SYNTHESIS OF 2-SUBSTITUTED 1,3-BENZOTHIAZOLES BY AZA-WITTIG REACTION OF 2-METHYLTHIO-*N*-TRIPHENYL-PHOSPHORANYLIDENEANILINE WITH ACID CHLORIDES

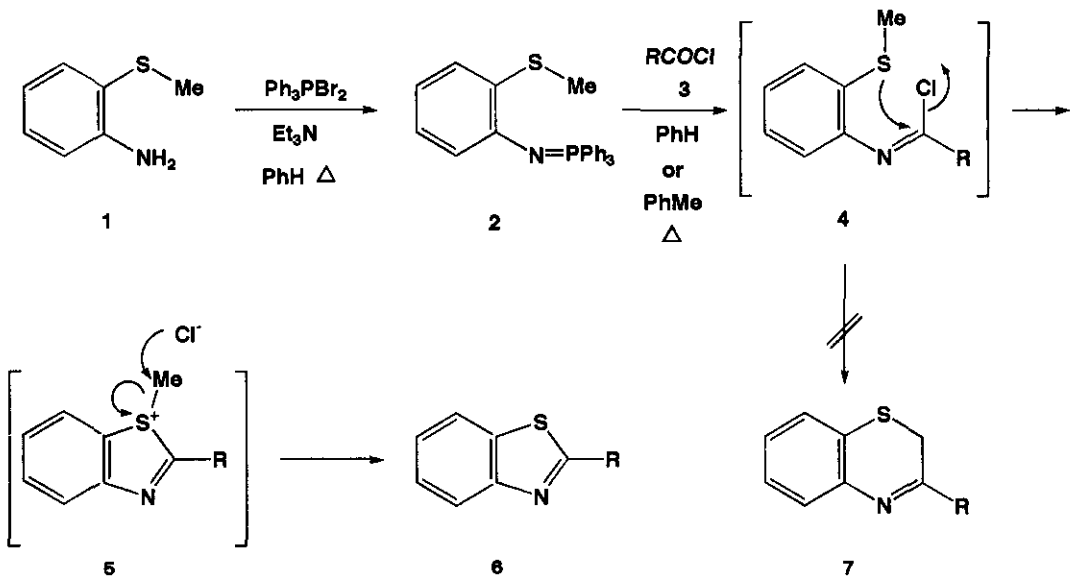
Masahiko Takahashi* and Masaru Ohba

Department of Materials Science, Faculty of Engineering, Ibaraki University, Hitachi, Ibaraki 316, Japan

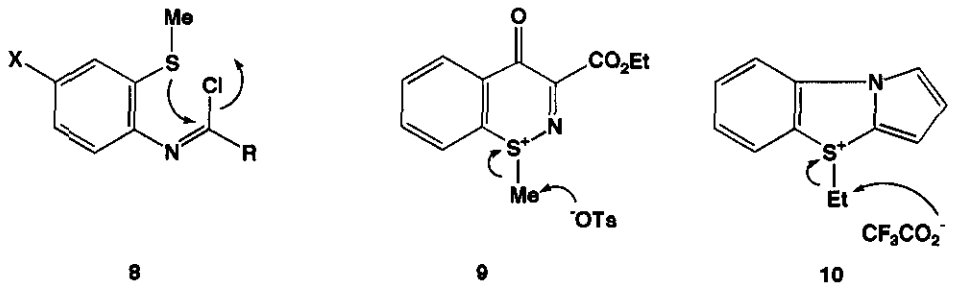
Abstract-The aza-Wittig reaction of 2-methylthio-*N*-triphenylphosphoranylidene-aniline (**2**) with acid chlorides (**3**) in refluxing benzene or toluene afforded 2-substituted 1,3-benzothiazoles (**6**)

