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Studies on Pyrimidine Derivatives and Related Compounds. LXIII.[1] Reactions of Thiazolium Salts with Dialkyl Acylphosphonates (Takamizawa Reaction 8)

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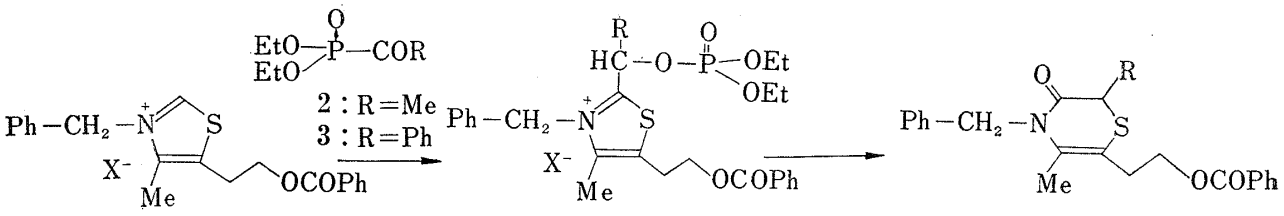
The reactions of diethyl acetyl- and diethyl benzoylphosphonate (**2**, **3**) with 3,4-dimethylthiazolium bromide (**8**) afforded 2-(1-diethylphosphoroyl)ethyl- and 2-(1-diethylphosphoroyl)benzyl-3,4-dimethylthiazolium bromides (**9**, **10**), which were decomposed to give 2-methyl- and 2-phenyl-4,5-dimethyl-2,3-dihydro-4H-1,4-thiazin-3-ones (**11**,**12**) by alkaline treatment. The reactions of **8** with dimethyl acetyl- and dimethyl benzoylphosphonate (**13**, **14**) gave the inner salts of O-methyl-O-1-(3,4-dimethyl-2-thiazolium)-ethyl- and O-methyl-O-1-(3,4-dimethyl-2-thiazolium)benzyl phosphoric acid (**15**, **16**). Similar adducts (**18**, **24**) were obtained from the reactions of **1b** with **13** and **14**. In a careful treatment, the inner salt (**26**) was found to be produced from 2-(1-diethylphosphoroyl)ethyl-3-benzyl-4-methyl-5-(2-benzoyloxy)ethylthiazolium bromide (**4**).

It has been previously reported[3] on the new reactions of thiamine and some other thiazolium compounds with diethyl acylphosphonates involving a novel rearrangement of thiazolium ring to 1,4-thiazines. During the course of the investigation of these reactions we succeeded[3d] in the isolation of the reaction intermediates, whose structures were confirmed both by chemically and by spectral evidences and clarified the reaction mechanism in the reactions of 3-benzyl-4-methyl-5-(2-benzoyloxy)ethylthiazolium halides (**1**) with diethyl acetyl (or benzoyl) phosphonates (**2**, **3**). The present paper deals with the reactions of 3,4-dimethylthiazolium iodide (**8**) and some other thiazolium salts with diethyl- and dimethyl acylphosphonates.



1a: X=Cl
b: X=Br
c: X=J

4 : R=Me, X=Br
5a: R=Ph, X=Cl
b: R=Ph, X=Br
c: R=Ph, X=J

6: R=Me
7: R=Ph

Chart 1

The 1:1 adduct, mp 120—121°, was obtained in a good yield by the reaction of **8** with **2** in the presence of triethylamine in dimethylformamide. The elemental analysis of the

1) Part LXII: A. Takamizawa, K. Hirai, S. Matsumoto, S. Sakai, and Y. Nakagawa, *Chem. Pharm. Bull.* (Tokyo), **17**, 910 (1969).
2) Location: *Fukushima-ku, Osaka.*
3) *a*) A. Takamizawa, Y. Sato, S. Tanaka, and H. Itoh, *Chem. Pharm. Bull.* (Tokyo), **14**, 407 (1966); *b*) A. Takamizawa and Y. Sato, *ibid.*, **14**, 742 (1966); *c*) A. Takamizawa, Y. Hamashima, Y. Sato, H. Sato, S. Tanaka, H. Itoh, and Y. Mori, *J. Org. Chem.*, **31**, 2951 (1966); *d*) A. Takamizawa, Y. Hamashima, and H. Sato, *J. Org. Chem.*, **33**, 4038 (1968).

adduct was in agreement with the expected formula, so it was assumed that the adduct has an analogous structure as that of **4** or **5**. The infrared spectrum showed a strong P=O band at 1278, and P–O–C bands at 1030 and 930 cm^{-1}. The nuclear magnetic resonance spectrum showed a typical CH_3–$\underset{|}{C}H$–O–P– four proton signal composed of a doublet and a quintet,[4] the latter splitting being caused by the coupling of the methine proton with phosphor nucleus, and the other signals gave also a good support for the structure of **9**. Alkaline treatment of **9** gave **11** in a good yield. From the data mentioned above it became clear that **8** gave the analogous product as the case of **1** in the reaction of **8** with diethyl acylphosphonate. The reaction of **8** with **3** afforded an oil (**10**), which gave **12** by an alkaline treatment,

