A Convenient Method for the Preparation of 4-Aryloxyphenols

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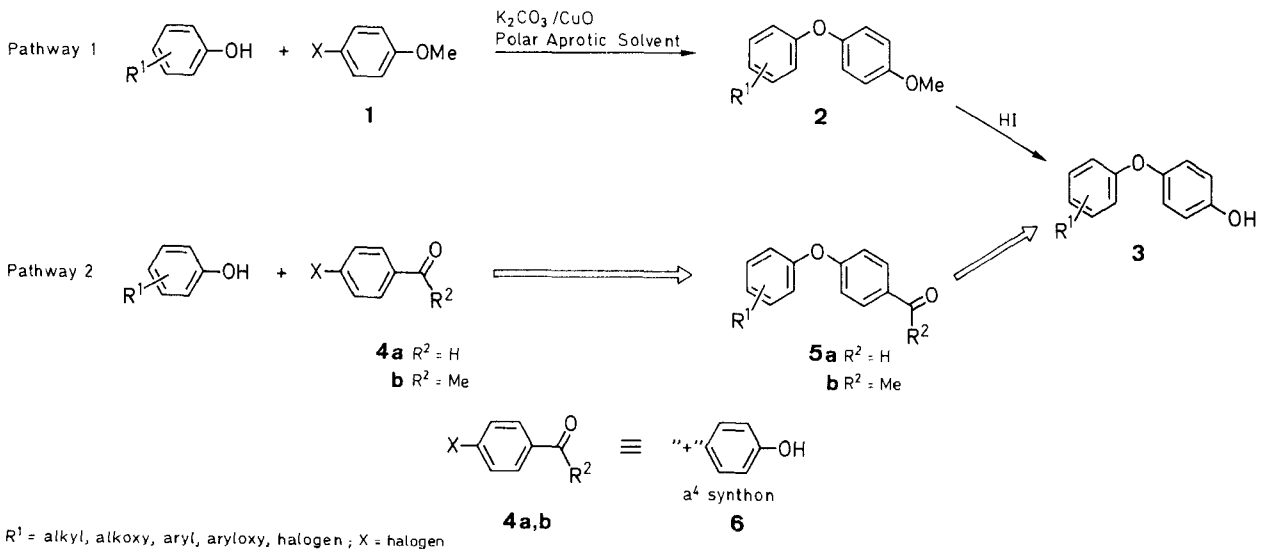
A convenient method for the preparation of 4-aryloxyphenols via the homologation of preformed phenols is described. Condensation of various 4-substituted phenols with either 4-fluorobenzaldehyde (**8**) or 4-fluoroacetophenone (**9**) yielded the corresponding 4-aryloxybenzaldehydes, **10**, and acetophenones, **11**, in 70–93% yield. Baeyer–Villiger oxidation of these materials with 3-chloroperoxybenzoic acid (MCPBA) yielded the corresponding 4-formyloxy and 4-acetoxyphenyl ethers which were hydrolyzed without purification to the desired 4-aryloxyphenols **12** in 72–94% yield. Both 4-fluorobenzaldehyde (**8**) and 4-fluoroacetophenone (**9**) are synthetically equivalent to the a^4 umpoled synthon **6**. Extension of this methodology of the preparation of 4,4'-[arylbis(oxy)]bisphenols from aromatic diols is also described. Condensation of various aromatic diols with **8** or **9** yielded the corresponding 4,4'-[arylbis(oxy)]bisbenzaldehydes **15** and acetophenones **16** in 71–89% yield. Baeyer–Villiger oxidation of these compounds with MCPBA yielded the desired 4,4'-[arylbis(oxy)]bisphenyl bisformates **17** and bisacetates **18** in 67–84% yield. Hydrolysis of these compounds afforded the desired 4,4'-[arylbis(oxy)]bisphenols **19** in 70–91% yield.

Recent studies in our laboratory have been directed toward the development of methodologies suitable for the preparation of 4-aryloxyphenols **3** via the homologation of preformed phenols. Of the methods available for effecting this transformation,[1–3] the Ullmann condensation/demethylation sequence shown in Scheme **A** (Pathway I) has been most widely used due in part to the straightforward nature of the synthesis and to the ready availability of 4-haloanisoles **1**. This method is however somewhat limited by the harsh reaction conditions employed and the moderate yields typically obtained in the initial condensation reaction.[4] These limitations are a result of the ability of electron donating groups situated *para* to the halogen substituents of aryl halides to significantly reduce their rate in the Ullmann condensation with phenols.[5–7] Since the structure of **3** dictates such a *para* relationship in **1**, these limitations are not easily circumvented. In addition, this method is also limited by the harsh reaction conditions required in the demethylation of the intermediate 4-aryloxyanisole **2**. Whereas yields for the demethylation of anisoles are generally good, their demethylation often requires treatment with strongly acidic or nucleophilic reagents,[8] conditions which can adversely affect sensitive functionality in an organic molecule.

