Photochemistry of Pyrimidin-4-ones in Aqueous Solution and Reactions of Dewar Pyrimidinones with Water and Hydrogen Sulphide: Isolation of Reversible Hydrates and Thiazines

Tamiko Takahashi, Shun-ichi Hirokami, and Masanori Nagata*
Laboratory of Chemistry, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-01, Japan
Takao Yamazaki
Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-01, Japan
Tadamasa Date
Chemistry Research Laboratory, Tanabe Seiyaku Co., Ltd., Toda, Saitama 335, Japan

Irradiation of the 2,3,6-trimethylpyrimidin-4-one (**1a**) in aqueous solution gave an unstable product (**3a**) that was observed by ^{1}H n.m.r. spectra and reverted to the starting pyrimidin-4-one (**1a**) at room temperature. The reversible compound (**3a**) could not be separated from a large amount of the starting pyrimidin-4-one (**1a**) by column chromatography. Irradiation of 2,3-dialkylpyrimidin-4-ones (**1e,f**), 3,6-dimethylpyrimidin-4-one (**1g**), and 3-methylpyrimidin-4-one (**1h**) in aqueous acetonitrile gave (*Z*)-2-acetyl-3-amino-*N*-methylprop-2-enamide (**4e**), 2-(aminoethylene)-3-oxo-octane-8-lactam (**4f**), (*Z*)-*N*-methyl-2-acetyl-3-aminoprop-2-enamide (**5g**), and (*Z*)-3-amino-2-formyl-*N*-methylprop-2-enamide (**5h**) as the major crystalline products, respectively. In order to isolate the reversible compounds (**3**), 1,3,6-trialkyl-5-oxo-2,6-diazabicyclo[2.2.0]hex-2-enes (**2a**) and (**2b**) and 7-oxo-9-t-butyl-6,10-diazatricyclo[4.4.0.0^{1,8}]dec-9-ene (**2c**) (Dewar pyrimidinones) were prepared and treated in aqueous solutions at 15–20 °C. The isolated reversible products were (*Z*)-*N*-acetyl-2-amino-*N*-methylbut-2-enamide (**3a**), (*Z*)-*N*-acetyl-3-amino-4,4,*N*-trimethylpent-2-enamide (**3b**), and (*Z*)-*N*-(3-amino-4,4-dimethyl-1-oxopent-2-enyl)-2-piperidone (**3c**). The reactions of the Dewar isomers (**2b**) and (**2c**) and 6-methyl-5-oxo-1,3-di-t-butyl-2,6-diazabicyclo-[2.2.0]hex-2-ene (**2d**) in acetonitrile solution containing hydrogen sulphide gave 2-amino-2,3,6-trialkyl-3,4-dihydro-2*H*-1,3-thiazin-4-ones (**8b**) and (**8d**) and 9a-amino-5,6,7,8,9a-hexahydro-2,6-di-t-butyl-4*H*-pyrido[2,1-*b*][1,3]thiazin-4-one (**8c**). The hydrates (**3a–c**) and 1,3-thiazines (**8b**) and (**8c**) reverted quantitatively to the corresponding pyrimidin-4-ones (**1a–c**) at room temperature. The mechanisms and intermediates of the reactions are discussed and an *X*-ray crystallographic study of 3-amino-2-formyl-*N*-methylbut-2-enamide (**4g**) is reported.

Much attention has been focussed on the photochemical reactions of nucleic acids and their derivatives with respect to physicochemically induced damage in biological systems since Sinsheimer and Hastings reported that exposure of aqueous uracil or uridine to u.v. light led to reversible formation of photoproducts. Similarly, uracil, cytosine, thymine, and their derivatives were converted reversibly into pyrimidinols in aqueous solution.[1]

We found that photolysis of the 2,3,6-trialkylpyrimidin-4-ones (**1**)[2] in aqueous solution, gave photoproducts which reverted to starting material without irradiation at room temperature.[2d] Here, we describe the complete experimental detail for the photohydration of pyrimidin-4-ones (**1a,e—h**) and isolation of the reversible products formed in the reactions of the isolated Dewar pyrimidinones (**2a—d**)[2c] (photochemical intermediates)[2a–e] with water and hydrogen sulphide.

The Dewar isomers were postulated as intermediates in the photochemistry of 4-amino-2,6-dimethylpyrimidine in aqueous solution[3] and of 1,3-dimethyluracil in methanol.[4]

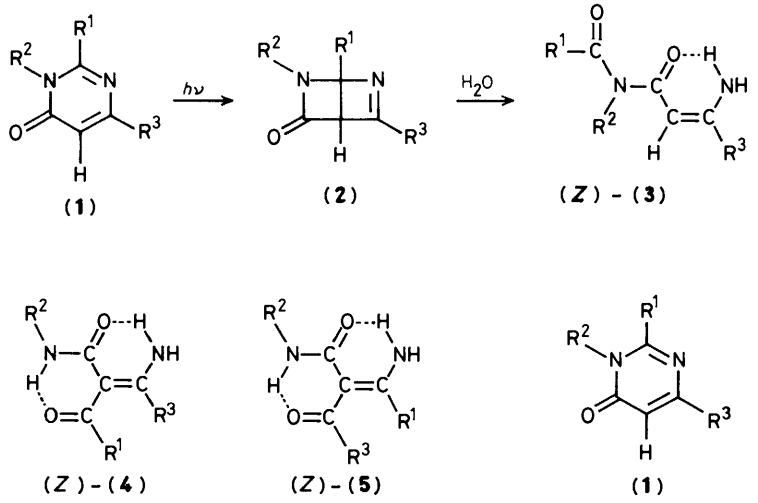
Results and Discussion

Photochemical Reactions of Pyrimidin-4-ones (**1**) *and Thermal Reactions of Dewar Pyrimidinones* (**2**) *in Aqueous Solution.*—When 2,3,6-trimethylpyrimidin-4(3*H*)-one (**1a**) [$\lambda_{max.}(H_2O)$ 269 (ε 4 860 dm^3 l^{-1} cm^{-1}) and 225 nm (ε 5 850)] was irradiated in aqueous acetonitrile with a high-pressure mercury lamp (100 W) through quartz under an argon atmosphere at 2 °C for 7 h, the ^{1}H n.m.r. spectrum showed formation of a photoproduct (**3a**) (43%) and a trace amount of 2-acetyl-3-amino-*N*-methylbut-2-enamide (**4a**).[5] The reversion of (**3a**) to starting material (**1a**) was observed in the dark at room temperature. Separation of the products by column chromatography on alumina gave (**4a**) (13%) and starting material (**1a**) (63%). Attempts to isolate product (**3a**) by column chromatography on alumina and on Sephadex LH-20 were unsuccessful.

Analogous photolysis of the pyrimidin-4-ones (**1e—h**) gave the corresponding products (**3e**) and (**4e,f**) (*Z*)-2-acetyl-3-amino-*N*-methylprop-2-enamide (**5g**) (32%), and (*Z*)-3-amino-2-formyl-*N*-methylprop-2-enamide (**5h**) (4%) in aqueous acetonitrile at 0—2 °C (Scheme 1).

Recently, we succeeded in isolating the Dewar pyrimidinones (**2a—c**)[2c] and expected that the reversible photoproducts (**3a—c**) could be isolated when the reactions of the Dewar isomers (**2a—c**) were carried out in aqueous solutions.

Treatment of 1,3,6-trimethyl-2,6-diazabicyclo[2.2.0]hex-2-en-5-one (Dewar pyrimidinone) (**2a**)[2c] in acetone solution containing water (10 v/v%) at 19 °C gave crystalline *N*-acetyl-3-amino-*N*-methylbut-2-enamide (**3a**) (46%) and 2,3,6-trimethylpyrimidin-4-one (**1a**) (33%) which were isolated by crystallization and by column chromatography on Sephadex



	R^1	R^2	R^3
a	Me	Me	Me
b	Me	Me	Bu^t
c	$-(CH_2)_4-$		Bu^t
d	Bu^t	Me	Bu^t
e	Me	Me	H
f	$-(CH_2)_5-$		H
g	H	Me	Me
h	H	Me	H

Scheme 1.

Table 1. Thermal reactions of the Dewar pyrimidinones (**2**) with water

Starting compd.	R^1	R^2	R^3	Solvent[a]	Temp. (°C)	Time (h)	Products (%) (1)	(3)	(4)	
(**2a**)	Me	Me	Me	A	19	2	33	46	N.d.[b]	
(**2a**)	Me	Me	Me	B	16	39	63	0	19	
(**2a**)	Me	Me	Me	C	35	51	14	0	17	*c*
(**2b**)	Me	Me	Bu^t	A	15	2	18	74	0	
(**2b**)	Me	Me	Bu^t	C	35	41	12	0	81	*d*
(**2c**)	$-(CH_2)_4-$		Bu^t	A	20	1	32	65	0	
(**2c**)	$-(CH_2)_4-$		Bu^t	C	35	37	85	0	10	
(**2d**)	Bu^t	Me	Bu^t	A	35	10	2	0	0	*e*

[a] A, acetone–H_2O (90:10, v/v); B, acetone–H_2O (70:30, v/v); C, CD_3CN–H_2O (94:6—95:5, v/v); [b] Not determined. [c] *N*-Methylacetoacetamide (**7a**) (14%) was obtained as a hydrolysis product of (**4a**) on alumina. [d] 3-Amino-4,4,*N*-trimethylpent-2-enamide (**6b**) (6%) was obtained as a hydrolysis product of (**4b**) on alumina. [e] The starting material (**2d**) (80%) was recovered.

