Scheme 5, Table 1). Yield 92%, from 4.0 g (25

mmole) 2-chlorobenzyl chloride (**2c**) and 4.3 g (25 mmole) 2-bromotoluene. ^{1}H-NMR: δ= 7.66-7.14 (m, 8H, $C_{arom.}$(H)), 4.33 (s, 2H, CH_2), 2.50 (s, 3H, CH_3). ^{13}C-NMR: δ= 138.0 (C_1), 137.3 (C_2), 136.6 ($C_{1'}$), 134.3 ($C_{2'}$), 130.2 ($C_{6,\,6'}$), 129.6 (C_3), 129.2 ($C_{3'}$), 127.4 ($C_{4'}$), 126.7 ($C_{5'}$), 126.6 (C_5), 126.1 (C_4), 36.9 (C_{CH2}), 19.2 (C_{CH3}). HRMS found: 216.0753 calculated: 216.0706

2' 3-Dichloro-2-methyldiphenylmethane (7, Scheme 5, Table 1). Yield 97%, from 4.0 g (25 mmole) 2-chlorobenzyl chloride (**2c**) and 5.1 g (25 mmole) 2-bromo-6-chlorotoluene. ^{1}H-NMR: δ= 7.51- 7.47 (m, 1H, $C_{3'}$(H)), 7.29 - 7.19 (m, 4H, $C_{4,\,4',\,5',\,6'}$(H)), 7.02 - 6.99 (m, 2H, $C_{5,\,6}$(H)), 4.11 (s, 2H, CH_2), 2.31 (s, 3H, $C_2(CH_3)$). ^{13}C-NMR: δ= 138.5 (C_1), 137.3 (C_2), 135.9 ($C_{1'}$), 134.2 ($C_{2'}$), 132.0 (C_3), 130.7 ($C_{6'}$), 130.1 (C_6), 130.0 ($C_{3'}$), 129.4 ($C_{4'}$), 127.6 (C_5), 126.8 ($C_{5'}$), 126.0 (C_4), 36.1 (C_{CH2}), 19.3 (C_{CH3}). HRMS found: 250.0320 calculated: 250.0316

2'-Chloro-2, 4, 6-trimethyldiphenylmethane (8, Scheme 5, Table 1). Yield 46%, from 4.0 g (25 mmole) 2-chlorobenzyl chloride (**2c**) and 5.0 g (25 mmole) bromomesitylene. ^{1}H-NMR: δ= 7.41 (dd, *J* = 7.8, 1.4, 1H, $C_{3'}$(H)), 7.14 (ddd, *J* = 7.8, 7.5, 0.8, 1H, $C_{4'}$(H)), 7.06 (ddd, *J* = 7.6, 7.5, 1.4, 1H, $C_{5'}$(H)), 6.95 (s, 2H, $C_{3,\,4}$(H)), 6.61 (dd, *J* = 7.6, 0.8, 1H, $C_{6'}$(H)), 4.07 (s, 2H, CH_2), 2.34 (s, 3H, $C_4(CH_3)$), 2.18 (s, 6H, $C_{2,\,6}(CH_3)$). ^{13}C-NMR: δ= 137.5 ($C_{1'}$), 137.2 ($C_{2,\,6}$), 135.9 (C_1), 134.3 (C_4), 132.6 ($C_{2'}$), 129.0 ($C_{6'}$), 128.9 ($C_{3,\,5}$), 128.2 ($C_{3'}$), 127.1 ($C_{4'}$), 126.8 ($C_{5'}$), 32.3 (C_{CH2}), 20.9 ($C_{4\text{-}CH3}$), 19.8 (C_{CH3}). HRMS found: 244.1154 calculated: 244.1019

3', 4'-Dichloro-2, 4, 6-trimethyldiphenylmethane (9, Scheme 5, Table 1). Yield 89%, from 6.0 g (25 mmole) 3, 4-dichlorobenzyl bromide (**2d**) and 5.0 g (25 mmole) bromomesitylene. ^{1}H-NMR: δ= 7.32 (d, *J* = 8.2, 1H, $C_{5'}$(H)), 7.14 (d, *J* = 2.0, 1H, $C_{2'}$(H)), 6.94 (s, 2H, $C_{3,\,5}$(H)), 6.87 (dd, *J* = 8.2, 2.0, 1H, $C_{6'}$(H)), 4.00 (s, 2H, CH_2), 2.34 (s, 3H, $C_4(CH_3)$), 2.23 (s, 6H, $C_{2,\,6}(CH_3)$). ^{13}C-NMR: δ= 140.6 ($C_{1'}$), 136.8 ($C_{2,\,6}$), 136.2 (C_1), 132.4 ($C_{3',\,4}$), 130.3 ($C_{4'}$), 130.2 ($C_{3,\,5}$), 129.7 ($C_{2'}$), 129.1 ($C_{5'}$), 127.2 ($C_{6'}$), 33.9 (C_{CH2}), 20.9 (C_{CH3}), 20.0 ($C_{4\text{-}CH3}$). HRMS found: 278.0633 calculated: 278.0629

