Diazotisation of aromatic amines and solvolysis of diazonium salts in ethylene glycol ethers

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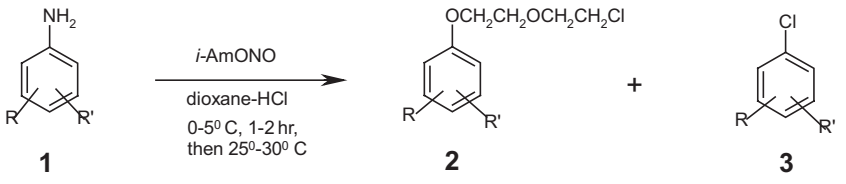
Aniline and unhindered alkyl-substituted anilines undergo solvolysis in dioxane and DME saturated with dry hydrogen chloride on diazotisation with isoamyl nitrite to give 2-(2-chloroethoxy)ethyl aryl ethers and 2-methoxyethyl aryl ethers respectively in 36-47% yields. 2,6-Dialkyl-substituted anilines give the corresponding chloro compounds as the major product along with the aryl ethers in lower yields. Diazotisation of aniline in ethylene glycol and monomethyl ethers of ethylene glycol and diethylene glycol gave the corresponding alcoholysis products in low yields. The solvolysis of aniline did not occur on diazotisation in diethyl ether or THF.

Keywords: aromatic amines, diazotisation, diazonium salts, solvolysis, aryl ethers, ethylene glycol ethers

Arenediazonium salts are among the most useful reagents in organic synthesis because several types of heteroatom nucleophiles[1,2] as well as carbon π-nucleophiles such as arenes and alkenes[3] can easily displace the diazonium group to form a variety of aryl–heteroatom and aryl–carbon bonds. This so-called dediazoniation reaction can occur both via a homolytic pathway involving aryl radicals and a heterolytic pathway characterised by S_N1 (involving highly reactive aryl carbocation intermediate), S_N2Ar or intermediate between S_N1 and S_N2Ar mechanisms depending on the presence or absence of a transition metal catalyst, pH of the reaction medium and the nature of the nucleophile, the diazonium salt and the solvent.[1-8] Recently, diazonium salts have also been used as the electrophilic reaction partner in palladium-catalysed Heck[9], Suzuki[10] and Stille[11] reactions which involve organopalladium intermediates. Although nucleophilic aromatic substitution in the absence of activating electron-withdrawing groups is rare, the diazonium group of arene diazonium salts, due to the exceptionally reactive diazonium ion leaving group, has been easily replaced with such weak nucleophiles as water,[1,2,4-8] alcohols,[12] acetonitrile,[13] trifluoroethanol,[14] trifluroacetic acid,[15] acetic acid[16] and acetic anhydride,[17] arguably involving an aryl carbocation intermediate. Ethers are weak nucleophiles that might be cleaved by the highly reactive electrophilic aryl carbocation to form aryl alkyl ethers, and such cleavage by benzynes has been reported.[18] However, little is known about this type of substitution reaction of diazonium group by ether nucleophiles, although ethereal solvents are quite often used in the reactions of the diazonium salts. We could find only one example of solvolysis by dioxane in which a diazonium salt of an azulene derivative was solvolysed by dioxane to give a (2-hydroxyethoxy)ethoxyazulene derivative in 20% yield along with hydrolysis (35%) and reductive dediazoniation (5%) products during diazotisation of the corresponding amine with $NaNO_2$ and concentrated sulfuric acid in dioxane.[19] Ethers, such as THF, DME, and dioxane are rather better known as reducing agents for the reductive dediazoniation at lower acidities, typically in acetate buffer.[20,21] These reactions occur by a free radical mechanism to effect displacement of the diazonium group by a hydrogen atom, and synthetic applications of reductive dediazoniation with dioxane have been documented.[22-24]

We now report our observations on the solvolysis of diazonium salts in anhydrous dioxane and other ethers of ethylene glycol during diazotisation of some alkyl-substituted anilines in these solvents saturated with hydrogen chloride gas. It was expected that in anhydrous medium the yields of the solvolysis products would improve due to suppression of hydrolysis. The reaction was first investigated in dioxane. A stock solution of hydrogen chloride in dioxane was prepared by passing dry hydrogen chloride gas in dry dioxane at about 20°C until saturated (4 M). Diazotisation of the anilines **1** (Scheme 1) in this solution with isoamyl nitrite at 0–5°C followed by stirring at 25–30°C for the time indicated in Table 1 gave 2-(2-chloroethoxy)ethyl aryl ethers **2** as a result of solvolysis of the diazonium salts.

