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Studies on Heterocyclic Compounds. V.[1] Photochemical Reactions of 2-(2,6-Dichlorobenzylidenehydrazino)pyrimidine and Its Related Hydrazones

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Under a nitrogen atmosphere, *anti*-isomers of 2-benzylidenehydrazinopyrimidines underwent isomerization easily to their *syn*-isomers by irradiation with ultraviolet light in a benzene solution, but in the presence of oxygen, photosensitized auto-oxidation occurred to afford 3-aryl-1,2,4-triazolo[4,3-*a*]pyrimidines. When irradiated in the same manner, 2-benzylidenehydrazino-1,3,5-triazine derivatives decomposed into benzaldehydes and 2-hydroxy-1,3,5-triazines.

Keywords——photoisomerization; photo-oxidation; hydrazone; 2-benzylidenehydrazinopyrimidine; nuclear Overhauser effect; 1,2,4-triazolo[4,3-*a*]pyrimidine; 1,2,4-triazole[4,3-*a*][1,3,5]triazine; 1,2,4-triazolo[1,5-*a*]pyrimidine; 1,2,4-triazolo[1,5-*a*][1,3,5]-triazine

In the preceding papers,[1,3] we have reported that 2-(2,6-dichlorobenzylidenehydrazino)-1,4,5,6-tetrahydropyrimidine hydrochloride (**1a**) (OT-24), a mild and long-acting antihypertensive agent, was established to be the *anti*-isomer (*E*-isomer) by nuclear Overhauser effect (NOE) experiments and readily isomerized to the *syn*-isomer (**1b**) (*Z*-isomer) by irradiation with ultraviolet light in aqueous or methanolic solution.[1] The compound (**1a**) was prepared by catalytic hydrogenation of 2-(2,6-dichlorobenzylidenehydrazino)pyrimidine (**2a**) (OT-23) over palladium–carbon in an acidic solution.[3]

Recently, the compound (**2a**) and some related 2-benzylidenehydrazinopyrimidine derivatives were proved to exhibit marked antibacterial activity.

This paper describes some informations on the photochemical reactions of these hydrazone derivatives observed during the course of the light-stability tests.

As reported previously[1] on the isomerization of **2a** to **2b**, the analogous compound (**3a**), 2-(2,6-dichlorobenzylidenehydrazino)-4,6-dimethylpyrimidine, was also found to isomerize to **3b** upon irradiation with a high-pressure mercury lamp.

For elucidation of the structures of **3a** and **3b**, NOE was used in a similar manner as in the cases of **2a** and **2b**.[1] When irradiated **3a** and **3b** on the NH proton, no NOE for CH proton of **3b** was detected, but a 31.8% NOE was observed for the CH proton of **3a**. Moreover, a 20.2% NOE enhancement of the NH proton on irradiation of the CH proton in **3a** was recognized, while no NOE on **3b**. The above results indicate that in the molecule of **3a** the azomethine proton must be located close to the NH proton, suggesting the *syn*-configuration to one another; while in the molecule of **3b** the CH and NH protons are not located on the same side of the C: N bond, implying the *anti*-configuration. Consequently, the structures of these isomers were assumed to be **3a** (*E*-isomer) and **3b** (*Z*-isomer) as shown in Chart 1.

Using the similar NOE experiments, the configurations of **4a** and **4b**, two isomers of 2-(2,6-dichlorobenzylidenehydrazino)-4-methylpyrimidine, were defined as *E*- and *Z*-isomers respectively. The results obtained are summarized in Table I.

1) Part IV: T. Tsujikawa, E. Mizuta, and M. Hayashi, *Yakugaku Zasshi*, **96**, 125 (1976).
2) Location: *Jusohonmachi, Yodogawa-ku, Osaka.*
3) T. Tsujikawa, M. Hayashi, and K. Masuda, *Yakugaku Zasshi*, **95**, 1271 (1975).

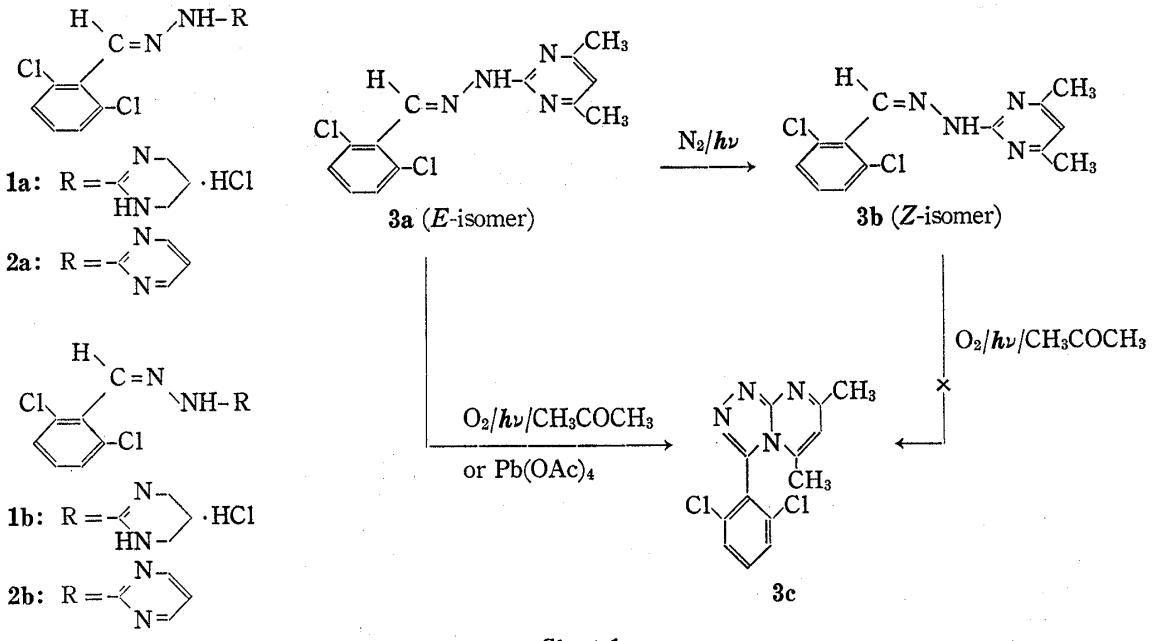
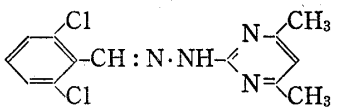
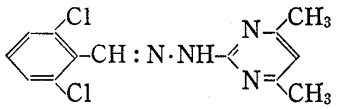