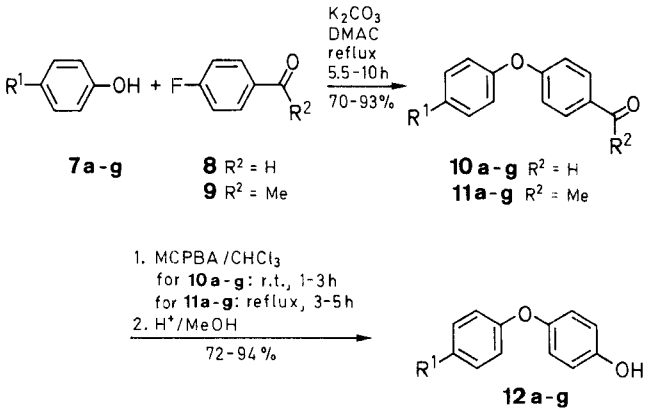
We realized that certain limitations of the initial Ullmann condensation could be circumvented if the phenolic hydroxyl of **3** was masked as an electron withdrawing group instead of being protected as its methyl ether. Such an approach would require a *para* relationship in the aryl halide between the electron withdrawing substituent and halogen, thus activating the aryl halide towards aromatic nucleophilic substitution. For this approach to be synthetically useful the masking group needed to be conveniently transformed in a second step into the phenolic hydroxy group of **3**. The facile Baeyer–Villiger oxidation/hydrolysis sequence for the conversion of electron rich benzaldehydes[9,10] and acetophenones[11–14] to phenols suggested to us that the aldehyde and ketone moieties of these compounds could be used as such masking groups. Thus the 4-aryloxyphenol residue could be derived from the corresponding 4-aryloxybenzaldehyde **5a** (R^2 = H) or 4-aryloxyacetophenone **5b** (R^2 = CH_3). As these materials could be conveniently prepared by condensation of the corresponding phenol with the activated 4-halobenzaldehyde **4a** (R^2 = H)[15–21] or 4-haloacetophenone **4b** (R^2 = CH_3),[22–28] the latter two compounds were seen as useful starting materials from which the 4-phenoxyphenol residue could be ultimately derived. The overall process which we envisioned is illustrated in Scheme **A** (Pathway 2). The 4-halobenzal-



Scheme A

dehydes and 4-haloacetophenones **4a, b** utilized in this synthesis are thus synthetically equivalent to the a[4] umpoled synthon **6** (Scheme **A**).[29]

An important extension of this methodology is the preparation of 4,4′-[arylbis(oxy)]biphenols **19** fom aromatic diols **14** as shown in Scheme **D**. Due to the presence of two reactive phenolic residues, methods for the preparation of **19** from **14** by an Ullmann condensation/demethylation sequence possess the added disadvantage that each aromatic diol must react twice with the 4-haloanisole in the initial condensation reaction. These materials are therefore often prepared by the Ullmann condensation of the less electron rich aromatic dihalides with 2 equivalents of 4-methoxyphenol.[30] In so far as certain aromatic diols are more readily prepared than the identically substituted aromatic dihalides, methodologies for the convenient preparation of 4,4′-[arylbis(oxy)]bisphenols from aromatic diols should prove to be a useful addition to the methodologies developed to date.

