[Chem. Pharm. Bull.
34(5)1980—1986(1986)]

1,3-Oxazines and Related Compounds. XII.[1] Facile Synthesis of 2,4-Disubstituted 6*H*-1,3-Oxazin-6-ones

YUTAKA YAMAMOTO,* YASUO MORITA, and KEIKO MINAMI

Tohoku College of Pharmacy, 4-4-1 Komatsushima, Sendai 983, Japan

(Received September 30, 1985)

A convenient method for synthesis of 2,4-disubstituted 6*H*-1,3-oxazin-6-ones (**8**) was developed. Acylaminoalkylidene-1,3-dioxane-4,6-diones (**5a**—**l**), which were prepared from *N*-acylimidates (**3a**—**l**) and Meldrum's acid (**4**), readily underwent thermolysis upon heating, leading to a variety of 2,4-disubstituted 6*H*-1,3-oxazin-6-ones (**8a**—**l**).

Keywords——6*H*-1,3-oxazin-6-one; Meldrum's acid; acylaminoalkylidene-1,3-dioxane-4,6-dione; *N*-acylimidate; thermolysis

A number of methods have been reported for the synthesis of 6*H*-1,3-oxazin-6-one derivatives (**8**), since the first derivative was synthesized by Barker.[2] However, they all possess limitations with respect to practical laboratory synthesis. These methods include intramolecular cyclizations of *N*-acyl-*β*-aminocrotonates[3] by pyrolysis, oxidative ring expansions of isoxazolones[4] and pyrroles,[5] reaction of isoxazolones and benzonitrile oxide,[6] and cycloaddition between *N*-iminopyridinium ylides and diphenylcyclopropenone.[7]

Various 1,3-oxazin-6-ones **8** were required in connection with our continuing studies on the ring transformations[8] of 1,3-oxazin-4-one derivatives. Further, 1,3-oxazin-6-ones **8** are available as 2-azabutadiene systems for use in Diels–Alder synthesis, and have attracted considerable attention for this reason. We now describe a preparatively useful and convenient procedure devised to gain an access to 1,3-oxazin-6-ones **8**, involving thermolysis of acylaminoalkylidene-1,3-dioxane-4,6-diones (**5**).

Synthesis of Acylaminoalkylidene-1,3-dioxane-4,6-diones (5)

It has been reported[3c] that the intramolecular cyclization of *N*-acyl-*β*-aminocrotonates to 1,3-oxazin-6-ones proceeds through *N*-acyliminoketene derivatives. It was thought that the 1,3-dioxane-4,6-diones (**5**) would provide an easy access to the important intermediate (**7**), because the 1,3-dioxane ring system readily undergoes thermolysis to form ketene derivative.[9]

Our first attempt at the synthesis of **5** by acylation of aminoalkylidene-1,3-dioxane-4,6-diones (**6**), which are easily available from Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione, **4**) and imidates **2** by the method of Maitte *et al.*[10] was unsuccessful; enamino derivatives **6** were treated with several acylating agents such as acyl chloride, acid anhydride and acyl imidazole. In all cases, quantitative recovery of **6** was obtained.

Next, our efforts were directed to the reaction of **4** with *N*-acylimidates **3**. When ethyl *N*-benzoylacetimidate (**3a**) prepared according to the literature[11] was allowed to react with **4** in chloroform ($CHCl_3$) under reflux in the presence of a catalytic amount of triethylamine (Et_3N), 5-(1-benzoylaminoethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**5a**) was obtained in 77% yield. Similar treatment of **3b**—**l** with **4** gave the corresponding 1,3-dioxane-4,6-diones (**5b**—**l**) (Chart 1). The results obtained are summarized in Table I.

Further, we developed a one-pot synthesis of **5** from imidate hydrochlorides **1**. For example, a suspension of ethyl acetimidate hydrochloride (**1**) ($R^2 = Me$) in $CHCl_3$ was treated

successively with 2.3 equivalents of Et_3N and an equimolar amount of benzoyl chloride. The mixture was stirred at room temperature overnight, an equimolar amount of **4** was added, and the whole was refluxed for 18 h to give **5a** in 41% yield. The yields obtained in this fashion are also shown in Table I.