Some dark red unidentified material was also formed in the reaction which was washed off with sodium hydroxide solution during work up. Diazotisation of aniline with solid sodium nitrite gave the product in comparable yield but *o*-toluidine afforded the product in better yield. However, with $NaNO_2$ the diazotisation proceeded slowly due to its low solubility in the reaction medium. Therefore, isoamyl nitrite was preferred for the subsequent diazotisation reactions. Sterically unhindered and less hindered anilines afforded the aryl ethers **2** in about 36–47% yieids, but 2,6-disubstituted anilines gave the chloroanilines **3** as the major products at the expense of the aryl ethers **2** (entries 7–9**).** Both electron-donating and electron-withdrawing groups inhibited the reaction. Thus, the reaction failed with *p*-anisidine, *p*-phenylenediamine, *p*-nitroaniline and *p*-chloroaniline as



a: R, R' = H **b**: R = H, R' = 2-Me **c**: R = H, R' = 4-Me
d: R = H, R' = 3-Me **e**: R = H, R' = 4-Et **f**: R = H, R' = 2-iPr
g: R = 2-Me, R' = 6-iPr **h**: R = 2-Me, R' = 6-tBu **i**: R = 2-iPr, R' = 6-iPr

Scheme 1

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Table 1 Solvolysis of aromatic diazonium salts in dioxane[a]

Entry	Amine **1**	Total reaction time[b]/h	Isolated yield/%	
			Ether[b] **2**	Chloroarene **3**
1	**a**	12 (14)	46(47)	0
2	**b**	22(12)	22(40)	0
3	**c**	72	43	0
4	**d**	18	36	0
5	**e**	14	39	0
6	**f**	18	42	0
7	**g**	24	14	41
8	**h**	17	11	34
9	**i**	15	19	32
10	**a**	18	41	0
11	**a**	18	9	0
12	**a**	30	7	0
13	**a**	35	4	0

[a]Reaction conditions: amine (5 mmol), isoamyl nitrite (5 mmol), HCl solution of dioxane (5 ml, 4M), 0–5°, 1–2 h, then 25–30°C.
[b]Values in parenthesis for sodium nitrite as the diazotising reagent.

well as with 2-aminopyridine, and the unreacted diazonium salt and decomposition products, if any, were washed away during the alkaline aqueous work up. The reaction also failed when aniline was diazotised with a lower concentration of dioxane in a mixture of dichloromethane-dioxane (5 : 1v/v).

Next, the reactivity of other ethereal solvents in solvolysing diazonium salts was investigated under similar conditions. The results are compiled in Table 2.

It was observed that the solvolysis occurred in DME with cleavage of one of the ether bonds as expected, but monomethyl ethers of ethylene glycol and diethylene glycol brought about alcoholysis through the hydroxyl oxygen without cleavage of any of the ether bonds. Ethylene glycol also behaved similarly. The poor yields of the products in these reactions may probably be due, at least partly, to the difficulty in their isolation from these high boiling water miscible solvents. Interestingly, in diethyl ether and THF, no solvolysis product could be isolated and, in the case of THF cleavage of the solvent molecule with HCl was observed. Furthermore, in contrast to the observed solvolysis in ethylene glycol, the solvolysis reaction did not take place in monohydric alcohols, such as methanol, propan-1-ol and butan-1-ol under similar conditions. The solvolysis reaction did not occur also in acetone, ethyl formate and ethyl acetate. The structures of all the products were determined by IR and ^{1}H and ^{13}C NMR spectroscopic analysis

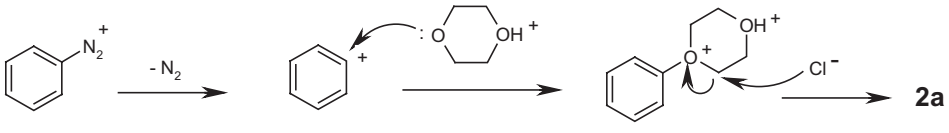
The mechanism of the reaction has not been investigated in detail. However, from the information that is available from the present study and from the literature, attack by the mono-protonated solvent molecule through the unprotonated oxygen atom on the aryl carbocation, formed by the heterolysis of the diazonium salt (S_N1) is suggested as a probability (Scheme 2).