Chart 1

Table I. Nuclear Overhauser Effect in 2-Benzylidenehydrazinopyrimidines

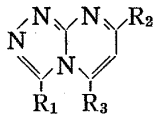
Structure	Compd. No.	NMR δ (ppm) –NH–	NMR δ (ppm) –CH:N–	NOE (%)	Isomer
	**3a**	11.32[a]	8.29[b]	31.8	*E*
		11.32[b]	8.29[a]	20.2	
	3b	9.75[a]	7.33[b]	0	*Z*
	**4a**	11.58[a]	8.39[b]	11.9	*E*
	4b	9.88[a]	7.37[b]	0	*Z*

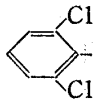
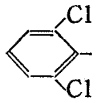
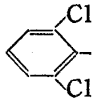
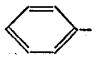
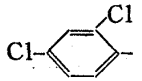
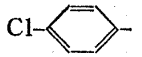
a) Irradiated.
b) Observed.

Attempts were made to isomerize *E*-isomers of 2-benzylidenehydrazinopyrimidine (**5a**), 2-(2,4-dichlorobenzylidenehydrazino)pyrimidine (**6a**) and 2-(4-chlorobenzylidenehydrazino)pyrimidine (**7a**) to their corresponding *Z*-isomers, (**5b**), (**6b**), and (**7b**). Though spots of *Z*-isomers were detected on the thin-layer chromatography (TLC) of these irradiated solutions, **5b**, **6b**, and **7b** could not be isolated in pure forms because of a possible reconversion of *Z*-isomer to *E*-isomer during the separation procedure.

The irradiations described above were all carried out under a nitrogen atmosphere. However, when a solution of **3a** was exposed to sunlight or irradiated with a high-pressure mercury lamp for a long time in the presence of air, the formation (trace) of an unknown fluorescent compound was detected by TLC. The irradiation under air-bubbling resulted in the formation (0.5—1.2%) of the above compound, and the addition of a small amount of benzophenone increased the yield of the compound to 15%. Finally, the compound was obtained in 37% yield, when acetone was used as photosensitizer instead of benzophenone. This photochemical reaction was scarcely affected by the addition of methylene blue or rose bengal, and no solvent effect by methanol or benzene was observed. Use of acetone as solvent and photosensitizer was found to be most effective for the formation of the unknown compound. Under the same condition, **3b** did not afford any fluorescent compound.

TABLE II. 1,2,4-Triazolo[4,3-*a*]pyrimidines



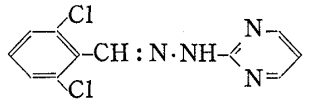
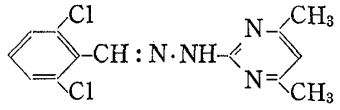
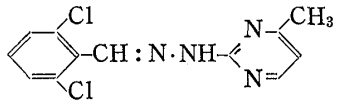
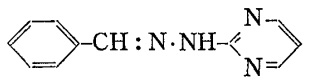
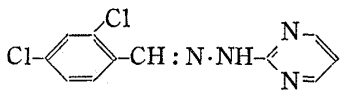
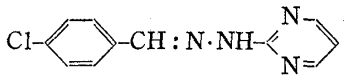
Compd. No.	Substituent R_1	Substituent R_2	Substituent R_3	Yield (%)	mp (°C)	Recrystd. from	Appearance	Formula	Analysis (%) Calcd. (Found) C	H	N	TLC *Rf*-value[a]
2c		H	H	40.2	204—205	Dil-EtOH	Colorless prisms	$C_{11}H_6Cl_2N_4$	49.84 (49.73)	2.28 (2.09)	21.13 (21.23)	0.50
3c		CH_3	CH_3	35.3	247—249	Dil-MeOH	Colorless prisms	$C_{13}H_{10}Cl_2N_4$	53.26 (53.27)	3.44 (3.50)	19.11 (19.60)	0.55
4c[b]		H CH_3	CH_3 H	74.0	144—146	$CHCl_3$+ petroleum ether (1:2)	Colorless power	$C_{12}H_8Cl_2N_4$	51.64 (51.76)	2.89 (2.67)	20.07 (20.27)	0.59
5c		H	H	61.0	201—202[c]							0.57
6c		H	H	75.3	235—237	EtOH	Colorless needles	$C_{11}H_6Cl_2N_4$	49.84 (49.95)	2.28 (2.00)	21.13 (21.03)	0.43
7c		H	H	51.3	278—280	EtOH	Colorless needles	$C_{11}H_7ClN_4$	57.28 (57.37)	3.06 (2.77)	24.29 (24.45)	0.27