LH-20. Similarly, the hydrates (**3b**) (74%) and (**3c**) (65%) and pyrimidin-4-ones (**1b**) (18%) and (**1c**) (32%) were obtained from the reactions of the Dewar pyrimidinones (**2b**) and (**2c**) with water.

The minor product (**4a**) that was formed in the photolysis of (**1a**) in aqueous solution could not be separated under the conditions. To isolate (**4a**), the Dewar isomer (**2a**) in acetone–water (30 v/v%) solution was set aside for 39 h at 16 °C. The hydrate (**3a**) reverted to (**1a**) and careful separation on a column of alumina gave (**1a**) (63%) and (**4a**) (19%).

When the Dewar isomers (**2a**) reacted with water in acetonitrile solution at 35 °C, 2-acetyl-3-amino-*N*-methylbut-2-enamide (**4a**) (17%), pyrimidin-4-one (**1a**) (14%), and *N*-methylacetoacetamide (**7a**) (14%) as a hydrolysis product of (**4a**) on a column of alumina were obtained. Analogously, the Dewar isomers (**2b**) and (**2c**) gave the corresponding hydrates [(**4b**) (81%) and (**4c**) (10%)] and pyrimidin-4-ones (**1b**) (12%) and (**1c**) (85%). The Dewar pyrimidinone (**2d**) (R^1 = R^3 = Bu^t) and (**2g**; R^1 = H and R^3 = Me) did not give the corresponding products (**3d**) and (**4d**). The Dewar isomer (**2g**)[1b] gave the hydrates (**5g**) (32%) (Scheme 1).

The reaction conditions and yields of the products are summarized in Tables 1 and 2. The The spectral data of (**3**) are listed in Table 3.

N-Methylacetoacetamide (**7a**) and 3-amino-4,4,*N*-trimethylpent-2-enamide (**6b**) were obtained from the reactions of the respective Dewar isomers (**2a**) and (**2b**) in aqueous acetonitrile at 35 °C. We presumed that the products (**7a**) and (**6b**) are formed by hydrolysis of the enamino ketones (**4a**) and (**4b**) on a column of alumina in the course of product separation. Hydrolysis of (**4b**) on alumina gave (**6b**) (45%) and 4,4,*N*-trimethyl-3-oxopentanamide (**7b**) (26%). The structures of (**7a**), (**6b**), and (**7b**) were deduced from their spectral data and those of (**7a**) and (**7b**) were confirmed by comparison with the spectral data of an authentic sample and by synthesis, respectively.

The hydrates (**3a**—**c**) reverted quantitatively to the

Table 2. Photolysis of the pyrimidin-4-ones (**1**) and reaction of Dewar pyrimidinone (**2g**) in aqueous acetonitrile solution[a]

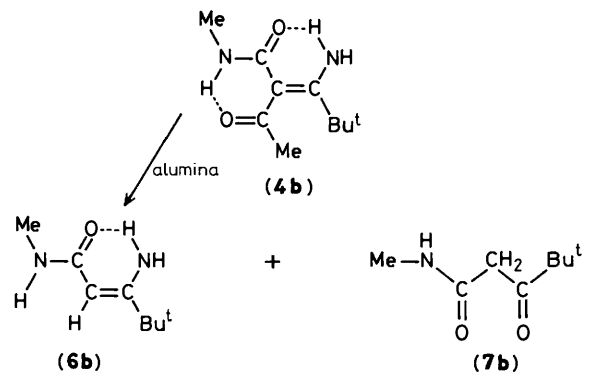
Starting compd.	R^1	R^2	R^3	Irrad'n time (h)	Recovered (**1**) (%)	Yield of products (%) (**3**)	(**4**)	(**5**)	
(**1a**)	Me	Me	Me	7	63	N.d.[f]	13	0	
(**1e**)	Me	Me	H	18	47	4	19	0	*b*
(**1f**)	$-(CH_2)_5-$		H	15	60	0	13	0	*c*
(**1g**)	H	Me	Me	16	34	0	0	48	*d*
(**2g**)[e]	H	Me	Me		N.d.[f]	0	0	32	*d*
(**1h**)	H	Me	H	6	53	0	0	4	

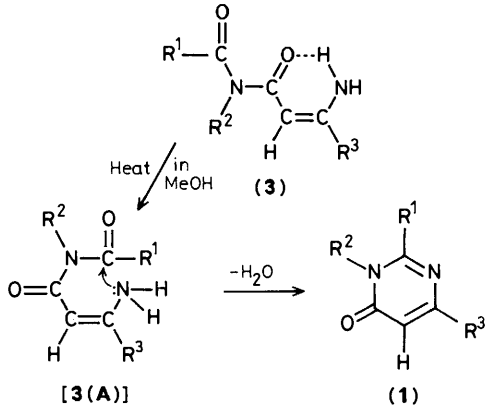
[a] Photolysis was carried out in H_2O–MeCN (85:15, v/v) at 0—2 °C. [b] Compound (**3e**) reverted quantitatively to the pyrimidin-4-one (**1e**) after 2 days at 15 °C. [c] ε-Caprolactam (11%) was obtained as a degradation product. [d] The products (**4e**) and (**5g**) were the same compound. [e] A mixture of (**1h**) and (**2h**) (70:30) was used for the reaction. [f] Not determined.

Table 3. ^{1}H N.m.r., i.r., and u.v. spectral data for the hydrates (**3**)

Compd. no.	^{1}H N.m.r.[a] (δ_H) R^1	R^2	R^3	2-H	NH_2	I.r.[b] (ν/cm^{-1})	U.v. (MeCN) [$\lambda_{max.}$/nm (ε)[c]]
(*Z*)-(**3a**)	2.42 (Me)	3.22 (Me)	2.07 (Me)	5.03	4.8—5.7 8.5—9.6	3 500, 3 300 1 665, 1 640 1 605	297(21 500) 225(4 950)
(*Z*)-(**3b**)	2.26 (Me)	3.09 (Me)	1.18 (Bu^t)	5.08	7.3—7.5 9.2—9.4	3 520, 1 660 1 630, 1 595	302(22 200)
(*Z*)-(**3c**)	$R^1 = R^2 = -(CH_2)_4-$ 2.3—2.5 (CH_2) 1.6—1.9 (2 × CH_2)	3.6—3.8 (CH_2)	1.14 (Bu^t)	6.03	6.5—7.7 8.8—9.6	3 520, 3 280 1 665, 1 620 1 600	308(19 600) 227(5 470)
(*Z*)-(**3e**)	2.42 (Me)	3.23 (Me)	7.18[d] (H)	5.01[e]	5.1—6.1 7.3—9.0	3 420, 3 350 1 652	n.m.[f]

[a] The ^{1}H n.m.r. spectra of the hydrates (**3a**) and (**3e**) were measured in $CDCl_3$ and of the hydrates (**3b**) and (**3c**) were measured in [$^2H_6$]Me_2SO. [b] The i.r. spectra of (**3a**—**c**) were measured in $CHCl_3$ and that of (**3e**) for the neat compound. [c] ε dm^3 l^{-1} cm^{-1}. [d] Doublet of doublets, *J* 8 and 18 Hz. [e] Doublet, *J* 8 Hz. [f] The u.v. spectrum was not measured.





	R^1	R^2	R^3
a	Me	Me	Me
b	Me	Me	Bu^t
c	$-(CH_2)_4-$		Bu^t

Scheme 2.

