

Solid-Liquid Phase Transfer Kinetics of *p*-Nitrobenzoate Esterification catalysed by Crown Ethers; a Comparison of the Catalytic Efficiency of Various Crown Ethers

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The kinetics of the esterification reaction between potassium *p*-nitrobenzoate and benzyl bromide catalysed by various crown ethers have been studied in a solid-chloroform phase-transfer system at 25 °C. The reaction was found to be first order in benzyl bromide, and the observed pseudo-first-order rate constants obtained at constant crown ether concentration were found to depend linearly on the concentration of the crown ether-salt complexes in the organic phase. Rate constants for both S_N1 and S_N2 mechanisms of benzyl bromide were determined and the S_N1 pathway was found to contribute to a negligible extent. The S_N2 rate constants in the presence of four crown ethers decreased in the order: oxydimethylenebisbenzo-15-crown-5 \gg dicyclohexano-18-crown-6 $>$ 18-crown-6 \sim 4'-methylbenzo-18-crown-6. Differences in the catalytic efficiencies of the crown ethers were ascribed to their different effects on the interionic ion pair distance $R-CO_2^- \cdots M^+$ on complexation.

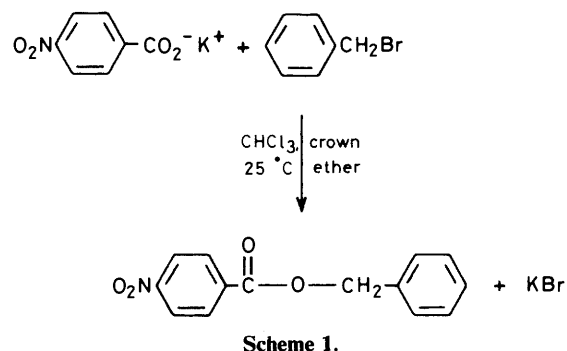
The efficiency of crown ethers as phase-transfer catalysts depends on their complexation constants with the reacting ion pairs, their ability to enlarge the interionic ion pair distance, and the lipophilicity of the ion-pair complexes.¹ Attempts to improve the catalytic efficiencies of these ligands in liquid-liquid systems through structural modification of the periphery crown ether rings have met with little success.² In comparison with crown ethers, quaternary ammonium salts and cryptands are generally more effective phase-transfer catalysts because they induce a large charge separation in the ion pair, yielding a more activated anion.^{3,4} Charge separation in a crown-ion pair complex depends on the structure of the crown ligand,⁵ but few quantitative data exist which correlate anion reactivity with crown ether structure.

In this paper we report a study of the efficiency of a series of crown ethers, including a bis-(crown ether), in catalysing the reaction between solid potassium *p*-nitrobenzoate and benzyl bromide in chloroform (Scheme 1). An anhydrous solid-liquid phase-transfer system was utilized to eliminate the effect of hydration on anion reactivity. The structures of the respective crown ethers are depicted in Scheme 2.

Experimental

Materials.—Potassium and sodium *p*-nitrobenzoates were prepared in water from *p*-nitrobenzoic acid (B.D.H.) and the respective metal hydroxides. The salts were recrystallized from 95% ethanol and dried overnight in a vacuum oven at 60 °C. For kinetic studies the salts were ground to a fine powder (100–150 mesh).

Dicyclohexano-18-crown-6 (2,5,8,15,18,21-hexaoxatricyclo-[20.4.0.0⁹.14]hexacosane) and 18-crown-6 (1,4,7,10,13,16-hexaoxacyclo-octadecane) were acquired from Aldrich. The latter was recrystallized from *n*-heptane; the former was purified by column chromatography on acidic alumina eluted with *n*-heptane, producing a mixture of the *cis*- and *trans*-isomers.⁶ 4'-Methylbenzo-18-crown-6 (2,3,5,6,8,9,11,12-octahydro-15-methyl-1,4,7,10,13,16-benzohexaoxacyclo-octadecan) was synthesized as described by Smid *et al.*⁷ Oxydimethylenebisbenzo-15-crown-5 [15,15'-oxydimethylenebis-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaoxacyclo-pentadecan)] was synthesized in 55% yield by modifying a recently published procedure:⁸ treating 4'-bromomethylbenzo-15-crown-5 with its hydrolysis product, 4-hydroxymethylbenzo-15-crown-5 in the presence of sodium hydride in tetrahydrofuran. Benzyl



bromide (Merck) was used without further purification. Chloroform (Merck) was dried by refluxing overnight over phosphorus pentoxide, and stored over molecular sieves (4 Å).

