Phase-transfer Reactions Catalyzed by Phosphoric Triamides Containing Hydrophobic Groups

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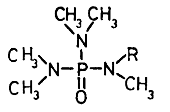
Aqueous organic two-phase reactions (halogen exchange, cyanation, and borohydride reduction) have been catalyzed by phosphoric triamides containing hydrophobic groups. The phosphoric triamides, which have a high cation binding ability, exibited high catalytic activity for the two-phase reactions. The catalytic activity of *N*-alkylteramethylphosphoric triamides (**1**) was higher than that of the corresponding pentamethyl derivatives and the difference has been explained in terms of the contribution of the dimeric species of **1** and/or hydrogen bonding between the NH of **1** and the anionic moieties of inorganic reagents.

Aqueous organic two-phase reactions are catalyzed by quaternary ammonium or phosphonium salts,1) crown ethers,2) cryptands,3) and α-phosphoryl sulfoxides4) and have found use in organic syntheses.5) Recently, it was found that *N*-alkylpentamethylphosphoric triamides (**1**)6) and *N*-alkyltetramethylphosphoric triamides (**2**) catalyzed two-phase reactions, the activity being dependent on the structure of the compounds.



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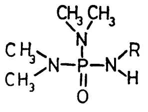

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In this report, the relationship between the structure and the catalytic activity will be discussed.

Experimental

Reagents. *N*-Alkylpentamethylphosphoric triamides (**1**) have been prepared by the reaction of the sodium salt of pentamethylphosphoric triamide7) and the corresponding alkyl halides in toluene at 0 °C. *N*-Alkyltetramethylphosphoric triamides (**2**) have been synthesized by the reaction of bis(dimethylamino)chlorophosphine oxide8) with the corresponding primary amine, in the presence of triethylamine, in refluxing benzene. **1** and **2** were purified by distillation under reduced pressure or recrystallization, and the structure confirmed by NMR, IR, and MS. The yields and physical properties are summarized in Table 1.

TABLE 1. YIELDS AND PHYSICAL PROPERTIES OF PHOSPHORIC TRIAMIDES

Name	Alkyl group (R)	Yield %	Bp/mmHg (mp) °C
Pentamethylphosphoric triamide derivatives			
1a	CH_3a)	—	68/1
1b	$PhCH_2$	81	117/0.5
1c	$PhCH=CH-CH_2$	80	155/1
1d	$Ph(CH_2)_3$	44	144/0.5
1e	$1-C_{10}H_7CH_2$	75	(116—119)b,c)
1f	$C_{12}H_{25}$	66	142/0.5
1g	$C_{16}H_{33}$	70	165/0.01
Tetramethylphosphoric triamide derivatives			
2a	CH_3	72	103/0.5
2b	$PhCH_2$	78	(84—90)b,c)
2c	$1-C_{10}HCH_2$	56	(119—124)b,c)

a) Commercial product. b) Hygroscopic. c) Uncorrected.

N-Benzylformamide,9) tridecyl methyl sulfoxife,10) 18-crown-6,11) and benzo-18-crown-612) were prepared by the methods described in the literature. *N*-Dodecyl-2-pyrrolidone (Mitsubishi Petrochemical) was distilled under reduced pressure prior to use. Other organic reagents were obtained from commercial sources and distilled under reduced pressure prior to use. Inorganic reagents and quaternary ammonium salts were obtained commercially, and used without further purification.

Reaction Procedure. The two-phase reactions were conducted under standard phase-transfer conditions2,3) and the yields determined by gas chromatography.

Measurements. The cation binding ability of the phosphoric triamides was evaluated by the procedure described by Smid *et al.*13) and the degree of association measured cryoscopically in benzene.

Results

Halogen Exchange Reaction. Table 2 shows the results of the reaction of octyl bromide with potassium

TABLE 2. REACTION OF $C_8H_{17}Br$a) WITH KIb) UNDER PHASE-TRANSFER CONDITIONSc)

Catalystd)	Time h	Yielde) %
None	24	<5
1a	24	5
1b	6	25
1c	6	77
1d	6	32
1e	6	11
1f	6	38
1g	6	21
2a	24	5
2b	6	73
2c	6	92
$PhCH_2NHCHO$	24	5
$C_{13}H_{27}SOCH_3$	24	26
NDPf)	24	5
18-Crown-6	6	16
Benzo-18-crown-6	6	68
$PhCH_2N(CH_3)_3^+Cl^-$	8	<5
$C_{16}H_{33}N(CH_3)_3^+Br^-$	2	100g)

a) No solvent was used for the substrate. b) Saturated aqueous solution, 5.0 mol equiv. c) Reaction temp, 80 °C; internal standard, tetralin. d) 0.08 mol equiv. e) GLPC analysis. f) *N*-Dodecyl-2-pyrrolidone. g) Emulsified reaction.

iodide under phase-transfer conditions. Both hexamethylphosphoric triamide (**1a**) and pentamethylphosphoric triamide (**2a**) were not effective catalysts for the halogen exchange. *N*-Alkylpentamethylphosphoric triamides (**1b**—**1g**) and *N*-alkyltetramethylphosphoric triamides (**2b**, **2c**) containing higher aliphatic or arylalkyl groups were however found to catalyze the reaction. In particular, the tetramethylphosphoric triamide derivatives showed high catalytic activity.