In recent years aza-Wittig reactions have emerged as a powerful method for the synthesis of heterocyclic compounds.[1] However, most of compounds prepared by this method are nitrogen heterocycles. In connection with our interest in development of sulfur-containing building blocks for heterocycles,[2] we searched the literature about sulfur-containing iminophosphoranes and found that they are a rather unknown class of compounds; annulation of 1,3,4-thiadiazole ring into a 1,2,4-triazine ring was achieved by the intramolecular reaction between a thioamide group and carbodiimide functions which were derived from iminophosphoranes.[3] *N*-(Alkylthiomethyl)iminophosphoranes were prepared and applied to the synthesis of functionalized *N*, *S*-acetals.[4] Thus, we focused our attention to the compounds which would serve as building blocks for both sulfur and nitrogen-containing heterocycles. A simple iminophophorane, 2-methylthio-*N*-triphenylphosphoranylideneaniline (**2**) bearing an active methylthio group seemed to be suitable for this purpose. We would like to report a new aza-Wittig reaction of **2** with acid chlorides (**3**) to 2-substituted 1,3-benzothiazoles (**6**).[5]

We planned to synthesize 1,4-benzothiazines (**7**) by cyclization of imidoyl chlorides (**4**) on treatment with bases,



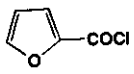
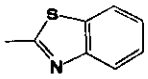
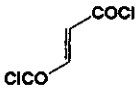
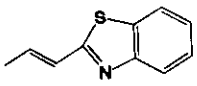
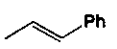
which could be formed from iminophophorane (**2**) and acid chloride (**3**). Iminophosphorane (**2**) was easily prepared[6] in 79% yield on treatment of **1** with triphenylphosphine dibromide in refluxing benzene in the presence of triethylamine. In order to prepare **4a** a mixture of **2** and benzoyl chloride (**3a**) in benzene was refluxed, and unexpectedly 2-phenyl-1,3-benzothiazole (**6a**) was obtained in 65% yield. The formation of **6a** would be explained by intramolecular nucleophilic attack of sulfur atom of the initially formed **4a** on the imidoyl chloride moiety to give **5** followed by nucleophilic attack of chloride ion to the methyl group of **5a**. The same type of reaction was already reported by Pilgram *et al.*;[7] the corresponding imidoyl chloride (**8**) was generated on treatment of *N*-acyl-2-methylthioaniline with phosgene. Further examples **9**[8] and **10**[9] about the nucleophilic displacement to methyl group on the sulfonium ion have appeared more recently.



Pilgram's method[7] for the preparation of 1,3-benzothiazoles is very limited; they prepared only 2-methyl- (86%), 6-chloro-2-cyclopropyl- (10%), and 2-dimethylaminobenzothiazoles (40%) by use of highly toxic

phosgene. In order to show the usefulness of our method we synthesized some 2-substituted 1,3-benzothiazoles (**6b-j**) in moderate yields and the results are shown in the Table. It has become apparent that 2-substituted 1,3-benzothiazoles having a variety of substituents such as aryl, heteroaryl, alkyl, and functionalized groups can be prepared by the present iminophosphorane-mediated cyclization.

Table. Synthesis of 2-substituted 1,3-benzothiazoles (6)

Acid Chlorides (3)	Products (6)	R	Solvents (at reflux for 24 h)	Yields %
PhCOCl	**6a**	Ph	Benzene	65
MeCOCl	**6b**	Me	Benzene	41
$ClCH_2COCl$	**6c**	$ClCH_2$	Benzene	32
$PhOCH_2COCl$	**6d**	$PhOCH_2$	Benzene	77
$PhCH_2COCl$	**6e**	$PhCH_2$	Toluene	72
	**6f**		Toluene	43
EtOCOCOCl	**6g**	CO_2Et	Toluene	70
$(COCl)_2$	**6h**		Toluene	5
	**6i**		Toluene	34
PhCH=CHCOCl	**6j**		Toluene	40

EXPERIMENTAL

All melting points were determined with a MRK MEL-TEMP II and uncorrected. Ir spectra were recorded on a JASCO A-102 spectrophotometer. Nmr spectra were taken with a JEOL GSX-400 and a JEOL JNM-PMX60. Mass spectra were obtained with a JEOL JMS DX-300.

