Anal. Calcd for $C_8H_{11}NOCl_3I$: C, 19.32; H, 2.23; N, 2.82. Found: C, 19.3; H, 2.2; N, 2.9.

***threo*-3-Amino-4-iodohexan-1-ol Hydrochloride (9).** A solution of oxazine **8** (4.0 g; 8 mmol) in methanol (35 mL) containing 2 N HCl (3 mL) was stirred for 11 h at room temperature. After removal of the solvent, the residue was taken up in dry ether, to give after filtration the hydrochloride **9** (2.8 g; 87% yield) as a low-melting solid: IR (Nujol) 3260 cm^{-1}; ^1H NMR (CD_3OD) δ 1.00 (t, 3 H), 1.30–1.80 (m, 4 H), 3.50 (m, 1 H), 3.80 (t, 2 H), 4.90 (br s, 4 H, OH, NH_3^+).

3-Benzamido-1-(benzyloxy)hexane (6). To a solution of hydrochloride **9** (2.0 g; 5 mmol) and azobisisobutyronitrile (0.8 g; 5 mmol) in benzene (15 mL) and methanol (3 mL) was added dropwise tri-*n*-butyltin hydride (2.9 g; 10 mmol), and the mixture was refluxed for 5 h. The solvents were removed under vacuum, and the residue was chromatographed on silica gel column (ethyl acetate) and directly benzoylated with benzoyl chloride (1.5 mL) and pyridine (1.5 mL) in CH_2Cl_2 (15 mL) to give **6** in 70% yield (1.1 g).

Acknowledgment. We thank M.P.I., Rome, for a grant.

Registry No. **1a**, 59874-81-6; **1b**, 104808-41-5; **1c**, 104808-42-6; **1d**, 104808-43-7; **1e**, 104808-44-8; **1f**, 104808-45-9; **1g**, 104808-46-0; **1h**, 51479-70-0; **1i**, 104808-47-1; **1j**, 104808-48-2; **1k**, 59874-82-7; **1l**, 104808-49-3; **1m**, 104808-50-6; **1n**, 97186-53-3; **1o**, 104808-51-7; **1p**, 104808-52-8; **1q**, 104808-53-9; **2a**, 104808-54-0; **2b**, 104808-55-1; **2c**, 104808-77-7; **2e**, 104808-58-4; **2f**, 104808-59-5; **2h**, 104808-61-9; **2i**, 104808-62-0; **2o**, 104808-67-5; **2p**, 104808-69-7; **2q**, 104808-70-0; *cis*-**3d**, 104808-56-2; *trans*-**3d**, 104808-57-3; **3g**, 104808-60-8; **3j**, 104808-63-1; **3k** (isomer 1), 104808-64-2; **3k** (isomer 2), 104808-78-8; **3l**, 104808-65-3; **3m**, 104808-66-4; **3n**, 104834-04-0; **3o**, 104808-68-6; **3p**, 104872-73-3; **3q**, 104808-71-1; **4**, 104808-72-2; **5**, 104808-73-3; **6**, 104808-74-4; **7**, 104808-75-5; **8**, 84820-38-2; **9**, 104808-76-6; (*E*)-$HOCH_2CH{=}CHPh$, 4407-36-7; (*E*,*E*)-$HOCH_2CH{=}CHCH{=}CHCH_3$, 17102-64-6; $HOCH_2CH{=}C(CH_3)_2$, 556-82-1; (*E*)-$HOCH_2CH{=}CHCH_2CH_3$, 1576-96-1; (*Z*)-$HOCH_2CH{=}CHCH_2CH_3$, 1576-95-0; (*E*)-$HOCH_2CH{=}CH(CH_2)_2CH_3$, 928-95-0; (*Z*)-$HOCH_2CH{=}CHCH_2OCH_3$, 30339-05-0; (*Z*)-$HOCH_2CH{=}CHCH_2OTHP$, 57323-06-5; (*E*)-$HOCH_2CH{=}CHCH_2OCH_3$, 22427-04-9; (*E*)-$HOCH_2CH{=}CHCH_2OTHP$, 77741-47-0; (*E*)-$HOCH_2CH{=}CHCH_2OCH_2Ph$, 69152-88-1; 3-(*Z*)-hexen-1-ol, 928-96-1; trichloroacetonitrile, 545-06-2.

Polymer-Supported Cryptands. Problems Arising in the Synthesis of Highly Loaded Polymers

Pier Lucio Anelli, Fernando Montanari, and Silvio Quici*

Centro CNR and Dipartimento di Chimica Organica e Industriale dell'Università, 20133 Milano, Italy

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The attachment of a hydroxymethyl[2.2.2]cryptand to lightly loaded chloromethylpolystyrene (≤1 mequiv of Cl/g) cross-linked with divinylbenzene leads to polymer-supported cryptands that are highly efficient catalysts in anion-promoted reactions carried out under phase-transfer conditions. However, the condensation with polystyrenes having a higher content of chloromethyl groups occurs in low yields, apparently affording immobilized cryptands with very low catalytic activity. This behavior results from extensive structural modifications of the bicyclic ligand, most likely promoted by neighboring chloromethyl groups.