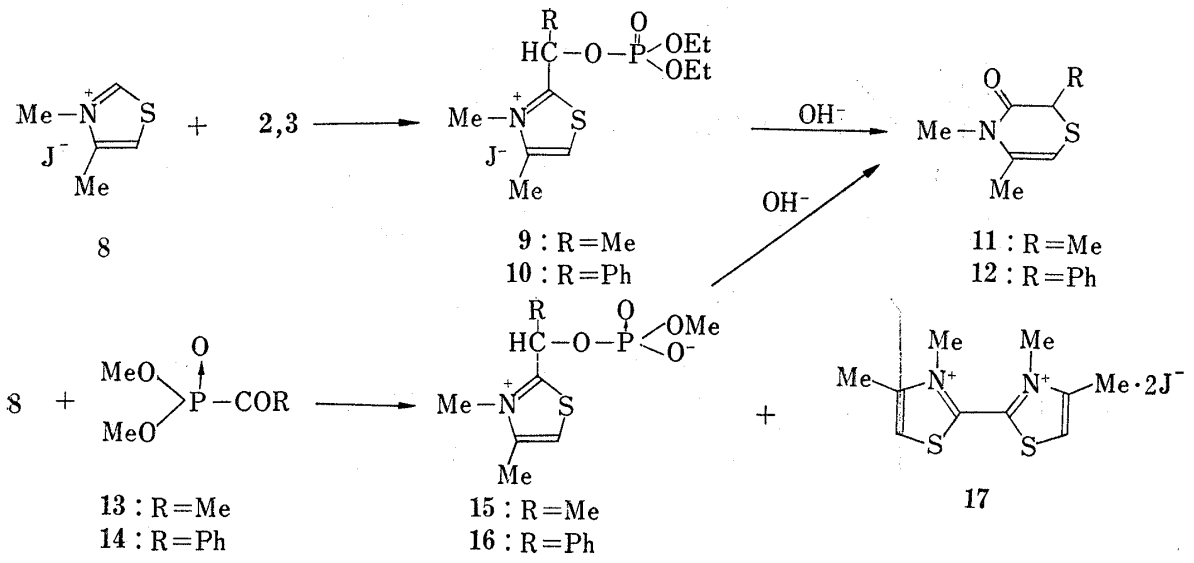


Chart 2

which suggest that **10** possesses quite analogous structure as that of **9**. From the reaction of **8** with dimethyl acetylphosphonate (**13**) was obtained **15**, mp 145—146°, which contrary to our expectations, contained no halogen, and the elemental analysis corresponded to the value less methyliodide than the 1:1 adduct of **8** and **13**. Moreover, **15** easily gave **11** in a good yield indicating that it is the similar intermediate as **9** and **10**. The infrared spectrum showed a P=O band at 1252, and P–O–C bands at 1100—1021 and 936 cm^{-1}. The NMR spectrum exhibited the proton signals as follows: 2.05 (q, 1H, thiazole–C_5–H, J=1.0), 4.34 (q-d, 1H, CH_3–$\underset{|}{C}H$–O–P, J_{HH}=6.8, J_{PH}=8.8), 5.98 (s, 3H, N–CH_3), 6.68 (d, 3H, O–CH_3, J_{PH}=10.8), 7.49 (d, 3H, thiazole–C_4–CH_3, J=1.0), 8.43 (d, 3H, CH_3–$\underset{|}{C}H$–O, J=6.8). Based on these data the structure of **15** was determined to be an inner salt of O-methyl-O-1-(3,4-dimethyl-2-thiazolium)ethylphosphoric acid. The structure of **16** which was quite analogously obtainable by the reaction of **8** with dimethyl benzoylphosphonate (**14**) was confirmed by the elemental analysis, infrared spectrum, and NMR spectral considerations (see Experimental section). It is interesting in obtaining inner salt in the reaction of **8** with **13** or **14**. From this point of view we reacted **1b** with **14** and obtained **18**, mp 185—188°, together with methyltriethylammonium bromide (**19**). **18** was assumed to have an analogous structure as that of **15** or **16** based on the data of the elemental analysis, infrared, and NMR spectrum, as well as the fact that **18** gave **7** and **20** by alkaline treatment. Furthermore, hydrogenation of **18** over palladium charcoal catalyst in the presence of sodium acetate in methanol gave **21**, which was proved to be identical with an authentic sample[3d] of **21** by

4) J.W. Emsley, J. Feeney, and L.H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 2, Pergamon Press, Ltd., Oxford, London, 1966, p. 1062.

their infrared spectra comparison. Contrary to our expectations were obtained **7**, 3-benzyl-4-methyl-5-(2-benzoyloxy)ethylthiazolin-2-one (**22**) and methylbenzamide (**23**), by the reaction of **18** with methylamine. The reaction of **1b** with **13** afforded an oil which gave **25** by an alkaline treatment suggesting that the product possesses analogous structure as that of **15**.