The structures of these products **5a**—**l** were characterized on the basis of analytical and spectroscopic data such as infrared (IR), proton nuclear magnetic resonance (^{1}H-NMR), and mass spectra (MS) (Table IV).

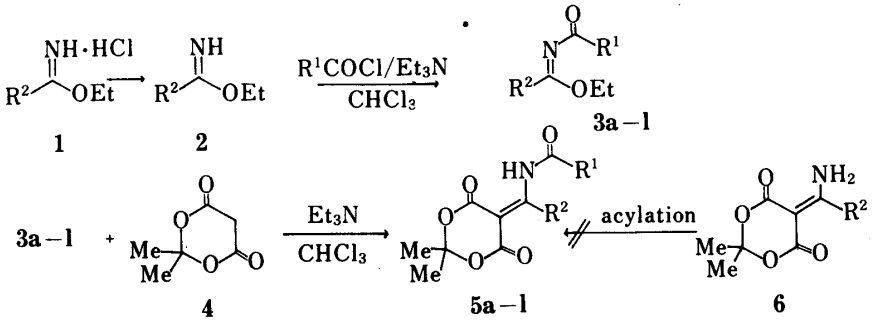

Chart 1

TABLE I. Preparation of Acylaminoalkylidene-1,3-dioxane-4,6-diones **5a**—**l**

Product No.	R^1	R^2	mp (°C) (Recrystn. solvent)	Yield[a] (%)
5a	Ph	Me	167—169 (dec.) (Et_2O–C_6H_6)	77 (41)
5b	Me	Me	135—137 (C_6H_6)	86
5c	Et	Me	110—112 (Et_2O–C_6H_6)	83
5d	iso-Pr	Me	63—64 (Et_2O–P.E.)	78
5e	*tert*-Bu	Me	90—92 (Et_2O–P.E.)	80
5f	$PhCH_2$	Me	182—184 (dec.) (C_6H_6)	85
5g	Ph	Ph	187 (dec.) (C_6H_6)	73
5h	Me	Ph	154—156 (dec.) (Et_2O–C_6H_6)	73 (48)
5i	Et	Ph	178—179 (dec.) (C_6H_6)	72
5j	iso-Pr	Ph	165—167 (dec.) (Et_2O–C_6H_6)	70
5k	*tert*-Bu	Ph	180—182 (dec.) (Et_2O–C_6H_6)	72
5l	$PhCH_2$	Ph	132—134 (Et_2O–C_6H_6)	67

a) The yields in the one-pot procedure are shown in parentheses, and they are based on the imidate hydrochloride **1**. Others are based on the *N*-acylimidate **3**. P.E. = petroleum ether.

Synthesis of 2,4-Disubstituted 6*H*-1,3-Oxazin-6-ones (8) by Thermolysis of Acylaminoalkylidene-1,3-dioxane-4,6-diones (5)

Acylaminoalkylidene-1,3-dioxane-4,6-diones (**5**) readily underwent thermal decomposition on heating above the melting point, giving the corresponding 2,4-disubstituted 6*H*-1,3-oxazin-6-ones (**8**) with loss of acetone and carbon dioxide. When 5-(1-benzoylaminoethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**5a**) was heated at 170—175 °C (bath temperature) without solvent until the evolution of carbon dioxide ceased (method A), 4-methyl-2-phenyl-6*H*-1,3-oxazin-6-one (**8a**) was obtained in 82% yield. Structural assignment of the product **8a** was accomplished on the basis of spectroscopic data and the following chemical derivatization; treatment of **8a** with 40% $MeNH_2$ aqueous solution in 95% EtOH gave 3,6-dimethyl-2-phenyl-4-pyrimidone (**9**), which was identified by comparison of the IR spectrum with that of an authentic sample.[12]

Similar thermolysis of 1,3-dioxane-4,6-diones (**5c**—**l**) afforded the corresponding 2,4-

