[Chem. Pharm. Bull. 29(10)2837—2843(1981)]

# Studies on Pyrimidine Derivatives. XXIII.[1] Synthesis of Acylmethylpyrimidines and Related Compounds *via* Imidoyl-substituted Oxosulfonium Ylides[2]

Hiroshi Yamanaka,* Shoetsu Konno, Takao Sakamoto, Setsuko Niitsuma, and Sayo Noji

*Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan*

(Received March 30, 1981)

The reaction of 2- and 4-chloropyrimidines with dimethyloxosulfonium methylide afforded the corresponding pyrimidinylmethylides. Pyrimidine derivatives containing a functionalized side chain such as acetonyl, phenacyl, ethoxycarbonyl, or N-phenylcarbamoyl were synthesized by acylation of the pyrimidinylmethylides followed by desulfurization of the resulting pyrimidinylacylmethylides.

**Keywords**——nucleophilic substitution; dimethyloxosulfonium methylide; chloropyrimidine; acylmethylpyrimidine; desulfurization; acetonyldiazine

There have been several papers[3–5] dealing with the reaction of 2- and 4-chloropyrimidines with active methylene compounds under basic conditions. However, this type of the reaction does not appear to represent a good procedure for the preparation of acylmethylpyrimidines, because in general the reported yields of the products were unsatisfactory. For example, Brown *et al.*[5] investigated the condensation of 2-chloro-4,6-dimethylpyrimidine (I) with dimethyl malonate and reported the overall yield of ethyl 4,6-dimethylpyrimidine-2-acetate to be less than 20% starting from I. We were unable to obtain a markedly better result.

On the other hand, dimethyloxosulfonium methylide (II)[6] generated from trimethyloxosulfonium chloride by the action of a strong base is known to have excellent nucleophilicity.

For example, Kunieda *et al.*[7] utilized this reagent (II) for the methylation of a 2,5-cyclic uridine and obtained the corresponding 2-methyl derivatives as illustrated below. Later Gilchrist *et al.*[8] reported the preparation of imidoyl-substituted oxosulfonium ylides by the reaction of II with various imidoyl chlorides. In that paper they stated that these reactions provided a very convenient method for the alkylation of heteroaromatic compounds such as 2-chloropyrimidine.

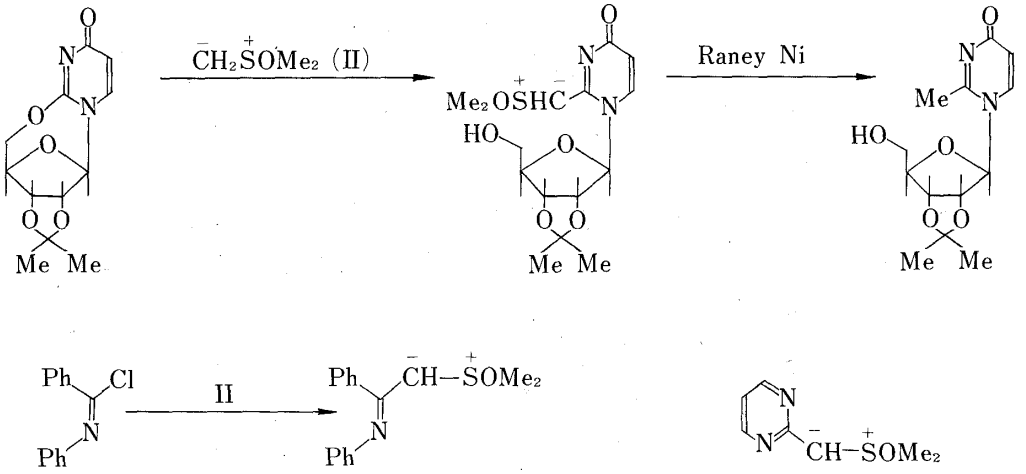


Chart 1

As a part of our investigations[9] on the synthesis of pyrimidine derivatives with a functionalized carbon substituent, we were interested in the application of Gilchrist' work to the preparation of these pyrimidine derivatives. The present paper describes the condensation of 2- and 4-chloropyrimidines with II, acylation of the resultant pyrimidinylmethyl sulfur ylide, and desulfurization of the acylated ylide to give 2- and 4-acylmethylpyrimidines.

When dimethyloxosulfonium methylide (II) prepared by Corey's method[6] was heated with 2-chloro-4,6-dimethylpyrimidine (I) in tetrahydrofuran, colorless crystals (mp 101.5—103°C) were obtained. The elemental analysis of this product (III) established its empirical formula to be $C_9H_{14}N_2OS$. The proton magnetic resonance (PMR) spectrum of III reveals the presence of four methyl groups. These data are consistent with the dimethyloxosulfonium 4,6-dimethylpyrimidinylmethylide structure. This compound was readily acylated by treatment with acetic anhydride, benzoyl chloride, or ethoxycarbonyl chloride in dioxane at room temperature to give the acetyl (IVa), benzoyl (IVb), or ethoxycarbonyl (IVc) derivative in good yield. Phenyl isocyanate also reacted with III under similar conditions and the N-phenylcarbamoyl derivative (IVd) was obtained in almost quantitative yield.