In addition to the well-known quaternary onium salts, lipophilic macrocyclic and macrobicyclic polyethers have been largely used as anion activators under phase-transfer conditions.[1] Their immobilization in insoluble polymer supports allows a very easy recovery and recycling of the catalyst.[2] This is especially important in the case of the expensive cryptands, which show very high catalytic efficiency and chemical stability for almost any kind of reaction carried out under aqueous organic two-phase conditions.[1b]

Factors affecting catalytic activity of polymer-supported quaternary onium salts[3] and crown ethers[4] have been thoroughly investigated and the extension of this study to polymeric cryptands appears important. In this context one of the main factors is the percent of ring substitution (prs). In this line it was necessary to synthesize a homogeneous series of immobilized cryptands in a wide range of loading. Cryptands with a low prs had been previously prepared by us;[5] however, unlike the quaternary salts and crown ethers, the synthesis of highly loaded catalysts by the attachment of a functionalized cryptand to chloromethylated polystyrenes turned out to be impossible. Many unexpected difficulties were met with, and they will be described in the present paper.

Results and Discussion

The polymeric catalysts here examined have structures 1 and 2.

Hydroxymethyl[2.2.2]cryptand **13** was condensed with commercial chloromethylated polystyrenes **3a–d**, 1% cross-linked with divinylbenzene, with 0.67, 1.04, 2.63, and 5.0 mequiv of Cl/g, respectively, to afford catalysts **1a–d**. Reactions were carried out in the presence of *t*-BuOK in boiling tetrahydrofuran (THF). Catalysts **1a** and **1b** were obtained in 39% and 53% yields (2.8 and 6.0 prs), respectively, but in the case of **1c** and **1d**, the yields of binding were much lower (8% and 9%, 2.6 and 5.9 prs, respectively).

Catalysts **1a** and **1b** were highly efficient, as was proved in nucleophilic aliphatic substitutions (Tables II and III, see also below), and the catalytic activities of **1c**,**d**, however, were very low (Table II). Binding yields, starting from **3c**,**d**, could be improved (up to 29%, catalysts **1e–g**) by

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(1) (a) Dehmlow, E. V.; Dehmlow, S. S. *Phase Transfer Catalysis*, 2nd ed.; Verlag Chemie: Weinheim, West Germany, 1983. (b) Montanari, F.; Landini, D.; Rolla, F. *Top. Curr. Chem.* **1982**, *101*, 147–200 and references therein.

(2) (a) Ford, W. T. *CHEMTECH* **1984**, 436–439. (b) Ford, W. T.; Tomoi, M. *Adv. Polym. Sci.* **1984**, *55*, 49–104.

(3) (a) Molinari, H.; Montanari, F.; Quici, S.; Tundo, P. *J. Am. Chem. Soc.* **1979**, *101*, 3920–3927. (b) Tomoi, M.; Ford, W. T. *J. Am. Chem. Soc.* **1981**, *103*, 3821–3832. (c) Anelli, P. L.; Montanari, F.; Quici, S. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1827–1830.

(4) (a) Anelli, P. L.; Czech, B.; Montanari, F.; Quici, S. *J. Am. Chem. Soc.* **1984**, *106*, 861–869. (b) Tomoi, M.; Yanai, N.; Shiiki, S.; Kakiuchi, H. *J. Polym. Sci.* **1984**, *22*, 911–926.

(5) (a) Montanari, F.; Tundo, P. *Tetrahedron Lett.* **1979**, 5055–5058. (b) Montanari, F.; Tundo, P. *J. Org. Chem.* **1981**, *46*, 2125–2130; (c) *Ibid.* **1982**, *47*, 1298–1302.

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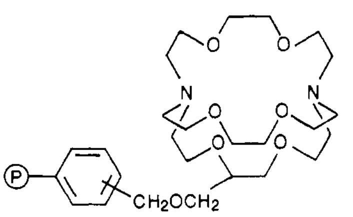
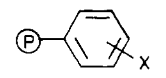
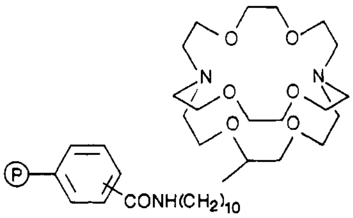