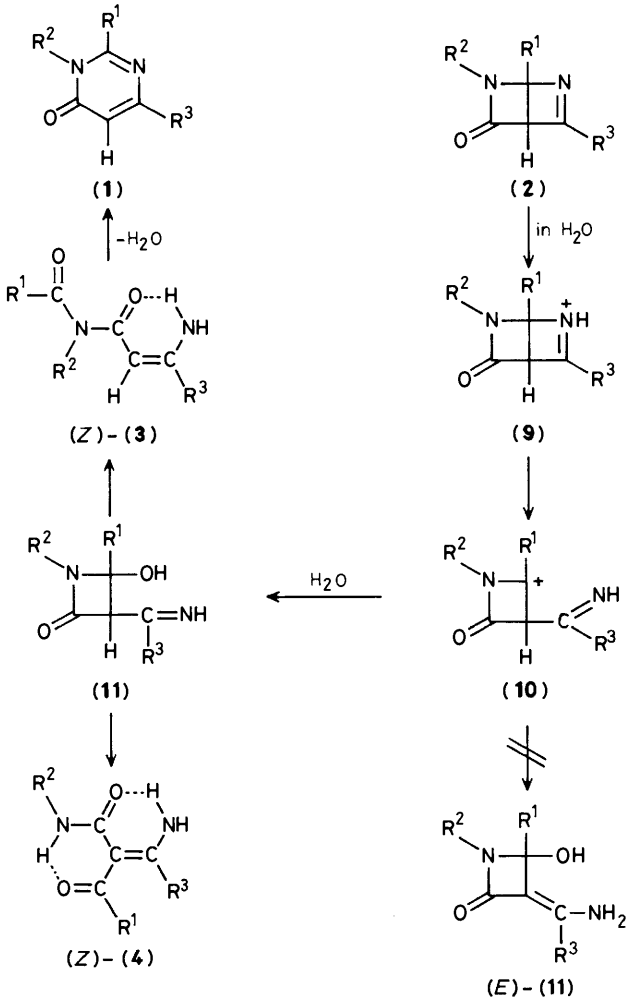
corresponding pyrimidin-4-ones (**1a**—**c**) (96—98%) in methanol at 16—23 °C (Scheme 2). Cyclization of compound (**3**) to (**1**) requires only rotation about the C(1)–C(2) bond and involves [**3(A)**] as an intermediate state of (**3**). The amine nitrogen attacks the imide carbonyl carbon and concomitant elimination of water molecule gives (**1**).

The structures of the hydrates (**3**), (**4**), and (**5**) were deduced from spectral data. Thus, the hydrates (**3**) and (**4**) showed $\lambda_{max.}$(MeOH) 305 ± 4 nm (ε 20 000—14 000 dm^3 mol^{-1} cm^{-1}) and the adducts [(**5g**) and (**5h**)] $\lambda_{max.}$ 273 ± 4 nm (ε 25 000). The i.r. spectra of the adducts (**3**), (**4**), and (**5**) indicated the presence of a primary amino group at 3 500—3 300 cm^{-1} and of one conjugated amide carbonyl group at 1 640—1 620 cm^{-1}. These results established the presence of an enamino ketone entity in the hydrates (**3**), (**4**), and (**5**), a feature which was confirmed by ^{1}H and ^{13}C n.m.r. spectral evidence.

The positions of the substituents in the imides (**3**) were determined by allowing the latter to revert to the pyrimidin-4-

Table 4A. Atomic co-ordinates ($\times 10^4$) for the non-hydrogen atoms of (**4g**)

	x/a	*y/b*	*z/c*
C(1)	2 115(2)	1 006(2)	1 629(3)
C(2)	2 699(2)	2 376(2)	1 409(3)
C(3)	1 925(2)	3 545(2)	1 694(3)
C(4)	2 438(3)	4 976(2)	1 465(4)
C(5)	4 049(2)	2 548(2)	923(3)
C(6)	2 403(3)	−1 454(2)	1 354(4)
N(1)	2 893(2)	−58(2)	1 302(3)
N(2)	685(2)	3 467(2)	2 174(3)
O(1)	944(1)	827(1)	2 083(2)
O(2)	4 869(2)	1 647(2)	632(3)



Scheme 3.

ones (**1**) (Scheme 2). Structural conformation of the enamino ketones (**4a**) and (**5g**) was established by comparison with spectral data of authentic samples [2b,5] and the structure of (**4b**) was confirmed by hydrolysis of (**4b**) on alumina to 3-amino-4,4,*N*-trimethylpent-2-enamide (**6b**) and 4,4,*N*-trimethyl-3-oxopentanamide (**7b**).

All the hydrates (**3**), (**4**), and (**5**) were single geometric isomers. In the ^{1}H n.m.r. spectra of the hydrates (**3**), the signals of the primary amino hydrogens were observed at δ_H 5—6 (br, 1 H) and at δ_H 9—10 (br, 1 H), indicating the presence of an intramolecular hydrogen bond between one of the carbonyl groups and one of the primary amine hydrogens. Furthermore, no new ^{1}H n.m.r. signal corresponding to the geometric isomer was observed in the thermal reversion of (**3**) to (**1**), suggesting the *Z*-form of the imides (**3**). The configuration about the double bond of the hydrates (**4**) and (**5**) was not defined by the spectral data.

A single-crystal *X*-ray diffraction study was carried out to establish the geometry of the hydrates. A single crystal of 3-amino-2-formyl-*N*-methylbut-2-enamide [2b] (**4g**) suitable for *X*-ray crystallographic analysis was chosen from a variety of the enamino ketone derivatives [2b] including the hydrates (**3**), (**4**), and (**5**). The *Z*-form of the enamino ketone (**4g**) was unambiguously established by crystallography (Figure 2). Atomic co-ordinates for non-hydrogen atoms of (**4g**) are shown in Table 4A. The primary amine nitrogen atom is involved in intramolecular hydrogen bonding to the carbonyl oxygen atom of the secondary amide group and similarly the secondary amide nitrogen atom is linked to the oxygen atom of the formyl group. The hydrogen bond lengths, 2.61 and 2.65 Å, respectively, are shorter than an average (2.88 Å), an indication that they are strong.

The structures of the enamino ketones (**3**), (**4**), and (**5**) were similar to that of (**4g**). Thus, the hydrates have a *Z*-configuration (Scheme 1).

Considering possible pathways from the Dewar isomers (**2**) to the hydrates (**3**) and (**4**), the structures require at some stage cleavage of the C(1)–N(2) bond and addition of the OH group to the C(1) atom of the Dewar isomer. The protonation takes place on the imine nitrogen to give an iminium cation (**9**),[2e] which rearranges to an azetidinyl cation (**10**) [2a–e] by fission of the C(1)–N(2) bond of (**9**). Nucleophilic attack by water results in formation of a 4-hydroxyazetidin-2-one (**11**).[1d] The ring opening of either the C(3)–C(4) bond or the N(1)–C(4) bond in (**11**) gives the imide (**3**) or the enamino ketone (**4**), respectively. Ring closure of (**3**) gives the pyrimidin-4-one (**1**) (Scheme 3). An increase of solvent polarity alters the relative ratio of the C(3)–C(4) to N(1)–C(4) bond cleavage as evidenced by the fact that cleavage of the C(3)–C(4) bond of the 4-hydroxyazetidin-2-ones (**11**) predominates in aqueous acetone whilst its relative ratio decreases in aqueous acetonitrile in favour of N(1)–C(4) bond cleavage (Table 1).

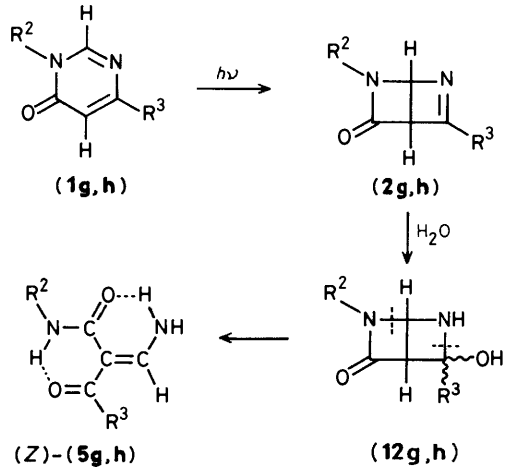
The extremely slow reaction of (**2d**) (Table 1) is due to the 1-t-butyl group. This indicates that the surrounding solvent molecules are kept away from the carbocation (**10**) by steric repulsion of the bulky t-butyl group and the cation (**10**) is not stabilized.

The addition of a water molecule to the imine bond of the Dewar isomers (**2g,h**) leads to the formation of the adducts (**12**) which undergo cleavage of the N(2)–C(3) and C(1)–N(6) bonds to give (**5**) (Scheme 4).

The rate of formation of the secondary carbocations from the Dewar isomars (**2g,h**) is slower that that of the tertiary carbocations from (**2a—c,e,f,**), and addition of water to the imine bond then predominates.