a) Tokyo Kasei "Spot-film" (Silica gel-f) (10×2.5 cm), solvent: $CHCl_3$+MeOH (10:1).
b) Mixture of two isomer (1:1).
c) lit.[5] mp 201—202°.

The fluorescent substance was isolated by column chromatography on silica gel, and crystallized from aqueous methanol to obtain colorless needles, $C_{13}H_{10}Cl_2N_4$, which melted at 247—249°. By comparison of elemental analyses, TLC, infrared (IR) and nuclear magnetic resonance (NMR) spectra, this compound was found to be identical with 3-(2,6-dichlorophenyl)-5,7-dimethyl-1,2,4-triazolo[4,3-*a*]pyrimidine (**3c**) (Table II), which was prepared by the reaction of **3a** with lead tetraacetate according to Bower's procedure.[4]

1,2,4-Triazolo[4,3-*a*]pyrimidines (**2c** and **4c**) were prepared from **2a** and **4a**, respectively, by the similar procedures. But **4c** was found to be a mixture (3:1) of two isomers by the NMR spectra which exhibited two singlet peaks due to two methyl groups. It was therefore assumed that they are a mixture of 5-methyl- and 7-methyl-3-(2,6-dichlorophenyl)-1,2,4-triazolo[4,3-*a*]pyrimidines, which failed to be separated. In **4c** obtained by treatment of **4a** with lead tetraacetate, the proportion of the two isomers was confirmed to be 1:1 by the

Table III. Sensitized Photochemical Oxidation Reactions of 2-Benzylidenehydrazinopyrimidines

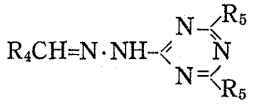
Compd. No.	Material	Irradiation				Product (yield,[a] %)	
		Photosensitizer	Solvent	Time (hr)	Atmosphere	1,2,4-Triazolo-[4,3-*a*]pyrimidine	Starting material (recovered)
2a		—	C_6H_6	16	Air	**2c** (trace)	(95.8)[b]
		Ph_2CO	C_6H_6	21	Air	**2c** (22.5)	(28.3)[c]
3a		—	MeOH	15	N_2	**3c** (0)	(46.4)[d]
		—	MeOH	15	Air	**3c** (0.5)	(67.5)[b]
		—	C_6H_6	15	Air	**3c** (1.2)	(54.2)[b]
		Ph_2CO	C_6H_6	22	Air	**3c** (15.0)	(80.0)[b]
		Rose bengal	C_6H_6	15	Air	**3c** (1.3)	(quantitative)[b]
		Methylene blue	C_6H_6 (MeOH, trace)	20	Air	**3c** (1.1)	(quantitative)[b]
		CH_3COCH_3	CH_3COCH_3	15	Air	**3c** (36.7)	(40.0)[b]
		CH_3COCH_3	CH_3COCH_3+MeOH (7:1)	15	Air	**3c** (40.2)	(37.5)[b]
4a		—	MeOH	6	N_2	**4c** (0)	(95.0)[e]
		Ph_2CO	C_6H_6	15	Air	**4c** (26.6)[f]	(60.0)[b]
5a		Ph_2CO	C_6H_6	30	Air	**5c** (15.1)	(76.8)[g]
6a		Ph_2CO	C_6H_6	15	Air	**6c** (0.9)	(84.5)[g]
7a		Ph_2CO	C_6H_6	15	Air	**7c** (26.6)	(60.0)[b]

a) Yields after chromatographic separation and crystallization.
b) Mixture of *Z*- and *E*-isomers.
c) *Z*-isomer: 15.8%; *E*-isomer: 12.5%.
d) *Z*-isomer: 40.0%; *E*-isomer: 6.7%.
e) *Z*-isomer: 53.0%; *E*-isomer: 42.0%.
f) Mixture of isomeric 5- and 7-methyl compounds (3:1).
g) *E*-isomer.
Ph: phenyl.

4) J.D. Bower and F.P. Doyle, *J. Chem. Soc.*, **1957**, 727.

NMR spectrum. Several related 2-benzylidenehydrazinopyrimidines were also irradiated in a similar manner to afford the corresponding 1,2,4-triazolo-[4,3-*a*]pyrimidines.

