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Catalytic activity and anion activation in S_N2 reactions promoted by complexes of silicon polypodands. Comparison with traditional polyethers

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The catalytic activity of silicon polypodands was evaluated in anion-promoted reactions under solid–liquid phase-transfer catalysis (SL-PTC) conditions and compared with that exhibited by common PTC agents. Results showed that these many-armed ligands are particularly efficient catalysts, even comparable with the more sophisticated crown ethers. Kinetics under homogeneous conditions indicated that the anion activation realized by silicon polypodands does not appreciably change with the number of chains and is comparable or slightly lower than that of traditional polyethers. In addition, the sequence of reactivity is determined by the cation ($NH_4^+ < K^+ < Na^+ < Li^+$), thus revealing an involvement of the metal ion in the transition state of the reactions ("metal ion electrophilic catalysis").

Introduction

We found in previous studies that silicon polypodands **1–7** (Scheme 1), a new class of open-chain ligands in which two or more polyether chains are linked to the same binding centre (silicon), are powerful complexing agents of alkali metal salts in low polarity media (*e.g.* chlorobenzene).[1,2] The complex forming ability of these polypodands is noticeably higher than that of the corresponding monopodand, showing a cooperative effect of the pendant arms in the complexation process. Consequently, they were successfully used as catalysts in a number of anion-promoted reactions under solid–liquid phase-transfer catalysis (SL-PTC) conditions including nucleophilic substitutions, reductions and alkylations.[1,2] In all cases the reactions were found to be faster than those catalyzed by the open-chain tris(polyoxaalkyl) amine TRIDENT (**8**) and even the macrocyclic polyether dicyclohexano-18-crown-6 DCH18C6 (**11**).[1,2]

In order to quantitatively evaluate the catalytic activity of this new class of polypodands as well as their ability to function as anion activation agents we conducted a kinetic study of typical nucleophilic substitution reactions under both SL-PTC and homogeneous conditions. The results are compared with those obtained with traditional phase-transfer agents, in particular the open-chain "TRIDENT" **8**, poly(ethylene glycol) ethers (PEGs **9**, **10**), dicyclohexano-18-crown-6 (DCH18C6, **11**) and the amphiphilic cryptand [2.2.2,C_{10}] **12**.

Results

Catalytic activity

The catalytic efficiencies of silicon polypodands **1**, **2**, **4**, **6**, TRIDENT **8** and PEG **10** were evaluated in the nucleophilic substitution reaction shown below as eqn. (1).

$$\underset{\mathbf{13}}{n\text{-}C_8H_{17}OSO_2Me} + NaI_{solid} \xrightarrow[\text{PhCl, }60^\circ\text{C}]{\text{catalyst}} \underset{\mathbf{14}}{n\text{-}C_8H_{17}I} + NaOSO_2Me_{solid} \qquad (1)$$