3, 3', 4-Trichlorodiphenylmethane (10, Scheme 5, Table 1). Yield 62%, from 6.0 g (25 mmole) 3, 4-dichlorobenzyl bromide (**2d**) and 3.3 g (25 mmole) 3-bromochlorobenzene. ^{1}H-NMR: δ= 7.36 (d, *J* = 8.2, 1H, C_5(H)), 7.26 (d, *J* = 2.1, 1H, C_2(H)), 7.24 - 7.20 (m, 2H, $C_{2',\,4'}$(H)), 7.15 (m, 1H, $C_{5'}$(H)), 7.00 (dd, *J* = 8.2, 2.1, 1H, C_6(H)), 3.90 (s, 2H, CH_2). ^{13}C-NMR: δ= 141.7 (C_1), 140.4 ($C_{1'}$), 134.5 (C_3), 132.5 ($C_{3'}$), 130.7 ($C_{2'}$), 130.5 (C_5), 130.3 ($C_{4'}$), 129.9 ($C_{5'}$), 128.9 (C_2), 128.3 (C_6), 127.0 ($C_{6'}$), 126.8 (C_4), 40.5 (C_{CH2}). HRMS found: 269.9645 calculated: 269.9770

3, 4, 4'-Trichlorodiphenylmethane (11, Scheme 5, Table 1). Yield 55%, from 6.0 g (25 mmole) 3, 4-dichlorobenzyl bromide (**2d**) and 3.3 g (25 mmole) 4-bromochlorobenzene. ^{1}H-NMR: δ= 7.36 (d, *J* = 8.2, 1H, C_4(H)), 7.29 (d, *J* = 8.4, 2H, $C_{3',\,5'}$(H)), 7.26 (d, *J* = 2.0, 1H, C_1(H)), 7.10 (d, *J* = 8.4, 2H, $C_{2',\,6'}$(H)), 7.00 (dd, *J* = 8.2, 2.0, 1H, C_5(H)), 3.90 (s, 2H, CH_2). ^{13}C-NMR: δ= 140.7 (C_1), 138.1 ($C_{1'}$), 132.4 (C_3), 132.3 ($C_{4'}$), 131.2 (C_2), 130.3 (C_5), 130.2 (C_4), 130.1 ($C_{3',\,5'}$), 128.7 ($C_{2',\,6'}$), 128.2 (C_6), 40.1 (C_{CH2}). HRMS found: 269.9776 calculated: 269.9770

2, 6, 3', 4'-Tetrachlorodiphenylmethane (12, Scheme 5, Table 1). Yield 70%, from 6.0 g (25 mmole) 3, 4-dichlorobenzyl bromide (**2d**) and 5.6 g (25 mmole) bromo-2, 6-dichlorobenzene. ^{1}H-NMR: δ= 7.34 (d, *J* = 8.0, 2H, $C_{3,\,5}$(H)), 7.32 (d, *J* = 8.3, 1H, $C_{5'}$(H)), 7.29 (d, *J* = 2.1, 1H, $C_{2'}$(H)), 7.16 (dd, *J* = 8.3, 7.5, 1H, C_4(H)), 7.04 (dd, *J* = 8.3, 2.1, 1H, $C_{6'}$(H)), 4.28 (s, 2H, CH_2). ^{13}C-NMR: δ= 138.1 (C_1), 135.7 ($C_{1'}$), 135.3 ($C_{2',\,6'}$), 132.1 (C_3), 130.1 (C_4), 130.0 (C_5), 130.0 ($C_{4'}$), 128.4 (C_2), 128.2 ($C_{3',\,5'}$), 127.6 (C_6), 35.5 (C_{CH2}). HRMS found: 303.9427 calculated: 303.9380

2, 3, 3', 4'-Tetrachlorodiphenylmethane (13, Scheme 5, Table 1). Yield 91%, from 6.0 g