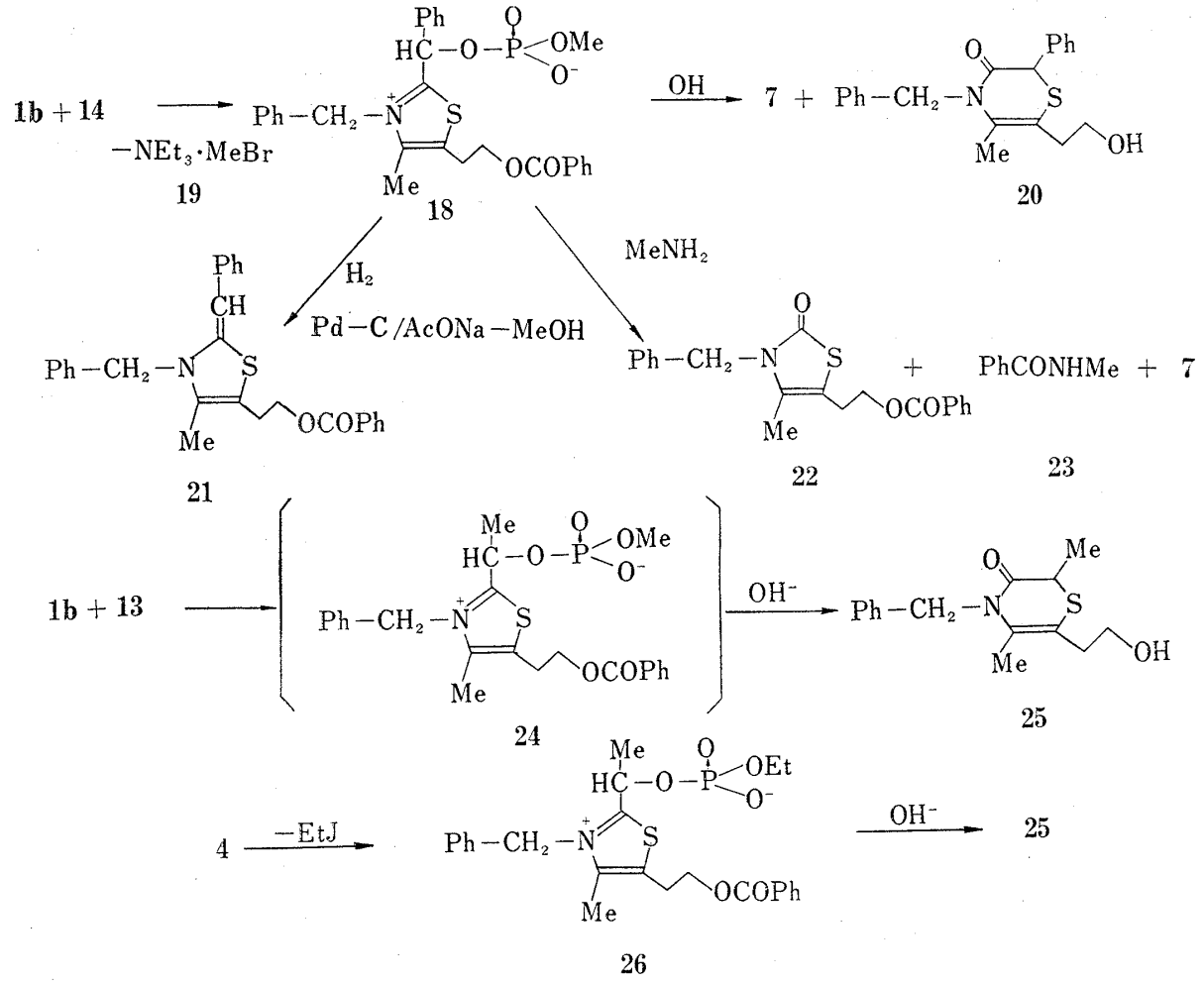


Chart 3

We clarified that the reactions of **1b** or **8** with **13** or **14** gave an addition products less methyl halide than the 1:1 adduct without exception as mentioned above, so we reinvestigated the reaction of **1b** with diethyl acetylphosphonate. We had already reported in the previous paper[3d] that the reaction of **1b** with **2** gave **4**. On standing the compound **4** for a few days at room temperature, we found another spot on the thin-layer chromatogram. The oil (**26**) newly obtained indicated the formula to be $C_{24}H_{28}O_6NSP$, which corresponded to the value less ethylbromide than **4**. The infrared spectrum showed C=O bands at 1714 and 1275, a P=O band at 1263, and P–O–C bands at 1118—1028 and 935 cm^{-1}. The NMR spectrum showed a proton signal due to ethoxyl group composed of a triplet and a quintet, a typical CH_3–CH< four proton signal composed of a doublet and a quintet, and the other signals gave a good support for the structure of **26**. Furthermore, alkaline treatment of **26** easily gave **25**. Consequently, the structure of **26** was concluded to be the inner salt same as **15** and **16**. The reaction of 3-benzyl-4-methylthiazolium bromide (**27**)[4] with **3** similarly gave an adduct (**28**), which afforded **29** in a good yield by treatment of alkali. The structures of both **28** and **29** were confirmed by their physical data. (See Experimental section.) An oil produced by the reaction of **30** with **3**, afforded **31** and **32** by alkaline treatment. Action of benzoylchloride or *p*-nitrobenzoylchloride on **32** gave **31** or *p*-nitrobenzoate (**33**).

