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Studies on Pyrimidine Derivatives. I.* Reaction of Pyrimidine N-Oxides with Enamines

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Reactions of 4,6-disubstituted pyrimidine N-oxides (Ia—f) with some enamines in the presence of benzoyl chloride were investigated. When Ia—f were treated with 1-morpholino-1-isobutene (II) in a similar manner given for the reaction of quinoline 1-oxide with II, α,α-dimethyl-(4,6-disubstituted 2-pyrimidine)acetaldehyde (IIIa—f) were obtained in moderate yields. Similarly, the reaction of Ia—f with 1-morpholino-1-cyclohexene (IV) and 1-morpholino-1-cycloheptene (VI) afforded 2-(4,6-disubstituted 2-pyrimidinyl)-cyclohexanones (V) and -cycloheptanones (VII), respectively.

However, the reaction of 4-ethoxy-6-methylpyrimidine 1-oxide with 1-piperidino-1-styrene under the same condition resulted in the formation of 2-phenacylpyrimidine (IX) in a poor yield.

Pyrimidine N-oxides used in this investigation were as follows: 4-methoxy-6-methyl- (Ia), 4-ethoxy-6-methyl- (Ib), 4-isopropoxy-6-methyl- (Ic), 4-benzyloxy-6-methyl- (Id), 4-methyl-6-phenyl- (Ie), and 4,6-dimethyl-pyrimidine 1-oxide (If).

As reported previously,[2] 4,6-disubstituted 2-cyanopyrimidines were synthesized by using Reissert-Henze reaction of the corresponding pyrimidine N-oxides. Recently Hamana, *et al.* reported[3,4] that quinoline 1-oxide reacted with enamines, such as 1-morpholino-1-cyclohexene and 1-morpholino-1-isobutene, in the presence of benzoyl chloride to give 2-(2-quinolyl)-cyclohexanone and α,α-dimethylquinolineacetaldehyde, respectively.

These two reactions seem apparently promising for the introduction of some carbon substituents into the 2-position of pyrimidine ring *via* its N-oxide. In this paper the authors wish to report the reaction of pyrimidine N-oxides with a variety of morpholinoenamines.

An ice-cooled mixture of 4-methoxy-6-methylpyrimidine 1-oxide and benzoyl chloride in chloroform was treated with 1-morpholino-1-isobutene (II), followed by the addition of hydrochloric acid to give a colorless oil (IIIa), bp 70° (1 mm Hg), in 70% yield. Elemental analysis of IIIa established its empirical formula as $C_{10}H_{14}O_2N_2$. The infrared (IR) spectrum of IIIa exhibits no band concerning the N-oxide function in the range of 1200—1300 cm^{-1} and shows the characteristic band of the aldehyde carbonyl group at 1729 cm^{-1}. The nuclear magnetic resonance (NMR) spectrum of IIIa indicates the presences of four methyl groups at 1.47 (6H, $(CH_3)_2C\langle$), 2.40 (3H, $CH_3\dot{C}=$), 3.92 (3H, $-OCH_3$), an olefinic proton 6.42, (1H, $-CH=C\langle$), and an aldehyde proton 9.88, (1H, $-CH=O$), respectively. Based on the spectral data described above, the structure of IIIa has been assigned as α,α-dimethyl-(4-methoxy-6-methyl-2-pyrimidine)acetaldehyde.

Similar treatment of the other 4,6-disubstituted pyrimidine N-oxides such as 4-ethoxy-6-methyl- (Ib), 4-isopropoxy-6-methyl-(Ic), 4-benzyloxy-6-methyl- (Id),[5] 4-methyl-6-phenyl-(Ie),[6] and 4,6-dimethyl-pyrimidine 1-oxide (If)[7] with II afforded the expected products (IIIb—

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* Dedicated to the memory of Prof. Eiji Ochiai.

[1] Location: *Aobayama, Sendai, 980, Japan.*

[2] H. Yamanaka, *Chem. Pharm. Bull.* (Tokyo), **6**, 633 (1958).