(25 mmole) 3, 4-dichlorobenzyl bromide (**2d**) and 5.6 g (25 mmole) bromo-2, 3-dichlorobenzene. ^{1}H-NMR: δ= 7.37 (dd, *J* = 8.4, 1.5, 1H, C_4(H)), 7.35 (d, *J* = 8.2, 1H, $C_{5'}$(H)), 7.27 (d, *J* = 1.9, 1H, $C_{2'}$(H)), 7.15 (dd, *J* = 8.4, 7.7, 1H, C_5(H)), 7.07 (dd, *J* = 7.7, 1.5, 1H, C_6(H)), 7.01 (dd, *J* = 8.2, 1.9, 1H, $C_{6'}$(H)), 4.08 (s, 2H, CH_2). ^{13}C-NMR: δ= 139.6 (C_2), 139.1 ($C_{1'}$), 132.5 (C_3), 132.4 ($C_{3'}$), 132.4 (C_4), 130.6 ($C_{2'}$), 130.5 ($C_{4'}$), 130.3 ($C_{5'}$), 130.3 ($C_{6'}$), 129.0 (C_1), 128.2 (C_6), 127.3 (C_5), 39.2 (C_{CH2}). HRMS found: 303.9422 calculated: 303.9380

4, 5-Dichloro-2-nitrotoluene (15, Scheme 6). The nitration of 3,4-dichlorotoluene **14** was carried out by a procedure described in the literature[37]. By threefold crystallisation of the crude product (yield 72 %) from ethanol pure **14** m.p. 57-59°C (uncorr., lit[37] 63-64°C), was obtained in a (22 %). ^{1}H-NMR: δ= 8.11 (s, 1H, C_3(H)), 7.48 (s, 1H, C_6(H)), 2.60 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 147.4 (C_2), 137.7 (C_5), 134.1 (C_6), 133.6 (C_4), 130.9 (C_1), 126.6 (C_3), 20.1 (C_{CH3}).

2-Amino-4, 5-dichlorotoluene (16, Scheme 6). The procedure described in the literature[24] gave, starting from 15, pure **16** in 60% yield, (m.p. 101-102°C, uncorr.). ^{1}H-NMR: δ= 7.12 (s, 1H, C_2(H)), 6.78 (s, 1H, C_5(H)), 5.27 (bs, 2H, NH_2), 2.03 (s, 3H, CH_3). ^{13}C-NMR: δ= 149.5 (C_6), 133.3 (C_2), 130.5 (C_3), 124.7 (C_1),118.4 (C_4), 116.7 (C_5), 19.1 (C_{CH3}).

2-Amino-4, 5-dichlorotoluene (16, Scheme 6) by reduction with Ru/C-hydrazine monohydrate. A modified procedure for **16** gave the compound in 98 % yield as a yellow powder.[25]

2-Bromo-4, 5-dichlorotoluene (17, Scheme 6). The compound was prepared in a 82% yield from **16** following the general procedure for diazotation and subsequent halogenation as described in ref[38] m.p. 85-86°C, uncorr. ^{1}H-NMR: δ= 7.60 (s, 1H, C_3(H)), 7.30 (s, 1H, C_6(H)), 2.35 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 138.0 (C_1), 133.3 (C_3), 131.7 (C_6), 131.3 (C_4),130.4 (C_5), 122.8 (C_2), 22.3 (C_{CH3}).

2, 6-Dichloro-4-nitrotoluene (20, Scheme 7). Following the known procedure[26] **20** was obtained in 45 % yield as a yellow solid starting from 0.5 mol of *para*-nitrotoluene **19**. ^{1}H-NMR: ($CDCl_3$/DMSO-d_6, 1/1): δ= 7.84 (s, 2H, $C_{3,4}$(H)), 2.23 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: ($CDCl_3$/DMSO-d_6, 1/1): δ= 145.7 (C_4), 141.9 (C_1), 135.9 ($C_{2,6}$), 122.4 ($C_{3,5}$), 17.8 (C_{CH3}).

4-Amino-2, 6-dichlorotoluene (21, Scheme 7) was prepared using the Fe/HCl-procedure described for compound **16** from 2, 6-dichloro-4-nitrotoluene **20** in an 81 % yield as a white solid. ^{1}H-NMR: δ= 6.48 (s, 2H, $C_{3,4}$(H)), 3.93 (bs, 2H, C_{NH2}(H)), 2.18 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 145.9 (C_4), 135.3 ($C_{2,6}$), 122.5 (C_1), 114.2 ($C_{3,5}$), 16.1 (C_{CH3}).

4-Bromo-2, 6-dichlorotoluene (22, Scheme 7). The compound was prepared from 75 mmole **21** in a 62% yield following the general procedure for diazotation and subsequent halogenation as described in the literature[38] ^{1}H-NMR: δ= 7.42 (s, 2H, $C_{4,5}$(H)), 2.40 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 136.1 ($C_{2,6}$), 133.6 (C_1), 130.4 ($C_{3,5}$), 119.0 (C_4), 17.1 (C_{CH3}).