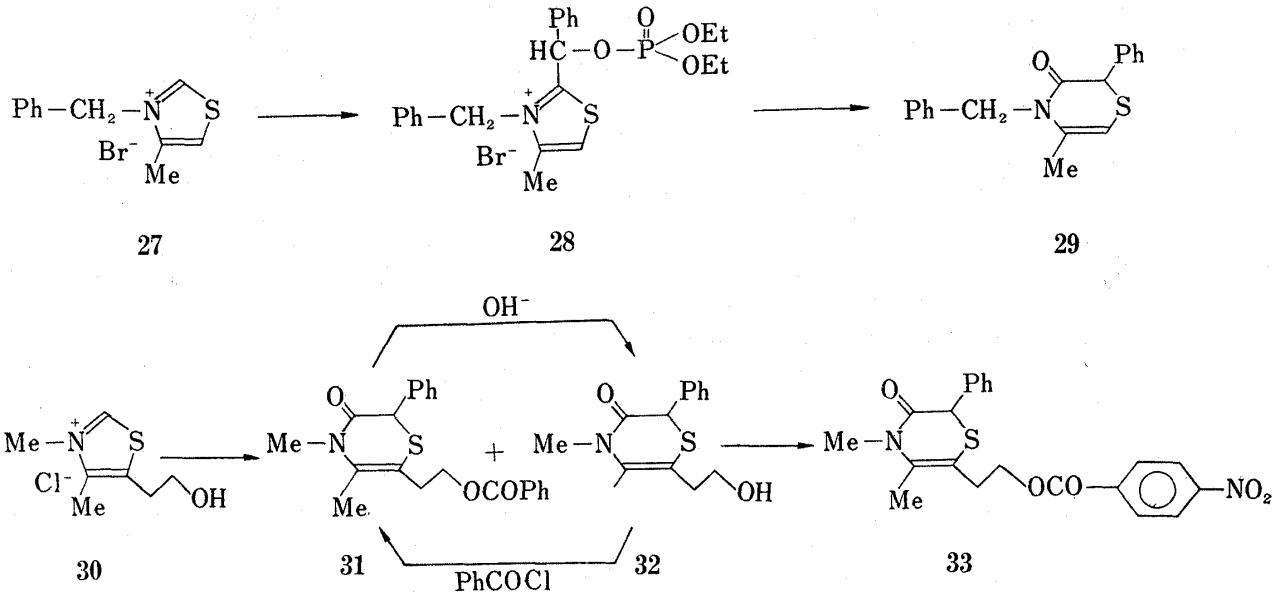


Chart 4

As described above, it has become clear that diethyl acylphosphonates easily reacted with thiazolium salts in general to give the 1:1 adducts which underwent ring expansion to 1,4-thiazine derivatives. It is also shown that the inner salts were obtained generally in these reactions. It may be considered that methoxyl group is more reactive than ethoxyl group, so the methoxyl group will undergo nucleophilic attack by halogen atom on it to give an inner salt involving the elimination of methyl halide. This assumption is also supported by the fact that an elimination reaction of ethylbromide in **4** is more slowly than that of methylbromide in **18**. These facts insist us to investigate the reactions of dialkyl acylphosphonates with other azolium compounds. Further work on these reactions is now in progress and will be described in near future.

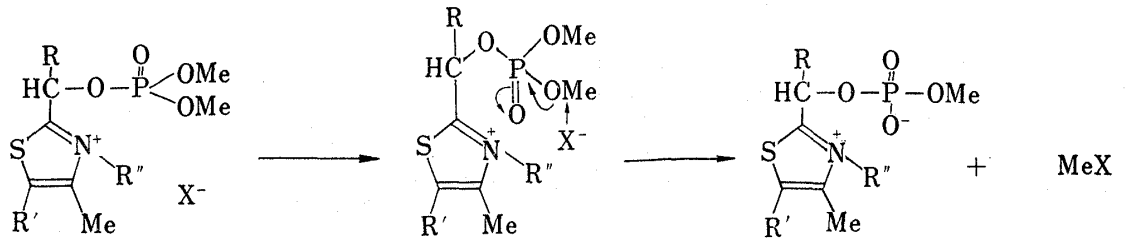


Chart 5

Experimental[5]

2-(1-Diethylphosphoryl)ethyl-3,4-dimethylthiazolium Iodide (9)——To an ice cooled mixture of **8** (1.21 g) and **2** (0.91 g) in dimethylformamide (10 ml) was added triethylamine (1.28 g) in nitrogen atmosphere and the mixture was stirred at 0—5° for 15 min, then the mixture reacted at room temperature for 24 hr. The resulting brown solution was concentrated *in vacuo* leaving brown crystalline residue, which was washed with ether and ethyl acetate. The light brown residue was recrystallized from acetone affording **9** as light brown rhombs, mp 120—121°. Yield, 62%. IR (Nujol, cm^{-1}): 1278 (P=O), 1030, 958 (P–O–C). *Anal.* Calcd. for $C_{11}H_{21}O_4NSIP$: C, 31.36; H, 5.03; N, 3.33; S, 7.61; I, 30.13; P, 7.35; OC_2H_5, 21.39. Found: C, 31.69; H, 5.18; N, 3.19; S, 7.38; I, 30.14; P, 7.63; OC_2H_5, 20.19.