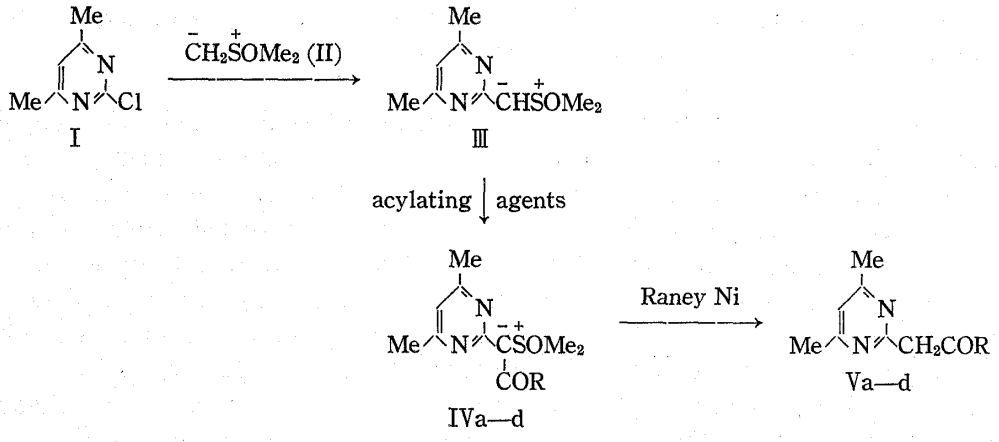


Chart 2

TABLE I. Physical and Analytical Data for Compounds IV and V

| Compd. No. | R | Yield (%) | mp (°C) or bp (°C/mmHg) | Appearance (recryst. solvt.) | Formula | Analysis (%) Calcd (Found) C | H | N | S |
|---|---|---|---|---|---|---|---|---|---|
| IVa | Me | 73 | 131—131.5 | Needles ($Et_2O$) | $C_{11}H_{16}N_2O_2S$ | 54.97 (54.74 | 6.71 6.59 | 11.66 11.59 | 13.34 12.99) |
| IVb | Ph | 80 | 167—170 | Needles (AcOEt–hexane) | $C_{16}H_{18}N_2O_2S$ | 63.55 (63.25 | 6.00 6.00 | 9.26 9.07 | 10.60 10.52) |
| IVc | OEt | 82 | 90—91 | Prisms ($Et_2O$) | $C_{12}H_{18}N_2O_3S$ | 53.31 (53.07 | 6.71 6.78 | 10.36 10.27 | 11.86 12.03) |
| IVd | NHPh | 95 | 178—179 | Plates ($Et_2O$–$CH_2Cl_2$) | $C_{16}H_{19}N_3O_2S$ | 60.55 (60.33 | 6.04 6.11 | 13.24 13.16 | 10.08 9.95) |
| Va | Me | 68 | 95/4 | Liquid | $C_9H_{12}N_2O$ | 65.83 (65.86 | 7.37 7.49 | 17.06 16.96) | |
| Vb | Ph | 67 | 76—77 (lit. 74—75.5) | Prisms ($Et_2O$–petr. ether) | a) | | | | |
| Vc | OEt | 71 | 62—66 (lit. 65—67) | Prisms (petr. ether) | a) | | | | |
| Vd | NHPh | 79 | 115—116 | Needles ($Et_2O$–hexane) | $C_{14}H_{15}N_3O$ | 69.69 (69.90 | 6.27 6.06 | 17.42 17.36) | |

a) These compounds have been reported in the literature.[5,11]

Desulfurization of these products (IVa—d) with deactivated Raney nickel[10] in boiling methanol for 30 minutes gave rise to the corresponding 2-acylmethylpyrimidines (Va—d). The use of freshly prepared Raney nickel or a prolonged reaction time in the presence of the deactivated nickel yielded a mixture from which it was difficult to purify the desired products, probably due to contamination with over-reduced by-products. Although the PMR spectra