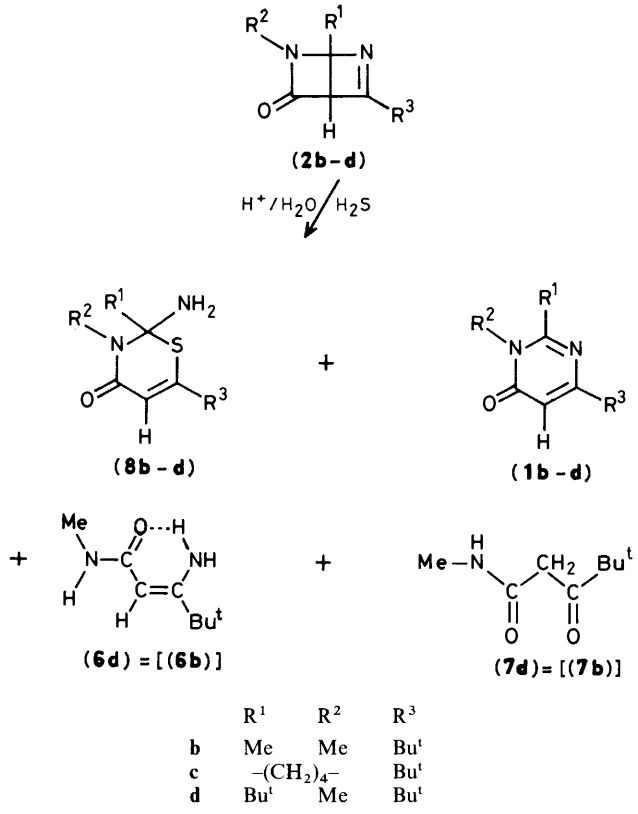
Reactions of the Dewar Pyrimidinones (**2**) *with Hydrogen Sulphide.*—The reaction of 1,6-dimethyl-5-oxo-3-t-butyl-2,6-diazabicyclo[2.2.0]hex-2-ene (**2b**) with hydrogen sulphide in acetonitrile solution at 0 °C gave crystalline 2-amino-3,4-dihydro-2,3-dimethyl-6-t-butyl-2*H*-1,3-thiazin-4-one (**8b**) (70%) and 2,3-dimethyl-6-t-butylpyrimidin-4-one (**1b**) (21%). Similarly, the 1,3-thiazines (**8c**) (52%) and the pyrimidin-4-ones (**1c**) (32%) from the Dewar isomer (**2c**) and (**8d**) (43%), (**1d**) (7%), 3-amino-4,4,*N*-trimethylpent-2-enamide (**6d**)[=(**6b**)] (27%), and 4,4,*N*-trimethyl-3-oxopentanamide (**7d**)[=(**7b**)] (11%) from the Dewar isomer (**2d**) were obtained (Scheme 5).

The rate of addition of H_2S to the Dewar pyrimidinones (**2**) is reduced when the methyl and methylene groups at the C(1) position of (**2**) are replaced by t-butyl. The relative reaction rate of (**2d**) with water as an impurity in the solution increases in the



	R^2	R^3
g	Me	Me
h	Me	H

Scheme 4.

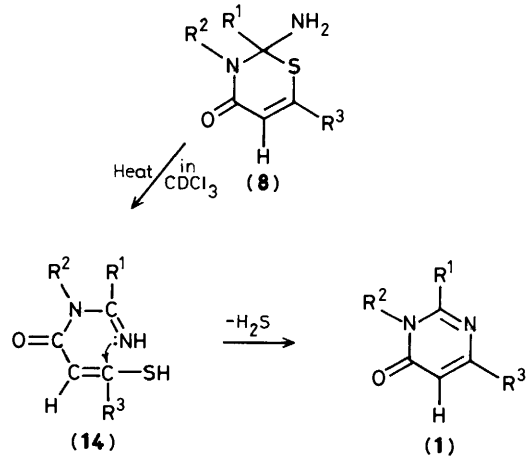


	R^1	R^2	R^3
b	Me	Me	Bu^t
c	$-(CH_2)_4-$		Bu^t
d	Bu^t	Me	Bu^t

Scheme 5.

presence of acid (H_2S) to give the hydrolysis products [(**6d**) = (**6b**) and (**7d**) = (**7b**)].

The structure of (**8b**) was deduced from spectral data. In the i.r. spectrum (KBr), primary amine and conjugated amide carbonyl frequencies appeared at 3 390 and 3 300 cm^{-1} and at 1 615 cm^{-1}, respectively. The ^1H n.m.r. spectrum ($CDCl_3$) exhibited the primary amine signal at δ_H 2.28 (br, 2 H). The mass spectrum showed the following peaks: *m/z* 214 (M^+, 44%) and 197 ($M^+ - NH_3$, 100%). The deuterium-labelled compound [**8b(D)**] was prepared from (**8b**) in [$^2H_4$]methanol and its mass spectrum showed the following peaks: *m/z* 216 (M^+, 30%) and



	R^1	R^2	R^3
b	Me	Me	Bu^t
c	$-(CH_2)_4-$		Bu^t
d	Bu^t	Me	Bu^t

Scheme 6.

197 ($M^+ - ND_2H$, 100%). From a comparison of these spectral results with those reported for 1,3-thiazine derivatives,[6] (**8b**) was assigned as the 2-amino-1,3-thiazine. The ^{13}C n.m.r. spectral data supported this structure. The structures of compounds (**8c**) and (**8d**) were assigned on the basis of spectral results and comparing of the latter with those of (**8b**).

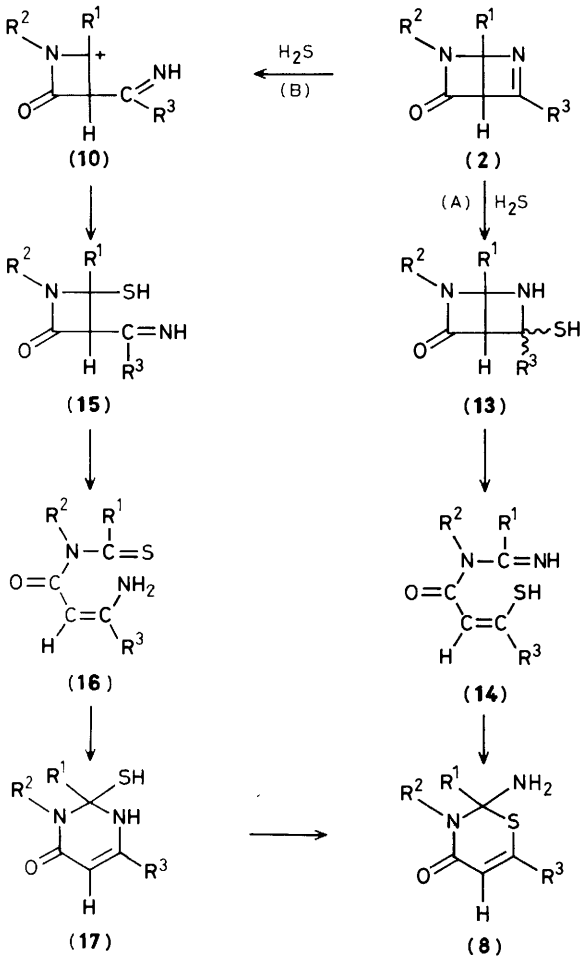
The 1,3-thiazine (**8b**) reverted to the pyrimidin-4-ones (**1b**) (98%), (**8c**) gave (**1c**) (95%), and (**8d**) led to the formation of (**1d**) (23%) and unidentified compounds (50%, w/w) in $CDCl_3$ at 35 °C (Scheme 6).

The 1,3-thiazines (**8b—d**) undergo S(1)–C(2) bond cleavage to give the amidines (**14**). Subsequent ring closure and elimination of hydrogen sulphide leads to the pyrimidin-4-ones (**1b—d**). The 1,3-thiazine (**8d**) gave (**1d**) and unidentified products. The rate of ring closure of the intermediate (**14d**) may be slowed down by steric repulsion of the two t-butyl groups (R^1 and R^3) and side reactions tend to dominate.

Two possible mechanisms for the formation of the 1,3-thiazines (**8**) are the addition of hydrogen sulphide to the imine bond of the Dewar isomers (**2**) to give adducts (**13**) (process **A**) and formation of the azetidinyl cations (**10**) by protonation of the imino nitrogen atom from hydrogen sulphide (process **B**). The adducts (**13**) give amidines (**14**) by cleavage of the N(2)–C(3) and C(1)–C(4) bonds. Ring closure by attack of the sulphur atom at the imino carbon gives (**8**) (process **A**). Addition of hydrogen sulphide to the azetidinyl cations (**10**) takes place to give azetidin-2-ones (**15**), followed by ring opening to yield the thioimides (**16**). Ring closure gives the 2-mercaptopyrimidines (**17**), which undergo ring opening by cleavage of the N(1)–C(6) bond and concomitant bond formation between the sulphur atom and the C(6) atom leads to (**8**) (process **B**) (Scheme 7). The two mechanisms could not be distinguished from the experimental results.

Experimental

M.p.s were measured with a Yanako melting point apparatus without corrections. The spectroscopic measurements were performed with the following instruments: i.r., JASCO A-102; u.v., Hitachi Model 200-10; mass spectra (m.s.), JEOL OISG-2 at 70 eV; ^1H and ^{13}C n.m.r., Varian EM-390 and Varian XL-200, respectively. Chemical shifts were reported in p.p.m. on the δ scale relative to a Me_4Si internal standard. Column



Scheme 7.

chromatography was performed on Merck 70—230 mesh alumina (activity II—III) or on Sephadex LH-20 (Pharmacia Fine Chemicals AB). The chromatographic isolations were accomplished by a medium pressure liquid chromatography (m.p.l.c.), using a column (25 × 2.5 cm) packed with Fuji-Davison silica gel BM-300 (200—400 mesh). Products isolated by m.p.l.c. were detected by an Oyo-Bunko UVILOG-5IIIA absorbance monitor at wavelength 280 nm.