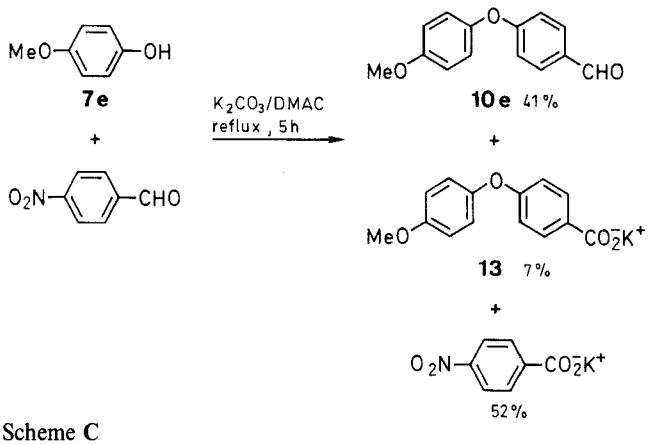


DMAC = *N,N*-dimethylacetamide

7–12	R^1	7–12	R^1
a	H	**e**	OMe
b	Cl	**f**	OPh
c	Br	**g**	CO_2Et
d	*t*-Bu		

Scheme **B**

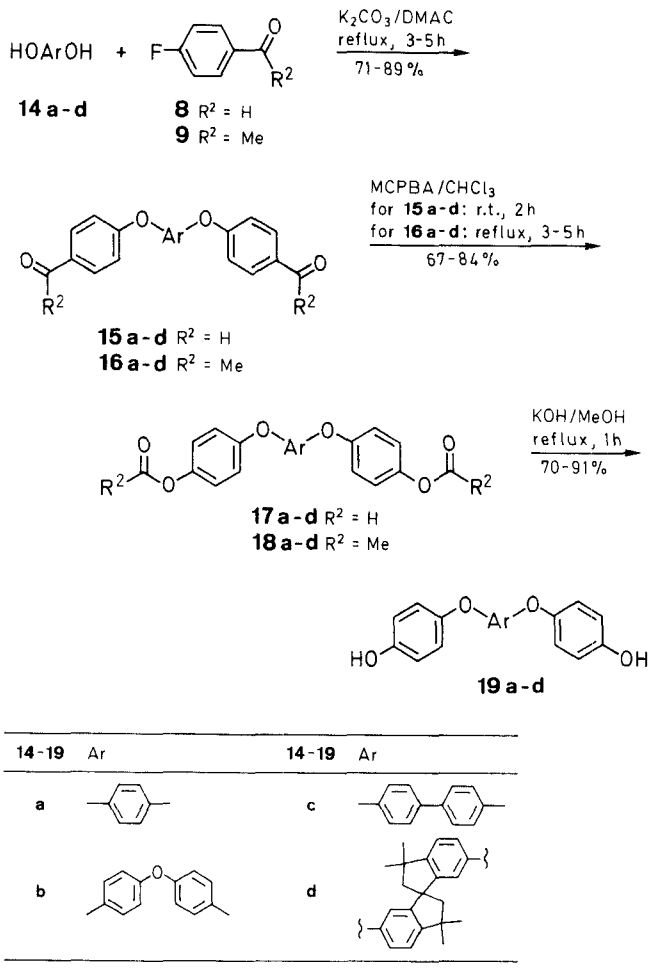
In the initial stages of our investigation the 4-aryloxyphenols **12a–g** were prepared from 4-fluorobenzaldehyde **8** by the 3-step procedure outlined in Scheme **B** (R^2 = H). Although 4-bromo and 4-iodobenzaldehyde would have been potentially useful in this synthesis, 4-fluorobenzaldehyde was chosen because of the facility with which it undergoes displacement reactions with phenols in the absence of copper catalysts.[15,16] Attempted condensation of 4-nitrobenzaldehyde with phenols gave a mixture of products. For example, condensation of **7e** with 4-nitrobenzaldehyde under the conditions described above yielded **10e** along with **13** and substantial quantities of potassium 4-nitrobenzoate (Scheme **C**). The latter two compounds are presumably generated by the potassium nitrite catalyzed oxidation of **10e** and 4-nitrobenzaldehyde, respectively. The instability of 4-nitrobenzaldehyde towards potassium nitrite oxidation was confirmed when treatment of an *N,N*-dimethylacetamide (DMAC) solution of 4-nitrobenzaldehyde with potassium nitrite under reflux conditions yielded large quantities of an insoluble solid determined to be potassium 4-nitrobenzoate by ^{1}H-NMR and mass spectral characterization.



Scheme **C**

The 4-aryloxybenzaldehydes **10a–g** were prepared in 70–89% yield by treatment of an *N,N*-dimethylacetamide solution of **7a–g** and 4-fluorobenzaldehyde **(8)** with a slight excess of potassium carbonate under reflux conditions. The reaction was typically complete within 5.5 to 10.0 hours, with the extent of reaction being monitored using ^{1}H-NMR by observing the disappearance of the resonance at $\delta = 10.1$ arising from the aldehydic proton of **8** and the concommitant appearance of a resonance at approximately $\delta = 9.8$ associated with the aldehydic proton of **10**. The resulting 4-aryloxybenzaldehydes **10a–g** were then oxidized by treatment with 3-chloroperoxybenzoic acid (MCPBA) in chloroform. This reaction was also conveniently followed using ^{1}H-NMR by observing the disappearance of the resonance arising from the aldehydic proton of **10** and the appearance of a resonance at approximately $\delta = 8.3$ corresponding to the formate proton of the resulting 4-formyloxyphenyl ethers. Within 1 to 2 hours the oxidation reaction was complete. Treatment of the crude 4-formyloxyphenyl ethers with a methanol solution containing a few drops of concentrated hydrochloric acid yielded the desired 4-aryloxyphenols **12a–g** in 75–94% yields.

It was also found that 4-fluoroacetophenone **(9)** was a useful starting material for the preparation of 4-aryloxyphenols **12a–g** by the procedure outlined in Scheme **B** (R^2 = Me). Thus, treatment of **7a–g** with **9** and a slight excess of K_2CO_3 under reflux conditions yielded the desired 4-aryloxyacetophenones **11a–g** in 78–93% yields. Baeyer–Villiger oxidation of the resulting products was typically complete at reflux within 3 to 6 hours utilizing 1.2 equivalents of MCPBA. The corresponding 4-acetoxyphenyl ethers so generated were treated without isolation with methanolic hydrochloric acid at reflux to yield the desired 4-aryloxyphenols **12a–g** in 72–85% yields.