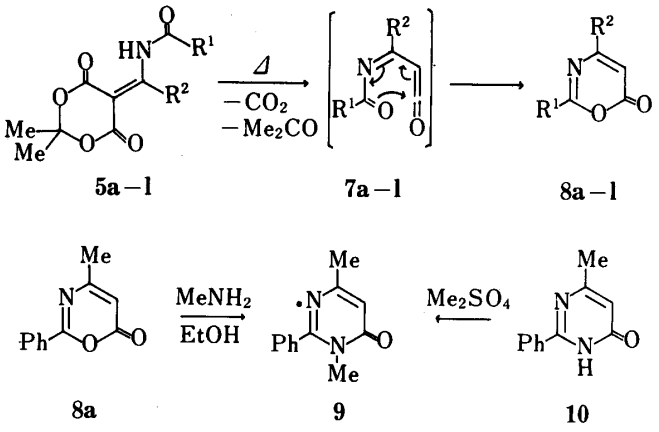

Chart 2

TABLE II. Preparation of 2,4-Disubstituted 6*H*-1,3-Oxazin-6-ones **8a—l**

Product No.	R^1	R^2	Bath temp. (°C)	mp (°C) (Recrystn. solvent) or bp (°C) (Torr)	Yield (%) (Method)
8a	Ph	Me	170—175	93—95 (Et_2O)[a]	82 (A), 74 (B)
8b	Me	Me		52—53[b]	33 (B)
8c	Et	Me	165—170	83 (8)	36 (A)
8d	iso-Pr	Me	165—170	90—91 (8)[c]	70 (A)
8e	*tert*-Bu	Me	165—170	80—81 (7)[d]	75 (A)
8f	$PhCH_2$	Me	180—185	103—105 (0.4)	32 (A)
8g	Ph	Ph	185—190	145—147 (C_6H_6)[e]	93 (A)
8h	Me	Ph	160—165	115—116 (Et_2O)[f]	91 (A)
8i	Et	Ph	180—185	71—73 (Et_2O)	91 (A)
8j	iso-Pr	Ph	170—175	124 (0.7)	88 (A)
8k	*tert*-Bu	Ph	180—185	105—106 (Et_2O)	92 (A)
8l	$PhCH_2$	Ph	170—175	91—92 (Et_2O)	91 (A)

a) Ref. 3*f*, mp 93 °C. *b*) Ref. 3*d*, mp 56—57 °C. *c*) Ref. 3*c*, bp 40—41 °C (0.1 Torr). *d*) Ref. 3*c*, bp 39—40 °C (0.3 Torr). *e*) Ref. 6*c*, mp 137—138 °C. *f*) Ref. 3*e*, mp 109—110 °C.

disubstituted 6*H*-1,3-oxazin-6-ones (**8c—l**) (Chart 2). The structures of these products **8c—l** were characterized on the basis of the spectroscopic and analytical data summarized in Table V.

Thermolysis of **5b** by method A gave rise to only an unidentified tarry material. Therefore, method A was modified by using decalin as a solvent. Thus, refluxing of **5b** in decalin afforded 2,4-dimethyl-1,3-oxazin-6-one (**8b**) in 33% yield (method B). When xylene or dibutyl ether was used, no thermal decomposition occurred. These results are summarized in Table II.

Our work provides an easy entry to the 2,4-disubstituted 1,3-oxazin-6-ones, and to the 2-azabutadiene system bearing several substituents.

Experimental

Melting points were obtained in a Mel-Temp melting point apparatus with an open capillary tube, and are uncorrected. IR spectra were taken on a Shimadzu IR-430 spectrometer. ^{1}H-NMR spectra were measured on a JEOL JNM-PMX 60 instrument. Chemical shifts are reported in δ values downfield relative to internal tetramethylsilane. The following abbreviations are used: s=singlet, d=doublet, t=triplet, m=multiplet, and br=broad.