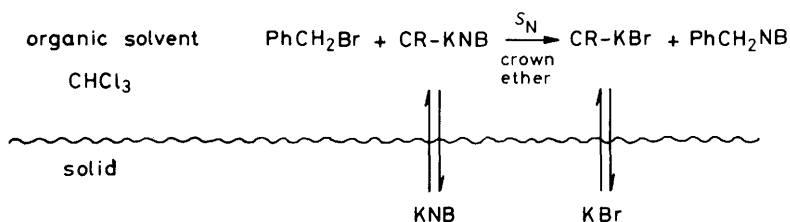
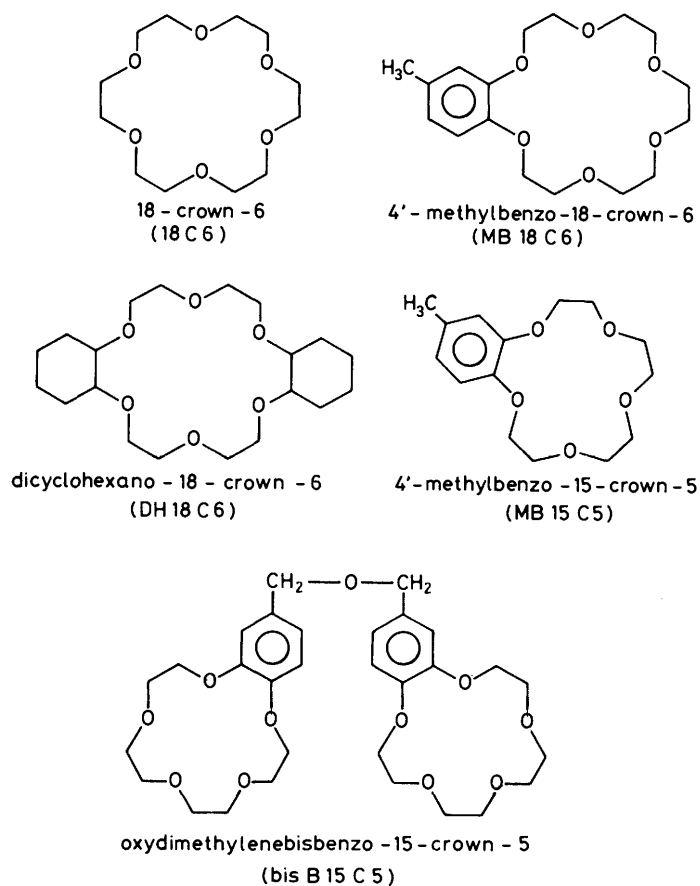
Phase Transfer Equilibrium.—To a water-jacketted reaction flask (20 ml) maintained at 25 ± 0.5 °C was added a 1.0×10^{-2} M-crown ether solution in chloroform (10 ml), and the solution was stirred for 15 min (to thermal equilibrium). Under constant stirring, 100–150 mesh potassium *p*-nitrobenzoate (KNB) was added. Initially at 0.5 min intervals, gradually increasing to 5 min intervals, 50 μ l samples of the clear solution were withdrawn and the concentration of the KNB-crown ether complex was determined with a Varian Super Scan 3 spectrophotometer, scanning between 250 and 300 nm. In some experiments, the effect of varying the stirring speed was studied.

Determination of Salt Transfer into the Organic Phase.—In a typical experiment, a 1.0×10^{-2} M-crown ether solution (10 ml; 0.1 mmol) was added to 150 mesh KNB salt (0.25 g, 1.2 mmol). After thermal and phase-transfer equilibrium was reached, a sample (50 μ l) of the clear solution was withdrawn and analysed for complex concentration. To determine the KNB-solubilizing effect of potassium bromide, ground KBr (0.06 g, 0.5 mmol) was added to the solution just analysed for complex concentration. Samples of the clear solution were withdrawn at 5 min intervals and any changes in the KNB-crown ether complex concentration were determined spectrophotometrically.