Materials. 2,6-Di-t-butylpyrimidin-4(3*H*)-one was synthesized by condensation[2c] of pivalamidine hydrochloride[7] and ethyl 4,4-dimethyl-3-oxopentanoate.[8] 2,3,6-Trimethylpyrimidin-4(3*H*)-one (**1a**),[2a] 2,3-dimethyl-6-t-butylpyrimidin-(4(3*H*)-one(**1b**),[2c] 6,7,8,9-tetrahydro-2-t-butyl-4*H*-pyrido[1,2-*a*]-pyrimidin-4-one (**1c**),[2c] 3-methyl-2,6-di-t-butylpyrimidin- 4(3*H*)-one (**1d**). 2,3-dimethylpyrimidin-4(3*H*)-one (**1e**),[2b] 7,8,9,10-tetrahydropyrimido[1,2-*a*]azepin-4(6*H*)-one (**1f**),[2b] and 3,6-dimethylpyrimidin-4(3*H*)-one (**1g**)[2b] were prepared from iodomethane and the corresponding pyrimidin-4(3*H*)-ones in alcoholic solutions containing potassium hydroxide. 3-Methylpyrimidin-4(3*H*)-one (**1h**) was prepared by desulphurization and methylation of 2-thiouracil.[9]

2,6-*Di-t-butylpyrimidin*-4(3H)-*one:* m.p. 165 °C; *m/z* 208 (M^+) (Found: M^+, 208.1544. $C_{12}H_{20}N_2O$ requires *M*, 208.1575).

For (**1d**): m.p. 46—49 °C; $\nu_{max.}(CHCl_3)$ 1 655 cm^{-1}; $\lambda_{max.}$(MeOH) 274 (ε 4 740 $dm^3\ l^{-1}\ cm^{-1}$), 222 nm (ε 4 420); $\delta_H(CDCl_3)$ 1.23 (9 H, s), 1.48 (9 H, s), 3.53 (3 H, s), and 6.32 (1 H, s); *m/z* 222 (M^+) (Found: M^+, 222.1702. $C_{13}H_{22}N_2O$ requires M^+, 222.1731).

For (**1h**): m.p. 126—128 °C (lit.,[9] 124—126 °C).

Preparation of Dewar Pyrimidinones (**2**).—The pyrimidin-4-one (2 g) in liquid ammonia–ether solution (280 ml) was irradiated under argon with a high-pressure mercury lamp (100 W) at −40 °C for 3—8 h.[2a] The solvent was evaporated and the residue was chromatographed on Sephadex LH-20.[2c] The prepared Dewar pyrimidinones were 1,3,6-trimethyl-2,6-diazabicyclo[2.2.0]hex-2-en-5-one (**2a**),[2a,c] 1,6-dimethyl-3-t-butyl-2,6-diazabicyclo[2.2.0]hex-2-en-5-one (**2b**),[2c] 9-t-butyl-6,10-diazatricyclo[4.4.0.0^{1,8}]dec-9-en-7-one (**2c**),[2c] 6-methyl-1,3-di-t-butyl-2,6-diazabicyclo[2.2.0]hex-2-en-5-one (**2d**), and 3,6-dimethyl-2,6-diazabicyclo[2.2.0]hex-2-en-5-one (**2g**).[2b,c] A mixture of (**1g**) and (**2g**) (7:3) was used for the reactions because (**2g**) was not separated by column chromatography.[2c]

Preparation of (**2d**). When (**1d**) (2.010 g, 9.05 mmol) was irradiated for 3 h, a mixture of (**2d**) and (**1d**) (37:63) was obtained. Column chromatography of the mixture gave (**2d**) (0.159 g, 8%) as colourless oil. The starting (**1d**) (1.439 g, 72%) and a mixture (0.324 g, 16%) of (**2d**) and (**1d**) were recovered.

For (**2d**): $\nu_{max.}(CHCl_3)$ 1 745 and 1 590 cm^{-1}; $\lambda_{max.}$(MeCN) 254 nm (ε 506 $dm^3\ l^{-1}\ cm^{-1}$); $\delta_H(CDCl_3)$ 1.12 (9 H, s), 1.20 (9 H, s), 2.88 (3 H, s), and 4.26 (1 H, s); *m/z* 222 (M^+) (Found: M^+, 222.1739. $C_{13}H_{22}N_2O$ requires *M*, 222.1731).

General Procedure for Reactions of Dewar Pyrimidinones (**2**) *in Aqueous Solution and Isolation of the Hydrates* (**3**)—(**5**).—The thermal reactions of the Dewar pyrimidinones (**2**) were carried out in aqueous acetone and in aqueous acetonitrile at 0—35 °C. The reaction progress was monitored routinely by ^1H n.m.r. spectroscopy. After removal of the solvent under reduced pressure, the residue was chromatographed on Sephadex LH-20 (180 g) and on silica gel.

Reactions of (**2a**) *with water.* (*a*) The Dewar isomer (**2a**) (103 mg, 0.743 mmol) was dissolved in acetone–H_2O (9:1, v/v; 19 ml) and the solution was set aside for 2 h at 19 °C. Separation of the reaction mixture by column chromatography on Sephadex LH-20 with $CHCl_3$–hexane (4:1, v/v) as eluant gave (*Z*)-*N*-acetyl-*N*-methyl-3-aminobut-2-enamide (**3a**) (53 mg) and pyrimidin-4-one (**1a**) (34 mg).

Recrystallization of (**3a**) from CCl_4–pentane gave colourless needles, m.p. 71—74 °C; *m/z* 156 (M^+, 29%) and 84 (100) (Found: C, 53.7; H, 8.0; N, 18.05. $C_7H_{12}N_2O_2$ requires C, 53.83; H, 7.74; N, 17.94%).

(*b*) Treatment of (**2a**) (471 mg, 3.41 mmol) in acetone–water (7:3, v/v) at 16 °C for 39 h gave the pyrimidin-4-one (**1a**) (296 mg) and crystalline (*Z*)-2-acetyl-3-amino-*N*-methylbut-2-enamide (**4a**) (99 mg), which were separated by column chromatography on alumina.

Recrystallization of (**4a**) from ethyl acetate–ether gave colourless prisms, m.p. 152—154 °C (lit.,[5] 146—148 °C). The enamino ketone (**4a**) was identical (spectra) with those of an authentic sample[5] which was obtained from hydrolysis of 3-(aminoethylidene)-4-methoxy-4-,*N*-dimethylazetidin-2-one on alumina.

(*c*) The reaction of (**2a**) (84 mg, 0.61 mmol) in CD_3CN (0.802 ml) containing water (43 mg, 2.39 mmol) gave (**1a**) (12 mg), (**4a**) (16 mg), *N*-methylacetoacetamide (**7a**) (10 mg), and unidentified products (34 mg) at 35 °C for 51 h.

N-Methylacetoacetamide was identical (spectra) with those of an authentic sample which was purchased from Tokyo Kasei Kogyo Co., Ltd.

Reactions of (**2b**) *with water.* (*a*) The Dewar isomer (**2b**) (38 mg, 0.21 mmol) was dissolved in acetone–H_2O (9:1, v/v; 10 ml) and the solution was set aside for 2 h at 15 °C. After removal of the solvent, the residue was dissolved in acetone–pentane. On

cooling, crystalline (*Z*)-*N*-acetyl-3-amino-4,4,*N*-trimethylpent-2-enamide (**3b**) (31 mg) separated and was filtered off.

Recrystallization of (**3b**) from acetone–pentane gave colourless needles, m.p. 104—107 °C; $\delta_C(CDCl_3)$ 25.7 (q, CH_3), 28.8 [q, $C(CH_3)_3$], 32.2 (q, NCH_3), 36.4 [s, $C(CH_3)_3$], 83.3 (d, C-2), 172.7 (s, CO or C-3), 172.8 (s, CO or C-3), 175.1 (s, CO or C-3); *m/z* 198 (M^+, 53%) and 126 (100) (Found: C, 60.5; H, 9.1; N, 13.9. $C_{10}H_{18}N_2O_2$ requires C, 60.58; H, 9.15; N, 14.13%).

Evaporation of the solvent from the liquid fraction under reduced pressure gave the pyrimidin-4-one (**1b**) (7 mg).

(*b*) The reaction of the Dewar isomer (**2b**) (81 mg, 0.45 mmol) was carried out in CD_3CN (0.548 ml) containing water (38 mg, 2.1 mmol) at 35 °C for 41 h. After removal of the solvent under reduced pressure, the residue was dissolved in methanol–benzene–ether. On cooling, (*Z*)-2-acetyl-3-amino-4,4,*N*-trimethylpent-2-enamide (**4b**) (72 mg) separated and was filtered off.