Preparation of *N*-Acylimidates (3). General Procedure——A solution of acyl chloride (33 mmol) in $CHCl_3$ (30 ml) was added dropwise over a period of 30 min to a stirred solution of an imidate **2** (30 mmol) and Et_3N (33 mmol) in

TABLE III. *N*-Acylimidates **3a**—**l**

Product No.	R^1	R^2	Yield (%)	bp (°C) (Torr)	Formula	Analysis (%) Calcd (Found) C	H	N	IR ν (neat) cm^{-1}	NMR ($CDCl_3$) δ
3a	Ph	Me	70	98—101 (2)[a]	—	—	—	—	1670	1.30 (3H, t, J=7 Hz), 2.01 (3H, s), 4.20 (2H, q, J=7 Hz), 7.1—7.9 (5H, m)
3b	Me	Me	71	52 (5)	$C_6H_{11}NO_2$	55.79 (55.91	8.58 8.71	10.85 10.90)	1670	1.30 (3H, t, J=7 Hz), 2.00 (3H, s), 2.16 (3H, s), 4.10 (2H, q, J=7 Hz)
3c	Et	Me	73	68 (3)	$C_7H_{11}NO_2$	58.72 (59.00	9.15 9.22	9.78 9.92)	1670	1.10 (3H, t, J=7 Hz), 1.26 (3H, t, J=7 Hz), 2.00 (3H, s), 2.43 (2H, q, J=7 Hz), 4.10 (2H, q, J=7 Hz)
3d	iso-Pr	Me	72	81—83 (10)	$C_8H_{15}NO_2$	61.12 (60.87	9.62 9.82	8.91 8.71)	1670	1.16 (6H, d, J=7 Hz), 1.30 (3H, t, J=7 Hz), 2.00 (2H, s), 2.33—2.83 (1H, m), 4.13 (2H, q, J=7 Hz)
3e	*tert*-Bu	Me	67	70—72 (3.5)	$C_9H_{17}NO_2$	63.13 (63.42	10.00 9.82	8.18 7.94)	1670	1.16 (9H, s), 1.23 (3H, t, J=7 Hz), 2.00 (3H, s), 4.10 (2H, q, J=7 Hz)
3f	$PhCH_2$	Me	80	120—121 (6)	$C_{12}H_{15}NO_2$	70.22 (70.50	7.37 7.40	6.82 6.70)	1670	1.26 (3H, t, J=7 Hz), 1.86 (3H, s), 3.73 (2H, s), 4.13 (2H, q, J=7 Hz), 7.30 (5H, s)
3g	Ph	Ph	70	129—130 (0.3)	$C_{16}H_{15}NO_2$	75.87 (75.78	5.97 6.08	5.53 5.38)	1660	1.46 (3H, t, J=7 Hz), 4.43 (2H, q, J=7 Hz), 7.20—8.16 (10H, m)
3h	Me	Ph	87	91—93 (0.8)[b]	—	—	—	—	1660	1.30 (3H, t, J=7 Hz), 2.00 (3H, s), 4.15 (2H, q, J=7 Hz), 7.10—7.55 (5H, m)
3i	Et	Ph	73	125—127 (7)[c]	—	—	—	—	1660	1.10 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 2.30 (2H, q, J=7 Hz), 4.30 (2H, q, J=7 Hz), 7.33—7.93 (5H, m)
3j	iso-Pr	Ph	75	130—132 (5)	$C_{13}H_{17}NO_2$	71.20 (71.25	7.82 7.89	6.39 6.19)	1660	1.16 (6H, d, J=7 Hz), 1.43 (3H, t, J=7 Hz), 2.26—2.83 (1H, m), 4.36 (2H, q, J=7 Hz), 7.26—7.93 (5H, m)
3k	*tert*-Bu	Ph	66	91—93 (0.9)	$C_{14}H_{19}NO_2$	72.07 (71.99	8.21 8.50	6.00 5.89)	1660	1.15 (9H, s), 1.23 (3H, t, J=7 Hz), 4.23 (2H, q, J=7 Hz), 7.33—7.8 (5H, m)
3l	$PhCH_2$	Ph	71	135 (0.7)	$C_{17}H_{17}NO_2$	76.38 (76.47	6.41 6.47	5.24 4.98)	1660	1.30 (3H, t, J=7 Hz), 3.63 (2H, s), 4.20 (2H, q, J=7 Hz), 7.05—7.66 (10H, m)

a) Ref. 11, bp 67—68 °C (0.05 Torr). *b*) Ref. 11, bp 77—78 °C (0.15 Torr). *c*) Ref. 13, bp 161—162 °C (17 Torr).