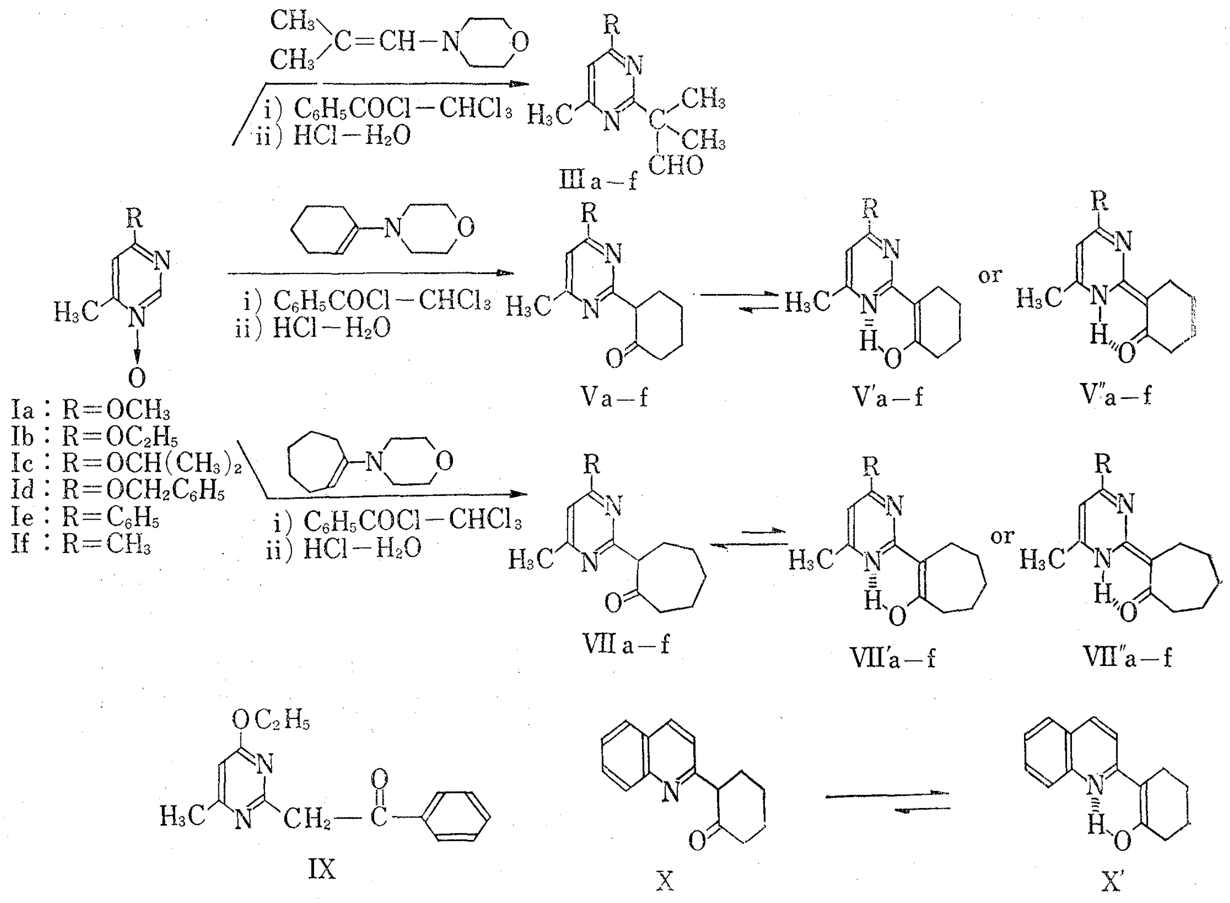
[3] M. Hamana and H. Noda, *Chem. Pharm. Bull.* (Tokyo), **13**, 912 (1965).

[4] M. Hamana and H. Noda, *Yakugaku Zasshi*, **89**, 641 (1969).

[5] H. Yamanaka, *Chem. Pharm. Bull.* (Tokyo), **7**, 158 (1959).

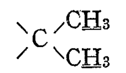
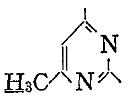
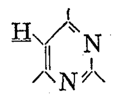
[6] H. Bredereck, R. Gompper, and H. Herlinger, *Chem. Ber.*, **91**, 2832 (1958).