2-Amino-3-chloro-5-nitrotoluene (25, Scheme 8). A 2 L, three-necked, round-bottomed flask, equipped with a mechanical stirrer was charged with 76.5 g (0.5 mol) of 2-methyl-4-nitroaniline **24** and 450 mL of 10 M HCl. Stirring of the yellow reaction mixture for 20 hours at room temperature resulted in a fine grey suspension. About 1 kg of crushed ice was added and a solution of 35 g (0.5 mol) chlorine gas in 100 mL of cold CCl_4 was added portionwise over a period of 30 minutes with vigorous stirring. The colour of the reaction mixture changed from grey to brown. After an additional 30 minutes, the organic solvent was removed under reduced pressure. Filtration gave an orange-brown residue, which was successively washed twice with 500 mL of ice water, 200 mL of 50 % ethanol/water and 500 mL of water and dried *in vacuo* affording 67.3 g (yield 72%) of the product. ^{1}H-NMR($CDCl_3$/DMSO-d_6, 1/1). δ= 8.14 (d, *J*= 2.5, C_2(H)), 7.93 (d, *J*= 2.5, 1H,

C_4(H)), 5.4 - 3.8 (bs, 2H, C_{NH2}(H)), 2.28 (s, 3H, C_{CH3}(H)). ^{13}C-NMR(CDCl$_3$/DMSO-d$_6$, 1/1): δ= 145.4 (C_2), 134.2 (C_5), 121.7 (C_6), 120.6 (C_4), 119.2 (C_1), 114.0 (C_3), 15.3 (C_{CH3}).

2, 3-Dichloro-5-nitrotoluene (26, Scheme 8). The compound was prepared from 48 mmole **25** in a 80 % yield following the general procedure for diazotation and subsequent halogenation as described in the literature.[38] ^{1}H-NMR: δ= 8.18 (d, *J*= 2.5, 1H, C_6(H)), 8.03 (d, *J*= 2.5, C_4(H)), 2.53 (s, 3H, CH_3). ^{13}C-NMR: δ= 145.8 (C_5), 139.9 (C_2), 139.8 (C_1), 134.0 (C_3), 123.4 (C_6), 122.9 (C_4), 21.5 (CH_3).

5-Amino-2, 3-dichlorotoluene (27, Scheme 8). The compound was prepared from 0.15 mole of **26** in a 78% yield as a purple solid using the Fe/HCl-procedure analogous to the procedure for compound **16**. ^{1}H-NMR: δ= 6.63 (d, *J*= 2.5,1H,C_4(H)), 6.50 (d, *J*= 2.5, 1H, C_6(H)), 5.41 (bs, 2H, C_{NH2}(H)), 2.20 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 150.6 (C_5), 140.1 (C_1), 133.8 (C_3), 119.1 (C_2), 117.4 (C_6), 115.0 (C_4), 23.2 (C_{CH3}).

5-Bromo-2, 3-dichlorotoluene (28, Scheme 8). The compound was prepared from 0.1 mole **27** in a 61% yield following the general procedure for diazotation and subsequent halogenation as described in ref[38] ^{1}H-NMR: δ= 7.46 (d, *J*= 2.2, 1H, C_6(H)), 7.29 (d, *J*= 2.2, 1H, C_4(H)), 2.39 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 139.9 (C_1), 133.7 (C_3), 131.9 (C_2), 130.4 ($C_{6,4}$), 119.6 (C_5), 21.0 (C_{CH3}).

1-N, N-Diethylcarbamoyl-3, 4-dichlorobenzene (31, Scheme 9). The compound was prepared by a modified literature procedure.[28] A 500 mL three-necked, round bottomed flask charged with 82 g (0.5 mol) of 3,4-dichlorophenol **30**, 68 g (0.5 mol) of *N,N*-diethylcarbamoylchloride and 200 mL of pyridine was stirred overnight at 100°C. After cooling to room temperature, a white precipitate was formed. The reaction mixture was poured into 100 mL water and extracted two times with 50 mL-portions of a 1/1 mixture of ether and pentane. The combined organic fractions were successively washed twice with 100 mL of 10 % HCl and twice with 100 mL of 10 % KOH and subsequently dried over Na_2SO_4. After removal of the solvent the protected phenol **31** was isolated as a clear liquid in 99 % yield (129 g). ^{1}H-NMR: δ= 7.34 (d, *J*= 8.8, 1H, C_5(H)), 7.24 (d, *J*= 2.7, 1H, C_2(H)), 6.97 (dd, *J*= 8.8, 2.7, 1H, C_6(H)), 3.34 (m, 4H, C_{CH2}(H)), 1.16 (m, 6H, C_{CH3}(H)). ^{13}C-NMR: δ= 153.0 ($C_{C=O}$), 150.1 (C_1), 132.2 (C_3), 130.1 (C_5), 128.3 (C_4), 123.7 (C_2), 121.2 (C_6), 42.1, 41.7 (C_{CH2}), 13.9, 13.0 (C_{CH3}).

