Studies on Organophosphorus Compounds XXXIII. Chemoselective Phase-Transfer Catalytic *S*-Alkylation of Dialkyl/diarylthiophosphinic Acids; A New Facile Route to *S*-Alkyl Dialkyl/diarylthiophosphinates

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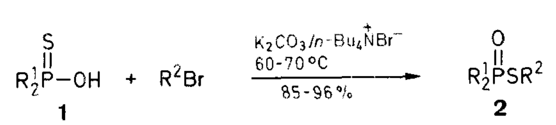
A phase-transfer catalytic (PTC) alkylation involving the reaction of alkyl bromide and dialkyl/diarylthiophosphinic acids in the presence of potassium carbonate and tetrabutylammonium bromide is described. The reaction proceeds by S_N2 mechanism and gives exclusively *S*-alkylated products.

As one of the important classes of sulfur-containing organophosphorus compounds with promising biological and chelating properties, *S*-alkylthiophosphinates were prepared by various methods. In the meantime, only few of these methods provide predominating *S*-alkylated products, due to the thiol-thione tautomerism of the substrates. *S*-Alkyldialkylthiophosphinates were synthesized by oxidation of *S*-alkyl dialkylthiophosphinite,[1] by reaction of R_2NSR on dialkylphosphinous acid,[2] or by treatment of sodium dialkylphosphinite with $RSSO_3Na$.[3]

The general drawback of these methods is associated with difficulties in preparing the phosphorus intermediates. On the other hand, reaction of sodium mercaptide[4] or xanthate[5] on dialkylphosphinyl chloride gives, as expected, *S*-alkyl dialkylthiophosphinate, but the yield is not satisfactory as a preparative method. Oxidative phosphinylation of a mercaptan affords, as reported by us,[6] *S*-alkyl dialkylphosphinates with 30% yield. Alkylation of dialkylthiophosphinic acid or its salts provides, as a rule, a mixture of *S*- and *O*-alkylated products, in which the distribution of two isomers is dependent on the structure of the alkylating agents.[7,8]

We report here a convenient method for the synthesis of *S*-alkyl dialkyl/diarylphosphinates based on a solid PTC alkylation of dialkyl/diarylthiophosphinic acid with alkyl bromide in the presence of potassium carbonate and tetrabutylammonium bromide (TBAB).



$$R^1_2\overset{S}{\overset{\|}{P}}{-}OH + R^2Br \xrightarrow[85\text{-}96\%]{K_2CO_3/n\text{-}Bu_4\overset{+}{N}Br^-,\ 60\text{-}70\,°C} R^1_2\overset{O}{\overset{\|}{P}}SR^2$$

1 **2**

2	R^1	R^2	**2**	R^1	R^2
a	n-C_5H_{11}	n-Bu	**j**	Ph	i-Bu
b	n-C_5H_{11}	i-Bu	**k**	Ph	s-Bu
c	n-C_5H_{11}	s-Bu	**l**	Ph	i-C_5H_{11}
d	n-C_5H_{11}	i-C_5H_{11}	**m**	c-C_6H_{11}	n-Bu
e	i-C_5H_{11}	n-Bu	**n**	c-C_6H_{11}	i-Bu
f	i-C_5H_{11}	i-Bu	**o**	c-C_6H_{11}	s-Bu
g	i-C_5H_{11}	s-Bu	**p**	c-C_6H_{11}	i-C_5H_{11}
h	i-C_5H_{11}	i-C_5H_{11}	**q**	n-C_8H_{17}	n-Bu
i	Ph	n-Bu			

The reaction proceeds chemoselectively and gives exclusively *S*-alkylated products as demonstrated by IR and ^{31}P-NMR studies. The catalytic effect of tetrabutylammonium bromide is obvious, since PTC *S*-butylation of dicyclohexylthiophosphinic acid provides significantly higher yield than that under non-

Table 1. *S*-Alkyl Dialkyl/arylthiophosphinates **2** Prepared

Product	Reaction Time (h)	Temp. (°C)	Solvent	Yield (%)	mp (°C) or bp (°C)/mbar	Molecular Formula[a] or Lit. Data
2a	0.25	60	–	85	149–150/0.3	$C_{14}H_{31}OPS$ (278.4)
2b	5.5	60	CH_3CN	40	145–148/0.5	$C_{14}H_{31}OPS$ (278.4)
2c	5.5	60	CH_3CN	34	128–131/0.3	$C_{14}H_{31}OPS$ (278.4)
2d	2	60	CH_3CN	54	149–152/0.4	$C_{15}H_{33}OPS$ (292.5)
2e	0.5	60	–	97	138–142/0.3	$C_{14}H_{31}OPS$ (278.4)
2f	1	60	–	78	128–131/0.3	$C_{14}H_{31}OPS$ (278.4)
2g	8	60	CH_3CN	36	127–129/0.3	$C_{14}H_{31}OPS$ (278.4)
2h	1	60	–	95	148–151/0.6	$C_{15}H_{33}OPS$ (292.5)
2i	1	60	–	91	183–184/0.4	bp 172–173/0.02[12]
2j	2	60	C_6H_6	38	179–181/0.3	mp 53.5[12]
2k	6	60	C_6H_6	41	116–117	$C_{16}H_{19}OPS$ (290.4)
2l	1	70	–	98	186–187/0.4	bp 158–159/0.04[12]
2m	0.5	70	–	95	185/0.4	$C_{16}H_{31}OPS$ (302.4)
2n	2	70	–	91	172–175/0.4	$C_{16}H_{31}OPS$ (302.4)
2o	8	70	–	63	61–62	$C_{16}H_{31}OPS$ (302.4)
2p	0.25	70	–	98	182/0.4	$C_{17}H_{33}OPS$ (316.5)
2q	0.25	80	CH_3CN	91	184–185/0.2	$C_{20}H_{43}OPS$ (362.5)

[a] Satisfactory microanalyses obtained: C ±0.25, H ±0.17, P ±0.38, S ±0.42.