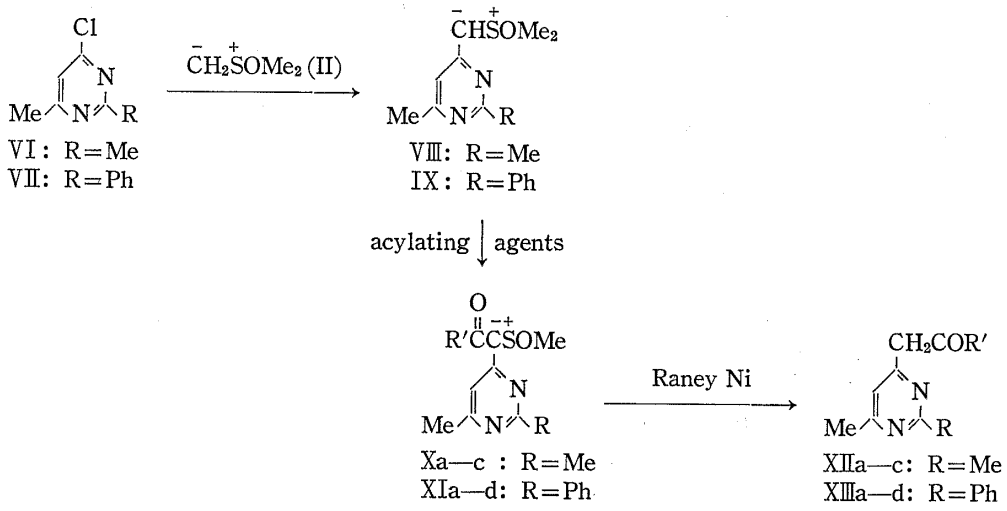


Chart 3

TABLE II. Physical and Analytical Data for Compounds X, XI, XII and XIII

| Compd. No. | R | R′ | Yield (%) | mp (°C) or bp (°C/mmHg) | Appearance (recryst. solvt.) | Formula | Analysis (%) Calcd (Found) C | H | N | S |
|---|---|---|---|---|---|---|---|---|---|---|
| Xa | Me | Me | 71 | 185—187 | Needles (THF–cyclohexane) | $C_{11}H_{16}N_2O_2S$ | 54.97 (54.76 | 6.71 6.78 | 11.66 11.50 | 13.34 13.11) |
| Xb | Me | Ph | 97 | 123—124.5 | Needles (THF–cyclohexane) | $C_{16}H_{18}N_2O_2S$ | 63.56 (63.51 | 6.00 6.16 | 9.27 9.11 | 10.58 10.66) |
| XIa | Ph | Me | 88 | 184.5—185 | Prisms ($Et_2O$–$CH_2Cl_2$) | $C_{16}H_{18}N_2O_2S$ | 63.56 (63.06 | 6.00 6.09 | 9.27 9.30 | 10.58 10.50) |
| XIb | Ph | Ph | 84 | 173—174 | Needles (THF–cyclohexane) | $C_{21}H_{20}N_2O_2S$ | 69.21 (68.83 | 5.53 5.84 | 7.69 8.04 | 8.78 8.93) |
| XIc | Ph | OEt | 81 | 150—151 | Needles ($CH_2Cl_2$–$Et_2O$) | $C_{17}H_{20}N_2O_3S$ | 61.43 (61.64 | 6.07 6.22 | 8.43 8.15 | 9.63 9.64) |
| XIIa | Me | Me | 76 | 73—74/0.5 (lit. 75—76/0.5) | Liquid | a) | | | | |
| XIIb | Me | Ph | 87 | 142—148/3 (lit. 146—150/0.1) | Liquid | a) | | | | |
| XIIc | Me | NHPh | 77 | 83—84 | Needles ($CH_2Cl_2$–petr. ether) | $C_{14}H_{15}N_3O$ | 69.69 (69.44 | 6.27 6.29 | 17.42 17.66) | |
| XIIIa | Ph | Me | 88 | 138/3 | Liquid | $C_{14}H_{14}N_2O$ | 74.31 (74.37 | 6.24 6.23 | 12.38 12.41) | |
| XIIIb | Ph | Ph | 95 | 108—110 | Needles ($CH_2Cl_2$–petr. ether) | $C_{19}H_{16}N_2O$ | 79.14 (78.90 | 5.59 5.66 | 9.72 9.44) | |
| XIIIc | Ph | OEt | 68 | 132/2 | Liquid | $C_{15}H_{16}N_2O_2$ | 70.29 (70.20 | 6.29 6.36 | 10.93 11.43) | |
| XIIId | Ph | NHPh | 63 | 132—134 | Needles ($CH_2Cl_2$–petr. ether) | $C_{19}H_{17}N_3O$ | 75.22 (75.24 | 5.65 5.80 | 13.85 13.61) | |

a) These compounds have been reported in the literature.[12,13]

of Va, b show the existence of tautomerism in $CHCl_3$ solution, there is no doubt in the structural assignment of the above products (Va—d), because 4,6-dimethyl-2-pyrimidinylmethyl phenyl ketone (Vb) and ethyl 4,6-dimethylpyrimidine-2-acetate (Vc) thus obtained were identical with specimens prepared by the known method.[5,11]