Recrystallization of (Z)-(**4b**) gave colourless leaflets, m.p. 156.5—157.5 °C; *m/z* 198 (M^+); $\nu_{max.}$(KBr) 3 420, 3 310, 1 610, and 1 580 cm^{-1}; $\lambda_{max.}$(MeOH) 308 nm (ε 14 000 $dm^3\ l^{-1}\ cm^{-1}$); $\delta_H(CDCl_3)$ 1.32 (9 H, s, Bu^t), 2.13 (3 H, s, CH_3), 2.89 (3 H, d, *J* 4.5 Hz, NCH_3), 5.2—6.7 (1 H, br, NH), 6.22 (1 H, br, *H*NH), and 10.7—12.7 (1 H, br, *H*NH) (Found: C, 60.35; H, 9.05; N, 13.9. $C_{10}H_{18}N_2O_2$ requires C, 60.58; H, 9.15; N, 14.13).

Evaporation of the solvent from the liquid fraction under reduced pressure gave an oily mixture (14 mg), which was chromatographed on alumina to give the pyrimidin-4-one (**1b**) (10 mg) and 3-amino-4,4,*N*-trimethylpent-2-enamide (**6b**) (4 mg).

Recrystallization of (**6b**) from $CHCl_3$–pentane gave colourless prisms, m.p. 113–115 °C; *m/z* 156 (M^+); $\nu_{max.}(CHCl_3)$ 3 540, 3 500, 3 320, 1 630, and 1 610 cm^{-1}; $\lambda_{max.}$(MeOH) 276 nm (ε 19 000 $dm^3\ l^{-1}\ cm^{-1}$); $\delta_H(CDCl_3)$ 1.17 (9 H, s, Bu^t), 2.83 (3 H, d, *J* 5 Hz, NCH_3), 4.48 (1 H, s, CH), 5.0 (1 H, br, NH), and 6.6 (2 H, br, NH_2) (Found: C, 61.45; H, 10.35; N, 17.75. $C_8H_{16}N_2O$ requires C, 61.50; H, 10.32; N, 17.93%). The pent-2-enamide (**6b**) may be formed by the reaction of (**4b**) on alumina. To confirm this reaction, hydrolysis of (**4b**) on a column of alumina was carried out.

Hydrolysis of (**4b**) *on Alumina.*—The enamino ketone (**4b**) (34 mg, 0.17 mmol) was adsorbed on a column of alumina (20 g) at 20 °C for 14 h. Elution with $CHCl_3$–MeOH (95:5, v/v) gave the pent-2-enamide (**6b**) (12 mg, 45%) and 4,4,*N*-trimethyl-3-oxopentanamide (**7b**) (7 mg, 26%) as crystals.

Recrystallization of (**7b**) from benzene–pentane gave colourless needles, m.p. 95.5—97 °C; *m/z* 157 (M^+); $\nu_{max.}$(KBr) 3 270, 3 100, 1 710, and 1 650 cm^{-1}; $\lambda_{max.}$(MeOH) 245 nm (ε 1 280 $dm^3\ l^{-1}\ cm^{-1}$); $\delta_H(CDCl_3)$ 1.18 (9 H, s, Bu^t), 2.85 (3 H, d, *J* 5 Hz, NCH_3), 3.51 (2 H, s, CH_2), and 6.7—7.5 (1 H, br, NH) (Found: C, 61.45; H, 9.5; N, 8.9. $C_8H_{15}NO_2$ requires C, 61.21; H, 9.62; N, 8.91%).

The 3-oxopentanamide (**7b**) (1.92 g, 96%) was synthesized by the reaction of methyl trimethylacetoacetate (2.10 g) with an excess of methylamine in methanol solution at 26 °C for 77 h. The synthesized compound was identical (spectra) with (**7b**).

Reaction of (**2c**) *with water.* (*a*) The Dewar isomer (**2c**) (144 mg, 0.700 mmol) was dissolved in acetone–water (9:1, v/v; 10 ml) and the solution was set aside for 1 h at 20 °C. After evaporation of the solvent, the residue was dissolved in CCl_4–pentane. On cooling, (*Z*)-*N*-(3-amino-4,4-dimethyl-1-oxo-2-pent-2-enyl)-2-piperidone (**3c**) (101 mg) separated and was filtered off.

Recrystallization of (**3c**) gave colourless needles, m.p. 91—93 °C; $\delta_C(CDCl_3)$ 20.3 (t, CH_2), 22.7 (t, CH_2), 28.9 [q, $C(CH_3)_3$] 34.8 [s, $C(CH_3)_3$], 34.8 (t, CH_2), 43.3 (t, CH_2), 86.2 (d, CH), 171.2 (s, CO or C-N), 172.7 (s, CO or C-N), and 174.1 (s, CO or C-N); *m/z* (rel intensity) 224 (M^+, 17%), 126 (100), and 99 (42).

Satisfactory analytical data for (**3c**) were not obtained because of the instability of the compound.

Evaporation of the solvent from the liquid fraction gave the pyrimidin-4-one (**1c**) (47 mg).

(*b*) The reaction of the Dewar isomer (**2c**) (82 mg, 0.40 mmol) was carried out in CD_3CN (0.658 ml) containing water (37 mg, 2.1 mmol) at 35 °C for 37 h. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel to give the pyrimidin-4-one (**1c**) (70 mg) and 2-(1-amino-2,2-dimethylpropylidene)-3-oxoheptane-7-lactam (**4c**) (9 mg) as crystals.

Recrystallization of (**4c**) from methanol–ether gave colourless prisms, m.p. 175—177 °C; *m/z* 224 (M^+); $\nu_{max.}(CHCl_3)$ 3 500, 3 400, 1 630, and 1 570 cm^{-1}: $\lambda_{max.}$(MeOH) 311 (ε 14 300 $dm^3\ l^{-1}\ cm^{-1}$) and 246sh nm (ε 1 860); $\delta_H[(CD_3)_2SO]$ 1.4—2.1 (4 H, m, 2 × CH_2), 1.37 (9 H, s, Bu^t), 2.31 (1 H, t, *J* 11 Hz, *H*CH), 2.75 (1 H, t, *J* 12 Hz, *H*CH), 3.2—3.5 (2 H, m, CH_2), 5.75 (1 H, br, NH), 5.89 (1 H, br, *H*NH), and 12.40 (1 H, br, *H*NH) (Found: C, 64.25; H, 8.9; N, 12.55. $C_{12}H_{20}N_2O_2$ requires C, 64.25; H, 8.99; N, 12.49%).

Reaction of (**2d**) *with water.* The Dewar isomer (**2d**) (132 mg, 0.595 mmol) was dissolved in acetone–water (9:1, v/v) and the solution was set aside for 10 h at 35 °C. Evaporation of the solvent gave an oily crystalline residue (109 mg) the ^1H n.m.r. spectrum of which indicated a mixture of the pyrimidin-4-one (**1d**) (3%) and the starting Dewar isomer (**2d**) (97%). The yield of (**1d**) was 2% and the recovered (**2d**) was 80%.

Reaction of (**2g**) *with water.* A mixture (2.004 g, 16.1 mmol) of (**2g**) (30%) and (**1g**) (70%) was dissolved in MeCN–H_2O (120 ml; 16:84, v/v) and the solution was set aside for 43 h at 0 °C. After evaporation of the solvent, the residue was chromatographed on alumina to give (*Z*)-2-acetyl-3-amino-*N*-methylprop-2-enamide (**5g**) (220 mg) as crystals. The pyrimidin-4-one (**1g**) (1.440 g) was also recovered.

Recrystallization of (**5g**) from benzene–methanol gave colourless prisms, m.p. 154—155 °C lit.[2b], mp, 154–155 °C). The amide (**5g**) was identical (spectra) with those of authentic sample.[2b]

General Procedure for the Photolysis of Pyrimidin-4-ones (**1**) *in Aqueous Solution and Isolation of the Products* (**3**)-(**5**). The pyrimidin-4-ones (**1**) (1.2—2.0 g) were irradiated in water (85 v/v%)-acetonitrile (250 ml; 85:15, v/v%) solution under an argon atmosphere at 0—2 °C with a high-pressure mecury lamp (100 W). The reaction progress was monitored routinely by ^1H n.m.r. spectroscopy. After irradiation, the solvent was evaporated under reduced pressure. The products were isolated by crystallization and/or by column chromatography on Sephadex LH-20 (180 g) and on alumina (40–80 g).

Photolysis of (**1a**) *in aqueous solution.* From (**1a**) (1.204 g, 8.71 mmol), a reaction mixture of (**1a**) (**3a**), and (**4a**) was obtained after irradiation for 7 h. The ^1H n.m.r. analysis indicated that the mixture contained (**1a**) (57%), (**3a**) (43%), and (**4a**) (trace amount). The column chromatography of the mixture on alumina gave (**4a**) (0.170 g, 13%). The starting material (**1a**) (0.764 g, 63%) was also recovered.