[7] R. Hunt, J. McOmie, and E. Sayer, *J. Chem. Soc.*, **1959**, 525.



Chart

Table I. NMR and IR Spectral Data of Compound IIIa—f

No.	IR(neat) $\nu_{C=O}$ (cm^{-1})	NMR[a]			
					-C$\underline{H}$O
IIIa	1729	1.47(6H, s)	2.40(3H, s)	6.42(1H, s)	9.88(1H, s)
IIIb	1732	1.46(6H, s)	2.40(3H, s)	6.38(1H, s)	9.85(1H, s)
IIIc	1725	1.46(6H, s)	2.39(3H, s)	6.34(1H, s)	9.85(1H, s)
IIId	1725	1.46(6H, s)	2.40(3H, s)	6.47(1H, s)	9.85(1H, s)
IIIe	1735[b]	1.45(6H, s)	2.57(3H, s)	7.47(1H, s)	9.98(1H, s)
IIIf	1730	1.47(6H, s)	2.44(6H, s)	6.85(1H, s)	9.85(1H, s)

[a] NMR spectra were taken in $CDCl_3$ solution and all signals are expressed by the ppm downfield from tetramethylsilane used as an internal standard.

[b] measured in $CHCl_3$ solution

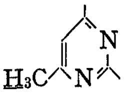
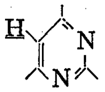
f), whose spectral data are summarized in Table I. As shown in the experimental section, the yields of IIIe,f seem to be somewhat lower than those of IIIa—d, but the reason is still obscure.

Following the similar fashion given for 1-morpholino-1-isobutene (II), Ia—f were allowed to react with 1-morpholino-1-cyclohexene (IV) to give 2-(2-pyrimidinyl)cyclohexanones (Va—f) in good yields. For instance, 2-(4-methoxy-6-methyl-2-pyrimidinyl)cyclohexanone (Va), mp 45—45.5°, was obtained in 80% yield by the reaction of Ia with IV and benzoyl chloride. The structure of Va was proposed as follows:

Compound Va was an empirical formula $C_{12}H_{16}O_2N_2$ and gave purple color with an aqueous solution of ferric chloride. The IR spectrum of Va exhibits no band concerning the N-oxide group, and a band at 1630 cm^{-1} which could be assigned to an enol C=C bond or a strongly chelated carbonyl group. The NMR spectrum of Va shows signals at 1.50—2.05 (4H, m), 2.20—2.70 (4.2H, m), 2.38 (3H, s), 6.20 (0.8H, s), 6.40 (0.2H, s), and 14.85—15.25 (0.8H, broad).

Observing the data described above, it is reasonably concluded that the structure of Va is 2-(4-methoxy-6-methyl-2-pyrimidinyl)cyclohexanone. Furthermore, these spectral data showed the existence of the intramolecular hydrogen bond between the ring nitrogen atom and the side chain oxygen atom. Accordingly, Va was considered to exist predominantly as the enol form (Va') or the enone form (Va'') in a chloroform solution, analogous to 2-substituted quinoline derivatives such as X and X'.[2,8] The spectral data of Va—f are summarized in Table II.

Table II. NMR and IR Spectral Data of Compound Va—f

No.	IR ($CHCl_3$) $\nu_{C=O}$ (cm^{-1})	NMR[a] Protons on cyclohexanone			NH or OH
Va	1630	1.50—2.05(4H, m) 2.20—2.70(4.2H, m)	2.38(3H, s)	6.20(0.8H, s) 6.40(0.2H, s)	14.85—15.25 (0.8H, b)
Vb	1635	1.55—2.10(4H, m) 2.20—2.70(4.2H, m)	2.37(3H, s)	6.16(0.8H, s) 6.37(0.2H, s)	15.09 (0.8H, broad s)
Vc	1638	1.57—2.06(4H, m) 2.20—2.74(4.2H, m)	2.34(3H, s)	6.12(0.8H, s) 6.32(0.2H, s)	14.97—15.30 (0.8H, b)
Vd	1635	1.50—2.05(4H, m) 2.20—2.70(4.2H, m)	2.37(3H, s)	6.25(0.8H, s) 6.48(0.2H, s)	14.98—15.35 (0.8H, b)
Ve	1639	1.50—2.20(4H, m) 2.24—3.00(4H, m)	2.51(3H, s)	7.17(1H, s)	14.28(1H, s)
Vf	1715 1635	1.59—2.03(4H, m) 2.22—2.70(4.3H, m)	2.42(6H, s)	6.65(0.7H, s) 6.86(0.3H, s)	14.00—15.20 (0.7H, b)

[a] NMR spectra were taken in $CDCl_3$ solution and all signals are expressed by the ppm downfield from tetramethylsilane used as an internal standard.