The radical mechanism is excluded because cuprous chloride did not show any catalytic effect on the reaction as against the general experience with the radical substitution reactions of the diazonium salts. Formation of the aryl carbocation is supported by the fact that the attacking species are weakly nucleophilic, the acidic medium is considerably polar, and the reaction is inhibited by both electron-withdrawing and heteroatom-electron-donating groups on the aromatic ring.[4,25] Both these types of groups at *para*-position are known to destabilise the aryl carbocation probably by -I effects. Resonance effects should not play any significant role in stabilising aryl carbocations due to the nearly orthogonal disposition of the orbitals involved. The failure to observe solvolysis in the monodentate nucleophilic solvents such as diethyl ether, THF and monohydric alcohols, may probably be due to insufficiently low concentration of the reactive unprotonated nucleophilic solvent molecules in the medium under the present conditions of high acidity. The observed solvolysis only in solvents having at least two nucleophilic oxygen atoms can thus be rationalised in terms of the presence of reactive mono-protonated nucleophilic species in the medium in sufficient concentration to effect the nucleophilic reaction. The alcoholysis and not the reaction through the ether oxygen in the bifunctional hydroxyether solvents might be due to preferential protonation of the more basic ether oxygen as well as due to greater stability and lower reversibility of the protonated oxonium ion product formed as compared to the alkylated oxonium ion intermediate. The solvolysis in dioxane and DME does not appear to occur via cleavage of the solvent molecule with HCl followed by nucleophilic attack by $ClCH_2CH_2OCH_2CH_2OH$ or $MeOCH_2CH_2OH$ thus formed through the hydroxy oxygen atom on the aryl carbocation, as (a) no cleavage products of dioxane or DME were isolated either from the reaction or after storing the acidic stock solutions for several days. (b) the yield of the solvolysis product in DME is considerably

Table 2 Solvolysis of aromatic diazonium salts in ethylene glycol ethers[a]

Entry	Amine	Solvent	Time/h	Product	Yield/%
1	Aniline	$MeOCH_2CH_2OMe$	18	2-Methoxy ethoxybenzene	41
2	2,6-Diisopropylaniline	$MeOCH_2CH_2OMe$	24	2,6-Diisopropyl-1-(2-methoxyethoxy)benzene	30(50)[b]
3	Aniline	$MeOCH_2CH_2OH$	35	2-Methoxy-ethoxybenzene	4
4	Aniline	$MeOCH_2CH_2OCH_2CH_2OH$	30	2-(2-Methoxy-ethoxy) ethoxybenzene	7
5	Aniline	$HOCH_2CH_2OH$	18	2-Phenoxyethanol	9

[a]Reaction conditions: amine (5 mmol), isoamyl nitrite (5 mmol), saturated HCl solution of the solvent (15 ml), 0–5°, 1–2 h, then 25–30°C.
[b]Value in parenthesis for 1-chloro-2,6-diisopropylbenzene.



Scheme 2

higher (41%) and the reaction time considerably lesser (18 h., Table 2, entry 1) than those in ethylene glycol monomethyl ether (4%, 35 h. Table 2, entry 3). It is not, however, possible to exclude the border line mechanism on the basis of all this information.

The aryl ethers **2** derived from the solvolysis in dioxane are important intermediates for the synthesis of compounds showing a wide spectrum of medicinal properties. For example, **2a** has been used in the synthesis of some benzomorphan derivatives which are useful for the treatment of neurodegenerative diseases, epilepsy, hypoglycemia, stroke, Morgues Alzheimer and Parkinson diseases, *etc.*[26] The ethers **2b, 2c** and **2d** have been used to synthesise novel pesticides by reaction with chloral.[27] The ether **2b** has also been used for the synthesis of potential analgesics.[28] These compounds are prepared by selective etherification of phenols with bis-2-chloroethyl ether.[27-30] The lower yields of these products in the present method is tolerable because it represents a simple, economical, one-step down-stream integration of the above process starting from readily available anilines and inexpensive dioxane precursors, bypassing the preparation of phenols and the alkylating reagents in separate steps.