TABLE IV. 2-Benzylidenehydrazino-1,3,5-triazines



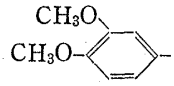
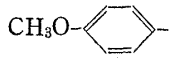
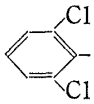
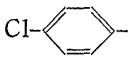
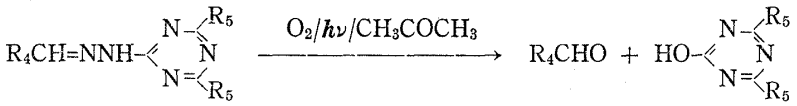
Compd. No.	Substituents R_4	Substituents R_5	Yield (%)	mp (°C)	Recrystd. from	Appearance	Formula	Analysis (%) Calcd. (Found) C	H	N
8a			62.4	182	EtOH	Pale yellow prisms	$C_{22}H_{31}N_7O_2$	62.10 (62.20)	7.34 (7.19)	23.04 (22.65)
9a			80.0	194—195	Dil-MeOH	Pale yellow pillars	$C_{19}H_{25}N_7O_3$	57.13 (57.15)	6.31 (6.24)	
10a			56.5	204	EtOH	Colorless pillars	$C_{20}H_{25}Cl_2N_7$	55.30 (55.46)	5.80 (5.86)	22.58 (22.81)
11a			64.8	248—249	MeO-$(CH_2)_2$OH	Colorless needles	$C_{20}H_{26}ClN_7$	60.07 (59.94)	6.55 (6.40)	24.52 (24.84)

TABLE V. Photochemical Reactions of 2-Benzylidenehydrazino-1,3,5-triaziazines

Material	Irradiation: Solvent	Irradiation: Time (hr)	Irradiation: Atmosphere	Product (yield, %)[a]: 2-Hydroxy-1,3,5-triazine	Product (yield, %)[a]: Benzaldehyde	Product (yield, %)[a]: Starting material (recovered)
8a	CH_3COCH_3+MeOH (3:1)	12	Air	**15**(54.2)	**17**(93.3)	—
9a	CH_3COCH_3+MeOH (3:1)	7	Air	**16**(80.8)	**18**(88.2)	—
10a	CH_3COCH_3+MeOH (3:1)	15	Air	**15**(21.8)	**19**(23.7)	**10a** (67.3)
11a	CH_3COCH_3+MeOH (3:1)	15	Air	**15**(55.6)	**20**(49.5)	**11a** (36.7)

a) Yields after chromatographic separation.



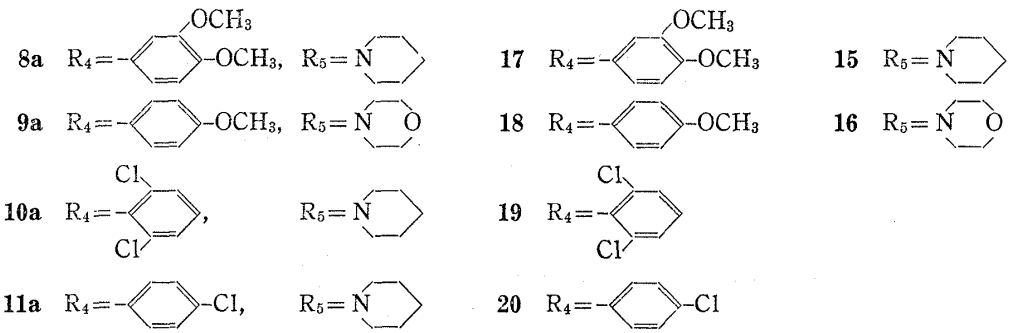


Chart 2

Next, the photo-oxidation of 2-benzylidenehydrazino-1,3,5-triazines (Table IV), analogues of 2-benzylidenehydrazinopyrimidines, was investigated. When 2-(3,4-dimethoxybenzylidenehydrazino)-4,6-dipiperidino-1,3,5-triazine (**8a**) (*E*-isomer) was irradiated in acetone-methanol (3: 1) with a high-pressure mercury lamp under air-bubbling, the products isolated were not 1,2,4-triazolo[4,3-*a*][1,3,5]triazine derivative (**8c**), but veratraldehyde and 2-hydroxy-4,6-dipiperidino-1,3,5-triazine (**15**). The similar photolysis was also observed in other 2-benzylidenehydrazino-1,3,5-triazines giving the corresponding benzaldehydes and 2-hydroxy-1,3-5, triazines. These results are summarized in Chart 2 and Table V. On the other hand, when **8a** was irradiated under a nitrogen atmosphere, a half of the material was isomerized to the *Z*-isomer (**8b**), which was hardly purified by silica gel column chromatography because **8b** was so labile that reconverted readily to **8a**.