Further attempts were made to extend this reaction to the other enamines *e.g.* 1-morpholino-1-cycloheptene (VI) and 1-piperidino-1-styrene (VIII). Although the reaction of Ib with VIII resulted in the formation of the desired compound (IX) in a poor yield, Ia—f were transformed into the 2-(2-pyrimidinyl)cycloheptanone derivatives smoothly. Namely, when VI was added dropwise to a solution of Ia and benzoyl chloride in chloroform, an exothermic reaction occurred and the solution turned to orange yellow. Treatment of the reaction mixture with diluted hydrochloric acid, followed by the purification using an alumina column chromatography, afforded yellow prisms, mp 53.5—55° (VIIa), whose empirical formula was $C_{13}H_{18}O_2N_2$. Compound VIIa gave purple color with ferric chloride, and formed the corresponding semicarbazone, mp 201—202°, $C_{14}H_{21}O_2N_5$. The spectral dara of VIIa shown in Table III, suggested that this product must have the structure of 2-(4-methoxy-6-methyl-2-pyrimidinyl)cycloheptanone, and the predominant tautomer is neither the enol form (VIIa') nor the enone form (VIIa''), but the keto form (VIIa).

The other pyrimidine N-oxides were also transformed to the expected products (VIIb—f) in the similar fashion given for the reaction of Ia with VI. The spectral data summarized in Table III.

In conclusion, the above investigation has provided a facile synthetic method for the pyrimidine derivatives having a carbonyl function on the side chain.

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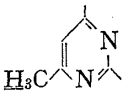
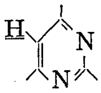
[8] R.F. Branch, A.H. Beckett, and D.B. Cowell, *Tetrahedron*, **19**, 401, 413 (1963).

Table III. NMR and IR Spectral Data of Compound VIIa—f

No.	IR ($CHCl_3$) $\nu_{C=O}$ (cm^{-1})	NMR[a]			
		Protons on cycloheptanone			N$\underline{H}$ or O$\underline{H}$
VIIa	1705	1.00—3.10(10H, m)	2.34(0.6H, s)	6.10(0.2H, s)	15.70—16.70
	1635	3.70—4.10(0.8H, m)	2.40(2.4H, s)	6.40(0.8H, s)	(0.2H, b)
VIIb	1705	1.20—3.10(10H, m)	2.33(0.6H, s)	6.05(0.2H, s)	15.30—16.20
	1635	3.70—4.10(0.8H, m)	2.38(2.4H, s)	6.35(0.8H, s)	(0.2H, b)
VIIc	1710	1.20—3.00(10H, m)	2.31(0.6H, s)	6.02(0.2H, s)	15.60—16.10
	1630	3.70—4.20(0.8H, m)	2.37(2.4H, s)	6.33(0.8H, s)	(0.2H, b)
VIId	1707	1.00—3.00(10H, m)	2.33(0.6H, s)	6.12(0.2H, s)	15.60—16.00
	1638	3.77—4.10(0.8H, m)	2.39(2.4H, s)	6.45(0.8H, s)	(0.2H, b)
VIIe	1708	1.10—3.20(10H, m)	2.53(3H, s)	7.14(0.3H, s)	15.31
	1637	3.90—4.23(0.7H, m)		7.30–7.70(0.7H)	(0.3H, broad s)
VIIf	1708	1.00—3.20(10H, m)	2.43(6H, s)	6.61(0.1H, s)	15.00—15.50
	1635	3.80—4.20(0.9H, m)		6.87(0.9H, s)	(0.1H, b)

a) NMR spectra were taken in $CDCl_3$ solution and all signals are expressed by the ppm downfield from tetramethylsilane used as an internal standard.