Scheme **D**

This methodology also proved useful in the preparation of 4,4'-[arylbis(oxy)]bisphenols from aromatic diols (Scheme **D**). Treatment of the aromatic diols **14a–e** with 2 equivalents of 4-fluorobenzaldehyde yielded the 4,4'-[arylbis(oxy)]bisbenzaldehydes **15a–d** in 71–78% yield. Baeyer–Villiger oxdiation of these materials yielded the bisformate esters **17a–d** in 78–84% yield which were hydrolyzed in methanolic potassium hydroxide to yield the 4,4'-[arylbis(oxy)]bisphenols **19a–d** in 70–88% yield. Alternatively **14a–d** could be condensed with 4-fluoroacetophenone to yield 4,4'-[arylbis(oxy)]-bisacetophenones **16a–d** in 70–88% yield. These materials were oxidized with MCPBA to yield the 4,4'-[arylbis(oxy)]bisphenyl bisacetates **18a–d** in 67–76% yield. Hydrolysis of the diacetates in methanolic potassium hydroxide yielded **19a–d** in 82–91% yield. The melting points of **19a–d** generated from the corresponding bisbenzaldehydes **15a–d** were somewhat lower than those derived from the corresponding bisacetophenones **16a–d**. The bisphenols **19a–d** generated from the corresponding bisbenzaldehydes **15a–d** could be further purified by conversion to the highly crystalline bisacetates then hydrolyzed to afford 4,4'-[arylbis(oxy)]bisphenols **19a–d** of identical melting points to those prepared from the bisacetophenones **16a–d**. Therefore, preparation of the 4,4'-[arylbis(oxy)]bisphenols **19a–d** from the aromatic diols **14a–d** and 4-fluoroacetophenone appears to be a more efficient route.

Melting points are uncorrected. HRMS were recorded on a MAT 731 or Vg ZAB 2F spectrometer using ionization potentials of 70–80eV. ^{1}H-NMR spectra were obtained on Varian EM-390 (90 MHz) or Varian XL-200 (50.3 MHz) spectrometer. ^{13}C-NMR spectra were recorded on a Varian XL-300 (75.4 MHz) or a GE-300 (75.4 MHz) spectrometer. The ^{1}H and ^{13}C-NMR chemical shifts are reported in ppm relative to internal TMS standard.

4-Aryloxybenzaldehydes 10a–g and 4-Aryloxyacetophenones 11a–g; General Procedure:

To a solution containing the substituted phenol **7a–g** (0.10 mol) and either 4-fluorobenzaldehyde (12.40 g, 0.10 mol) or 4-fluoroacetophenone (13.80 g, 0.10 mol) in DMAC (100 mL) is added anhydr. K_2CO_3 (14.88 g, 0.12 mol). The mixture is refluxed and monitored by ^{1}H-NMR. After 5.5–10.0 h, the mixture was allowed to cool to r.t. and diluted with H_2O (100 mL) depositing the product as either a solid or viscous oil. In those instances (**10f, 11f**) where the product is deposited as a solid it is isolated from solution by filtration and purified by recrystallization. In those cases where an insoluble oil is generated the diluted mixture is extracted with $CHCl_3$ (2 × 100 mL). The $CHCl_3$ extracts are combined, dried ($MgSO_4$), and concentrated *in vacuo*. The resulting oil is distilled under reduced pressure to yield the desired product. A small sample of this product is further purified by recrystallization (Table 1).

4-Aryloxyphenols 12a–g via Baeyer–Villiger Oxidation of 4-Aryloxybenzaldehydes 10a–g and 4-Aryloxyacetophenones 11a–g; General Procedure:

To a stirred solution of the 4-aryloxybenzaldehydes **10a–g** (0.04 mol) in (100 mL) is added MCPBA (80–85%, 10.75 g, 0.05 mol). The mixture is stirred at r.t. for 1–3 h and monitored by ^{1}H-NMR. In similar fashion the 4-aryloxyacetophenones **11a–g** (0.04 mol) in $CHCl_3$ (100 mL) are treated with MCPBA (80–85%, 12.50 g, 0.06 mol) and heated at reflux for 3–5 h and monitored by ^{1}H-NMR. After such time the mixture is washed with sat. aq $NaHSO_3$ (100 mL), sat. aq $NaHCO_3$ (2 × 100 mL), and H_2O (100 mL). The $CHCl_3$ layer is concentrated *in vacuo* and the resulting oil dissolved in MeOH (100 mL, EtOH is used in the preparation of **12g**) containing a few drops of conc. HCl and either stirred at r.t. for 1 h (preparation from **10a–g**) or heated at reflux for 1–3 h (preparation from **11a–g**). After such time the solvent is removed *in vacuo* and the resulting oil vacuum distilled (Table 2).