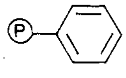
1



3, X = CH2Cl
4, X = COOH



2



microporous polystyrene, 1% cross-linked with divinylbenzene

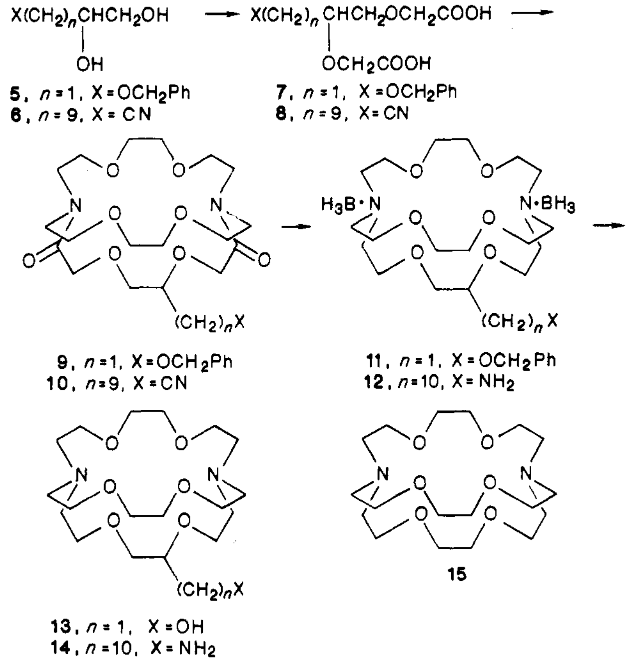
using different bases and solvents (Table I), but catalytic activities were only slightly increased, remaining noticeably lower then those of **1a,b** (Table II). As for **1a,b**, nitrogen and oxygen elemental analyses of **1c–g** are mutually consistent, indicating the apparent presence of cryptand units in the polymeric materials. Furthermore, infrared spectra are very similar for all catalysts **1a–g** in the ν_{C-O} region (1000–1200 cm^{-1}). The low catalytic activities should mean that for **1c–g** extensive structural modifications of the bicyclic ligand occurred. What is more likely is that the already linked cryptands undergo quaternization at bridgehead nitrogens by still unreacted neighboring chloromethyl groups. Hofmann degradation of the quaternized cryptand can, in principle, also occur, thus leading to the opening of the bicyclic structure.

In order to get further information, [2.2.2]cryptand **15** was refluxed with chloromethylpolystyrenes **3a–d** in THF in the presence of *t*-BuOK (i.e., under the reaction conditions leading to catalysts **1a–d**).

Polymers **1h–m** were thus obtained. Nitrogen and oxygen elemental analyses (Table IV) indicated that the cryptand residues were bonded to the polymer matrices, their amounts increasing with the CH_2Cl loading. Furthermore, IR spectra of polymers **1h–m** show strong ν_{C-O} absorptions at 1000–1200 cm^{-1} and disappearance of ν_{C-Cl} absorption at 1265 cm^{-1}. Catalytic activities of polymers **1h–m** (Table II) are noticeably lower than those of catalysts **1a,b** and of the same order of magnitude as those of **1f,g** (Table II). This seems to indicate that in the preparation of **1c–g** and **1h–m** similar processes occurred, i.e., quaternization of bridgehead nitrogens and possible, subsequent ring opening. The presence of small amounts of nitrogen even in polymers **1h,i** derived from chloromethylated polystyrenes **3a,b** with low chlorine content suggests that this side reaction can be concomitant with the binding of hydroxymethyl[2.2.2]cryptand **13** through the Williamson reaction: this side reaction is most likely negligible for polystyrenes **3a,b**, as shown by the very high efficiency of catalysts **1a,b**, whereas it seems to be prevalent for polystyrenes **3c,d** with higher contents of chloromethyl groups.

We also tried preparing a series of differently loaded polymer-supported cryptands following an alternative synthetic route. Catalysts **2a** (5.1 prs) and **2b** (20.7 prs) were obtained from carboxylated polystyrenes **4a** and **4b** (11.9 and 29.7 prs, respectively) and ω-aminodecyl[2.2.2]cryptand **14**. Carboxylated polymers **4a** and **4b** were prepared from polystyrene or from bromopolystyrene, 1% cross-linked with divinylbenzene, by lithiation and subsequent quenching with anhydrous CO_2, as described by Fréchet.[6] In this case the loadings were limited by the carboxylation reaction,[7] and 20.7 prs was the highest functionalization of polymer-supported cryptand **2** which could be realized.[8]

Scheme I



Hydroxymethyl[2.2.2]cryptand **13** and ω-aminodecyl[2.2.2]cryptand **14** were synthesized from *O*-monobenzylglycerol (**5**) and from 11-cyano-1,2-undecanediol (**6**), respectively, following a synthetic route similar to others previously described (Scheme I).[5]

The catalytic activity of polymer-supported cryptands **1** and **2** was evaluated in nucleophilic substitutions by I$^-$ on *n*-octyl bromide (eq 1) and by I$^-$, Br$^-$, and Cl$^-$ on *n*-octyl methanesulfonate (eq 2–4). The reactions were carried

$$n\text{-}C_8H_{17}Br + I^- \rightarrow n\text{-}C_8H_{17}I + Br^- \qquad (1)$$

$$n\text{-}C_8H_{17}OMes + Y^- \rightarrow n\text{-}C_8H_{17}Y + MesO^- \qquad (2\text{–}4)$$

$$Y = I \text{ (eq 2)};\ Y = Br \text{ (eq 3)};\ Y = Cl \text{ (eq 4)}$$

out in toluene–H_2O at 60 °C in the presence of 0.05 molar equiv of catalyst, with the stirring speed maintained at 1300 rpm in order to minimize the influence of diffusion. Under these conditions they followed a pseudo-first-order kinetic (eq 5). The observed rate constants are reported

$$\text{rate} = k_{\text{obsd}}[\text{substrate}] \qquad (5)$$

in Table III, together with those obtained, under the same conditions, with polymer-supported crown ethers **16** and **17** and phosphonium salts **18** and **19**.

