Tris(polyoxaalkyl)amines (Trident), a New Class of Solid-Liquid Phase-Transfer Catalysts

Gêrard Soula

Sociéte Rhone-Poulenc Recherches, Centre de Recherches des Carrières, 69192-Saint-Fons Cedex, France

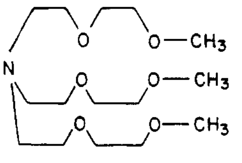
Received April 24, 1984

A new class of solid-liquid phase-transfer catalysts has been prepared. These tris(polyoxaalkyl)amines (I) are designed to obtain the best balance between straightforward synthesis (cheap starting materials), high activity, easy recovery, and low toxicity. The catalysts are synthesized from ethylene glycols by a simple one-step method in yields in the range of 65-81%. They show high catalytic effects in aliphatic nucleophic substitutions and aromatic nucleophilic substitutions on activated and unactivated molecules. In the Ullman synthesis (a new PTC reaction) there is a synergic effect of anionic activation by tridents and by copper salts. Reactions have been carried out at temperatures up to 180 °C without evidence of decomposition of the tris(polyoxaalkyl)amines. The behavior and catalytic activity of these catalysts are discussed.

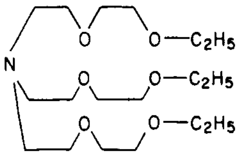
Since 1967 with the discovery by C. J. Pedersen[1,2] of the ability of crown ethers to form complexes with alkali metal and similar cations, there has been rapid and broad development of this class of compounds and of other ligands such as Lehn's cryptands[3] and the so-called octopus molecules.[4] More recently, Vögtle and his co-workers[5] showed the ability of polypodants and particulary of acyclic cryptands to form complexes with alkali and alkaline earth metal salts.

In order to carry out solid-liquid phase-transfer catalysis and the recovery of metals, we described, at the same time, in different patents[6-8] the synthesis and the properties of tris(polyoxaalkyl)amines. We report here results concerning the preparation of these tris(polyoxaalkyl)amines and among these compounds we have selected TDA-1 to act as phase-transfer catalyst which represents the best efficiency/price/toxicity compromise.

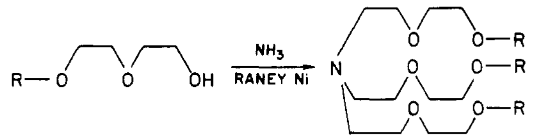
Preparation of Tris(polyoxaalkyl)amines. Tris(polyoxaalkyl)amines may be called "acyclic cryptands" or, as we prefer, "tridents". In this study, the tridents, tris(3,6-dioxaheptyl)amine (TDA-1), **1**, and tris(3,6-dioxaoctyl)amine (TDA-2), **2**, were synthesized by using a simple method from the mono ether of bis(ethylene glycol) (eq 1[8]).



1



2

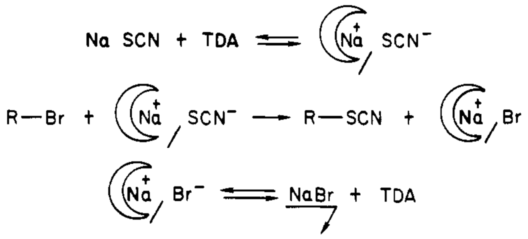


(1)

This process is cheap and industrially feasible and it is a simpler method than those which have been described previously.[5,6]

We shall describe first, a typical reaction carried out under PTC conditions[9-11] in order to show the activity of the TDA-1. We will then show some of the new possibilities of solid-liquid PTC methods which we have found.

Scheme I



Reaction of Alkyl Halide with NaSCN. This reaction has been extensively studied with PTC, liquid-liquid or solid-liquid PTC, with different catalysts[12-16] (eq 2).

$$C_6H_{13}\text{-Br} + Na^+SCN^- \xrightarrow{\text{"PTC"}} C_6H_{13}\text{-SCN} + NaBr \quad (2)$$

In this case, the characteristic behavior of tris(polyoxaalkyl)amines can be seen. In 20 mL of dry chlorobenzene, at 100 °C, 0.01 mol of NaSCN is completely soluble in the presence of a stoichiometric amount of tris(polyoxaheptyl)amine (TDA-1). Upon addition of 0.008 mol of *n*-bromohexane at this temperature, the reaction occurs with precipitation of sodium bromide. NaSCN forms a complex with TDA-1, which is soluble in chlorobenzene, whereas under the same conditions NaBr does not form a complex with the trident. In the presence of a catalytic amount of TDA-1, solid NaSCN is gradually solubilized and the reaction with the alkyl bromide takes place. In fact, the results are the same with a stoichiometric or a catalytic amount of TDA-1 (RSCN yield = 98%) after 15 min in the former case and after 2.5 h in the latter. The reaction pathway may be summarized as shown in Scheme I.