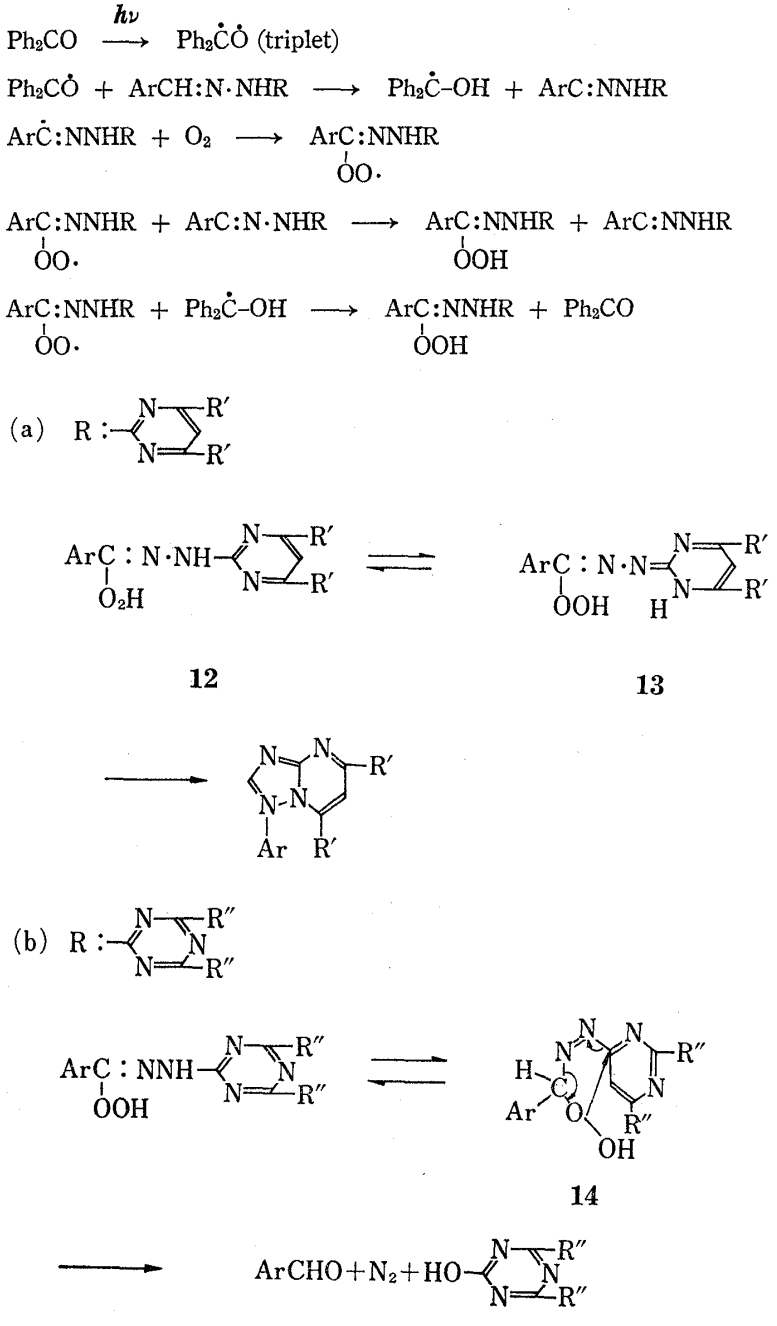
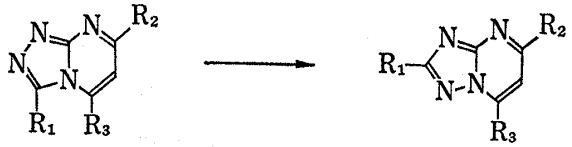


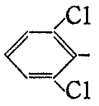
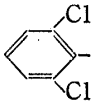
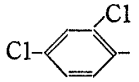
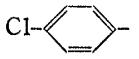
Chart 3

From the above findings it can assumed that the photochemical reactions described above are grouped as the type-I photo-oxygenation according to Gollnick's classification.[5] Namely, its main feature is the abstraction of hydrogen by the sensitizer (in its excited triplet state) followed by the addition of oxygen to the newly formed radical. The mechanisms of the present reactions are summarized as shown in Chart 3.

It has already been pointed out that the products in the photochemical reactions of 1,3,5-triazines differ from those in the case of pyrimidines. This can be explained by two possible processes, (a) and (b), *via* the intermediary hydroperoxy compounds, as shown in Chart 3. In the case of 1,3,5-triazines, the existence of **13**-type tautomer would be improbable due to the inductive effects of the substituents (secondary amino groups) of triazine rings. Consequently the formation of 1,2,4-triazolo[4,3-*a*][1,3,5]triazine derivatives *via* the process (a) would not occur.

TABLE VI. Isomerization of 1,2,4-Triazolo[4,3-*a*]pyrimidine to 1,2,4-Triazolo[1,5-*a*]pyrimidine



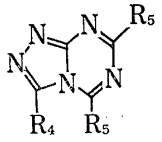
Starting material compd. No.	Reaction condition			Product	
	Reagent	Temp. (°C)	Time (hr)	Compd. No.	Substituents R_1	R_2, R_3
2c	85% HCO_2H	Reflux	10	**2d**		H
3c	85% HCO_2H	90	6	**3d**		CH_3
6c	85% HCO_2H	Reflux	6	**6d**		H
7c	85% HCO_2H	Reflux	6	**7d**		H

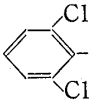
	Product							
	mp (°C)	Yield (%)	Recrystd. from	Appearance	Formula	Analysis (%), Calcd. (Found) C	H	N	TLC[a] *Rf*-value
2d	138—140	83.3	Dil-EtOH	Colorless prisms	$C_{11}H_6Cl_2N_4$	49.84 (49.73)	2.28 (2.07)	21.13 (21.34)	0.80
3d	209—210	83.4	EtOH	Colorless prisms	$C_{13}H_{10}Cl_2N_4$	53.26 (53.38)	3.44 (3.49)	19.11 (19.21)	0.83
6d	194—195	85.0	EtOH	Colorless needles	$C_{11}H_6Cl_2N_4$	49.84 (49.85)	2.28 (2.01)	21.13 (21.14)	0.73
7d	243—244	87.6	EtOH	Colorless needles	$C_{11}H_7ClN_4$	57.28 (57.38)	3.06 (2.88)	24.29 (24.42)	0.68

a) Tokoy Kasei "Spot-film" (Silica gel-f) (10 cm × 2.5 cm), solvent: $CHCl_3$+CH_3OH (10:1).