Photolysis of (**1e**) *in aqueous solution.* From (**1e**) (1.990 g, 16.0 mmol), a reaction mixture of (**1e**), (*Z*)-*N*-acetyl-3-amino-*N*-methylprop-2-enamide (**3e**), and (*Z*)-2-acetyl-3-amino-*N*-methylprop-2-enamide (**4e**) was obtained after irradiation for 18 h. The separation of the mixture by column chromatography on Sephadex LH-20 gave (**3e**) (81 mg) as an oil and (**4e**) (274 mg) as crystals. The starting material (**1e**) (0.935 g) was also recovered.

The spectra of the compound (**4e**) were identical with those of the pent-2-enamide (**5g**).

Compound (**3e**) was unstable and attempts to purify it by distillation and by chromatography on Sephadex LH-20 were unsuccessful. The structure was assigned on the basis of ^1H

n.m.r. and i.r. spectral results and was confirmed by conversion of (**3e**) into the pyrimidin-4-one (**1e**) (*ca.* 100%) at 15 °C.

Photolysis of (**1f**) *in aqueous solution.* From (**1e**) (1.988 g, 12.1 mmol), 2-(aminoethylene)-3-oxo-octane-8-lactam (**4f**) (279 mg, 13%) as crystals and ε-caprolactam (149 mg, 11%) as a degradation product, were obtained after irradiation for 15 h followed by separation of the reaction mixture on alumina. Starting material (**1f**) (1.194 g) was also recovered.

Recrystallization of (**4f**) from benzene–methanol–hexane gave colourless needles, m.p. 163—166 °C; *m/z* 182 (M^+); $\nu_{max.}$(KBr) 3 290, 3 180, and 1 640 cm^{-1}; $\lambda_{max.}$(MeOH) 297 (ε 13 500 $dm^3\ l^{-1}\ cm^{-1}$), 244 nm (ε 5 560); δ_H[$(CD_3)_2SO$] 1.56 (6 H, m, 3 × CH_2), 2.2—2.7 (2 H, m, CH_2), 2.9—3.5 (2 H, m, CH_2), 7.18 (1 H, dd, *J* 9 and 15 Hz, CH), 7.41 (1 H, t, *J* 7.5 Hz, NH), 8.02 (1 H, br, *H*NH), 9.32 (1 H, d, *J* 15 Hz, *H*NH) (Found: C, 59.25; H, 7.7; N, 15.15. $C_9H_{14}N_2O_2$ requires C, 59.32; H, 7.74; N, 15.37%).

The ε-caprolactam obtained was identical (m.p. and spectra) with an authentic sample.

Photolysis of (**1g**) *in aqueous solution.* From (**1g**) (2.009 g, 16.2 mmol), a mixture of (**1g**) and (**5g**) was obtained after irradiation for 16 h. Separation of the reaction mixture by chromatography on alumina gave (**5g**) (1.098 g) and starting material (**1g**) (0.686 g).

Photolysis of (**1h**) *in aqueous solution.* From (**1h**) (2.013 g, 18.3 mmol), crystalline (*Z*)-*N*-methyl-3-amino-2-formylprop-2-enamide (**5h**) (88 mg) was obtained after irradiation for 6 h. The reaction mixture was separated by column chromatography on alumina.

Recrystallization of (**5h**) from methanol–ether gave colourless prisms, m.p. 131—132 °C; *m/z* 128 (M^+); $\nu_{max.}$(KBr) 3 350, 3 250, 3 220, 1 645, and 1 615 cm^{-1}; $\lambda_{max.}$(MeOH) 268 nm (ε 26 100 $dm^3\ l^{-1}\ cm^{-1}$), 238sh nm (ε 10 500); δ_H([$^2H_6$]Me_2SO) 2.70 (3 H, d, *J* 5 Hz, NCH_3), 7.59 (1 H, dd, *J* 8 and 16 Hz, CH), 8.5—9.0 (2 H, br, 2 × NH), 8.88 (1 H, s, CH), and 9.4—9.8 (1 H, br, NH) (Found: C, 46.65; H, 6.35; N, 21.75. $C_5H_8N_2O_2$ requires C, 46.87; H, 6.29; N, 21.87%).

The experimental conditions for the thermal reactions of the Dewar pyrimidinones (**2**) in aqueous solutions and the yields of the products are summarized in Table 1. The yields of the products formed by the photolysis of the pyrimidin-4-ones (**1**) in aqueous solution are listed in Table 2. The spectral data of the imides (**3**) are shown in Table 3.

General Procedure for the Reactions of the Hydrates (**3**) *and Isolation of the Products.*—The imides (**3**) were dissolved in methanol (5 ml) and the solutions were set aside at 16—23 °C for 2—7 days. After evaporation of solvent the residues were crystallized to give the products.

Reversion of (**3a**) *to* (**1a**). From (**3a**) (16 mg, 0.10 mmol), the pyrimidin-4-one (**1a**) (14 mg, 98%) was obtained after 5 days.

Reversion of (**3b**) *to* (**1b**). From (**3b**) (31 mg, 0.16 mmol), the pyrimidin-4-one (**1b**) (27 mg, 96%) was obtained after 7 days.

Reversion of (**3c**) to (**1c**). From (**3c**) (20 mg, 0.089 mmol), the pyrimidin-4-one (**1c**) (18 mg, 98%) was obtained after 2 days.

General Procedure for the Reactions of Dewar Pyrimidinones (**2**) *with* H_2S.—The reaction of the Dewar isomer (**2**) was carried out in freshly distilled acetonitrile (50 ml) containing H_2S (2.3—2.6 g, 68—77 mmol) at 0 °C for 15—19 h. After evaporation of the solvent and excess reagent, the products were separated by crystallization and/or by column chromatography on Sephadex LH-20 (180 g) and on alumina (20 g).

Reaction of (**2b**) *with* H_2S. From the Dewar isomer (**2b**) (0.136 g, 0.756 mmol), a mixture of 2-amino-3,4-dihydro-2,3-dimethyl-6-t-butyl-2H-1,3-thiazin-4-one (**8b**) and the pyrimidin-4-one (**1b**) was obtained. Crystallization of the mixture from CCl_4–pentane gave (**8b**) (113 mg, 70%) as colourless fine plates.

For (**8b**), m.p. 89—91 °C; *m/z* 214 (M^+, 44%), 197 ($M^+ - NH_3$, 100) (Found: M^+, 214.1169. $C_{10}H_{18}N_2OS$ requires *M*, 214.1139); $\nu_{max.}$(KBr) 3 390, 3 300, and 1 615 cm^{-1}; $\lambda_{max.}$(CH_3CN) 285 nm (ε 3 780 $dm^3\ l^{-1}\ cm^{-1}$), 253 nm (ε 4 400), and 228 nm (ε 4 790); δ_H($CDCl_3$) 1.21 (9 H, s, Bu^t), 1.83 (3 H, s, CH_3), 2.28 (2 H, br, NH_2), 3.06 (3 H, s, NCH_3), and 6.14 (1 H, s, 5-H); δ_C($CDCl_3$) 26.6 (q, 2-CH_3), 27.8 (q, NCH_3), 29.1 [q, (CH_3)$_3$C], 37.3 [s, (CH_3)$_3$*C*], 78.4 (s, C-2), 113.0 (d, C-5), 160.1 (s, C-4/C-6), and 165.5 (s, C-6/C-4).

The pyrimidin-4-one (**1b**) (28 mg, 21%) was obtained after separation of the liquid fraction by column chromatography on alumina.

Reaction of (**2c**) *with* H_2S. From the Dewar pyrimidinone (**2c**) (0.154 g, 0.748 mmol), a mixture of 9a-amino-5,6,7,8,9,9a-hexahydro-2-t-butyl-4*H*-pyrido[2,1-*b*][1,3]thiazin-4-one (**8c**) and pyrimidin-4-one (**1c**) was obtained. Crystallization of the reaction mixture from CCl_4–pentane gave (**8c**) (93 mg, 52%) as colourless prisms.

For (**8c**): m.p. 74—75 °C; *m/z* 240 (M^+, 1.5%), 223 ($M^+ - NH_3$, 100) (Found: M^+, 240.1288. $C_{12}H_{20}N_2OS$ requires M^+, 240.1295); $\nu_{max.}$(KBr) 3 390, 3 320, and 1 610 cm^{-1}; $\lambda_{max.}$(CH_3CN) 280 nm (ε 4 570 $dm^3\ l^{-1}\ cm^{-1}$), 229 nm (ε 4 640); δ_H($CDCl_3$) 1.22 (9 H, s, Bu^t), 1.5—2.3 (6 H, m, 3 × CH_2), 2.13 (2 H, br, NH_2), 2.8—3.3 (2 H, m, CH_2), 4.1—4.4 (2 H, m, CH_2), and 6.17 (1 H, s, 5-H); δ_C($CDCl_3$) 19.5 (t, CH_2), 23.7 (t, CH_2), 29.1 [q, (CH_3)$_3$C], 37.3 [s, (CH_3)$_3$*C*], 39.0 (t, CH_2), 39.3 (t, CH_2), 78.9 (s, C-9a), 112.6 (d, C-3), 160.2 (s, C-4/C-2), and 165.9 (s, C-2/C-4).