The method described above was applicable to the preparation of 4-acylmethylpyrimidines. Namely, the reactions of 4-chloro-2,6-dimethylpyrimidine (VI) and 4-chloro-6-methyl-2-phenylpyrimidine (VII) with II afforded the corresponding dimethyloxosulfonium 2,6-dimethyl-4-pyrimidinylmethylide (VIII) and dimethyloxosulfonium 6-methyl-2-phenyl-4-pyrimidinylmethylide (IX), respectively. The acylation of VIII and IX with acetic anhydride, benzoyl chloride, ethoxycarbonyl chloride, or phenyl isocyanate followed by desulfurization of the resultant acyl-ylides (Xa—c, XIa—d) gave the desired 4-acylmethylpyrimidines (XIIa—c, XIIIa—d) without any difficulties. These data are summarized in Table II. Among these final products, 2,6-dimethyl-4-pyrimidinylmethyl methyl ketone (XIIa) and 2,6-dimethyl-4-pyrimidinylmethyl phenyl ketone (XIIb) were identical with authentic specimens prepared by the known method.[12,13]

In order to determine the scope of this reaction, chlorodiazines other than chloropyrimidines such as 3-chloro-6-phenylpyridazine (XIV), 2-chloro-5,6-diphenylpyrazine (XV) and 4-chloroquinazoline (XVI) were tested. As shown in Chart 4, among these compounds XV and XVI were readily converted to the corresponding acetonyl derivatives (XVII, XVIII), while Raney nickel desulfurization of the pyridazine derivative (XIX) resulted in the formation of α-methyl-6-phenyl-3-pyridazineethanol (XX), instead of the expected carbonyl compound. The spectral data for XVII, XVIII and XX are in good agreement with the proposed structure. On the other hand, the reactions of 2-chloropyridine, 4-chloro-2,6-dimethylpyridine and 4-chloroquinoline 1-oxide failed to give any significant products, and considerable amounts of the starting materials, were recovered.

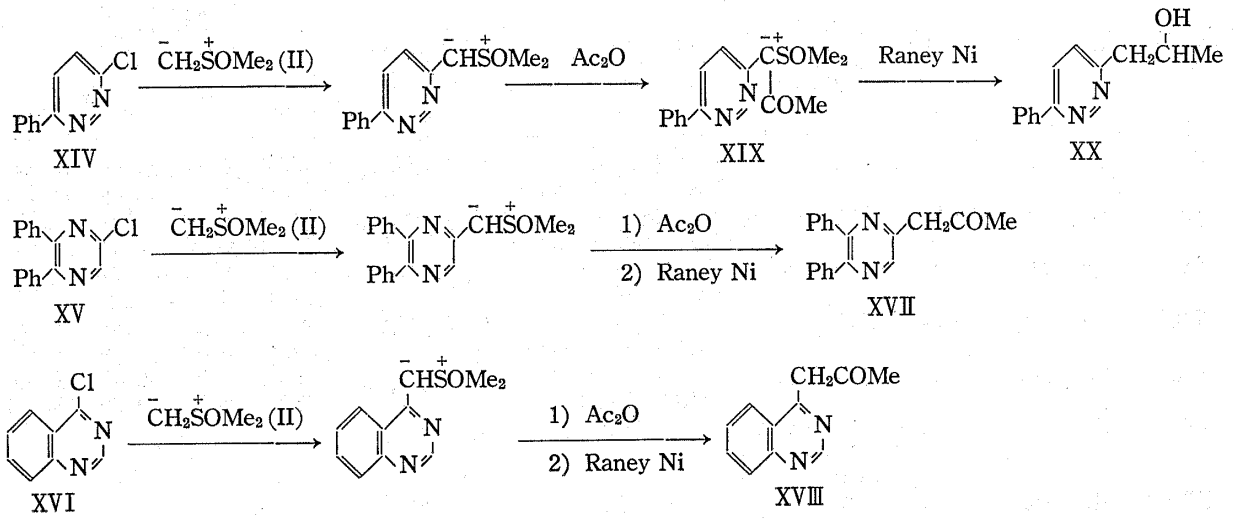


Chart 4

Based on the above experiments, it is concluded that the replacement of an active chlorine atom by an acylmethyl group *via* the sulfur-ylide is widely applicable to the synthesis of diazine derivatives, although it was unsuccessful in the mono azine series.

## Experimental

All melting points and boiling points are uncorrected. Infrared (IR) spectra were measured with a JASCO IRA-1 spectrometer. Mass spectra (MS) were taken with a Hitachi M-52G spectrometer. PMR spectra were taken at 60 MHz with Hitachi-Perkin-Elmer R-20 and JEOL JNM-PMX 60 spectrometers.

Chemical shifts are expressed as ppm downfield from tetramethylsilane (TMS) as an internal standard. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, and b=broad.

**General Procedure for the Preparation of Dimethyloxosulfonium Pyrimidinylmethylide**——Chloropyrimidine (1 mol equiv.) was added to a THF solution of dimethyloxosulfonium methylide (II) (2 mol equiv.), prepared by the procedure described in the literature.[6] The mixture was refluxed under a stream of $N_2$ for 5 h with stirring. The resulting precipitates (trimethyloxosulfonium chloride) were filtered off, and the filtrate was concentrated to dryness *in vacuo*. The residue was purified by recrystallization or alumina column chromatography.