5) T. Matsuura, *Yukigoseikagaku Kyokaishi*, **26**, 217 (1968).

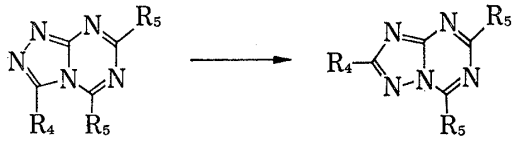
TABLE VII. 1,2,4-Triazolo[4,3-*a*][1,3,5]triazines

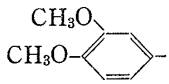
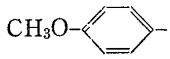
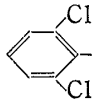
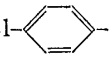
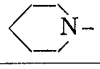


Compd. No.	Substituents R_4	Substituents R_5	Yield (%)	mp (°C)	Recrystd. from	Appearance	Formula	Analysis (%) Calcd. (Found) C	H	N	TLC *Rf*-value[a]
8c	CH_3O		58.8	170—171	Dil-EtOH	Colorless prisms	$C_{22}H_{29}N_7O_2 \cdot \frac{1}{2}H_2O$	61.09 (61.48)	6.99 (6.78)	22.67 (22.61)	0.39
9c	CH_3O		60.3	234—235	MeO-$(CH_2)_2OH$	Colorless plates	$C_{19}H_{23}N_7O_3$	57.42 (57.29)	5.83 (6.05)		0.40
10c			33.0	217—219	Dil-MeOH	Colorless pillars	$C_{20}H_{23}Cl_2N_7$	55.56 (55.60)	5.36 (5.35)	22.66 (22.31)	0.60
11c	Cl		75.0	243—247	Dil-MeOH	Colorless prisms	$C_{20}H_{24}ClN_7$	60.37 (60.06)	6.08 (6.04)	24.64 (24.67)	0.56

a) Tokyo Kasei "Spot-film" (Silica gel-f) (10 cm × 2.5 cm), solvent: $CHCl_3$+MeOH (10:1).

TABLE VIII. Isomerization of 1,2,4-Triazolo[4,3-*a*][1,3,5]triazine to 1,2,4-Triazolo[1,5-*a*][1,3,5]triazine



Starting material compd. No.	Reaction condition Temp. (°C)	Reaction condition Time (hr)	Product Compd. No.	Product Substituents R_4	Product Substituents R_5
8c	215—220	0.5	**8d**	CH_3O 	
9c	240—245	0.25	**9d**		
10c	230	10	**10d**		
11c	235—240	1.5	**11d**	Cl 	

	Product mp (°C)	Yield (%)	Recrystd. from	Appearance	Formula	Analysis (%) Calcd. (Found) C	H	N	TLC *Rf*-value[a]
8d	170—172	50.0	EtOH	Colorless powder	$C_{22}H_{29}N_7O_2$	62.39 (62.48)	6.90 (7.08)	23.15 (23.20)	0.90
9d	240	30.0	MeO-$(CH_2)_2OH$	Colorless pillars	$C_{19}H_{23}N_7O_3$	57.42 (57.59)	5.83 (6.08)		0.67
10d	205—207	30.8	Dil-EtOH	Colorless prisms	$C_{20}H_{23}Cl_2N_7$	55.56 (56.09)	5.36 (5.32)	22.66 (22.78)	0.87
11d	253—254	65.0	EtOH	Colorless needless	$C_{20}H_{24}ClN_7$	60.37 (60.27)	6.08 (6.04)	24.64 (24.74)	0.89

a) Tokyo Kasei "Spot-film" (Silica gel-f) (10 cm × 2.5 cm), solvent: $CHCl_3$+CH_3OH (10:1).

Unsuccessful photo-oxidation of **3b** to **3c** may be accounted for by the difficulty in H_2O_2-elimination because of the fixation of a hydroperoxy group and pyrimidine ring in the *anti*-configuration in connection with the C: N bond in **13** derived from **3b**.

1,2,4-Triazolo[4,3-*a*]pyrimidine derivatives obtained by photolysis were found to be identical in all respects with authentic specimens prepared by the oxydation of the corresponding hydrazones with lead tetraacetate. Furthermore, it was confirmed that these triazolopyrimidines are readily rearranged into 1,2,4-triazolo[1,5-*a*]pyrimidines on heating with formic acid according to Sirakawa's method.[6]

1,2,4-Triazolo[4,3-*a*][1,3,5]triazines, which were also synthesized by treatment of the corresponding hydrazones with lead tetraacetate, were converted into 1,2,4-triazolo[1,5-*a*]-[1,3,5]triazines by melting according to the method reported by Deshpande, *et al.*[7] The structure of 1,2,4-triazolo[1,5-*a*]-pyrimidines and 1,2,4-triazolo[1,5-*a*][1,3,5]triazines were assigned on the basis of the comparable results presented by Sirakawa[6] and Deshpande, *et al.*[7] The 1,2,4-triazolopyrimidines and 1,2,4-triazolo[1,3,5]triazines thus prepared are listed in Tables II, VI, VII, and VIII.