Table 2. Spectral Data of Compounds **2**

Compound	IR (KCl) ν (cm^{-1})			^{31}P-NMR δ	MS m/z (%)	
	P–S–C	P=O	P–C		M$^+$	others
2a	500, 535	1180	710	57.59	279 (53)	152 (100)
2b	500, 535	1175	710	57.59	279 (63)	152 (40)
2c	505, 540	1175	710	56.93	279 (53)	221 (89)
2d	495, 535	1180	710	57.51	293 (58)	152 (100)
2e	500, 535	1180	750	58.59	279 (66)	221 (50)
2f	510, 540	1180	750	58.17	279 (100)	207 (63)
2g	500, 535	1180	750	58.51	279 (83)	221 (52)
2h	500, 540	1180	740	58.37	293 (43)	221 (51)
2i	525, 570	1200	760–700	39.47	291 (39)	201 (100)
2j	525, 570	1200	760–700	42.82	291 (100)	201 (86)
2k	530, 560	1200	740	41.56	291 (59)	201 (82)
2l	525, 570	1200	760–700	39.32	305 (17)	201 (100)
2m	535, 560	1180	750	67.21	303 (38)	164 (100)
2n	530, 558	1175	760–720	68.62	303 (59)	164 (100)
2o	525, 570	1200	760–700	68.48	303 (69)	164 (51)
2p	535, 560	1175	750	68.48	317 (55)	164 (100)
2q	580, 610	1255	750	28.34	363 (78)	113 (100)

catalytic alkylation. In the meantime, the yield of *S*-butylation of dioctylthiophosphinic acid in the presence of TBAB approaches to 91% within 0.25 hours, while the non-catalytic alkylation lasts 14 hours in order to achieve 84% yield.

The variation in polarity of solvent did not affect the product yield. Moreover, this chemospecific PTC *S*-alkylation could be carried on smoothly without solvent. Although the structure variation in alkyl groups of dialkylthiophosphinic acids has no significant influence on the reaction, the yield is evidently dependent on the alkyl bromide. The bulky alkyl bromide gives, as a rule, lower yield. As a typical S_N2 reaction, the *S*-alkylation process is governed by the nature of the leaving group, i.e., an alkyl bromide reacts smoothly while the corresponding chloride gives no reaction at all. It is necessary to point out that Makosza and his colleagues used alkali metal carbonates and tetraalkylammonium salt for the generation and reactions of a variety of carbanions.[9]

The present new method affords higher chemoselectivity and high yield of the alkylation reaction and it is simple to perform. Seventeen *S*-alkyl(aryl)thiophosphinic acids, among which fourteen compounds have not been reported hitherto, were synthesized by the present method (Table 1).

Melting points were determined on a Mettler FP 61 apparatus, potentiometric titration was performed with a glass electrode on a Metrohm 636 Titroprocessor, IR spectra were recorded on a Shimadzu 400 spectrophotometer. ^{31}P-NMR spectra were obtained on a FX 90Q spectrometer using 85% H_3PO_4 as external standard and $CDCl_3$ as solvent. Mass spectra were measured with a Finnigan 4021 spectrometer. Silicon-loaded paper chromatography was performed as described previously,[10] using *i*-PrOH/$CHCl_3$/NH_4OH (6:3:1) as eluent.

Dicyclohexylthiophosphinic acid (mp 136–137°C) and diphenylthiophosphinic acid (mp 147–148°C) were prepared by reaction of diethylphosphite with the appropriate Grignard reagents followed by addition of elemental sulfur and subsequent hydrolysis.[11] By an analogous method di(*n*-amyl)thiophosphinic acid and di(*i*-amyl)thiophosphinic acid (mp 66–68°C) were prepared with 88% and 93% yield, respectively.

S-Butyl Di(*i*-amyl)thiophosphinate (2e); Typical Procedure:

A mixture of di(*i*-amyl)thiophosphinic acid (**1**; $R^1 = n\text{-}C_5H_{11}$, 22.3 g, 0.1 mol), K_2CO_3 (13.8 g, 0.1 mol), TBAB (1 g), and *n*-butyl bromide (16.4 g, 0.12 mol) is heated at 60°C with vigorous stirring. The completion of the reaction is monitored by silicon-loaded paper chromatography until no more dialkylthiophosphinic acid can be detected. After cooling to room temperature, the reaction mixture is treated with ether (50 mL). The organic layer is then washed with water (3 × 30 mL), dried (Na_2SO_4), and evaporated. Upon fractional distillation, *S*-butyl di(*i*-amyl)thiophosphinate (**2e**) is obtained; yield: 27.1 g (97%); bp 138–142°C/0.4 mbar (Tables 1 and 2).

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