Experimental

Dioxane, DME and THF were dried by the usual method (Na, benzophenone). Other high boiling solvents were used after simple distillation at atmospheric pressure. Hydrogen chloride was generated by standard method (H_2SO_4 + HCl + NaCl) under a hood. The saturated stock solutions of hydrogen chloride in ethereal solvents were prepared by passing the dry hydrogen chloride in the solvent at about 20°C with protection from atmospheric moisture with a calcium chloride guard tube. The molarity of the solution was determined by diluting known volume of the solution with water and titrating with standard sodium hydroxide. IR spectra were recorded on Nicolet Protégé 460 ES-P FT IR spectrophotometer of neat liquid film placed between KBr disks. NMR spectra were recorded on Bruker Spectrospin DPX 300 MHz FT NMR spectrometer in $CDCl_3$ with TMS as internal standard.

Typical procedure

To the saturated solution of hydrogen chloride in dioxane (15 ml, 4 M) taken in a round bottom flask fitted with calcium chloride guard tube, the aromatic amine (5 mmol) was added at room temperature and the suspension was cooled with stirring to 0–5°C. A solution of isoamyl nitrite (0.635 g, 5 mmol) in dioxane (2 ml) was added to this solution dropwise and the stirring was continued at this temperature for 1–2 h. The solid amine salt slowly disappeared as the diazotisation progressed. The temperature was allowed to rise slowly and then maintained at 25–30°C. The stirring was continued and the progress of the reaction was monitored by TLC (silica gel). After the completion of the reaction (Table 2), the solvent was removed under reduced pressure. The residue was taken up in ether (30 ml) and washed successively with water (2 × 5 ml), and 0.1 M NaOH (3 × 5 ml) to remove most of the coloured material and finally with water (2 × 5 ml) and brine (5 ml). The ether layer was dried (anhyd. Na_2SO_4), filtered and evaporated. Column chromatography (silica gel) of the crude product gave the chloroarenes by elution with hexane and the aryl ether products by elution with 5% ethyl acetate in hexane as colourless liquids. The characterisation of the novel compounds **2e**, **2f**, **2g**, **2h** and **2i** and of 2,6-diisopropyl-1-(2-methoxyethoxy)benzene must be regarded as formally tentative but the structures are well supported by the data available.

Spectroscopic data

[2-(2-Chloroethoxy)ethoxy]benzene[29,30] **2a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.63 (t, *J* = 6.0 Hz, 2H, $C\underline{H}_2Cl$), 3.80 (t, *J* = 6.0 Hz, 2H, $CH_2OC\underline{H}_2CH_2Cl$), 3.85 (t, *J* = 4.8 Hz, 2H, $C\underline{H}_2OCH_2CH_2Cl$), 4.11 (t, *J* = 4.8 Hz, 2H, $PhOC\underline{H}_2$), 6.89–6.96 (m, 3H, aromatic *ortho, para*), 7.24–7.29 (t, *J* = 7.9 Hz, 2H, aromatic *meta*); ^{13}C NMR (75 MHz, $CDCl_3$): δ 42.6 ($\underline{C}H_2Cl$), 67.2 ($O\underline{C}H_2CH_2Cl$), 69.6 ($PhOCH_2\underline{C}H_2$), 71.4 ($PhO\underline{C}H_2$), 114.5 (aromatic *ortho*), 120.8 (aromatic *para*), 129.3 (aromatic *meta*), 158.5 (quaternary); IR (KBr)**:** ν_{max} 1247 s,1131 s (C–O), 754 s (C–Cl) cm^{-1}

1-[2-(2-Chloroethoxy)ethoxy]-2-methylbenzene[27,28] **2b:** ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.23 (s, 3H, $C\underline{H}_3$), 3.63 (t, *J* = 5.7, Hz, 2H, $C\underline{H}_2Cl$), 3.76–3.89 (m, 4H, $C\underline{H}_2OC\underline{H}_2$), 4.11 (t, *J* = 4.7 Hz, 2H, $ArOC\underline{H}_2$), 6.78–6.88 (m, 2H, aromatic C_3–H, C_6–H), 7.11–7.15 (t, *J* = 6.3 Hz, 2H, aromatic C_4–H, C_5–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.2 ($\underline{C}H_3$), 42.8 ($\underline{C}H_2Cl$), 67.7 ($O\underline{C}H_2CH_2Cl$), 69.9 ($ArOCH_2\underline{C}H_2$), 71.5 ($ArO\underline{C}H_2CH_2$), 111.1 (aromatic C_6), 120.6 (aromatic C_4), 126.7, 130.7 (aromatic C_3, C_5), 156.8 (aromatic C_1); IR (KBr): ν_{max} 1246 s, 1123 s CC–O), 751 s (C–Cl) cm^{-1}.