4,4'-[Arylbis(oxy)]bisbenzaldehydes 15a–d and 4,4'-(Arylbis-(oxy)]bisacetophenones 16a–d from Aromatic Diols 14a–d; General Procedure:

To a solution containing an aromatic diol **14a–d** (0.10 mol), and either 4-fluorobenzaldehyde (24.80 g, 0.20 mol) or 4-fluoroacetophenone (27.60 g, 0.02 mol) in DMAC (250 mL) is added anhydr. K_2CO_3 (24.80 g, 0.20 mol). The mixture is heated at reflux and monitored by ^{1}H-NMR. After 3–5 h, the mixture is allowed to cool to r.t. and diluted with H_2O, precipitating the product from solution. The product is isolated from solution by filtration, dried, and purified by recrystallization (Table 3).

4,4'-[Arylbis(oxy)]bisphenyl Bisformates 17a–d by the Baeyer–Villiger Oxidation of 4,4'-[Arylbis(oxy)]bisbenzaldehydes 15a–d; General Procedure:

To a stirred solution containing the 4,4'-[arylbis(oxy)]bisbenzaldehyde **15a–d** (0.04 mol) in $CHCl_3$ (100 mL) is added MCPBA (80–85%, 21.50 g, 0.10 mol). The mixture is stirred at r.t. and monitored by ^{1}H-NMR. After 2 h the reaction mixture is washed with $NaHSO_3$ (100 mL), $NaHCO_3$ (2 × 100 mL) and H_2O (100 mL). The $CHCl_3$ layer is then concentrated *in vacuo* and the resulting solid purified by recrystallization (Table 4).

4,4'-[Arylbis(oxy)]bisphenyl Bisacetates 18a–d by the Baeyer–Villiger Oxidation of the 4,4'-[Arylbis(oxy)]bisacetophenones 16a–d; General Procedure:

To a stirred solution of 0.04 mol of 4,4'-[arylbis(oxy)]bisacetophenone **16a–d** in $CHCl_3$ (100 mL) is added 21.50 g (0.10 mol) of 80–85% MCPBA. The mixture is stirred under reflux for 3–5 h and monitored by ^{1}H-NMR. After such time the mixture is washed

Table 1. 4-Aryloxybenzaldehydes **10** and 4-Aryloxyacetophenones **11** Prepared

Fluoro-arene	Product	Yield (%)	mp (°C) (solvent)	bp (°C)/Torr	Molecular Formula[a] or Lit. Data	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
8	**10a**	71	oil	148–151/2.2	191–193/22[30]	6.93–7.55 (m, 7H), 7.85 (d, 2H, J = 9), 9.93 (s, 1H)
8	**10b**	70	47–48.5 (hexane)	178–181/2.5	$C_{13}H_9ClO_2$[a] (232.6)	6.88–7.17 (m, 4H), 7.37 (d, 2H, J = 9), 7.87 (d, 2H, J = 9), 9.98 (s, 1H)
8	**10c**	77	67–68 (hexane)	186–189/2.5	$C_{13}H_9BrO_2$[a] (277.1)	6.83–7.14 (m, 4H), 7.50 (d, 2H, J = 9), 7.85 (d, 2H, J = 9), 9.95 (s, 1H)
8	**10d**	75	oil	243–245/43	$C_{17}H_{18}O_2$[a] (254.3)	1.37 (s, 9H), 7.02 (d, 2H, J = 9), 7.05 (d, 2H, J = 9), 7.42 (d, 2H, J = 9), 7.84 (d, 2H, J = 9), 9.93 (s, 1H)
8	**10e**	89	59.5–60.5 (hexane)	185–189/2.5	60.5[33]	3.83 (s, 3H), 6.82–7.12 (m, 6H), 7.72 (d, 2H, J = 9), 9.92 (s, 1H)
8	**10f**	85	46–48 (hexane)	–	$C_{19}H_{14}O_3$[a] (290.3)	6.87–7.50 (m, 11H), 7.84 (d, 2H, J = 9), 9.93 (s, 1H)
8	**10g**	71	60–61 (pentane)	204–206/4.5	$C_{16}H_{14}O_4$[a] (270.3)	1.40 (t, 3H, J = 8), 4.39 (q, 2H, J = 8), 7.03–7.27 (m, 4H), 7.92 (d, 2H, J = 9), 8.15 (d, 2H, J = 9), 9.99 (s, 1H)
9	**11a**	83	51 (hexane)	159–161/3.5	49[30] 153–154/2[33]	2.55 (s, 3H), 6.93–7.51 (m, 7H), 7.96 (d, 2H, J = 9)
9	**11b**	93	67.5–68	191–193/4.9	66–68[22]	2.56 (s, 3H), 6.83–7.10 (m, 4H), 7.32 (d, 2H, J = 9), 8.95 (d, 2H, J = 9)
9	**11c**	82	78–79 (hexane)	195–199/4.0	$C_{14}H_{11}BrO_2$[a] (291.1)	2.57 (s, 3H), 6.83–7.07 (m, 4H), 7.49 (d, 2H, J = 9), 7.95 (d, 2H, J = 9)
9	**11d**	85	oil	172–174/1.2	160–165/0.1[22]	1.39 (s, 9H), 2.56 (s, 3H), 6.80–7.10 (m, 4H), 7.40 (d, 2H, J = 9), 7.93 (d, 2H, J = 9)
9	**11e**	78	58–59 (hexane)	198–201/3.2	60–61[34] 233/16[34]	2.53 (s, 3H), 3.83 (s, 3H), 6.80–7.10 (m, 6H), 7.91 (d, 2H, J = 9)
9	**11f**	83	87.5–88.5 (hexane)	–	$C_{20}H_{16}O_3$ (304.3)	2.54 (s, 3H), 6.87–7.45 (m, 11H), 7.94 (d, 2H, J = 9)
9	**11g**	81	47–48 (pentane)	212–214/3.5	$C_{17}H_{16}O_4$ (284.3)	1.39 (t, 3H, J = 8), 2.59 (s, 3H), 4.40 (q, 2H, J = 8), 7.00–7.20 (m, 4H), 7.93–8.23 (m, 4H)