The equilibria 1 and 3 are considerably displaced toward the right and the catalyst is released after each reaction. This is an extremely clear example of how the catalyst in

---

[1] Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017.
[2] Pedersen, C. J. *J. Am. Chem. Soc.* **1970**, *92*, 391.
[3] Dietrich, B.; Lehn, J. M.; Sauvage, J. P. *Tetrahedron Lett.* **1969**, 2885.
[4] Vögtle, F.; Weber, E. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 814.
[5] Heimann, U.; Herzhoff, M.; Vögtle, F. *Chem. Ber.* **1979**, *112*, 1392.
[6] Soula, G. Eur. Patent 5094, 1978.
[7] Soula, G. Eur. Patent 16673, 1979.
[8] Soula, G.; Linguenheld, L. French Patent 2455570, 1979.
[9] Keller, W. E. "Compendium of phase transfer reactions and related synthetic methods"; 1st ed.; Fluka A. G., 1979.
[10] Weber, W. P.; Gokel, G. W. "Phase Transfer Catalysis in Organic Synthesis"; Springer-Verlag: Berlin, 1977.
[11] Stark, C. M.; Liotta, C. "Phase Transfer Catalysis"; Academic Press: New York, 1978.
[12] Reeves, W. P.; White, M. R.; Bier, D. *J. Chem. Educ.* **1978**, *55*, 56.
[13] Landini, D.; Maia, A. M.; Montanari, F.; Pirisi, F. M. *Gazz. Chim. Ital.* **1975**, *105*, 863.
[14] Cinquini, M.; Tundo, P. *Synthesis* **1976**, 516.
[15] Jonczyk, A.; Ludwikow, M.; Makosza, M. *Angew. Chem., Int. Ed. Engl.* **1978**, *90*, 58.
[16] Lehmkuhl, H.; Rabet, F.; Hauschild, K. *Synthesis* **1977**, 184.

0022-3263/85/1950-3717$01.50/0 © 1985 American Chemical Society

Table I. Compared Efficacy of Phase-Transfer Catalysts in the Reaction of Hexyl Bromide with NaSCN (Eq 2)[a,c]

catalyst	yield, % with 100% catalyst[b,d]	yield, % with 10% catalyst[b,e]
without catalyst	0	0
TDA-1	98	98
hexadecyltributylphosphonium bromide	7.4	30.2
tetrabutylammonium bromide	24.4	98
18-crown-6	94	98
dibenzo-18-crown-6	4.7	50.2
bis(ethylene glycol)	<2	7.6
tetrakis(ethylene glycol)	35	77
bis(ethylene glycol) dimethyl ether	<2	0
tetrakis(ethylene glycol) dimethyl ether	76	62
tetrakis(ethylene glycol) bis(8-quinolyl) ether	98	98

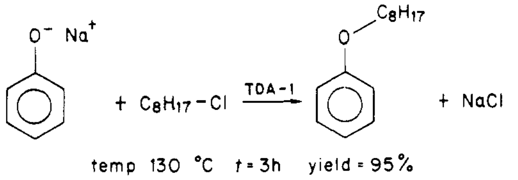
[a] This comparative study was carried out on the suggestion of one of the referees. [b] Molar %. [c] Solvent chlorobenzene, 100 °C. [d] 15 min [e] 2 h 30 min.

solid–liquid (PTC) is selective in its choice of alkali salts thus permitting a high turn-over of the catalyst.

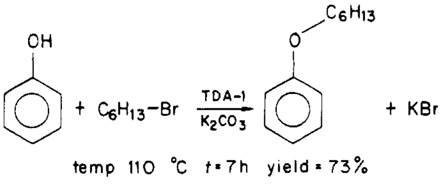
In order to compare the efficacy of tridents to that of other catalysts we have carried out the previous reaction (eq 2) under identical conditions. The catalysts checked include those which have been most extensively used in solid–liquid systems and which are commercialy available. The results reported in Table I correspond to stoichiometric and to catalytic amounts of catalyst. Under both conditions TDA-1 gives a 98% yield. This value is also obtained with tetrakis(ethylene glycol)–di-8-quinolyl ether (a podant prepared by Vögtle[30]) under stoichiometric and catalytic conditions and by 18-crown-6 and TBAB under catalytic conditions. However, with TBAB, byproducts arising from decomposition of the catalyst were also observed.

The following examples illustrate the behavior of tridents in other cases of solid–liquid PTC.

Reactions of Alkyl Halides with Alkali Phenates. This reaction is of great industrial importance. In each instance of solid–liquid PTC, phenolic compounds themselves in combination with K_2CO_3 or the preformed alkali phenate may be used (eq 3 and 4).