5) All melting points were determined using a stirred Yamato Kagaku silicon oil bath. Infrared spectra were measured using a JASCO IR-S recording spectrophotometer. Proton magnetic resonance spectra were obtained using Varian A-60 Mc apparatus with tetramethylsilane as internal standard.

2-(1-Diethylphosphoryl)benzyl-3,4-dimethylthiazolium Iodide (10)——It was obtained as an oil by the similar method as that of **9** by reacting **8** (1.21 g), **3** (1.21 g), and triethylamine (1.28 g) in dimethylformamide (10 ml). The product was used for the next reaction without further purification.

2,4,5-Trimethyl-2,3-dihydro-4H-1,4-thiazin-3-one (11)——a) A mixture of **9** (0.211 g), ethanol (5 ml), and aqueous 10% sodium hydroxide (2 ml) was stirred at room temperature for 2 hr. After the concentration of the reaction mixture *in vacuo*, the residue was suspended in H_2O and extracted with $CHCl_3$. The oily residue after removal of the solvent was purified by distillation to give colorless oil, bp 80° (0.1 mmHg) (bath temperature). Yield, 0.065 g (82.7%). IR (film, cm^{-1}): 1660 (C=O). NMR ($CDCl_3$, τ): 4.55 (quartet, 1H, thiazole-C_5-H, $J=1.2$ cps), 6.68 (quartet, 1H, CH_3-C<u>H</u><, $J=7.0$ cps), 6.83 (singlet, 3H, N-CH_3), 7.95 (doublet, 3H, thiazole C_4-CH_3, $J=1.2$ cps), 8.58 (doublet, 3H, C<u>H</u>$_3$-CH<, $J=7.0$ cps). *Anal.* Calcd. for $C_7H_{11}ONS$: C, 53.49; H, 7.05; N, 8.91; S, 20.38. Found: C, 53.21; H, 7.15; N, 9.32; S, 20.31.

b) To 80% ethanol solution (10 ml) containing 1 g of sodium hydroxide was added 0.54 g of **15**, and the mixture was warmed at 80° for 5 hr. After that the mixture was concentrated to leave oily residue, which was extracted with $CHCl_3$. The $CHCl_3$ extract was washed, dried, and concentrated leaving **10** as oily residue, bp 75—78° (0.1 mmHg). Yield, 0.22 g.

2-Phenyl-4,5-dimethyl-2,3-dihydro-4H-1,4-thiazin-3-one (12)——a) **10** obtained above was treated with alcoholic sodium hydroxide in a similar manner mentioned above. The product was purified through aluminium oxide column chromatography. Recrystallization of the solid from ether gave **12** as colorless sticks, mp 91—92°. Yield, good. IR (Nujol, cm^{-1}): 1658 (C=O). NMR ($CDCl_3$, τ): 2.70 (singlet, 5H, C_6H_5-), 4.60 (multiplet, 1H, thiazine-C_6-<u>H</u>, $J=1.6$ cps), 6.75 (singlet, 3H, N-CH_3), 8.02 (doublet, 3H, thiazine C_5-CH_3, $J=1.0$ cps). *Anal.* Calcd. for $C_{12}H_{13}ONS$: C, 65.74; H, 5.98; N, 6.39; S, 14.60. Found: C, 65.46; H, 5.89; N, 6.15; S, 14.57.

b) To a mixture of sodium hydroxide (0.2 g), ethanol (3 ml), and H_2O (0.5 ml) was added **16** (0.15 g), the mixture was warmed at 70—90° for 3 hr. The reaction mixture was concentrated to leave oily residue, which was extracted with $CHCl_3$, and the $CHCl_3$ extract was washed with water, dried and concentrated to leave crystalline residue, which was recrystallized from ether to give **12** as colorless sticks, mp 91—92°. Yield, 0.05 g.

Reaction of 8 with Dimethyl Acetylphosphonate (13)——To an ice cooled mixture of **8** (1.21 g) and **13** (0.76 g) in dimethylformamide (10 ml) was added triethylamine (1.28 g) dropwise, then the mixture reacted at room temperature for 60 hr affording red brown solution. Concentration of the solution *in vacuo* left oily residue, which was submitted to silicagel chromatography. Elution with acetone gave **11** as an oil (0.16 g). From the methanol elucible fraction was obtained light brown solid, which was recrystallized from methanol–acetone giving **15** as light brown sticks, mp 145—146°. Yield, 0.96 g. *Anal.* Calcd. for $C_8H_{14}O_4NSP\cdot H_2O$: C, 35.70; H, 5.99; N, 5.21; P, 11.50; OCH_3, 11.51. Found: C, 35.91; H, 6.23; N, 5.09; P, 11.17; OCH_3, 12.63.