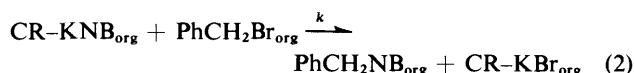
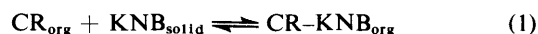
Kinetic Measurements.—In a typical experiment, chloroform (8 ml) containing crown ether (1.0×10^{-2} M; 0.08 mmol) and 150 mesh KNB (0.25 g, 1.2 mmol) was placed in a flask kept at 25 ± 0.5 °C. After stirring for 15 min, 2.5M-benzyl bromide in chloroform (2 ml; 5.0 mmol) was added. At intervals, depending on the reaction rate, a sample (50 μ l) of the clear chloroform solution was withdrawn and immediately diluted with chloroform (10 ml) to quench the reaction. The benzyl *p*-nitrobenzoate product was determined quantitatively by h.p.l.c. with a Waters Associate 6000 instrument using a μ -Porasil column eluted with CHCl_3 -*n*-heptane (1:8 v/v). The reaction was usually monitored up to about 15% conversion.

Results and Discussion

In this solid-liquid phase transfer system, potassium *p*-nitrobenzoate is transferred to chloroform by means of the crown ether, and the soluble crown ether-potassium *p*-nitrobenzoate complex (CR-KNB) is converted into benzyl *p*-nitrobenzoate



(BzNB) by treatment with benzyl bromide. The mechanism of this heterogeneous process is depicted in Scheme 3 and equations (1)–(3).



The following assumptions are made. (a) The phase-transfer processes (1) and (3) are much faster than the nucleophilic substitution reaction (2). (b) The concentration of the CR-KNB complex depends only on the initial crown ether concentration in the organic phase. (c) Crown ether complexation to KNB is appreciably greater than to KBr, implying that the concentration of the CR-KNB remains essentially constant during the reaction. The rate of product formation is given by equation (4), where k_{obs} is the pseudo-first-order rate constant. Integration yields equation (5). Depending on reaction

$$\frac{d[\text{PhCH}_2\text{NB}]}{dt} = k[\text{PhCH}_2\text{Br}][\text{CR-KNB}] = k_{\text{obs}} [\text{PhCH}_2\text{Br}] \quad (4)$$

$$-\ln[\text{PhCH}_2\text{Br}]_0 - [\text{PhCH}_2\text{NB}] = k_{\text{obs}} t - \ln[\text{PhCH}_2\text{Br}]_0 \quad (5)$$

conditions, benzyl bromide can undergo either $S_{\text{N}}1$ or $S_{\text{N}}2$ reactions;⁹ hence the rate of product formation can be expressed as equation (6). Combining (4) and (6) yields equation (7), and thus k_1 and k_2 can be obtained by measuring k_{obs} as a

$$\frac{d[\text{PhCH}_2\text{NB}]}{dt} = k_1[\text{PhCH}_2\text{Br}] + k_2[\text{PhCH}_2\text{Br}][\text{CR-KNB}] = \{k_1 + k_2[\text{CR-KNB}]\}[\text{PhCH}_2\text{Br}] \quad (6)$$

$$k_{\text{obs}} = k_1 + k_2[\text{CR-KNB}] \quad (7)$$

function of the crown ether-salt complex concentration.

Phase-transfer Equilibration and Extent of Salt Transfer.—Using conditions similar to those employed in the kinetic studies, we found that phase-transfer equilibrium can be attained within 2 min. Figure 1 shows plots of u.v. absorbance *versus* time for transfer of KNB to chloroform containing oxydimethylenebisbenzo-15-crown-5 and dicyclohexano-18-crown-6. The time needed to reach equilibrium is not affected by the rate of stirring or a change in particle size from 100 to 150 mesh, but the use of non-ground KNB increases the equilibration time to 5 min. These results justify the previously made assumption that the phase-transfer step is much faster than ester formation, the half-lives for which lie between 10^2 and 10^3 min, depending on the crown ether used.