(3)



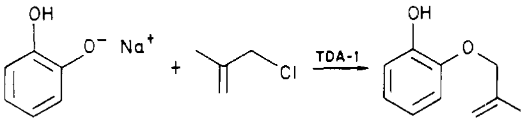
(4)

After 3 h at 130 °C with TDA-1/PhO^-Na^+ = 0.05 the yield was 95%. Under the same conditions but without the catalyst, the yield was 4%. With K_2CO_3, TDA-1/PhOH = 0.05, and toluene as a solvent and after 7 h at 110 °C the alkyl phenyl ether yield was 73%. In the absence of a catalyst the yield was 6%. This procedure has special advantages when it is applied to an ambident reagent. It is well-known that pyrocatecholate gives C-alkylation with methallyl chloride in the presence of water.[17] With preformed sodium pyrocatecholate and TDA-1, we obtained high selectivity in O-alkylation in aprotic, nonpolar solvents.[18] In order to minimize di-O-alkylation, the conversion of the starting material was limited to 75% max. Table II shows the influence of the solvent upon the yield and the selectivity of this reaction.

Table II. Reaction of Sodium Pyrocatecholate with Methallyl Chloride Catalyzed by TDA-1

solvent[a,b]	*t*, h	yield, %	selectivity, %
toluene	5	55	92
chlorobenzene	4	67	95
chlorobenzene	6	74	93
anisole	6.30	73.5	93.5
acetonitrile[c]	10.30	67.5	90

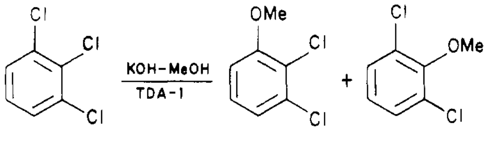
[a] Reaction at 100 °C. [b] Without TDA-1 the yield is <5%. [c] In refluxing acetonitrile.



(5)

Nucleophilic Aromatic Substitution on Activated Aryl Halide Substrates. The diphenyl ether synthesis can be accomplished by liquid–liquid PTC[19] at about 110 °C with $R_4N^+X^-$. Under these conditions it is necessary to operate under pressure and the temperature of the reaction is limited by the stability of the catalyst. When solid–liquid PTC was used with the tridents (TDA), the reaction takes place at atmospheric pressure and without any appreciable decomposition of the catalyst even at 180 °C.[20] Table III shows some examples of this reaction.

Nucleophilic Aromatic Substitution on Unactivated Aryl Halide Substrates. Sam and Simmons[21] showed that KOH/crown ether in methanol solution, after the evaporation of methanol, gives a complex containing only 11% KOH. The predominant form is CH_3OK (89%) which results from the reaction of KOH with methanol during complex formation. After heating a 1.0 M solution of this mixture in *o*-dichlorobenzene at 90 °C for 16 h a 40–60% yield of *o*-chloroanisole was obtained. In order to prepare dichloroanisoles from 1,2,3-trichlorobenzene, we used a KOH–CH_3OH solution containing only a catalytic amount of TDA-1;[22] CH_3OH distilled simultaneously with the addition of KOH–CH_3OH during the reaction (eq 6). The yield was 94% after 2 h at 140 °C. Without the catalyst, under the same conditions, the yield was 8%. This is an efficient method to prepare and use CH_3OK as it avoids the use of potassium metal and stoichiometric amounts of crown ether.



(6)

Ullman Synthesis. Bacon and Hill[23,24] showed that basic solvents such as pyridine and quinoline are necessary to carry out the synthesis of diaryl ethers from nonactived aryl halides with a copper salt catalyst (eq 7). Although the mechanism of this reaction is not clearly understood, it is thought that the solvent forms a complex with the copper salt and hence solubilizes it, allowing the interaction

---

[17] Desimone, R. French Patent 2 281 914, 1976.

[18] Michelet, D.; Soula, G. French Patent 2 459 216, 1979.

[19] Markert, J.; Schwander, H. Ger. Patent 2 620 791, 1976.

[20] Soula, G. Eur. Patent 22 387, 1979.

[21] Sam, D. J.; Simmons, H. E. *J. Am. Chem. Soc.* **1973**, *96*, 2252.

[22] Soula, G. Eur. Patent 35 927, 1980.

[23] Bacon, R. G.; Hill, H. A. *J. Chem. Soc.* **1964**, 1100.

[24] Bacon, R. G.; Hill, H. A. *J. Chem. Soc.* **1964**, 1108.

Table III. Nucleophilic Aromatic Substitution on Activated Aryl Halides with Solid Reagents in the Presence of TDA-1 (0.05 mol equiv) as Catalyst

aryl halide[a]	nucleophile (Na salt)	product	t, h	yield, %[c]
4-chloronitrobenzene	phenol	4-phenoxynitrobenzene	9	95 (3)
4-chloronitrobenzene	4-aminophenol	4′-amino-4-phenoxybenzene	13	83 (8)
4-chloronitrobenzene	methanethiol	4-thiomethoxynitrobenzene	2	72
4-chlorobenzonitrile[b]	phenol	4-phenoxybenzonitrile	8	85 (3)
2-chloro-5-(trifluoromethyl)nitrobenzene	phenol	2-phenoxy-3-(trifluoromethyl)nitrobenzene	4	92 (18)

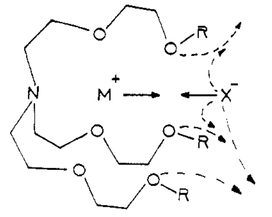
[a] Solvent used is chlorobenzene at reflux. [b] Reaction occurs in *o*-dichlorobenzene at 180 °C. [c] Yield obtained in the same conditions without catalyst.