TABLE IV. Spectral and Analytical Data for Acylaminoalkylidene-1,3-dioxane-4,6-diones **5a—l**

Compd. No.	IR ν (KBr) cm^{-1}	NMR ($CDCl_3$) δ	Formula (m/e M^+)	Analysis (%) Calcd (Found)		
				C	H	N
5a	1730, 1670	1.73 (6H, s), 3.20 (3H, s), 7.46—8.10 (5H, m), 13.76 (1H, br)	$C_{15}H_{15}NO_5$ (289)	62.28 (62.53	5.23 5.25	4.84 4.66)
5b	1750, 1720 1675	1.73 (6H, s), 2.31 (3H, s), 3.05 (3H, s), 12.86 (1H, br)	$C_{10}H_{13}NO_5$ (227)	52.86 (52.61	5.77 5.55	6.17 5.91)
5c	1745, 1720 1685	1.23 (3H, t, J=7 Hz), 1.73 (6H, s), 2.56 (2H, q, J=7 Hz), 3.06 (3H, s), 12.85 (1H, br)	$C_{11}H_{15}NO_5$ (241)	54.76 (55.06	6.27 6.18	5.81 5.67)
5d	1745, 1730 1670	1.26 (6H, d, J=7 Hz), 1.73 (6H, s), 2.36—2.80 (1H, m), 3.10 (3H, s), 12.93 (1H, br)	$C_{12}H_{17}NO_5$ (255)	56.46 (56.16	6.71 6.62	5.49 5.22)
5e	1745, 1730 1675	1.33 (9H, s), 1.73 (6H, s), 3.06 (3H, s), 13.16 (1H, br)	$C_{13}H_{19}NO_5$ (269)	57.98 (57.86	7.11 7.06	5.20 4.93)
5f	1750, 1720 1670	1.70 (6H, s), 3.06 (3H, s), 3.80 (2H, s), 7.33 (5H, s), 12.90 (1H, br)	$C_{16}H_{17}NO_5$ (303)	63.36 (63.27	5.65 5.61	4.62 4.32)
5g	1750, 1715 1670	1.80 (6H, s), 7.30—8.13 (10H, m), 13.20 (1H, br)	$C_{20}H_{17}NO_5$ (351)	68.37 (68.64	4.88 4.99	3.99 3.73)
5h	1750, 1730 1685	1.76 (6H, s), 2.13 (3H, s), 7.1—7.6 (5H, m), 12.13 (1H, br)	$C_{15}H_{15}NO_5$ (289)	62.28 (62.36	5.23 5.27	4.84 4.55)
5i	1760, 1730 1670	1.07 (3H, t, J=7 Hz), 1.76 (6H, s), 2.43 (2H, q, J=7 Hz), 7.10—7.55 (5H, m), 12.17 (1H, br)	$C_{16}H_{17}NO_5$ (303)	63.36 (63.52	5.65 5.65	4.62 4.32)
5j	1750, 1730 1670	1.20 (6H, d, J=7 Hz), 1.80 (6H, s), 2.66 (1H, m), 7.17—7.63 (5H, m), 12.30 (1H, br)	$C_{17}H_{19}NO_5$ (317)	64.34 (64.36	6.04 5.99	4.41 4.19)
5k	1740, 1730 1675	1.26 (9H, s), 1.80 (6H, s), 7.10—7.56 (5H, m), 12.50 (1H, br)	$C_{18}H_{21}NO_5$ (331)	65.24 (65.47	6.39 6.23	4.23 4.00)
5l	1750, 1730 1675	1.70 (6H, s), 3.65 (2H, s), 7.06—7.56 (10H, m), 12.10 (1H, br)	$C_{21}H_{19}NO_5$ (365)	69.03 (69.05	5.24 5.16	3.83 3.60)