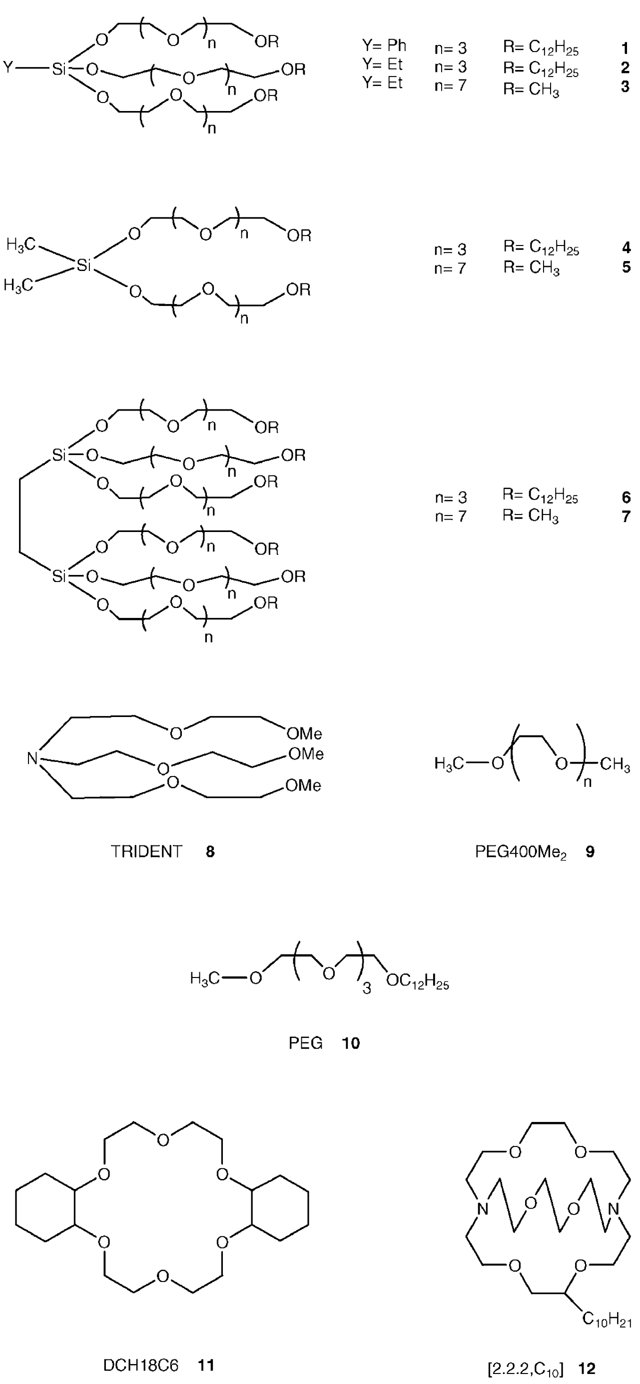
The rate of displacement of the methanesulfonate group in *n*-octyl methanesulfonate (**13**) by iodide was measured at 60 °C in a solid–liquid NaI–chlorobenzene two-phase system, in the presence of the same catalytic amount of ligand (0.1 mol equivalents) and with a 5 : 1 molar ratio of inorganic salt : substrate, by stirring the heterogeneous mixture at 1000 ± 100 rpm. Kinetic determinations were performed (GLC analysis) by following the disappearance of the substrate **13** and/or the appearance of the reaction product **14** with respect to an internal standard (dodecane). In all cases the reactions were found to obey a *pseudo*-first-order kinetic equation [eqn. (2)], up to at least 75% conversion.

$$\text{rate} = k_{obsd}[\text{substrate}] \qquad (2)$$

The observed rate constants (k_{obsd}, s^{-1}, see Table 1 for data) for the silicon polypodands examined, **1**, **2**, **4** and **6**, are found to depend on the ligand, progressively increasing, about fourfold, on going from **4**, through **1** and **2**, to **6**. Such a trend parallels the increasing complexing ability of these polyethers (from 1.2 to 3.5 NaI moles per mole) with the number of chains and binding sites (Scheme 1). As shown in Table 1, the observed catalytic activity is as much as 14-fold higher than that of the corresponding monopodand PEG **10**, confirming once again the "cooperative effect" of the polyether chains in the activation process. Interestingly, catalytic efficiency is comparable with, or even better than, that of TRIDENT **8** and is very close to that of crown ether DCH18C6 **11** in the case of polypodand **6** with six polyether arms (Table 1).

Anion activation and metal ion effect

In order to quantitatively evaluate the anion activation effected by this novel class of polypodands, kinetic measurements were conducted under homogeneous conditions by reacting comparable amounts of substrate **13** [eqn. (3)] or **15** [eqn. (5)] and preformed complex (Ligand^{M^+})I^-.



Scheme 1

Table 1 Extent of complexation[a,b] and catalytic efficiency of silicon polypodands **1**, **2**, **4**, **6** and ligands **8**, **10**, **11** in the reaction shown in eqn. (1)[c]

Catalyst	NaI moles per ligand mole	$10^5\ k_{obsd}$ (s^{-1})	k_{rel}
4	1.2	28.5	3.7
1	1.3	49.5	6.5
2	1.8	60	7.9
6	3.5	104	13.7
8 (TRIDENT)	0.95	46	6
10 (PEG)	0.16	7.6	1
11 (DCH18C6)	1.0	104.5	13.8

[a] Defined as moles of NaI complexed per mole of ligand. [b] Average of at least four titrimetric determinations. The error is estimated to be 5–10%. [c] A chlorobenzene solution (10 ml) of substrate **13** (0.5 M), catalyst (0.05 M), and internal standard (0.25 M) with 25 mmol of NaI.