Table IV. Diaryl Ether Synthesis from Unactivated Aryl Halides with Cuprous Chloride[a] and TDA[b] as Catalyst

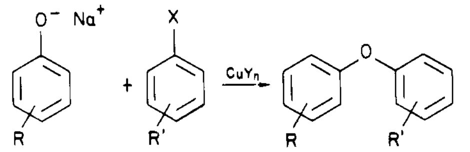
aryl halide	reagent (Na salt)	product	solvent (TDA)	T, °C	t, h	yield,[c] %	yield,[d] %
3-methylchlorobenzene	3-fluorophenol	3-fluorophenyl 3-methylphenyl ether	none (TDA-1)	180	8.5	66	5
3-cyanochlorobenzene	phenol	3-cyanophenyl phenyl ether	anisole (TDA-2)	155	6	85	15
4-(trifluoromethyl)chlorobenzene	3-methylphenol	3-methylphenyl 4-(trifluoromethyl)phenyl ether	anisole (TDA-1)	155	6	75	3
3-nitrochlorbenzene	phenol	3-nitrophenyl phenyl ether	anisole (TDA-2)	155	6	72	12
2-fluorochlorobenzene	3-methylphenol	2-fluorophenyl 3-methylphenyl ether	none (TDA-1)	133	24	75	11

[a] The amount of CuCl is 0.01 mol equiv. [b] TDA is used in the same concentration (0.01 mol equiv). [c] Without apparent reason, sometimes the reaction stops at different levels. It seems that the cuprous chloride is very sensitive to the presence of water and other impurities. In the particular case of water, it may be the formation of cuprous oxide, which does not form a complex with TDA, is the main reason. [d] Yield obtained under the same conditions without TDA.

Scheme II



of the copper salt with the aryl halide. We wished to avoid this kind of solvent and to solubilize the solid alkali phenates and solid copper salts by the introduction of catalytic amounts of tridents.[25]



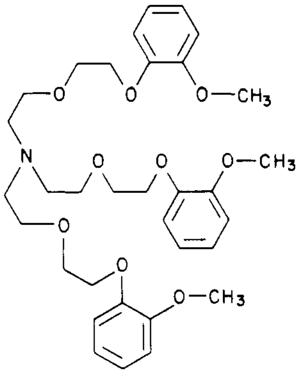
(7)

X = Br, Cl; Y = Br, Cl; n = 1, 2

Cuprous chloride was chosen as the copper catalyst. The reactions were carried out with 10% of TDA-1 and 10% of CuCl. Table IV shows some Ullmann syntheses in the presence of cuprous chloride and TDA in different solvents.

Discussion

With these simple tridents it is possible to complex and solubilize a large variety of metal salts in organic solvents: alkali metals salts such as NaSCN and KSCN, as well as transition metal salts such as $ReCl_3$, $RuCl_3$, $PdCl_2$.[7] This property is, of course, not only due to the nature of the trident but also, and to a greater extent, to the flexibility of the molecule. It is now proved by Vögtle et al.[26,27] that in KSCN complexation by tris[5-(2-methoxyphenoxy)-3-oxapentyl]amine, 3, all ten donor centers, including the three terminal OCH_3 groups, participate in the coordination of the metal ion which is located at the center of the pseudocavity (Vögtle's terminal group concept[28]).



3

Although it has not been demonstrated, we can suppose that the tris(polyoxaalkyl)amines form complexes with alkali metals in the same manner. Throughout all these examples of solid–liquid PTC, the role of trident is clearly demonstrated. It seems that the mechanism proposed for the reaction of NaSCN with *n*-bromohexane is applicable to other types of reactions.

However, it appears that not only the cation but also the anions play an important role in the solubilization process. To enhance reaction rates, it is important that complex formation between the reagent and the trident occurs; it is also imperative that no complexation occurs with the salt produced in the reaction. During the course of the reaction only the anion changes; the cations remains unchanged. Consequently, the trident should have a high sensitivity to the nature of the anion (Scheme II). A small anion with a high charge density interacts so strongly with the cation that it can destroy complexation by electrostatic repulsion with the ligands. This is the case with F⁻, Cl⁻, or Br⁻. A larger anion, having a low charge density, does

---

(25) Soula, G.; Linguenheld, L. Eur. Patent 21868, 1979.

(26) Vögtle, F.; Muller, W. M.; Wehner, W.; Buhleier, E. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 548.

(27) Vögtle, F.; Weber, E. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 753.