The function $[\text{CR-KNB}]/[\text{CR}]_0$ can be used as a measure of the efficiency of a crown ether in transferring the solid KNB

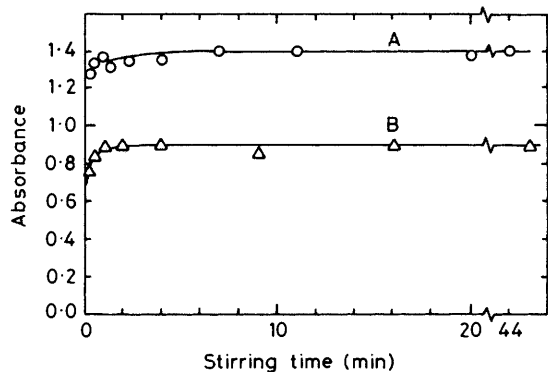


Figure 1. Plots of the absorbance of the crown ether-potassium *p*-nitrobenzoate complex versus stirring time in solid- CHCl_3 phase-transfer processes at 25 °C: A, [bisB15C5] = $5.0 \times 10^{-3}\text{M}$ at λ_{max} 280 nm; B, [DH18C6] = $5.0 \times 10^{-3}\text{M}$ at λ_{max} 272 nm; cell length = 1.0 cm (the sample was diluted 200 times before u.v. measurement)

Table 1. Efficiency of transfer of solid potassium *p*-nitrobenzoate into chloroform by crown ethers at 25 °C

Crown ether	Fraction of crown ether complexed to crown ether	Concentration range of crown ether, $10^2[\text{CR}]_0/\text{M}$
18-Crown-6	0.95	0.50—5.0
4'-Methylbenzo-18-crown-6	0.95	0.60—5.0
Dicyclohexano-18-crown-6	0.95	0.5—6.0
Oxymethylenebisbenzo-15-crown-5	1.0	0.13—2.3

salt into the organic phase. No detectable amount of salt is transferred in the absence of crown ether, but Table 1 shows that the above function reaches 0.95 for 18C6, MB18C6, and DH18C6, and 1.0 for bisB15C5, implying that nearly every crown ether molecule in the CHCl_3 solution is bound to a K^+ ion. At 25 °C a complex concentration of 0.06M in CHCl_3 can be easily attained.

Since KBr is a reaction product, it conceivably could compete with KNB for crown ether and, consequently, lower the CR-KNB concentration during the reaction. However, during the reaction the concentration of CR-KNB was found to be constant up to at least 20% conversion of PhCH_2Br . Also, addition of solid KBr in an amount equal to that produced after 20% conversion has no effect on the concentration of CR-KNB. Apparently the reaction product CR-KBr decomposes into solid KBr and free crown ether, the latter solubilizing solid KNB to maintain a constant CR-KNB concentration. The different behaviour of KBr and KNB depends on such factors as the crystal lattice energy of the salt, and the complex formation constants of the crown ether with the two salts.¹

Kinetic Measurements.—Plots of $\ln([\text{PhCH}_2\text{Br}]_0 - [\text{PhCH}_2\text{NB}])$ versus reaction time for the bisB15C5-catalysed reaction of solid KNB with PhCH_2Br at various crown ether concentrations are shown in Figure 2. The observed pseudo-first-order rate constants k_{obs} calculated from the least-squares straight lines (correlation coefficients better than 0.998) are listed in Table 2 together with other reaction variables. It was ascertained that no reaction occurred in the absence of crown ether.

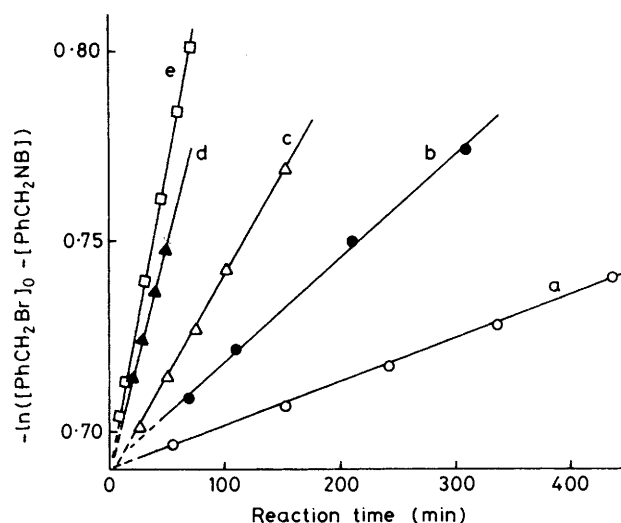


Figure 2. Plots of $-\ln([\text{PhCH}_2\text{Br}]_0 - [\text{PhCH}_2\text{NB}])$ versus reaction time for the solid- CHCl_3 phase-transfer reaction between potassium *p*-nitrobenzoate and benzyl bromide catalysed by oxymethylenebisbenzo-15-crown-5 at 25 °C: a, $[\text{CR}]_0 = 1.3 \times 10^{-3}\text{M}$; b, $[\text{CR}]_0 = 3.0 \times 10^{-3}\text{M}$; c, $[\text{CR}]_0 = 5.0 \times 10^{-3}\text{M}$; d, $[\text{CR}]_0 = 1.2 \times 10^{-2}\text{M}$; e, $[\text{CR}]_0 = 1.5 \times 10^{-2}\text{M}$