Experimental[9)]

Reaction of Ia—f with 1-Morpholino-1-isobutene (II) in the Presence of BzCl——General Procedure: To a solution of I (1.0 equivalent) and II (2.0 equivalents) in $CHCl_3$, BzCl (1.1 equivalents) was added dropwise with stirring at a temperature not exceeding 40°. The mixture was then warmed at 30—40° for 2 hr, and after cooling, poured into 3N HCl. The reaction mixture was condensed under reduced pressure to give a residue, which was treated with C_6H_6. The C_6H_6 layer was extracted with 3N HCl and the extract was made alkaline with K_2CO_3. The liberated oil was dissolved in C_6H_6 and the solution was dried over anhyd. K_2CO_3. After removal of the solvent, the residue was purified by column chromatography (Al_2O_3–ether), followed by distillation *in vacuo* to yield III.

The results of elemental analysis of the products are recorded in Table IV.

α,α-Dimethyl-(4-methoxy-6-methyl-2-pyrimidine)acetaldehyde (IIIa)——From Ia (1 g, 0.0071 mole), II (2.0 g, 0.014 mole), BzCl (1.1 ml, 0.008 mole), and $CHCl_3$ (7 ml), IIIa was obtained according to the general procedure. Colorless liquid, bp 70° (1 mmHg), yield 0.95 g (70%).

α,α-Dimethyl-(4-ethoxy-6-methyl-2-pyrimidine)acetaldehyde (IIIb)——From Ib (1 g, 0.0065 mole), II (1.8 g, 0.013 mole), BzCl (1.0 ml, 0.072 mole), and $CHCl_3$ (7 ml), IIIb was obtained according to the general procedure. Colorless liquid, bp 73° (1 mmHg), yield 0.88 g (65%).

α,α-Dimethyl-(4-isopropoxy-6-methyl-2-pyrimidine)acetaldehyde (IIIc)——From Ic (1 g, 0.0059 mole), II (1.7 g, 0.012 mole), BzCl (0.9 ml, 0.0065 mole), and $CHCl_3$ (7 ml), IIIc was obtained according to the general procedure. Colorless liquid, bp 75—80° (1 mmHg), yield 0.85 g (65%).

α,α-Dimethyl-(4-benzyloxy-6-methyl-2-pyrimidine)acetaldehyde (IIId)——From Id (1 g, 0.0046 mole), II (1.3 g, 0.0098 mole), BzCl (0.75 ml, 0.005 mole), and $CHCl_3$ (6 ml), IIId was obtained according to the general procedure with the exception of using 20% HCl on extracting IIId from C_6H_6 solution. Colorless liquid, bp 130—135° (1 mmHg), yield 0.75 g (60%).

α,α-Dimethyl-(4-phenyl-6-methyl-2-pyrimidine)acetaldehyde (IIIe)——From Ie (1 g, 0.005 mole), II (1.4 g, 0.01 mole), BzCl (0.77 ml, 0.0055 mole), and $CHCl_3$ (8 ml), IIIe was obtained according to the general procedure. The product was recrystallized from petr. ether (bp 63—70°). Colorless needles, mp 85°, bp 125° (1 mmHg, yield 0.2 g (15%).

α,α-Dimethyl-(4,6-dimethyl-2-pyrimidine)acetaldehyde (IIIf)——From If (1 g, 0.008 mole), II (2.3 g, 0.016 mole), BzCl (1.2 ml, 0.009 mole), and $CHCl_3$ (8 ml), IIIf was obtained according to the general procedure. Colorless liquid, bp 65° (1 mmHg), yield 0.22 g (15%).

Reaction of Ia—f with 1-Morpholino-1-cyclohexene (IV) in the Presence of BzCl——General Procedure: To a solution of I (1.0 equivalent) and IV (2.0 equivalents) in $CHCl_3$, BzCl (1.1 equivalents) was added dropwise with stirring and cooling (below 40°). The reaction mixture was allowed to stand at room temperature

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9) All melting points were uncorrected. IR spectra measurements were performed with a JASCO IR A-1 spectrometer and NMR spectra were taken at 60 MHz with a Hitachi-Perkin-Elmer R-20 spectrometer.