(28) Tummler, B.; Maass, G.; Vögtle, F.; Sieger, H.; Heimann, U.; Weber, E. *J. Am. Chem. Soc.* **1979**, 101, 2588.

not interact with the cation–trident complex, thus permitting the formation of stable complexes. Fortunately, in anionic nucleophilic substitution, the nucleophile is generally softer than the leaving group anion. Thus the equilibria 1 and 3 are displaced toward the right, permitting a high turn-over of catalyst. However, it is necessary to note that the anion is not really a "naked" ion as it is with the cryptand. Consequently, the anionic activation will be less effective than that observed with cryptand.[29,30]

We have shown by this method that it is possible to perform not only classical nucleophilic substitutions but also other reactions not achievable by the liquid–liquid PTC technique (such as dichloroanisole synthesis from KOH–MeOH or the Ullmann synthesis with cuprous chloride). Another good point of interest is that even at high temperatures, the trident acts as a phase-transfer catalyst without the loss of the useful properties observed at lower temperatures.

Toxicity. Different studies showed that TDA-1 was of very low toxicity. The LD_{50} was found to be 4.5 g/kg. TDA-1 is nonirritating to the skin and has no mutagen activity.

The simplicity of the preparation of tridents, the facility with which it is possible to recover the catalyst after reaction, their high activity in solid–liquid PTC and their low toxicity suggest that tridents such as TDA-1 are very promising catalysts.

Experimental Section

All products synthetized were characterized by ^1H, NMR, IR, and mass spectroscopy and gave satisfactory analytical results.

^1H NMR spectra were recorded on a JEOL FX 100 spectrometer with tetramethylsilane as internal standard. IR spectra were obtained with a Perkin-Elmer 457 spectrometer and mass spectrometry analyses were recorded on a AEI MS 902 instrument. Atomic absorption spectrometry analyses were performed on Perkin-Elmer instrument 403 and X-ray fluorescence spectrometer Philipps PW 1400 spectrometer.

Gas chromatographic analyses were performed on a Perkin-Elmer 900 instrument with flame-ionization detector by using a column packed with silicon rubber SE-30 on Chromosorb.

Reagents and solvents were all commercialy available materials and were purified by standard procedures.

The experimental procedures are illustrated by the following typical reactions.

Preparation of Tris(3,6-dioxaoctyl)amine (TDA-2). Dehydrated Raney nickel (195 g) and 1.400 g of 3,6-dioxaoctanol [bis(ethylene glycol)monoethyl ether] are introduced into a four-necked round-bottomed flask equipped with a stirrer, an ammonia and hydrogen inlet, a column, and a condenser for collecting the water entrained by the stream of gas. The slurry obtained is heated to 150 °C, at which temperature a stream of gas consisting of 51 g of ammonia and 2 g of hydrogen per hour is passed through. The mixture is then heated to 185 °C and this temperature is maintained for 3 h when about 60% of the alkylene glycol ether has been converted into amines. The ammonia supply is then cut off and the stream of hydrogen is maintained for a further 2 h at 185 °C. After cooling, the Raney nickel is filtered and the filtrate is distilled in vacuo. This yields 800 g of tris(3,6-dioxaoctyl)amine having a boiling point of 195 °C at 0.5 mmHg and 180 g of 9-aza-3,6,12,15-tetraoxaheptadecane (bp 143 °C (0.5 mmHg)). This secondary amine may be recycled.

Preparation of Tris(3,6-dioxaheptyl)amine (TDA-1). The operation described in the preceding example is carried out with 7500 g of Raney nickel, 25 000 g of 3,6-dioxaheptan-1-ol, 1700 g/h of gas. The yields are 15 125 g of tris(3,6-dioxaheptyl)amine of boiling point 160 °C (0.5 mmHg) and 3241 g of 8-aza-2,5,11,14-tetraoxapentadecane of boiling point 125 °C (0.5 mmHg).

Reaction of *n*-Bromohexane with Sodium Thiocyanate in Chlorobenzene Catalyzed by TDA-1. A 100-mL three-necked, round-bottomed flask equipped with a magnetic stirring bar, reflux condenser, and dropping funnel was charged with 20 mL of dried distilled chlorobenzene, solid NaSCN (0.81 g, 0.01 mol), and tris(3,6-dioxaheptyl)amine (3.23 g, 0.01 mol, under stoichiometric conditions, 0.32 g, 0.01 mol, under catalytic conditions). The solution was placed in a bath at 100 °C and was maintained under a nitrogen atmosphere while *n*-bromohexane (1.32 g, 0.008 mol) was quickly added. After 15 min at 100 °C, under stoichiometric conditions (or 2 h 30 min at 100 °C, under catalytic conditions), the bromohexane had disappeared and only *n*-hexyl thiocyanate as the new product was detected by GLC; the product yield was 98%.