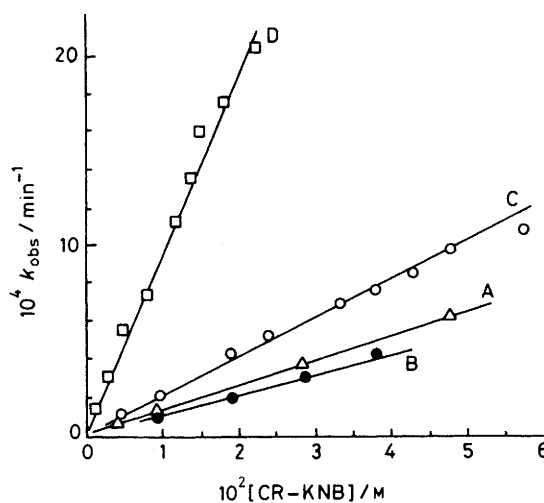


Figure 3. Plots of k_{obs} versus $[\text{CR-KNB}]$ in the solid- CHCl_3 phase-transfer reactions catalysed by various crown ethers at 25 °C: A, 18C6, B, MB18C6, C, DH18C6, D, bisB15C5

Figure 3 depicts plots of k_{obs} versus the complexed salt concentration $[\text{CR-KNB}]$. All crown ethers show linear relations with intercepts very close to zero. The intercepts, representing k_1 for benzyl bromide in CHCl_3 at 25 °C [equation (7)], are less than 10^{-6}min^{-1} . Small $\text{S}_{\text{N}}1$ rate constants are expected since in a low polarity solvent such as chloroform the $\text{S}_{\text{N}}1$ pathway is insignificant. The same reaction gave $k_1 = 10^{-5}\text{min}^{-1}$ in the more polar solvent dichloromethane.⁹

The $\text{S}_{\text{N}}2$ rate constants calculated from the slopes of the plots of Figure 3 are listed in Table 3. The k_2 values in the presence of 18C6, MB18C6, or DH18C6 differ by not more than a factor of 1.5, but the k_2 value in the presence of bisB15C5 is about ten times larger.

The much higher k_2 value with bisB15C5 is most likely caused by the larger $\text{CO}_2^- \cdots \text{K}^+$ interionic distance in its complex with this bis-crown ether. At the concentrations

Table 2. Pseudo-first-order rate constants, k_{obs} for the reaction between potassium *p*-nitrobenzoate and benzyl bromide in a solid- CHCl_3 phase-transfer system catalysed by various crown ethers at 25 °C

Crown ether	$10^2[\text{CR}]_0$ M	$[\text{PhCH}_2\text{Br}]_0$ M	Wt. KNB g	$10^2[\text{CR-KNB}]$ M	$10^4 k_{\text{obs}}$ min^{-1}	Conversion (%)
18C6	0.48	0.481	0.15	0.46	0.69	0.9
	1.00	0.506	0.15	0.95	1.24	4.5
	3.00	0.253	0.10	2.85	3.63	5.7
	5.00	0.252	0.20	4.75	6.17	6.0
MB18C6	1.00	0.503	0.25	0.95	0.98	3.6
	2.00	0.503	0.25	1.92	1.92	6.3
	3.00	0.503	0.25	2.88	3.09	9.7
	4.00	0.503	0.25	3.80	4.72	11.0
DH18C6	0.50	0.500	0.25	0.48	1.08	3.8
	1.00	0.500	0.25	0.95	2.19	10.8
	2.00	0.500	0.25	1.90	4.25	16.4
	2.52	0.490	1.00	2.39	5.23	15.0
	3.50	0.500	0.25	3.33	6.87	10.6
	4.00	9.500	0.25	3.80	7.45	7.6
	4.50	0.500	0.25	4.28	8.49	10.9
	5.00	0.500	0.25	4.75	9.83	16.8
6.00	0.500	0.25	5.70	10.8	17.0	
BisB15C5	0.13	0.501	0.25	0.13	1.16	4.8
	0.30	0.501	0.25	0.30	2.85	10.1
	0.50	0.501	0.25	0.50	5.38	7.5
	0.80	0.501	0.25	0.80	7.28	5.0
	1.20	0.501	0.25	1.20	11.1	5.5
	1.35	0.501	0.25	1.35	13.5	9.5
	1.50	0.501	0.25	1.50	15.8	10.4
	1.80	0.501	0.25	1.80	17.5	8.3
2.25	0.248	0.25	2.25	20.4	9.6	