TABLE IV. Analyses of Compound IIIa—f

No.	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
IIIa	$C_{10}H_{14}O_2N_2$	61.83	7.27	14.42	62.06	7.49	14.42
IIIb	$C_{11}H_{16}O_2N_2$	63.44	7.74	13.45	63.06	7.90	13.53
IIIc	$C_{12}H_{18}O_2N_2$	64.84	8.16	12.60	65.13	8.38	12.53
IIId	$C_{16}H_{18}O_2N_2$	71.09	6.71	10.36	71.25	6.90	10.37
IIIe	$C_{15}H_{16}ON_2$	74.97	6.71	11.66	74.61	6.79	11.73
IIIf	$C_{10}H_{14}ON_2$	67.38	7.92	15.72	68.02	8.24	15.55

for 1—2 hr, then poured into 3N HCl and condensed under reduced pressure to leave a residue, which was dissolved in 3N HCl. After washing with C_6H_6, the aqueous solution was made alkaline with K_2CO_3 and the liberated solid or oil was extracted with C_6H_6. The C_6H_6 extract was dried and evaporated to give the crude product (V) which was recrystallized from MeOH. Depending on the case, the crude product (V) was purified by distillation *in vacuo* with subsequent recrystallization from MeOH.

The elemental analysis data are shown in Table V.

2-(4-Methoxy-6-methyl-2-pyrimidinyl)cyclohexanone (Va)——From Ia (1 g, 0.0071 mole), IV (2.4 g, 0.015 mole), BzCl (1.1 ml, 0.008 mole), and $CHCl_3$ (7 ml), Va was obtained according to the general procedure. Yellow needles, mp 45—45.5°, bp 120° (2 mmHg), yield 1.2 g (80%).

2-(4-Ethoxy-6-methyl-2-pyrimidinyl)cyclohexanone (Vb)——From Ib (1 g, 0.0064 mole), IV (2.2 g, 0.013 mole), BzCl (1.0 ml, 0.0072 mole), and $CHCl_3$ (7 ml), Vb was obtained according to the general procedure. Yellow prisms, mp 68—69°, bp 120° (1 mmHg), yield 1.4 g (85%).

2-(4-Isopropoxy-6-methyl-2-pyrimidinyl)cyclohexanone (Vc)——From Ic (1 g, 0.0059 mole), IV (2.0 g, 0.012 mole), BzCl (0.9 ml, 0.0065 mole), and $CHCl_3$ (7 ml), Vc was obtained according to the general procedure. Yellow prisms, mp 80—80.5°, bp 120—125° (1 mmHg), yield 1.3 g (90%).

2-(4-Benzyloxy-6-methyl-2-pyrimidinyl)cyclohexanone (Vd)——From Id (1 g, 0.0046 mole), IV (1.5 g, 0.0092 mole), BzCl (0.7 ml, 0.005 mole), and $CHCl_3$ (6 ml), Vd was obtained according to the general procedure with the exception of using 20% HCl on extracting Vd from C_6H_6 solution. Yellow needles, mp 83°, bp 200° (1 mmHg), yield 1.0 g (70%).

2-(4-Phenyl-6-methyl-2-pyrimidinyl)cyclohexanone (Ve)——From Ie (1 g, 0.005 mole), IV (1.7 g, 0.01 mole), BzCl (0.77 ml, 0.0055 mole), and $CHCl_3$ (8 ml), Ve was obtained according to the general procedure. To remove impurities, the product was passed through a column of Al_2O_3 using C_6H_6 as an eluant. Yellow needles, mp 80—82°, yield 0.6 g (45%).

2-(4,6-Dimethyl-2-pyrimidinyl)cyclohexanone (Vf)——From If (1 g, 0.008 mole), IV (2.7 g, 0.016 mole), BzCl (1.2 ml, 0.009 mole), and $CHCl_3$ (7 ml), Vf was obtained according to the general procedure. Yellow prisms, mp 68—69°, bp 120° (2 mmHg), yield 0.85 g (50%).