[a] Satisfactory HRMS obtained: $m/z \pm 0.0005$.

Table 2. 4-Phenoxyphenols **12a–g** Prepared from 4-Phenoxybenzaldehydes **10a–g** and Acetophenones **11a–g**

Substrate	Product	Yield (%)	mp (°C) (solvent)[a]	bp (°C)/Torr	Molecular Formula[b] or Lit. Data	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
10a	**12a**	83	83–84 (PE)	165–167/3.0	84[4]	5.40 (br s, 1H), 6.70–7.47 (m, 9H)
11a	**12a**	85	83–84.5 (PE)	165–167/3.0		
10b	**12b**	84	79.5–81.0 (hexane)	168–171/2.4	$C_{12}H_9ClO_2$ (220.6)	5.08 (br s, 1H), 6.70–7.02 (m, 6H), 7.23 (d, 2H, J = 9)
11b	**12b**	82	80–81.5 (hexane)	167–169/2.5		
10c	**12c**	94	82–83 (hexane)	178–182/2.3	88[1]	4.57 (br s, 1H), 6.63–6.98 (m, 6H), 7.35 (d, 2H, J = 9)
11c	**12c**	78	82–83 (hexane)	179–181/2.5		
10d	**12d**	83	oil	172–174/19	$C_{16}H_{18}O_2$ (242.3)	1.3 (s, 9H), 4.58 (br s, 3H), 6.67–7.03 (m, 6H), 7.30 (d, 2H, J = 9)
11d	**12d**	79	oil	172–174/1.9		
10e	**12e**	94	89.5–90.5 (hexane)	174–178/2.3	91–91.5[1]	3.80 (s, 3H), 6.27 (br s, 1H), 6.67–7.02 (m, 8H)
11e	**12e**	79	89–90 (hexane)	177–181/3.0		
10f	**12f**	78	99–100 (hexane)	–	103–104[36]	5.92 (br s, 1H), 6.67–7.47 (m, 13H)
11f	**12f**	80	99–100 (hexane)	–		
10g	**12g**	75	112–114 (hexane/EtOAc)	221–224/2.5	$C_{15}H_{14}O_4$ (258.3)	1.36 (t, 3H, J = 8), 3.95 (br s, 1H), 4.36 (q, 2H, J = 8), 7.08 (m, 6H), 8.00 (d, 2H, J = 9)
11g	**12g**	72	112–114 (hexane/EtOAc)	226–229/2.9		

[a] PE = petroleum ether.
[b] Satisfactory HRMS obtained: $m/z \pm 0.0005$.