Formamide, sulfoxide, and 2-pyrrolidone derivatives having hydrophobic groups in the molecules exhibited low catalytic activity. Benzo-18-crown-6 was effective as a catalyst, while 18-crown-6 was not. Benzyltrimethylammonium chloride was also not effective. Hexadecyltrimethylammonium bromide (CTAB) showed the highest catalytic activity of all the catalysts used.

Table 3. Reaction of $C_8H_{17}Br$[a] with NaCN[b] under phase-transfer conditions[c]

Catalyst[d]	Time h	Yield[e] %
None	24	11
1a	8	22
1b	10	47
1c	10	70
1d	10	34
1e	10	68
2a	8	24
2b	10	76
2c	10	91
$PhCH_2NHCHO$	10	7
$C_{13}H_{27}SOCH_3$	10	6
NDP[f]	10	4
Benzo-18-crown-6	8	84
$C_{16}H_{33}N(CH_3)_3^+Br^-$	6	98[g]

a) No solvent was used for the substrate. b) 33 wt % aqueous solution, 1.5 mol equiv. c) Reaction temp, 80 °C; internal standard, naphthalene. d) 0.05 mol equiv. e) GLPC analysis. f) *N*-Dodecyl-2-pyrrolidone. g) Emulsified reaction.

Cyanation. Table 3 shows the results of the reaction of octyl bromide with sodium cyanide. The cyanation, as well as the halogen exchange reaction, was catalyzed by **1b**—**1e** and **2b**—**2c**, the catalytic activity of the latter being higher than that of the former. Benzo-18-crown-6 and CTAB showed high catalytic activity, but CTAB emulsified the system with increasing conversion of the reaction.

Reduction of Ketone. The results of the reduction of acetophenone and 2-octanone with sodium borohydride are shown in Table 4. The reduction proceeded very slowly in the absence of phosphoric triamide catalysts. This reaction, and the two reactions described above, were catalyzed by the phosphoric triamides, especially **2b** and **2c**.

Interaction between Phosphoric Triamides and Picrate Salts. The cation binding ability of the phosphoric triamides was investigated by the extraction method described by Smid *et al.*[13] and the results of the extraction of potassium picrate by the phosphoric triamides are shown in Table 5. The cation binding ability of **1a** and **2a** was very low. Tetramethylphosphoric triamides containing the benzyl (**2b**) or 1-naphthylmethyl (**2c**) group exhibited high cation binding ability, compared with the other phosphoric triamides. Pentamethylphosphoric triamides possessing benzyl (**1b**), cinnamyl (**1c**), or 1-naphthylmethyl (**1e**) groups also proved efficient in the extraction of potassium picrate. The pentamethylphosphoric triamides having a dodecyl (**1f**) or hexadecyl (**1g**) group showed very low cation binding ability.

Table 4. Reduction of ketones[a] with $NaBH_4$[b] under phase-transfer conditions[c]

Ketone $RCOCH_3$	Catalyst[d]	Time h	Yield[e] %
R=Ph[f]	None	8	10
	1b	8	65
	1e	8	69
	2b	6	94
	2c	6	92
$R=C_6H_{13}$[g]	None	24	3
	1b	8	93
	1e	8	87
	2b	3	>95
	2c	3	>95

a) 25.5 mmol. b) 0.76 mol equiv. c) Benzene (4 ml) was used as solvent; 1 wt % aqueous NaOH (1 ml); room temp. d) 0.10 mol equiv. e) GLPC analysis. f) Internal standard, diphenyl. g) Internal standard, ethylbenzene.

Table 5. Extraction of potassium picrate by phosphoric triamides[a]

Phosphoric triamide	Potassium picrate extracted[b] %
1a[c]	1
1b	4
1c	8
1d	1
1e	11
1f	1
1g	1
2a[c]	1
2b	12
2c	12

a) Solvent system, H_2O–CH_2Cl_2 (50: 50, v/v); [Picric acid]$=7.0\times10^{-5}$ M: [KOH]$=0.01$ M; [Phosphoric triamide]$=7.0\times10^{-3}$ M. b) Based on total amount of potassium picrate. The picrate concentration was measured by optical spectroscopy, using $\varepsilon=1.8\times10^4$ in CH_2Cl_2. c) [Phosphoric triamide]$=7.0\times10^{-2}$ M.

The cation binding ability of the phosphoric triamides was largely independent of the species of alkali cations,[6] in contrast with the observations on crown ethers.[13]

Association of Phosphoric Triamides. Table 6 shows the degree of association of the phosphoric triamides in benzene which for **2b** and **2c** was 1.2, and for **1b** and **1e** was 1.0. **1b** and **2b** were found to be present as monomeric forms in dioxane.