Details of the antibacterial activity and the structure–activity relationship will be reported in the near future.

Experimental[8]

Hydrazones (*E*-isomers)——2-(2,6-Dichlorobenzylidenehydrazino)pyrimidine (**2a**),[3] 2-(2,4-dichlorobenzylidenehydrazino)pyrimidine (**6a**),[3] 2-(4-chlorobenzylidenehydrazino)pyrimidine (**7a**)[3] and 2-benzylidenehydrazinopyrimidine (**5a**)[6] were prepared by the methods described in literatures.

General Procedure for preparing Other Hydrazones: (A) A solution of 2,6-dichlorobenzaldehyde (5.1 g) and 2-hydrazino-4,6-dimethylpyrimidine (4 g) in EtOH (60 ml) was refluxed for 3 hr. After cooling, the resulting precipitate was collected and recrystallized from EtOH to give 2-(2,6-dichlorobenzylidenehydrazino)-4,6-dimethylpyrimidine (**3a**) as colorless needles (5.1 g, 59.3%), mp 174—175°. *Anal.* Calcd. for $C_{13}H_{12}Cl_2N_4$: C, 52.90; H, 4.10; N, 18.98. Found: C, 52.91; H, 3.97; N, 19.33.

2-(2,6-Dichlorobenzylidenehydrazino)-4-methylpyrimidine (**4a**) was prepared by the similar procedure. Colorless powder, mp 172—173°, 48.3%. *Anal.* Calcd. for $C_{12}H_{10}Cl_2N_4$: C, 51.27; H, 3.58; N, 19.93. Found: C, 51.29; H, 3.49; N, 19.95.

(B) A solution of 2,6-dichlorobenzylideneaminoguanidine acetate (3.2 g) and acetylacetone (1 ml) in EtOH (30 ml) was refluxed for 24 hr. After cooling, the resulting precipitate was collected and recrystallized from EtOH to give **3a** as colorless needles (1.0 g, 30.9%), mp 174—175°. The mixed mp and IR spectra were identical with those of the sample (**3a**) obtained by the procedure (A).

(C) A solution of 2,6-dichlorobenzaldehyde (5 g) and 2-hydrazino-4,6-dipiperidino-1,3,5-triazine (7.9 g) in EtOH (200 ml) was refluxed for 4 hr. After cooling, the resulting precipitate was recrystallized from EtOH to afford 2-(2,6-dichlorobenzylidenehydrazino)-4,6-dipiperidino-1,3,5-triazine (**10a**). The reactions were carried out in a similar manner to give the compounds in Table IV.

Photo-oxidation of Hydrazones——The apparatus described previously was used.[1]

(A) A solution of **3a** (1.5 g) in MeOH (300 ml) was irradiated with a high-pressure mercury lamp (UM-103 reactor: Ushio Electric Co. Ltd.) under a nitrogen atmosphere for 15 hr. MeOH was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel to give 2-(2,6-dichlorobenzylidenehydrazino)-4,6-dimethylpyrimidine (*Z*-isomer) (**3b**) (0.6 g, 40.0%). Colorless needles, mp 179—182°. *Anal.* Calcd. for $C_{13}H_{12}Cl_2N_4$: C, 52.90; H, 4.12; N, 18.98. Found: C, 52.67; H, 3.88; N, 19.26.

Z-Isomer (**4b**) was prepared by the similar photoisomerization of **4a**. Colorless powder, mp 129—130°, 53.0% (recovered **4a**: 42.0%). *Anal.* Calcd. for $C_{12}H_{10}Cl_2N_4$: C, 51.27; H, 3.59; N, 19.93. Found: C, 50.98; H, 3.41; N, 19.81.

(B) A solution of **5a** (3.0 g) and benzophenone (0.3 g) in benzene (400 ml) was irradiated with a high-pressure mercury lamp under bubbling with air passed through the inlet tube from compressed air source for 30 hr. Benzene was evaporated *in vacuo* and the residue was chromatographed on silica gel and eluted

6) K. Sirakawa, *Yakugaku Zasshi*, **80**, 956 (1960).
7) R.J. Deshpande and A.V. RamaRao, *Synthesis*, **1974**, 863.
8) All melting points were uncorrected. The IR spectra were taken with a Hitachi Model 215 spectrophotometer and all NMR spectra were measured on a Varian HA-100 spectrometer using tetramethylsilane as the internal standard. All values reported for NOE's are mean values of at least five measurements by at least two operators.

with $CHCl_3$ to recover benzophenone (0.3 g) and 2-benzylidenehydrazinopyrimidine (2.3 g), then with $CHCl_3$–MeOH (10: 1) to give 3-phenyl-1,2,4-triazolo[4,3-*a*]pyrimidine (**5c**) (455 mg, 15.1%), colorless needles, mp 198—200° (lit.[6] mp 201—202°), which was identical with an authentic sample[6] in comparisons of IR spectrum and TLC. TLC (Tokyo Kasei "Spot film-f," solvent: $CHCl_3$). The irradiated solution: *Rf* 0.11 for *E*-isomer, *Rf* 0.17 for *Z*-isomer; The recovered 2-benzylidenehydrazinopyrimidine: *Rf* 0.11 for *E*-isomer.