Table 3. 4,4′-[Arylbis(oxy)]bisbenzaldehydes **15** and 4,4′-[Arylbis(oxy)]bisacetophenones **16** Prepared

Fluoro-arene	Product	Yield (%)	mp (°C) (solvent)	Molecular Formula[a]	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)	^{13}C-NMR (DMSO-d_6/TMS) δ
8	**15a**	78	157–158 (DMAC/*i*-PrOH)	$C_{20}H_{14}O_4$ (318.3)	7.02–7.18 (m, 8H), 7.85 (d, 4H, J = 9), 9.93 (s, 2H)	117.45, 122.24, 131.36, 132.05, 151.44, 162.53, 191.55
8	**15b**	76	133–134 (DMAC/*i*-PrOH)	$C_{26}H_{18}O_5$ (410.4)	7.00–7.23 (m, 12H), 7.90 (d, 4H, J = 9), 9.99 (s, 2H)	117.16, 120.37, 122.13, 131.18, 132.06, 150.19, 153.75, 162.83, 191.52
8	**15c**	71	150–151 (DMAC/*i*-PrOH)	$C_{26}H_{18}O_4$ (394.4)	7.11 (d, 4H, J = 9), 7.15 (d, 4H, J = 9), 7.63 (d, 4H, J = 9), 7.89 (d, 4H, J = 9), 9.99 (s, 2H)	117.79, 120.65, 128.59, 131.46, 132.09, 136.02, 154.37, 162.26, 191.58
8	**15d**	78	158–161 (DMCA/*i*-PrOH)	$C_{35}H_{32}O_4$ (516.6)	1.34 (s, 6H), 1.36 (s, 6H), 2.23 (d, 2H, J = 13), 2.41 (d, 2H, J = 13), 6.52 (m, 2H), 6.96–7.02 (m, 6H), 7.31 (d, 2H, J = 9), 7.83 (d, 4H, J = 9), 9.86 (s, 2H)	29.90, 31.37, 42.89, 57.12, 58.80, 115.61, 116.90, 119.58, 123.76, 130.90, 131.90, 148.67, 152.15, 153.90, 162.83, 191.29
9	**16a**	79	179–180.5 (DMF/*i*-PrOH)	$C_{22}H_{18}O_4$ (346.4)	2.59 (s, 6H), 7.04 (d, 4H, J = 9), 7.12 (s, 4H), 7.97 (d, 4H, J = 9)	26.50, 117.12, 121.73, 130.68, 132.03, 151.99, 161.95, 196.54
9	**16b**	89	179–180 (DMF/*i*-PrOH)	$C_{28}H_{22}O_5$ (438.5)	2.56 (s, 6H), 6.93–7.15 (m, 12H), 7.97 (d, 4H, J = 9)	26.33, 116.79, 120.05, 121.58, 130.53, 131.79, 150.84, 153.92, 162.12, 196.53
9	**16c**	76	223–224 (DMF)	$C_{28}H_{22}O_4$ (422.5)	2.59 (s, 6H), 6.97–7.33 (m, 8H), 8.00 (d, 4H, J = 9)	26.37, 117.37, 120.32, 128.46, 130.55, 132.04, 136.66, 155.00, 161.70, 196.57
9	**16d**	84	201–202 (DMF/*i*-PrOH)	$C_{37}H_{36}O_4$ (544.7)	1.40 (s, 12H), 2.23 (d, 2H, J = 13), 2.41 (d, 2H, J = 13), 2.55 (s, 2H), 6.59 (m, 1H), 6.83–7.05 (m, 6H), 7.20 (d, 4H, J = 9), 7.90 (d, 4H, J = 9)	26.47, 29.94, 31.39, 42.86, 57.14, 58.86, 115.29, 116.61, 119.27, 123.70, 130.62, 131.46, 148.39, 152.04, 154.31, 161.60, 196.30

[a] Satisfactory HRMS obtained: $m/z \pm 0.0005$; except for **16a**: $m/z + 0.0029$.

Table 4. 4,4′-[Arylbis(oxy)]bisphenyl Bisformates **17a–d** and Bisacetates **18a–d** Prepared