1-[2-(2-Chloroethoxy)ethoxy]-4-methylbenzene[27] **2c**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.26 (s, 3H, $C\underline{H}_3$), 3.62 (t, *J* = 5.8 Hz, 2H, $C\underline{H}_2Cl$), 3.77–3.84 (m, 4H, $C\underline{H}_2OC\underline{H}_2$), 4.08 (t, *J* = 4.7 Hz, 2H, $ArOC\underline{H}_2$), 6.80 (d, *J* = 8.5 Hz, 2H, aromatic C_2–H, C_6–H), 7.06 (d, *J* = 8.3 Hz, 2H, aromatic C_3–H, C_5–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3 ($\underline{C}H_3$), 42.7 ($\underline{C}H_2Cl$), 67.4 ($O\underline{C}H_2CH_2Cl$), 69.7 ($ArOCH_2\underline{C}H_2O$), 71.4 ($ArO\underline{C}H_2$), 114.4 (aromatic C_2, C_6), 129.8 (aromatic C_3, C_5), 130.7 (aromatic C_4), 156.4 (aromatic C_1); IR (KBr): ν_{max} 1245 s, 1131 s (C–O), 816 m (C–Cl) cm^{-1}.

1-[2-(2-Chloroethoxy)ethoxy]-3-methylbenzene[27] **2d**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 3H, $C\underline{H}_3$), 3.64 (t, *J* = 5.8 Hz, 2H, $C\underline{H}_2Cl$), 3.80–3.88 (m, 4H, $C\underline{H}_2OC\underline{H}_2$), 4.11 (t, *J* = 4.7 Hz, 2H, $ArOC\underline{H}_2$), 6.70–6.78 (m, 3H, aromatic C_2–H, C_4–H, C_6–H), 7.15 (t, *J* = 7.7 Hz, 1H, aromatic C_5–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5 ($\underline{C}H_3$), 42.7 ($\underline{C}H_2Cl$), 67.2 ($\underline{C}H_2CH_2Cl$), 69.8 ($ArOCH_2\underline{C}H_2$), 71.5 ($Ar–O–\underline{C}H_2$), 111.4 (aromatic C_6), 115.4 (aromatic C_2), 121.7 (aromatic C_4), 129.1 (aromatic C_5), 139.4 (aromatic C_3), 158.6 (aromatic C_1); IR (KBr): ν_{max} 1262 s, 1160 s, 1131 s (C–O), 776 s, (C–Cl) cm^{-1}.

1-[2-(2-Chloroethoxy)ethoxy]-4-ethylbenzene **2e**: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.13 (t, *J* = 7.8 Hz, 3H, $C\underline{H}_3$), 2.51 (q, *J* = 7.5 Hz, 2H, $C\underline{H}_2CH_3$), 3.58 (t, *J* = 5.7 Hz, 2H, $C\underline{H}_2Cl$), 3.73–3.81 (m, 4H, $C\underline{H}_2OC\underline{H}_2$), 4.04 (t, *J* = 4.5 Hz, 2H, $ArOC\underline{H}_2$), 6.77 (d, *J* = 7.9 Hz, 2H, aromatic C_2–H, C_6–H), 7.11 (d, *J* = 8.1 Hz, 2H, aromatic C_3–H, C_5–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.8 ($\underline{C}H_3$), 27.9 ($\underline{C}H_2$–CH_3), 42.7 ($\underline{C}H_2Cl$), 67.5 ($\underline{C}H_2CH_2Cl$), 69.8 ($ArOCH_2\underline{C}H_2$), 71.5 ($ArO\underline{C}H_2$), 114.5 (aromatic C_2, C_6), 128.7 (aromatic C_3, C_5), 136.8 (aromatic C_4), 156.7 (aromatic C_1); IR (KBr): ν_{max} 1248 s, 1132 s (C–O), 830 s (C–Cl) cm^{-1}.