Table 6. Association of phosphoric triamides in benzene and dioxane

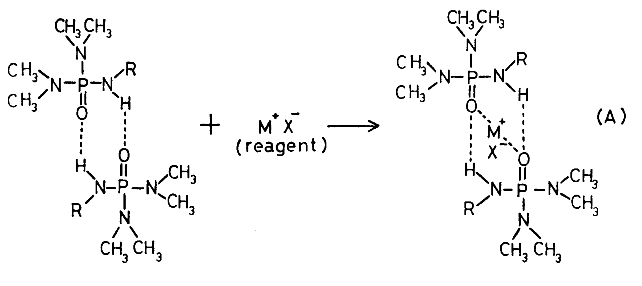
Phosphoric triamide	Concn M	Degree of association in benzene	Degree of association in dioxane
1b	0.055	1.0	
1b	0.013		1.0
1e	0.037	1.0	
2b	0.051	1.2	
2b	0.011		1.0
2c	0.039	1.2	

Discussion

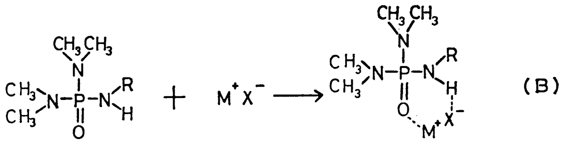
It has been shown that the phosphoric triamides containing hydrophobic groups are effective as phase-transfer catalysts. The catalytic activity of some of the phosphoric triamides was comparable to that of benzo-18-crown-6, and somewhat lower than that of CTAB. The activity was considerably higher than that of formamide, sulfoxide, and pyrrolidone derivatives containing hydrophobic groups. The donor numbers of the corresponding compounds containing methyl, in place of the higher groups are as follows:[14] hexamethylphosphoric triamide, 38.8; *N*,*N*-dimethylformamide, 26.6; dimethyl sulfoxide, 29.8; *N*-methyl-2-pyrrolidone, 27.3. On the basis of this data, it is suggested that the phosphoric triamides containing hydrophobic groups interact strongly with the cationic moieties of inorganic reagents through pole-dipole interactions.

The mechanism of two-phase reactions catalyzed by ammonium or phosphonium salts was first proposed by Starks,[1] and supported by Herriot and Picker.[15] In the system, the onium salts are thought to extract the anionic reagent into the organic phase. In the reactions catalyzed phosphoric triamides, the compounds which were efficient extractors of potassium picrate from the aqueous to the organic phase (CH_2Cl_2), exhibited high catalytic activity for the two-phase reactions (see Tables 2, 3, 4, and 5). These observations may be explained in terms of the mechanism proposed by Starks,[1] *i.e.*, the phosphoric triamides, and the onium salts, transfer the inorganic reagent from the aqueous phase to the organic phase, and thereby catalyze the two-phase reaction.

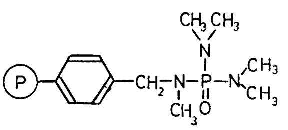
The catalytic activity of the phosphoric triamides was found to be dependent on the structure of the hydrophobic groups. In this study, the activity of the phosphoric triamides having arylalkyl groups such as benzyl or 1-naphthylmethyl groups was higher than those having alkyl groups such as dodecyl or hexadecyl.



The catalytic activity of **2** is higher than that of **1**, although the electron-donating power of the dialkylamino group is stronger than that of the monoalkylamino group.[16] This result may be explained as follows; **2** slightly associates in benzene (Table 6) and the hydrogen of NH in **2** is weakly acidic (**2** reacts easily with NaH) suggesting the participation of a dimeric species. This is formed through hydrogen bonding, in the two-phase reaction (Scheme **A**).



Moreover, it appears reasonable to assume that the anionic moiety (X^-) of the inorganic reagent (M^+X^-) may interact with the acidic hydrogen of **2** through hydrogen bonding (Scheme **B**). The enhanced interaction of **2** with M^+X^-, as described in schemes **A** and **B**, will result in an increase in the solubility of M^+X^- in the organic phase, and thereby an increase in the catalytic activity of **2**. In the case of **1** which does not contain an acidic hydrogen, the interaction of **1** with X^- is not expected.



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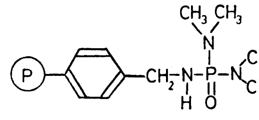

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Solid-phase catalysts (**3** and **4**), prepared by the reaction of chloromethylated polystyrene resin cross-linked with divinylbenzene and the sodium salts of pentamethylphosphoric triamide or tetramethylphosphoric triamide, were found to be effective for two-phase reactions.[17] In the tri-phase[18] and the two-phase system, the activity of the tetramethyl derivative **4** was higher than that of the pentamethyl derivative **3**. Such a difference between **3** and **4** may be interpreted by assuming a strong interaction of **4** with M^+X^- through hydrogen bonding as shown in scheme **B**, since the cooperative interaction of the phosphoric triamide groups, with M^+X^- as shown in scheme **A**, may be assumed to occur with difficulty in the immobilized system.[19]

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