Reaction of *n*-Bromohexane with Sodium Thiocyanate in Chlorobenzene Catalyzed by Several Catalysts (Table I). The reaction was performed as above. The *n*-hexyl thiocyanate was detected by GLC; the product yields are reported in Table I.

Reaction of *n*-Octyl Chloride with Sodium Phenate. *n*-Octyl chloride (171 g, 1.15 mol), 11.6 g (0.1 mol) of anhydrous solid sodium phenate, and 1.6 g (0.005 mol) of tris(3,6-dioxaheptyl)amine were successively introduced into a 500-mL three-necked round-bottomed flask. The heterogeneous reaction mixture was stirred and heated at 130 °C. The yield of *n*-phenoxyoctane was 95% after 3 h. (Determination by GC with standard.)

Reaction of *n*-Bromohexane with Phenol and K_2CO_3. Anhydrous toluene (370 mL) 27.7 g K_2CO_3 (0.2 mol), 37.7 g of phenol (0.4 mol), 66 g of *n*-bromohexane (0.4 mol), and 5.4 g of tris(3,6-dioxaheptyl)amine (0.016 mol) were successively introduced into a 1-L three-necked round-bottomed flask. The reaction mixture was stirred and heated at 110 °C for 7 h. The mixture was then quenched with water (200 mL). The organic phase was separated, dried over silica gel, and distilled; 52 g of phenoxyhexane was recovered (75% yield).

Reaction of Sodium Pyrocatecholate with Methallyl Chloride in Different Solvents. Toluene (70 mL), 6.6 g (0.05 mol) of sodium pyrocatecholate, 9.1 g (0.1 mol) of distilled methallyl chloride, and 1.6 g (0.005 mol) of tris(3,6-dioxaheptyl)amine were successively introduced into a 250-mL three-necked round-bottomed flask equipped with a mechanical stirrer, a reflux condenser, and a thermometer. A steam of argon was passed through, and the heterogeneous reaction mixture was heated at 100 °C for 5 h. The degree of conversion of the sodium pyrocatecholate was 55%. The yield of the monoether formed was 92% as analyzed by GLC.

Reaction of Sodium Phenate with *p*-Nitrochlorobenzene. Chlorobenzene (100 mL), 32 g (0.2 mol) of *p*-nitrochlorobenzene, 23 g (0.2 mol) of sodium phenate, and 3.2 g (0.01 mol) of tris(3,6-dioxaheptyl)amine were successively introduced into a 500-mL three-necked round-bottomed flask equipped with a mechanical stirrer, a thermometer, and a reflux condenser. The heterogeneous reaction mixture was stirred and heated at 130 °C for 9 h. The mixture was then cooled to 25 °C and quenched with water (100 mL). The organic phase was separated, dried over silica gel, and then analyzed by GLC to show unreacted *p*-nitrochlorobenzene (5%) and *p*-phenoxynitrobenzene (95%). The nitrochlorobenzene was distilled and the product yield after recrystallization from 100 mL of dried ethanol was 92%.

Reaction of Sodium *p*-Aminophenate with *p*-Nitrochlorobenzene. Chlorobenzene (100 mL), 15.7 g (0.1 mol) of *p*-chloronitrobenzene, 13.1 g (0.1 mol) of sodium *p*-aminophenate, and 1.6 g (0.005 mol) of tris(3,6-dioxaheptyl)amine were successively introduced into a 500-mL three-necked round-bottomed flask equipped with a mechanical stirrer, a thermometer, and a reflux condenser. The mixture was then stirred and heated at 130 °C for 13 h and the resulting solution was filtered while hot. After filtration, 300 mL of hexane was added and this caused the precipitation of the *p*-(4-aminophenoxy)nitrobenzene. The yield of the product was 83%.

Reaction of Sodium Thiomethylate with *p*-Nitrochlorobenzene. Chlorobenzene (1 L), 157 g (1 mol) of *p*-nitrochlorobenzene, 140 g (2 mol) of sodium thiomethylate, and 32 g (0.1 mol) of tris(3,6-dioxaheptyl)amine were successively introduced into

---

[29] Landini, D.; Maia, A.; Montanari, F.; Tundo, P. *J. Am. Chem. Soc.* **1979**, 101, 2526.

[30] Vögtle, F. "Host Guest Complex Chemistry II"; Topics in Current Chemistry; Springer-Verlag: Berlin, 1982.

a 2-L three-necked round-bottomed flask equipped with a mechanical stirrer, a thermometer, and a reflux condenser. The mixture was stirred and heated for 2 h at the reflux temperature of the chlorobenzene and then cooled. The salts formed, together with the unconverted sodium thiomethylate, were removed by filtration and the chlorobenzene then evaporated. The *p*-thiomethoxynitrobenzene was distilled. The yield of the reaction was 72%.