1-[2-(2-Chloroethoxy)ethoxy]-2-isopropylbenzene **2f**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21 [d, *J* = 4.4, 3H, $CH(CH_3)C\underline{H}_3$], 1.23 [d, *J* = 4.1 Hz, 3H, $CH(C\underline{H}_3)CH_3$], 3.35 [m, 1H, $C\underline{H}(CH_3)_2$], 3.64 (t, *J* = 2.9 Hz, 2H, $C\underline{H}_2Cl$), 3.82 (t, *J* = 5.8, 2H, $CH_2OC\underline{H}_2CH_2Cl$), 3.88 (t, *J* = 4.7, 2H, $C\underline{H}_2OCH_2CH_2Cl$), 4.12 (t, *J* = 4.7 Hz, 2H, $ArOC\underline{H}_2$), 6.76 (d, *J* = 8.0 Hz, 1H, aromatic C_6–H)), 6.86 (t, *J* = 7.4 Hz, 1H, aromatic C_4–H), 7.06 (t, *J* = 7.6 Hz, 1H, C_5–H), 7.14 (d, *J* = 7.3 Hz, 1H, C_3–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.6 [$CH(\underline{C}H_3)_2$], 26.8 [$\underline{C}H(CH_3)_2$], 42.8 ($\underline{C}H_2Cl$), 67.7 ($\underline{C}H_2CH_2Cl$), 69.9 ($ArOCH_2\underline{C}H_2$), 71.5 ($ArO\underline{C}H_2$), 111.5 (aromatic C_6), 120.9 (aromatic C_4), 126.1 (aromatic C_5), 126.5 (aromatic C_3), 137.2 (aromatic C_2), 155.8 (aromatic C_1); IR (KBr): ν_{max} 1241 s, 1133 s (C–O), 751 s (C–Cl) cm^{-1}.

1-[2-(2-Chloroethoxy)ethoxy]-2-isopropyl-6-methylbenzene **2g**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21 [d, *J* = 6.9, Hz, 6H, $CH(C\underline{H}_3)_2$], 2.30 (s, 3H, $ArC\underline{H}_3$), 3.39 [sep, *J* = 6.8 Hz, 1H, $C\underline{H}(CH_3)_2$], 3.68 (t, *J* = 5.8, Hz, 2H, $C\underline{H}_2Cl$), 3.86 (t, *J* = 5.7, 4H, $C\underline{H}_2OC\underline{H}_2$), 3.93 (t, *J* = 2.5 Hz, 2H, $ArOC\underline{H}_2$), 7.0 (d, *J* = 4.9, 2H, aromatic C_3–H, C_5–H)), 7.10 (t, *J* = 4.6 Hz, aromatic C_4–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.4 ($Ar\underline{C}H_3$), 23.9 [$CH(\underline{C}H_3)_2$], 26.1 [$\underline{C}H(CH_3)_2$], 42.7 ($\underline{C}H_2Cl$), 70.5 ($\underline{C}H_2CH_2Cl$), 71.5 ($ArOCH_2\underline{C}H_2$), 72.4 ($ArO\underline{C}H_2$), 124.2 (aromatic C_4), 128.5 (aromatic C_3, C_5), 130.8 (aromatic C_6), 141.7 (aromatic C_2), 154.2 (aromatic C_1); IR (KBr)**:** ν_{max} 1256 s, 1193 s, 1134 s (C–O), 783 s (C–Cl) cm^{-1}.

1-t-Butyl-2-[2-(2-Chloroethoxy)ethoxy]-3-methylbenzene **2h**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.39 [s, 9H, $C(C\underline{H}_3)_3$], 2.32 (s, 3H, $ArC\underline{H}_3$)), 3.67 (t, *J* = 5.9 Hz, 2H, $C\underline{H}_2Cl$), 3.84–3.95 (m, 4H, $C\underline{H}_2OC\underline{H}_2$), 4.00 (t, *J* = 4.7 Hz, 2H, $ArOC\underline{H}_2$), 6.94 (t, *J* = 7.3 Hz, 1H, aromatic C_5–H), 7.04 (d, *J* = 7.3 Hz, 1H, aromatic C_4–H), 7.17 (d, *J* = 7.8 Hz, 1H, aromatic C_6–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.2 ($Ar\underline{C}H_3$), 31.1 [$C(\underline{C}H_3)_3$], 35.0 [$\underline{C}(CH_3)_3$], 42.7 ($\underline{C}H_2Cl$), 70.5 ($\underline{C}H_2CH_2Cl$), 71.2 ($ArOCH_2\underline{C}H_2$), 71.7 ($ArO\underline{C}H_2$), 123.4 (aromatic C_5), 124.9 (aromatic C_4), 129.9 (aromatic C_6), 131.4 (aromatic C_3), 142.6 (aromatic C_1), 156.4 (aromatic C_2); IR (KBr): ν_{max} 1132 s (C–O), 753 s (C–Cl) cm^{-1}.