These results call for a few comments. Where a comparison among polymer-supported cryptands, crown ethers, and quaternary onium salts with similar features (prs,

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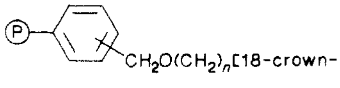
[6] Farral, M. J.; Fréchet, J. M. J. *J. Org. Chem.* **1976**, *41*, 3877–3882.

[7] We have not been able to exceed 2.54 mequiv of CO_2H/g (29.7 prs). Fréchet has reported the preparation of a polystyrene with a slightly higher functionalization (2.9 mequiv of CO_2H/g).[6]

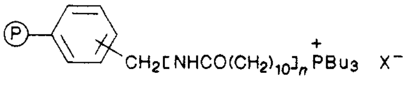
[8] Polymer-supported cryptands having a high loading degree have been prepared by Manecke by copolymerization of styrene with vinyl-substituted cryptands.[9] However, in this case it was assumed that only cryptand units near the surface of polymer beads were easily accessible.[10]

[9] Manecke, G.; Reuter, P. *Makromol. Chem.* **1981**, *182*, 1973–1984.

[10] Manecke, G.; Reuter, P. *J. Mol. Catal.* **1981**, *13*, 355–365.



16, $n = 1$
17, $n = 9$



18, $n = 0$
19, $n = 1$

spacer chain, cross-linking, etc.) is possible, cryptands are shown to be the most efficient catalysts, as previously emphasized.[11] This behavior is similar to that found for the correspondent lipophylic phase-transfer catalysts under two-phase conditions.[1b,12,13] Comparison is particularly interesting in the case of crown ethers, whose reactivity is often high for large and polarizable anions like I^- but becomes much lower for harder anions like Br^- and Cl^-. This behavior is connected with the dramatic diminution of complexation constants occurring with crown ethers, but to a much lesser extent with cryptands.[1b,4a]

Reactivities of catalysts **1** and **2** noticeably decrease for almost all reactions[14] by increasing prs (**1a** and **2a** vs. **1b** and **2b**, respectively). Such a decrease compares with that found in polymer-supported quaternary onium salts[3b,c] and is related to a higher polarity at the catalytic site for higher prs. A similar phenomenon occurs in polymer-supported crown ethers, although it can be partially masked by the concomitant increase of complexation constants.[4a]

Insertion of a spacer chain between the catalytic site and the polymer backbone is always accompanied by higher catalytic activities.[5] Unexpectedly, spaced cryptands **2a,b** are less reactive than directly bonded cryptands **1a,b**. Our feeling is that this behavior derives from the concomitance of several factors: the presence of unreacted carboxylic groups,[15] the different linkage between the polymer backbone and the cryptand unit, the eventual increase of cross-linking, etc.

In conclusion, the preparation of recyclable and highly reactive polymer-supported phase-transfer catalysts, binding cryptand units to functionalized polystyrene matrices, is only possible for lightly loaded polymers. This is particularly disappointing taking into account that wide ranges of loading are possible for the less stable quaternary salts[3c] and the less efficient crown ethers.[4a]

Experimental Section

^1H NMR spectra were recorded at 90 MHz on a Varian EM-390 spectrometer with Me_4Si as an internal standard. Infrared spectra were obtained with a Perkin-Elmer 377 spectrometer. GLC analyses were performed on a Hewlett-Packard Model 5840 flame ionization instrument (2 ft × 0.125 in. UCW 982-10% on Chromosorb W column). Satisfactory combustion analyses were obtained (C, ±0.40; H, ±0.20; N, ±0.40) for all new compounds. Oxygen and nitrogen elemental analyses of polymer samples were performed by Mikroanalytisches Labor Pascher, Bonn, West Germany.

Organic and inorganic reagents, ACS grade, were used without further purification. The styrene–divinylbenzene copolymer used was Bio-Beads S-X1, purchased from Bio-Rad Laboratories, Richmond, CA. Chloromethylated polystyrenes, 200–400 mesh, cross-linked with 1% divinylbenzene with 0.67, 1.04, 2.63, and 5.0 mequiv of Cl/g were purchased from Fluka AG, Buchs, Switzerland. 3-(Benzyloxy)-1,2-propanediol,[17] 11-cyanoundecane-1,2-diol,[18] and *n*-octyl methanesulfonate[19] were prepared following standard procedures.