TABLE V. Analyses of Compound Va—f

No.	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
Va	$C_{12}H_{16}O_2N_2$	65.43	7.32	12.72	65.86	7.11	12.85
Vb	$C_{13}H_{18}O_2N_2$	66.64	7.74	11.96	66.26	7.64	11.83
Vc	$C_{14}H_{20}O_2N_2$	67.71	8.12	11.28	68.14	8.34	11.45
Vd	$C_{18}H_{20}O_2N_2$	72.95	6.80	9.45	73.00	6.90	9.61
Ve	$C_{17}H_{18}ON_2$	76.66	6.81	10.52	76.49	6.83	10.55
Vf	$C_{12}H_{16}ON_2$	70.56	7.90	13.72	70.44	7.90	13.72

Reaction of Ia—f with 1-Morpholino-1-cycloheptene (VI) in the Presence of BzCl——General Procedure: To a solution of I (1.0 equivalent) in $CHCl_3$, BzCl (1.5 equivalents) was added dropwise with stirring and cooling (below 20°). After stirring for an additional 40 min, VI (1.0 equivalent) was added slowly with stirring at a temperature not exceeding 40°. The reaction mixture was refluxed for 1.5 hr. After cooling, the mixture was poured into 3N HCl, condensed to dryness under reduced pressure and the residue was dissolved in $CHCl_3$, washed with 3N Na_2CO_3 and dried over anhyd. K_2CO_3. The $CHCl_3$ was removed and the residue was passed through a column of Al_2O_3 using ether as an eluant. The first fraction gave VII, which was purified by recrystallization.

2-(4-Methoxy-6-methyl-2-pyrimidinyl)cycloheptanone (VIIa)——From Ia (1.4 g, 0.01 mole), VI (1.81 g, 0.01 mole), BzCl (1.86 g, 0.015 mole), and $CHCl_3$ (6 ml), VIIa was obtained according to the general procedure. Recrystallization from MeOH gave yellow prisms, mp 53.5—55°, bp 126—130° (2 mmHg), yield 0.99 g (42%). Semicarbazone, mp 201—202° (acetone). *Anal.* Calcd. for $C_{14}H_{21}O_2N_5$: C, 57.71; H, 7.27; N, 24.04. Found: C, 57.98; H, 7.54; N, 24.18.

2-(4-Ethoxy-6-methyl-2-pyrimidinyl)cycloheptanone (VIIb)——From Ib (1.54 g, 0.01 mole), VI (1.81 g, 0.01 mole), BzCl (1.86 g, 0.015 mole), and $CHCl_3$ (6 ml), VIIb was obtained according to the general procedure. Recrystallization from MeOH gave yellow needles, mp 61.5—63°, bp 138—140° (1.5 mmHg), yield 1.57 g (63%). Semicarbazone, mp 164.5—165.5° (EtOH). *Anal.* Calcd. for $C_{15}H_{23}O_2N_5$: C, 58.99; H, 7.59; N, 22.94. Found: C, 58.77; H, 7.60; N, 22.45.

2-(4-Isopropoxy-6-methyl-2-pyrimidinyl)cycloheptanone (VIIc)——From Ic (1.0 g, 0.006 mole), VI (1.09 g, 0.006 mole), BzCl (1.12 g, 0.009 mole), and $CHCl_3$ (4 ml), VIIc was obtained according to the general procedure. Recrystallization from MeOH gave yellow prisms, mp 65.5—67°, bp 123° (2 mmHg), yield 0.85 g (57%).

2-(4-Benzyloxy-6-methyl-2-pyrimidinyl)cycloheptanone (VIId)——From Id (1.3 g, 0.006 mole), VI (1.09 g, 0.006 mole), BzCl (1.12 g, 0.009 mole), and $CHCl_3$ (5 ml), VIId was obtained according to the general procedure. Recrystallization from petr. ether (bp 50—55°) gave yellow needles, mp 90—91°, yield 0.9 g (48%).