The pyrimidin-4-one (**1c**) (49 mg, 32%) was obtained after separation of the liquid fraction by column chromatography on alumina.

Reaction of (**2d**) *with* H_2S. From the Dewar isomer (**2d**) (0.134 g, 0.604 mmol), crystalline 2-amino-3,4-dihydro-3-methyl-2,6-di-t-butyl-2H-1,3-thiazin-4-one (**8d**) (67 mg, 43%), the pyrimidin-4-one (**1d**) (10 mg, 7%), 3-amino-4,4,*N*-trimethylpent-2-enamide (**6d**) [=(**6b**)] (25 mg, 27%), and 4,4,*N*-trimethyl-3-oxopentanamide (**7d**) [=(**7b**)] (7.0 mg, 11%) were obtained after separation of the reaction mixture on Sephadex LH-20.

Recrystallization of (**8d**) from benzene–pentane gave colourless prisms, m.p. 83—84 °C; *m/z* 256 (M^+, 4.7%), 239 ($M^+ - NH_3$, 1.3), and 57 (100) (Found: M^+, 256.1603. $C_{13}H_{24}N_2OS$ requires *M*, 256.1608); $\nu_{max.}$($CHCl_3$) 3 440, 3 360, and 1 620 cm^{-1}; $\lambda_{max.}$(MeCN) 282 nm (ε 3 750 $dm^3\ l^{-1}\ cm^{-1}$) and 225 nm (ε 2 810); δ_H($CDCl_3$) 1.10 (9 H, s, Bu^t), 1.22 (9 H, s, Bu^t), 2.27 (2 H, br, NH_2), 3.22 (3 H, s, NCH_3), and 6.03 (1 H, s, 5-H); δ_C($CDCl_3$) 25.9 [q, (CH_3)$_3$C], 29.0 [q, (CH_3)$_3$C], 30.2 (q, NCH_3), 37.3 [s, (CH_3)$_3$*C*], 46.9 [s, (CH_3)$_3$*C*], 88.3 (s, C-2), 113.9 (d, C-5), 159.2 (s, C-4/C-6), and 166.6 (s, C-6/C-4).

General Procedure for the Reactions of the Thiazines (**8**).—Solution of the thiazines (**8**) in $CDCl_3$ (0.41—0.58 ml) were set aside for 64—88 h at 35 °C. The reaction progress was routinely monitored by ^1H n.m.r. spectroscopy. After evaporation of the solvent, the products were separated by crystallization and/or by column chromatography on alumina (20 g).

Reaction of (**8b**). From (**8b**) (23 mg, 0.11 mmol), the pyrimidin-4-one (**1b**) (19 mg, 98%) was obtained after 88 h.

Reaction of (**8c**). From (**8c**) (22 mg, 0.092 mmol), the pyrimidin-4-one (**1c**) (18 mg, 95%) was obtained after 64 h.

Reaction of (**8d**). From (**8d**) (20 mg, 0.078 mmol), the pyrimidin-4-one (**1d**) (4 mg, 23%) and unidentified products (10 mg, 50 w/w %) were obtained after 87 h.

Single-crystal X-Ray Crystallographic Analysis of 3-Amino-2-formyl-N-methylbut-2-enamide (**4g**).—A single crystal of (**4g**) was grown from methanol solution.

Crystal data. $C_6H_{10}N_2O_2$, *M* = 142.1. Monoclinic, *a* = 9.666 5(8) Å, *b* = 9.810 5(6) Å, *c* = 7.548 4(5) Å,

$\beta = 99.873(6)°$, $V = 705.2$ Å^3, space group $P2_1/c$, $Z = 4$, $D_x = 1.339$ g cm^{-3}, λ(Cu-K_α) = 1.541 4 Å, μ(Cu-K_α) = 6.42 cm^{-1}. A colourless needle (0.4 × 0.1 × 0.6 mm) was used for data collection. Unit-cell dimensions were found by a least-squares fit to the observed value $39.7° < 2\theta < 80°$ for 17 strong reflections.

Data collection and processing. Rigaku AFC/3 diffractometer, $2\theta/\omega$ mode, ω scan speed 4.0° min^{-1}, graphite-monochromated Cu-K_α radiation; 1 052 unique reflections, giving 937 [$|F_0| > \sigma(|F_0|)$].

After three-dimensional difference Fourier synthesis, 931 reflections were used for refinement because six reflections [(0,0,2), (0,1,2), (1,0,2), (0,0,4), (1,0,4), and (2,0,4)] which were considered to be measured wrong in view of the counting statistics were deleted. No significant changes in the measurement of the intensities were observed during the course of data collection. No absorption corrections were made.

Structure Analysis and Refinement.—The structure was solved by direct methods using Multan programs [10] and refined by the block-diagonal least-squares technique on F. Hydrogen atoms were located by difference synthesis. In the final least-squares refinement, the anisotropic temperature factors for the non-hydrogen atoms and the isotropic temperature factors for the hydrogen atoms were used. The weighting scheme $w(hkl) = -0.000\,23|F|^2 + 0.042\,19|F| - 0.006\,40$ gave satisfactory agreement analyses. Final R and R_w values were 0.051 and 0.056. The atomic scattering factors were taken from the International Tables for X-ray Crystallography.[11]

Tables of the atomic co-ordinates for the hydrogen atoms, anisotropic temperature factors for the non-hydrogen atoms, isotropic temperature factors for the hydrogen atoms, bond lengths, bond angles, and structure drawings of (**4g**) (Tables 4—7 and Figures 1 and 2) are available on request from the Cambridge Crystallographic Data Centre.*

The structure drawing (Figure 2) of (**4g**) was made by using a computer program Chem 3D (Cambridge Scientific Computing Inc.).

Acknowledgements

We are indebted to Miss K. Hatakeyama for her helpful assistance.

References

1 (*a*) R. L. Sinsheimer and R. Hastings, *Science*, 1949, **110**, 525; (*b*) S. Y. Wang, ed. 'Photochemistry and Photobiology of Nucleic Acids,' Academic Press, New York, vol. I, 1976.
2 (*a*) S. Hirokami, T. Takahashi, M. Nagata, Y. Hirai, and T. Yamazaki, *J. Org. Chem.*, 1981, **46**, 1769; (*b*) T. Takahashi, S. Hirokami, K. Kato, M. Nagata, and T. Yamazaki, *ibid.*, 1983, **48**, 2914; (*c*) S. Hirokami, T. Takahashi, K. Kurosawa, M. Nagata, and T. Yamazaki, *ibid.*, 1985, **50**, 166; (*d*) T. Takahashi, S. Hirokami, M. Nagata, and T. Yamazaki, *Tetrahedron Lett.*, 1985, **26**, 3247; (*e*) S. Hirokami, T. Takahashi, M. Nagata, and T. Yamazaki, *J. Org. Chem.*, 1987, **52**, 2455.
3 K. L. Wierzchowski, D. Shugar, and A. R. Katritzky, *J. Am. Chem. Soc.*, 1963, **85**, 827.
4 M. Arys, T. B. Christensen, and J. Ericksen, *Tetrahedron Lett.*, 1984, **25**, 1521.
5 Y. Hirai, S. Hirokami, M. Nagata, M. Morita, and T. Yamazaki, *J. Org. Chem.*, 1980, **45**, 936.
6 (*a*) M. Yokoyama, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 1610; (*b*) M. Yokoyama, M. Nakamura, H. Ohteki, T. Imamoto, and K. Yamaguchi, *J. Org. Chem.*, 1982, **47**, 1090.
7 D. J. Brown and R. F. Evans, *J. Chem. Soc.*, 1962, 4039.
8 Ger. Patent 2 412 784, 1975 (*Chem. Abstr.*, 1976, **84**, 43341p).
9 L. Bauer, G. E. Wright, B. A. Mikrut, and C. L. Bell, *J. Heterocycl. Chem.*, 1965, **2**, 447.
10 P. Main, M. M. Woolfson, and G. Germain, 1971, Multan. A Computer program for Automatic Solution of Crystal Structure, University of York.
11 J. A. Ibers and W. C. Hamilton, eds., 'International Tables for X-Ray Crystallography,' Kynoch Press, Birmingham, 1974, vol. IV, pp. 73—83.

* See 'Instructions for Authors' (1989), *J. Chem. Soc., Perkin Trans. 1*, 1989, Issue 1.

Received 25*th April* 1988; *Paper* 8/01602J