4-[(Benzyloxy)methyl]-3,6-dioxaoctane-1,8-dicarboxylic Acid (7). Potassium (20 g, 0.5 mol) was added to a solution of 18.2 g (0.1 mol) of 3-(benzyloxy)propane-1,2-diol (**5**) in 500 mL of *t*-BuOH in an argon atmosphere. The mixture was stirred until complete disappearance of the metal and then heated to reflux. A solution of 22.7 g (0.24 mol) of chloroacetic acid in 100 mL of *t*-BuOH was added in 30 min; stirring and reflux were maintained for 15 h. The solvent was evaporated under vacuum and the residue acidified with aqueous 6 N H_2SO_4, extracted with ethyl acetate (3 × 50 mL), and dried with Na_2SO_4. Evaporation of the solvent afforded 34.0 g of crude product, which was dissolved in 200 mL of absolute EtOH and reacted with 15.8 g (0.24 mol) of 85% KOH dissolved in 150 mL of EtOH. The resulting white precipitate was filtered in an argon atmosphere and washed with EtOH (2 × 20 mL), then dissolved in water (100 mL), and acidified with aqueous 6 N H_2SO_4. Extraction with ethyl ether (4 × 100 mL) and evaporation afforded 20 g (67%) of **7** as a thick oil: ^1H NMR ($CDCl_3$) δ 3.30–3.80 (m, 5 H), 4.10 (s, 2 H), 4.30 (s, 2 H), 4.55 (s, 2 H), 7.30 (m, 5 H), 11.0 (br s, 2 H).

4-(9-Cyanononyl)-3,6-dioxaoctane-1,8-dicarboxylic Acid (8). Potassium (10.0 g, 0.25 mol) was added to a solution of 10.65 g (0.05 mol) of 11-cyanoundecane-1,2-diol (**6**) in 200 mL of *t*-BuOH in an argon atmosphere. The mixture was stirred until complete disappearance of the metal and then heated to reflux. A solution of 12.28 g (0.13 mol) of chloroacetic acid in 50 mL of *t*-BuOH was added in 30 min; stirring and reflux were maintained for 15 h. The solvent was evaporated under vacuum, and the residue was acidified with aqueous 6 N H_2SO_4 and extracted with ethyl acetate (3 × 80 mL). The organic phase was washed with water (50 mL) and with brine (50 mL) and then dried over $MgSO_4$. After evaporation of the solvent, the oily residue (19.6 g) was dissolved in 200 mL of absolute ethanol/benzene (1:1) containing 0.3 g of *p*-toluenesulfonic acid and refluxed for 15 h with continuous circulation of condensed vapors through anhydrous Na_2SO_4. Evaporation of the solvent and purification by column chromatography (silica gel; ethyl ether) afforded 9.25 g (48%) of the diethyl ester of **8** as a colorless oil: IR (film) 2240, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20–1.90 (m, 22 H), 2.35 (t, 2 H), 3.45–3.70 (m, 3 H), 4.10–4.40 (m, 8 H).

A solution of 3.5 g (0.053 mol) of 85% KOH in 3 mL of water was added to the obtained diethyl ester dissolved in 100 mL of CH_3OH. The mixture was stirred at room temperature for 24 h, and the solvent was evaporated. The residue was acidified with aqueous 3 N HCl, extracted with CH_2Cl_2, dried over $MgSO_4$, and evaporated, affording **8** as an oil in quantitative yield: ^1H NMR ($CDCl_3$) δ 1.20–1.90 (m, 16 H), 2.35 (t, 2 H), 3.40–3.90 (m, 3 H), 4.00–4.40 (m, 4 H), 10.65 (br s, 2 H, D_2O exchange).

5-[(Benzyloxy)methyl]-2,9-dioxo-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (9). A solution of 6.11 g (20.5 mmol) of **7** and 7.8 g (61.5 mmol) of oxalyl chloride in 50 mL of anhydrous benzene was stirred overnight at room temperature. After evaporation of the solvent, the remaining oxalyl chloride was removed by addition and evaporation of benzene (3 × 30 mL). The oily product, in quantitative yield [IR (film) 1800 cm^{-1}, absence of the CO band of the acid], was used without further purification. A solution of the bis acid chloride in 500 mL of anhydrous benzene and a solution of 5.24 g (20 mmol) of 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane and 4.44 g (44 mmol)

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[11] Cinquini, M.; Colonna, S.; Molinari, H.; Montanari, F.; Tundo, P. *J. Chem. Soc., Chem. Commun.* **1976**, 394–396.

[12] Landini, D.; Maia, A.; Montanari, F.; Tundo, P. *J. Am. Chem. Soc.* **1979**, *101*, 2526–2530.

[13] Nucleophilic aliphatic substitutions by I^- are faster when, instead of octyl methanesulfonate, octyl bromide is the substrate. A similar behavior has already been found[3c] for reactions catalyzed by polymer-supported quaternary salts.

[14] Exceptions are the identical reactivities of catalysts **1a** and **1b** in Br–I exchange reactions, although reactivities are different for all the other reactions tested. We do not have any explanation for that.

[15] Amidation leading to catalysts **2** occurs in 43–70% yield (see Table I). Fair yields and the formation of free carboxyl groups have also been observed in amidations and esterifications of carboxylated polystyrenes.[16]

[16] (a) Letsinger, R. L.; Kornet, M. J.; Mahadevan, V.; Jerina, D. M. *J. Am. Chem. Soc.* **1964**, *86*, 5163–5165. (b) Letsinger, R. L.; Mahadevan, V. *J. Am. Chem. Soc.* **1966**, *88*, 5319–5324.

[17] Czech, B. *Tetrahedron Lett.* **1980**, 4197–4198.