2-(4-Phenyl-6-methyl-2-pyrimidinyl)cycloheptanone (VIIe)——To a solution of Ie (1.86 g, 0.01 mole) and VI (1.81 g, 0.01 mole) in $CHCl_3$, BzCl (1.86 g, 0.015 mole) was added dropwise with stirring and cooling (below 5°). After stirring for 1.5 hr on an ice-salt bath, the reaction mixture was treated with 3N HCl (10 ml). The separated orange solid was removed by filtration and the filtrate was condensed under reduced pressure to give a residue which was dissolved in $CHCl_3$. The $CHCl_3$ layer was washed with 3N Na_2CO_3, dried over anhyd. K_2CO_3 and evaporated to dryness. The residue was passed through a column of Al_2O_3 using petr. ether (bp 30—40°)–C_6H_6 as an eluant, and the eluate was distilled to give 0.59 g (21%) of red liquid (VIIe), bp 163—170° (0.01 mmHg). Semicarbazone, mp 203—205° (decomp.) (acetone–MeOH). *Anal.* Calcd. for $C_{19}H_{23}ON_5$: C, 67.63; H, 6.87; N, 20.76. Found: C, 67.35; H, 6.83; N, 20.53.

2-(4,6-Dimethyl-2-pyrimidinyl)cycloheptanone (VIIf)——To a solution of If (1.24 g, 0.01 mole) in $CHCl_3$ (7 ml), BzCl (1.86 g, 0.015 mole) was added dropwise with stirring and cooling (below 0°). After stirring for an additional 30 min on an ice-salt bath, VI (1.81 g, 0.01 mole) was added dropwise at the temperature not exceeding 10°. The resulting mixture was stirred for 4 hr at −5—10°. The oily residue obtained according to the general procedure was passed through a column of Al_2O_3 using cyclohexane–C_6H_6 (9: 1) as an eluant to give yellow solid (VIIf), which was recrystallized from MeOH. Yellow needles, mp 83—85°, yield 0.5 g (23%).

TABLE VI. Analyses of Compound VIIa—f

No.	Formula	Analysis (%)					
		Calcd.			Found		
		C	H	N	C	H	N
VIIa	$C_{13}H_{18}O_2N_2$	66.64	7.74	11.96	66.47	7.72	11.65
VIIb	$C_{14}H_{20}O_2N_2$	67.71	8.12	11.28	67.48	7.94	11.23
VIIc	$C_{15}H_{22}O_2N_2$	68.67	8.45	10.68	69.04	8.25	10.67
VIId	$C_{19}H_{22}O_2N_2$	73.52	7.14	9.03	73.59	7.11	9.07
VIIe	$C_{18}H_{20}ON_2$	77.11	7.19	9.99	76.72	7.09	10.01
VIIf	$C_{13}H_{18}ON_2$	71.52	8.31	12.83	71.97	8.36	12.81

Reaction of Ib with 1-Piperidino-1-styrene in the Presence of BzCl——To a well cooled solution of Ib (1 g, 0.0065 mole) in $CHCl_3$ (7 ml), BzCl (1.0 ml, 0.0072 mole) was added dropwise, maintaining the temperature at 0°. After stirring for 30 min at room temperature, VIII (2.3 g, 0.015 mole) was added dropwise at 0°, and the mixture was stirred for an additional 2.5 hr on an ice-salt bath. After standing overnight at room temperature, the reaction mixture was poured into 3N HCl, condensed under reduced pressure and the residue was dissolved in ether and the ether layer was extracted with 3N HCl. The HCl solution was washed with ether, made alkaline with K_2CO_3 and the liberated dark brown oil was extracted with $CHCl_3$. Evaporation of the $CHCl_3$ gave dark brown liquid, which was purified by column chromatography [Al_2O_3–petr. ether (60—70°)] to give a small amount of orange solid (IX). Recrystallization from petr. ether (bp 45—50°) gave pale orange needles, mp 80.5—82°. *Anal.* Calcd. for $C_{15}H_{16}O_2N_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.30; H, 6.36; N, 11.16. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1700, 1640. NMR ($CDCl_3$, TMS, ppm): 1.38 (3H, t, J=7.5 Hz), 2.39 (3H, s), 4.38 (0.3H, q, J=7.5 Hz), 4.40 (0.7H, q, J=7.5 Hz), 4.45 (0.6H, s), 6.14 (0.7H, s), 6.35 (0.3H, s), 7.2—7.6 (3.7H, m), 7.6—8.1 (2H, m), 14.5—15.8 (0.7H, b).

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