**Dimethyloxosulfonium 4,6-Dimethyl-2-pyrimidinylmethylide (III)**——From 2-chloro-4,6-dimethylpyrimidine (I) (1.17 g, 0.012 mol) and II (0.026 mol), III was obtained according to the general procedure as colorless needles (AcOEt–hexane), mp 101.5—103°C, yield 1.66 g (70%). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1575, 1585. PMR ($CDCl_3$): 2.24 (6H, s), 3.47 (6H, s), 4.34 (1H, s), 6.29 (1H, s). *Anal.* Calcd for $C_9H_{14}N_2OS$: C, 54.51; H, 7.12; N, 14.13; S, 16.17. Found: C, 54.28; H, 6.91; N, 14.04; S, 16.26.

**Dimethyloxosulfonium 2,6-Dimethyl-4-pyrimidinylmethylide (VIII)**——From 4-chloro-2,6-dimethylpyrimidine (VI) (2.25 g, 0.016 mol) and II (0.039 mol), VIII was obtained according to the general procedure as a yellow liquid, which was chromatographed on an alumina column with $Et_2O$. The yield was 1.42 g (45%). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1580. PMR ($CDCl_3$): 2.20 (3H, s), 2.43 (3H, s), 3.48 (6H, s), 3.56—4.15 (1H, b), 6.12 (1H, s). In the subsequent experiments, this material was used without further purification.

**Dimethyloxosulfonium 6-Methyl-2-phenyl-4-pyrimidinylmethylide (IX)**——From 4-chloro-6-methyl-2-phenylpyrimidine (VII) (7.16 g, 0.035 mol) and II (0.088 mol), IX was obtained according to the general procedure as colorless needles ($CH_2Cl_2$–$Et_2O$), mp 134—135°C, yield 8.80 g (97%). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1600, 1580. PMR ($CDCl_3$): 2.32 (3H, s), 3.45 (6H, s), 3.88 (1H, s), 6.18 (1H, s), 7.30—7.58 (3H, m), 8.23—8.50 (2H, m). *Anal.* Calcd for $C_{14}H_{16}N_2O_2S$: C, 64.60; H, 6.20; N, 10.76; S, 12.29. Found: C, 64.49; H, 6.09; N, 10.55; S, 12.52.

**General Procedure for the Acetylation of Dimethyloxosulfonium Pyrimidinylmethylide (III, VIII, and IX). A Typical Example: Dimethyloxosulfonium Acetyl (4,6-dimethyl-2-pyrimidinyl)methylide (IVa)**——A solution