$CHCl_3$ (50 ml) in an ice-salt bath. The reaction mixture was allowed to stand at room temperature overnight. The solvent was removed under reduced pressure, and benzene (50 ml) was added to the residue. The precipitated solid was filtered off, and the filtrate was evaporated. The residual oil was purified by distillation. The results obtained are summarized in Table III.

Preparation of Acylaminoalkylidene-1,3-dioxane-4,6-diones (5). General Procedure——A solution of an *N*-acylimidate **3** (10 mmol), Meldrum's acid (1.44 g, 10 mmol), and a few drops of Et_3N in $CHCl_3$ (10 ml) was heated under reflux for 18 h, then the solvent was removed under reduced pressure. The remaining crude product **5** was purified by recrystallization from the solvent indicated in Table I. Table IV summarizes the spectral and analytical data for the 1,3-dioxane-4,6-diones (**5**) obtained.

One-Pot Procedure for Preparation of Acylaminoalkylidene-1,3-dioxane-4,6-diones (5a, h)——A solution of Et_3N (2.33 g, 23 mmol) in $CHCl_3$ (10 ml) and a solution of acyl chloride (11 mmol) in $CHCl_3$ (10 ml) were successively added dropwise to a suspension of an imidate hydrochloride **1** (10 mmol) in $CHCl_3$ (10 ml) in an ice-salt bath. The reaction mixture was allowed to stand at room temperature overnight. Then Meldrum's acid (1.44 g, 10 mmol) was added and the resulting mixture was heated under reflux for 18 h. The reaction mixture was washed with H_2O (15 ml × 3), and dried over $MgSO_4$. The solvent was removed under reduced pressure. The remaining crude product was purified by recrystallization from the solvent indicated in Table I.

Thermolysis of 5 to 2,4-Disubstituted 6*H*-1,3-Oxazin-6-ones (8) (Method A). General Procedure——Acylaminoalkylidene-1,3-dioxane-4,6-diones **5a, c—l** (5 mmol) were each heated without solvent at the temperature indicated in Table II in an oil bath until the evolution of carbon dioxide ceased (*ca.* 10 min). The resulting product was purified by distillation or recrystallization from the solvent indicated in Table II. Table V summarizes the spectral and analytical data for the 6*H*-1,3-oxazin-6-ones **8**.

Thermolysis of 5b to 2,4-Dimethyl-6*H*-1,3-oxazin-6-one (8b) (Method B)——A solution of acetylamino-

TABLE V. Spectral and Aalytical Data for 2,4-Disubstituted 6*H*-1,3-Oxazine-6-ones **8a—l**