Reaction of 8 with Dimethyl Benzoylphosphonate (14)——To an ice cooled solution of **8** (1.21 g) and **14** (1.08 g) in dimethylformamide (10 ml) was added triethylamine (1.28 g) in nitrogen atmosphere and the mixture was stirred at 2—5° for 20 min, then the mixture reacted at room temperature for 40 hr. The reaction mixture was filtered. The filtered mass (0.145 g) was recrystallized from large amount of methanol to give 2,2′-bis(3,4-dimethylthiazolium)diiodide (**17**) as yellow cubics, mp 260—265°. *Anal.* Calcd. for $C_{10}H_{14}N_2S_2I_2$: C, 25.01; H, 2.94; N, 5.84; S, 13.34; I, 52.85. Found: C, 24.83; H, 2.62; N, 5.96; S, 13.24; I, 52.67. The filtrate was concentrated *in vacuo* leaving brown residue, which was washed with ether to give brown solid. Recrystallization from ethanol–acetone gave **16** as colorless plates, mp 210—213°. Yield, 1.07 g. IR (Nujol, cm^{-1}): 1252 (P=O), 1099—1014 (P–O–C). NMR (d_6-DMSO, τ): 2.02 (diffused quartet, 1H, thiazole-C_5-<u>H</u>), 2.53 (singlet, 5H, C_6H_5), 3.32 (doublet, 1H, C_6H_5-C<u>H</u>–O–P, $J_{HP}=9.5$ cps), 6.10 (singlet, 3H, N-CH_3), 6.85 (doublet, 3H, OCH_3, $J_{HP}=11.0$ cps), 7.50 (doublet, 3H, thiazole-C_4-CH_3, $J=0.8$ cps). *Anal.* Calcd. for $C_{13}H_{16}O_4NSP$: C, 49.83; H, 5.15; N, 4.47; P, 9.89; OCH_3, 9.91. Found: C, 49.19; H, 4.99; N, 4.28; P, 9.87; OCH_3, 9.63.

Reaction of 1b with 14——To a mixture of **1b** (4.18 g) and triethylamine (2.02 g) in dimethylformamide (25 ml) was added **14** (2.14 g) in nitrogen atmosphere and the mixture was stirred at 2—5° for 30 min, then the mixture reacted at room temperature for 20 hr. The resulting dark green solution was concentrated *in vacuo* leaving dark green crystalline residue, which was washed with ether, ethyl acetate, and acetone The light brown crystalline residue was recrystallized from methanol–acetone or acetonitrile affording **18** as colorless sticks, mp 185—188° (decomp.). Yield, 5.8 g. IR (Nujol, cm^{-1}): 3400 (OH) 1716, 1280 (COO), 1258 (P=O), 1099—1038 (P–O–C). NMR ($CDCl_3$, τ): 1.97—3.33 (multiplet, 16H, aromatic proton, C_6H_5-C<u>H</u>–), 3.72, 4.17 (AB quartet, 2H, C_6H_5-C<u>H</u>$_2$-N, $J=17.1$ cps), 5.42 (triplet, 2H, -C<u>H</u>$_2$-O, $J=6.0$ cps), 6.68 (triplet, 2H, -CH_2-CH_2O-, $J=6.0$ cps), 6.73 (doublet, 3H, CH_3O, $J=11.0$ cps), 7.70 (singlet, 3H, thiazole C_4-CH_3). *Anal.* Calcd. for $C_{28}H_{28}O_6NSP\cdot H_2O$: C, 61.65; H, 5.54; N, 2.57; P, 5.87; OCH_3, 5.68. Found: C, 62.05; H, 5.36; N, 2.65; P, 5.64; OCH_3, 6.20.

Alkaline Treatment of 18——A solution of **18** (0.5 g) in 80% ethanol (15 ml) containing 1 g of sodium hydroxide was warmed at 50° for 2 hr to result brown solution, which was concentrated and the residue was extracted with $CHCl_3$. The $CHCl_3$ extract was washed, dried, and submitted over aluminium oxide chromato-

graphy. Elution with ether gave 0.05 g of **7** as colorless sticks, mp 103—104° (lit. [3b] mp 104—106°). Elution with ethyl acetate gave 0.17 g of **20** as colorless needles, mp 107—109° (lit.[3b] mp 108—109°).

Catalytic Hydrogenation of 18 with Palladium-Charcoal——**18** (0.55 g) and sodium acetate (0.25 g) were dissolved in 40 ml of methanol and hydrogenated at atmospheric pressure at room temperature over 0.5 g of 10% palladium–charcoal catalyst. Complete hydrogenation was observed about after approximately 25 ml of hydrogen had been consumed within 3.5 hr. The solution was filtered free of the catalyst by suction and the filtrate was concentrated, neutralized, and extracted with $CHCl_3$. The crystalline residues after removal of the solvent were chromatographed over aluminium oxide and eluted with ether giving **21** as yellow plates, mp 107—108°, which was proved to be identical with an authentic specimen by their infrared spectra comparison. Yield, 0.08 g.