1-N, N-Diethylcarbamoyl-2, 3-dichlorotoluene (32, Scheme 9). The compound was prepared by a modified literature procedure.[30] A 1 L, three-necked, round-bottomed flask equipped with a thermometer, a mechanical stirrer, and a gas inlet, was charged with a mixture of 50.0 g (0.19 mol) of **31** in 300 mL of dry THF and 25 g (0.22 mol) of *N, N, N', N'*-tetramethylethylenediamine (TMEDA). The flask was flushed with nitrogen and cooled to below -90°C. To the mixture was added 170 mL of a solution of 1.3 M (0.22 mole) *sec*-BuLi in hexane while maintaining the temperature of the mixture between -80 and -90°C. The light yellow reaction mixture was stirred for 2 hours at -80°C. Subsequently 45 g (0.32 mol, excess) of methyl iodide was added, after which the reaction mixture was stirred for another hour. During this period the temperature was allowed to reach 0°C. To the clear reaction mixture 100 mL of water was added. Threefold extraction with 50 mL portions of pentane was carried out. After drying the combined organic fractions over $MgSO_4$, the solvent was removed *in vacuo* and 51.9 g of a brown oil remained, corresponding to a 99% yield. ^{1}H-NMR: δ= 7.28 (d, *J*= 8.8, 1H, C_5(H)), 6.96 (d, *J*= 8.8, 1H, C_4(H)), 3.42 (m, 4H, C_{CH2}(H)), 2.28 (s, 3H, C_{CH3}(H)), 1.24 (m, 6H, C_{CH3}(H)). ^{13}C-NMR: δ= 153.4 ($C_{C=O}$), 148.9 (C_6), 133.3 (C_2), 131.6 (C_1), 129.5 (C_3), 127.3 (C_4), 121.6 (C_5), 42.2, 42.0 (C_{CH2}), 14.6 (C_{CH3}), 14.3, 13.3 (C_{CH3}).

2, 3-Dichloro-6-hydroxytoluene (33, Scheme 9). The compound was prepared by a modified literature procedure.[30] In a 1-L, three-necked, round-bottomed flask, equipped with a thermometer, a magnetic

stirring bar and a gas inlet, 51.9 g (0.19 mol) of **32** was dissolved in 300 mL of dry THF under an inert atmosphere. Cautious, portion-wise addition of 7.6 g (0.2 mol) of $LiAlH_4$ over a period of 30 minutes resulted in an exothermic reaction. The reaction mixture was stirred overnight at room temperature, then treated with 20 mL of ethanol and 50 mL of 10 % HCl. The resulting suspension was subjected to continuous extraction with diethyl ether during 5 h. Removal of the solvent and crystallisation of the remaining solid from pentane resulted in 22.3 g (yield 62 %) of the desired compound as a white solid. ^{1}H-NMR: δ= 7.15 (d, *J*= 8.7, 1H, C_4(H)), 6.64 (d, *J*= 8.7, 1H, C_5(H)), 4.84 (bs, 1H, C_{OH}(H)), 2.33 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 152.6 (C_6), 133.3 (C_2), 127.3 (C_4), 124.9 (C_3), 124.6 (C_1), 114.1 (C_5), 13.6 (C_{CH3}).

2, 3-Dichlorotolyl-6-triflate (34, Scheme 9). A 100 mL three-necked, round-bottomed flask equipped with a gas inlet, a thermometer, and a magnetic stirring bar, was charged with 4.4 g (25 mmole) of phenol 33, 50 mL of pyridine and 25 mL of CH_2Cl_2. The mixture was brought under an inert atmosphere and cooled at 0°C. Triflic anhydride (7.8 g, 27 mmole) was added over a period of 30 min. The mixture was stirred overnight at room temperature, then poured in 100 mL water, after which two extractions with 50 mL portions of diethyl ether were carried out. The combined organic fractions were washed with 50 mL of brine and subsequently dried over $MgSO_4$. Removal of the solvent under reduced pressure gave 6.8 g (yield 90%) of a white powder. ^{1}H-NMR: δ= 7.40 (d, *J*= 8.8, 1H, C_5(H)), 7.16 (d, *J*= 8.8, 1H, C_6(H)), 2.46 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 146.2 (C_1), 134.5 (C_2), 132.9 (C_3), 131.9 (C_4), 127.9 (C_5), 120.1 (C_6), 23.7 (C_{CH3}).