Table III. Spectral Data for Compounds IV, V, X, XI, XII and XIII

| Compd. No. | IR $\nu_{max}^{KBr}$ $cm^{-1}$ | PMR $\delta$ (ppm) in $CDCl_3$ |
|---|---|---|
| $IV_a$ | 1600, 1550[a] | 2.30 (3H, s) ,2.44 (6H, s), 3.66 (6H, s), 6.75 (1H, s). |
| $IV_b$ | 1600, 1535[a] | 2.21 (6H, s), 3.76 (6H, s), 6.62 (1H, s), 7.0—7.4 (5H, m). |
| $IV_c$ | 1645, 1600[a] | 1.25 (3H, t, $J$=7.0 Hz), 2.41 (6H, s), 3.65 (6H, s), 4.19 (2H, q, $J$=7.0 Hz), 6.70 (1H, s). |
| $IV_d$ | 1620, 1580[a] | 2.38 (6H, s), 3.85 (6H, s), 6.47 (1H, s), 6.93—7.65 (5H, m), 12.0—12.3 (1H, b). |
| $V_a$ | 1735, 1655[a] | 2.09 (0.9H, s), 2.29 (2.1H, s), 2.47 (6H, s), 4.08 (1.4H, s), 5.59 (0.3H, s), 6.77 (0.3H, s), 7.02 (0.7H, s), 13.3—14.0 (0.3H, b). |
| $V_d$ | 1680[a] | 2.45 (6H, s), 3.93 (2H, s), 6.88 (1H, s), 7.0—7.60 (5H, m), 10.0—10.37 (1H, b). |
| $X_a$ | 1600, 1567 | 2.26 (3H, s), 2.50 (3H, s), 2.65 (3H, s), 3.67 (6H, s), 7.10 (1H, s). |
| $X_b$ | 1590, 1545 | 2.22 (3H, s), 2.48 (3H, s), 3.72 (6H, s), 6.63 (1H, s), 7.10—7.45 (5H, m). |
| $X_c$ | 1590, 1560 | 2.35 (3H, s), 2.62 (3H, s), 3.70 (6H, s), 5.28 (1H, s), 6.85—7.55 (5H, m), 12.60—12.93 (1H, b). |
| $XI_a$ | 1590, 1580 | 2.32 (3H, s), 2.53 (3H, s), 3.63 (6H, s), 7.10 (1H, s), 7.48 (3H, m), 8.43 (2H, m). |
| $XI_b$ | 1555, 1523 | 2.33 (3H, s), 3.70 (6H, s), 6.75 (1H, s), 7.28—7.55 (8H, m), 7.90—8.15 (2H, m). |
| $XI_c$ | 1650 | 1.35 (3H, t, $J$=7.0 Hz), 2.50 (3H, s), 3.73 (6H, s), 4.26 (2H, q, $J$=7.0 Hz), 7.30—7.58 (4H, m), 8.30—8.55 (2H, m). |
| $XI_d$ | 1580, 1550 | 2.47 (3H, s), 3.72 (6H, s), 6.90—7.70 (9H, m), 8.18—8.45 (2H, m). |
| $XII_c$ | 1697, 1597 | 2.45 (3H, s), 2.72 (3H, s), 3.74 (2H, s), 7.0—7.70 (6H, m), 9.50—10.0 (1H, b). |
| $XIII_a$ | 1715, 1650[a] | 2.07 (0.9H, s), 2.27 (2.1H, s), 2.46 (0.9H, s), 2.53 (2.1H, s), 3.87 (1.4H, s), 5.27 (0.3H, s), 6.50 (0.3H, s), 6.97 (0.7H, s), 7.35—7.65 (3H, m), 8.20—8.60 (2H, m), 15.22 (0.3H, s). |
| $XIII_b$ | 1690, 1600 | 2.48 (3H, s), 4.42 (0.7H, s), 6.00 (0.65H, s), 6.67 (0.7H, s), 7.05 (0.3H, s), 8.25—8.35 (8H, m), 8.25—8.55 (2H, m). |
| $XIII_c$ | 1740[a] | 1.27 (3H, t, $J$=7.0 Hz), 2.55 (3H, s), 3.80 (2H, s), 4.22 (2H, q, $J$=7.0 Hz), 7.70 (1H, s), 7.38—7.60 (3H, m), 8.35—8.60 (2H, m). |
| $XIII_d$ | 1670 | 2.55 (3H, s), 3.82 (2H, s), 7.00—7.65 (9H, m), 8.35—8.65 (2H, m), 9.55—9.95 (1H, b). |

a) Taken in $CHCl_3$.

of $Ac_2O$ (1 g, 0.01 mol) in dry dioxane (20 ml) was added dropwise to a solution of III (2 g, 0.01 mol) in dry dioxane (30 ml) with constant stirring in an ice bath. The mixture was stirred at room temperature for an additional 1 h, and concentrated to dryness *in vacuo*. The residual solid was purified by recrystallization to give IVa. The other compounds were similarly prepared. Physical and analytical data for the compounds (IVa, Xa, and XIa) are listed in Tables I and II. Spectral data (IR and PMR) are listed in Table III.

**General Procedure for the Benzoylation and Ethoxycarbonylation of III, VIII and IX. A Typical Example: Dimethyloxosulfonium Benzoyl (4,6-dimethyl-2-pyrimidinyl)methylide (IVb)**——A solution of benzoyl chloride (1.41 g, 0.01 mol) in dry dioxane (20 ml) was added dropwise to a solution of III (3.96 g, 0.02 mol) in dry dioxane (70 ml), keeping the temperature below 20°C by ice-cooling. The reaction mixture was stirred at room temperature for 1 h. The resulting precipitates (III hydrochloride) were filtered off and the filtrate was concentrated to dryness *in vacuo*. The residual solid was purified by recrystallization to give IVb. The other compounds were similarly prepared. Physical and analytical data for the compounds (IVb, c, Xb and XIb, c) are listed in Tables I and II. Spectral data are listed in Table III.

**General Procedure for the Reaction of III, VIII and IX with Phenyl Isocyanate. A Typical Example: Dimethyloxosulfonium 4,6-Dimethyl-2-pyrimidinyl-phenylcarbamoylmethylide (IVd)**——A solution of phenyl isocyanate (0.6 g, 0.005 mol) in dry dioxane (10 ml) was added dropwise to a solution of III (1 g, 0.005 mol) in dry dioxane (20 ml), keeping the temperature below 20°C by ice-cooling. The reaction mixture was stirred at room temperature for 1 h, and then concentrated to dryness *in vacuo*. The residual solid was purified by recrystallization to give IVd. The other compounds were similarly prepared. Physical and analytical data for the compounds (IVd, Xc and XIa) are listed in Tables I and II. Spectral data are listed in Table III. Xc (mp 148—150°C, crude yield 90%) and XId (mp 162—165°C, crude yield 90%) were used without purification in the subsequent desulfurization.