Reaction of Potassium Phenate with *p*-Chlorobenzonitrile. *o*-Dichlorobenzene (200 mL), 27.5 g (0.2 mol) of *p*-chlorobenzonitrile, 29.04 g (0.22 mol) of potassium phenate, and 3.2 g (0.01 mol) of tris(3,6-dioxaheptyl)amine were successively introduced into a 500-mL three-necked round-bottomed flask equipped with a mechanical stirrer, a thermometer, and a reflux condenser. The reaction mixture was stirred and heated at the reflux temperature of the *o*-dichlorobenzene for 8 h. The salts formed were removed by filtration and the solvent removed by distillation. The yield of the reaction was 85%.

Reaction of Sodium Phenate with 3-Nitro-4-chloro(trifluoromethyl)benzene. Chlorobenzene (200 mL), 22.5 g (0.1 mol) of 3-nitro-4-chloro(trifluoromethyl)benzene, 13 g (0.11 mol) of sodium phenate, and 3.2 g (0.01 mol) of tris(3,6-dioxaheptyl)amine were successively introduced into a 500-mL three-necked round-bottomed flask equipped with a mechanical stirrer, a thermometer, and a reflux condenser. The mixture was stirred and heated at the reflux temperature of the chlorobenzene for 4 h. After cooling, the salts were filtered and the solvent then evaporated. The yield of the reaction was 92%.

Reaction of 1,2,3-Trichlorobenzene with MeOH–KOH. Into a 4-L three-necked round-bottomed flask, equipped with a mechanical stirrer, an addition funnel, and a distillation column with a condenser and a receiver was charged 1.815 kg of 1,2,3-trichlorobenzene (10 mol) and 160 g of tris(3,6-dioxaheptyl)amine. The mixture was heated to 140 °C and a solution of 1.306 kg of KOH (86%) in 2.5 kg of methanol was added dropwise over 2 h with simultaneous distillation of the methanol. When the addition was complete, the stirring was continued for another 2 h at 135 °C; the mixture was then cooled and quenched with water (1 L). After separation of the organic phase the aqueous phase was extracted 3 times with 500 mL of chlorobenzene. The organic phases were mixed and then dried over sodium sulfate. The chlorobenzene was evaporated and the products were distilled: 2,6-dichloroanisole, bp 117 °C (20 mm), 496 g; 2,3-dichloroanisole, bp 128 °C (20 mm), 756 g. After acidification of the aqueous phase and extraction with chlorobenzene (500 mL), 2,6-dichlorophenol (23%) was recovered. The overall yield of the reaction was 97%.

Preparation of 3-(3′-Fluorophenoxy)toluene. 3-Chlorotoluene (110 g, 0.87 mol), 8 g (0.06 mol) of sodium *m*-fluorophenate, 0.6 g (0.006 mol) of cuprous chloride, and 1.9 g (0.006 mol) of tris(3,6-dioxaheptyl)amine were introduced into a 500-mL round-bottomed flask equipped with a stirrer and heated by an oil bath. The mixture was allowed to reflux for 8 h (180 °C) before cooling. Water (100 mL) was added and the solution was neutralized (pH 7) with concentrated aqueous hydrochloric acid. The organic layer was then separated and distilled. 3-(3′-Fluorophenoxy)toluene (7.9 g, 66% yield) was recovered.

Preparation of 3-Phenoxybenzonitrile. 3-Chlorobenzonitrile (100 g, 0.73 mol), 98 g (0.84 mol) of sodium phenate, 7.2 g (0.0072 mol) of cuprous chloride, 9 g (0.028 mol) of tris(3,6-dioxaheptyl)amine, and 570 g of anisole were introduced into a 1-L round-bottomed flask equipped as in the preceding example. The mixture was heated under reflux (155 °C) for 6 h and under a nitrogen atmosphere. The degree of conversion was 85%, and the yield with respect to distilled *m*-phenoxybenzonitrile was 70%.

Comparative Example. The procedure carried out under b was repeated except that no tris(3,6-dioxaheptyl)amine was added. The degree of conversion after 6 h was 15%.

Preparation of 3-Methylphenyl 4-(Trifluoromethyl)phenyl Ether. Sodium *m*-cresolate (65 g, 0.5 mol), 90.25 g (0.5 mol) of *p*-chloro(trifluoromethyl)benzene, 5 g (0.005 mol) of cuprous chloride, 18 g (0.056 mol) of tris(3,6-dioxaheptyl)amine, and 300 g of anisole were introduced into a 1-L round-bottomed flask equipped as in the other examples. After refluxing for 6 h at 150 °C, the mixture was cooled. Water (300 mL) was added in order to dissolve the salts which have been formed in the reaction. The resulting solution was neutralized to pH 7. The organic layer was separated and distilled. Distillation yielded 98 g of 3-methylphenyl 4-(trifluoromethyl)phenyl ether.