Action of Methylamine on 18——To a cooled solution (−70°) of **18** (1.0 g) in ethanol (10 ml) was added 8.6% methylamine solution in ethanol (25 ml) was added under stirring. The solution was stirred at the temperature for 1 hr, then the bath was removed and the mixture was stirred at room temperature for 10 hr. The solution was concentrated and the residue was submitted over silicagel chromatography and eluted using ether at first. From the first fraction was obtained **7** as colorless sticks, mp 102—104° (0.075 g). From the folllowing fraction was obtained **22** (0.13 g), mp 77—79°. After that acetone was used as a solvent and was obtained 0.1 g of methylbenzamide (**23**) as colorless plates, mp 80—82°.

Reaction of 1b with 13——To a cooled mixture of **1b** (2.09 g) and triethylamine (1.1 g) in dimethylformamide (15 ml) was added **13** (0.76 g) in nitrogen atmosphere, the mixture was stirred at 0—5° for 20 min, then the mixture reacted at room temperature for 20 hr. The reaction mixture was concentrated *in vacuo* leaving dark brown oil. Acetone was added to the oil and the precipitated solid (methyltriethylammonium bromide) was removed by filtration (0.2 g), and the filtrate was concentrated. To the residue was added 80 % ethanol (30 ml) containing 3 g of sodium hydroxide and the solution was heated on a steam bath for 30 min. The reaction mixture was concentrated and the residue was extracted with $CHCl_3$. The $CHCl_3$ extract was washed, dried, and concentrated leaving oily residue, which was chromtographed over silicagel and obtained 0.6 g of **25** as light brown oil.

Inner Salt of O-Ethyl-O-1-{3-benzyl-4-methyl-5-(2-benzoyloxy)ethylthiazolium(2)} ethylphosphoric Acid——**4** was allowed to stand at room temperature for a week resulting an appearance of another spot on the thin-layer chromatogram (methanol–silicagel). The oil was submitted to silicagel chromatography and eluted with methanol affording **26** as a colorless oil. IR (film, cm^{-1}): 1714, 1275 (COO), 1263 (P=O), 1118—1028, 935 (P–O–C). NMR ($CDCl_3$, τ); 1.98—3.10 (multiplet, 10H, aromatic proton), 3.92, 4.17 (AB quartet, 2H, C_6H_5–$C\underline{H}_2$–, J=18.0 cps), 4.17 (quintet, 1H, CH_3–$C\underline{H}$–O–P, $J_{HH}=J_{HP}$=6.5 cps), 5.43 (triplet, 2H, –$C\underline{H}_2$–O–, J=6.0 cps), 6.08 (quintet, 2H, CH_3–$C\underline{H}_2$–O–P, $J_{HH}=J_{PH}$=7.1 cps), 6.63 (triplet, 2H, –$C\underline{H}_2$–CH_2O–, J=6.0 cps), 7.65 (singlet, 3H, thiazole C_4–CH_3), 8.50 (doublet, 3H, $C\underline{H}_3$–CH–O–P, J=6.5 cps), 8.82 (triplet, 3H, $C\underline{H}_3$–CH_2–O–P, J=7.1 cps). *Anal.* Calcd. for $C_{24}H_{28}O_6NSP$: C, 58.86; H, 5.76; N, 2.80; P, 6.33. Found: C, 59.76; H, 5.99; N, 2.63; P, 6.12. **26** easily gave **25** by treating with aqueous alkali.

2-(1-Diethylphosphoroyl)benzyl-3-benzyl-4-methylthiazolium Bromide (28)——**28** was obtained by the similar method as that of **9** using 0.9 g **27**, 0.8 g of triethylamine, and 0.8 g of **3** in dimethylformamide (10 ml). Recrystallization of the solid from acetone–ethyl acetate gave colorless needles, mp 114—116°. Yield, 0.97 g. IR (Nujol, cm^{-1}): 1270 (P=O), 1026, 994 (P–O–C). NMR ($CDCl_3$, τ): 2.36—3.30 (multiplet, 12H, aromatic proton, C_6H_5–$C\underline{H}$< and, thiazole C_5–$\underline{H}$), 3.95, 4.20 (AB quartet, 2H, C_6H_5–$C\underline{H}_2$–, J=16.8 cps), 6.15 (quintet, 4H, CH_3–$C\underline{H}_2$–OX, $J_{HH}=J_{PH}$=7.1 cps), 7.56 (doublet, 3H, thiazole C_4–CH_3, J=0.8 cps), 8.81 (triplet of doublet, 3H, $C\underline{H}_3$–CH_2O–, J_{HH}=7.1 cps, J_{PH}=1.0 cps), 8.91 (triplet of doublet, 3H, $C\underline{H}_3$–CH_2–O–, J_{HH}=7.1 cps, J_{PH}=1.0 cps). *Anal.* Calcd. for $C_{22}H_{27}O_4NBrSP$: C, 51.56; H, 5.32; N, 2.74; S, 6.26; P, 6.04; OC_2H_5, 17.57. Found: C, 51.17; H, 5.70; N, 3.02; S, 6.89; P, 5.67; OC_2H_5, 17.21.