Compd. No.	IR ν[a] cm^{-1}	NMR ($CDCl_3$) δ	Formula (*m/e* M^+)	Analysis (%) Calcd (Found)		
				C	H	N
8a	1755	2.30 (3H, s), 6.00 (1H, s), 7.33—7.59 (3H, m), 8.15—8.29 (2H, m)	—	—	—	—
8b	1750	2.20 (3H, s), 2.36 (3H, s), 5.95 (1H, s)	—	—	—	—
8c	1760	1.30 (3H, t, J=7 Hz), 2.23 (3H, s), 2.70 (2H, q, J=7 Hz), 6.00 (1H, s)	$C_7H_9NO_2$ (139)	60.42 (60.12	6.52 6.48	10.07 9.91)
8d	1760	1.30 (6H, d, J=7 Hz), 2.21 (3H, s), 2.60—3.11 (1H, m), 5.93 (1H, s)	—	—	—	—
8e	1770	1.33 (9H, s), 2.23 (3H, s), 5.93 (1H, s)	—	—	—	—
8f	1760	2.18 (3H, s), 3.86 (2H, s), 5.93 (1H, s), 7.30 (5H, s)	$C_{12}H_{11}NO_2$ (201)	71.62 (71.48	5.51 5.59	6.96 6.83)
8g	1750	6.53 (1H, s), 7.26—8.36 (10H, m)	—	—	—	—
8h	1740	2.43 (3H, s), 6.45 (1H, s), 7.26—7.56 (3H, m), 7.83—8.10 (2H, m)	—	—	—	—
8i	1760	1.36 (3H, t, J=7 Hz), 2.76 (2H, q, J=7 Hz), 6.50 (1H, s), 7.36—7.65 (3H, m), 7.90—8.13 (2H, m)	$C_{12}H_{11}NO_2$ (201)	71.62 (71.88	5.51 5.48	6.96 6.81)
8j	1750	1.40 (6H, d, J=7 Hz), 2.63—3.20 (1H, m), 6.50 (1H, s), 7.36—7.66 (3H, m), 7.90—8.10 (2H, m)	$C_{13}H_{13}NO_2$ (215)	72.54 (72.39	6.09 6.22	6.51 6.24)
8k	1750	1.43 (9H, s), 6.50 (1H, s), 7.40—7.65 (3H, m), 7.90—8.13 (2H, m)	$C_{14}H_{15}NO_2$ (229)	73.34 (73.38	6.59 6.81	6.11 5.93)
8l	1740	3.96 (2H, s), 6.46 (1H, s), 7.30—8.06 (10H, m)	$C_{17}H_{13}NO_2$ (263)	77.55 (77.69	4.98 4.90	5.32 5.21)

a) Spectra of **8a, b, g—i, k, l** were taken in KBr. Those of **8c—f, j** were taken neat.

ethylidene-1,3-dioxane-4,6-dione (**5b**) (1.14 g, 5 mmol) in decalin (20 ml) was refluxed for 2 h whilst nitrogen gas was slowly bubbled through the solution. The decalin was distilled off under vaccum. The remaining solid was sublimed at 50 °C (bath temp.)/0.7 Torr to give 0.2 g (33%) of **8b**.

Synthesis of 4-Methyl-2-phenyl-6*H*-1,3-oxazin-6-one (8a) by Using Method B——A solution of **5a** (1.44 g, 5 mmol) in decalin (20 ml) was refluxed for 4 h while nitrogen gas was bubbled through the solution. The solvent was removed under vaccum. The residual solid was recrystallized from ether to give 0.69 g (74%) of **8a**. The IR spectrum was identical with that of the sample of **8a** obtained by Method A.

Reaction of 8a with $MeNH_2$——$MeNH_2$ (40% aqueous solution) (10 ml) was added with stirring to a suspension of **8a** (0.93 g, 5 mmol) in 95% EtOH (10 ml) in an ice bath. Stirring was continued for a further 30 min. The reaction mixture was concentrated under reduced pressure, followed by extraction with $CHCl_3$. The $CHCl_3$ layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The residual solid was recrystallized from hexane to give 3,6-dimethyl-2-phenyl-4-pyrimidone (**9**), mp 88—89 °C, 0.97 g (93%). The IR spectrum of **9** was identical with that of an authentic sample prepared by the procedure described below.

Synthesis of 9——A solution of **10** (1.86 g, 10 mmol) in 10% NaOH solution was treated with dimethyl sulfate (1.5 g), according to the reported procedure[12] to give 0.84 g (42%) of **9**, mp 88—89 °C. The IR spectrum was identical with that of the sample of **9** obtained in the above run.

Acknowledgement The authors are grateful to Dr. S. Suzuki of this College for mass spectral measurements.