3, 4-dichlorobenzyltributyltin (35, Scheme 9). A 100 mL Schlenk vessel equipped with a magnetic stirring bar and a reflux condenser was charged with 6.5 g of Zn dust (Merck p.a.) and 50 mL of dry diethyl ether. After flushing with nitrogen a few drops of dibromoethane were added and the suspension heated until reflux. After the evolution of gas had ceased and the mixture had cooled to room temperature **2d** (12 g, 50 mmole) was added and the mixture was stirred overnight. The reaction mixture was transferred into a 100 mL centrifugal vessel. Tributyltin chloride (16.3 g, 50 mmole) was added, after which a weakly exothermic reaction took place. The reaction mixture was stirred overnight at room temperature. After removal of the solvent from the grey suspension, the remaining oil was diluted with 50 mL of hexane, the mixture subjected to centrifugation and the upper layer decanted. The precipitate was washed twice with 10 mL hexane. The hexane fractions were combined and the solvent removed under vacuum resulting in 4.3 g (yield 19 %) of a colourless oil, which was used as such.

3', 4, 4', 5-Tetrachloro-2-methyldiphenylmethane (TCBT-89, Scheme 6). A 100 mL, three-necked, round-bottomed flask equipped with a mechanical stirrer, a gas inlet and a thermometer was flushed with nitrogen and charged with a solution of 12.0 g (50 mmole) of **17** in 80 mL dry THF. The mixture was cooled to -70°C and 31 mL of a solution of 1.6 M *n*-BuLi in hexane was added over 5 min while the temperature was kept at -70°C. The colour of the reaction mixture changed from clear white to purple/pink. After stirring for an additional 15 minutes, 6.8 g (50 mmole) of anhydrous $ZnCl_2$ was added and stirring continued for another 15 minutes followed by 12.0 g (50 mmole) of **2d** and 1.2 g (1 mmole, 2 mol %) of $Pd(PPh_3)_4$. The yellow reaction mixture was heated at 60°C for 15 minutes and then allowed to cool to room temperature. Pentane (100 mL) and 100 mL of a saturated aqueous solution of NH_4Cl were added. The layers were separated and the water layer was extracted twice with 50 mL of pentane. The combined organic fractions were washed with 50 mL of water, dried over $MgSO_4$ and filtered over Al_2O_3 to remove residual palladium. Removal of the solvent under reduced pressure afforded a yellow oil, which solidified on standing. Crystallisation from methanol resulted in 5.7 g of white crystals (yield 36 %). ^{1}H-NMR: δ= 7.35 (d, *J*= 8.2, 1H, C_5(H)), 7.24 (s, 1H, C_6(H)), 7.18 (d, *J*= 2.0,

1H, $C_{2'}$(H)), 7.14 (s, 1H, C_3(H)), 6.93 (dd, *J*= 8.2, 2.0, $C_{6'}$(H)), 3.88 (s, 2H, C_{CH2}(H)), 2.18 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 139.3 (C_2), 137.9 ($C_{1'}$), 136.6 (C_1), 131.7 ($C_{3'}$) , 131.5 (C_3), 130.9 (C_5), 130.1 (C_4), 130.0 ($C_{4'}$), 129.6 (C_6), 129.6 ($C_{2'}$), 128.8 ($C_{5'}$), 127.9 ($C_{6'}$), 37.1 (C_{CH2}), 18.5 (C_{CH3}). HRMS found: 317.9570 calculated: 317.9537

3, 3', 4', 5-Tetrachloro-4-methyldiphenylmethane (TCBT-94, Scheme 7). The compound was prepared by an analogous method used for **TCBT-89** from 20.0 g (83 mmole) of **22** and 22.0 g (92 mmole) of benzyl bromide **2d** using 5.0 g (5 mol %) of $Pd(PPh_3)_4$ to give, after workup, 27.95 g of a crystalline product (95 %). Twofold crystallisation from petroleum ether (b.p. 40-60°C) afforded 10.8 g (yield 41 %) of the pure, white tetrachlorobenzyltoluene. ^{1}H-NMR: δ= 7.38 (d, *J*= 8.2, 1H, $C_{5'}$(H)), 7.27 (d, *J*= 2.1, 1H, $C_{2'}$(H)), 7.08 (s, 2H, $C_{2,6}$(H)), 6.98 (dd, *J*= 8.2, 2.1, $C_{6'}$(H)), 3.83 (s, 2H, C_{CH2}(H)), 2.42 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 139.9 ($C_{1'}$), 139.3 ($C_{3,5}$), 135.6 ($C_{1,4}$), 132.7 ($C_{3'}$), 131.6 ($C_{4'}$), 130.7 ($C_{2'}$), 130.6 ($C_{5'}$), 128.2 ($C_{6'}$), 128.1 ($C_{2,6}$), 39.9 (C_{CH2}), 17.1 (C_{CH3}). HRMS found: 317.9554 calculated: 317.9537