Table 2 Second-order rate constants k ($M^{-1}\ s^{-1}$) of the nucleophilic substitution of the methanesulfonic group in *n*-octyl methanesulfonate by $(\text{Ligand}^{Na^+})I^-$ complexes in chlorobenzene, at 60 °C[a]

Ligand	$10^3\ k$ ($M^{-1}\ s^{-1}$)[b]	k_{rel}
5	4.42	1
3	4.63	1.04
7	6.72	1.5
8 (TRIDENT)	10.7	2.4
12 ([2.2.2,C_{10}])	14.6	3.3
11 (DCH18C6)	19	4.3
9 (PEG400Me_2)	21	4.7

[a] [Substrate] = 2–4 × 10^{-2} M; $[(\text{Ligand}^{Na^+})I^-]$ = 3–5 × 10^{-2} M. [b] Average of at least two determinations. The error in these values is estimated to be 5%.

Rates were measured by potentiometric titration of the halide (I^-). The reactions, shown in eqns. (3) and (5), were found to follow a second-order kinetic equation [eqn. (4)] to conversions of nearly 75%. Results are reported in Tables 2–4 together with those of ligands **8–12** for sake of comparison.

$$\underset{\mathbf{13}}{n\text{-}C_8H_{17}OSO_2Me} + (\text{Ligand} \supset M^+)I^- \xrightarrow[60°C]{PhCl} n\text{-}C_8H_{17}I + \underset{\mathbf{14}}{(\text{Ligand} \supset M^+)MeSO_3^-} \quad (3)$$

$$M^+ = Li^+,\ Na^+,\ K^+$$

$$\text{rate} = k[\text{substrate}][(\text{Ligand}^{M^+})I^-] \quad (4)$$

The data collected in Table 2 show that, in the series of silicon polypodands **3**, **5** and **7** ($n = 7$, $R = CH_3$, see Scheme 1) the second-order rate constant k ($M^{-1}\ s^{-1}$), determined for the reaction shown in eqn. (3) with NaI, increases, by about 1.5-fold, on changing from the polypodand **5**, which has two polyether chains, to **7**, which has six chains. In addition, the polypodands have a reactivity comparable (TRIDENT **8**) or slightly lower than that of traditional catalysts such as PEG400Me_2 **9**, DCH18C6 **11** and [2.2.2,C10] **12**. Depending on the ligand, it follows the order: PEG400Me_2 ≈ DCH18C6 > [2.2.2,C10] > TRIDENT > **7** > **3** ≈ **5** (Table 2).

Interestingly, the sequence found with the complexes $(\text{Ligand}^{Na^+})I^-$ noticeably changes also with the metal ion M^+ ($M^+ = Li^+, Na^+, K^+$). The ligand being the same, the rate constants k ($M^{-1}\ s^{-1}$) increase, in the order $K^+ < Na^+ < Li^+$. As shown in Table 3, the highest difference of reactivity, $\Delta k = k_{Li^+}/k_{K^+} = 5$, is observed with the polypodand **5**, whereas this difference diminishes on increasing the number of arms ($\Delta k = 2.8$ and 1.9 for **3** and **7**, respectively). A similar trend is obtained with crown ether **11** ($\Delta k = 2.6$) whereas the behaviour is completely different with cryptand **12**. With the latter, in fact, the rate constants k ($M^{-1}\ s^{-1}$) are lower and independent of the cation (Table 3).

An even more evident cation effect has been found in the demethylation reaction of methyldiphenyl phosphate **15** by complexes $(\text{Ligand}^{M^+})I^-$ ($M^+ = Li^+, Na^+, K^+, NH_4^+$)

Table 3 Effect of the metal ion M^+ and ligand on the second-order rate constant k ($M^{-1}\ s^{-1}$) of the reaction shown in eqn. (3)[a,b]

	$10^3\ k$ ($M^{-1}\ s^{-1}$)		
Ligand	Li^+	Na^+	K^+
5	18.9 (5)	4.4 (4.3)	3.8 (1)
3	12.5 (2.8)	4.6 (1.02)	4.5 (1)
7	9.4 (1.9)	6.7 (1.4)	4.9 (1)
11 (DCH18C6)	26 (2.6)	19 (1.4)	10 (1)
12 ([2.2.2,C_{10}])	15.3 (1.05)	14.6 (1.0)	14.5 (1)

[a] Same reaction conditions as Table 2. [b] $\Delta k = k_{M^+}/k_{K^+}$ in parentheses.