Table 3. Second-order rate constants (k_2) for the reaction between potassium *p*-nitrobenzoate and benzyl bromide catalysed by crown ethers in CHCl_3 at 25 °C

Crown ether	$10^2 k_2$ $\text{l mol}^{-1} \text{min}^{-1}$	Range of crown ether concentration, $10^2[\text{CR}]/\text{M}$
18C6	1.30	0.50—5.00
MB18C6	1.13	0.60—5.00
DH18C6	1.84	0.50—6.00
BisB15C5	9.66	0.13—2.25
MB15C5	0.14 ^a	1.00—7.00

^a With sodium *p*-nitrobenzoate instead of potassium *p*-nitrobenzoate as the nucleophile

employed in these studies, the crown ether-salt complex in CHCl_3 is undoubtedly an ion pair. Moreover, the observation that k_2 is independent of the concentration of the crown ether-ion pair complex indicates that the reaction proceeds *via* the ion pairs and that no reactive free ions are involved.

Previous studies with fluorenyl carbanion and picrate salts^{5,7,10} have shown that the interionic ion-pair distance in a crown ether-ion-pair complex is sensitive to the structure of the crown ether and the types of cation and anion composing the ion pair. Frequently, both tight and loose crown-ether-complexed ion pairs can be found, with distinctly different optical absorption maxima. In systems where 1:1 crown ether-cation complexes are formed (*e.g.* 18C6 and K^+), crown-ether-complexed tight ion pairs are frequently observed in less polar media like CHCl_3 or diethyl ether, especially for less delocalized anions. Potassium picrate, which has λ_{max} 357 nm in tetrahydrofuran and is a tight ion pair in this solvent, yields 1:1 crown ether complexes with 18C6, MB18C6, and DH18C6 with absorption maxima now at 365, 365 and 370 nm, respectively, while the bisB15C5 complex

absorbs at 378 nm, a value close to that for the loose ion pair.^{10,11} The interionic ion pair distances in the complexes appear to increase in the order 18C6 ~ MB18C6 < DH18C6 << bisB15C5.⁵ This change corresponds with the increase in k_2 found for these crown ethers. A small spectral change is observed on complexing the crown ether with potassium *p*-nitrobenzoate, especially with the bis-crown ether, but the carboxylate spectra are much less sensitive to changes in the interionic ion pair distance than those of phenolates or carbanion salts. The recently studied decarboxylation of potassium 6-nitrobenzoxazole-3-carboxylate in benzene and the catalytic effect of added crown ethers and polyethers on this reaction could also be rationalized on the basis of a crown-ether-dependent $\text{CO}_2^- \cdots \text{K}^+$ distance in the crown ether-ion pair complex.¹²

A series of experiments with sodium *p*-nitrobenzoate and MB15C5 yielded a k_2 value of $1.4 \times 10^{-3} \text{ l mol}^{-1} \text{ min}^{-1}$ (Table 3), ten times smaller than that for KNB-18C6. Sodium picrate and MB15C5 yield a complex in CHCl_3 with λ_{max} 357 nm, suggesting an interionic ion pair distance smaller than that found in the 18C6 complexes with potassium picrate. Hence, the low k_2 value for the MB15C5-sodium *p*-nitrobenzoate complex is not surprising.

In conclusion, the rate-determining step in the solid-liquid phase-transfer reaction between potassium *p*-nitrobenzoate and benzyl bromide catalysed by crown ethers is the S_N2 reaction in the liquid phase. The reactivity of the nucleophile appears to be a sensitive function of the interionic ion pair distance and by appropriate modification of the complexing crown ligand the efficiency of these phase-transfer catalysts can be significantly improved.

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