3', 4, 4', 5-Tetrachloro-3-methyldiphenylmethane (TCBT-88, Scheme 8). The compound was prepared by an analogous method as described for **TCBT-89** from 13.8 g (58 mmole) of **28** and 15.2 g (63 mmole) of benzyl bromide **2d** using 5.0 g (5 mol %) of $Pd(PPh_3)_4$ to give, after workup, 19.1 g of a white solid. Two crystallisations from hexane resulted in 2.2 g (yield 12 %) of a white solid. ^{1}H-NMR: δ= 7.36 (d, *J*= 8.2, $H_{5'}$), 7.24 (d, *J*= 2.0, 1H, $H_{2'}$), 7.19 (d, *J*= 1.4, 1H, H_2), 6.98 (dd, *J*= 8.2, 2.0, 1H, $H_{6'}$),6.92 (d, *J*= 1.4, 1H, H_3), 3.34 (s, 2H, C_{CH2}(H)), 2.40 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 140.2 (C_5), 138.9 ($C_{1,1'}$), 138.6 ($C_{3,3'}$), 132.9 (C_4), 132.6 ($C_{4'}$), 130.7 ($C_{2'}$), 130.6 (C_6), 129.5 ($C_{5'}$), 128.2 (C_2) ,128.2 ($C_{6'}$), 40.1 (C_{CH2}), 21.2 (C_{CH3}). HRMS found: 317.9632 calculated: 317.9537

3, 3', 4, 4'-Tetrachloro-2-methyldiphenylmethane (TCBT-87, Scheme 9). A 250 mL, three-necked, round-bottomed flask equipped with a reflux condenser, a magnetic stirring bar and a gas inlet-thermometer combination was charged with 10.3 g (35 mmole) of triflate **34**, 18 g (40 mmole) of 3,4-dichlorobenzyltributyltin (**35**), 1.7 g (40 mmole) of lithium chloride and 2.0 g (1.7 mmole, 5 mol %) of $Pd(PPh_3)_4$ dissolved in 100 mL of dry DMF. The mixture was stirred under an inert atmosphere for 48 hours under reflux an then poured in 200 mL of 5M HCl after which four extractions with 50 mL portions of hexane were carried out. The organic fraction was dried over $MgSO_4$, the solvent removed under reduced pressure and the resulting oil purified by flash chromatography over a short silica column with pentane. Crystallisation from pentane gave 2.5 g (yield 22%) of white crystals. ^{1}H-NMR: δ= 7.34 (d, *J*= 8.2, 1H, $C_{5'}$(H)), 7.28 (d, *J*= 8.2, 1H, C_5(H)), 7.16 (d, *J*= 2.0, 1H, $C_{2'}$(H)), 6.95 (d, *J*= 8.2, 1H, C_6(H)), 6.91 (dd, *J*= 8.2, 2.0, 1H, $C_{6'}$(H)), 3.95 (s, 2H, C_{CH2}(H)), 2.30 (s, 3H, C_{CH3}(H)). ^{13}C-NMR: δ= 139.6 (C_2), 137.5 ($C_{1,1'}$), 137.0 (C_3), 133.5 ($C_{3'}$), 132.6 (C_4), 131.6 ($C_{4'}$), 130.5 ($C_{6'}$), 130.3 (C_6), 128.9 ($C_{2'}$), 127.8 ($C_{5'}$), 127.6 (C_5), 39.2 (C_{CH2}), 17.5 (C_{CH3}). HRMS found: 317.9489 calculated: 317.9537

REFERENCES

1. Fürst, P.; Krüger, C.; Meemken, H. A., Groebel, W.; *Z. Lebensm. Unters. Forsch.*, **1987**, *185*, 394.
2. Rönnefahrt, B.; *Deutsche Lebensmittel-Rundschau*, **1987**, *83-7*, 214.
3. Friege, H.; Stock, W.; Alberti, J.; Poppe, A.; Juhnke, I.; Knie, J., Schiller, W.; *Chemosphere*, **1989**, *18*, 1367.
4. Poppe, A.; Alberti, J.; Friege, H., Rönnefahrt, B.; *Vom Wasser*, **1988**, *70*, 33.