**General Procedure for the Desulfurization of Dimethyloxosulfonium Acylpyrimidinylmethylides (IV, X and IX) with Raney Ni. A Typical Example: 4,6-Dimethyl-2-pyrimidinylmethyl Methyl Ketone (Va)**——Deactivated Raney Ni[10] (5 g, wet weight) was added to a solution of IVa (0.96 g, 0.004 mol) in $CH_3OH$ (40 ml). The mixture was refluxed for 30 min with vigorous stirring, then the Raney Ni was removed by filtration and the fitrate was concentrated *in vacuo*. The residual liquid was dissolved in $Et_2O$ and dried over anhydrous $Na_2SO_4$. After removal of the solvent, the residual liquid was purified by distillation under reduced pressure to give Va. The other compounds were similarly prepared. Physical and analytical data for the compounds (Va—d, XIIa—c and XIIIa—d) are listed in Tables I and II. Spectral data are listed in Table III.

**5,6-Diphenyl-2-pyrazinylmethyl Methyl Ketone (XVII)**——From 2-chloro-5,6-diphenylpyrazine (XV)[14] (4.80 g, 0.018 mol) and II (0.045 mol), dimethyloxosulfonium 5,6-diphenyl-2-pyrazinylmethylide was obtained according to the procedure described for IIIa as yellow prisms (AcOEt), mp 172—173°C, yield 5.36 g (93%). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1560. PMR ($CDCl_3$): 3.43 (6H, s), 4.13 (1H, s), 7.13 (5H, s), 7.17 (5H, s), 7.80 (1H, s). *Anal.* Calcd for $C_{19}H_{18}N_2OS$: C, 70.79; H, 5.63; N, 8.69; S, 9.93. Found: C, 70.58; H, 5.66; N, 8.46; S, 9.66. The pyrazinylmethylide (1.50 g, 0.0046 mol) was treated with $Ac_2O$ (0.57 g, 0.0056 mol) according to the procedure described for IVa to give 1.55 g (91%) of dimethyloxosulfonium acetyl (5,6-diphenyl-2-pyrazinyl)methylide as yellow prisms (benzene–hexane), mp 171—173°C. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1570, 1550. PMR ($CDCl_3$): 2.20 (3H, s), 3.58 (6H, s), 7.24 (10H, b), 8.47 (1H, s). *Anal.* Calcd for $C_{21}H_{20}N_2O_2S$: C, 69.21; H, 5.53; N, 7.69; S, 8.78. Found: C, 68.93; H, 5.61; N, 7.46; S, 8.83. The acetylpyrazinylmethylide (0.8 g, 0.0022 mol) was treated with deactivated Raney Ni (2.5 g) according to the procedure described for Va to give 0.382 g (60%) of XVIII, as yellow prisms ($Et_2O$), mp 115—117°C. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1725. PMR ($CDCl_3$): 2.30 (3H, s), 4.00 (2H, s), 7.28 (10H, s), 8.43 (1H, s). *Anal.* Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 78.93; H, 5.67; N, 9.62.

**Methyl 4-Quinazolinylmethyl Ketone (XVIII)**——From 4-chloroquinazoline (XVI)[15] (1.8 g, 0.011 mol) and II (0.022 mol), dimethyloxosulfonium 4-quinazolinylmethylide was obtained according to the procedure described for IIIa as a liquid, yield 2.6 g. Without further purification, the liquid was treated with $Ac_2O$ (1.9 g, 0.019 mol) as in the case of IVa to give 1.7 g (55%) of dimethyloxosulfonium acetyl (4-quinazolinyl) methylide as yellow needles, mp 185.5—187°C (dec.). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1580, 1560. PMR ($CDCl_3$): 1.83 (3H, s), 3.73 (6H, s), 7.40—8.40 (4H, m), 9.27 (1H, s). *Anal.* Calcd for $C_{13}H_{14}N_2O_2S$: C, 59.54; H, 5.34; N, 10.69; S, 12.21. Found: C, 59.31; H, 5.51; N, 10.48; S, 12.18. The acetylquinazolinyl methylide (0.5 g, 0.0019 mol) was treated with deactivated Raney Ni (5 g) as in the case of Va to give 0.2 g (57%) of XVIII as yellow needles ($Et_2O$–hexane), mp 127—129°C (lit.[16] mp 121—122°C). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1625, 1615. PMR ($CDCl_3$): 2.21 (3H, s), 5.94 (1H, s), 7.10—8.13 (5H, m), 13.63—15.30 (1H, b).