Table 4 Second-order rate constants for the demethylation reaction of **15** by (Ligand$^{M^+}$)I$^-$ complexes in chlorobenzene, at 60 °C[a]

	k^b (M^{-1} s^{-1})			
Ligand	Li^+ (1.28)[c]	Na^+ (1.02)[c]	K^+ (0.75)[c]	NH_4^+ (0.69)[c]
7	0.18	0.019	0.011	0.008
9 (PEG400Me$_2$)[d]	0.67	0.05	0.013	0.0098
11 (DCH18C6)[d]	0.53	0.11	0.02	0.016
12 ([2.2.2,C10])[d]	0.018	0.0181	0.0179	0.0184

[a] [Substrate **15**] = 0.5–2 × 10^{-2} M; [(Ligand$^{M^+}$)I$^-$] = 0.2–2 × 10^{-2} M. [b] Average of at least two determinations. The error in these values is estimated to be 5%. [c] Metal ion charge *vs.* ionic radius. [d] See ref. 4.

(Ligand = **7**, **9**, **11**, **12**) in chlorobenzene at 60 °C (eqn. 5).

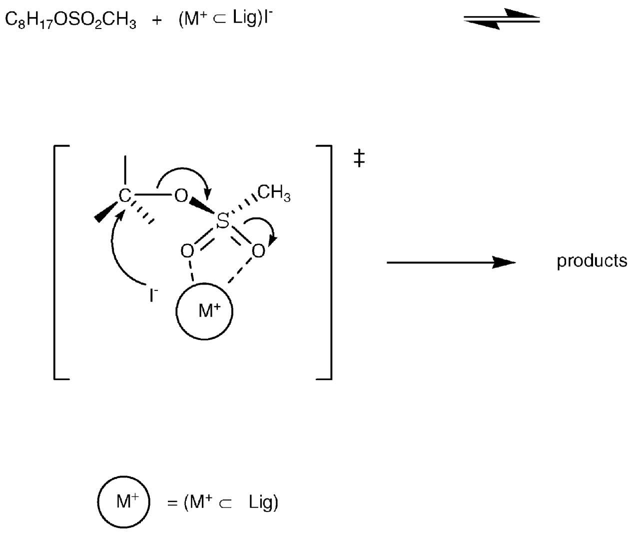
$$\underset{\mathbf{15}}{(PhO)_2POOMe} + (Ligand \supset M^+)I^- \xrightarrow[60\,^{\circ}C]{PhCl} (Ligand \supset M^+)(PhO)_2POO^- + MeI \qquad (5)$$

The data of Table 4 indicate that the second-order rate constants k (M^{-1} s^{-1}) depend on the ligand as well as on the cation, increasing on going from ammonium to the corresponding lithium complex. The enhancement of reactivity $\Delta k = k_{Li^+}/k_{NH_4^+}$ is more pronounced with crown ether **11** and PEG400Me2 **9** (33 and 68 times, respectively) in comparison with that of the polypodand **7** (22.5 times), whereas no metal ion effect was again found with cryptand **12**.

Discussion

Silicon polypodands **1–7** are efficient SL-PT catalysts. Their catalytic activity increases with the number of polyether chains in line with the increasing amount of salt complexed per mole of podand (Table 1).

Kinetics under homogeneous conditions show that the anion activation realized by this series of polypodands does not appreciably change (only 1.5 times) with the number of binding sites and polyether chains and is comparable with or slightly lower than that of traditional catalysts, in particular TRIDENT **8** and crown ether **11** (Table 2). It is worth noting, however, that the lower anion activation effected by silicon polypodands is largely compensated by their high complexation extents and for this reason their catalytic activity even approaches that of the cyclic polyether **11** (Table 1).