2-Phenyl-4-benzyl-5-methyl-2,3-dihydro-4H-1,4-thiazin-3-one (29)——A mixture of **28** (0.26 g), sodium hydroxide (0.25 g), ethanol (3 ml), and H_2O (0.5 ml) was stirred at room temperature for 3 hr. The mixture was concentrated and the residue was extracted with $CHCl_3$. The $CHCl_3$ extract was purified through aluminium oxide column chromatography to give colorless sticks (ether), mp 80—81°. Yield, 0.11 g. IR (Nujol, cm^{-1}): 1656 (CO). NMR ($CDCl_3$, τ): 2.67 (singlet, 5H, aromatic proton), 2.76 (doublet, 5H, aromatic proton), 4.55 (multiplet, 1H, thiazine–C_6–H), 4.78, 5.18 (AB quartet, 2H, C_6H_5–$C\underline{H}_2$–, J=16.4 cps), 5.45 (doublet, 1H, C_6H_5–$C\underline{H}$–, J=1.6 cps), 8.13 (doublet, 3H, thiazine C_5–CH_3, J=1.1 cps). *Anal.* Calcd. for $C_{18}H_{17}ONS$: C, 73.20; H, 5.80; N, 4.74; S, 10.84. Found: C, 73.31; H, 5.81; N, 4.48; S, 10.71.

Reaction of 30 with 2 Equivalent of Diethyl Benzoylphosphonate (3)——To an ice cooled suspension of **30** (9.2 g) and triethylamine (20.2 g) in dimethylformamide (80 ml) was added **3** (24.2 g) in nitrogen atmosphere and the mixture was stirred at 2—10° for 30 min, then the mixture reacted at room temperature for 24 hr resulting brown solution. The solution was concentrated *in vacuo* leaving brown residue, which did not crystallized. The residue was dissolved in $CHCl_3$ and $CHCl_3$ solution was shaken with 10% sodium carbonate solution and dried. The residue after removal of the solvent was chromatographed over aluminium oxide and eluted with $CHCl_3$. From the first fraction was obtained colorless solid, which was recrystallized from ether to afford **31** as colorless sticks, mp 90°. Yield, 6.2 g (33.7%). IR (Nujol, cm^{-1}): 1711, 1665,

1273, 1118. NMR ($CDCl_3$, τ): 2.02—2.65 (multiplet, 5H, aromatic proton), 2.80 (singlet, 5H, aromatic proton), 5.51 (singlet, 1H, C_6H_5–C<u>H</u>〈), 5.85 (double triplet, 2H, –CH_2–C<u>H_2</u>–O–, J=6.0, 4.2 cps), 6.74 (singlet, 3H, N–CH_3), 7.40 (multiplet, 2H, –C<u>H_2</u>–CH_2–O–), 7.97 (singlet, 3H, thiazine C_5–CH_3). *Anal.* Calcd. for $C_{21}H_{21}O_3NS$: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.99; H, 5.82; N, 3.96.

From the second fraction was obtained **32** as colorless oil, bp 200—210° (0.06 mmHg) (bath temp.). Yield, 4.3 g (32.7%). IR (film, cm^{-1}): 3550, (OH), 1652 (C=O), 1033 (OH). NMR ($CDCl_3$, τ): 2.75 (singlet, 5H, aromatic proton), 5.48 (singlet, 1H, C_6H_5–C<u>H</u>〈), 6.59 (triplet, 2H, –CH_2–C<u>H_2</u>–O, J=5.8 cps), 7.68 (triplet, 2H, –C<u>H_2</u>–CH_2–O–, J=5.8 cps), 8.00 (singlet, 3H, thiazine C_5–CH_3), 8.38 (broad singlet, OH). *Anal.* Calcd. for $C_{14}H_{17}O_2NS$: C, 63.86; H, 6.51; N, 5.32. Found: C, 64.09; H, 6.67; N, 5.60.

Hydrolysis of 31——A solution of **31** (3.0 g) in 75% ethanol (20 ml) containing sodium hydroxide (1.0 g) was warmed at 70° for 1 hr. The reaction mixture was concentrated leaving oily residue, which was extracted with $CHCl_3$, and $CHCl_3$ extract was washed, dried, and concentrated. The residue was purified by distillation, and obtained 2.0 g (93%) of **32** as colorless oil.

2-Phenyl-6-(2-*p*-nitrobenzoyloxy)ethyl-4,5-dimethyl-2,3-dihydro-4H-1,4-thiazin-3-one (33)——**31** (0.257 g) reacted with *p*-nitrobenzoylchloride (0.3 g) at room temperature for 40 hr in pyridine (3 ml). The solution was concentrated. The residue was extracted with $CHCl_3$ and $CHCl_3$ extract was washed with cooled aqueous sodium hydroxide, H_2O, and dried. Purification through column chromatography gave **33** as colorless needles (ether), mp 88°. Yield, 0.29 g (72%). *Anal.* Calcd. for $C_{21}H_{20}O_5N_2S$: C, 61.16; H, 4.89; N, 6.79; S, 7.77. Found: C, 61.22; H, 5.00; N, 6.84; S, 7.82.