[18] Anelli, P. L.; Montanari, F.; Pollak, V.; Quici, S. *Gazz. Chim. Ital.* **1986**, *116*, 127–131.

[19] Williams, M. R.; Mosher, H. S. *J. Am. Chem. Soc.* **1954**, *76*, 2984–2987.

Table I. Catalysts 1a–g and 2a–b: Analytical Data

cat.	starting polymer[a]	base	solvent	elem anal.[b] % N	% O	mequiv of[c] [2.2.2]/g	% ring[c] subst	% yield of binding
1a	**3a** (7.2)	*t*-BuOK	THF	0.62	2.91	0.24	2.8	39
1b	**3b** (11.4)	*t*-BuOK	THF	1.25	5.32	0.46	6.0	53
1c	**3c** (31.3)	*t*-BuOK	THF	0.53	2.35	0.20	2.6	8
1d	**3d** (68.2)	*t*-BuOK	THF	0.95	4.48	0.37	5.9	9
1e	**3c** (31.3)	*t*-BuOK	DMF	1.40	6.05	0.52	7.5	24
1f	**3c** (31.3)	BuLi	THF	0.97	3.98	0.35	4.7	15
1g	**3c** (31.3)	*t*-BuOK[d]	THF	1.57	7.17	0.60	9.1	29
2a	**4a** (11.9)			1.60	4.67	0.38[e]	5.1[e]	43
2b	**4b** (29.7)			3.90	11.00	0.93[e]	20.7[e]	70

[a] prs in parentheses. [b] Average of two values. [c] Average of the hypothetical values calculated from oxygen and nitrogen elemental analysis. [d] Three molar equivalents of *t*-BuOK. [e] Calculated from nitrogen elemental analysis.

Table II. Activities of Catalysts 1[a]

cat.	$10^6 k_{obsd}$, s^{-1} X = Br, Y = I	X = OMes, Y = Br
1a	225	66.6
1b	225	36.1
1c	3.5	
1d	2.7	
1e	3.1	
1f	12.8	
1g	33.3	4.5
1h[b]		
1i	47.7	4.0
1l	64.2	5.2
1m	37.1	2.4

[a] In toluene–H_2O at 60 °C, for reactions $n\text{-}C_8H_{17}X + Y^- \rightarrow n\text{-}C_8H_{17}Y + X^-$ (eq 1 and 3). [b] Not tested, due to the very low functionalization.

Table III. Catalytic Activity of Polymer-Supported Cryptands. Comparison with Polymer-Supported Crown Ethers and Phosphonium Salts[a]

cat.	% ring subst	$10^6 k_{obsd}$, s^{-1} X = Br, Y = I	X = OMes, Y = I	X = OMes, Y = Br	X = OMes, Y = Cl
1a	2.8	225	123	66.6	11.4
1b	6.0	225	72.2	36.1	3.7
16[b]	6.8	34.6	47.8	1.6	*d*
18[c]	6.1	38.0	22.7	23.9	16.6
2a	5.1	183	58.1	20.0	
2b	20.7	109	30.7	8.8	
17[b]	7.6	55.0	85.5	3.5	
19a[c]	8.7	67.5	33.8	22.8	
19b[c]	25.4	31.6	16.1	10.8	

[a] In toluene–H_2O at 60 °C, for reactions $n\text{-}C_8H_{17}X + Y^- \rightarrow n\text{-}C_8H_{17}Y + X^-$ (eq 1–4). [b] Taken in part from ref 4a. [c] Taken in part from ref 3c. [d] Too small to be evaluated.

Table IV. Catalysts 1h–m: Analytical Data

cat.	starting polymer[a]	elem anal.[b] N %	O %	mequiv of bonded[c] [2.2.2]/g
1h	3a (7.2)	≤0.3[d]	1.35	
1i	3b (11.4)	0.48	2.21	0.2
1l	3c (31.3)	1.65	7.20	0.62
1m	3d (68.2)	1.93	7.20	0.72

[a] prs in parentheses. [b] Average of two values. [c] Average of the apparent values calculated from oxygen and nitrogen analysis. [d] The detection limit of the analytical method is 0.3%.

of triethylamine in 500 mL of anhydrous benzene were simultaneously dripped (8 h) into 1200 mL of the same solvent under vigorous stirring. After filtration of triethylamine hydrochloride and evaporation of the solvent, the crude reaction mixture was purified by column chromatography on silica gel eluting with EtOAc–CH_3OH to give 6.15 g (58%) of **9** as a viscous oil: IR (film) 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.30–4.30 (m, 33 H), 4.50 (s, 2 H), 7.30 (m, 5 H).

5-(9-Cyanononyl)-2,9-dioxo-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (10). Starting from **8**, **10** was obtained as a viscous oil in 47% yield following the procedure described for **9**: IR (film) 2240, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10–1.90 (m, 16 H), 2.35 (t, 2 H), 2.50–4.70 (m, 31 H).