Substrate	Product	Yield (%)	mp (°C) (solvent)	Molecular Formula[a] or Lit. mp (°C)	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)	^{13}C-NMR (DMSO-d_6/TMS) δ
15a	**17a**	78	112–114 (MeOH/H_2O)	$C_{20}H_{14}O_6$ (350.3)	6.83–7.23 (m, 12H), 8.33 (s, 2H)	118.78, 120.18, 122.03, 144.65, 152.31, 159.06
15b	**17b**	84	144.5–155.5 (*i*-PrOH)	$C_{26}H_{18}O_7$ (442.4)	6.81–7.20 (m, 16H), 8.33 (s, 2H)	118.96, 119.88, 120.48, 122.27, 144.91, 152.22, 153.37, 155.74, 159.22
15c	**17c**	83	192–193.5 (*i*-PrOH)	$C_{26}H_{18}O_6$ (426.4)	7.00–7.26 (m, 12H), 7.55 (d, 4H, J = 9), 8.33 (s, 2H)	119.71, 122.33, 128.22, 128.41, 135.82, 145.18, 155.14, 156.37, 159.21
15d	**17d**	80	127–128 (MeOH/H_2O)	$C_{35}H_{32}O_6$ (548.6)	1.40 (s, 6H), 1.42 (s, 6H), 2.31 (d, 2H, J = 13), 2.44 (d, 2H, J = 3), 6.59 (d, 2H, J = 3), 6.89 (m, 12H), 8.50 (s, 2H)	30.33, 31.81, 43.19, 57.59, 59.55, 115.42, 118.55, 118.62, 122.22, 123.10, 144.60, 147.98, 152.37, 155.86, 156.16, 159.94
16a	**18a**	76	106–106.5 (*i*-PrOH)	110–113[35]	2.29 (s, 6H), 6.90–7.16 (m, 12H)	21.02, 118.98, 120.43, 122.69, 145.95, 152.77, 155.19, 169.55
16b	**18b**	73	153–154 (*i*-PrOH)	152[35]	2.29 (s, 6H), 7.00–7.18 (m, 16H)	21.06, 118.89, 110.90, 120.48, 122.69, 145.89, 152.48, 153.35, 155.33, 169.58
16c	**18c**	74	200–201 (DMF/*i*-PrOH)	$C_{28}H_{22}O_6$ (454.5)	2.31 (s, 6H), 6.96–7.23 (m, 12H), 7.55 (d, 2H, J = 9)	21.06, 119.10, 119.62, 122.74, 128.24, 135.76, 146.18, 154.96, 156.59, 169.57
16d	**18d**	67	149–150 (*i*-PrOH)	$C_{37}H_{36}O_6$ (576.7)	1.36 (s, 12H), 2.09–2.56 (m, 10H), 6.56 (d, 2H), 6.78–7.33 (m, 12H)	20.87, 30.51, 31.97, 43.73, 58.35, 60.27, 115.41, 119.16, 119.38, 123.73, 124.07, 147.02, 148.39, 153.12, 156.17, 157.39, 169.72

[a] Satisfactory HRMS obtained: $m/z \pm 0.0014$; except for **17b, c**: $m/z + 0.0033$.

Table 5. 4,4′-[Arylbis(oxy)]bisphenols **19a–d** Prepared

Substrate	Product	Yield (%)	mp (°C) (solvent)	Molecular Formula[a] or Lit. mp (°C)	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)	^{13}C-NMR (DMSO-d_6/TMS) δ
17a	**19a**	76	188–189 (toluene/*i*-PrOH)	191–195[35], 188[30]	6.67–7.00 (m, 12H), 9.30 (br, s)	116.33, 118.84, 120.32, 148.8, 153.2, 153.6
18a	**19a**	83	190.5–192 (toluene/*i*-PrOH)			
17b	**19b**	88	202–204 (*i*-PrOH)	208–212[35] 206–207[30]	6.70–7.13 (m, 16H), 9.37 (br s, 2H)	116.24, 118.70, 119.74, 120.42, 148.56, 152.06, 153.70, 153.80
18b	**19b**	83	214–215 (*i*-PrOH)			
17c	**19c**	70	242–245 (*i*-PrOH)	$C_{24}H_{18}O_4$ (370.4)	6.73–7.20 (m, 12H), 7.58 (d, 4H, J = 9)	116.32, 117.29, 121.03, 127.76, 133.77, 147.80, 154.02, 157.77
18c	**19c**	82	249–250.5 (*i*-PrOH)			
17d	**19d**	80	207–210 (*i*-PrOH)	$C_{33}H_{32}O_4$ (492.6)	1.30 (s, 12H), 2.10 (d, 2H, J = 13), 2.41 (d, 2H, J = 13), 6.26 (d, 2H), 6.67–6.90 (m, 10H), 7.20 (d, 2H, J = 9), 9.40 (br s, 2H)	30.23, 31.46, 42.56, 57.20, 59.12, 112.23, 116.50, 120.34, 123.11, 145.89, 148.44, 151.53, 153.53, 157.72
18d	**19d**	91	208–209 (*i*-PrOH)			

[a] Satisfactory HRMS obtained: $m/z \pm 0.0003$.

with sat. aq $NaHSO_3$, (100 mL) with sat. aq $NaHCO_3$ (2 × 100 mL), and with H_2O (100 mL). The $CHCl_3$ layer is concentrated *in vacuo* and the resulting solid purified by recrystallization (Table 4).

4,4′-[Arylbis(oxy)]bisphenol 19a–d by the Hydrolysis of 4,4′-[Arylbis(oxy)]bisphenyl Bisacetates 17a–d and 4,4′-[Arylbis(oxy)]bisphenyl Bisformates 18a–d; General Procedure:
To a stirred solution of 0.02 mol of **17a–d** or **18a–d** in MeOH (100 mL) is added a 0.5 M KOH/MeOH solution (10 mL). The solution is heated at reflux for 1 h. After such time the solvent is removed *in vacuo*, the residue is suspended in H_2O (100 mL) and precipitated from solution by acidification with conc. HCl. The precipitate is isolated from solution by filtration and recrystallized (Table 5).

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