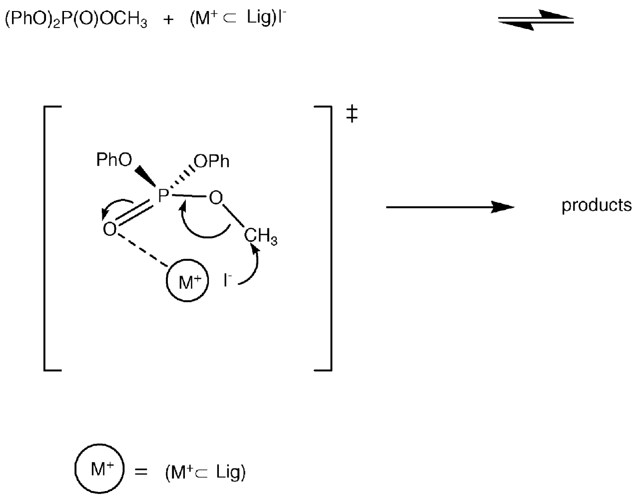


Scheme 2

In addition, the kinetic data highlight the importance of the metal ion M^+ in determining the rate of the S_N2 reactions eqn. (3) and eqn. (5) (Tables 3 and 4). They can both be explained on the basis of a transition state where the complexed cation (Ligand$^{M^+}$) interacts at the same time with the ion paired I$^-$ and the leaving group (Schemes 2 and 3).[3,4] In the activation process the metal cation in the ion pair (Ligand$^{M^+}$)I$^-$ stabilizes the negative charge developing on the oxygens of the methanesulfonic [eqn. (3)] or phosphonic group [eqn. (5)], whereas the nucleophile I$^-$ simultaneously attacks the carbon following a concerted push–pull mechanism ("metal ion electrophilic catalysis"). The catalytic effect increases with increasing the Lewis acidity of the cation ($NH_4^+ < K^+ < Na^+ < Li^+$) and is mainly related to the ability of the polyether to shield the cation charge.[3,4] Interestingly, crown ether DCH18C6 **11** and PEG **9**, that are anion activators less efficient than cryptand **12**,[5–9] are found to play a major role here. These ligands indeed form stable inclusion complexes where the metal cation, even if partially shielded by the ethereal oxygens, still keeps a remarkable density of charge and hence can interact with the leaving group in the transition state (Schemes 2 and 3). With these polyethers the higher participation of the cation (Na^+ and Li^+ in particular) in the transition state largely compensates the lower activation of the anion realized by the ligand as proved by the comparison with cryptand **12**. With the latter the reactivity does not appreciably change with the metal ion M^+ and is lower than that of the corresponding complexes with **11** and **9**. Since cryptands efficiently shield cations, and hence are excellent anion activators, the lower reactivity found clearly proves that, in this case, the participation of the cation is inhibited (Table 3).[5–9]

Analogously, the enhancement of reactivity $\Delta k = k_{Li^+}/k_{K^+}$ (Table 3) progressively increases on going from polypodand **7** (less than 2 times) to **3** (2.8 times) to **5** (5 times). The results can be explained in the same way by assuming that the metal ion electrophilic catalysis changes depending on the topology of the polypodand.[10]

Finally it is worth noting the effect of the cation participation in the demethylation reaction shown in eqn. (5). As shown in Table 4, with a metal ion of high charge density (ion charge/ionic radius) like lithium (z/r = 1.23 Å^{-1}), where the electrophilic catalysis is the dominant effect, the reactivity of silicon polypodand **7** is up to 10 times higher than that of cryptand **12**. With this cation the trend of reactivity is: PEG **9** > crown **11** > polypodand **7** ≫ cryptand **12**. By contrast, with cations of lower charge density (NH_4^+) (0.69 Å^{-1}) the sequence obtained: cryptand **12** > crown **11** > PEG **9** > polypodand **7**, is that expected when the anion activation is prevailing.



Scheme 3

Conclusion

The results as a whole proved that polypodands **1–7** are efficient catalysts in anion-promoted reactions under solid–liquid PTC conditions. The high catalytic activity is mainly due to the excellent complexing ability of these many-armed ligands. As a result, silicon polypodands **1–7**, that combine low cost and ease of synthesis with high complexation extent and good anion activation, can be considered a promising alternative to the traditional, more expensive, macrocyclic polyethers in a number of solid–liquid phase transfer catalyzed reactions.