**Dimethyloxosulfonium Acetyl(6-Phenyl-3-pyridazinyl)methylide (XIX)**——Dimethyloxosulfonium 6-phenyl-3-pyridazinyl methylide was obtained from 3-chloro-6-phenylpyridazine (XIV)[17] (3.24 g, 0.017 mol) and II (0.0425 mol) according to the procedure described for III, as yellow prisms (AcOEt–MeOH), mp 151—153°C, yield 3.40 g (81%). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1600, 1540. PMR ($CDCl_3$): 3.50 (6H, s), 3.80 (1H, s), 6.72 (1H, d, $J$=8 Hz), 7.20—7.60 (4H, m), 7.80—8.10 (2H, m). *Anal.* Calcd for $C_{13}H_{14}N_2OS$: C, 63.40; H, 5.73; N, 11.38; S, 12.99. Found: C, 63.17; H, 5.58; N, 11.12; S, 12.79. The pyridazinylmethylide (1.40 g, 0.059 mol) was treated with $Ac_2O$ (0.7 g, 0.00683 mol) as in the case of IVa to give 1.00 g (98%) of XIX, as colorless needles (AcOEt), mp 146—148°C. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1570, 1550. PMR ($CDCl_3$): 2.33 (3H, s), 3.78 (6H, s),

7.50—8.10 (5H, m), 8.10—8.43 (2H, m). *Anal.* Calcd for $C_{15}H_{16}N_2O_2S$: C, 62.49; H, 5.59; N, 9.72; S, 11.10. Found: C, 62.32; H, 5.68; N, 9.46; S, 10.96.

**α-Methyl-6-phenyl-3-pyridazineethanol (XX)**——Deactivated Raney Ni (2.5 g) was added to a solution of XIX (0.5 g, 0.00174 mol) in $CH_3OH$ (30 ml) and the mixture was refluxed for 2 h with vigorous stirring. The reaction mixture was worked up according to the procedure described for Va. The crude product was purified by chromatography on an alumina column with AcOEt to give 0.122 g (33%) of XX, as colorless plates ($Et_2O$), mp 103—105°C. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3400. PMR ($CDCl_3$): 1.37 (3H, d, $J$=7 Hz), 3.10 (2H, d, $J$=6 Hz), 3.97 (1H, d, $J$=4 Hz, exchangeable with $D_2O$), 4.00—4.70 (1H, m), 7.23—7.77 (5H, m), 7.77—8.17 (2H, m). MS *m/e*: 214 ($M^+$). *Anal.* Calcd for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59; N, 13.08. Found: C, 72.89; H, 6.44; N, 13.01.

**Reactions of 2-Chloropyridine, 4-Chloro-2,6-dimethylpyridine, and 4-Chloroquinoline 1-Oxide with II**——When an attempt was made to react the above three chloro-compounds with II as in the case of I, no precipitate was obtained. The unchanged starting materials were each recovered in about 70% yield from the reaction mixture.

**Acknowledgement** The authors wish to thank Dr. S. Ogawa, Messrs. K. Tanji, M. Shiraiwa and Y. Aizawa for their experimental assistance. Thanks are also due to the staff of the Central Analysis Room of this Institute for elemental analysis and measurements of PMR spectra and Mass spectra.

## References and Notes

1) Part XXII: T. Sakamoto, T. Sakasai, and H. Yamanaka, *Chem. Pharm. Bull.*, **29**, 2485 (1981).
2) S. Niitsuma, T. Sakamoto, and H. Yamanaka, *Heterocycles*, **10**, 171 (1978).
3) R.C. Elderfield and I. Serlin, *J. Org. Chem.*, **16**, 1669 (1951).
4) V.P. Mamaev and O.A. Zagulyaeva, *Kim. Geterotsikl. Soedin. Sb.* **1**, **1967**, 354 [*Chem. Abs.*, **70**, 87723e (1969)].
5) D.J. Brown and P. Waring, *Aust. J. Chem.*, **27**, 2251 (1974).
6) E.J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).
7) T. Kunieda and B. Witkop, *J. Am. Chem. Soc.*, **93**, 3487 (1971).
8) R. Faragher and T.L. Gilchrist, *J. Chem. Soc., Perkin I*, **1977**, 1196.
9) T. Sakamoto and H. Yamanaka, *Heterocycles*, **15**, 583 (1981).
10) W-2 Raney Ni prepared in the usual way was washed with water until the washings were neutral. The resulting Raney Ni was stored in 2% NaCl solution for 3 days and washed thoroughly with water.
11) B. Roth and J.M. Smith, *J. Am. Chem. Soc.*, **71**, 616 (1949).
12) H.R. Sullivan and W.T. Caldwell, *J. Am. Chem. Soc.*, **77**, 1559 (1955).
13) H. Yamanaka, H. Abe, and T. Sakamoto, *Chem. Pharm. Bull.*, **25**, 3334 (1977).
14) P.J. Nelson and K.T. Potts, *J. Org. Chem.*, **27**, 3243 (1962).
15) St. v. Niementowshi, *J. Prakt. Chem.*, [2], **51**, 564 (1895).
16) T. Higashino, *Chem. Pharm. Bull.*, **10**, 1048 (1962).
17) M. Ogata, *Chem. Pharm. Bull.*, **11**, 1522 (1963).