2-Methylthio-*N*-triphenylphosphoranylideneaniline (2)

A Typical Procedure : A solution of bromine (16.0 g, 0.10 mol) in dry benzene (200 ml) was added dropwise to a stirred solution of triphenylphosphine (26.3 g, 0.10 mol) at 0-5°C under nitrogen atmosphere. The mixture was stirred in the ice bath for 4 h. A solution of **1** (13.9 g, 0.10 mol) and triethylamine (20.2 g, 0.20 mol) in dry benzene (100 ml) was added to the mixture at room temperature and the mixture was refluxed for 30 h The precipitates of triethylammonium bromide formed were removed by filtration and the mother liquor was concentrated *in vacuo*. The crude solids were collected by filtration and were recrystallized from benzene-hexane to give **2** (31.8 g, Y.79%), mp 158-160°C. Ir (KBr): 1560, 1460, 1425, 1320, 1100, 1010 cm^{-1}. Ms: 399 (M^+, 100%), 366 (90), 352 (M^+-SMe, 29), 308 (19), 290 (14), 262 (Ph_3P, 16), 183 (15). ^{1}H-Nmr ($CDCl_3$): δ 2.44 (s, 3H), 6.38-7.98 (m, 19H). *Anal.* Calcd for $C_{25}H_{22}NPS$: C, 75.20; H, 5.51; N, 3.51. Found: C, 75.43; H, 5.69; N, 3.49.

2-Phenyl-1,3-benzothiazole (6a)

Iminophosphorane (**1**) (2.0 g, 5.0 mmol) was dissolved into hot dry benzene (50 ml) under nitrogen atmosphere, and to this solution benzoyl chloride (0.70 g, 5.0 mmol) was added. After the mixture was refluxed for 24 h, removal of the solvent left a residue. Addition of hexane (40 ml) to the residue yielded precipitates of triphenylphosphine oxide, which were collected by filtration. Evaporation of the mother liquors left a solid, which was recrystallized from hexane to give **6a**, mp 115-117°C. It was identical with the commercially available authentic specimen.

2-Methyl-1,3-benzothiazole (6b)

After removal of triphenylphosphine oxide the residue was purified by bulb to bulb distillation followed by column chromatography on silica gel with an eluent of ethyl acetate-chloroform (2:3). Oil (lit.,[10] bp 123-124°C/20 mmHg).

2-Chloromethyl-1,3-benzothiazole (6c)

After removal of triphenylphosphine oxide the residue was purified by bulb to bulb distillation and sublimation under reduced pressure. mp 31-32°C (lit.,[11] mp 34°C).

2-Phenoxymethyl-1,3-benzothiazole (6d)

mp 75-77°C (hexane) (lit.,[11] mp 82-83°C).

2-Benzyl-1,3-benzothiazole (6e)

The product was purified by bulb to bulb distillation. Oil (lit.,[10] bp 165°C/1 mmHg).

2-(2-Furyl)-1,3-benzothiazole (6f)

mp 101-103°C (hexane) (lit.,[12] mp 104-105°C).

Ethyl 1,3-benzothiazole-2-carboxylate (6g)

mp 68-70°C (hexane) (lit.,[13] mp 69.8-70.5°C).

2,2'-Bi(1,3-benzothiazole) (6h)

After refluxing, the insoluble materials in the hot reaction mixture were removed by decantation. The insoluble materials in the cooled reaction mixture were collected by decantation of the solvent, triturated with ethanol, collected by filtration, and recrystallized from pyridine. mp 308-309°C (lit.,[14] mp 308-309°C).

***trans*-1,2-Di(2-1,3-benzothiazolyl)ethene (6i)**

After refluxing, the reaction mixture was cooled to form black precipitates, which were collected by filtration and were recrystallized from pyridine-toluene. mp 228-230°C (lit.,[15] mp 230-231°C).

2-Styryl-1,3-benzothiazole (6j)

mp 109-111°C (hexane) (lit.,[16] mp 112°C).

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