5-[(Benzyloxy)methyl]-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane 1,10-Bisborane Derivative (11). A sample of 5.85 mL (58.5 mmol) of a 10 M solution of borane–dimethyl sulfide in hexane was diluted with 30 mL of anhydrous THF and then added to a solution of 6.15 g (11.7 mmol) of **9** in 120 mL of THF. The mixture was stirred and refluxed for 48 h. The excess of borane was destroyed with methanol and the solvent evaporated to dryness in vacuum. The residue was taken up with 100 mL of methylene chloride, after filtration of the insoluble part the solvent was removed, and the crude material was purified by column chromatography (silica gel; EtOAc–$CHCl_3$) to give 4.30 g (70%) of **11** as a waxy solid: IR (Nujol) 2360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.80–4.20 (m, 43 H), 4.50 (s, 2 H), 7.30 (m, 5 H).

5-(10-Aminodecyl)-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane 1,10-Bisborane Derivative (12). Starting from **10**, **12** was obtained as a waxy solid in 40% yield following the procedure described for **11**. In this case the cyano function is also reduced: IR (Nujol) 2340 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00–1.90 (m, 20 H), 2.60–4.10 (m, 43 H).

5-(Hydroxymethyl)-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (13). A sample of 3.66 g (7 mmol) of **11** and 40 mL of 6 N HCl were refluxed for 3 h. After evaporation in vacuo of the solvent, the residue was taken up with water (20 mL), and the pH was adjusted to 12 with lithium hydroxide. The aqueous mixture was extracted with $CHCl_3$ (3 × 100 mL) and the organic phase dried over molecular sieves (4 Å) and evaporated to afford 2.62 g (92%) of pure **13** as a viscous oil: ^1H NMR ($CDCl_3$) δ 2.30–3.00 (m, 13 H), 3.40–4.00 (m, 25 H).

5-(10-Aminodecyl)-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (14). **14** was obtained from **12** as a viscous oil in quantitative yield following the procedure described for **13**: ^1H NMR ($CDCl_3$) δ 1.00–1.80 (m, 20 H), 2.35–2.95 (m, 14 H), 3.30–3.80 (m, 23 H).

Polymer-Supported Cryptands 1a–g. Hydroxymethyl-[2.2.2]cryptand **13** was linked to commercially available 1% cross-linked chloromethylated polystyrenes **3a–d** by refluxing the amount of polymer corresponding to 1.0 mmol of Cl with 1.2 mmol of **13** in anhydrous THF (50 mL for 1 g of polymer) and 1.5 mmol of *t*-BuOK for 4 days. The polymer was filtered, washed with water, methanol, ethyl ether, methylene chloride, ethyl ether, methanol, methylene chloride, and ethyl ether, and dried for 3 h (65 °C, 2 torr), affording catalysts **1a–d**.

Catalyst **1e** was obtained from **3c** as reported above by using DMF as solvent at 65 °C.

Catalyst **1f** was obtained from **3c** as reported above by using BuLi as base.

Catalyst **1g** was obtained from **3c** as reported above by using 3.0 mmol of *t*-BuOK.

The amount of cryptand bonded to the polymer was estimated by oxygen and nitrogen elemental analysis (Table I).

Catalysts 1h–m. A sample of 1% cross-linked chloromethylated polystyrenes **3a–d** corresponding to 1.0 mmol of Cl, 1.2 mmol of [2.2.2]cryptand **15**, and 1.5 mmol of *t*-BuOK were refluxed in THF (50 mL for 1 g of polymer) for 4 days. The resulting polymer was filtered, washed, and dried as described for **1a–g**. The content of bonded cryptand units was evaluated by oxygen and nitrogen elemental analysis (Table IV).

Polymer-Supported Cryptands 2a–b. A sample of carboxylated polystyrene corresponding to 1 mmol of COOH group in 15 mL of thionyl chloride was stirred and refluxed for 3 h. The polymer was filtered in an argon atmosphere and washed with anhydrous toluene and ethyl ether. The conversion of the carboxylic acid into the corresponding chlorocarbonyl function was found quantitative by IR (KBr pellets). This polymer was added to a solution of 1.2 mequiv of **12** and 1.5 mequiv of anhydrous triethylamine in 15 mL of $CHCl_3$. The mixture was stirred and refluxed for 15 h. After filtration the polymer was washed with methanol, water, methanol, methylene chloride, and twice with ethyl ether and dried for 3 h (65 °C, 2 torr). The amount of bonded cryptand was estimated by nitrogen elemental analysis (Table I).

Kinetic Measurements. Kinetics were run in a 50-mL flask equipped with a Teflon-lined screw cap and magnetic stirrer and thermostated at 60 °C with circulating butyl phthalate. The temperature was controlled to within ±0.01 °C by a Exacal 200 Bath Circulator. Stirring speed (1300 ± 50 rpm) was controlled by using a strobe light. The flask was charged with 12.5 mL of a 4 M aqueous solution of potassium salt (KX, X = I, Br, Cl), 3 mL of toluene, tetradecane as internal standard (2 mL of a 0.1 M solution in toluene), and 0.25 mequiv of catalyst. The mixture was left at 60 °C for 12 h at 200 rpm stirring speed in order to condition the catalyst. *n*-Octyl methanesulfonate or *n*-octyl bromide (5 mL of a 1 M solution in toluene) was added at zero time and the mixture stirred at 1300 rpm. The reactions were followed by GLC analysis. The pseudo-first-order rate constants (k_{obsd}) were obtained by plotting ln [substrate] vs. time and determining the slope of the straight lines.