References

1) Part XI: Y. Yamamoto and Y. Morita, *Annual Report of Tohoku College of Pharmacy*, **31**, 83 (1984).
2) C. C. Barker, *J. Chem. Soc.*, **1954**, 317.
3) *a*) F. Eiden and B. S. Nagar, *Naturwissenschaften*, **50**, 402 (1963) [*Chem. Abstr.*, **59**, 7525*h* (1963)]; *b*) H. R. Kricheldorf, *Angew. Chem.*, **84**, 107 (1972); *c*) W. Steglich, E. Buschmann, and O. Hollitzer, *ibid.*, **86**, 596 (1974); *d*) G. Maier and U. Schäfer, *Justus Liebigs Ann. Chem.*, **1980**, 798; *e*) P. de Mayo, A. C. Weedon, and R. W. Zabel, *Can. J. Chem.*, **59**, 2328 (1981); *f*) S. Goetze and W. Steglich, *Chem. Ber.*, **109**, 2323 (1976); *g*) J. Stefan

and W. Steglich, *ibid.*, **114**, 1337 (1981).
4) E. M. Beccalli, *J. Org. Chem.*, **49**, 4287 (1984).
5) S. Giambrone, G. Dattolo, and A. Roccaro, *Atti Accad. Sci., Lett. Arti Palermo, Parte 1*, **33**, 359 (1973) [*Chem. Abstr.*, **83**, 206047*t* (1974)]; R. A. Y. Jones and N. Sadighi, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 2259; M. Takahashi, N. Inaba, H. Kirihara, and S. Watanabe, *Bull. Chem. Soc. Jpn.*, **51**, 3312 (1978).
6) *a*) G. Lo Vecchio, F. Foti, F. Risitano, and G. Grassi, *Chim. Ind.* (Milan), **58**, 450 (1976) [*Chem. Abstr.*, **86**, 139961*h* (1977)]; *b*) *Idem, Tetrahedron Lett.*, **1977**, 2119; *c*) F. Risitano, G. Grassi, F. Foti, F. Caruso, and G. Lo Vecchio, *J. Chem. Soc., Perkin Trans. 1*, **1979**, 1522; *d*) G. Grassi, F. Foti, F. Risitano, and F. Caruso, *J. Chem. Res.*, **1983**, 172.
7) T. Sasaki, K. Kanematsu, and A. Kakehi, *J. Org. Chem.*, **36**, 2451 (1971); J. J. Barr, R. C. Storr, and V. K. Tandon, *J. Chem. Soc., Perkin Trans. 1*, **1980**, 1147.
8) T. Kato, Y. Yamamoto, and M. Kondo, *Chem. Pharm. Bull.*, **23**, 1873 (1975); Y. Yamamoto and Y. Azuma, *Heterocycles*, **6**, 1817 (1977); Y. Yamamoto, Y. Azuma, and K. Miyakawa, *Chem. Pharm. Bull.*, **26**, 1825 (1978); Y. Yamamoto and Y. Azuma, *Heterocycles*, **9**, 185 (1978); Y. Yamamoto and Y. Morita, *Chem. Pharm. Bull.*, **33**, 975 (1985).
9) Y. Oikawa, K. Sugano, and O. Yonemitsu, *J. Org. Chem.*, **43**, 2087 (1978); K. Mohri, Y. Oikawa, K. Hirao, and O. Yonemitsu, *Heterocycles*, **19**, 515 (1982); *idem, ibid.*, **19**, 521 (1982); I. Iwataki, S. Makisawa, and K. Saito, Jpn. Patent 79106466 [*Chem. Abstr.*, **92**, 58755*r* (1980)]; M. Sato, H. Ogasawara, K. Oi, and T. Kato, *Chem. Pharm. Bull.*, **31**, 1896 (1983); M. Sato, K. Sekiguchi, H. Ogasawara, and C. Kaneko, *Synthesis*, **1985**, 224.
10) J. P. Célérier, E. Dloisy, P. Kapron, G. Lhommet, and P. Maitte, *Synthesis*, **1981**, 130.
11) M. A. Perez, C. A. Dorado, and J. L. Soto, *Synthesis*, **1983**, 483.
12) S. Senda, K. Hirota, and O. Otani, *Yakugaku Zasshi*, **94**, 571 (1974).
13) H. L. Wheeler, P. T. Walden, and H. F. Matcalf, *J. Am. Chem. Soc.*, **20**, 64 (1898).