1-[2-(2-Chloroethoxy)ethoxy]-2,6-diisopropylbenzene **2i**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.22 [d, *J* = 6.8 Hz, 12H, $CH(C\underline{H}_3)_2$], 3.39 [sep, *J* = 6.8 Hz, 2H, $C\underline{H}(CH_3)_2$], 3.68 (t, *J* = 7.6 Hz, 2H, $C\underline{H}_2Cl$), 3.84–3.91 (m, 6H, $ArOC\underline{H}_2C\underline{H}_2OC\underline{H}_2$), 7.09 (s, 3H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1 [$CH(\underline{C}H_3)_2$], 26.2 [$\underline{C}H(CH_3)_2$], 42.8 ($\underline{C}H_2Cl$), 70.6 ($\underline{C}H_2CH_2Cl$), 71.6 ($ArOCH_2\underline{C}H_2$), 73.8 ($ArO\underline{C}H_2$), 124.0 (aromatic C_4), 124.7 (aromatic C_3, C_5), 141.8 (aromatic C_2, C_6) 152.9 (aromatic C_1); IR (KBr): ν_{max} 1235 s, 1196 s, 1134 s (C–O), 796 s, 759 s (C–Cl) cm^{-1}.

1-Chloro-2-isopropyl-6-methylbenzene[31] **3g**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.42 [d, *J* = 5.4 Hz, 6H, $CH(C\underline{H}_3)_2$], 1.57 (s, 3H, $ArC\underline{H}_3$), 2.65 [sep, *J* = 6.8 Hz, 1H, $C\underline{H}(CH_3)_2$], 6.25–6.33 (m, 3H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1 ($ArC\underline{H}_3$), 22.7 [$CH(\underline{C}H_3)_2$], 30.3 [$\underline{C}H(CH_3)_2$], 123.9 (aromatic C_3), 126.3 (aromatic C_5), 128.2 (aromatic C_4), 133.7 (aromatic C_1), 136.3 Aromatic C_6), 145.9 (aromatic C_2); IR(KBr): ν_{max} 1469 s, 1455 s, 1041 s, 779 s (C–Cl) cm^{-1}.

1-t-Butyl-2-Chloro-3-methylbenzene[32] **3h**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.49 [s, 9H, $C(C\underline{H}_3)_3$], 2.38 (s, 3H, $ArC\underline{H}_3$) 7.09 (m, 2H, aromatic C_4–H, C_6–H), 7.27 (dd, *J* = 2.7, 3.5 Hz, 1H, C_5–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.7 ($ArC\underline{H}_3$), 29.8 [$C(\underline{C}H_3)_3$], 36.3 [$\underline{C}(CH_3)_3$], 125.3 (aromatic C_6), 125.9 (aromatic C_4), 128.8 (aromatic C_5), 133.0 (aromatic C_2), 138.0 (aromatic C_3), 146.6 (aromatic C_1); IR (KBr): ν_{max} 1042 s, 778 s (C–Cl) cm^{-1}.

1-Chloro-2,6-diisopropylbenzene[33] **3i**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23 [d, 12H, *J* = 6.8 Hz, $CH(C\underline{H}_3)_2$], 3.49 [sep, *J* = 6.8 Hz, 2H, $CH(C\underline{H}_3)_2$], 7.12–7.18 (m, 3H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.8 [$CH(\underline{C}H_3)_2$], 30.6 [$\underline{C}H(CH_3)_2$], 123.9 (aromatic C_3, C_5), 126.6 (aromatic C_4), 132.8 (aromatic C_1), 146.0 aromatic C_2, C_6); IR (KBr): ν_{max} 1031 s, 791 s (C–Cl) cm^{-1}