5. Wester, P. G., van der Valk, F.; *Bull. Environ. Contam. Toxicol.*, **1990**, *45*, 69.
6. Parkinson, A., Safe, S. *Polychlorinated Biphenyls (PCBs): Mammalian and environmental toxicology*, Springer Verlag, Heidelberg, 1987;
7. Safe, S., *et al.*; *Environ. Health Perspect.*, **1985**, *60*, 47.
8. Safe, S., Phil, D.; *Crit. Rev. Toxicol.*, **1990**, *21*, 51.
9. McFarland, V. A., Clarke, J. U.; *Environ. Health Perspect.*, **1989**, *81*, 225.
10. Ehmann, J., Ballschmitter, K.; *Fres. Zeit. Anal. Chem.*, **1984**, *332*, 904.
11. van Haelst, A. G., Thesis, Amsterdam 1996.
12. Tamao, K.; Sumitani, K.; Kiso, Y.; Zembayashi, M.; Fujioka, A.; Kodama, S.; Minato, A., Kumada, M.; *Bull. Chem. Soc. Jpn.*, **1976**, *49*, 1958.
13. Sekiya, A., Ishikawa, N.; *J. Organometall. Chem.*, **1976**, *118*, 349.
14. Foà, M., Cassar, L.; *J. Chem. Soc. Dalton Trans.*, **1975**, 2572.
15. Fahey, D. R.; *J. Am. Chem. Soc.*, **1970**, *92*, 402.
16. Ku, Y. Y.; Patel, R. R., Sawick, D. P.; *Tetrahedron Lett.*, **1996**, *37*, 194.
17. Johnson, D. K.; Ciavarri, J. P.; Ishmael, F. T.; Schillinger, K. J.; van Geel, T. A. P., Stratton, S. M.; *Tetrahedron Lett.*, **1995**, *36*, 8565.
18. Ebert, G. W., Rieke, R. D.; *J. Org. Chem.*, **1988**, *53*, 4482.
19. Milstein, D., Stille, J. K.; *J. Am. Chem. Soc.*, **1979**, *101*, 4992.
20. Negishi, E.; Matsushita, H., Okukado, N.; *Tetrahedron Lett.*, **1981**, *22*, 2715.
21. Pelter, A.; Rowlands, M., Clements, G.; *Synthesis*, **1987**, 51.
22. Pilkington, B. L.; *Ger. Offen. Patent*, **1990**, 4114430.
23. McMurry, J. *Organic Chemistry*, Brooks/Cole, Calif., 1984; 497.
24. Vogel, A. I. *Practical Organic Chemistry* 5^{th} *ed.*, Longman, Scientific & Technical, London, 1989; 890.
25. Furst, A.; Berlo, R. C., Hooton, S.; *Chem. Rev.*, **1965**, *65*, 51.
26. Weinstock, L. M., Demarco, A. M.; *Org. Prep. Proc. Int.*, **1981**, *13*, 103.
27. Smith Jr., W. J., Campanaro, L.; *J. Am. Chem. Soc.*, **1953**, *75*, 3602.
28. Lustig, E.; Benson, W. R., Duy, N.; *J. Org. Chem.*, **1967**, *32*, 851.
29. Snieckus, V.; *Chem. Rev.*, **1990**, *90*, 879.
30. Sibi, M. P., Snieckus, V.; *J. Org. Chem.*, **1983**, *48*, 1937.
31. Greene, T. W., Wuts, P. G. M. *Protective groups in organic synthesis* 2^{nd} *ed.*, Wiley Interscience, N. York, 1991;
32. Ritter, K.; *Synthesis*, **1993**, 735.
33. Quesnelle, C.; Familoni, O. B., Snieckus, V.; *Synlett*, **1994**, 349.
34. Cotton, F. A.; Faut, O. D., Goodgame, D. M.; *J. Am. Chem. Soc.*, **1961**, *83*, 344.
35. Hartley, F. R.; *Organometal. Chem. Rev. A.*, **1970**, *6*, 119.
36. Coulson, D. R.; *Inorg. Synth.*, **1972**, *13*, 121.
37. Cohen, J. B., Dakin, H. D.; *J. Chem. Soc.*, **1902**, 1344.
38. Vogel, A. I. *Practical Organic Chemistry* 5^{th} *ed.*, Longman, Scientific & Technical, London, 1989; 934.