Experimental

General methods

GLC data were obtained with a Hewlett-Packard 6890 by using a HP-5.5% phenylmethylsiloxane column (30 m × 320 mm × 0.25 mm). Potentiometric titrations were carried out with a Metrohm 751 GPD Titrino using a combined silver electrode isolated with a potassium nitrate bridge. Karl Fisher determinations were performed with a Metrohm 684 KF coulometer. ^{1}H and ^{31}P NMR spectra were recorded on Bruker AC 300 and AMX 300 spectrometers, using as external references TMS and 85% H_3PO_4, respectively.

Materials and solvents

Dry (Fluka) chlorobenzene ($H_2O \leq 20$ ppm) was used. Alkali metal iodides were AnalaR grade commercial products, kept in a desiccator under vacuum. Silicon polypodands **1–7** were prepared following a previously reported procedure.[11,12] Their structures were also proved by ^{1}H, ^{13}C and ^{29}Si NMR spectroscopy.[12] Ligands **8–10** were utilized as purchased.

Dicyclohexano-18-crown-6 (DCH18C6) **11** was an AnalaR grade commercial product (mixture of isomers, purity $\geq 97\%$) and was used as such. Merck Kryptofix 222D ([2.2.2,C_{10}]) **12** (50% toluene solution) was used as purchased after removal of the organic solvent under vacuum.

Octyl methanesulfonate **13**, bp 92–94 °C at 0.03 mmHg, n_D^{20} 1.4392, was prepared according to the literature (bp 98 °C at 1.5 mmHg, n_D^{20} 1.4390).[13]

Methyldiphenyl phosphate **15** was a commercial product (purity 80%) utilized after purification by column chromatography (silica gel; eluant $Et_2O : ETP = 1 : 1$) bp 125 °C at 0.04 mmHg, $n_D^{20} = 1.5371$ (bp 122 °C at 0.03 mmHg, $n_D^{20} = 1.5372$).[14]

Extent of complexation

The extent of complexation of polypodands **1–7** and polyethers **8–11** was determined by stirring a standardized chlorobenzene solution (10–20 ml) of ligand (0.02–0.05 M) with 1.1–50 molar equivalents of MI as solid phase, in a flask thermostatted at 60 °C. The system was magnetically stirred for 2–4 h, then kept without stirring for an additional 10 min to allow good separation of the two phases. Aliquots (5–8 ml) of the organic phase were centrifuged, samples (2–3 ml) were withdrawn and potentiometrically titrated with 0.01 M $AgNO_3$. Potentiometric titrations of cryptates $(M^+ \subset [2.2.2,C10])I^-$ were carried out in acid medium in order to avoid the simultaneous titration of the free ligand.[5]

Kinetic measurements under SL-PTC conditions

In a typical procedure a standardized chlorobenzene solution (10 ml) of methanesulfonate **13** (1 M) and internal standard (dodecane) (0.5 M) was added, in a flask thermostatted at 60 ± 0.1 °C, to a standardized solution (10 ml) of catalyst (0.1 M) which had previously been stirred over solid NaI (25 mmol) for 1 h, to obtain the complex formation. Timing and stirring were started. Aliquots of the organic phase were withdrawn (after stopping the stirring for 30–60 s to allow adequate separation), centrifuged, separated from any eventual solid precipitate and analyzed by GLC (see General methods). The reaction rates were measured by following the disappearance and/or appearance of substrate and reaction product. The *pseudo*-first-order rate constants (k_{obsd}) were computer generated by plotting log[substrate] *vs.* time and determining the slope of the straight lines.

Kinetics under homogeneous conditions

Standardized chlorobenzene solutions (5 ml) of substrates **13** or **15** (0.15–0.30 M) were added to a standardized solution (0.02–0.04 M) of complexed MI (15 ml) in a 30 ml flask thermostatted at 60 ± 0.1 °C. The solution of preformed complex $(\text{Ligand}^{M^+})I^-$ was prepared as described above. Samples (2–5 ml), withdrawn periodically, were quenched in ice-cold MeOH (50 ml) and the unreacted iodide was potentiometrically titrated with 0.01 M $AgNO_3$. The second-order rate constants k (M^{-1} s^{-1}) were evaluated using a least squares computer program from the equation: $1/([B_0]-[A_0]) \cdot \ln([BA_0]/[AB_0]) = kt$, where A = substrate and B = complexed MI or *vice versa*. All rates involved at least 8 samplings and gave correlation coefficients of 0.997 or better.

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