(C) A solution of **3a** (3.0 g) in acetone (350 ml) was irradiated with a high-pressure mercury lamp with air-bubbling for 13 hr. Acetone was evaporated *in vacuo* and the residue was chromatographed on silica gel and eluted with $CHCl_3$–MeOH (10: 1) to give a mixture (1.2 g) of **3a** and **3b** and **3c** (1.08 g, 36.7%). The compound (**3c**) was identified with an authentic specimen in comparisons of IR spectrum and TLC.

(D) A solution of 2-(3,4-dimethoxybenzylidenehydrazino)-4,6-dipiperidino-1,3,5-triazine (**8a**) (3.0 g) in acetone (300 ml) and MeOH (100 ml) was irradiated with a high-pressure mercury lamp with air–bubbling for 12 hr. After the reaction mixture was concentrated under reduced pressure, the residue was chromatographed on silica gel. Elution with $CHCl_3$ afforded veratraldehyde (mp 44—45°, 1.1 g) and that with $CHCl_3$–MeOH (10: 1) gave 2-hydroxy-4,6-dipiperidino-1,3,5-triazine (**15**) (1.0 g), colorless powder, mp 269—270° (dec.). Both compounds were consistent with authentic specimens in all respects by comparisons of IR spectra and TLC. The photochemical reactions in Table V were worked up in the manner similar to that described above.

(E) A solution of **3b** (0.5 g) in acetone (300 ml) was irradiated with a high–pressure mercury lamp with air-bubbling for 15 hr. In the TLC of the resulting solution, the formation of **3c** was not confirmed.

2-Hydroxy-4,6-dipiperidino-1,3,5-triazine (15)——A solution of 2-chloro-4,6-dipiperidino-1,3,5-triazine (3.0 g) in 10% HCl (20 ml) was refluxed for 4 hr. After cooling, the resulting mixture was neutralized with $NaHCO_3$ and the precipitate was collected and recrystallized from EtOH to give **15** (1.0 g), colorless pillars, mp 269—271° (dec.). *Anal.* Calcd. for $C_{13}H_{21}N_5O$: C, 59.29; H, 8.04; N, 26.59. Found: C, 59.20; H, 8.07, N, 26.61.

2-Hydroxy-4,6-dimorpholino-1,3,5-triazine (**16**) was prepared by the similar procedure. Colorless powder (EtOH), mp>300°, 55.3%. *Anal.* Calcd. for $C_{11}H_{17}N_7O_3$: C, 49.43; H, 6.41; N, 26.20. Found: C, 48.87; H, 6.40; N, 25.98.

3-Aryl-1,2,4-triazolo[4,3-*a*]pyrimidines (Table II)——General Procedure: To a solution of **2a** (2.0 g) in MeOH (40 ml) was added $Pb(OAc)_4$ (3.64 g), and the reaction mixture was stirred at room temperature (r.t.) for 2 hr and concentrated under reduced pressure. The residue was treated with H_2O (50 ml) and the resulting crystals were collected and recrystallized from 80% EtOH to afford 3-(2,6-dichlorophenyl)-1,2,4-triazolo[4,3-*a*]pyrimidine (**2c**). The compounds (**3c**, **4c**, **5c**, **6c**, and **7c**) were prepared by the similar procedures.

2-Aryl-1,2,4-triazolo[1,5-*a*]pyrimidines (Table VI)——General Procedure: A solution of **3c** (0.3 g) in 85% HCOOH (5 ml) was heated at 90° for 6 hr and concentrated under reduced pressure. The residue was recrystallized from EtOH to afford 2-(2,6-dichlorophenyl)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**3d**). The compounds (**2d**, **6d**, and **7d**) were prepared by the similar procedures.

3-Aryl-1,2,4-triazolo[4,3-*a*][1,3,5]triazines (Table VII)——General Procedure: To a solution of 2-(3,4-dimethoxybenzylidenehydrazino)-4,6-dipiperidino-1,3,5-triazine (**8a**) (4.3 g) in MeOH (200 ml) was added $Pb(OAc)_4$ (4.9 g), and the reaction mixture was stirred at r.t. for 2 hr. After insoluble substance (trace) was filtered off, the filtrate was concentrated *in vacuo* and the residue was triturated with Et_2O (100 ml). The collected crystals were recrystallized from 80% EtOH to give 3-(3,4-dimethoxyphenyl)-5,7-dipiperidino-1,24-triazolo-[4,3-*a*][1,3,5]triazine (**8c**). The compounds (**9c**, **10c**, and **11c**) were prepared by the similar procedures.

2-Aryl-1,2,4-triazolo[1,5-*a*][1,3,5]triazines (Table VIII)——General Procedure: **8c** was heated at 215—220° for 35 min and the resulting residue was recrystallized from EtOH to afford 2-(3,4-dimethoxyphenyl)-5,7-dipiperidino-1,2,4-triazolo[1,5-*a*][1,3,5]triazine (**8d**). The compounds (**9d**, **10d**, and **11d**) were prepared by the similar procedures.

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