Preparation of *m*-Phenoxynitrobenzene. *m*-Chloronitrobenzene (7.9 g, 0.05 mol), 5.8 g (0.05 mol) of sodium phenate, 0.5 g (0.005 mol) of cuprous chloride, and 1.60 g (0.005 mol) of tris(3,6-dioxaheptyl)amine in 50 mL of anisole were introduced into a 100-mL Erlenmeyer flask, equipped with a magnetic stirring bar, under a nitrogen atmosphere. The mixture was heated under reflux for 6 h, and the degree of conversion reached 72%.

Preparation of 3-(2′-Fluorophenoxy)toluene. 1-Chloro-2-fluorobenzene (20 g, 0.15 mol), 1.37 g (0.01 mol) of sodium *m*-cresolate, 0.099 g (0.001 mol) of cuprous chloride, and 0.32 g (0.001 mol) of tris(3,6-dioxaheptyl)amine were introduced into a 100-mL Erlenmeyer flask equipped with a magnetic stirring bar and maintained under a stream of nitrogen. The mixture was heated under reflux for 24 h. The degree of conversion with respect to 1-fluoro-2-(3′methylphenoxy)benzene reached 75%.

Acknowledgment. I acknowledge the financial support of the Rhone-Poulenc Company, the helpful discussion with Professor J. Metzger, Prof. R. Gallo, and Prof. D. Seyferth, and the invaluable help of fellow workers listed in the references in the development of this work.

Registry No. 1, 70384-51-9; 2, 75888-21-0; $\mathrm{Me(OCH_2CH_2)_2NH(CH_2CH_2O)_2Me}$, 5732-47-8; $\mathrm{Et(OCH_2CH_2)_2NH(CH_2CH_2O)_2Et}$, 77455-70-0; $\mathrm{HO(CH_2)_2O(CH_2)_2OCH_3}$, 111-77-3; $\mathrm{HO(CH_2)_2O(CH_2)_2OEt}$, 111-90-0; $\mathrm{CH_3(CH_2)_5SCN}$, 6803-40-3; $\mathrm{CH_3(CH_2)_5Br}$, 111-25-1; $\mathrm{Na^+SCN^-}$, 540-72-7; $\mathrm{PhO(CH_2)_7CH_3}$, 1818-07-1; $\mathrm{CH_3(CH_2)_7Cl}$, 111-85-3; $\mathrm{PhO^-Na^+}$, 139-02-6; $\mathrm{PhO(CH_2)_5CH_3}$, 1132-66-7; PhOH, 108-95-2; *o*-$\mathrm{HOC_6H_4OCH_2C(CH_3){=}CH_2}$, 4790-71-0; *p*-$\mathrm{HOC_6H_4O^-Na^+}$, 30008-10-7; $\mathrm{CH_2{=}C(CH_3)CH_2Cl}$, 563-47-3; *p*-$\mathrm{O_2NC_6H_4OPh}$, 620-88-2; *p*-$\mathrm{O_2NC_6H_4Cl}$, 100-00-5; *p*-$\mathrm{O_2NC_6H_4O}$-*p*-$\mathrm{C_6H_4NH_2}$, 6149-33-3; *o*-$\mathrm{ClC_6H_4F}$, 348-51-6; *p*-$\mathrm{H_2NC_6H_4O^-Na^+}$, 15267-98-8; *p*-$\mathrm{MeSC_6H_4NO_2}$, 701-57-5; $\mathrm{MeS^-Na^+}$, 5188-07-8; *p*-$\mathrm{PhOC_6H_4CN}$, 3096-81-9; *p*-$\mathrm{ClC_6H_4CN}$, 623-03-0; $\mathrm{PhO^-K^+}$, 100-67-4; *m*-$\mathrm{FC_6H_4O}$-*m*-$\mathrm{C_6H_4Me}$, 65295-57-0; *m*-$\mathrm{ClC_6H_4Me}$, 108-41-8; *m*-$\mathrm{FC_6H_4O^-Na^+}$, 35535-79-6; *m*-$\mathrm{PhOC_6H_4CN}$, 50789-45-2; *m*-$\mathrm{ClC_6H_4CN}$, 766-84-7; *m*-$\mathrm{MeC_6H_4O}$-*p*-$\mathrm{C_6H_4CF_3}$, 71558-32-2; *m*-$\mathrm{MeC_6H_4O^-Na^+}$, 3019-89-4; *p*-$\mathrm{ClC_6H_4CF_3}$, 98-56-6; *m*-$\mathrm{O_2NC_6H_4OPh}$, 620-55-3; *m*-$\mathrm{ClC_6H_4NO_2}$, 121-73-3; *o*-$\mathrm{FC_6H_4O}$-*m*-$\mathrm{C_6H_4Me}$, 78850-78-9; 3-nitro-4-phenoxy-α,α,α-trifluorotoluene, 1960-59-4; 3-nitro-4-chloro-α,α,α-trifluorotoluene, 121-17-5; 2,6-dichloroanisole, 1984-65-2; 2,3-dichloroanisole, 1984-59-4; 2,6-dichlorophenol, 87-65-0; 1,2,3-trichlorobenzene, 87-61-6.