(2-Methoxyethoxy)benzene[34]: ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.45 (s, 3H, $OC\underline{H}_3$), 3.75 (t, *J* = 4.7 Hz, 2H, $C\underline{H}_2OCH_3$), 4.12 (t, *J* = 4.7 Hz, 2H, $PhOC\underline{H}_2$), 6.94 (t, *J* = 7.8 Hz, 3H, aromatic *o*, *p*), 7.28 (t, *J* = 7.9, Hz, 2H, aromatic *m*); ^{13}C NMR (75 MHz, $CDCl_3$): δ 59.1 ($O\underline{C}H_3$), 67.0 ($\underline{C}H_2OCH_3$, 71.0 ($PhO\underline{C}H_2$), 114.5 (aromatic *o*), 120.8 (aromatic *p*), 129.3 (aromatic *m*), 158.7 (aromatic quaternary); IR (KBr): ν_{max} 1247 s, 1128 s (C–O), 754 s (C–Cl) cm$^{-1.}$

2,6-Diisopropy1-1-(2-methoxyethoxy)benzene: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23 [d, *J* = 6.8 Hz, 12H, $CH(C\underline{H}_3)_2$], 3.37 [m, 2H, $C\underline{H}(CH_3)_2$], 3.48 (s, 3H, $OC\underline{H}_3$)), 3.75 (t, *J* = 4.6 Hz, 2H, $C\underline{H}_2OCH_3$), 3.90 (t, *J* = 4.6 Hz, 2H, $ArOC\underline{H}_2$), 7.09 (s, 3H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1 [$CH(\underline{C}H_3)_2$], 26.2 [$\underline{C}H(CH_3)_2$], 59.2 ($O\underline{C}H_3$), 71.9 ($\underline{C}H_2OCH_3$), 73.6 ($ArO\underline{C}H_2$), 124.0 (aromatic C_4), 124.6 (aromatic C_3, C_5), 141.8 (aromatic C_2, C_6), 153.0 (aromatic C_1); IR (KBr): ν_{max} 1190 s, 1129 s (C–O) cm^{-1}.

[2-(2-Methoxyethoxy)ethoxy]benzene[35]: ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.39 (s, 3H, $OC\underline{H}_3$), 3.57 (t, *J* = 4.5 Hz, 2H, $C\underline{H}_2OCH_3$), 3.72 (t, *J* = 4.5 Hz, 2H, $C\underline{H}_2CH_2OCH_3$), 3.85 (t, *J* = 4.8 Hz, 2H, $PhOCH_2C\underline{H}_2O$), 4.14 (t, *J* = 4.9 Hz, 2H, $PhOC\underline{H}_2$), 6.93–6.96 (m, 3H, aromatic *o*, *p*), 7.27 (t, *J* = 7.7 Hz, 2H, aromatic *m*); ^{13}C NMR (75 MHz, $CDCl_3$): δ 59.0 ($O\underline{C}H_3$), 67.3 ($\underline{C}H_2OCH_3$), 69.8 ($\underline{C}H_2CH_2OCH_3$), 70.7 ($PhOCH_2\underline{C}H_2$), 71.9 ($PhO\underline{C}H_2$), 114.6 (aromatic *o*), 120.8 (aromatic *p*), 129.4 (aromatic *m*), 158.7 (aromatic quaternary); IR(KBr): ν_{max} 1245 s, 1112 s (C–O) cm^{-1}.

2-Phenoxyethanol[36]: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.25 (br. s, 1H, $O\underline{H}$), 3.94 (t, *J* = 4.4, Hz, 2H, $C\underline{H}_2OH$), 4.07 (t, *J* = 4.4 Hz, 2H, $PhOC\underline{H}_2$), 6.90–6.99 (m, 3H, aromatic *o*, *p*), 7.29 (t, *J* = 7.9 Hz, 2H, aromatic *m*); ^{13}C NMR (75 MHz, $CDCl_3$): δ 61.3 ($\underline{C}H_2OH$), 69.0 ($PhO\underline{C}H_2$), 114.5 (aromatic *o*), 121.0 (aromatic *p*), 129.5 (aromatic *m*), 158.5 (aromatic quaternary); IR (KBr): ν_{max} 3393 s (O–H), 1054 s cm^{-1}.

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