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Registry No. **5**, 4799-67-1; **6**, 104911-02-6; **7**, 80525-59-3; **8**, 104911-03-7; **8** diethyl ester, 104911-07-1; **9**, 104911-04-8; **10**, 104911-05-9; **11**, 104911-08-2; **12**, 104911-09-3; **13**, 74339-03-0; **14**, 104911-06-0; **15**, 23978-09-8; *n*-$C_8H_{17}Br$, 111-83-1; I^-, 20461-54-5; *n*-$C_8H_{17}OMe_5$, 16156-52-8; Br^-, 24959-67-9; Cl^-, 16887-00-6; chloroacetic acid, 79-11-8; oxalyl chloride, 79-37-8; 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane, 23978-55-4.

2-(4-Pyridyl)ethyl as a Protective Group for Sulfur Functionality

Alan R. Katritzky,* Ichiro Takahashi, and Charles M. Marson

Department of Chemistry, University of Florida, Gainesville, Florida 32611

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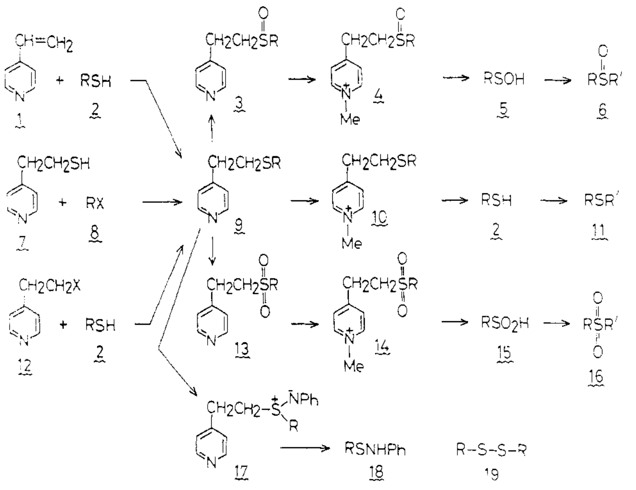
2-(4-Pyridyl)ethyl sulfides have been prepared from a variety of alkyl and aryl thiols and from alkyl and acyl halides. These sulfides and their corresponding sulfoxides and sulfones were each depyridylethylated by quaternization and subsequent treatment with mild base to give respectively the thiols, sulfenic acids, sulfinic acids, and sulfenamides. During one of these protection–deprotection sequences, methyl 1-octyl sulfoxide was readily converted by aerial oxidation into the corresponding sulfone.

Other publications[1,2] from this laboratory have reported the use of 2-(4-pyridyl)ethyl as a protective group, which is easily removed by quaternizing agents such as methyl iodide. In particular, we have shown that carboxylic acids[1] and heterocyclic NH groups[2] can be protected in this way. Other workers have utilized 2-(4-pyridyl)ethyl as a constituent of the group $PyCH_2CH_2OCO$–, used in the protection of amino functionality.[3,4] The technique of pyridylethylation has also been used to activate the cyano group in 4-cyanopyridine by easily reversible quaternization.[5] This paper records some applications of 2-(4-pyridyl)ethylation in the manipulation of sulfur functionality.

Strategy

Our overall strategy is outlined in Scheme I. Pyridylethyl sulfides **9a–g** and thiol esters **9h,i** were prepared (i) by the pyridylethylation of thiols **2a–d**, (ii) by the alkylation or acylation of 2-(4-pyridyl)ethanethiol (**7**), and (iii) by the alkylation of thiol **2d** using the 2-(4-pyridyl)ethyl alkylating agent **12j**. The 2-(4-pyridyl)ethyl sulfides **9** could be converted by oxidation to sulfoxides **3** and sulfones **13**. Each of these three classes of compounds **3**, **9**, and **13** could then be quaternized to give the corresponding methyl quaternary salts **4**, **10**, and **14**. In practice, these now decomposed either spontaneously or on treatment with mild base to give, respectively, the corresponding sulfenic acid **5**, thiol **2**, or sulfinic acid **15**. These products were usually trapped as the sulfoxide **6**, the

Scheme I



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[1] Katritzky, A. R.; Khan, G. R.; Schwartz, O. A. *Tetrahedron Lett.* **1984**, *25*, 1223.

[2] Katritzky, A. R.; Khan, G. R.; Marson, C. M., in preparation.

[3] Kunz, H.; Barthels, R. Angew. *Chem., Int. Ed. Engl.* **1983**, *22*, 783.

[4] Kunz, H.; Barthels, R. Ger. Offen. DE 3141923, 1983; *Chem. Abstr.* **1983**, *99*, 140398e. Kunz, H.; Birnbach, S. *Tetrahedron Lett.* **1984**, *25*, 3567.

[5] Bailey, T. D.; McGill, C. K. U.S. Patent 4158093, 1979; *Chem. Abstr.* **1979**, *91*, 123636y.

0022-3263/86/1951-4914$01.50/0